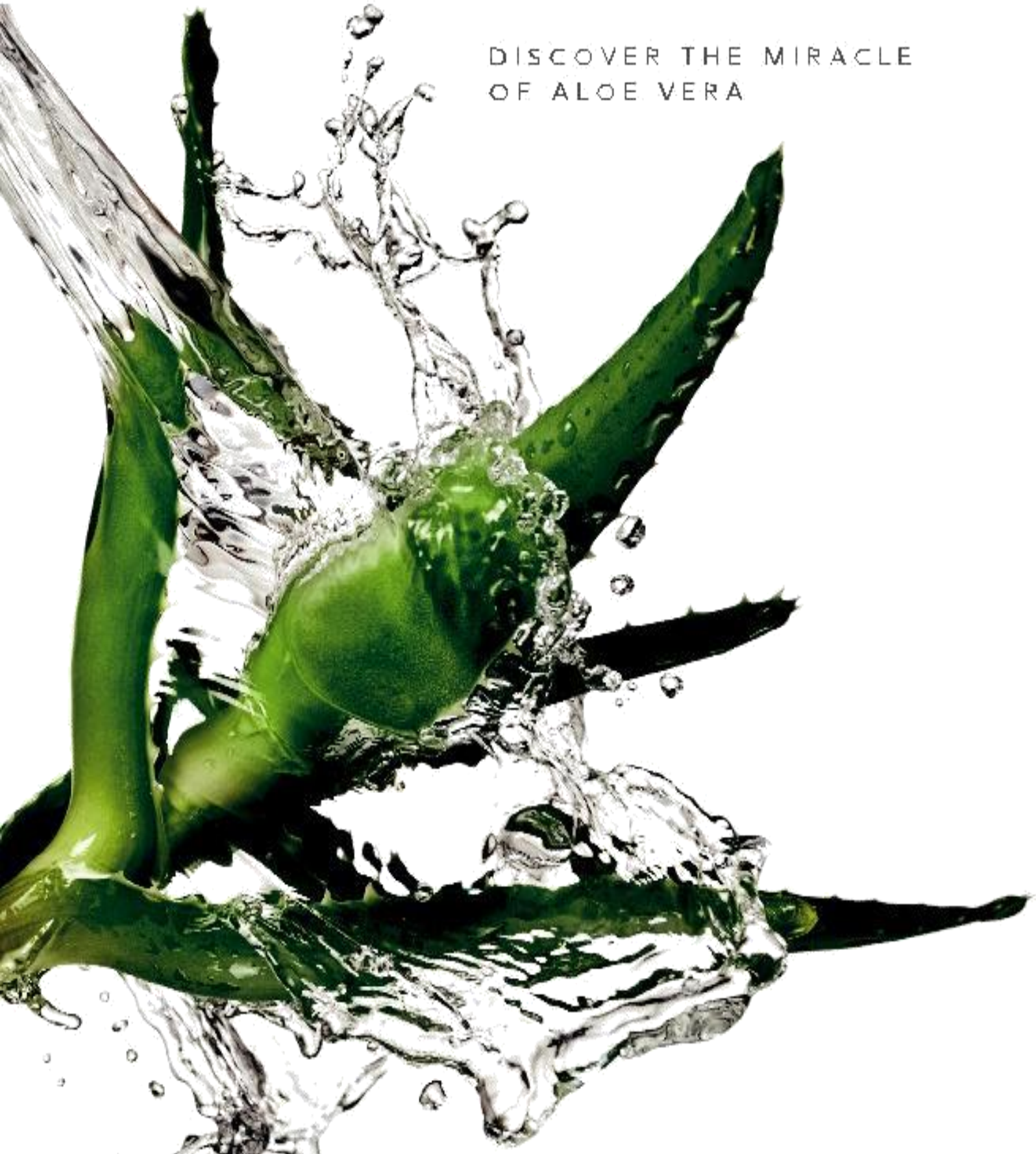
Aloe
JOURNAL

DISCOVER THE MIRACLE
OF ALOE VERA



Aloe Vera

A Long, Illustrious History - Dating From Biblical Times

Aloe Vera looks like a cactus but it isn't – the plant is a member of the lily family which includes garlic and onion.

Inside the leaf is a jelly-like substance. Early users of Aloe Vera discovered that when the jelly was applied to a wound, it would heal faster – a remarkable feat in a time, long before anti-biotic ointments, when the infection of a minor wound was often fatal.

Descriptions and instructions for twelve different recipes for the internal and external uses of Aloe Vera can be found in an Egyptian relic, the Eberpapyrus, dating to around 1,500 BC. By 400 BC, the properties of Aloe Vera was well accepted from China to India. Today, Aloe Vera is cultivated throughout the world. Terms including; the potted physician and nature's medicine chest, attempted to describe the significant historical uses of Aloe Vera.

The properties of Aloe Vera, due to its long history of use, were mostly folkloric. Early attempts to scientifically validate its uses produced mixed results; different assessme nts of the anecdotal evidence and a wide chasm between the proponents of Aloe Vera and the detractors. The highly charged debate, between the two camps, contributed to public confusion, diminishing interest in the supplemental value of Aloe Vera products. Thankfully, improved, more modern scientific methods are beginning to restore the reputation of Aloe Vera.

Advocates for Aloe Vera evolved into three distinct camps: jelly only, extracted isolates and whole leaf.

1. The jelly only camp are purists, relying on the historical uses of the clear "fillet" contained on the inside of the leaf.
2. The extracted isolates group search for "magic bullets", one or more of the identified beneficial substances, contained in the plant, that might result in process and/or pharmaceutical patents.
3. During the past few years, scientists have discovered yet another remarkable array of substances concentrated in the skin of the leaf. Today, the whole leaf approach is adding new dimensions to the properties of this remarkable plant.

Dr. Robert H. Davis, Ph.D. presented a ground breaking research report to the International Aloe Vera Science Council, The Conductor – Orchestra Concept of Aloe Vera. which underscores the nature of the whole leaf approach, the benefits, and possibilities it affords.

Today, there is an impressive accumulation of research supporting Dr. Davis' position which was highlighted by an enlightening seminar presented by Dr. Ivan Danoff M.D., Ph.D., entitled The Therapeutic Component in Aloe Vera.

A NOTE OF CAUTION: Aloe Vera is not a panacea! Reasonable people recognize that the juice from a orange is a beneficial addition to their diet - because the juice contains vitamin C; as is apple juice – because it contains pectin; as is grape juice – because it offers anti oxidants; or the juice from any number of other fruits and vegetables.

The decision to drink the juice from an Aloe Vera plant, considering the volumes of research surrounding the plant, may be as simple as deciding to drink orange juice!

Decide for yourself.

The Complete Story of Aloe Vera

The semi-tropical plant, Aloe Vera, has a long and illustrious history dating from biblical times. It has been mentioned throughout recorded history and given a high ranking as an all-purpose herbal plant.

Aloe's thick, tapered, spiny leaves grow from a short stalk near ground level. It is not a cactus, but a member of the tree lily family, know as Aloe *barbadensis*. Aloe is related to other members of the Lily family such as the onion, garlic and turnip families. Aloe's relationship to the lily family is evident from the tubular yellow flowers produced annually in the spring that resemble those of the Easter lily.

There are over 250 species of aloe grown around the world. However, only two species are grown today commercially, with Aloe *barbadensis* Miller and Aloe *aborescens* being the most popular. The Aloe plant is grown in warm tropical areas and cannot survive freezing temperatures.

In the United States, most of the Aloe is grown in the Rio Grande Valley of South Texas, Florida and Southern California. Internationally, Aloe can be found in Mexico, the Pacific Rim countries, India, South America, Central America, the Caribbean, Australia and Africa.

The leaves of the Aloe plant grow from the base in the rosette pattern. Mature plants can grow as tall as 2 and a half inches to 4 feet with the average being around 28 to 36 inches in length. Each plant usually has 12-16 leaves that, when mature, may weigh up to three pounds. The plants can be harvested every 6 to 8 weeks by removing 3 to 4 leaves per plant.

The original commercial use of the Aloe plant was in the production of a latex substance called Aloin, a yellow sap used for many years as a laxative ingredient. This product became synonymous with the name "Aloe" and recorded in the trade, technical and government literature during the early 20th century. This terminology created much confusion later when Aloe's other main ingredient, Aloe Gel, a clear colorless semi-solid gel, was stabilized and marketed. This Aloe Vera Gel, beginning in the 50's, has gained respect as a commodity used as a base for nutritional drinks, as a moisturizer, and a healing agent in cosmetics and OTC drugs.Chemical analysis has revealed that this clear gel contains amino acids, minerals, vitamins, enzymes, proteins, polysaccharides and biological stimulators. Public interest in Aloe has grown quickly, and now there is a considerable amount of research into the various components of Aloe to find out more about their properties and to characterize these components so that more specific research can provide clues to the "magic" that is attributed to Aloe Vera.

This "magic" concept brought the industry under the Federal Food and Drug Administration's microscope in the late 70's and early 80's. The claims made to the consumer about uses and effectiveness of Aloe were exaggerated.

Aloe Vera Gel, like most natural juices, both fruit and vegetable, is an unstable product when extracted and is subject to discoloration and spoilage from contamination by microorganisms. The great success of Aloe as a commodity for use in nutritional foods and cosmetics is due to the proper stabilizing procedures that enable processors to store and ship the Aloe Gel without fear of spoilage throughout the market places of the world.Research conducted around the world leaves little doubt that certain biochemical properties of Aloe will be proven facts. Such attributes as moisturizing and penetrating properties are known, but the attributes such as its healing abilities and analgesic action to bacterial activity has not been clearly defined and documented through properly controlled scientific research and testing.

Today, the Aloe industry has established high ethical standards for businesses and their Aloe products. Through the International Aloe Science Council, the industry has solidified its dedication to providing the world with the highest quality Aloe. The wide acceptance of Aloe by society in so many consumer products suggests that the IASC is moving in the proper direction. The image of Aloe has never been higher. The IASC has a dedicated group of professionals committed to the further growth, research and marketing of quality Aloe Vera Gel and Aloe products made from this Gel. This is because the IASC knows the future of Aloe is full of promise for those willing to make the necessary effort.

Aloe Vera - Information

Scientific Papers describing the uses and powers of the Aloe Vera Plant: Especially the Cold Processed Whole Leaf Aloe Vera is truly amazing!

These Articles From Doctors, Scientists And Health Practitioners show a remarkable pattern for Aloe Vera (Aloe Barbadensis):

Whole-Leaf Aloe Vera, Almost A Panacea
By Bruce Eric Hedendal, D.C., Ph.D.

Aloe Vera, The Whole Leaf Advantage
By Ivan Danhof, M.D., Ph.D.

Aloe Vera Leaf Handling and Constituent Variability
By Ivan Danhof, M.D., Ph.D.

Digestion and The Immune System and Aloe Vera MPS
By John C. Pittman, M.D.

Immune Enhancing Effects Of Aloe Vera
By John C. Pittman, M.D.

Aloe Vera In Dentistry
By James Harrison, D.D.S., F.A.G.D.

The Rediscovery Of Aloe Vera
By Alfred Garbutt, D.C.

Aloe Vera Psoriasis Treatment Protocol
By Donovan J. Anderson, M.D.

Aloe Vera Wound Care Protocol
By Donovan J. Anderson, M.D.

Fundamentals Of Aloe Vera Mucopolysaccharides
By Ivan Danhof, M.D., Ph.D.

Internal Uses Of Aloe Vera
By Ivan Danhof, M.D., Ph.D.

Aloe Vera and The Heart, Actions And Activities

Polysaccharide, The Magic Bullet
By Robert H. Davis, Ph.D.

The Conductor - Orchestra Concept Of Aloe Vera
By Robert H. Davis, Ph.D.

Biological Activity Of Aloe Vera
By Robert H. Davis, Ph.D.

Aloe Vera - The Cancer Solution
By Robert E. Willner, M.D., Ph.D.

Aloe Vera - A Natural Solution To Drug-Resistant Bacteria, Viruses & Fungi
By David E. Williams, M.D.

A Holistic Protocol For The Immune System
By Scott J. Gregory

Aloe Vera: Its Potential Use In Wound Healing and Disease Control In Oral Conditions
By Timothy E. Moore, D.D.S./M.S.,P.C.

Aloe Vera Produces Anti-Inflammatory, Immune Strengthening Effects On Skin
By Steven R. Schechter, N.D.

Effect Of Orally Consumed Aloe Vera Juice On Gastrointestinal Function In Normal Humans
By Jeffrey Bland, Ph.D.

Aloe Vera Medicinal Substances, Present & Future Potentials
By Wendell D. Winters

Aloe Vera and The Human Immune System
By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Aloe Vera and The Human Digestive System
By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

The Healing Properties Of Aloe Vera
By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Aloe Vera in Alternative Medicine Practice
By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Aloe Vera: Ancient Herb In New Form Delivers Proven Effects
By Keisuke Fujita, M.D., Ph.D.; Hidehiko Beppu, Ph.D.; Kaoru Kawai, Ph.D. & Kan Shinpo, Ph.D.

The External Use Of Aloes
By J. E. Crewe, M.D.

Aloe Vera In The Treatment Of Burns and Scalds

By J. E. Crewe, M.D.

Aloe Vera's Effectiveness As An Anti-Inflammatory Agent

By Hiroko Saito

Antiarthritic Activity Of Anthraquinones Found In Aloe Vera For Podiatric Medicine

By Robert H. Davis, Ph.D.; Patrick S. Agnew, B.S. & Eugene Shapiro, B.S.

Aloe Vera and Gibberellin, Anti-Inflammatory Activity In Diabetes

By Robert H. Davis, Ph.D. & Nicholas P. Maro

Aloe Vera Gel In Peptic Ulcer Therapy: Preliminary Report

By Julian J. Blitz, D.O.; James W. Smith, D.O. & Jack R. Gerard, D.O.

Aloe Vera and Other Topical Antibacterial Agents In Wound Healing

By John P. Heggers, Ph.D. & Wendell Winters, Ph.D.

Wound Healing, Oral and Topical Activity Of Aloe Vera

By Robert H. Davis, Ph.D.; Mark G. Leitner, R.Ph., D.P.M.; Joseph M. Russo, D.P.M. & Megan E. Byrne, B.S.

Aloctin A, An Active Substance Of Aloe Arborescens Miller As An Immunomodulator

By Ken'ichi Imanishi

Tumor Inhibitors 114 Aloe Emodin: Antileukemic Principle Isolated From Rhamnus frangula L

By S. Morris Kupchan & Aziz Karim

Prevention Of Atheromatous Heart Disease

By O.P. Agarwal, M.D., F.I.C.A.

Whole-Leaf Aloe Vera, Almost A Panacea

By Bruce Eric Hedendal, D.C., Ph.D.

An Overview of One of the Most Accepted, Yet Misunderstood, Medicinal Plants in History

There is a voluminous amount of anecdotal evidence showing that authentic, **properly prepared Aloe vera has powerful healing properties in humans and animals**. The virtues of Aloe vera have been recorded for thousands of years by many ancient civilizations, including Egypt, Persia, Greece, India and Africa. Although today it is found throughout the world as a common household plant, Aloe is, without doubt, one of the most accepted, yet misunderstood medicinal plants in history. It is not just "good for burns."

Historical evidence indicates that Aloe vera originated in the warm, dry climate of Africa, although today the plant is found worldwide. From Europe, the Spanish carried Aloe to their New World possessions in South America and the Caribbean. Spanish missionaries in the west always planted Aloe around their settlements and carried it on their journeys to aid the sick. Today Aloe is used worldwide, particularly in the U.S. and Canada, both internally as a drink and in cosmetics and ointments. Japan currently imports over fifty million dollars of Aloe per year to treat people with ulcers and digestive problems.

Although the modern medical community has given the health benefits of Aloe vera limited official standing, there have been numerous worldwide scientific studies by authoritative and respected medical researchers revealing Aloe's ubiquitous health benefits for people and animals as well.

Let's briefly examine how it could be that H. R. McDaniel, M.D., pathologist and researcher at the Dallas-Fort Worth Medical Center, has said, **"The use of Aloe vera will be the most important single step forward in the treatment of diseases in the history of mankind."**

In clinical studies of whole-leaf Aloe vera's internal and external uses during the past six months, I have personally witnessed mitigations or complete resolutions of the following:

Abrasions	Colds	Herpes simplex & zoster	Staph infections
Acne	Colic	Hypertension	Stings
Actinic keratoses	Constipation	Infections	Sunburns
AIDS	Contusions	Insect bites	Tendinitis
Allergic reactions (reversal of anaphalaxis)	Dandruff	Menstrual cramps & irregularity	Ulcerations
Allergies	Denture (gum) sores	Nausea	Ulcerative colitis
Arthritis	Dermatitis	Parasites (especially protozoan infections)	Vaginitis
Boils	Diabetes	Peptic & duodenal ulcers	Varicose veins
Bruises	Edema	Psoriasis	Viral infections
Burns	Epstein-Barr virus (chronic fatigue syndrome)	Radiation dermatitis	Warts
Bursitis	Fungal infections	Rashes	Yeast infections
Candida	Genital herpes	Reflex esophagitis	
Carbuncles	Gingivitis	Seborrhea	
Chapped/cracked skin	Hemorrhoids	Sprains	

One brand of cold-processed whole-leaf Aloe vera ("Brand A") demonstrated the highest in active polysaccharides in independent lab tests by Ivan Danhof, M.D., Ph.D.

I know you must be thinking that no one plant or product could affect - in some positive way - all of the above. If so, it would be a miracle. Webster defines a miracle as "an extraordinary event manifesting outstanding or unusual event, thing, or accomplishment; and a divinely natural occurrence that must be learned humanly." By this definition, it is no wonder why thousands of Aloe vera users worldwide have commonly referred to it as a "miracle plant." Is Aloe vera really a miracle plant? Many facts and continued research are available, so you may decide for yourself. Organized medicine and pharmacology have not embraced Aloe, because it cannot be patented and its usage threatens literally hundreds of prescription and non-prescription drugs. **Aloe vera is hypoallergenic and has no known side effects even in large doses.**

Taken internally, Aloe vera generally makes people feel better. "Feeling better" may not seem scientific enough, but may relate to **Aloe's ability to detoxify the body**, a phenomenon reported by Jeffrey Bland, Ph.D., formerly of the Linus Pauling Institute, in his scientific paper, "Effect of Orally Consumed Aloe Vera Juice on Gastrointestinal Function in Normal Humans," published in 1985. Dr. Bland studied for one week the effects of Aloe vera juice consumption on urinary indican, stool specific gravity and gastric and bowel motility.

Urinary indican values decreased, indicating lowered bowel bacterial conversion of tryptophan and possible improved protein digestion and absorption, as well as reduced bowel putrefaction. **This change, by itself, could help prevent colon cancer.**

Specific gravity of the stool was reduced on the average of 0.37 with decreased stool transit time, without diarrhea. Stool cultures were generally more normal, especially in the two-thirds of test subjects that had, prior to the trial, high amounts of bowel yeast (Candida albicans). Aloe promoted a more favorable balance of gastrointestinal symbiotic bacteria and decreased yeast populations. All subjects who had indigestion, irritable bowel syndrome, colitis, and gastritis reported symptomatic relief after this short, seven-day research study.

The Aloe vera in this 1985 study was yellowish in color, had a somewhat bitter taste, was pasteurized and contained preservatives. Since this study, new 1990's technology has improved the healing potential of Aloe with the advent of whole-leaf processing. This technique removes only the aloin (a cathartic). But uses the entire whole leaf instead of merely the clear inner gel. Scientific research has proved that the outer leaf and rind, which previously were thrown away, contain 200% more of the active therapeutic ingredients.

However, over 95% of the Aloes on the market today still use only the inner gel and stabilize the Aloe in a high-heat process that degrades some of the enzymes, polysaccharides and mucopolysaccharides. High heat (pasteurization and/or autoclave methods) break down the constituents in Aloe that are the most valuable for healing. Heat also kills the live enzymes necessary for digestion. Most Aloes are heat processed.

"Brand A" whole-leaf Aloe concentrate is one of only a few Aloes that are cold-processed. There is no FDA control of Aloe labeling as it is an FDA-approved food. With only 10% Aloe and 90% water, companies can label their product a 100% Aloe drink! Most of these Aloe vera products are very low or even devoid of these active enzymes and polysaccharides that scientists feel are essential for the anti-viral, anti-inflammatory, immune-enhancing and tissue-healing effects of real Aloe vera.

Aloe vera's mucopolysaccharides are long-chain sugars found in large amounts in the plant and properly prepared whole-leaf Aloe juice and juice concentrates. We have just begun in the last few years to recognize the major role that mucopolysaccharides (MPS) play in human and animal health.

Carrington Laboratories, Inc., has isolated one of these and trademarked it "Acemannan." They are working for FDA drug approval as a potent immune-modulating and anti-viral material. It works by interacting with the immune system, enhancing rather than overriding it. Acemannan is a potent stimulator of macrophage activity. In animals, this naturally occurring polysaccharide has been shown to increase production of tumor necrosis factor-alpha and interleukin-1 by the macrophage. In fact, on November 4, 1991, Carrington Laboratories, Inc., announced approval by the USDA to market Acemannan as an aid in the treatment of canine and feline fibrosarcoma. Currently, there is no effective treatment for this disease. Acemannan causes tumor necrosis to occur in this form of fibrosarcoma, with encapsulation of cancerous tissue, facilitating surgical removal.

This unique mechanism of this major active ingredient of the Aloe vera plant, coupled with its direct anti-viral activity, explains why whole leaf Aloe, in addition to wound care, shows promise in a wide range of human and animal diseases including AIDS, cancer and ulcerative colitis. Other aspects of MPS are that they are found in every single cell in the body. They play a crucial role in performing bodily functions by:

- Forming a lining throughout the colon to keep toxic waste from re-entering the body.
- Providing a life-saving barrier against microbial invasion for each cell (especially viruses).
- Providing critical lubrication of joints.
- Helping to maintain the capacity of movement of fluids.
- Allowing the transfer of gases in the lungs.
- Facilitating absorption of water, electrolytes and nutrition in the GI tract.

MPS are as vital to a healthy body as bricks are to a brick house. The human body stops manufacturing MPS around puberty. After this, one must begin to receive the MPS from outside sources. One of the very best sources comes from whole leaf Aloe vera. Experts agree that MPS contribute to good health and their deficiency can produce drastic degenerative diseases. But not all Aloes are alike. Consumers of Aloe are beginning to learn that if an Aloe product looks like water (instead of yellowish or reddish), it probably is water or heavily diluted.

As discussed, "100% Aloe vera" can be put on the label of an Aloe beverage or product that only contains a fraction of Aloe. A manufacturer can put one gallon of pure Aloe in 100 gallons of water, mix it, and call it "100% Aloe vera;" and it's legal. Where is the FDA when you really need it?

To repeat, real Aloe vera does not look like or taste like water. This fact is emphasized because even if the consumer has no other information to judge the Aloe he is buying (although independent lab tests are now available), then the product's appearance and taste are the first line of defense against being defrauded. If an Aloe is not at least yellowish in color, you are not buying Aloe vera, no matter what the seller claims. You have the right to ask the seller for proof. Hopefully, the FDA will demand this in the near future.

Scientific studies on Aloe vera have been published for decades proving its effectiveness in a multitude of conditions: radiation and other burns, cancer in animals, HIV, digestive problems, skin ulcer and wound healing, immune modulation, infections (virus, bacteria and fungus), toxicity, pruritis, hyperglycemia, hypercholesterolemia, and inflammatory conditions (external or internal), to name a few.

The references at the end of this article highlight just some of the international scientific research studies on Aloe vera over the years and the studies are accelerating in 1992.

Cold processed whole leaf Aloe vera is perhaps my number one daily health supplement that I take without fail, and the one I prescribe most frequently for most patients, as well as members of my family. My own skin, scalp, digestion, elimination and energy have all improved since I started on Brand "A" whole leaf Aloe products. My own research with "God's miracle plant" will continue. "So far, so good," is an understatement.

With all the chemicals being used in apples today, I think a new maxim will emerge: **"Drinking Aloe today, keeps the doctor away."**

References and additional Literature

Aloe Vera, The Whole Leaf Advantage

Excerpts By Ivan E. Danhof, M.D., Ph.D.

In the evolution of processing methods of Aloe vera leaves, The hand-filleting procedure was developed to avoid contamination of the internal gel fillet with the yellow sap found in the pericyclic cells of the vascular bundles located just beneath the thick green rind of the leaf. The yellow sap has a number of laxative anthraquinones, the major being aloin. As the laxative action of these anthraquinones may be associated with considerable abdominal cramping in humans, these agents, although widely used from the 17th through the 20th centuries, have been replaced by laxative agents possessing fewer undesirable side-effects.

Aloin contains a glucose molecule attached to the parent anthracane ring. If the glucose is cleaved off, the resulting product is Aloe-emodin, which has, depending on its concentration, a red through brown through black coloration, which is in cosmetic products. Thus, the presence of aloin or its derivatives is undesirable both for internal consumption and topical usage.

Only recently have processing methods using the entire whole leaf been perfected so the undesirable elements can be selectively removed, while maximizing the desired constituents. Among the desirable constituents are the polysaccharides (glucomannans), glycoproteins and associated growth factors.

In Table I, the data reveals that the quantity of desirable polysaccharides is 2 1/2 to 3 times the yield using the hand filleting methods.

Occasionally an individual sample may contain more than the amounts indicated in the table; this may occur if the leaves are dehydrated. These ranges will encompass 95% of routine samples based on current in-hand data.

Table I
Yields and Aloe Leaf Processing

Process Fraction	Hand Filleting (%)	Whole Leaf (%)
Total Solids (without preservatives or additives)	**0.45 - 0.65**	**1.30 - 3.50**
Polysaccharides	**0.12**	**0.16**

The major undesirable constituents, the polyhydroxyanthraquinones, can be selectively removed through filtration through charcoal and other absorbents so the remaining level of aloin is 1 ppm or less.

Table II data compares various processing methods and the effect on yield (total solids), aloin concentration, and the distribution of sizes of constituents. **The whole leaf method can produce an Aloe juice which is high in total solids, high in retained high dalton (molecular weight) polysaccharides with their scientifically demonstrated benefits,** while the aloin concentration is at a very acceptable low level.

Table II
Methods Of Leaf Preperation and Constituents

Method Of Preparation	pH	Aloin (ppm)	(%) H_20	(%) Total Solids
Hand-filleting	4.27	6	99.25	0.48
Roller	4.30	32	99.61	0.39
Leaf Splitter	4.24	18	99.61	0.42
Whole Leaf	4.09	1	98.62	1.38

Cold Versus Heat Processing Methods

Data suggest that the time interval between leaf harvesting and processing (sun exposure) should be minimized (less than 24 hrs); heat exposure during processing should be minimized, especially if high temperatures are maintained for an hour or more.

Advantages Of The Whole Leaf Cold Processing Methods

Advantages of the whole leaf, cold-processed, approaches include the following:

1. Maximizes the yield of desirable constituents.
2. Increases cost effectiveness of processing.
3. Increased total solids concentration.
4. Increased polysaccharide concentrations.
5. Virtual absence of undesirable anthraquinones.
6. Improved desirable characteristics for cosmetic usage.
7. Increased concentration in permeability factors increasing transdermal penetration.
8. Improved taste palatability.
9. Increased concentration of growth factors responsible for accelerating of healing.
10. Increased concentration of factors responsible for the stimulation of the immune system.

Aloe Vera Leaf Handling And Constituent Variability

By Ivan E. Danhof, M.D., Ph.D.
Excerpt From The book: Remarkable Aloe, Aloe Through The Ages

What Is The Best Aloe Vera?

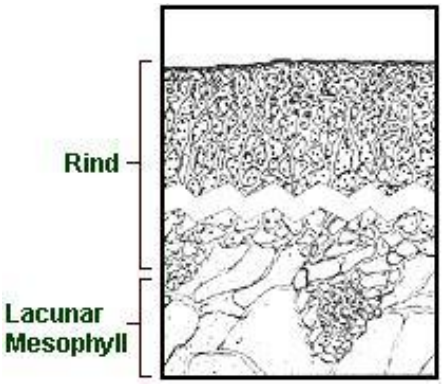
The question, "What is the best Aloe Vera" is often asked. I answer the query with another question, "What do you want the Aloe Vera product to do." The *BEST* Aloe Vera is one which contains the constituents that have the actions and benefits the final product should contain and does not contain materials with negative effects.

An Aloe Vera leaf contains more than 200 different constituents - each of them in relatively small quantities. The juice contains, on average, more than 99% water, thus all the constituents together amount to less than 1%. This implies that actions and benefits may be brought about by very small amounts of active ingredients. It also points to the fact that the leaf should be harvested and processed to assure that the active constituents are present in satisfactory amounts and are not adversely altered by the method of preparation.

To answer our initial question, the *BEST* Aloe Vera is a preparation which: maximizes the desired constituents, minimizes any ingredient with negative effects, maintains the constituents in an unaltered and active form, preserves the actions and benefits, and is present in the final product in amounts which, indeed, can bring about the desired result when the product is used as recommended.

Where are the Aloe Vera Constituents Made?

In figure 1, is a photomicrographic section through the outer portion of an Aloe leaf. The rind consists of 15-18 layers of cells interspersed with chloroplasts (small round bodies), where the constituents are synthesized, and with inclusions containing calcium oxalate and magnesium lactate crystals.



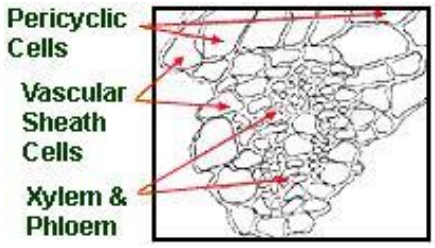
A composite photomicrographic section through the outer layers of the leaf of Aloe barbadensis Miller, showing the thick green rind and the outer portion of the lacunar mesophyll (mucilage).

Just beneath the thick green rind are located the vascular bundles. As shown in Figure 2, the outer support of the vascular bundle is provided by the sheath cells. Inside the vascular bundles are three types of tubular structures: the xylem (transports water and minerals from roots to leaf) the phloem (transports starches and other synthesized materials to the roots), and the large pericyclic tubules (containing the yellow latex or sap which is very high in the laxative anthraquinones, especially aloin).

The anthraquinones absorb ultra violet rays of the sun and prevent overheating of the central portion of the Aloe leaf, the water storage organ. Note that the pericyclic portion of the vascular bundle is adherent to the rind, while the remainder of the vascular bundle protrudes into the lacunar (large spaces) parenchyma or mesophyll, which is very thick and slimy. This provides a movable layer between the more solid inner gel fillet and the stiff outer rind. This liquid layer is termed the mucilage.

The innermost and major portion of the leaf is the spongy parenchyma or mesophyll constituting the gel filet. This layer has more structural integrity than the slimy mucilage layer.

All of the carbohydrate (polysaccharides) and glycoprotein (enzymes) constituents of the Aloe leaf are made in the thick green find. Carbohydrates synthesized in excess of that needed for energy metabolism are transported to the gel fillet for storage of water and minerals and carbohydrates.



The various portions of the tubules of a vascular bundle are labeled. The pericyclic tubules contain the laxative agents of the yellow sap or latex. Xylem and phloem vessels serve in water and nutrient transport, respectively.

The carbohydrates are transported by the phloem vessels to small cellulose-containing vessels in the gel fillet, which constitutes most of the pulp of the fillet. Water is then osmotically attracted to the carbohydrates serving as the water storage organ of the plant.

The carbohydrates (and small amounts of lipids or fats) consist of carbon, oxygen and hydrogen. These are derived from carbon dioxide from the air taken into the leaf through the stomata (pores) at night, and water from the ground. There is no sunlight to energize the photosynthesis mechanism to change the CO2 into carbohydrate. The entrapped CO2 is stored as malic acid, which gives the internal part of the leaf an acidic pH of about 4.0. When sunlight hits the leaf, some of the malic acid can be changed to the carbohydrate used as fuel by the plant's synthetic machinery. Only a portion of the carbohydrate is used for energy, the remainder being stored in the mucilage and gel fillet.

Digestion and The Immune System and Aloe Vera MPS

By John C. Pittman, M.D.

Poor digestion results in two primary problems:

1. Food is not broken down into the elemental building blocks necessary for the body to rebuild itself and generate energy for metabolism. At a cellular level, toxins are not removed from the cells, sufficient nutrients are not moved in to the cell, and not enough energy is produced for cell functioning. **This affects all cells including the immune system cells such as white blood cells, which then lack the fuel and the oxygen to carry out their normal function.**
2. Even more significant is that maldigestion results in food remnants in the gut causing several pathological reactions. First, there is irritation of the intestines, causing increased permeability of the cells in the intestinal wall. Undigested protein can then leak across into the lymph system and then into the general circulation, with the immune system reacting to contain the foreign invaders. The immune system becomes overtaxed and runs down. Oxygen and fuel gets used up; **the immune cells wear out faster and do not reproduce in sufficient numbers**.

Undigested food remnants can also become a breeding ground for candida and several types of parasites. Candidiasis produces toxins that cause increased digestion dysfunction, food allergies, fatigue and a host of other problems. **Ultimately, this causes the immune system to become even further depressed.** The inflammation in the intestines causes further damage by causing reactions that produce oxidative free radicals as waste by-products. Then negatively charged oxygen molecules begin to chop holes in cell membranes in an attempt to grab a positive charge. This results in further damage to the intestinal walls and ever increasing permeability. The leaky gut syndrome increases with more food particles going into the blood.

Research has shown that Aloe mucopolysaccharides have a remarkable ability to normalize all of these damaging processes, which has the effect of enhancing the immune system function through improved digestion. Aloe mucopolysaccharides act as a potent anti-inflammatory agent, stopping the damage and leakage of the intestinal wall, thereby taking the stress off the immune system.

Aloe mucopolysaccharides have direct anti-bacterial, anti-viral, anti-fungal/yeast and anti-parasite effects. Chronic yeast growth can be controlled so the normal, healthy flora can then thrive more easily. Furthermore, the macrophages, monocytes, antibodies and T-cells are stimulated. Phagocytosis (when large white blood cells engulf particles) is dramatically increased to ingest foreign proteins, such as the HIV virus. **Aloe mucopolysaccharides increases the number and intensity of all immune cells in the body.**

The key to integrating healthy digestion with a healthy immune system is the oral ingestion of Aloe mucopolysaccharides.

Immune Enhancing Effects Of Whole Leaf Aloe Vera

By John C. Pittman, M.D.

Galactomannans are a class of long chain sugars derived from plants, which have been shown in laboratory and clinical studies to have a wide variety of immune stimulating and protective effects within the body. In studying the different sources of this polymer, **it has been discovered that the Aloe barbadensis plant contains the greatest concentration of acetylated mannan which is also the most active form of mannans**. This "acemannan" has been shown to have many effects in the body, mostly impacting on the gastrointestinal and immune systems, which are intricately related. Before elaborating on acemannan's beneficial effects, it is appropriate to discuss the type of pathology often present in individuals experiencing immune system depression.

The most striking commonality found in individuals suffering with immuno-depressive conditions (Epstein-Barr virus, Chronic Fatigue Syndrome, systemic candidiasis, HIV infection and others) is their high incidence of digestive dysfunction and maldigestion. This has several effects that contribute to stress on the immune system and therefore its weakening. Maldigestion means that the consumed food is not properly broken down into the elemental building blocks needed for the body to rebuild itself and to generate energy for metabolism. This results in a type of starvation at the cellular level, with all tissue suffering malnourishment and therefore decreased effectiveness of all internal chemical processes. These processes include breakdown and transport of toxins out of the cell, movement of nutrients into the cell, and energy production for cell functioning. This effects all cells in the body, including those of the immune system such as white blood cells, (macrophages, monocytes, and lymphocytes) and red blood cells which carry oxygen. **Not only do we lack enough fuel but we're low on oxygen too.**

However, it is not this cellular starvation alone that causes the immune depression. Maldigestion also results in partially digested food remnants which can be involved in several pathological reactions. First, these remnants become irritants and cause inflammation of the mucosal wall of the intestines. Many powerful enzymes and damaging chemicals are released, injuring the intestinal wall causing increased intestinal mucosal permeability. The foreign proteins of the digested food can then leak across the mucosa into the lymphatic channels of the intestinal wall and from there gain access to the circulation. Here, these absorbed proteins are recognized as foreign and attacked by cells of the immune system. Antibodies bind to the protein, then call in macrophages and monocytes. T-cells arrive later, releasing enzymes and using oxygen to drive the metabolic breakdown of the foreign protein. **The total result is that the immune system is constantly turned off and draining down like a battery.** As these allergic reactions to food breakdown products continue, the cells of the immune system wear out faster, run out of fuel and aren't reproduced in sufficient numbers.

In addition to this chronic hyperimmune state, undigested food remnants provide fuel for the overgrowth of fermentative fungal organisms such as Candida albicans as well as several types of parasites. Overgrowth of Candida in the intestine has significant effects throughout the body due to the absorption of toxic by-products of its metabolism. This can result in worsening of food allergies, hypoglycemia, digestive disturbances, excessive mucus, bloating, flatulence, skin rashes, and extreme fatigue. This chronic infection further drains the immune system and complicates the picture.

Further damage is inflicted on all cell membranes from the effects of the generalized inflammation occurring as a result of maldigestion. These metabolic reactions utilize large amounts of oxygen and produce oxidative free radicals as waste by-products. These negatively charged oxygen molecules are desperately trying to balance their electrical charge and immediately begin to chop holes in cell membranes

as they grab positive charges. The result here is further damage to the intestinal mucosa and ever worsening of the increased permeability.

All these processes work together in a vicious sequence of events leading to progressive weakening of the immune system. It is clear that many mechanisms are at play in orchestrating these processes. Without definitive therapy directed at each component of immune system pathology, this is a downward spiral to death. Fortunately, a thorough multidimensional treatment protocol addressing each component has been shown to reverse these processes. Also, Aloe appears to play a key role on many different levels in boosting immune function.

As the biologic activities of Aloe derived acemannan have been elucidated, **it has been shown to have a remarkable ability to normalize all of these damaging processes and therefore contribute significantly to the enhancement of immune system function**. At the intestinal level, acemannan acts as a potent anti-inflammatory agent, neutralizing many of the enzymes responsible for damaging the mucosal wall; in effect, quenching the fire. This results in decreased leakiness of the intestinal wall and less absorption of allergic stimulating foreign protein. Acemannan has direct virucidal, bactericidal, and fungicidal properties which can help control Candida overgrowth so that normal gastrointestinal bacterial flora can be restored. Acemannan also stimulates intestinal motility, helping to move allergenic proteins from the small intestine into the colon. All these processes help to normalize gastrointestinal wall structure and function and therefore stop the vicious cycle of immune system damage.

Acemannan also has direct effects on the cells of the immune system, activating and stimulating macrophages, monocytes, antibodies and T-cells. It has been shown in laboratory studies to act as a bridge between foreign proteins (such as virus particles) and macrophages, facilitating phagocytosis (ingestion of the protein by the macrophage). This receptor site activation is a key component in boosting cell-mediated immunity which is deficient in HIV infection. It increases the number and intensity of action of macrophages, killer T-cells, and monocytes, as well as increasing the number of antibody forming B-cells in the spleen. Acemannan also protects the bone marrow from damage by toxic chemicals and drugs such as AZT.

These various effects while seemingly widespread and unrelated, are in fact due to one simple process at the cell membrane level. **Acemannan, a mucopolysaccharide, is a long chain sugar which interjects itself into ALL cell membranes.** This results in an increase in the fluidity and permeability of the membrane allowing toxins to flow out of the cell more easily and nutrients to enter the cell. This results in improved cellular metabolism throughout the body and an overall boost in energy production. **The vicious cycle of maldigestion and cellular starvation is finally broken as the acemannan normalizes absorption of nutrients and increases tolerance for allergenic foods.** The immune system is now stronger, under control, and better prepared for any new threat.

As humans living in the late twentieth century, our bodies' metabolic and detoxification systems are under ever-increasing stress from foreign chemicals, nutrient depleted food, and immune damaging infectious agents. In order to control and prevent the inevitable progression of immune system destruction that these stresses cause, therapy must be multifactorial involving all levels of health, diet, and lifestyle. These different areas consist of destruction of pathogenic organisms, metabolic detoxification, intestinal cleansing, increasing cellular metabolism, antioxidant agents to combat free radicals, and direct stimulation of immune system cells. **Acemannan, the active ingredient in cold-processed, whole-leaf Aloe has been demonstrated in laboratory testing and clinical use to be effective on all levels of this therapeutic program.**

It is because of these versatile and comprehensive characteristics that Concentrated Whole Leaf Aloe Vera juice is strongly recommended in the treatment of immune deficiency disorders. It plays a prominent role along with other therapies, nutritional supplements, and medications in the multidimensional treatment of these illnesses. The healing powers of Aloe have been known for centuries, but now we have the scientific foundation that allows appreciation of this amazing plant and its important role in restoring and maintaining our health.

Whole Leaf Aloe Vera In Dentistry

By James Harrison, D.D.S., F.A.G.D.

Post-treatment dental discomfort and pain are among the most unpleasant forms of misery we humans inflict upon ourselves. In providing relief from this, the blessed Aloe Vera plant displays yet another example of Heavenly mercy.

This story started for me on a weekend in July of 1991. Dr. Bruce Hedendal gave me a bottle of "Whole leaf" Aloe vera concentrate. He said that a report by Lee Ritter, N.D., showed that all Aloes were not equal, in fact some had no active ingredients whatsoever.

I had been using an Aloe product, which cost approximately $23.00 a gallon, for the past six months, but had not noticed any particular benefit. I was using it simply because I had heard of Aloe's legendary benefits. The bottle said, "100% pure, tastes like spring water," and according to the Ritter report, it was water. I was skeptical that this whole leaf Aloe product would produce any more noticeable benefits than before, but that is what this article is about.

Within two days of using the products, I noticed a tremendous increase in energy. I had been riding a hypoglycemic roller coaster for years, fueling up on caffeine and sugar to climb out of the slumps, only to find myself in another some hours later. That first week, I felt good, but I really was not paying attention to it. It was approximately two weeks into using the new Whole Leaf Aloe Vera that I noticed that I was thinner. Because my weight had been creeping up, I had been avoiding the scale; but that morning I had to check it out. To my surprise, I was a full five pounds lighter. It was only then that I realized why I had lost the weight. I was no longer feeding with sugar and caffeine the roller coaster slumps, but I was cruising nicely along near the top.

I had been using the Aloe Vera on my forehead, which had many patches of recurrent actinic keratosis, a pre-cancerous condition, which had in the past been removed with cryotherapy (liquid nitrogen). It took a month of using the concentrate, but these patches have gone into remission.

I have been an allergy sufferer my entire life, but the situation had been getting progressively worse over the last five years. When I first started using the new Whole Leaf Aloe Vera, the allergy symptoms got much worse, but then they started to clear. I have had a few bad days over the past five months, but generally I am greatly improved.

I have also experienced another benefit worth mentioning. I have suffered with a painful shoulder for two years. The pain is gone. During this time, I mentioned these benefits to others, who also started using these products, and they reported back (in most cases) equally enthusiastic stories.

The next two incidents encouraged me to introduce the products into my practice of dentistry. The first was when a four year old boy fell onto some sharp oyster shells and cut his foot open. I reached him first and covered his wound with 5X Aloe gel. He stopped crying within seconds. It was a deep cut. We cleaned and bandaged it with an Aloe Vera dressing and he was out playing in minutes.

The second incident was in my dental practice. The patient needed his wisdom tooth extracted, and while the site was getting numb we talked about Aloe Vera. He said his wife's grandmother had married a Native American back in the thirties and had used Aloe Vera ever since. He reported that she is now ninety-seven years old, looks like she is fifty, and acts like she is forty. He suggested that we try Aloe Vera on his wound.

I irrigated the socket with the Whole Leaf Aloe Vera concentrate, and after the sutures were in place, I filled the socket with the 5X Aloe gel. That evening I called to see how the patient was doing. His comments were that **"if his tongue didn't feel the space he would not be aware that anything had happened."** He continued to apply Whole Leaf Aloe Vera for that week and when it came time to remove the sutures, the area appeared pink and healed over. I was quite impressed.

We have since used the Aloe Vera for all surgeries with uniformly gratifying results. One person among many, Mr. Harold Gans, wrote, "I suppose it is unusual for a patient to tell a dentist that he feels he had not even been treated by him. I honestly feel as if I had not been in your chair. I never felt any pain at any time, nor any discomfort after leaving your office..."

What makes that letter so rewarding is that we worked on Mr. Gans for two plus hours, removing numerous teeth, performing bone recontouring, and inserting an upper immediate denture. The check-up the next day showed some mild hematomas, but little swelling. The tissue was a healthy pink. I have not had to prescribe pain medication, except for one very drug-oriented patient, in four months.

I hope these anecdotal stories have piqued your interest to read further, because I have some ideas about what may be happening.

Why Aloe May Work

Carrington Laboratories, Inc., has been trying to gain FDA approval for the use of acemannan as a drug. Acemannan is the name given to the large molecular-weight sugars called mucopolysaccharides that are found in Aloe Vera. They assert that this is the "active" ingredient and have spent considerable time and money doing in-vitro and in-vivo research. Their work has shown that Aloe Vera interacts with the body's immune system, enhancing rather than overriding this system. It stimulates the macrophages, one of the principal immune response steering mechanisms of the body. These studies have shown direct anti-viral activity. On November 4, 1991, Carrington announced that conditional approval was granted by the USDA for the use of Acemannan as an aid in the treatment of canine and feline fibrosarcoma. Although this is an isolate of the plant and may represent only a small fraction of its active ingredients, it is a large step forward and may open the door for Aloe to gain approval for other uses.

Trevor Lyons, B.D.S., L.D.S., R.M., a Canadian dentist, deserves recognition as a true pioneer in our quest for the solutions to periodontal disease, as well as the systemic manifestations resulting from this infection. His book, *Introduction to Protozoa and Fungi in Periodontal Infections*, is a masterpiece of literature review and original research.

There are many thought-provoking ideas presented that will provide answers to many puzzling questions. His basic premise is that one-celled animals, protozoa such as Entamoeba gingivalis, Entamoeba histolytica, Trichomonas tenax, are not opportunistic, but, in fact, precede the host's oral and systemic declines *(Lyons, p. 15)*. Equally important in oral and systemic pathology are the fungi most notably Candida albicans. Again, rather than being opportunistic, these fungi actually suppress the host's immune system, are capable of causing death, and have been shown to be distributed throughout all of the host's organs upon autopsy.

Yeasts and trophozoites, contrary to what was previously believed, do not appear to be normal inhabitants of the mouth. They are associated with oral and/or systemic disease, and if left untreated in an apparently symptomless host, will lead to the deterioration of the oral and general health of the patient *(Lyons, p 73, p. 15)*.

Dr. Lyons, through meticulous and step-by-step development of his theory, proves that these heretofore accepted, "normal" inhabitants should be our target organisms in the treatment of many oral and systemic diseases. He has documented and published proof that the elimination of those parasites restores the host to a state of well being.

Another forward-thinking holistic dentist, Dr. Douglas Cook, from Surfing, WI, read between the lines of Dr. Lyons' work and gleaned the idea of why the Aloe Vera is so effective on so many people. In an interview with Dr. Lyons, he confirmed this information. **Aloe Vera is one of the most potent protozoaand yeast-killing solutions that he had ever worked with.** However, Dr. Lyons did not have at his disposal, nor did he know about, these new, highly concentrated Whole Leaf Aloe Vera solutions.

Most of Dr. Lyons' successes, which are monumental, were produced using traditional allopathic medicine. Many of these medicaments used are highly toxic to the host, as well as the target organisms. Possibly, nature has provided the perfect solution to this parasite problem: Aloe Vera.

In 1929, Kofoid reported finding Entamoeba in the bone marrow of some arthritic subjects. In 1981, Snyderman and McCarty reported similar pathology in rheumatoid arthritis and destructive periodontal disease. In 1982, Dr. Paul Keys, the former head of dental research at the United States National Institute of Health, reported the almost invariable relationship between oral protozoa and periodontal deterioration. E. gingivalis found at the base of periodontal pockets and E. histolytica found in ulcers of the colon *(Lyons, p. 28)* behave similarly, causing the lesion to spread laterally as the amoebae migrate parallel to the floor of the ulcer.

Could these one-celled animals really be that destructive? R. Mueller, in 1988, reported a new theory of enzyme destruction. Polymorphs produce a proteolytic (protein-digesting) enzyme, "elastase" which is normally bound to a circulating liver enzyme, "proteinase inhibitor" forming "elastase proteinase inhibitor complex" (EPIC). The leukocytes are disrupted by the contact with amoebae leaving the leukocytes in an uncontrolled state of maximum production and release of elastase. The EPIC balance becomes overpowered, leading to rapid, uncontrolled, lytic activity. This concept fits well with the understanding that destructive periodontal disease may be considered an autoimmune disease *(Genco and Mergenhagen, 1982)* and shows that "the supreme irony of this state of parasitism is that the very cells which should protect the host in fact destroy the host and are then, in turn, consumed by this predator parasite, Entamoeba gingivalis." *(Lyons, p. 34)*

These parasites also are capable of being infected with a virus. From within this safe harbor protected from the patient's immune response, a continuous stream of pathogenic particles could eventually destroy the host. Could this be the reason why Epstein-Barr and HIV patients are helped with Aloe Vera? Does the Aloe Vera destroy the virus' hideout? Whatever research eventually shows, the destruction of these one-celled invaders will leave the host with a stronger immune system.

Many dentists have been dismayed over the rampant decay in the cervical areas of some of their patients' teeth. These lesions tend to rapidly spread along and below the gingival margin. Within just a few months this mostly painless destruction may render the tooth unsalvageable. Dr. Lyons has shown that this rapid decay is caused by Candida, which is capable of both aerobic and anaerobic metabolism.

Antibiotics and antifungals have proven effective if the right ones at the right times are used. Reports from the literature show that neither E. gingivalis nor E. histolytica is capable of initiating infection

without the concomitant presence of bacteria *(Levine, 1973, p. 147; Grollman & Grollman, 1970, p. 649)*. And, while antibiotic therapy may be cidal to trophozoites, it may be working due to the change in the bacterial environment.

Aloe Vera, on the other hand, non-toxic to the host, has been reported (in anecdotal stories) effective in the treatment of most digestive and gastrointestinal problems, arthritis, skin lesions, multiple sclerosis, diabetes, and periodontal disease, etc.! Could it be that Dr. Lyons, who first recorded the destruction of the protozoa with Aloe Vera, may have found the reason why Aloe Vera appears to be so effective with so many different problems?

Use Of Whole-Leaf Aloe

It has been my finding, as well as Dr. Lyons' and Dr. Cook's, that the use of topical antimicrobial therapy, although helpful, should be combined with systemic treatment.

A therapeutic dose of mucopolysaccharides of 15 mg/kg has been established as virucidal. To my knowledge, no amoebacidal dose has yet been established, but working on the 15 mg/kg dose per day, approximately two ounces of the concentrate per day should be effective for the average adult. It is important to take part of the dose before bed, preferably on an empty stomach, since the parasites are particularly active at night *(Lyons, p. 26)*.

It is very important to keep the dose within acceptable ranges, so that the "kill" does not produce a flood of toxins, antigens, viruses and viroid particles, which are released into the body upon the parasites' death and disintegration. This is called the Herxheimer Reaction, and will vary depending on the nature and quality of the material released and the host's (patient's) tolerance to those foreign substances. If this reaction becomes severe, it is best to discontinue the Aloe Vera and work on other detoxification programs such as colonics and diet changes, etc.

The best way to start on an oral disinfection program would be to purchase a good soft-bristled toothbrush. Dr. Phillips has developed a baby-soft brush and a technique quite effective in removing plaque and stimulating the tissue. You may purchase these items from Periodontal Health Brush, Inc.

As your dentifrice, the 5X Aloe gel works to clean the gums and gently kill the pathogens. If you use an oral irrigation machine, mixing a couple of tablespoons of Aloe concentrate into the water will help kill the pathogens living at the bottom of the pockets. Homozon, a magnesium oxide powder, which releases oxygen in the presence of acid, can be used as a dentifrice or a packing on the gums, then followed with the Aloe Vera. Don't forget to brush your tongue and be gentle with the floss.

It is best to institute a program of oral disinfection prior to rigorous scaling and curettage, due to the potential spread of protozoa and yeast throughout the body through the open blood vessels abounding in the infected gums.

Hopefully, as research catches up with these ideas, we will learn how and why Aloe Vera is so effective in helping our bodies heal themselves. I, for one, see the need for more in office diagnosis of specific pathogens, based on the use of the phase-contrast microscope, as well as the incorporation of a program for heavy metal detoxification.

The Rediscovery Of Aloe Vera

By Alfred Garbutt, D.C.

Aloe vera is a plant of African origin that is related to the lily. Aloe vera means true aloe in Latin. The healing benefits of Aloe vera have been recorded throughout the world for thousands of years. The American medical and pharmaceutical communities most likely have not accepted it because it can't be patented nor a prescription written for it. Nevertheless, there are a significant number of records and research articles about the benefits of Aloe vera.

I have been studying therapeutic nutrition for over 26 years and have frequently read about these benefits. There was the occasional stomach upset in a child that would respond but overall I witnessed little results with the Aloe products available. I didn't want to waste people's money so I stopped recommending the internal use of Aloe Vera until this past year.

My continual study of therapeutic nutrition brought me across vital information as to why the previous products had little, if any benefit.

They were lacking or low in a key active ingredient that was necessary for the body to heal itself. This active ingredient is called mucopolysaccharide (MPS), which is a long chain of sugars that bond with water. In the body this type of natural chemical glues cells together, lubricates joints and enhances the immune system.

Over 95% of the Aloe products on the market are either diluted or improperly processed. Using only the inner gel of the Aloe vera leaf provides a lower concentration of MPS. **The outer leaf and rind have 200% more of the active ingredient than the inner gel. Processing the plant with high heat also destroys many of the beneficial ingredients of Aloe. The best products should be cold processed using the whole leaf** with the aloin removed. Aloin is the irritating chemical in the plant that can cause diarrhea or intestinal cramping.

Ivan Danhof, M.D., Ph.D. is considered the leading expert in the world on Aloe vera. Dr. Danhof states, "The only material shown to have beneficial effects in scientific studies are attributable to the polysaccharides." Experts in the subject recommend between 600 - 1,200 mgs of MPS per day for a healthy adult. Unhealthy people would commonly use 1,200 - 3,000 mgs per day, those with severe diseases using much higher amounts.

The vast majority of Aloe vera products available in the USA have 0 - 1,400 mgs MPS per liter. Even with the best of these, you would need to drink one liter each day to get enough of the mucopolysaccharides. When I found a product that was 10 times the concentrate with over 12,000 mgs MPS per liter, I finally saw the results with my patients that I expected and wanted. **Whenever you buy Aloe vera products for internal use, always check how much MPS is in the bottle.** If you must drink 1-3 liters per day to equal 3-4 ounces of a 10 times concentrate then that cheaper bottle is not truly the most economical for what you get.

A few of the body problems that doctors are researching or using Aloe vera for are: mouth and stomach ulcers, intestinal disorders such as irritable bowel, to expel worms, sleep disorders, chronic vaginal irritation, inflammation associated with diabetes, digestive problems, viral infections, excess yeast (candida) in the bowel and stressed immune system.

There are medical doctors doing research with cancer and AIDS patients taking very large doses of concentrated Aloe vera and observing promising responses.

A 10 times concentrated Aloe gel can also have remarkable benefits for the skin when applied topically. Aloe can penetrate deep into the tissues where it can moisturize, have antiseptic properties, stimulate the growth of new healthy cells and have a cleansing detoxifying effect. A morning and evening application of pure Aloe gel can be a simple yet beneficial procedure towards slowing down the deterioration of your skin, especially if you live in Southern California which is technically a desert. We just artificially make it look green by pumping in a lot of water during the summer months.

Whole Leaf Aloe Vera - Psoriasis Treatment Protocol

By Donovan J. Anderson, M.D.
Willow Valley Medical Center, August 29, 1996

Psoriasis is a chronic disease that is found more prevalently in the USA than in less developed countries. Its cause is unknown. It is characterized by scaly, shiny lesions that break out on the erythematous areas of the skin. Although unsightly and irritating, psoriasis is neither painful nor contagious.

Specialists who treat psoriasis frequently, believe it is brought on by genetic factors in combination with several factors including diet, immediate environment, and lack of vitamins A and D. The lesions respond well to sunshine, concentrations of ultraviolet rays, and recently they have been found to respond well to saline rich muds of the Dead Sea resorts. (I wonder if the mud from the Salton Sea would work?)

The Aloe program includes an applied regimen of regular daily topical applications of Aloe vera gel. Large daily doses of Aloe drinking juice, supplemented by a specific regimen of megavitamins and anti-oxidants. And with a strict all natural diet which excludes any intake of processed foods, "junk" foods, fast food meals, sugar or foods heavy in animal fat or other high LDL cholesterol. We also find that more fresh fruits and vegetables help the skin to heal faster.

1. After showering with mild soap,
2. spray the affected area with Aloe liquid spray.
3. Apply Aloe gel 4 times per day is best. 2 times minimum.
4. Drink at least 4 oz of Aloe drink per day.
5. Take multivitamin and mineral combination. (TVM-49)
6. Get at least 1 hour of sunshine to the affected skin each day or UV light.
7. Eat natural diet with fruits and vegetables with as little animal products as possible.
8. Try to limit processed foods and "junk" foods.
9. I strongly recommend a potent antioxidant such as pycnogenol or grape seed extract (Proanthenols Bio-Complex).

The Aloe juice and gel must be high quality, Cold processed Whole leaf, Stabilized. Should have a minimum of 8,000 mg of Mucopolysaccharides per liter (MPS). The typical Aloe gel sold at the pharmacy OTC is single strength, fillet only. It doesn't work I have tried it. Whole leaf has 5 times more healing power than single strength fillet gel. Aloe juices OTC generally are single strength or 1,00 to 1,400 mg MPS/liter. Some have as low as 40mg/MPS/liter. Others have high MPS counts because they add maltose as sweeteners that are measured the same as MPS but have no healing power. **I personally recommend Life Plus Aloe products.** They have no sweeteners or flavors. I find that they are quite tasty and they have a 30 day money back guarantee. The price per mg of MPS is the most competitive on the market.

Whole Leaf Aloe Vera
Wound Care Protocol

By Donovan J. Anderson, M.D.
Willow Valley Medical Center, August 29, 1996

Excerpts from - A Holistic Protocol for the Immune System By Scott J. Gregory, O.M.D. Fifth Edition Aloe Vera For over five thousand years, folk medicine has celebrated the juice of the aloe vera plant for its unique healing properties. Only recently, however, has modern medicine begun to unlock the deeper secrets of aloe and to place the "miracle plant" under laboratory scrutiny. The aloe plant is a succulent, consisting of thick green leaves with a gelatinous substance inside. Aloe juice, properly processed, contains a wide variety of healing constituents. The principal attributes are: antiseptic, anti-inflammatory, and anti-viral. Antiseptic: The plant produces six antiseptic agents: Lupeol, a natural salicylic acid, urea nitrogen, cinnamic acid, phenol, and sulfur all demonstrate anti-microbial effects. Lupeol and salicylic acid also have analgesic effects. Anti-Inflammatory: Aloe contains three plant sterols, which are important fatty acids-HCL cholesterol (which lowers fats in the blood), campesterol, and B-sitosterol. All are helpful in reducing symptoms of allergies and acid indigestion. These compounds also aid in arthritis, rheumatic fever, both internal and external ulcers, and inflammation of the digestive system. The stomach, small intestine, liver, kidneys, and pancreas can all benefit from these antiinflammatory effects. Anti-viral, anti-bacterial: Recent research has suggested some exciting new possibilities. Aloe not only provides vigorous overall immune system support, but aids directly in the destruction of intravascular bacteria. The reason is aloe's unique polysaccharide component. The body's natural "complement system"a critical defense system involving a series of proteins-only needs to be activated in order to attack bacteria. It is the polysaccharides that trigger these proteins-in a sequence called the "cascade phenomenon"to take on a doughnut shape and insert themselves into the surface membranes of bacteria. Through this action they literally create holes in the bacteria, exposing the pathogens' interior to surrounding fluids, causing their death. In an article in the Medical World News, December 1987 issue, titled "Aloe Drug May Mimic AZT without Toxicity," Dr. H. Reginald McDaniel stated, "A substance in the aloe plant shows preliminary signs of boosting AIDS patients' immune systems and blocking the human immune-deficiency virus' spread without toxic side effects." In the summer of 1989, internationally recognized AIDS expert Terry L. Pulse, M.D., conducted a systematic study of a unique nutritional regimen combining the use of an aloe vera drink with a supplementation powder and fatty acid capsules. The objective was to determine if this nutritional regimen would help to restore the patients immune systems and increase their ability to fight current and future infections. Twenty-eight patients remained with the study through its 180-day period. Whereas initial rating showed 16 patients classified with full-blown AIDS, at 180 days all 16 had improved so dramatically that none could any longer be placed in that category. Additionally, two were accorded a MWR (Modified Walter Reed scale) classification of 0-or HIV negative-at the end of the study. Subsequently, an additional five patients achieved a 0 rating on the MWR scale. Dr. Pulse's and Dr. McDaniel's studies, though preliminary, became the catalyst for rapidly-expanding interest in the anti-viral and immune-enhancing potential of aloe. A unique feature of the polysaccharides or long-chain carbohydrates in aloe is their remarkable ability to pass through the stomach and digestive tract and into the circulatory system without being broken down by stomach acid or digestive enzymes. By a process called endocytosis, they are taken up into the cells of the intestinal lining intact and extruded into the circulatory system, where they are able to fulfill their immune-supporting functions. Whole-Leaf Aloe Concentrate In the past decade the marketplace has been flooded with aloe drinks, and almost all of these have been flooded with water. In fact, many are, so dilute as to be of almost no benefit. Recent years, however, have seen the promising development of new technologies enabling the best processors not only to produce stable concentrates of aloe, but to utilize the whole leaf. It is now known that the polysaccharides are concentrated close to the rind, where these sugars are produced, though these layers were previously discarded due to the presence of undesirable aloe resins, aloin or aloe emodin. But now, state-of-the-art filtering technologies permit the removal of these highly purgative components without significantly reducing the healing agents of aloe. Within the rapidly-growing field of aloe research, no one has done more than Dr. Ivan Danhof, M.D., Ph.D., of Grand Prairie, Texas, to highlight the advantages of wholeleaf processing and to advance further study. Recognized as one of the world's top experts on aloe, Dr. Danhof has helped to pioneer critical work aimed at isolating aloe's healing agents

and developing the most favorable processing and stabilizing techniques. Importantly, these new techniques use only limited heat (called " cool processing"). Dr. Danhof is also closely affiliated with one of the world's leading manufacturers of whole-leaf aloe concentrate, and this concentrate is commercially available through the International Health Foundation, of Portland, Oregon. For each batch of whole leaf aloe concentrate produced, IHF uses an independent research laboratory to verify concentration and quality. IHF's aloe drinks come in two levels of concentration-177 milligrams of polysaccharides per ounce, and 450 milligrams of polysaccharides per ounce. That translates into 5,654 and 14,400 milligrams per quart-a polysaccharide level equivalent to many gallons of common aloe drinks on health food store and nutrition cent shelves.

Fundamentals Of Aloe Vera Mucopolysaccharides

By Ivan Danhof, M.D., Ph.D.

The Aloe vera mucopolysaccharide (MPS) is a long chain sugar molecule composed of individual mannose and glucose sugar molecules connected together. There is wide range in the size of the mucopolysaccharide molecule.

The varying sizes determine their **healing properties**:

Small *50-600 molecules*	Reduces inflammation - which is involved in such diseases as ulcerative colitis, arthritis, and gastric reflux. Also helps with the reduction of blood sugar with both type I and II diabetes.
Medium *up to 1,500 molecules*	Where as vitamins and minerals can only function outside the cells, mucopolysaccharides are very effective intracellular antioxidants and free radical scavengers - very important in preventing and treating arteriosclerosis, heart disease and Parkinson's disease. With the ever increasing pollution on the planet and loss of nutrients in the soil, the increase in free radicals and loss of cellular oxygen will only become worse with time. This makes Aloe vera mucopolysaccharides even more important than ever.
Large *up to 5,000 molecules*	Has a direct anti-bacterial and anti-viral effect. Important with all the new infectious diseases cropping up and the older ones becoming more virulent from long term use of antibiotics.
Very Large *up to 9,000 molecules*	The very large molecules are immune modulating, which have a powerful healing effect on AIDS, cancer and many different immune system disorders. It is also this large molecule that causes the body to produce a natural chemical, tumor necrosis factor, that functions to shut off the blood supply to tumors.

Internal Uses Of Aloe Vera

Excerpts By Ivan E. Danhof, M.D., Ph.D.

History - Internal Uses Of Aloe Vera

Historical evidence encompassing more than 4,000 years testifies to the high regard of ancient peoples to the benefits of Aloe vera.

In the 1930's, interest in the internal gel was enhanced when the material was found to be remarkably effective in treating radiation-induced dermatitis. Since that time, a number of external and internal uses for the internal gel of Aloe have been reported in the literature, some of which are truly remarkable. Owing to increasing anecdotal reports purporting to corroborate beneficial effects of drinking the ground, preserved, internal gel of Aloe, a number of scientific investigations have been undertaken to evaluate the validity of the anecdotal reports.

A few of the scientifically documented beneficial uses of drinking Aloe beverages will be delineated in contradistinction to untold numbers of anecdotal reports which represent subjective impressions or appraisals.

Gastrointestinal Disorder

For over 300 years the curanderos and curanderas in the Rio Grande Valley of Texas and the northern states of Mexico have recommended internal Aloe gel for "Las enferemedades del estomago y los intestinos, pero especialment para las ulceras." (The diseases of the stomach and intestines, but especially for ulcers.) As a result of these anecdotal reports, scientific investigations have been undertaken in animal models (laboratory rats) which have shown that if Aloe gel is administered prior to the ulcer-inducing stress (immobilization), there is an 80% decrease in the number of ulcers formed compared with the control animals given saline instead of the Aloe gel. Similarly, if the Aloe gel was given after the ulcers were formed, healing was three times as fast compared to the healing in the control animals. *(Galal et al, 1975)*

In a second laboratory investigation, Aloe gel pretreatment was 85% effective in preventing stomach lesions, and 50% better than the controls in healing the gastric ulcerations. *(Kandil and Gobran, 1979)*

Additional studies showed that a common group of plant constituents, the triterpenes, including lupeol, possess ulceroprotective activity against the formation of gastric ulcerations in albino rats induced by immobilization restraint. *(Gupta et al, 1981)* Other investigations have shown that Aloe gel preparations contain lupeol as well as other triterpenoids. *(Suga and Hirata, 1983)*

Aloe gel mixed with heavy liquid petrolatum (2:1) was given to 12 patients, 7 males and 5 females, ages 24 to 84 years, with definitive x-ray evidence of duodenal ulcers. All 12 patients showed complete recovery with no recurrence for at least a year after ulcer healing. This study suffers, however, from the fact that (1) Duodenal ulcers are often self-healing without any treatment, and (2) There was no control group of patients treated in a similar manner without the administration of Aloe. Nonetheless, the physicians who conducted the study represent trained, clinically-experienced observers, and thus even these uncontrolled observations have some scientific merit. *(Blitz et al, 1963)*

Atherosclerosis And Coronary Heart Disease

Coronary heart disease associated with the accumulation of blood fats (Lipids) in the lining of the arteries is still one of the major causes of death in the Western world. Several studies in animal models as well as in human subjects have suggested that the ingestion of Aloe gel may have a beneficial effect by lowering serum cholesterol, serum triglycerides, and serum phospholipids, which, when elevated, seem to accelerate the deposition of fatty materials in the large and medium-sized arteries, including the coronary arteries of the heart.

In one study, albino laboratory rats were fed high cholesterol diets with the experimental group fed the polysaccharide (Glucomannan) from Aloe. Compared with the control animals, the group fed the Aloe fraction showed:

1. Decreased total cholesterol levels.
2. Decreased triglyceride levels.
3. Decreased phospholipid levels.
4. Decreased nonesterified fatty acid levels.
5. Increased HDL cholesterol (the "good" cholesterol) levels.
6. Markedly increased HDL/Total cholesterol ratios.

The evidence suggests that the ingestion of Aloe gel, may have a salubrious effect on fat (Lipid) metabolism which, if active in human subjects, would tend to decrease the risk of coronary artery disease in people. *(Joshi and Dixit, 1986)*

Monkeys given Triton, which causes marked increases in blood lipids, were divided into two groups. The first group was given Aloe, while the second group received the drug, clofibrate, which is used clinically to lower serum cholesterol and triglyceride levels. The following data show the reduction in the various parameters compared with the control animals.

There was a marked in the beneficial HDL/Total Cholesterol ratios. *(Bixit and Joshi, 1983)*

Aloe-Treated Monkeys	PARAMETER	Clofibrate-Treated Monkeys
61.7%	Total Cholesterol	47.6%
37.8%	Triglycerides	50.0%
51.2%	Phospholipids	
	Non-esterified Fatty Acids	41.7%
45.5%		23.9%

A third investigation was performed studying 5,000 patients who were fed the husks of a local Indian plant, isabgal, which provided fiber, and Aloe gel as a beverage. There were some remarkable effects in three important areas:

1. **Lipid Metabolism**
    a. Decreased total cholesterol.
    b. Decreased triglycerides.
    c. Increased HDL cholesterol.
    d. **Carbohydrate Metabolism**
        a. Decreased fasting blood sugar levels in diabetic patients.
        b. Decreased post-prandial (after a meal) elevation in blood sugar levels in diabetic patients.

c. **Angina pectoris** (chest pain from insufficient delivery of oxygen to the heart.)

a. Decreased frequency of anginal attacks.

These data in the human study suggest that the benefit from the regimen, at least in part attributable to the ingested Aloe beverage, may have salubrious effects on several systems in the body. *(Agarwal, 1985)*

Anti-Cancer Actions

One of the common experimental cancer models is sarcoma-180. When Aloe was administered to mice bearing S-180 tumors, the tumor growth was inhibited. *(Soeda, 1969; Suzuki, 1979)*

Similarly, Alexin B, a specific molecule species derived from Aloe, was shown to possess anti-cancer activity against lymphocytic leukemia. *(Suzuki, 1979a)* Additional investigations revealed that another molecular species derived from Aloe, Aloctin-A, had anti-tumor activity, but the action was to bolster the immune system rather than a direct anti-tumor activity. *(Imanishi et al, 1981)*

Immune System

There are several mechanisms which contribute to the immunological protection enjoyed by normal persons. Among these mechanisms the ingestion of bacteria and other potentially harmful agents by certain white blood cells (a process termed phagocytosis) and the formation of antibodies (formed by another group of white cells, the beta-lymphocytes) are probably the most important. Scientific evidence suggests that Aloe gel contains substances which are active both in stimulating phagocytosis as well as stimulating the formation of antibodies.

In one study, the Aloe fractions were shown to increase phagocytosis when injected into guinea pigs. *(Stepanava et al, 1977)* In another study, mice were injected intraperitoneally with Escherichia coli, which caused a serious infection to develop in the abdominal cavity, namely, peritonitis. Injects of materials from two species of Aloe (Aloe barteri and Aloe ferox) both stimulated phagocytic activity in the animals. *(Delaveau et al, 1980)* It was demonstrated that phagocytic activity was depressed in adult patients with bronchial asthma. A mixture of amino acids derived from Aloe enhanced the depressed phagocytic function of the white blood cells in these asthma patients. *(Yagi et al, 1987)* In an additional study when certain materials (lectins) purified from Aloe were added to human lymphocytes raised in tissue cultures, the human white cells were stimulated to produce antibodies. *(Suzuki et al, 1979)*

Perhaps the most remarkable studies concern the effect of Aloe fractions on the status of patients with HIV which causes AIDS. The polysaccharide fraction of Aloe was shown to exhibit antiviral activity and enhance cell function. The polysaccharide was given orally, 250 milligrams four times a day, to 8 patients with ARC (AIDS Related Complex), with Walter Reed staging from 3 to 6. Eight of eight patients showed improvement within 90 days of therapy with an average reduction of 2 Walter Reed stages. Fever and night sweats were eliminated in all patients; diarrhea was alleviated in two of three patients, and opportunistic infections (which are usually responsible for the death of the AIDS patient) were controlled or eliminated in six of eight patients. Two patients, unemployable because of the intensity of their symptoms, returned to full employment. Three of three patients showed a decline in HIV core antigen (P-24). Initially positive HIV cultures became negative in three patients. Clinical toxicity and side-effects were entirely absent. Acute toxicity studies in animals showed no toxicity whatever at dosages 100 times those used in the pilot human experiments. *(McDaniel and McAnalley, 1988)* These experiments however, were uncontrolled, and additional studies, utilizing appropriate scientific study design would need to be done before the data would be acceptable to the scientific community.

In plasma there are four interacting systems which serve vital protective functions. These include the following:

1. Intrinsic coagulation (blood clotting)
2. Plasminogen(prevention and dissolving of intravascular clots)
3. Kinninogen (inflammation)
4. Complement (destruction of intravascular bacteria)

The latter system, the complement system, consists of a series of proteins which require activation. When activated these proteins interact sequentially - a cascade phenomenon - and form circular, doughnut-shaped proteins, which are inserted into the surface membranes of bacteria, literally causing "holes" which permit the interior of the bacterium to become exposed to the environment, causing the death of the organism. Normally this complement system is stimulated by the presence of polysaccharides on the surface of the invading organism. Studies have shown that the polysaccharides (glucomannans) of Aloe can perform this function. *(t'Hart et al, 1988; t'Hart et al, 1989)*

There are several additional beneficial actions of ingested Aloe presented in the literature. True, many of the anecdotal reports have been studied in animal models, giving credence to the anecdotal information. Other reported benefits in human subjects have yet to be documented by scientific investigations. A number of studies are currently underway in various laboratories across the country and in other countries as well.

Three salient points are of vital significance in providing credibility to scientific studies: (1) How are the polysaccharides handled in the digestive tract? (2) As the juice is so "dilute" is there really sufficient material absorbed to account for the reported benefits? (3) What amount of juice would be required orally, on the average, to provide a beneficial effect?

The answers are:

- The polysaccharides are not digested by the enzyme systems in the human digestive tract; these mannose-containing molecules are absorbed by endocytosis, i.e., they are taken up into the cell intact.
- Apparently, from the animal experiments, very small amounts of Aloe constituents are required to produce a beneficial effect.
- In human subjects, beneficial actions are readily apparent with the ingestion of 2 ounces twice daily.

References

Whole Leaf Aloe Vera And The Heart

While the polysaccharides are the largest single group of Aloe constituents possessing some remarkable actions and activities, they are not alone, but share pharmacological properties with a large number of Aloe constituents.

As you may be aware, plants have been the mainstay source of medically important materials (medicines) for literally thousands of years. Among these plants, the Foxglove has a special place because it was the original source of the cardiac glycoside, digitalis. Digitalis works by slowing a runaway heart rhythm as well as increasing the force of the contraction of the heart muscle, especially in cases of congestive cardiomyopathy - (cardio = heart; myo = muscle; pathy = disease) commonly referred to as congestive heart failure. In failing hearts, digitalis offers three potential therapeutic actions:

Chronotropic (Heart Rate Effects)

Trough **Chronotropic (Heart Rate) effects**, the heart rate is slowed so the diastolic period (the time between actual muscular contractions [the systolic period]) is longer. It is during the diastolic period that the heart chambers are filled with blood, ready for the next beat. But just as important, this is the time when the heart relaxes and receives its own nourishment. If the heart rate is too fast, the diastolic cardiac nourishment period is too short. This makes the heart less efficient in pumping and circulating blood.

Dromotropic (Speed Of Conduction Of The Electrical Impulses Through The Heart)

Through the **Dromotropic effect**, the electrical impulses are slowed. The heart's electrical impulses permit the atria (top chambers) to beat first, which fills the ventricles with blood, followed by contraction of the ventricles which distributes blood to the body, (The right ventricle pumps blood to the lungs while the left ventricle pumps blood to the rest of the body.) Digitalis somewhat slows the conduction velocity through the heart's electrical system, thus increasing its efficiency and allowing it to work better with less effort.

Inotropic (Force Of Heart Contraction)

Through the **Inotropic effect**, the force of the heart contraction is increased. With increased strength in the heart's contraction, the cardiac output (amount of blood ejected from the right and left ventricles during a single beat) is increased, thus giving the body a better supply of fresh blood... improving circulation and stamina.

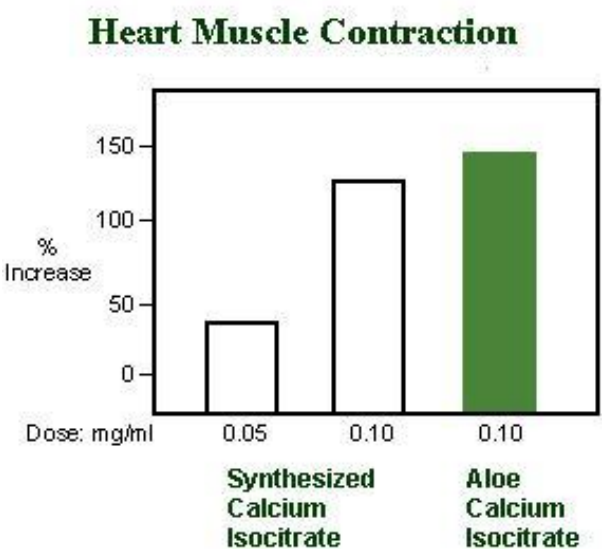
You may be wondering at this point: *Why are we talking about digitalis?* Is there digitalis in Aloe juice or extract? The answer, of course, is No. However, the Aloe extract does contain a mineral called calcium isocitrate which is capable of mimicking the positive inotropic action of digitalis, as demonstrated in the isolated cardiac tissues of animals. Indeed, some Japanese researchers isolated this mineral from Aloe saponaria. Recently, it has been shown that this mineral is also found in Aloe aborescens and Aloe barbadensis, but the amount varies among the species.

Initially, investigators made some rather crude preparations, which, when tested in isolated rabbit atria (top heart chambers, as explained above), showed a remarkable increase in the force of the contraction (positive inotropic action). (The reason researchers use isolated portions of heart tissue in such studies is to avoid any effects of the nervous system and/or circulating, hormones which, might act with the

material being tested and make the results invalid.)

With further study and refinement of the material, the researchers were able to identify the active material in their success in producing the inotropic action with Aloe components. The active material was shown to be the mineral salt, calcium isocitrate, which had increased the force of contractions in isolated atria tissue from guinea pigs.

To confirm their findings, the researchers synthesized the calcium isocitrate and tested its activity using the same types of isolated heart tissue.



The results, as the graph shows, duplicated those produced with the material extracted from Aloe juice. Interestingly, other salts from the Aloe juice also showed positive inotropic activity.

Studies have also shown that calcium citrate, a salt advocated for the treatment of osteoporosis (a condition found in older women which causes bones to lose calcium and become weak and brittle), is well absorbed by the human gastrointestinal tract. Some researchers believe that the human body absorbs the calcium isocitrates just as well as it does the calcium citrate. However, no data from studies in human subjects, are available to confirm this belief.

The presence of this beneficial compound is no surprise to Aloe researchers. All of these salts are insoluble in alcohol and thus, would be expected to be found in the polysaccharide Aloe fractions precipitated with alcohol in the laboratory.

Reference

Yagi A; Shibata S; Nishioka I; et al: Cardiac Stimulant Action of Constituents of Aloe saponaria. *J Pharm Sci* 71:739-741, 1982.

Polysaccharide – The Magic Bullet

By: Robert H. Davis, Ph.D.

The Aloe leaf has polysaccharide in the parenchymal cells which is used by the plant for energy. Mucilage is a different storage form. All polysaccharides are not the same. When mucilage is placed over a wound, the wound remains moist and does not drop as does dry wounds. Epidermal and fibroblast growth factors come from the mucilage and stimulate the fibroblast directly for growth and repair. The cells as a result migrate within the wound in a proper manner to increase wound healing. The occlusive nature (cover) of mucilage increases wound healing from a mechanical and endocrine viewpoint. Mucilage is also a good anti-inflammatory agent. Some polysaccharides are immune stimulatory and this immune property improves wound healing probably through the macrophage. The big polysaccharides appear to be immune stimulatory whereas the smaller ones have anti-inflammatory activity. When an animal bites into the Aloe leaf, a hole is made in the leaf so that there is opportunity for the gel fillet to leak to the outside. However, this does not occur. The mucilage in combination with the Aloe gel hardens which seals the hole. Mucilage always hardens and acts as a container for the inner gel fillet. The transformation which occurs here is a sol-gel transformation of mucilage. Aloe vera tends to improve the penetration of water whereas mucilage tends to block the escape of water from a wound. We have been able to transfer the sol-gel transformation of mucilage and Aloe to an animal wound in which it improves an incisional wound some 130%. If Aloe and mucilage are placed between two sticks, it takes some 1200 gms of force to pull the sticks apart. Wound healing does not just require immune stimulation by polysaccharides but Aloes healing comes from growth factors, amino acids, glycoproteins, gibberellin, auxin and minerals such as zinc as well as polysaccharides. These biologically active agents synergize to give us the miracle of Aloe vera. Polysaccharide is not a magic bullet in that these other biological agents make major contributions to the biological activity of Aloe vera.

In the making of Aloe vera, two major processing procedures are used by the Aloe industry to give us Aloe vera. The fillet method removes the rind by a mechanical means and the fillet is washed. The whole leaf method grinds up the whole leaf and removes the rind by filter. The anthraquinones are removed by charcoal. The amount of aloin left is less than 5 parts per million. This amount is not detectable by the deification reflex. When the Aloe vera is freeze dried for both the fillet and whole leaf methods and the powders are stored on the shelf for eight years, no difference was recorded in biological activity. Both

methods yield the expected activity that was recorded in the beginning. Processing of Aloe vera is supposed to breakdown the polysaccharide polymer (depolymerase enzyme) into fragments that have little or no activity. This may or may not be true as we have not seen the evidence. However, if it is true in Aloe vera, to assume that the smaller polymers resulting from enzyme breakdown of the polysaccharide do not have biological activity is a presumption. In fact, there are a number of small ploymers that have great biological activity and are immune stimulators which are being sold successfully on the open market. The breakdown of the polysaccharide in Aloe by enzymes must be presented and the resulting polymers must be evaluated across the board for biological activities using the original Aloe vera as the control test substance. In all the work that has been done with the polysaccharide, we have never seen Aloe vera as the test control to which the polysaccharide is compared. These things must be done before we claim that the various polysaccharides are the magic bullets. Are they much more potent than the mother Aloe vera from which they were extracted? This must be shown by peer review.

Aloe vera contains a large polysaccharide molecule which we have called the conductor. This molecule leads the many biologically active substances into a symphony of biological events to heal wounds, reduce inflammation and eliminate pain. The conductor molecule fits into the fibroblasts, similar to a lock and a key mechanism so as to set up a cascade of important biological events, supported by Aloe substances which are part of the orchestra. The polarity of water is needed for the polysaccharide to communicate with the active substances to synergistically achieve the maximum desired benefits. We opposed the theory that there is only one active molecule (a polysaccharide) responsible for all its beneficial effect. We are convinced that all the biologically active substances in Aloe are necessary to achieve the maximum-end-benefit. Only Aloe can attach the entire spectrum of human conditions because specific synergisms are brought into sharper focus. We have observed that if the polysaccharide from Aloe is washed extremely well – that is to remove all agents from it, the polysaccharide has very little biological activity. In fact, what is called polysaccharide is a polysaccharide with active orchestra members attached to it giving it biological activity along the lines we have discussed. If the polysaccharide is prepared in different ways, some activities may be lost and others remain. The “magic bullet” apparently requires a communication with orchestra agents to have its best influence.

Aloe vera is a biological vehicle in that it acts as a physical or physiological carrier for active biological agents but, also adds biological activity to the test agent no matter what the pharmacologic agent under consideration is. In effect, it is a physical carriage plus added Aloe vera activity. This is the orchestra of active substances surrounding the polysaccharide conductor. Thus the Aloe vera can add to the biological activity of most test substances. Substances can by synergized and put into Aloe for a biological vehicle effect. Can the conductor (the polysaccharide) do this most important biological vehicle effect by itself without the surrounding orchestra agents? I think not. It needs the rest of the team. If it can, it needs to be published as data under peer review and not just a “commercial blurb” put out to stir up controversy. Aloe

vera contains water soluble compounds such as amino acids, enzymes and carbohydrates as well as oil soluble compounds such as vitamins, sterols and anthraquinones. Possibly, pharmacologic agents of both solubility's can be placed in Aloe and carried through the skin to blood vessels. In an indirect way, the biological agents in Aloe can help the conductor (the polysaccharide) produce the biological response at the cell receptor. To suggest that the polysaccharide works alone is presumptive and it is unwise to call it the magic bullet. The polysaccharide has biological activity but not of the order obtained by synergizing with the surrounding biological compounds.

Aloe vera has been called a modulator in that it brings biological systems into balance. Using the Gowda 50% ethanol extraction procedure on Aloe vera, we found that 78% of the anti-inflammatory activity was present in the supernatant. The wound healing activity was present in the precipitate with the polysaccharide and other precipitated agents. Nevertheless, in the supernatant most of the anti inflammatory activity was present in the supernatant without the presence of the polysaccharide. Some of the wound healing orchestra compounds were precipitated with the polysaccharide to help with the wound healing activity. The carrageenan-inflamed synovial pouch response to Aloe vera confirms our biological results based on the Gowda experiment. The fibroblast stimulation activity of Aloe vera recorded in wound healing was clearly observed. The fibroblast response in the air pouch was not a chronic inflammation but rather a growth-repair response. Aloe stimulates the fibroblast directly to increase wound tensile strength. It stimulates glucosamine to form collagen and proteoglycan but zinc and vitamin C must be present. Mast cells of animals treated with carrageenan were found in connective tissue and pouch fluid. They were particularly increased in the inner being of the air pouch as a result of the inflammation. Aloe vera reduced the inflammation and the pouch was vascularity but at the same time Aloe vera increased the pouch wall weight. This increase in air pouch punch biopsy weight by Aloe represents a healing and repair response. Aloe stimulates directly growth and repair by directly stimulating fibroblasts. Aloe vera has no anti-fibrosis effect but stimulates the fibroblast for growth and repair as seen in wound healing. Both of these studies clearly demonstrate that Aloe vera inhibits inflammation and stimulates wound healing at the same time which is the miracle of Aloe. We have not seen data to show that the magic bullet (the polysaccharide) can do this. In fact, this wonderful dual biological characteristic appears to be exclusive for Aloe vera.

The polysaccharide is an immune stimulator which increases the immune response to an antigen. La Badie has shown that Aloe vera can act as an adjuvant to enhance the immune response to an antigen. He found that there are two functionally and chemically distinct immunomodulatory compounds in the gel of Aloe vera. One fraction could enhance antibody formation and another could inhibit antibody formation such that La Badie called Aloe vera an immune modulator. Davis and La Badie showed that the Aloe vera can inhibit and stimulate phagocytosis as well as "mop up" oxygen radicals. Aloe vera acts as an immune stimulator on wound healing and an immune inhibitor on inflammation. Aloe vera can prevent and regress

the autoimmune condition of adjuvant inducted arthritis. This condition involves both antibody and cellular immunity. Aloe vera can inhibit the infiltration of polymorphonuclear leukocytes into a site of irritiation. This represents a block on leukotrienes. Under-nourished individuals have impaired immune responses which may be co-factors in the immunodeficient virus infection. This makes people more susceptible to viral infection. The many nutritional components in Aloe vera may help the infected individual fight off a disease as a co-factor as well as play a role in regulating the immune system (cell mediated immunity). No single component such as the polysaccharide can do the complete job. A treatment of many compounds as seen in Aloe vera would seem to be more beneficial for a multi-factorial syndrome. The global AIDS problem may be out of control because there is no treatment. If the polysaccharide can contribute in this area, possibly, Aloe vera can even make a better contribution because it is multifaceted. Aloe vera has 200 biologically active agents as well as polysaccharide to act as a biological vehicle and a treatment possibility.

Yagi presented data on the isolation of a glycoprotein (Aloe glycoprotein) which has bradykinindegrading activity and a proteolytic activity against bradykinin. The Aloe glycoprotein has hemagglutinating and cytoagglutinating activity. It has mitogenic activity for lymphocytes. This glycoprotein is called Aloctin A. This glycoprotein has strong anti-tumor activity whose activity varies with the dose at microgram amounts. Aloctin A is non toxic and at very small doses causes complete regression of tumors. Like the polysaccharide, the glycoportein appears to have an anti-tumor effect based on cell division and immune system response. Thus, the polysaccharide is not the only magic bullet, glycoprotein is another one. In fact, Aloe vera has many magic bullets such as gibberellin, auxin, sterols and chromones to mention a few. All of these compounds are found around the polysaccharide in the orchestra.

The penetration of topical agents through the skin may be influenced by the drug, the vehicle and the skin. Little attention has been given to the influence of Aloe vera and mucilage on the penetration through the skin. The stratum corneum acts as a barrier to drug penetration through the skin but also acts as a reservoir for molecules when a drug is applied on the skin. When hydrocortisone is applied to the skin, 99% fails to penetrate the skin stratum corneum and is wasted. Placing hydrocortisone in Aloe vera enhances the penetration and adds to the biological activity of hydrocortisone. Aloe vera increases the penetration of skin by water hydration, occlusiveness and by increasing compound solubility. Aloe vera increases the penetration through the skin whereas the polysaccharide mucilage acts as an occlusive seal forming a firm cover to keep moisture in the skin. Aloe can aid water soluble and insoluble compounds as a biological carrier so that it can be a good carrier for all kinds of drugs as well as contributing Aloe activity to the drug it carries. Can Aloe polysaccharides alone aid in skin penetration and add its biological activity to an agent it carries? We think it can not by itself. It needs the orchestra environment of biologically active

compounds to complete the task. The properties of a large polysaccharide are completely different from those of a small polysaccharide. What is said of the smaller one cannot be attributed to the larger one. In any event, we need to see the data to prove that the magic bullet – the polysaccharide – can act in a fashion similar to Aloe vera. The FDA must see the data recorded in commercial blurbs" backing up all the claims made by people who say "If you don't have our polysaccharide, you don't have active Aloe vera." This is not true based on scientific evidence. These claims are false and are made by people motivated by money and not by evidence.

Gibberellin is a growth factor found in Aloe plants that has anti-inflammatory and wound healing activity in laboratory animals. It does this in normal and diabetic animals. Gibberellin's wound healing activity is related to its ability to stimulate protein synthesis as well as the RNA-DNA cellular systems. It stimulates wound healing (open and incisional wounds) in a dose-response manner. Aloe vera and gibberellin can stimulate fibroblasts directly to form collagen and proteoglycans for wound healing. We also feel that Aloe vera (or gibberellin) can stimulate or modulate the macrophage to produce the traditional growth factors which stimulate fibroblasts. It appears that Aloe vera or gibberellin can do the same thing as proposed by the polysaccharide. Because of the contribution of other agents, they probably do a better job on open and incisional wounds. However, studies need to be designed to show this. Aloe vera and gibberellin are anti-inflammatory even in the diabetic. They improve wound healing, reduce edema and pain. Aloe vera has an additive "vehicle effect" with gibberellin on wound tensile strength. Gibberellin blocks hydrocortisone's inhibition on wound healing similar to Aloe vera.

Hydrocortisone inhibits wound healing by blocking the formation of connective tissue. This increases the spread of infection. Aloe vera and gibberellin counteracts these detrimental effects of steriods. Gibberellin and Aloe vera block the steriod inhibition on wound tensile strength. Aloe vera contains three sterols that have good anti-inflammatory activity. They exhibit anti-inflammation in a dose-response fashion and may be a major contributor to the anti–inflammation in Aloe. Aloe vera blocks a wide variety of irritants that act by different biochemical pathways. However, it has no chronic anti-inflammatory activity because it stimulates the fibroblast for wound healing. However, we wonder if it aids the hydrocortisone's chronic anti-inflammatory activity since Aloe vera prevents and regresses adjuvant induced arthritis. Aloe vera acts as a biological vehicle for aspirin and it synergizes with its analgesic and anti-inflammatory activity.

Summarizing the main effects of Aloe vera, we must conclude that gibberellin, sterols, chromones, aspirin like compounds and auxins are magic bullets in Aloe vera. Mucilage improves wound healing. Glycoprotein is anabolic and produces both anti-cancer effects and immune system responses that are anti-tumor. Both of these must be considered magic bullets as well as the polysaccharide found in the parenchyma cells of the Aloe leaf. Is it wise to precipitate the polysaccharide with alcohol and throw out

all these wonderful biological agents? Is it wise to say that only the polysaccharide is worthwhile when you are aware of this data? I think not. It is exceptable to isolate the various compounds and evaluate them by themselves. However, do not run down Aloe vera from which they came. The data presented here refutes the concept that “If Aloe vera doesn’t have a certain polysaccharide, it’s not Aloe vera.” It rejects the concept that only the polysaccharide is active and important in Aloe vera.

The Conductor - Orchestra Concept Of Aloe Vera

By Robert H. Davis, Ph.D.

The Model For Aloe Vera

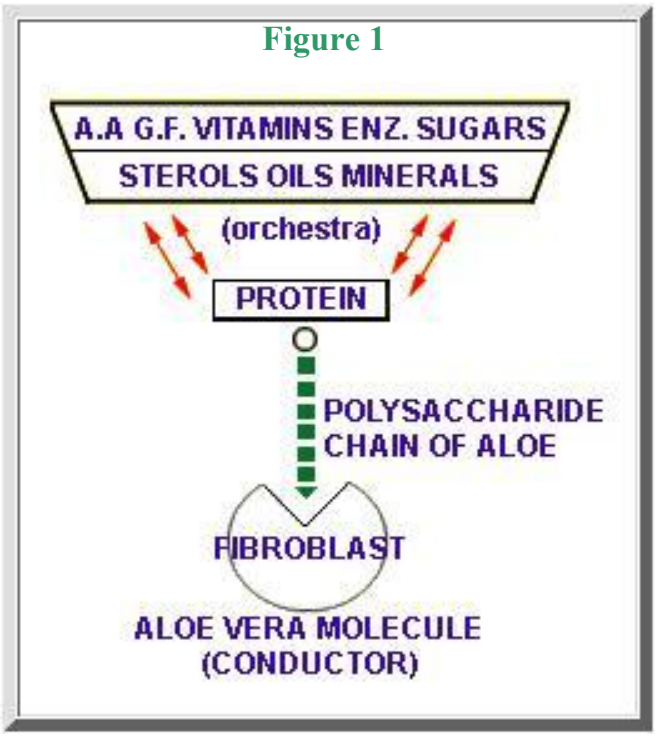
The modern symphony orchestra combines instruments from strings, woodwinds, brass and percussion to form an ensemble capable of beautiful musical expressions. Each of these musical arrangements uniquely blends the sound of various instruments into one given tone. As an orchestra tunes up, each instrument creates its own distinctive musical notes. Out of this chaos comes the miracle of Mozart and the wonder of Beethoven.

One key element of the orchestra is the conductor. An outstanding conductor develops an orchestra by a combining many aspects of musical training. His role is to understand the potential contribution of each instrument and provide the leadership needed to create a synergy of sounds. Although his position is important, the talented orchestra players are the essential elements that must work together to produce the magic of a musical symphony.

How Aloe Vera Mimics The Orchestra

"The Conductor-Orchestra concept" was developed to better define the relationships that exist among over 200 biologically active compounds within Aloe vera *(Figure 1)*. One of these molecules, a polysaccharide, acts as the conductor that leads a symphony composed of these 200+ biologically active compounds. The polysaccharide molecule consists of mannose molecules joined by beta I-4 linkages to form a chain. As the conductor, the polysaccharide modulates the biological activity between surrounding orchestra molecules to work synergistically.

Figure 1



This conductor-orchestra relationship creates an infinite array of biological activities. The protein at one end of the polysaccharide helps direct the mannose phosphate at the other end into the insulin-like growth factor receptor. As part of the fibroblast, it produces collagen and proteoglycans to improve wound healing. The Aloe vera molecule can also stimulate macrophages to produce a variety of important biologically active substances. And it can recognize the receptors on other cell surfaces as well as recognize the individual players within the orchestra. In addition, the biological compounds indirectly help the conductor produce the biological response occurring at the cell receptor. Altogether, the Aloe vera molecule leads an orchestra of compounds working to produce a symphony of therapeutic effects. To suggest that the conductor - the

polysaccharide - works alone in this complex array of activity is presumptive. Although there's knowledge to gain from the isolation of biological compounds and activities. It seems unwise to search for a "magic bullet."

What Is The Role Of Water In The Aloe Vera Relationship

The important question remains unanswered - How does the polysaccharide (the conductor) communicate and relate to the 200 biologically active compounds in the orchestra? Aloe is 99.5% water and 0.5% solids. The water is removed by tyophilization but must be added again to recover the biological activities of Aloe vera. Water, although a rather commonplace compound, is necessary for the activity of life. Water is not just a solvent for organic molecules such as polysaccharides, but it plays a major role in the relationship between the polysaccharide and the 200 active compounds in Aloe. The interaction between the conductor and the orchestra arises from water's polarity. The water molecules in Aloe vera have large oxygen atoms that draw electrons from two hydrogen atoms, giving water a positive and negative charge at either end of the molecule. This polarity enables water to dissolve active agents and to mold complex molecules. The orchestra molecules as well as the conductor polysaccharide possess both polar and non-polar parts. The polar parts react well with water whereas the non-polar or hydrophobic parts avoid water. The polarity of water molecules aligns their negative ends with the positive ends of other molecules. A chain of these polarized water molecules act to connect the conductor polysaccharide with the orchestra molecules in Aloe vera. This allows the conductor to communicate with the 200 orchestra compounds such as amino acids, vitamins and sterols. Information is given to the conductor in a similar way to influence the polysaccharides control over the orchestra.

Standardization: The Aloe Vera Unit

The conductor-orchestra theory has been adopted by key Aloe vera suppliers and new manufacturing standards are being developed around this theory. A standardized "unit" of Aloe vera should be established by the industry that samples a predetermined amount of product for testing. This Aloe unit can then be tested and deliver a measurable biological-chemical response. Other approaches to determine the activity of Aloe vera, such as selectively testing only one, single component of this complex molecule, is unwarranted and unscientific based on our current knowledge. Clearly, a "magic bullet" approach is not valid. Science has proven that Aloe vera, in its natural composition, keeps the body in a healthy physiological state. This does not mean that the study and fractionation of Aloe vera is unimportant. Individual active components such as the polysaccharide may prove very exciting for specific applications. However, the study of Aloe vera and its complete compliment of components is necessary to fully understand the potential of Aloe vera.

The Yin Yang Theory And Aloe

The Yin Yang theory is used in eastern culture to indicate the active and passive principles that bring balance to the universe. These two forces interact to bring all things into existence. In a similar manner, Aloe vera moderates the balance of its own biological systems. Aloe vera has an inhibitory system that blocks pain and inflammation as well as a stimulatory system that improves growth and wound healing. Also, independent laboratory testing of Aloe vera fractions has shown their activity to include modulation of antibodies and cellular immunity. One example of the normalizing influence of Aloe vera is its

inhibition of the auto-immune condition demonstrated in adjuvant arthritis. Overall, the beneficial effects of Aloe vera often result because two components act in such a way (Yin Yang) to normalize the balance of activity.

A Receptor For Aloe Vera

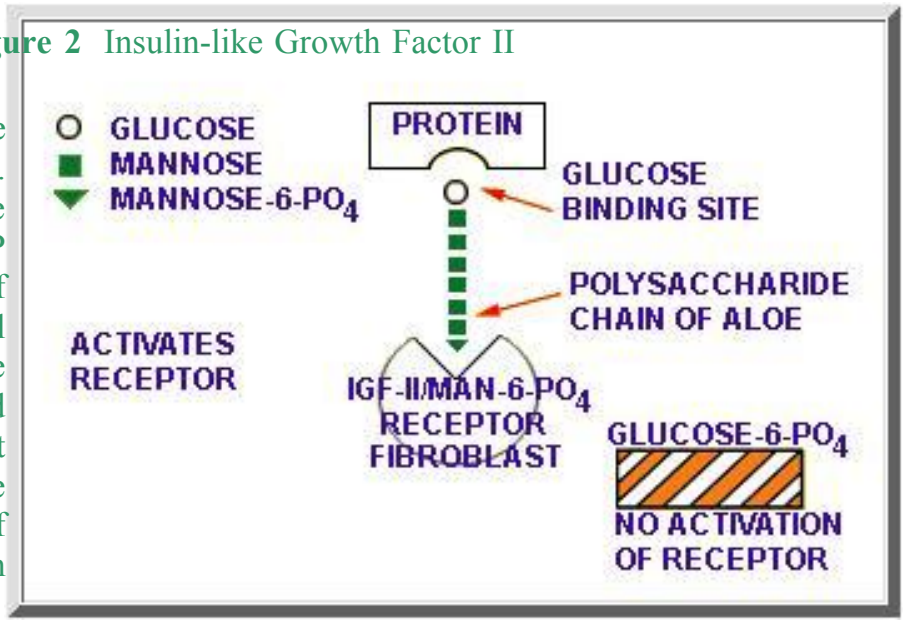


Figure 2 Insulin-like Growth Factor II

It has been well established that the (IGF-II) and mannose-6-phosphate (M-6-P) bind to the same receptor on the fibroblast *(Figure 2)*. These two ligands bind at separate binding sites within the IGF-II/M-6-P receptor. However, the exact effect of these ligands binding to their individual binding sites is still unclear. One possible theory is that the binding of either ligand is capable of activating fibroblast proliferation. This would indicate that free M-6-P is a growth substance capable of yielding the same response as IGF-II. In Aloe, M-6-P is located at the end of the polysaccharide chain that fits into the receptor. This may be important in understanding how Aloe heals wounds and inhibits inflammation. It has been demonstrated that M-6-P improves wound healing in a straight line, dose-response fashion when compared with controls. For example, Glucose-6-phosphate, when used as a control, does not activate the receptor in the fibroblast. The binding site for this glucose is at the other end of the polysaccharide chain of Aloe and is probably a weak to moderate covalent bond. Lack of response by this control indicates that M-6-P is specific to the receptor. This may be important in understanding how Aloe heals wounds and inhibits inflammation.

The receptor dynamics are part of the overall Aloe vera conductor-orchestra theory. One exciting characteristic of this theory is that the conductor-orchestra unit has little or no toxicity at very high gm/kg doses. Most of us working with Aloe vera have recorded no toxicity. In fact, we feel that Aloe vera can modulate, reduce and may even eliminate toxicity of other biological agents.

Mechanism Of Action Of Aloe Vera: Wound Healing

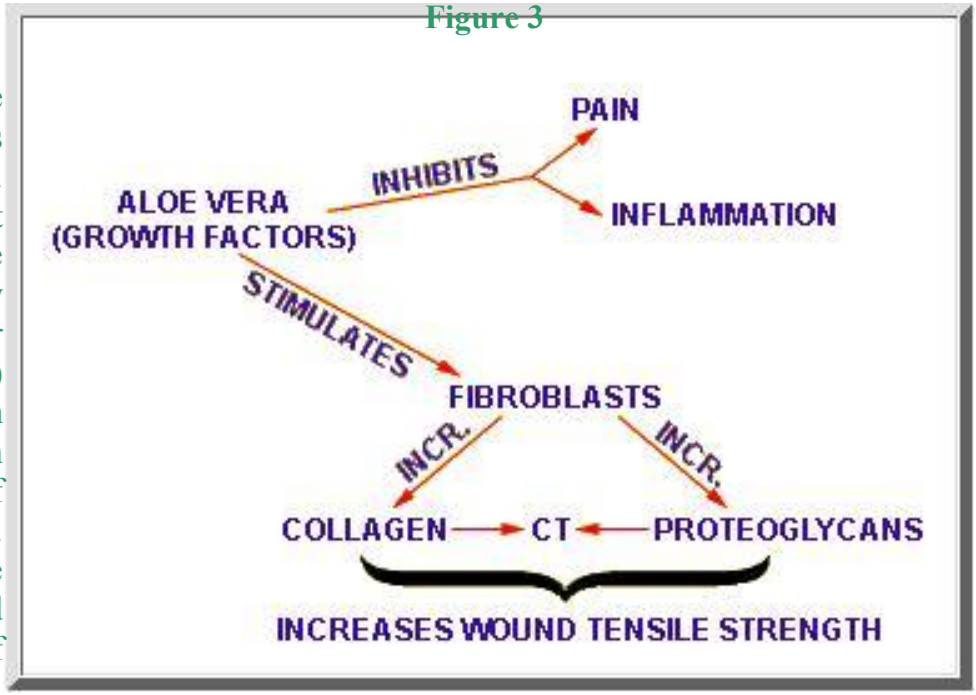
The concept that the Aloe vera molecule synergizes with plant growth factors to repair and produce growth, broadly portrays the activity of Aloe vera *(Figure 3)*. Three characteristics of growth factor activity in Aloe are:

1. **Inhibition of pain & inflammation**
2. **Stimulation of fibroblasts to functionally produce collagen & proteoglycans**
3. **Increased wound tensile strength**

The mechanism of Aloe's inhibition of pain and inflammation will be detailed in the next section, first we must understand how Aloe vera enhances wound healing.

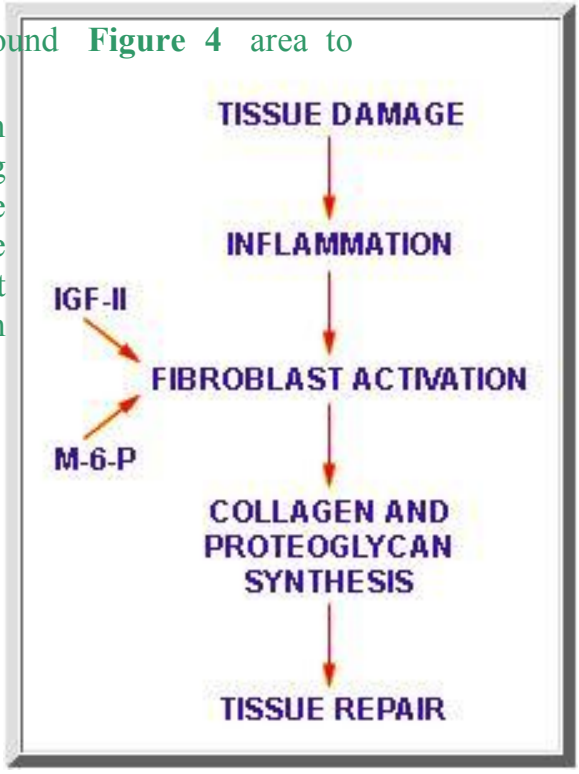
During the healing process, Aloe vera's stimulation of the fibroblast produces and adds new collagen to tissue. However, we should note that macrophages can also secrete substances that can similarly stimulate fibroblasts. Whether the effect is direct (from Aloe) or indirect (from microphages), new collagen forms between the margins of wounds when Aloe is present. These collagen bonds are responsible for increased tensile strength. Therefore, if the tensile strength increases, it is assumed the collagen productions is increased by Aloe. This is a different approach than the Danhof response of Aloe based on the uptake of tritiated thymidine, which only represents an increase in fibroblasts number. Whereas, we are demonstrating a functional increase in collagen and proteoglycans through wound tensile-strength.

Figure 3



When skin is injured, fibroblasts migrate into the wound area to proliferate and produce collagen as well as proteoglycans. Proteoglycans form the ground substance in which collagen fibers embed. This represents a remodeling of connective tissue. Cells in the wound area communicate with each other by growth factors. Growth factors in Aloe are attracted to the wound area and bind to the fibroblast IGF receptor to produce collagen and proteoglycans which increase the tensile strength *(Figure 4)*.

Figure 4



Connective tissue is mainly composed of collagen, which makes up one third of our body protein. Also, connective tissue contains large complex chains of modified sugars that form the framework for collagen. These modified sugars hold water and give connective tissue flexibility and resistance. In wound healing, collagen and proteoglycans repair and remodel this connective tissue. To produce collagen for repair, glucose from the diet is stimulated by Aloe vera and forms glucosamine within the fibroblast. Then, in the presence of zinc and vitamin C, glucosamine forms procollagen. In addition, procollagen can be formed directly from external amino acids. Next, Aloe pushes the fibroblast to convert the secreted procollagen to collagen. The glucosamine and procollagen form the "core protein" as a frame for connective tissue. Also, they form hyaluronic acid as a frame for "link" proteins are essential components for connective tissue. In addition, this connective tissue can double and triple if the necessary sugars and amino acids are stimulated by Aloe vera in the fibroblast.

This activity demonstrates how wound healing is enhanced when connective tissue, subjected to mechanical forces and damages, repair themselves by the Aloe-fibroblast stimulating influence to make collagen and proteoglycans. Aloe vera acts as a mechanism to promote the active biological agents that heal damaged tissue.

Aloe Vera And Inflammation

Inflammation is the response of living tissue to a damaging stimulus. It is a defense mechanism against a traumatic insult. On a molecular basis, the inflammatory process involves complex regulators, potentiators and mediators. A uniform response occurs regardless of the nature of the irritant event, though the inflammatory process may act as a double edge sword by also creating a threat to an organism. Inflammation by be acute or chronic. The acute inflammation response to a tissue insult involves the release of vasoactive substances. This increases the permeability of capillaries so that fluid goes into interstitial tissue and produces edema. Then, polymorphonuclear leukocytes (PMN's) move out of the capillaries and are attracted to the injury site by a mediator called leukotrienes. The PMN's increase their metabolism and oxygen consumption as they phagocytize the trauma debris. However, the products resulting from this increased metabolism contain oxygen radicals that attack the membrane lipids and produce further inflammation. If the irritant remains under the skin, chronic inflammatory response occurs. Connective tissue forms around the irritant and, over a long period of time, attempts to push the trauma outside the body. Lysozymes, products of these inflammatory cells, function in a manner to modulate neutrophil (PMN) activity.

Topical steroids are usually applied to block acute and chronic inflammation but their properties also retard wound healing. They decrease edema by reducing capillary permeability, vasodilation and stabilizing lysosomal membranes. Steroids can actually increase the spread of infection by inhibiting connective tissue formation.

Aloe vera is also used to inhibit acute inflammation. But, unlike steroids, it stimulates fibroblast growth to improve wound healing and block the spread of infection. This is the miracle of Aloe.

Studies have shown that since only about 1% of steroids can penetrate the stratum corneum of the skin, 99% is unavailable and wasted. Our data has shown that Aloe vera can act as a vehicle for steroids - to improve absorption and act as an efficient carrier. This is a significant economic consideration for Aloe vera.

The complexity of Aloe vera's components makes the study of its anti-inflammatory activity a difficult task. Aloe vera does not have a single mechanism of action. Aloe vera contains amino acids such as phenylalanine and tryptophane that have anti-inflammatory activity. The salicyclic acid in Aloe prevents the biosynthesis of prostaglandins from arachidonic acid. This explains, in part, how Aloe reduces vasodilation and decreases the vascular effects of histamine, serotonin and other mediators of inflammation. Since prostaglandins play an integral role in regulating both inflammation and immune reactions, Aloe vera can affect both of these systems by blocking prostaglandin synthesis. The analgesic effect of Aloe vera is synergistic with aspirin. Since Aloe vera has both stimulatory and inhibitory components. Aloe can modulate both immune and inflammatory reactions. It can act as a stimulator of wound healing and antibody production. Aloe

can block prostaglandin and modulate the production of lymphocytes and macrophage derived mediators (lymphokinins) including interleukins and interferons.

Besides Aloe's effects on inflammatory and immune reactions, it also acts as a scavenger of free oxygen radicals produced by PMN's. The vitamin C in Aloe that inhibits inflammation picks up oxygen radicals to block the inflammatory process. Vitamin E, a known antioxidant, is also a component of Aloe vera. These biological effects of the orchestra work in collaboration with the conductor (polysaccharide) to produce these valuable therapeutic effects.

Aloe Vera Is A Biological Vehicle

Compounds that are poorly absorbed through the stratum corneum of the skin need a vehicle to aid them in penetration. Glucocorticoids and vitamin C are not absorbed well and, as a result, most of the material is wasted when applied topically. A vehicle must be found that solubilizes steroids and Vitamin C while at the same time hydrates the stratum corneum. As previously mentioned. Aloe vera's anti-inflammatory, wound healing and analgesic properties make Aloe a "biological vehicle" that helps to nullify the detrimental activity of glucocorticoids but at the same time aids the penetration. Similarly, vitamin C is not readily absorbed by the tissue. However, vitamin C has been shown to help in the synthesis of collagen, since it may counterbalance the collagen breakdown to reduce the development of autoantibodies. In certain diseases, such as rheumatoid arthritis, the levels of vitamin C are low. Our data, thus far, suggests that Aloe vera aids in the absorption of vitamin C and adds to its biological activity. Although all the factors that control the absorption of vitamin C are not know, previous studies show esterifying ascorbic acid increases the availability to tissues so that the therapeutic dose can be reduced. In a similar manner, Aloe vera's activity as a biological vehicle to increase the absorption of vitamin C may be just as possible.

Aloe vera can solubilize water soluble compounds as well as lipid soluble substances. Also, it can hydrate the stratum corneum cell membranes to aid a range of materials in penetrating the skin. The biological activity of Aloe can add and even synergize with many agents in producing therapeutic effects so that we call Aloe vera a "biological vehicle."

Summary

Aloe vera contains polysaccharides that act as a conductor to direct biological activities among an orchestra of various molecules. Many agents within Aloe have been isolated, identified and demonstrated to synergize with one another over a large biological spectrum. A standard preparation of Aloe vera with a well-defined unit for each biological activity is necessary for future research. The conductor-orchestra theory opposes the idea that suggests that one molecule in Aloe (a polysaccharide) is responsible for the beneficial effects and that the standardization should be based on that polysaccharide. A greater understanding between the conductor and orchestra is needed to better define how Aloe vera synergizes its many activities. This understanding will change many pharmacologic concepts in the future. The conductor-orchestra concept will be practiced as the central format by which the Aloe industry will operate.

Biological Activity Of Aloe Vera

By Robert H. Davis, Ph.D.

An examination of the biological activity of steroids and synthetics revealed that they are both active yet toxic. In the search for natural substances, such as vitamins and amino acids, that have biological activity, we serendipitously discovered that **Aloe vera had many biologically active compounds that had anti-inflammatory, wound healing, analgesic and anti-arthritic activity**.

Ingredients In Aloe Vera Gel

Mannose and glucose are the most significant sugars found in the Aloe vera gel, and they can be used to assay the activity of Aloe vera. The gel contains important sterols which can have anti-inflammatory activity. Amino acids such as tryptophane and phenylaianine reduce inflammation. Studies have shown that vitamin C & B complex can maintain adrenalectomized animals, and that minerals such as zinc are very important in wound healing. Anthraquinones have good anti-inflammatory activity, but their activity is usually obtained by working through an inflammation pattern. Salicylic acid and aspirin are also highly biologically active.

The Aloe Leaf

The rind is the manufacturing plant for carbohydrates, fats, proteins and vitamins. These Aloe vera constituents are transported throughout the leaf by the phloem, and other materials are brought up from the roots by way of the xylem. These two mechanisms aid in transporting the Aloe vera under the influence of the wind. Mucilage was once thought to take part in this transport process, but researchers now feel that it acts as a container for the gel fillet or the storage of Aloe vera.

If one takes the liquid mucilage and freeze dries it, one finds that the mucilage looks and acts like a bandage. It has occlusive “coverlike” properties as well as biological activity. The topical anti-inflammatory activity of mucilage at the 1% dosage is 3.8% in decreasing edema, whereas at the 5% dose level, it is 33.7%.

A consideration of the sol-gel transformation becomes very evident as an animal bites the Aloe leaf. The sol which is a colloidal system under the influence of many factors can be converted into a colloidal gel. If this system could be transported to the human wound, one would have an excellent topical wound healing treatment.

In the Aloe leaf synthesis, carbon dioxide and water are converted to an “active carbon that is used to make carbohydrates, lipids, protein and vitamins. The Aloe vera cell, visible at a magnification of about 40,000, is surrounded by a cell wall, has a large nucleus and two cell membranes the cytoplasm of which manufacturers mucopolysaccharide. The mucopolysaccharide is stored within the lumen of the cell.

Biological Activity of Aloe Vera

Aloe vera could prevent adjuvant arthritis 72%, and cause a regression of 22 to 26% at a dosage of 150 mg/kg per day. In another experiment, we proved that Aloe vera was effective in reducing inflammation over a broad spectrum of irritants in experimental animals. The percent inhibition by Aloe vera ranged from 76.9% against gelatin to 22.7% against dextran. In evaluating vitamin C's influence on localized adjuvant arthritis, we found that it could reduce edema 80%, inhibit PMN infiltration, and decrease the pain induced by the adjuvant arthritis. However, there was no influence on the paw temperature. Anthranilic acid, a metabolite of tryptophane, could inhibit PMN infiltration as was evident in the peritoneal fluid of adjuvant arthritic rats.

The topical treatment of adjuvant arthritis with combined Aloe, RNA and vitamin C produced a 25.2% prevention inhibition and 45.1% regression inhibition at a dosage of 1.5% concentration of each.

Phenylaianine synergized with hydrocortisone acetate in reducing localized edema. We also obtained a good vehicle response on anti-inflammatory activity using Aloe vera for hydrocortisone acetate. The combination of Aloe vera and hydrocortisone was definitely additive in nature. We observed the vehicle effect of Aloe vera for hydrocortisone acetate on inhibiting the infiltration of PMN's as well as the topical application of the steroid.

Aloe vera is also a good vehicle for vitamin C and other important agents. Tryptophane and phenylalanine had good local anti-inflammatory activity in inhibiting PMN infiltration. In fact, the inhibition effect approaches that of the steroid. While phenylalanine was able to inhibit granuioma tissue weight in adrenalectomized Tanimals synergistically with cortisone, tryptophane did not synergize with the steroid.

When we placed a cotton pellet under the skin of a rat we found that Aloe vera was unable to inhibit the growth of granuloma tissue. Aloe vera had no antifibrosis effect over a dosage range of 50 to 400 mg/kg administered for 12 days.

While Aloe vera had no chronic anti-inflammatory influence, we wondered if it could inhibit the detrimental effects of the steroid on wound healing. Aloe vera could inhibit edema in diabetic animals in a dose-response fashion up to 80% over a dosage range from 10 to 100 mg/kg.

A similar response was obtained in diabetic animals by Aloe vera in inhibiting the infiltration of PMN'S. Aloe vera definitely can block the vasoactive substances responsible for inflammation, can constrict small blood vessels, can block PMN filtration, as well as inhibit production of oxygen radicals.

We evaluated the influence of mucilage in Aloe vera on skin penetration of 5% trypan blue over six hours. We found that Aloe vera at a 10% dose could increase the trypan blue penetration 24%. However, 10% mucilage was occlusive, that is it acts as a cover for wounds and blocks the penetration of trypan blue. A combination of Aloe vera and mucilage revealed that the mucilage could block the penetrating ability of Aloe vera. Mucilage acts as a cover for wounds but does not increase the penetrability through the skin.

Wound Healing And The Aloe Vera Molecule

The effect of Aloe vera on skin fibroblasts was measured by Danhof in 1983 *(Danhof 1987)*. He found that tritated thymidine uptake by skin fibroblasts was increased in a dose-response fashion by Aloe vera. He also found that the anthraquinones in the yellow sap killed the fibroblasts. This "killing of fibroblasts" has potential as an anti-inflammatory assay if Aloe vera was used to protect against this "killing effect."

Years ago we felt that wounds should not be covered. However, we found that dry wounds drop, and prevent the migration of cells and the influence of wound healing growth factors. With Aloe vera acting as a cover, the wound remains moist, and there is an excellent migration of epidermal and fibroblast cells. So there is an increase in covered wound healing over that of uncovered wounds. Aloe vera increased the wound healing over a dosage range of 1 to 100 mg/kg in a dose-response fashion.

This was the first study that demonstrated that Aloe vera was effective in animals.

Aloe vera is a modulator. It has an inhibitor system capable of blocking the immune system observed in the adjuvant arthritic animal, and it can block the mediators responsible for inflammation.

Aloe vera also has a stimulatory system in which it can increase antibody production and stimulate wound healing by means of growth factors such as gibberellin, auxin and mannose phosphate. The isolation of the wound healing and anti-inflammatory activities using the 50% ethanol extraction of Aloe vera revealed that the supernatant contained 78% of the anti-inflammatory activity whereas the precipitate had only 32%. On the other hand, the supernatant had 0% wound healing activity whereas the precipitate had 160% wound healing activity in reference to the original Aloe vera. This 160% value is likely due to the fact that the anti-inflammatory activity is masking some of the wound healing effect seen in the original Aloe vera.

All of our studies seem to indicate that Aloe vera is both orally and topically active on wound healing and inflammation even in the diabetic animal. For example, studies show that Aloe vera can improve wound healing in the diabetic in a clear cut dose-response fashion over a dosage of 1 to 100 mg/kg.

Gowda demonstrated that mannose phosphate is the significant constituent in the 50% Aloe vera extract *(Gowda 1979)*. At the same time, Morgan showed that the mannose phosphate will bind to the insulin like growth factor receptor *(Morgan 1987)*. Willenberg's study exhibited the anti-inflammatory activity of mannose phosphate *(Willenberg 1989)*. Its ability to improve wound healing is evident.

The effect of mannose phosphate on topical croton-oil-induced inflammation was dose-related. The plateau of the dose-response curve was seen, however, at 25% inhibition. Glucose-6-phosphate had no effect and served as a control. Mannose phosphate improved wound healing in a dose-response straight-line fashion, but not response was seen with glucose-6-phosphate. The mannose phosphate of Aloe vera activates the insulin like growth factor receptor.

The "Aloe vera molecule" consists of a protein at one end and mannose-6-phosphate at the other end. The polysaccharide chain contains one glucose which is covalently linked to the protein with six mannose sugars moving toward the insulin, like the growth factor receptor of the fibroblast. The "Aloe vera molecule" can stimulate the fibroblast to increase collagen and proteoglycans.

We feel that the protein part of the Aloe vera molecule acts to guide the polysaccharide chain into the receptor. The mechanism of action of Aloe vera at the present time seems to inhibit pain and inflammation, but also can, by means of the growth factors, stimulate the fibroblast to increase wound tensile strength.

We have developed a wound tensile strength assay in which the length of the curve extends from day three to day ten. A dose-response relationship with Aloe vera on wound tensile strength was obtained on a two-day treatment as well as on a four-day treatment basis at doses of 50 to 300 mg/kg per day.

The slopes of both curves were similar. However, we have decided to use the four-day treatment as the curve on which to best assay Aloe vera on wound tensile strength. Gibberellin, a plant growth hormone,

stimulated wound healing in a dose-response straight-line fashion over a dosage range from 2 to 100 mg/kg. Auxin was also shown to have good biological activity. Gibberellin could also block PMN infiltration even in diabetic animals up to 60%.

Aloe vera may have an additive or a synergistic relationship with over 100 compounds to produce biological activity. It is possible that Aloe vera acts as a kind of conductor which produces music with an orchestra of many biological active ingredients. It seems presumptuous for us to consider, or even to postulate that any one substance is responsible for the biological activity seen in the Aloe vera gel.

The Air Pouch Synovium

We made an air pouch in animals by administering 30 ml of air under the skin. In seven days we administered 1% carrageenan into the pouch, and two hours later we administered 10% Aloe vera to determine what effect Aloe vera would have on the air pouch synovium.

We found that Aloe vera could stimulate the pouch wall weight by increasing the number of fibroblasts. This agrees with previous findings that the alcohol precipitate of Aloe had its greatest effect on wound healing by stimulating the fibroblast. Aloe vera decreased by 60% the mass cell count and wall vascularity.

The effect of Aloe vera on a 1% carrageenan-irritated simulated joint synovium model proves conclusively that Aloe vera stimulates the fibroblasts, as seen in the wound healing studies, and inhibits inflammation, as evidenced by the decrease in vascularity and the reduction in mass cell count.

Summary

We have shown that some of the constituents of Aloe vera have biological activity similar to amino acids, vitamin C and growth factors like gibberellin and Auxin. Some attention was given to how the Aloe leaf makes and stores the gel. Mention was also made of the fact that we have seen what we call the "Aloe vera Cell" in our laboratory at 40,000 magnification. In addition we have shown that the "Aloe vera molecule" probably does not act alone, but rather acts in either an additive or synergistic fashion with some of the 100 constituents of the Aloe vera.

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Whole Leaf Aloe Vera
The Cancer Solution

By Robert E. Willner, M.D., Ph.D.

The Aloe plant has become the basic ingredient of a large number of commercial preparations in the form of creams, lotions, gels and shampoos. The juice of the Aloe is being used for cleansing of the colon and intestinal problems. Toxicity and side effects are relatively rare and not usually severe. Almost every conceivable benefit has been claimed for Aloe over the centuries - most of them justified.

Whole Leaf Aloe Vera has anti-leukemic activity

Because it is a plant, chemical analysis has revealed a host of substances, one of which has been shown in mice to have anti-leukemic activity. *(S.N. Kupchan, 1976)*

Whole Leaf Aloe Vera has anti-cancer activity

The anti-cancer activity of Aloe indicate that its action is through stimulation of the scavenging white blood cells of the immune system. *(L. Ralamboranto, Archives of the Pasteur Institute, 1982)*

The many studies carried out by Russian scientists have done more to establish a respectable place in modern medicine for Aloe than any other group of investigators. N.V. Gribel and V.G. Pashinskii, in Vopr Onkol., 1986, showed that Whole Leaf Aloe juice reduced tumor mass and the frequency of metastases in rats.

Whole Leaf Aloe Vera protects against infection

R. Berkow in the Merck Manual, wrote of Aloe's ability to protect individuals with weakened immune systems against infection.

S. Solar, publishing in the Archives of the Pasteur Institute in 1980, showed that Aloe could prevent infection in mice if used several days before exposure.

J.Y. Brossat and his group, in the same journal the following year, demonstrated that Aloe was effective in preventing serious infections from bacteria, parasites and even fungus. These studies give great credence to those individuals who drink Aloe on a daily basis as a protective against disease.

Whole Leaf Aloe Vera - The Logical Choice in Health Maintenance

Y. Sato wrote of Aloe's protective effect on the skin against X-rays and K. Saki demonstrated its protection of the liver, particularly against alcohol. All of this evidence makes Whole Leaf Aloe Vera a logical choice in health maintenance and, in particular, as a cancer preventative because of its obvious protection and benefits to the immune system.

Whole Leaf Aloe Vera
A Natural Solution To Drug-Resistant Bacteria, Viruses & Fungi

Excerpts By David E. Williams, M.D.

There are a growing number of antibiotic-resistant strains of bacteria as well as several highly virulent forms of viruses now threatening our health. Conventional antibiotic and antiviral approaches to control or eliminate these threats have largely been unsuccessful. **But, some earlier, more natural remedies offer valid alternatives.** Knowing the details on how to obtain and use these remedies may be some of the most important information you'll ever learn.

The major changes taking place in our healthcare system will at times require you to find your own solutions to the problems these changes can cause.

The gel of the Aloe vera plant has been known to have healing powers for centuries. Practically everybody is aware of Aloe vera gel for treating burns, skin inflammation, acne, diabetic leg ulcers, shallow wounds, gastrointestinal ulcers and constipation. In higher concentrations (60, 80 and 90 percent) **Whole Leaf Aloe vera extracts can eliminate dozens of harmful bacteria**. The diseases associated with these bacteria are some of the most common and fatal of our time.

Bacteria & Fungi Known To Be Eliminated By Aloe Vera:

Bacteria	Causes
Streptococcus pyogenes	Rheumatic fever, strep throat & scarlet fever
Serratia marcescens	Endocarditis, pneumonia & bacteremia
Klebsiella pneumoniae	Pneumonia
Escherichia coli	Diarrhea & fatal food poisoning
Staphylococcus aureus	Food poisoning & toxic shock syndrome
Pseudomonas aeruginosa	Severe & fatal blood or urinary tract infections
Citrobacter	Diarrhea & blood poisoning
Candida albicans	Vaginal, respiratory & skin infections, thrush & endocarditis
Trichophyton	Fungal infections of the skin, nails or hair
Mycobacterium tuberculosis	Tuberculosis, lupus & erythematosus

Whole Leaf Aloe Vera
A Holistic Protocol
For The Immune System"

Excerpts By Scott J. Gregory
O.M.D. Fifth Edition

Aloe Vera

For over five thousand years, folk medicine has celebrated the juice of the Aloe vera plant for its unique healing properties. Only recently, however, has modern medicine begun to unlock the deeper secrets of Aloe and to place the "miracle plant" under laboratory scrutiny. The Aloe plant is a succulent, consisting of thick green leaves with a gelatinous substance inside. **Aloe juice, properly processed, contains a wide variety of healing constituents. The principal attributes are: antiseptic, anti-inflammatory, and anti-viral.**

Aloe Vera - Antiseptic

The Aloe Vera plant produces **six antiseptic agents**: Lupeol, a natural salicylic acid, urea nitrogen, cinnamic acid, phenol, and sulfur all demonstrate anti-microbial effects. Lupeol and salicylic acid also have analgesic effects.

Aloe Vera - Anti-Inflammatory

Aloe contains **three plant sterols**, which are important fatty acids-HCL cholesterol (which lowers fats in the blood), campesterol, and B-sitosterol. All are **helpful in reducing symptoms of allergies and acid indigestion**. These compounds also aid in arthritis, rheumatic fever, both internal and external ulcers, and inflammation of the digestive system. The stomach, small intestine, liver, kidneys, and pancreas can all benefit from these anti-inflammatory effects.

Aloe Vera - Anti-Viral, Anti-Bacterial

Recent research has suggested some exciting new possibilities. **Aloe not only provides vigorous overall immune system support, but aids directly in the destruction of intravascular bacteria**. The reason is Aloe's unique polysaccharide component. The body's natural "complement system" a critical defense system involving a series of proteins only needs to be activated in order to attack bacteria. It is the polysaccharides that trigger these proteins in a sequence called the "cascade phenomenon" to take on a doughnut shape and insert themselves into the surface membranes of bacteria. Through this action they literally create holes in the bacteria, exposing the pathogens' interior to surrounding fluids, causing their death.

Aloe Vera - Effects in HIV and AIDS

In an article in the *Medical World News*, December 1987 issue, titled "Aloe Drug May Mimic AZT without Toxicity," Dr. H. Reginald McDaniel stated, "A substance in the Aloe plant shows preliminary signs of boosting AIDS patients' immune systems and blocking the human immune-deficiency virus'

spread without toxic side effects."

In the summer of 1989, internationally recognized AIDS expert Terry L. Pulse, M.D., conducted a systematic study of a unique nutritional regimen combining the use of an Aloe vera drink with a supplementation powder and fatty acid capsules. The objective was to determine if this nutritional regimen would help to restore the patients immune systems and increase their ability to fight current and future infections.

Twenty-eight patients remained with the study through its 180-day period. Whereas initial rating showed 16 patients classified with full-blown AIDS, at 180 days all 16 had improved so dramatically that none could any longer be placed in that category. Additionally, two were accorded a MWR (Modified Walter Reed scale) classification of 0 - or HIV negative - at the end of the study. Subsequently, an additional five patients achieved a 0 rating on the MWR scale.

Dr. Pulse's and Dr. McDaniel's studies, though preliminary, became the catalyst for rapidly-expanding interest in the **anti-viral and immune-enhancing potential of Aloe**.

A unique feature of the polysaccharides or long-chain carbohydrates in Aloe is their remarkable ability to pass through the stomach and digestive tract and into the circulatory system without being broken down by stomach acid or digestive enzymes. By a process called endocytosis, they are taken up into the cells of the intestinal lining intact and extruded into the circulatory system, where they are able to fulfill their immune-supporting functions.

Whole-Leaf Aloe Concentrate

In the past decade the marketplace has been flooded with Aloe drinks, and almost all of these have been flooded with water. In fact, many are, so dilute as to be of almost no benefit. Recent years, however, have seen the promising development of new technologies enabling the best processors not only to produce stable concentrates of Aloe, but to utilize the whole leaf. **It is now known that the polysaccharides are concentrated close to the rind**, where these sugars are produced, though these layers were previously discarded due to the presence of undesirable Aloe resins, aloin or Aloe emodin. But now, state-of-the-art filtering technologies permit the removal of these highly purgative components without significantly reducing the healing agents of Aloe.

Within the rapidly-growing field of Aloe research, no one has done more than Dr. Ivan Danhof, M.D., Ph.D. Recognized as one of the world's top experts on Aloe, Dr. Danhof has helped to pioneer critical work aimed at isolating Aloe's healing agents and developing the most favorable processing and stabilizing techniques. **Importantly, these new techniques use only limited heat (called "cool processing").**

Whole Leaf Aloe Vera: Its Potential Use In Wound Healing And Disease Control In Oral Conditions

By Timothy E. Moore, D.D.S./M.S.,P.C.

Aloe vera has been shown to enhance defense mechanisms, and it has a variety of components to help combat periodontal disease and other oral conditions. As a periodontist utilizing Aloe vera in various consistencies for the last 14 years with over 6,000 documented patients who have been treated with applications, I've observed remarkable healing, reduced edema, and pain control.

There are eight main uses of Aloe vera in dental practice:

1. Applications directly to the sites of periodontal surgery.
2. Applications to the gum tissues when they have been traumatized or scratched by toothbrush-dentifrice abrasion, sharp foods, dental floss, and toothpick injuries.
3. Chemical burns are relieved quickly from accidents with aspirin.
4. Extraction sites respond more comfortable and dry sockets do not develop when Aloe vera is applied.
5. Acute mouth lesions are improved by direct application on herpetic viral lesions, aphthous ulcers, canker sores, and cracks occurring at the corners of our lips. Gum abscesses are soothed by the applications as well.
6. Other oral diseases chronic in nature respond with Lichen Planus and Benign Pemphigus. Even gun problems associated with tongue and Burning Mouth Syndrome are improved.
7. Denture patients with sore ridges and ill-fitting dentures and partials can benefit as funguses and bacterial contamination reduce the inflammatory irritations.
8. Aloe vera can also be used around dental implants to control inflammation from bacteria contamination.

Other oral disorders such as Candidiasis, Desquamative Gingivitis, Vesiculobullous diseases, acute monocytic leukemia, hematological disorders and nutritional problems all respond to Aloe vera use. Even diabetes mellitus, Sjorgen's Syndrome, menopausal patients and medications which can cause Xerostomia or dry mouth.

Interest is gathering momentum across our country as researchers are becoming interested in alternative therapy utilizing natural products versus synthetic agents. Aloe vera research is currently being undertaking at Oklahoma University, Baylor University, and Loma Linda.

Lastly, it was a privilege to use Aloe vera on the bombing victims in the April 1995 disaster in Oklahoma City. The attendants, doctors and especially the injured learned that the healing capabilities of Aloe vera far exceeded their expectations in pain control and healing time reduction.

Aloe vera has an unlimited future in new applications, and I sense in dentistry we are just on the cutting edge of promising utilization for anti-inflammatory procedure, antiviral, and immunological benefits for our patients.

Aloe Vera Produces Anti-Inflammatory, Immune Strengthening Effects On Skin

Excerpts By Steven R. Schechter, N.D.

The succulent leaf of the Aloe vera plant is one of nature's most revered therapeutic herbs. Throughout history, Aloe vera has been regarded as a miraculous healing plant.

Many cultures observed that Aloe produced remarkable benefits. Historical and religious documents of the Egyptians, Romans, Greeks, Hebrews, Chinese, Indians, Algerians, Moroccans, Tunisians and Arabians report its effectiveness for both internal and external uses.

Aloe vera - Traditional Herbal Medicine

From traditional herbal medicine, Aloe vera is reported useful for the following symptoms: fever, skin diseases, constipation, gonorrhea, jaundice, rheumatic diseases, hemorrhoids, coughs & colds, edema, sciatica, lumbago, rheumatism, retention of urine, indigestion, flatulence, abdominal tumors, carbuncles, muscle spasms during menstruation, ulcers, colitis, inflammations, vaginitis & cervicitis (used as a douche), conjunctivitis, and enlargement or inflammation of the liver, spleen & other glands.

During the summer of 1967, I was hired to conduct research at the world's first medical laser laboratory at Children's Hospital in Cincinnati. Every day, after completing my experiments, I would go into the room where the research animals were housed to help them heal from laser burns.

Aloe Vera and Skin Disorders / Burns

After using several preparations, I observed that Aloe vera gel produced the most impressive healing of various skin disorders including burns, lesions and cancers. I also tested the gel on myself after an accidental laser burn, and then on a few willing patients at the laboratory. Each time, Aloe consistently and quickly produced results.

Aloe is a well-known burn remedy and is used in trauma centers in California, Illinois, New York, Texas and other states. One reason Aloe has a range of beneficial effects, even being gently rubbed onto the surface - is that it has the ability to penetrate the skin.

Research conducted by Ivan E. Danhof, Ph.D., M.D., retired professor of clinical pharmacology and physiology at the University of Texas, and author of a three-book series on Aloe, shows **Aloe vera gel penetrates human skin almost four times faster than water**. Because Aloe is a super penetrator, it is added to moisturizers and shampoos, and aftershave creams. As a super emollient and emulsifier, **Aloe vera gel penetrates and moisturizes the under layers of skin**.

Danhof and other researchers observed that when Aloe vera is combined with other healing substances, it can help these substances penetrate the skin easily and deeply. Research shows Aloe produces an anti-aging effect on skin as strong as retinoic acid. **Yet, unlike retinoic acid, the polysaccharides in Aloe vera are not irritating to skin.**

Aloe Vera - Anti-bacterial, Anti-inflammatory, Pain-relieving

Each year, everyone is exposed to more than 60,000 chemical pollutants and 200 radioactive toxins that can cause a range of severe inflammations, infections and internal and external pains. Researchers report Aloe vera to contain anti-bacterial, anti-inflammatory, and pain-relieving properties.

Aloe vera gel contains ingredients that neutralize harmful, foreign skin substances. Then, it helps blood cells remove these pathogens before they can spread. These anti-inflammatory substances help treat acne and other skin irritations.

Since the earliest use of X-rays, and subsequently radio-therapy, doctors have observed that radiation can cause severe skin reactions. Any remedy that protects from severe radiation reactions works by either externally healing skin or internally stimulating various immune processes.

Aloe Vera reduces Skin reactions due Radiation

Numerous research studies document the effectiveness of Aloe in preventing or treating reactions to radiation. For example, emulsions of juices from Aloe were applied externally after radiation treatment to 260 human patients. Researchers claimed the emulsions were far more therapeutic than most synthetic preparations in reducing skin reactions due to irradiation. They said Aloe emulsions were “recommended for preventing the development of local reactions in radiation therapy, in the treatment of dry and moist epidermitis (inflammation of the outer layers of the skin) and treating radiation burns of the second and third degrees.” Aloe was also found to accelerate tissue repair and normal cell growth, and to help treat other dermatological problems.

Interestingly, the primary active ingredients of other immune-stimulating herbs like echinacea, astragalus and Oriental mushrooms are also their polysaccharides. Like Aloe vera, the therapeutic benefits of green-lipped sea mussels, shark fin soup, and the anti-cancer effect of shark cartilage **are all due to naturally occurring mucilaginous polysaccharides**.

Used properly for the disorders it is known to benefit, Aloe vera is a powerful healer that has been successfully employed for millennia.

Effect Of Orally Consumed Aloe Vera Juice

On Gastrointestinal Function In Normal Humans

Excerpts By Jeffrey Bland, Ph.D.
Linus Pauling Institute of Science & Medicine

Preventive Medicine, March/April 1985

Abstract

This study evaluated the effect of oral Aloe vera juice supplementation on gastric pH, stool specific gravity, protein digestion/absorption, and stool microbiology. Results indicate that supplemental oral Aloe vera juice is well tolerated by most individuals and has favorable effects upon a number of gastrointestinal parameters. A discussion of the potential role of Aloe vera juice on inflammatory bowel disorders based upon this work is presented.

Introduction

Members of the genus Aloe Barbadensis and Aloe vera have been used historically for medical purposes. Going back to ancient Phoenician literature, historical records chronicle the application of internal contents of the leaves of the Aloe plant for the treatment of burns, wounds, and other dermatological conditions. The pharmacological principle(s) in Aloe has been the subject of great controversy throughout this history. In recent years, individuals have extracted the Aloe plant looking for specific nutritional agents, alkaloids, sapponins, fatty acid materials, glycoproteins, or terpenoid substances that may account for its unique ability to promote healing of the dermis. This research has uniformly resulted in failure to identify the active principle in Aloe. It has been suggested that the extract of the Aloe plant promotes tissue reparation through the complex synergistic interaction of many substances, including vitamins, mineral amino acids, and other small constituent molecules that are members of the terpenoid family. Substances such as Aloe-Emodin or Aloe Resin-A have been evaluated recently from Aloe extraction concentrates as being terpenoids, characteristic of Aloe potency.

A great challenge still exists to phytochemists to try to better define what the physiochemical agents in Aloe are that demonstrate activity. The clinical evidence mounts, however, that topical application of Aloe extracts or the excised phloem material of the Aloe plant itself has repeatedly been demonstrated to have significant ability in promotion vascularizing, reducing edema and inflammation, while promoting epidermal growth and differentiation.

Recent studies of Cera, Heggers, and Hagstrom in animals have indicated that the topical administration of Aloe extract to dogs with certain forms of dermatitis can result in significant improvement of the dermatological condition when contrasted to control animal. They postulate that Aloe vera has both bacteriostatic and prostaglandin-suppressor activity when applied to the dermis.

Concomitant with these observations of the abilities of the extract of the Aloe plant as a bacteriostatic substance when administered topically are the historical reports that Aloe vera, when ingested orally, also has a systemic influence both on improvement of gastrointestinal function and possibly even other important physiological relationships. Individuals who have suffered from indigestion, irritable bowel syndrome, colitis, and excess acid stomach, have reported relief from these conditions by the oral administration of Aloe vera juice. The physiological effects of orally administered Aloe vera juice on

gastrointestinal function has not been studied under controlled conditions. Such a study is essential to establish the role that orally administered Aloe vera juice plays in imparting favorable gastrointestinal functional changes.

To address this particular question, the following study was designed. This study evaluates the impact of orally consumed Aloe vera juice on gastrointestinal function by evaluation of colonic bacterial activity, gastrointestinal pH, impact upon stool specific gravity, and gastrointestinal motility in normal subjects.

Study Design

This study involved ten healthy subjects - five men (median age: 42; standard deviation: 14 years), and five women (median age: 32; standard deviation: 5 years) - engaged in a semicontrolled Aloe vera juice oral supplementation study protocol. During the course of this study, they were not asked to eat any special foods nor to engage in an alternative scheduling of their time, but rather maintain their normal diets and lifestyles.

The subjects' initiated entry into the study by reporting after fasting overnight for an evaluation of their gastric acid secretion by the Heidelberg radiotelemetry procedure. This procedure involves the swallowing of a small pH sensitive capsule, which then transmits back to a receiver worn around the waist the internal pH of the stomach and duodenum. This procedure allows for in vivo quantification of gastrointestinal pH with position of the capsule in the gastrointestinal tract and also after the challenge with various foods.

After time was allowed for the capsule to equilibrate in the stomach, a meal replacement bar was consumed to stimulate hydrochloric acid output. This meal replacement bar contained 40% of its calories as protein, 50% of its calories as carbohydrate, and 10% of its calories as fat with RDA levels of vitamins and minerals. After one hour, six ounces of water was consumed and the patient asked to sit upright to allow the capsule to travel into the duodenum where the pH was monitored for another two and one-half hours. A stool sample and a morning urine sample were also taken after the completion of the Heidelberg gastrogram.

The urine was analyzed for the presence of indoxyl-sulfate, a metabolite of tryptophan produced in the bowel by the action of gastrointestinal bacteria on unabsorbed dietary protein. Indoxyl-sulfate in the urine is indicative of the degree to which either dietary protein is being malabsorbed or intestinal colonic bacteria are engaged in a putrefactive process. The stool sample had its specific gravity measured and was assayed for microbiota by a stool culture with specific focus on pathogenic bacteria.

After completion of these first battery of tests, each subject was then asked to consume six ounces of Aloe vera juice (concentrate juice) taken in two-ounce increments three times daily each day for seven days. After seven days on an ad lib diet with Aloe vera juice supplementation, each subject was then evaluated by the identical procedure to that in the initial phase of the experiment. The only modification of the program was the addition of six ounces of Aloe juice at the first hour of the Heidelberg gastrogram rather than six ounces of water.

Comparison of the post-Aloe vera supplementation stool culture, urinary indican, and Heidelberg gastrogram to that of the pre-Aloe vera challenge allowed for the determination of the impact that Aloe vera juice supplementation has upon gastrointestinal function as measured through bacterial activity of the colon, bowel transmit time, gastric pH, and stool density.

Results

TABLE 1
Urinary Indican Levels
Before & After Aloe Vera Trial

Evaluation of the data collected on each subject before and after Aloe vera juice supplementation produced information on the average changes in urinary indican, stool specific gravity, gastric pH, and bowel motility.

As can be seen from Table 1, urinary indican values were seen to decrease on the average, one full unit after the Aloe vera juice intake for one week. This is indicative of lowered bowel bacterial conversion of tryptophan and possibly improved protein digestion and absorption after the Aloe vera juice treatment.

Subject	Sex	Before*	After*
N.M.	F	Trace	Trace
P.S.	F	2	Negative
L.Z.	F	Trace	Trace
S.G.	F	4	1
S.M.	F	3	2
L.B.	M	1	2
P.M.	M	4	1
M.A.	M	1	Trace
J.B.	M	3	2
J.F.	M	3	3

Average change - 1.0 indican units

*Values rated from zero to 4: highest indican = 4

Increased urinary indican is reflective of reduced protein digestion and absorption and increased bowel putrification of the amino acid tryptophan, and the lower value of urinary indican seen after the Aloe vera juice supplementation trial, suggests improved protein digestion assimilation with reduced bacterial putrefaction.

Table 2 displays the stool's specific gravity data before and after the week's supplementation with Aloe vera juice. It can be seen that stool specific gravity is reduced on the average 0.37 units, suggesting improved water holding characteristics of the stool and decreased bowel transit time. It is important to note that none of the subjects in the study complained of diarrhea or loose stools while taking Aloe vera, but rather specific gravity of the stool was reduced more toward what would be considered as ideal value.

TABLE 2
Stool Specific Gravity
Before & After Aloe Vera Trial

Subject	Sex	Before*	After*	Subject	Sex	Before*	After*
N.M.	F	0.92	0.92	P.S.	F	1.27	1.00
L.Z.	F	1.50	1.25	S.G.	F	1.43	1.07
S.M.	F	2.70	1.30	L.B.	M	2.20	1.70
P.M.	M	1.44	1.08	M.A.	M	1.18	1.00
J.B.	M	1.12	1.10	J.F.	M		

Table 3 displays the gastric pH one hour after administration of the meal replacement bar and right after oral supplementation of either water or Aloe vera juice. It can be seen that the effect of Aloe vera juice administration is to increase the pH of the intestinal contents by, on the average, 1.88 units. Aloe vera juice, therefore, participates as a buffering agent in the gut which has its optimal pH range above pH5 and, therefore, may be viewed as an alkalizing substance.

Average change - 0.3 after Aloe treatment

Table 4 indicates that the time for the capsule to be transferred to the duodenum after Aloe supplementation was prolonged by approximately 1.2 hours. Table 4 also confirms that out of ten subjects in the study, six had markedly altered stool cultures by microbiological assay and four of these six who had indications of yeast overgrowth in their stools prior to Aloe, had reduction in yeast abundance after Aloe vera

TABLE 3
Gastric pH One Hour After
The Administration Of The
Meal Replacement Bar

supplementation. This indicates that orally administered Aloe vera juice may have some bacteriostatic or fungostatic activity in the digestive tract and aid in the promotion of favorable balance of gastrointestinal symbiotic bacteria. These observations are consistent with the previously acknowledged bacteriostatic properties of Aloe vera juice applied topically.

TABLE 4

Time Of Capsule Transfer To Duodenum & Stool Culture Effects Of Aloe Vera

Subject	Sex	Change In Time Of Capsule To duodenum (hrs)	Qualitative Effect Of Aloe On Stool Culture
N.M.	F	-1	No difference
P.S.	F	0	Lowered yeast
L.Z.	F	0	Lowered bacteria
S.G.	F	+1	No difference
S.M.	F	-2	Lowered bacteria
L.B.	M	0	Lowered yeast
P.M.	M	-2	Lowered yeast
M.A.	M	-1	No difference
J.B.	M	0	No difference
J.F.	M	0	Markedly lower yeast

Subject	Sex	Before*	After*
N.M.	F	1.4	3.4
P.S.	F	3.2	4.1
L.Z.	F	3.2	4.0
S.G.	F	3.1	5.4
S.M.	F	3.2	5.3
L.B.	M	2.7	4.0
P.M.	M	1.6	4.7
M.A.	M	4.2	4.5
J.B.	M	3.2	4.1
J.F.	M	4.1	4.7

Average change after Aloe vera administration +1.88 pH units

Discussion

The tolerance of the subjects to Aloe vera juice supplementation was in general, quite good. One subject complained of gas and another of transient gut pain, which after continued supplementation throughout the week diminished. The other eight subjects were asymptomatic with no diarrhea, nausea, intestinal bloating, or distress.

Four of the subjects noted an improved bowel regularity with greater gastrointestinal comfort after eating. Three of the subjects indicated that they felt some enhancement of energy and a sense of well-being, although this could not be confirmed quantitatively due to the protocol not being blinded or placebo-controlled.

The most marked objective difference between the pre-Aloe and post-Aloe supplementation periods in the various subjects, was the decrease in stool specific gravity indicating a greater water-holding characteristic of the stool and improved gastrointestinal motility with reduced bowel transit time. This would indicate that the Aloe vera supplementation had a tonic effect on the intestinal tract, thereby promoting a reduced transit time with decreased residence of fecal material in the colon. This mild tonic effect was not accompanied by any diarrhea and, therefore, would not be considered operating as a true laxative.

Secondarily, the effect of Aloe vera juice supplementation appeared to be that of altering colonic biota. Those subjects that had heavy overgrowth of fecal bacteria and some yeast infection, were found to have improved fecal colonization and decreased yeast after the Aloe vera juice supplementation. This may indicate that the Aloe vera contains an agent or agents which are mycostatic or bacteriostatic or that the improved gastrointestinal function and altered pH of the bowel as it relates to Aloe vera juice supplementation sets the stage for different populations of bacteria to flourish in the gut. The alkalizing effect of Aloe vera juice was also quite apparent in that the average gastrointestinal pH after Aloe supplementation was found to increase 1.86 units, indicating a more alkaline buffer capacity of the Aloe vera juice supplemented intestinal contents. This would support the hypothesis that Aloe vera juice supplementation may act also as a mild antacid in that its pH is 8.6 with a reasonably good buffering capacity.

Lastly, the reduction in urinary indican after Aloe vera juice supplementation indicates that the improvement in colonic bacterial activity or protein digestion / absorption after juice supplementation is seen as lowered bowel putrefaction. The indication that dietary protein is better absorbed and less available for putrefaction may also indicate why some individuals have in the past found Aloe vera to be helpful in the management of various food allergic symptoms or arthritis-like pain. It is known from the

work of Dr. Hemmings that incomplete protein breakdown products from such reactive foods as gluten from wheat or casein from milk can be transported through the "leaky" gastrointestinal mucosa into systemic circulation and initiate either antibody-antigen reactions in systemic circulation which can aggravate the symptoms of arthritis or may participate in direct antigen assault upon the gastrointestinal mucosa increasing the risk to inflammatory bowel disorders.

It has also been suggested that some of these incomplete protein breakdown products may have chemical reactivity similar to that of the endorphins and, if absorbed into systemic circulation, may actually initiate brain biochemical changes associated with what has been termed "cerebral allergy". When these incomplete protein breakdown products, through poor protein digestion / absorption, are delivered to the bloodstream and initiate, antigen-antibody complexes. These complexes can be trapped in the liver or in joint spaces and initiate inflammatory processes that have the clinical manifestations of pain and edema. This may explain why Rasmussen and his colleagues have found that a dietary fast can be helpful in reducing the symptoms of rheumatoid arthritis in stricken patients. They found that while on a dietary fast rheumatoid arthritic patients had significant reduction in morning stiffness, in pain score, improvement in hand-grip force, improvement in joint index, and a reduction of the biochemical signs of active disease. This may have resulted from decreased load of incomplete protein breakdown products in the blood which reduces antigen-antibody complex formation and degranulation of neutriphiles with accompanying inflammatory process associated with arthritis. Agents which would promote proper integrity of the gastrointestinal mucus and aid in the digestion and assimilation of dietary protein as amino acids rather than as oligopeptides would be substances that would reduce the relative load of dietary antigens on the blood as agents which exacerbate arthritic symptoms.

Recently, it has been found that in individuals who suffer from caeliac disease, which is associated with wheat sensitivity, that wheat protein contains a dietary antigen, alpha-gliaden, which can activate T-suppressor cell activity and reduce the body's immunity. This may account for why celiac disease is often associated with the symptoms of inflammatory bowel disease. Improved digestion and management of these dietary protein antigens would facilitate an improved immunological status of the gut with reduced inflammatory activity. It has also been found that non-steroidal anti-inflammatory drugs that are commonly used to treat the symptoms of arthritis actually increase the permeability of the gut to antigens and may increase the antigen-antibody complex formation and increase the long-term progression of the disease. It is also known that alcohol abuse can also lead to a "leaky" gut with increasing risk of exposure to dietary antigens.

The function of Aloe vera juice in promoting, proper gastrointestinal function, based upon the information from this preliminary study, may be to regulate gastrointestinal pH while improving gastrointestinal motility, increasing stool specific gravity, and reducing populations of certain fecal micro-organisms, including yeast. This could have significant advantage to some individuals by promoting proper dietary protein digestion and absorption and reducing bowel putrifactive processes in the colon.

This study sets the stage for a more detailed evaluation of the effect of Aloe vera juice on gastrointestinal function in patients with active inflammatory disease including inflammatory bowel disorders, colitis, and potentially forms of autoimmune disease, including rheumatoid arthritis. The impact of Aloe vera juice supplementation in these patients under controlled conditions, should allow for evaluation as to the effectiveness of this complex mixture as contributors in improved gastrointestinal function. The beneficial effect of Aloe juice supplementation could also be due to the reduction in the delivery of antigens to the gut mucosa which, if uncontrolled, are associated with inflammatory bowel disease or the absorption of these antigens into the systemic circulation through a permeable mucosa thus initiating antigen-antibody complex formation.

From this study, it can be confirmed that Aloe vera juice supplementation in normal individuals is well tolerated and did not produce any covert or overt adverse effects on gastrointestinal physiology. Oral supplementation resulted in improved bowel motility, increased stool specific gravity, and reduced indication of protein putrefaction in the colon. Clinical improvements in

intestinal function while supplementing with Aloe included reduced bloating after meals and reduced flatulence, indicating improved colonic bacterial function.

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Aloe Medicinal Substances

Present And Future Potentials

Excerpts By Wendell D. Winters
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The uses of substances derived from Aloe vera plants in a folk medicine role are widely recognized. The actual value of these Aloe substances and other plant derived substances in helping to improve pathologic conditions, relieve complaints and restore health has been debated from antiquity to the present.

Evolving historical patterns of the use of plant substances in traumatic conditions and in systemic illnesses have revealed that man may have first observed animals who were injured or ill to be eating or rolling in patches of certain plants. Subsequently, early man found that these plants would aid in healing human illnesses. Initially, Aloe substances were mainly used as healing aids for topical skin problems and conditions and this has remained their most wide spread use to the present. However, over the years the use of these and some other plant substances has been extended into scientific experimental treatments for internal upsets and conditions.

Less well recognized, but just as important, has been another evolution which is continuing in the use of Aloe substances. This has been the change in the use of Aloe from mainly folk medicine applications to more recent uses as **phytotherapeutics**, i.e., plant substances used in scientifically recognized therapeutic roles. Thus, **Aloe substances are joining kampo and chinese traditional medicine substances as major members of the world group of medically active phytotherapeutic agents**.

Another pattern of evolution in Aloe and other phytotherapeutic substances is taking place today. This pattern follows the usual pathways observed for other crude plant medicinal substances in which they are gradually replaced by chemical drugs. For example, the usual process has been to isolate the active ingredients from crude plant medicinal substances and then develop derivatives. This first move to change from crude plant medicinal substances to chemical drugs has been driven by increasing scientific interest in the pharmacological mechanisms of the crude plant substances acting as drugs against such diseases as AIDS and cancer. In the usual situation of this type, active components from crude plant drugs are isolated and purified by means of sequential chemical processes and their structures are determined. Then the bioeffects of these purified active plant components are studied using in vitro experiments, in animal therapy models and then later, and in much more detail, in human subjects with applicable disorders. Table 1 presents uses and origins of some representative plant substances which have allowed this evolution.

Table 1
Uses & Origins Of Representative Plant Substances

Plant Substance	**Use**	**Origin**
Quinine	antimalarial	S.A. cinchona tree bark
tubocurarie	muscle relaxant during surgery / seizures	liana tree bark
digoxin	element in progesterone in birth control pills	wild yams of C.A.
reserpine	control hypertension	shrub of S.E. Asia
vincristine	acute childhood leukemia Hodgkins disease	rosy periwinkle
salicyclic acid	headaches	willow tree leaves

digitalis	cardiac disorders	fox glove
Chinese Traditional Medicine & Kampo	wide range of disorders	several mixtures of medicinal plant substances
Aloe	wide range of disorders	extracts of leaf, juice, covering of several medicinal Aloe

There are several major reasons why the evolutions in uses and in the forms of phytotherapy substances are continuing to occur and why these evolutions will continue at an even more rapid pace in the future. First, medicinal plants from the land and sea only grow in a few areas of the world and they are difficult to discover, so their supply is very limited. Second, not all medicinal plants can be cultivated away from their native origins. Third, the content of the medically active substances in the plants has been found to vary considerably according to the method, the time and the place of collection, the weather before and during the harvest period, and the water and soil used for culturing. These and other plant cultivation factors will make it difficult to maintain in the long term a constant supply of original plant substances of consistent potency. With an ever increasing market demand for the plant medicinal active substances, this major disadvantage of crude plant substances stands out when compared to synthesized drugs which are free of these problems.

In addition, the Aloe substances, like the other crude drugs, are usually used for more than one illness or set of symptoms. They also are usually used in combination with other drugs and given for a long time in small doses. Moreover, **Aloe is a complex mixture of a wide variety of biologically active components. These Aloe substances are in some way integrated naturally to mainly exert what appears to be a synergistic effect and also to counteract side effects.**

Although we are now in the "age of chemical drugs for medical use," Aloe applications have been and continue to be based mostly on "folk medicine experiences." It is granted that many chemical components have been isolated from various Aloe materials and some of their chemical and bioactive properties have been determined. However, only a few of these isolated Aloe substances exhibit the same pharmacological effects of the whole Aloe. Therefore, it appears that in the case of Aloe bioactivities, the whole may not be equal to the sum of its parts, but may be many times greater than the sum of its parts - a multiplier effect!

For Aloe substances today, it is most important now to determine what the most productive pathway will be to follow in the future. I believe this pathway should have the following major markers:

1. identification of the bioactive components in Aloe.
2. determine the mechanism of action / mode of action.
3. chemical analysis of the active and inactive components.
4. evaluation of the main pharmacologic properties.

In summary, the present posture of Aloe substances is presented in the following as it relates to several major areas of importance to scientific investigators and potential sponsors of research.

For example, at the present time the major uses and applications of Aloe substances are shown in Table 2. In addition, the scientific research and development areas now being investigated, which will be the areas of continuing scientific research and medical substance applications in the future (as suggested by the scientific research topics discussed at the recent first International Congress of Phytotherapy) are presented in Table 3.

Table 2
Usages & Applications Of Aloe

A. In Vivo Uses Identified by Folk Traditional Medicine
    1. Healing of minor cutaneous injuries, such a blisters, abrasions, cuts,

burns, bites and scalds

2. Protection and care of external skin, such as cleansing, moisturizing, tightening and in mixes as sunscreens and anti-chapping compounds

B. In Vivo Identified by Scientific Studies
   1. Anti-inflammatory
   2. Anti-microbial
   3. Diet supplementary

C. In Vitro Bioactivities Identified by Scientific Studies
   1. Cellular modulation
      a. cell attachment
      b. growth stimulation
      c. wound healing
   2. Immunological alterations
      a. immunodiffusion precipitation
      b. hemagglutination
      c. mitogenic stimulation of immune cells
      d. lectin reactions with immune cells

Table 3
Topics Of Scientific Research Reports Presented At The International Congress Of Phytotherapy *(Seoul, Korea October 15-19,1991)*

Neurologic Studies
Aging
Inflammation Studies
Wound Healing Studies
Immune Factors and Immunologic Modulation Studies
Pharmochemistry Reports
Antimicrobial Studies
Gastrointestinal Studies
Neoplasia Studies
Metabolic Studies
Phytotherapy Clinical Application Studies

It is important to note that phytotherapeutic substances, i.e., plant derived substances used in treatments of medical conditions, when employed in a folk medicine setting do not perform in all medical situations. Moreover, little is known about the site of action of Aloe substances, namely whether they act at the systemic, organ, tissue, cell or subcellular levels or at the surface-cytoplasmic, nuclear-genetic or structural biological and metabolic levels of cells. Accordingly, it is obvious that swallowing boiled leaf extracts will not dissolve blood vessel fatty plaques or blood clots. Likewise, drinking tea brewed from plant parts will not reverse myocardial infarction damage or lung cancer. The point made is that we all recognize that there are major limits to traditional folk medicine uses and that it is dangerous to advise the use of plant substances in folk healing approaches over the advantages of modern day medicine.

In conclusion, while **numerous medicinal Aloe remedies have been proven to folk medicine satisfactions by time and usage, without any scientific reason behind why or how they work**, current scientific studies are being directed to identify and understand the operational mechanisms of action of Aloe substances. Such studies, when completed, promise to even further expand the potential usages and biomedical applications of Aloe.

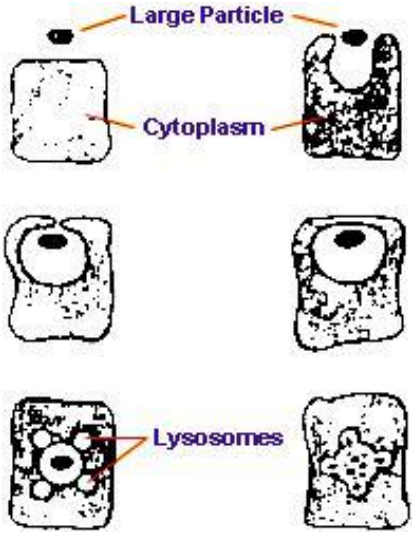
Whole Leaf Aloe Vera And The Human Immune System

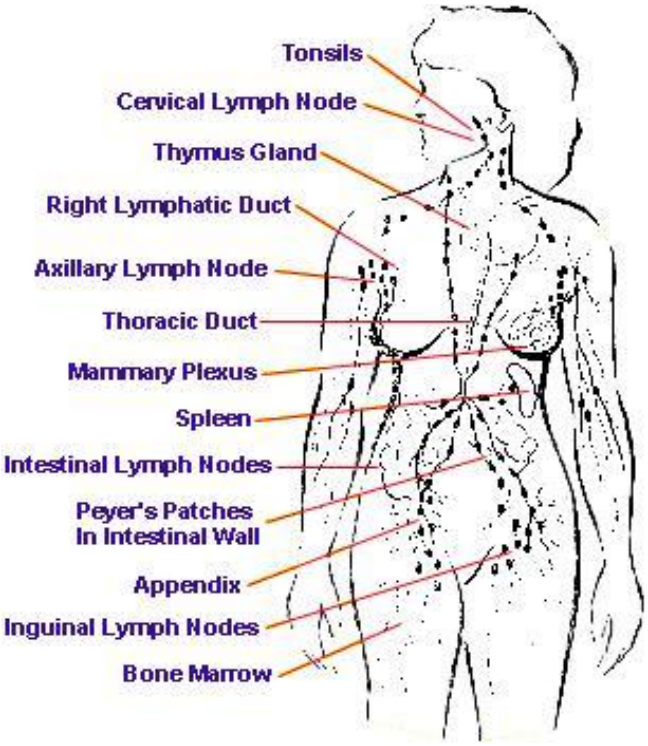
By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Specialised molecules in Aloe vera whole leaf extract interact with some special "receptor" substances that are embedded into the outer membrane of our immune system cells. The result is that the immune system cells are galvanized into action. In particular, the class of cells known as "phagocytes" increase the activities by which they attack, and then engulf bacteria, waste products and debris. This increase in scavenging activities cleanses and protects the body, with knock-on benefits for a whole cascade of different medical conditions. The literature indicates that a common mechanism in this respect probably exists in both humans and animals and that both can benefit enormously from use of Aloe vera.

Mechanism of phagocytosis.

A. Extracellular particle activates a specialised cell.
B. Cell sends out arms to engulf the particle.
C. Cell encloses the particle by forming a large vesicle or vacuole.
D. The vacuole moves into the cytoplasm.
E. Lysosomes attach to the vacuole.
F. Lysosomes digest the vacuole's contents.





The Nature Of The Immune System And Phagocytes

The Immune System provides the defence mechanisms of the body. It is concerned with defence against foreign cells and foreign substances. It Involves the white blood cells (leukocytes) and some special plasma proteins called "antibodies." Very especially important are the types of white blood cells known as "lymphocytes." These cells, while they form a most important component of the white cells in the blood, they actually travel extensively within the body. Many of them, originating in the bone marrow, travel to the thymus gland, where their further development is influenced, and they then establish themselves in a number of centres around the body, especially the lymph glands in the neck, armpit and groin areas and in the spleen. Here they constitute centres of "lymphoid tissue." The tonsils and the appendix also constitute centres of lymphoid tissue and hence should be regarded as part of the immune system.

Two other very important type of cell in the body's defences, both of which are also white cells, are the "macrophage," a name derived from the Greek and really meaning "big eater" and the "neutrophil." Both of these cell types carry out the process called "phagocytosis." This is a process of engulfing foreign particles and cells, and this includes the debris from body cells which may have been killed by bacterial toxins or by environmental poisons which have found their way into the body. The engulfing process consists of the cell sending out processes of its own cell substance until they join up around the offending item and consequently draw it into the cell. Once within the cell the engulfed particle is enclosed within a membranous "vesicle" which separates it from the rest of the cell. Digestive enzymes and oxidising substances can then be poured into the vesicle from the cell to digest or otherwise destroy the offending item.

This process of phagocytosis plays an important part of the overall processes of immunity. The actual phagocytosis step is really a cleaning up operation after some of the earlier immune processes have taken place. In the earlier stages, antibody proteins are likely to have been produced against the offending item, which coat it and make it more "palatable" to phagocytosis. Also, if the offending item is a bacterial cell, or even a moribund body cell, it may have been killed by the action of "killer" lymphocytes. Nonetheless, phagocytosis is an extremely important step and can be seen as a cleansing process. The phagocytosed item is "neutralised" and ends up being destroyed and eliminated. The digestive and oxidising processes that take place within the phagocyte destroys the structure of the offending item and makes it unrecognisable as what it was. The effect is therefore both protective and cleansing. The phagocyte may even migrate to a place from which it will be eliminated, as when it migrates to an area of pus, such as a boil, and the pus is eventually shed from the surface.

Obviously, anything which can make the process of phagocytosis more effective and more active is going to be significant for the processes of immunity. Such a substance will be an immune system stimulant. **Aloe vera is such a substance.**

Scientific Literature References To The Immunostimulant Action Of Aloe

Solar S et al. 1979: Mise en evidence et etude propietes immunostimulantes d'un extrait isole et partiellement purifie a partir d'Aloe vahome. *Archives de l'Institut Pasteur de Madagascar* 47 9-39.

Shida T; Yagi A; Nishimura H; Nishioka I 1985: Effect of Aloe Extract on Peripheral Phagocytosis in Adult Bronchial Asthma. *Planta Med.* pp273-275.

Yagi A 1987: Effect of Amino Acids in Aloe Extract on Phagocytosis by peripheral neutrophils in Adult Bronchial Asthma. *Jpn J. Allegrol.* 36 (12) 1094-1101.

t'Hart LA; Van Den Berg AJ; Klus L; Van Dijk; Labadle RP 1989: Two functionally and chemically distinct immunomodulatory compounds in the gel of Aloe Vera. *J Ethnopharmacol* May-Jun 23 (1) 661-71.

Womble D; Helderman JH 1988: Enhancement of Allo-Responsive of Human Lymphocytes by Acemannan (Carrisym). *Int. J Immunopharmacol.* 10 (8) 967-974.

t'Hart LA; Van Den Berg AJ; Klus L; Van Dijk; Labadle RP 1989: An anti-complimentary polysaccharide with immunological adjuvant activity from the leaf parenchyma gel of Aloe vera. *Planta Med* 55 (6) 509-12.

t'Hart LA; Nibbering PH; Van Den Barselaar MT; Van Dijk H; Van Den Berg AJ; Labadie RP 1990: Effects of low molecular constituents from Aloe vera gel on oxidative metabolism and cytoxic and bacterial activities of human neutrophils. *Int J Immuno-pharmacol* 12 (4) 427-434.

Davis RH; Parker WL; Sampson RT; Murdoch DP 1991: Isolation of a stimulatory system in an Aloe extract. *J Am Podiatr Med Assoc* 81 (9) 473-498.

Sheets MA et al. 1991: Studies on the effect of acemannan on retrovirus infections: clinical stabilization of feline virus-infected cats. *Mol. Biother.* 3 41-45.

Pittman JC 1992: Immune enhancing effects of Aloe. *Health Conscious* 13 (1) 28-30.

Winters WD 1993: Immunoreactive Lectins in Leaf Gel from Aloe barbadensis Miller.

Imanishi K 1993: Aloctin A, an Active Substance of Aloe arborescens Miller as immuno-modulator.

Karaca K; Sharma JM; Norgren R 1995: Nitric Oxide production by chicken macrophages activated by Acemannan. *Int. J. Immuno pharmacol.* 17 (3) 183-8.

Scientific Literature References To Stimulation Of Phagocytosis

The following references relate to human adult bronchial asthma and identified a positive effect upon phagocytosis in these patients.

Shida T; Yagi A; Nishimura H; Nishioka I 1985: Effect of Aloe Extract on Peripheral Phagocytosis in Adult Bronchial Asthma. *Planta Med.* pp273-275.

Yagi A 1987: Effect of Amino Acids in Aloe Extract on Phagocytosis by peripheral neutrophils in Adult Bronchial Asthma. *Jpn J. Allegrol.* 36 (12) 1094-1101.

The following recent references relates to work with chickens in which the complex carbohydrates from Aloe was found to increase the output of Nitric Oxide by macrophages. Nitric Oxide is one of the lethal chemicals produced by macrophages for killing and neutralising harmful bacteria and for the destruction of foreign substances and debris. Obviously, then an increased output of Nitric Oxide provides a means by which macrophage cells can increase effectiveness of phagocytic activity.

Karaca K; Sharma JM; Norgren R 1995: Nitric Oxide production by chicken macrophages activated by Acemannan. *Int. J. Immuno pharmacol.* 17 (3) 183-8.

The following reference relates to the stimulation of immune activity in mice by local activation of a substance known as "complement" and by increase in antibody production. In its conclusions it makes reference to the "activation...of human polymorphonuclear leucocytes." Once again it is clear that major immuno-stimulatory activity is being reported.

t'Hart LA; Van Den Berg AJ; Klus L; Van Dijk; Labadle RP 1989: An anti-complimentary polysaccharide with immunological adjuvant activity from the leaf parenchyma gel of Aloe vera. *Planta Med* 55 (6) 509-12.

In addition, the following article by J.C. Pittman cites that "Acemannan has direct effects on the immune system, activating and stimulating macrophages, monocytes, antibodies and T-cells." T-cells are one of the major classes of lymphocytes. Pittman also says that "It (acemannan) has been shown in laboratory studies to act as a bridge between foreign proteins (such as virus particles) and macrophages, facilitating phagocytosis." Acemannan is a trade name given to a mannose-rich polysaccharide extracted from Aloe vera.

Pittman JC 1992: Immune enhancing effects of Aloe. *Health Conscious* 13 (1) 28-30.

The Knock-On Benefits For A Whole Cascade Of Different Medical Conditions

The consequences of having a more effective immune system are extremely far-reaching. **Perhaps the most obvious and most expected change is that the body is very much strengthened with regard, not only to fight infection, but also with regard to keeping infections at bay in the first place.** The work that has been done in this area includes both bacterial and virus infections of various types. The biochemical literature shows clearly that this is the case.

In order to present a balanced picture, it has to be stated that not all plant substances which stimulate the immune systems of animals and humans do so in a useful, efficacious and supportive way. There is a whole range of such plant substances, loosely classified under the heading of "lectins" which, although they are immuno-stimulatory, nonetheless fail to produce a good and useful effect on the immune system that is of demonstrable benefit to its performance. The special importance of Aloe is that its immune-active effects have been clearly shown to be of functional benefit.

Next, it is clear, and well known, that the body's fight against tumours is also mediated through the immune system, which has an ability to kill and remove tumour cells. The outcome is presumed to be determined mainly by the vigour of the immune system response to the tumour. There is even one form of cancer therapy, known as "immunotherapy" which involves culturing the patient's own immune cells (killer cells) outside the body in the laboratory and then re-injecting them. However, clear evidence exist showing that under laboratory conditions Aloe preparations are capable of slowing or stopping the growth of tumours or even causing them to shrink. This can be demonstrated both with active, growing tumours in vivo and also with tumour cells culture. So far there are no trials on human cancer, but anecdotal accounts certainly exist of Aloe being effective against tumours.

The whole area of auto-immune disorders is one where we might well expect benefit from the use of a substance, such as Aloe, which makes the immune system more effective. Auto-immune disease is perhaps rather a special case, since the defects which exist do not relate so much to a deficiency of immune function, but rather, it is a mis-direction of immune function. However, there is some evidence which favours a conclusion of efficacy for Aloe in auto-immune conditions. This need cause no surprise in view of Aloe's known anti-inflammatory properties combined with its tendency to normalize immune function. Here there is offered a simple list of conditions which might well be expected to be benefited by a better direction of function in the immune system - i.e. auto-immune conditions. Pernicious anaemia, Hashimoto's thyoiditis (i.e. one type of thyroid insufficiency), Graves disease (i.e. Thyrotoxcosis), Type 1 Diabetes, Rheumatoid arthritis, Systemic Lupus and Lupus erthematosus, Myasthenia gravis, Auto-immune haemolytic anaemia, Goodpasture's syndrome (a type of glomerulonephritis, i.e. kidney disease), Addison's disease (deficiency of the adrenal cortex), Mixed connective tissue disease and Scleroderma. Multiple sclerosis has an auto-immune element.

Most of these diseases have not yet been subjected to trials with Aloe vera. However, it is the nature of the fundamental actions of Aloe which leads to the conclusion that the application of Aloe to these conditions could well produce favourable results.

The gastro-intestinal tract is a significant location for immune function. There are concentrations of immune (i.e. lymphoid) tissues throughout the intestines. The small intestines contain the special areas called "Peyers patches," but the large intestine, together with the appendix, is also a rich area for lymphoid tissue. Bowel health and function is an area of particular interest for the application of Aloe vera amongst Alternative and Complementary health professionals at the present time. The scientific data which exists on this area is generally supportive to their conclusions in this respect, but there is relatively little such data available at present, the subject having attracted the attention of only a few scientific investigators. Nonetheless, there are several reasons for believing that immune function is extremely important to the functions of the intestine, and this too will be reviewed in future Aloe vera newsletters now being planned. The existence of this connection raises the distinct possibility that Aloe vera will be found, in future biomedical studies, to benefit such conditions as colitis, including ulcerative colitis, polyposis of the colon, diverticulitis, irritable bowel syndrome and Crohn's disease. Much anecdotal evidence from Alternative health professionals and their patients already suggests that this is the case.

Candidiasis - infection of the intestines with Candida albicans - is an obvious case in which immune system response is obviously crucial - and it seems apparent that it is a stimulatory effect which would be needed.

Lastly, and particularly interestingly, their are diseases known or believed to involve the immune system in a major way. The most obvious of these is allergies. On the face of it the last thing which the immune system might appear to need in such cases is stimulation, because the trouble appears to arise from an over-stimulated condition of the immune system in which the system attacks foods and environmental non-foods in an unnecessary and unproductive way. However, allergies can also be viewed as a mis-direction of immune function and it is possible that Aloe may in future be found to help to put the immune system back into a better ordered state of function and to alleviate allergic conditions. So far no scientific work seems to have been done in this direction. Other conditions within which the immune

system appears to play a major part, as yet undefined, would include ME (myalgic encephalomlyelitis). This presentation has been limited to demonstrating the existence of the immune-stimulatory effect and listing conditions which either definitely do benefit from Aloe treatment or can be expected to do so with varying degrees of confidence. Future issues of the Aloe vera newsletter will explore many of these aspects rather more fully and will also introduce the other fundamental modes of action of Aloe and their likely benefits to disease conditions.

The author wishes to state clearly that, whilst this article quotes some work which has been done by others, which has involved animals, that he is in no way involved himself in working with laboratory animals, nor would he either condone or justify that type of work.

Whole Leaf Aloe Vera And The Human Digestive System

Excerpts By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Trials indicate that Aloe vera heals peptic ulcers, controls intestinal secretions to normal levels, influences the bowel flora, controls gastric and intestinal pH, improves the functioning of the pancreas and limits adverse bacteria in the colon, reducing putrification.

The Normal Digestive System

In looking closely at the functions of the Digestive System, it is much the usual thing to examine minutely the functions of its individual parts. Whilst it may well be necessary to do some analysis of that kind, it is usually far more instructive to consider the digestive system as a whole. The reason why this is so important is that the functions of each part of this system interact with those of every other part. Hence, if the digestive system is in difficulties, the job of restoring it to normal should not be tackled piecemeal, but rather in a completely wholistic manner. Before we can consider exactly what Aloe vera does within the Digestive System it is necessary to understand the normal functions of digestion and the more common forms of malfunction which may be encountered in practice. Whilst the first part may be accomplished by reading the appropriate chapter of any textbook of anatomy and physiology, a simple overall explanation is provided here by reference to the diagram below.

The food, upon entering through the mouth and undergoing mastication, becomes mixed with the saliva. As saliva contains a starch digesting enzyme, salivary amylase, the digestion of starch begins almost at once. On passing down into the stomach, the food meets the gastric juice which contains the protein-digesting enzyme pepsin and hydrochloric acid, HCI, which is there to provide the very low (i.e. acidic) pH at which the pepsin works best. Under good conditions, therefore, protein digestion proceeds apace in the stomach phase of digestion. The highly acid conditions in the stomach are also of importance in destroying bacteria which enter with the food. Most of the potentially harmful bacteria are killed by a sufficiently strong acid environment, while the more beneficial, acid producing bacteria, like Lactobacillus acidophilus are more likely to survive and to subsequently implant themselves to grow and reproduce in the intestines. A relative lack of stomach acid can therefore be harmful both because it impedes digestion of proteins by pepsin and allows some of the undesirable bacteria to pass through.

However, too much acid can be a serious disadvantage also, as we shall see below. This phase may characteristically last for about 2 hours before the stomach starts to empty, but is very variable. In particular the time of residence in the stomach is lengthened by a high fat content in the meal, which may delay emptying for quite a long time. When the stomach empties, its contents are passed on into the duodenum, which is the first part of the small intestine. Here the very acid, partly digested, fluid material, now called “chyle,” meets the pancreatic juice and the bile, which are both secreted into the duodenum, respectively from the exocrine pancreas and from the liver and gall bladder, (digest fats), trypsin, chymotrypsin and carboxypeptidase (to continue the digestion of proteins) and pancreatic amylase (to continue the digestion of starch). The pancreatic juice therefore amounts to a quite formidable battery of enzymes able to break down all the main bulk nutrients. The bile contains many wastes and toxins, for it is one of the functions of the liver to clear the blood of toxins and excrete them into the bile for passing

out of the body. However, it also contains the bile salts, taurocholic and glycocholic acids, which are potent fat emulsifiers. These play an important part in fat digestion by breaking down the larger fat droplets into smaller ones.

The duodenum is in many ways the hub of the digestive process, where numerous key steps are concentrated. It is extremely important that the control of pH within the duodenum should be correct. The pancreatic enzymes have their working optimum on the alkaline side of neutrality, so they cannot work properly if the combined effect of the slightly alkaline bile and the pancreatic juice should fail to neutralize the strong acid of the chyle. Under these conditions, the chyle will remain acid and the intestinal phase of digestion cannot get properly underway. The situation will also expose the relatively delicate tissues of the duodenum to un-neutralized acid from the stomach and may encourage ulceration of the duodenum.

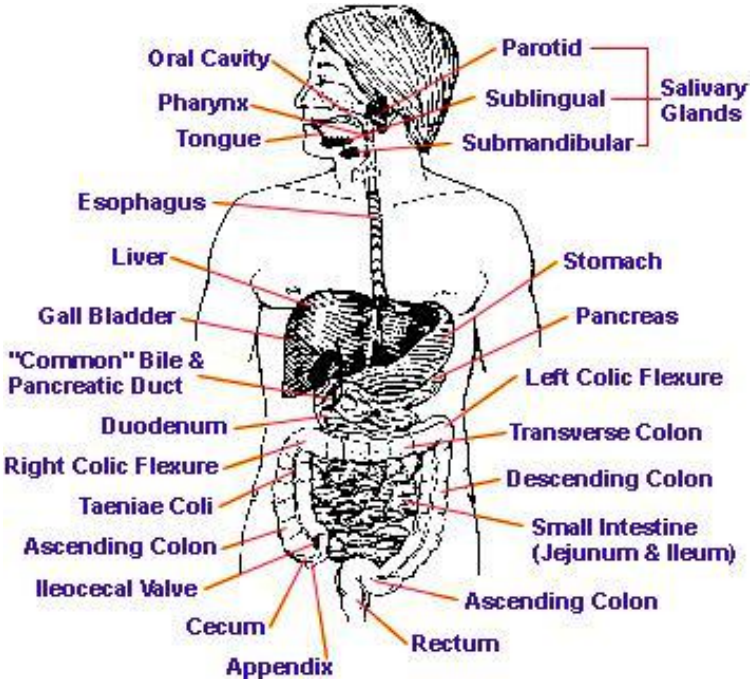


Figure 1

Most of the human digestive system is tubular in nature. The digestive tube is separated from the body wall by a coelomic cavity. A membrane of connective tissue and epithelium, the peritoneum, covers the inner body wall (parietal peritoneum) and extends as mesentery to cover the outer gut tube (visceral peritoneum). The digestive tube shows a number of specialised regions which participate in the digestive process.

Digestion and absorption normally proceed, with fats being emulsified and partly broken down by pancreatic lipase, to be absorbed further down the small intestine, partly as fatty acids and glycerol and partly as tiny fat droplets which go into the blood as “chylomicrons.” Proteins are attacked extensively by the pancreatic proteases as intestinal digestion proceeds, and are joined by other enzymes which break down smaller peptides, some of these enzymes being produced in the intestinal juice itself otherwise known as the “succus entericus.” Eventually, proteins are reduced to free amino acids and absorbed. Starches are reduced mainly to maltose, a disaccharide which has then to be broken down to glucose by the action of the maltase enzyme in the succus entericus. Common sugar or sucrose, is split by sucrase from the succus entericus. As the food passes to the jejunum, (the mid part of the small intestine) and the ileum (the final part of the small intestine), these various digestive and absorptive processes begin to approach completion.

In the large intestine, or colon, much water is reabsorbed, which is a very important function. With this, the colon also reabsorbs many important mineral salts. This reabsorption of mineral salts is significant because, although much absorption of minerals also occurs in the small intestine, this is never complete. This is more than just the absorption of dietary minerals. The digestive juices are mineral rich. If any

significant proportion of the mineral reserves that are "invested" in the digestive process failed to be reabsorbed, that would represent a serious loss to the body. This is prevented by having a colon which is competent at mineral absorption. Under the best conditions, some small proportion of the total starch intake will remain by the time the food residues reach the colon. This will then provide an energy source for the Lactobacillus acidophilus and other desirable acid-forming bacteria. These, if they are well established there, will inhibit the growth of undesirable putrefactive bacteria and even pathogens, and are known to have some anti-tumour properties. They will also manufacture significant amounts of vitamins which supplement dietary sources of vitamins. High protein content should never be allowed to reach the colon, since it will lead to the production of alkali rather than mild acid. This will favour the undesirable putrefactive bacteria, pathogens and Candida albicans, and, through the decarboxylation of amino acids, will produce quantities of toxic amines which become absorbed and intoxicate the body and all the organs within it.

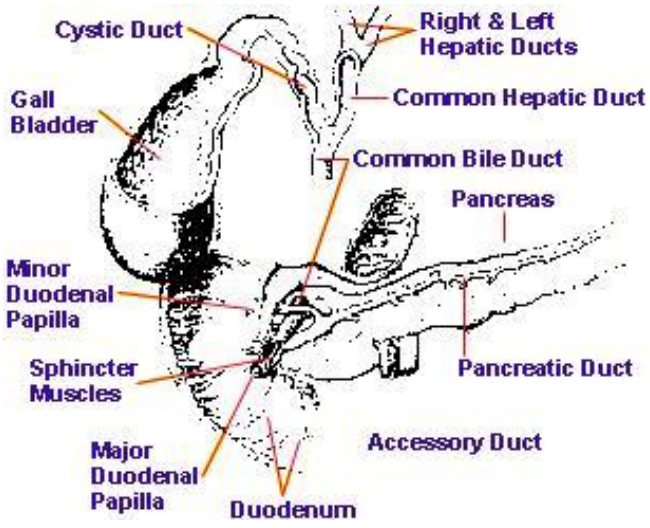


Figure 2

Illustration to show the positional relationship of the Duodenum to the Gall Bladder, Bile Duct and Pancreas.

Disturbances Of Digestion

So, digestive disturbance may begin from either too much acid or too little acid and pepsin in the stomach. If the stomach phase of digestion is less effective than it should be, then protein may well pass down into the lower bowel to undergo putrefaction and an overwhelming production of toxins. That is doubly likely if the pancreas is also sluggish or incompetent in the production of an enzymatically active pancreatic juice. The condition of both stomach and pancreas can be read diagnostically in the iris of the eye.

When putrefaction sets in, the intestines themselves become compromised and are often ineffective in their normal functions. They are liable to become pocketed, bulged, and affected by diverticuli. Their ability to carry out peristalsis (the muscular movements which advance the food residues along the intestine), becomes sluggish, the tissues of the intestinal wall become toxic, weakened and vulnerable to infection and ulceration. These effects are obviously going to be noticed eventually in terms of bowel diseases of one kind or another. High up in the intestine there is danger of ulceration wherever a substantial excess of un-neutralized acid prevails, over and above that which is required in any part of the gastrointestinal system. There is obviously a strong correlation between over-acidity and the occurrence of either gastric or duodenal ulcers - even though some other factors may have to be present also to cause breakdown of the normal protection of the stomach or duodenal wall. In the small intestine, conditions of inflammation and/or abnormal levels of secretion may well occur if the pH of the contents are wrong or if the small intestinal tissues are not being properly nourished through errors of the digestive process higher up in the tract, especially errors of function in the stomach, liver or pancreas.

What has been described above is a maze of possible symptoms that may be cross-connected in diverse ways. Whilst some improvements may sometimes be gained by a piecemeal and symptomatic approach, a wholistic approach to the overall working of the digestive system, as has already been stated, is far more likely to provide a truly effective and lasting solution. To gain insight into how Aloe affects the working of the digestive system as a whole, it is necessary to consider at some length the work of Dr. Jeffrey Bland as reported in his paper "Effect of Orally Consumed Aloe vera juice on Gastrointestinal Function in Normal Humans." Dr Bland wrote this paper from the Linus Pauling Institute of Science & Medicine at Palo Alto, California. It was published in *Preventive Medicine* in the Issue of March / April 1985.

In the tests reported by Bland, the dose of unconcentrated Aloe vera juice was 6 ounces per day (i.e. about 170ml), divided into 3 aliquots of 2 ounces (59ml). The duration of the test was only 7 days and no special measures were taken with regard to diet during the test period. Several parameters were measured which, taken together, were regarded as providing as a good and reliable index of the functioning of the gastrointestinal system. These were (1) a stool culture to indicate the distribution of bacterial types (2) levels of indican in the urine as an indication of the putrefactive capability of the intestinal flora and hence of the flora's capacity to manufacture toxic amines from intestinal amino acids (3) stool density (4) bowel transit time and (5) gastric pH.

The results indicated about a 40% reduction in the indican levels. This was taken to indicate that either bowel putrefactive activity was reduced, or else the digestion and assimilation of dietary protein higher up the tract was improved, or possibly both. Indican is derived from the amino acid tryptophane, but it was being used is a likely indicator of overall amino acid decarboxylating activity, and therefore of toxic amine production generally. The markedly diminished indican levels in the urine were taken, quite correctly, I think, to represent a considerable improvement in overall gastrointestinal function. It is a finding which carries with it implications for gastric function, pancreatic function, better bowel flora composition and, correlated to that, bowel contents pH and lower putrefective activity.

The stool cultures indicated an improved composition of the bacterial flora of the gut following the Aloe vera test. It is interesting that this improvement was attained without the use of bowel flora products containing supplements of live bacteria. Clearly, the Aloe vera itself was creating conditions within which a better spectrum of bacteria could survive and grow. The advantages of this are well known to nutritionists, and are clearly linked to lower putrefactive activity as outlined above. One especially interesting finding was that the yeast count in the stool cultures diminished markedly.

The specific gravity of the stools was reduced on average by 0.37 units. This was interpreted as an important shift towards a more ideal value. It was taken to indicate a better water-holding capacity of the stools and a faster transit time through the gastrointestinal system. It was reported that no-one suffered from diarrhea or loose stools during the test. Clearly, the Aloe vera was not acting as a laxative at all. The better bowel transit time was interpreted as an improvement of muscular tone throughout the gastrointestinal system.

The study clearly established that Aloe vera exerted a marked effect upon gastrointestinal pH. Whilst this was profoundly interesting, it was the least satisfactory part of the study because the pH changes in different sections of the gastrointestinal tract were not separately reported and differentiated. However, Bland's tabulated results suggest that a reduction in average gastric acidity was the most pronounced finding, being a reduction by 1.88 pH units. In accord with explanations I have given above, a reduction in stomach acidity will only be of benefit to people who originally had hyperacidity. It is noticeable in Bland's results that two individuals with a starting gastric acidity of less than pH 2 (i.e., very acid), showed a pH change of 2.55 units whilst those with a relatively non-acid pH of above 4 only showed an average change of 0.45 units. It appears, therefore, that people who experienced major change of gastric pH were the people who really needed on account of previous hyperacidity. Although the subjects for this study were "normal humans," the explanations given earlier in this fact sheet make it clear just why these people would have been closer to possible gastrointestinal upset than the others and also make it clear that the observed reduction in gastric pH would have been beneficial. It also becomes clear that here also is one reason why, in abnormal human subjects, conditions of gastric and duodenal ulceration would be much relieved by Aloe vera juice.

It now seems clear that the combined effect of all these various parameters of function should be taken into account when assessing the effect of Aloe upon gastrointestinal function. Thinking piecemeal, symptomatically and non- wholistically is just not good enough to generate the level of understanding required.

No other studies appear to vie with the Bland study for detailed monitoring and whole-system investigation. More such studies are obviously needed in which Aloe vera is used for rather longer and in which people with named digestive abnormalities are included in the study. Conditions such as colitis, diverticulitis, ulcerative colitis, Crohn's disease and irritable bowel syndrome (IBS) specifically need to be investigated. From what is known of the nature of these complaints and what is known of the actions of Aloe vera, there is every reason to expect such trials to be positive. A great many Alternative Practitioners, working with their individual patients, are already informally reporting success with these named complaints.

There is a scientific study from the Ukraine which concluded very positively that "In cases of functional disorders of the small intestine the process of juice secretion and enzymatic activity, Aloe extract may be recommended for stimulating the secretory function of the small intestine." This suggests that a small intestinal condition such as Crohn's disease is likely to be helped. The fact that in this case the Aloe was injected may not, of course, be essential to its efficacy.

Peptic Ulcer

Some Japanese work concerns peptic ulcer, as does the work of Blitz and colleagues in Florida (1963). In the latter study 12 patients with peptic ulcer were selected and Aloe vera gel was the sole source of treatment. It is notable that the gel was used by Blitz because in the Japanese work some components of the exudate fraction of the leaf (which is absent from gel) were recognised as being important. The twelve patients were "diagnosed clinically as having peptic ulcer, and having unmistakable roentgenographic evidence of duodenal cap lesions." The results of the Blitz work are summarized as "All of these patients had recovered completely by the end of 1961, so that at this writing at least 1 year has elapsed since the last treatment." Also **"Clinically, Aloe vera gel has dissipated all symptoms"**; and **"Aloe vera gel provided complete recovery."** It is, indeed, tantalizing when one has only a small quantity of good information on such an important subject. The chances are that the misery of thousands of peptic ulcer sufferers could be removed through Aloe vera, but no one has proved it on a large enough scale, or to the satisfaction of the medical profession. The lucky members of the public are the ones who know about it.

Another study in 1978 is significant insofar as it identifies in several papers that two factors in Aloe which diminish stomach secretion are, aloenin and Aloe-ulcin. They obtained these from Aloe Arborescens. Aloenin is one of the individual components of the exudate fraction of the leaf. It is a phenolic compound of the type called a "quinonoid phenylpyrone." The fact that aloenin has this property means that it would have an action not unlike that of a drug such as cimetedine, marketed as Tagamet, which has a huge usage as a chemical drug for the treatment of peptic ulcer by suppression of stomach secretion. It is to be hoped that the action of substances from the gel or whole leaf extract upon peptic ulcer will be found to be by a less crude and less suppressive mechanism, which, hopefully might have something to do with correcting the underlying causes of peptic ulcer. Nonetheless, the Japanese findings show that, a named component of the exudate fraction (aloenin) seems to have a synergistic effect (i.e. a mutually enhancing effect) with the action of the other leaf components. As for Aloe-ulcin, the Japanese identified it with magnesium lactate. It is, frankly, hard to become convinced by that part of the evidence, because there is so little magnesium in Aloe: it takes much more to have known physiological effects. Therefore, this author does not draw any firm conclusions about Aloe-ulcin, but this need not affect, in any way, the overall conclusions in relation to peptic ulcer.

The clinical evidence, both from the work of Blitz and from the Japanese work, is clear, in spite of their small numbers of patients. **The effectiveness of Aloe Vera for peptic ulcer seems established,** even if some component of the exudate, such as aloenin, might ideally be added for maximum effect. **There is, in my view, quite enough evidence to support the use of Aloe vera Whole Leaf Extract as a component of treatment for every peptic ulcer case encountered.**

This completes the case in favor of using Aloe vera Whole Leaf Extract for maintaining, improving and healing the digestive tract.

The Healing Properties Of Aloe Vera

By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Aloe vera contains Glucomannan, a special complex polysaccharide composed largely of the sugar mannose. It interacts with special cell-surface receptors on those cells which repair damaged tissues, called fibroblasts, stimulating them, activating their faster growth and replication. Plant hormones in Aloe, called gibberellins, also accelerate healing by stimulating cell replication. These combined actions make Aloe a uniquely potent healing Herb.

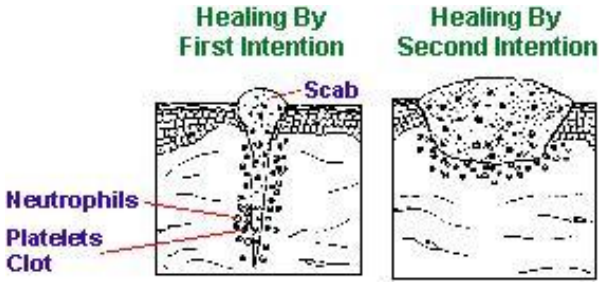


Figure 1
The illustrations show the immediate effects of a trauma which penetrates the skin. Where there is a sharp cut producing a narrow incision, this is called "healing by first intention" (left). Where the injury has much more width, the healing which follows is called "healing by second intention" (right). The penetrated epidermis is shown (top layer), the trauma to the substratum of tissues beneath and the migration of white cells, especially neutrophils, to the site.

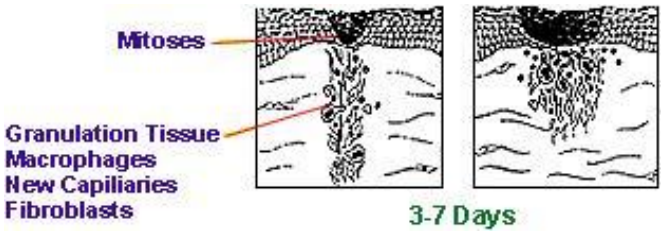
Processes Which Heal Damaged Tissues

Wounding does not just cause trauma to one cell type. Whichever part of the body is wounded, the skin is broken and it is also likely that sub-dermal connective tissues are damaged. Such damage makes it inevitable that blood vessels will have been cut through, spilling some blood within the wound, which then clots. Therefore, even if the wound is quite superficial, so long as the skin itself is penetrated, at least three tissue types are involved. Obviously, much deeper wounds are likely to involve muscle tissue. I do not address here the question of very serious injury involving bone, nerves and internal organs.

Within a few hours of wounding, a single layer of epidermal cells starts to migrate from the skin edges to form a delicate covering over the raw area beneath. The chief feature of this process, at least at first, is the movement of already existing epidermal cells over the wound surface, though it is very likely backed up by some cell multiplication. Some 36 to 72 hours after wounding, the predominant cell-type in the inflammation fluid is seen to be macrophages. Whilst these cells are well known as phagocytes there is good evidence that they do more than just phagocytose. The microphage infiltration is followed a day or two later by a proliferation of fibroblasts, cells which produce fibres of collagen and also produce other tissue proteins. By the sixth day thick fibres are present which show the staining reactions of collagen and these tend to be orientated parallel to the skin surface and across the axis of the wound, giving the repair some strength. At the same time, the fibroblasts are producing "proteoglycans" (macro-molecules which combine polysaccharide and protein elements), and these form the underlying matrix for the new connective tissue which is being formed.

Both macrophage infiltration and fibroblast proliferation are accompanied by ingrowth into the wound of small capillary buds which are derived from intact small blood vessels of the dermis (i.e. the skin layer beneath the outer epidermis) near the wound edges. Initially these buds consist of solid ingrowths of endothelial cells, but they soon acquire a lumen. At first these new blood vessels are rudimentary in structure and, compared with normal vessels, they are very leaky. The newly vascularized, collagen-producing tissue is called "granulation tissue" because it appears granular on its surface due to the little knots of delicate bloods vessels which show there.

Figure 2
The illustrations show the same two lesions as in Figure 1 but after 3-7 days, showing the laying down of "granulation tissue" and new blood vessels.



Another process important in wound-healing is wound contraction. In the case of larger open wounds, after two or three days the wound area starts to contract. This is a real movement of the wound margins and is independent of the rate at which covering by new epithelium takes place. This does not seem to be related to the formation of collagen in the wound either and, indeed, appears to happen before very much collagen has been laid down. The effect is ascribed to a different type of cell having a mixture of the properties of fibroblasts and smooth muscle cells and consequently called "myofibroblasts." These cells do, in fact, contain actin, the contractile protein of muscle and it appears to be this protein which shortens in order to produce contraction of the wound area.

Various controlling influences are at work in the process of healing, several of them involving chemical messengers that provide communication between cells and hence directing the onward flow of events. For example, in the case of the migration and multiplication of epithelial cells, the loss of cell-cell contact by the cells at the edge of the wound may well be a factor which starts their migration. On the other hand, there are thought to be substances which normally inhibit the migration of epithelial cells, called "chalones." It may be the lack of these chalones which initiates the migration into the wound, or alternatively there may be yet other chemical messengers which give these cells a positive stimulus. Relatively little is known about this or about the causes of the migration of the blood vessels. However, there is a little more information about the fibroblasts. These do appear to be subject to stimulation by external chemical messengers. It is most likely that these cells are stimulated, or their functions modified by, cell messengers from the damaged tissues, possibly by glycoproteins of the type called "fibronectins." If these particular substances do not actually stimulate multiplication, they certainly do affect other aspects of fibroblast function. They are very much concerned with the laying down of collagen fibres. In response to injury of tissue, fibroblasts are stimulated to migrate, to multiply and to accelerate their production of both collagen and proteoglycan matrix. The fact that these substances are of a glycoprotein nature may well be important in relation to the way in which Aloe influences these same cells.

The Ways In Which Aloe Influences The Healing Processes

It is necessary to turn now to the specific "Healing" effect of Aloe. This is certainly a separate type of action from the Anti-Inflammatory effect described in Newsletter No. 2. The latter effect, as we have seen, calls for the inhibiting of certain processes, such as cholesterol synthesis, the inhibiting of prostaglandin formation, or the inhibiting of bradykininase enzyme. By complete contrast with this, a healing action calls, as we have seen, for the positive stimulation of those cells which grow and multiply to effect the formation and physical strengthening of wound tissues. The process of healing has more in common with the process of immune stimulation - since both are positive stimulatory processes, not inhibitory.

Effect Of Mannans And Glucomannans

It is not surprising, therefore, that since these two processes of immune stimulation and healing have something in common, that they should also be linked in another way. Both seem to reside, at least in part, in the high molecular weight carbohydrate-rich fraction of Aloe. In Newsletter No. 1 it has been clearly shown how the immune stimulation effect is mediated through this fraction. That the healing action is also at least partly mediated through this fraction is also clearly demonstrated in the published literature. For example, a paper by Tizard, Carpenter, & McAnalley, 1989, entitled "The Biological

Activities of Mannans and related complex Carbohydrates," addresses itself more generally to the question of the biomedical effects of mannose-containing carbohydrates of this type, wherever they come from. The authors conclude that "mannose containing products increase macrophage activity and promote wound-healing. Stimulation of macrophages will increase cell and tissue growth, fibroblast activity and fibroblast proliferation. Aloe, containing mannose, "may also promote wound-healing in this way."

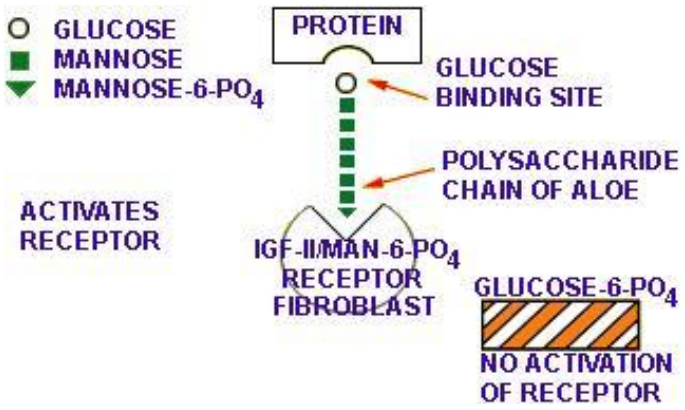
The stimulatory nature of the immune system effects were cited by J.C. Pittman in 1992 in a short review and summary entitled "Immune enhancing effects of Aloe." This quotation was "Acemannan has direct effects on the immune system, activating and stimulating macrophages, monocytes, antibodies and T-cells." Acemannan is a trade name which has been applied to the mannose-rich polysaccharide fraction from Aloe.

Prof. Davis et al. found that Aloe vera increases Collagen (protein) and proteoglycan synthesis, and that this results in increased tissue repair without loss of anti-inflammatory activity. They suggested that the mechanism might be that mannose-6-phosphate fits the growth factor receptors on the surface of the fibroblasts, enhancing their activity. This paper is Davis, Didonato, & Hartman, "Anti-inflammatory and wound-healing activity of a growth substance in Aloe vera," 1994. This very mechanism has been referred to above, showing a route to the stimulation of fibroblasts - cells which produce collagen (protein) fibres to strengthen the new tissue formations which heal wounds. Inherent within this idea, is the concept that fibroblast cells - which are key cells in forming the structure of connective tissue - possess special receptors of the type discussed, which are sensitive to mannose-6-phosphate and hence to mannose-containing polysaccharides, mannose-containing glycoproteins, and breakdown products derived from these large mannose-rich molecules. Macrophages and other immune cells have similar surface receptors. This is reflected in a paper by Winters (1993). After presenting experimental results, Winters declares "These results suggest that these Aloe lectins were active at alpha D-glucose and mannose sites and not at n-acetyl glucosamine sites." The white blood cells being used in this work appear to have been predominantly lymphocytes.

Figure 3
The illustrations above show the same two lesions as in Figure 1 but after some weeks when the healing process is "resolving" and normal tissue structure is being restored.

Hence, it appears that the "final common pathway" for initiating both the immune-stimulatory effect and the tissue-healing effect of Aloe, is the stimulation of predominantly mannose-sensitive cell-surface receptors. In the one case the cell-surface involved is that of immune system cells, and in the other it is the surface of the fibroblasts of connective tissues. The following diagram has been drawn up by Professor Davis, to illustrate the way in which the glucomannan - a mixed polysaccharide comprising mainly mannose sugar but containing also a little glucose - interacts with the cell surface of the fibroblast.

It shows a section of a glucomannan molecule, linked to protein by a glucose sugar unit and by a chain of mannose sugar units to the cell surface receptor. The cell is shown as being the fibroblast. It does seem most likely that the glucomannan does react with the fibroblasts directly. However, there is an alternative theory which is not yet excluded - that the macrophages are stimulated first and then release chemical messengers, which in turn stimulate the fibroblasts.



Plant Growth Hormones

Prof. Davis considers that gibberellin (a plant growth hormone) in Aloe increases wound-healing by increasing protein synthesis. It has been said to do this by binding to a section of DNA and consequently affecting the copying of the DNA so as to make protein. The authors Davis, Didonato, & Hartman, in "Anti-inflammatory and wound-healing activity of a growth substance in Aloe vera," 1994, say that gibberellin, isolated from Aloe, increased wound-healing more than 100% in mice. Indole-3-acetic acid, an auxin, which is also a plant growth hormone, was also reported to increase protein synthesis by increasing up take of amino acids. Little work directly upon gibberellin in Aloe appears to have been published, but one paper which mentions it specifically is "Aloe vera and gibberellin: anti-inflammatory activity in diabetes," by Davis & Maro, 1989. Some of the amino acids have also been referred to as growth-stimulants by Prof. Davis's group, but no definite role for these has yet been clarified, nor attributed with any certainty to any individual amino acids.

Summary

From all the foregoing, it can be seen that the mechanisms of the healing action are multi-factorial. That is to say, they are the result of a good many factors coming together and exerting their own distinct influences simultaneously, to produce the overall effects. The knowledge which has been gathered is impressive, though it falls short of complete explanation or complete understanding. Nonetheless, it serves to give a fair mental image of the types of processes that are going on when Aloe exerts its effects.

In the future Newsletter, it will be possible to consider ways in which the three prime known actions of Aloe work in concert, not only with each other, but also with the known secondary effects of Aloe, to produce important beneficial effects upon chronic illness. It also becomes possible to address the question, as to which medical conditions which have not yet been subjected to medical trials with Aloe, most stand to benefit, on theoretical and inferential grounds, from the future application of the therapeutic effects of Aloe.

References Confirming The Wound-Healing Powers Of Aloe

In the following list of publications most refer to observations upon the actual practical healing of wounds. However, a few references have been included which simply report a mitogenic effect, i.e. an effect in stimulating cellular multiplication of a tissue, since that is such a fundamental component of the healing process.

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Freytag A 1954: Suggested role of Traumatic acid in Aloe wound healing. *Parmazle* 9 705.

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Winters WD; Benavides R; Clouse WJ 1981: Effects of Aloe Extracts on human normal and tumor cells in vitro. *Economic Botany* 35 (1) pp. 89-95.v.

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Yagi A; Machll H; Shida T; Nishloka L 1985: Effect of Aloe Lectin on Deoxyribonucleic acid synthesis in baby hamster kidney cells. Stimulation of RND Synthesis by an Glycoprotein. *Experientia* 41 669-671.

Davis RH; Kabbani JM; Maro NI 1987: Aloe vera and wound healing. *J Am Podiatr Med Assoc.* 78 (2) 165-9.

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Fan YJ; Li M Yang WL; Qin L; Zou J 1989: Protective effect of extracts from Aloe Vera L. Var. Chinensis (Haw.) Berg. On experimental Hepatic lesions & a primary clinical study on the injection of in patients with Hepatitis. *Chung Kuo Chung Yao Tsa Chin* 14 (12) 746-748.

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Heggers JP; et al (8 authors) 1992 (Dec.): Wound healing potential of Aloe & other chemotherapeutic agents. Presented in part at the 6th Internat. Congress on Traditional and Folk Medicine.

Heggers JP; Pelly RP; Robson MC 1993: Beneficial effects of Aloe in wound healing. *Phytotherapy Research* 7 548-552.

Skohan SJ; Davis RH 1993: Principals of wound healing and growth factor considerations. *J. Amer. Podiatric. Med. Assoc.* 83 (4) April. 223-227.

Heggars JP; et al (7 authors) 1994: Beneficial effect of Aloe on wound healing in an excisional model. Presented at the 26th Ann. Meeting of the American Burns Assoc. April.

Davis RH; Didonato JJ; Johnson WS; Stewart CB 1994: Aloe vera, Hydro-cortisone, & sterol influence on wound tensile strength and anti-inflammation. *J. Amer. Podiatric. Med. Assoc.* 84 614-621.

Davis RH; Di Donato JJ; Hartman GM; Haas RC 1994: Anti-inflammatory & wound healing activity of a growth substance in Aloe vera. *J. Amer. Podiatric Med. Assoc.* 84 (2) Feb., 77-81.

Many potential users of Aloe ask "If Aloe stimulates cell division, can it not also stimulate the growth of cancer cells?" In the following paper tests were done with normal human cells and also human cancer cells and the results showed that although the growth of the normal cells were stimulated, that of the cancer cells was not.

Winters WD; Benavides R; Clouse WJ 1981: A note from "Effects of Aloe extracts on human normal & tumor cells in vitro. *Economic Botany* 35 (1) pp. 89-95.

Fractions of leaf extracts from Aloe vera and Aloe saponaria were prepared by differential centrifugation and tested by in vitro assays for the presence of lectin-like activities and for effects on the attachment and growth of human normal and tumour cells. Fractions of extracts of fresh leaves had high levels of lectin-like substances measured by immunodifusion and haemagglutinin assays. **Substances in fluid fraction from both fresh leaf sources were found to markedly promote attachment and growth of human normal, but not tumour, cells and to enhance healing of wounded cell monolayers.** Results from cell assays suggested that the observed growth promotion and wound healing effects of Aloe substances in vitro may be analogous to what has been observed in vivo during healing of wounds and burns.

Aloe Vera, Aloe In Alternative Medicine Practice

Excerpts By Lawrence Plaskett, B.A., Ph.D., C.Chem., F.R.I.C.

Aloe vera can easily be incorporated into practice in Clinics of Nutritional Medicine, Naturopathy, Herbalism, Iridology, Kinesiology, Vega Testing and Mora Therapy, Colonics, Aromatherapy and Reflexology. It can be similarly used by Practitioners of Dowsing and Radionics. Within more orthodox practice, it can be used in conjunction with Physiotherapy.

This newsletter examines the rationale that lies behind the use of Aloe in these contexts. It looks at what is involved in incorporating Aloe into practice, gives guidance on the types of product that are needed and recommends a range of Possible doses.

The Practitioner's Thinking Which Lies Behind Treatment With Whole Leaf Aloe Vera

Practitioners who have assimilated the contents of Aloe vera Information Service News Letters 1-4 will by this time have abundant reasons for regarding **Whole Leaf Aloe Vera** with a great deal of respect as a **powerful herbal remedy** with multifaceted potency within the widest field of "healing." At the same time many readers may have been quite properly impressed with **Aloe's powers in specific healing directions**, such as those applying to those named medical conditions which have been subjected to trials with Aloe for potential therapeutic application.

For yet other people, who perhaps suffer from no illness or significant symptoms, **the attraction of Aloe may well be its potential for maintaining good health by a general "toning up" effect, which is inherent in Aloe's fundamental actions**, especially those having to do with maintaining or improving the condition of the immune system and increasing the oxygen consumption, and therefore the activity levels, within the tissues. These, effects, most emphatically, appear to offer a very positive route to the avoidance of the partially de-oxygenated, low-activity and toxic condition which is recognised, naturopathically and vitalistically, as constituting the state of "chronicity." Furthermore, whilst this state of "chronicity" is the major predisposing factor towards chronic illness, it does not yet form part of the philosophy and outlook of mainstream medicine. Notwithstanding this, the concept is nonetheless wholly compatible with the principles of modern medical biochemistry.

It will be clear why Aloe gets dubbed with emotive terms such as "The Silent Healer" and even "Panacea." This happens, even among quite well informed users of Aloe, not just people who are easily influenced by hype and imagination. **It does so because the nature of the fundamental actions of Aloe are to improve the status of some vitally important systems of the body which affect many functions.** In this way it improves, generally, the biochemical status, activity levels and metabolic and functional competence of cells. Obviously, any such influence will be a most positive factor in keeping the individual safer than they would otherwise be, from developing chronic diseases in general. The painstaking process, which no doubt will have to be gone through, of thoroughly testing Aloe in clinical trials against every known chronic disease, is, to a certain extent superfluous within the philosophy of anyone who truly understands the fundamental modes of action of this remarkable herb.

The fundamental changes which Aloe is capable of making within the body will help the body to fend off each and every chronic disease. Much though that may sound like a heresy to strictly orthodox clinicians, whose medical philosophy requires them to look at each and every labeled medical condition as though it were a separate entity, this author, who is himself so deeply rooted in medical science, now regards this as a truism, and that conclusion emanates from deep enquiry into the biochemical actions of Aloe at the cellular level. There is, indeed, every reason, through a process of scientific inference, to believe that each and every chronic disease will be found to respond to greater of lesser degree, to Aloe. The most likely exception to this is those genetic illnesses determined by genetic error, but even with these there is a chance that the overall medical condition of the patient will be better for a certain toning up of cellular metabolism, such as Aloe can bring. This author's exploration of the literature has found a general absence of negative results when people have tried the use of Aloe against chronic disease. Some of the papers on the subject report that 100% of patients responded to Aloe or very nearly so.

How does Aloe relate to specific Disciplines within Alternative and Complementary Medicine?

Nutritional Medicine

For the Practitioner whose prime field is Nutritional Medicine, Aloe vera can be seen in the role of a quite unique adjunct of the Therapy. Although Aloe is often advocated for its content of nutrients, this is not really a key point, nor even a very significant point at all about Aloe. Naturally, Aloe, being a plant juice, contains some protein, carbohydrate and lipid, contains minerals, such as calcium, magnesium, sodium and potassium, and some of the vitamins, but the amounts of these are low. Because Aloe is the juice of a plant which is adapted to water-storage, its juice is very dilute, the gel containing about 0.5 - 0.7% of total solids and the Whole Leaf Extract about 1.0 - 2.0% of total solids. Most other plant juices are much more concentrated than this. Given these low concentrations, and the modest volumes of the juice which are used for therapy, the quantities of nutrients taken in with a daily dose of Aloe, are very small compared to dietary intakes. Therefore, one does not use Aloe for its nutrient content.

Instead, **Aloe is to be uniquely valued for its content of active biochemicals**. These are substances which interact with living cells in very small amounts, producing significant changes to cell metabolism and cell behaviour. These substances interact with specialized receptors on the cell surface to produce these changes, in a way which might be described as "pharmacological." Yet the substances within Aloe which are doing this are entirely non-toxic natural substances and they leave no residues in the tissues. Any practitioner who is a purist and, perhaps, does not much like the use of the word "pharmacological" in this connection, can rest assured that Man has always been exposed to active substances of this kind in his foods. Aloe itself, of course, is not a food, but pharmacologically active substances of the same general type are well distributed among unprocessed whole foods. None of our foods contain the same range of active cell-stimulating constituents as Aloe in the same proportions, but the principles involved in using Aloe are much the same as when one uses some foods as medicines.

Naturally, much of what one does when using foods as medicines involves selecting the foods for their nutrient content. Unlike Aloe, we eat enough of various individual foods, or can do, to contribute significantly to the dietary supply of specified vitamins, minerals etc. That is one most important element of food therapy. The other aspects of food therapy, but one which is often forgotten, due to focusing primarily upon the nutrients, is the way that the various whole unprocessed foods contribute pharmacologically active substances which constantly stimulate or otherwise modify the behaviour and metabolism of our cells. We are used to the idea that food processing can damage our food by causing extensive losses of nutrients but, almost certainly, there is another huge area of understanding - one which we are only just beginning to glimpse at the present time - which concerns the way in which the processing of food damages these pharmacologically active substances which are in natural, unprocessed foods but which may be absent, or nearly so, from processed foods.

The presence of special bioactive substances in plant-derived foods is the subject of two important books by Jean Carper *The Food Pharmacy*, 1989 and *Food Your Miracle Medicine*, 1993. Some of the components she identifies are nutrients and others simply have very powerful anti-oxidant effects, but is seems rather clear than some of them exert actions of a pharmacological kind.

Just because the pharmacologically active substances in Aloe, and also those in foods, interact with cell surface receptors, and because drugs also do the same thing, there is no need whatsoever to regard these substances as being drug-like in their action. Not only do these natural therapeutic agents leave no residues in the tissues, but, since there are some such substances in foods, it is true to say that Man has evolved with a certain level of exposure to these substances as his normal experience. That is an experience which must have ranged over at least three million years of the history of Man. Moreover, going back far longer than that, Man's evolutionary ancestors, during the whole of the period when the mammals were evolving and changing towards today's forms, a period of more than the last 80 million years, the tissue cells of plant-eating mammals have been subject to these same forms of pharmacological stimulation. Indeed, the flowering plants (Angiosperms), which are the principal source of foods for mammals and Man today, themselves evolved over a somewhat longer time-scale from the Cretaceous period of some 100 - 120 million years ago.

It is therefore very arguable that the tissue cells of Man have developed under conditions in which exposure to such stimulatory biochemicals has been expected, normal, and perhaps entirely necessary to survival. **If so, the partial withdrawal of such substances from the diet, which is inherent in the switch to processed food, may well be catastrophic to the health of Man.** And we must remember that some people today consume hardly any fresh plant foods. The consumption of fresh fruit and vegetables, which is shown in national statistics of diet and food consumption, is actually very unevenly distributed between individuals.

It is by no means surprising, therefore, if we find today that people in countries with a western lifestyle, Aloe, which has unique powers, and possibly other herbs also, where they contain concentrates of bioactive substances, are very badly needed to offset the loss of these actively stimulatory compounds from the food. Even more so, of course, they are needed to effect cures from chronic diseases among people who have followed the western lifestyle for many years.

Aloe, of course, must be classified as an adjunct to the Nutritional Therapist, simply because Aloe itself is not a food. **But it is a powerful one, containing more potent stimulatory substances than any food, in its own unique combination.** Used in this way it greatly enhances the efforts of the Practitioner to support the patient's immune system, to promote healing, to cleanse and to relieve inflammatory conditions. The writer is both a practitioner of Nutritional Medicine and is engaged in the training of Nutritional Medicine Practitioners. His student / Practitioners almost all understand and most use the powers of Aloe.

Naturopathy

Because of the nature of Aloe's actions, this plant is a natural ally of the Naturopathic Practitioner. Its cleansing effect, which is so completely in accord with the precepts of the Western Naturopathic system of thought, is most probably mediated through the effects of Aloe upon the immune system and those which it exerts upon the alimentary system. The healing action depends partly upon the direct stimulatory effect upon fibroblasts and other cell types and partly upon the consequences of the tissues being better cleansed. For the dedicated naturopathic it is obvious to use a potent cleansing herb to augment the benefits of their other cleansing procedures.

Herbalism

To a herbalist Aloe is home ground, as it is unquestionably a herbal remedy. Herbalists should also note all that has been said above about the relative lack of nutrients in Aloe. But then the same is true of herbs in general. They are often recommended in herbal texts for their content of some specified nutrient, such as iron, for example, and yet they rarely contain any significant amount of the named nutrient in the small quantity of herb likely to be consumed in a day's dose. It usually takes either foods or concentrated nutritional supplements to deliver a significant amounts of nutrients and the claim to do so with small doses of herbs is almost always misleading. Most active herbs, like Aloe, depend for their action upon pharmacologically active compounds present in small concentrations. The herbalist therefore needs to be aware of using the herbs for these specific biomedical effects which depend upon interactions between the living cell and the active compounds.

In my experience, herbalists may be mainly scientific in their emphasis, or mainly naturopathic, using the herbs within either of these appropriate concepts. Whichever way the herbalist leans, he or she will usually be happy with the information about Aloe and the way in which it is very readily justified in either the scientific or the naturopathic mode.

Iridology

Iridology is a purely diagnostic discipline which only makes any sense when it is naturopathically interpreted, since the iris only yields information in naturopathic terms. Iridologists are therefore almost always either naturopathic, nutritional or herbal Practitioners who are used to using these various disciplines as a means of therapy once the iridology diagnosis has been reached. They will almost certainly find that Aloe has the strongest possible appeal to them as a powerful therapeutic tool, which will make real changes in the iris signs, which signify progress being made in identifiable parts of the body with cleansing, healing and the relief of inflammation. The writer is both a Practitioner of Iridology and is engaged in the training of Iridologists. His student / Practitioners almost all understand and use the powers of Aloe.

Osteopathy And Massage

Physical therapists obviously treat conditions which manifest as physical problems. These may arise from injuries or from metabolic deterioration of structural parts. Conditions which arise without any influence from outside physical trauma and are hence internally generated, usually have underlying causes from nutritional deficiencies or imbalance, toxicity and/or subtle energy imbalances.

When osteopaths or masseurs treat a patient for a condition which results from injury they are faced with both damage and inflammation. **Both the healing and anti-inflammatory actions of Aloe can be engaged at once to assist in these cases.** Aloe will work here very positively. It is, perhaps, in an adjunct role to the main therapy of the Practitioner, but in most cases it will be found to be a very potent and worthwhile adjunct.

When the complaint is internally generated, osteopathy itself is likely to provide helpful treatment, without, perhaps, touching the metabolic disorders which lay at the foundation of the trouble. To deal with this problem some osteopaths and masseurs embrace naturopathic means of treatment as well as their main therapy. Aloe is, of course, a major contribution to working in this way. It should appeal to physical practitioners whether or not they have already adopted a naturopathic approach to aspects of their treatment. Its use calls for no additional training and, by its cleansing action and its various cell-stimulating actions, it will tend to help metabolic problems, even though the nutritional defects should never be ignored.

Practitioners of therapeutic massage who do massage directed to the purpose of lymphatic drainage, have a particular reason for seeking the help of Aloe as an adjunct of their treatment. The cell-types of the lymphatic system are one and the same with those of the immune system. When the flow of the lymphatic

vessels is stimulated by the massage, the flow through the lymph glands is necessarily improved. These important concentrations of lymphatic cells are thereby helped in their cleansing by the massage and if Aloe is used at the same time, then these two actions, both aiming at essentially the same end, will augment one another and the benefits may well be synergistic.

Much that has been said in this section could also be said about other physical therapies, including the often distinctly non-Alternative field of Physiotherapy. Some Physiotherapists have nonetheless embraced some aspect of Alternative and Complementary therapy and hence may be able to gain in the same way from the use of Aloe.

Acupuncture And Homeopathy

These therapies are considered together here because they are prime energy therapies of great importance within the field as a whole. Aloe, so far as we know, does not become directly involved in the correction of subtle energy imbalances, but rather does so indirectly through relieving the Life Force from some of the burdens of toxicity and enhancing vitality through its stimulating actions upon tissue cells of different types. Therapists who are primarily subtle energy therapists will therefore regard Aloe as working upon a different level.

Not all training courses for acupuncturists and homeopaths stress sufficiently the way that the flow of energy, whilst being helped by these therapies, can also be synergistically facilitated by employing nutritional means. Therefore some of these Practitioners may not have got into using Nutrition as the valuable adjunct which it is. Those who have not done so, or whose patients simply "do not want to know" about diet and vitamin supplements may well find Aloe an easy option to introduce, so far as patient acceptance is concerned, and should be well pleased most of the time, with the results. The emphasis here is upon making the Practitioner's work easier and gaining additional leaps forward for the patient. Those energy medicine Practitioners who do use diet and supplements as well should gain even more of a fillip to their treatments from employing Aloe as well. One needs to remember here that Aloe does not replace any aspect of Nutrition, so the benefits of Aloe plus Nutrition are generally found to be additive.

The same observations I have made about acupuncturists and homeopaths apply also to those osteopaths who use cranial osteopathy and, through that version of their therapy, work directly upon the subtle energies of the patient.

Kinesiology - VEGA Testing - MORA Testing and Therapy

The use of subtle testing of patients via muscle testing and by using the higher human faculties combined with electronic methods, is done, of course to diagnose conditions, but also to select treatment, either homeopathic, herbal or, nutritional, while in the case of MORA, direct treatment is being applied through the equipment. These Practitioners will probably want to ask, through their diagnostic techniques, whether Aloe should be used. The known effects of Aloe are, as we have seen in previous NewsLetters, so broad spectrum in their relationship to pathologies, that probably there will be few who are not diagnosed as requiring or benefiting from Aloe. Perhaps, however, these methods will be able to pick out the most prime cases for concentrating upon Aloe treatment.

However, one can go much further and say that these diagnostic procedures will very frequently find labeled conditions for which treatment must then be found. If the diagnosed labeled condition is inflammatory, involves damage and therefore requires healing, involves the digestive system or else a need for fighting infection or tumours or requires cleansing action, then Aloe is likely to have a role. These Practitioners will either employ their technique and/or their equipment to help them decide, or may

decide to use Aloe anyway, once the cause of the problem has been found.

Much of what has been said in this section could also be applied to Practitioners who work via Dowsing and/or Radionics, in relation to their likely use of Aloe.

Reflexology

Reflexologists both diagnose and treat through the feet. They find sites of previously unsuspected chronic inflammation, disorders of the digestive system which were, perhaps, not clearly diagnosable before, and find organs which may be struggling with chronicity for reasons connected with nutrition, toxicity and subtle energy imbalances. Application of Aloe by these Practitioners is likely to have much in common with that of Practitioners of other diagnostic approaches, like the kinesiologists. They will be able to apply Aloe to conditions they have uncovered and make the Aloe synergize with their main therapy.

Colonic Irrigation

Any cleansing therapy can synergize with the cleansing action of Aloe. Aloe being taken by mouth during the same period when colonic washout therapy is being applied will strengthen cleansing effect simply by combining these two approaches to cleansing which operate in different ways, one, the Aloe, internally and the other essentially externally, bearing in mind that the colonic lumen is regarded as being outside the body. The benefits here will be much the same as those of combining Aloe with any other, distinctly different approach to cleansing, and the effects are almost certain to be synergistic. There is, however, one further bonus. The colonics therapist can use Aloe directly in the washout fluid, or leave the Aloe containing fluid in contact with the bowel lining for a time, to work directly upon inflammatory conditions itself.

Aromatherapy

The effects of Aromatherapy are presumed to be partly subtle and partly physiological. The subtle energy effects of the Therapy will interact with Aloe indirectly, rather than directly, as in the case of energy therapies, acupuncture and homeopathy. Insofar as the effects of Aromatherapy are physiological, they will interact directly with Aloe, working at the same material level to augment cleansing and re-establishment of balance within the body.

What will it take for Practitioners to incorporate Aloe into their Practice?

Of course, whichever of the above disciplines one practices, the use of Aloe is an addition to the rest of the therapy you are giving. It is something which the patient must do for themselves when they are not with you. For the osteopathic, massage, acupuncture or reflexology patient that might be a new departure since the main treatment is something which the practitioner does to them. For patients of nutritional medicine, herbalism and homeopathy, they are all used to the idea that the treatment involves regular administration of remedies or nutrients to themselves. The introduction of Aloe into treatment should not give any difficulty for any of these groups, since the administration is very easy, involving, in the case of Whole Leaf Extract, only measuring out and taking a small quantity of liquid one, two or three times per day. Advice to keep the bottle in the refrigerator once opened is appropriate.

Topical Use

The use of Aloe vera Whole Leaf Extract will be the usual form of treatment, since internal administration is usually required. However, application to the surface is a secondary form of application which will be wanted fairly often either instead of internal use or in addition to it. For application of Aloe to the skin, or to the accessible mucous membranes, creams and ointments have a long-standing role, both in home treatment and in hospital applications. These are readily available from manufacturers. Their use for appropriate superficial conditions can be thoroughly recommended. Alternatively the concentrated Whole Leaf Extract can be applied topically also using either cotton wool pads, or other means. It has both an advantage and a disadvantage in this application. The ointments and creams are manufactured with "body" which helps them to adhere to the surface, but this very fact means that they usually have a lower Aloe content. The choice of brand should be made critically, as with Whole Leaf Extract.

Selection Of The Right Aloe Products For Practitioner Use

Any user of Aloe should bear in mind the recent history of Aloe, which is that whilst it has marvellous credentials as a curative herbal remedy, it has been much abused by the unscrupulous acts of certain suppliers. They have diluted the extracts with water and extended it dishonestly by the addition of inactive maltodextrin, dextrose or glycerol. It has also been subject to other forms of abuse which were not dishonest, but involved processing the plant in ways which failed, to various degrees, to preserve its biological activity. There are also operators who market only a distillate from Aloe. From what is known of the active ingredients of Aloe, there is absolutely no reason to expect that any significant amount of these will be present in such distillates.

The next question concerns the selection between a Whole Leaf Aloe vera and a Gel product. Most of the products on the market at present are products from the Gel of the leaf. There is certainly nothing wrong with that and Gel is the most long-established and longest recognised form of Aloe apart from the exudate, or "aloin" fraction, which is of a quite different nature. Previously, Whole Leaf Aloe Extracts were not used because they would always have contained the "aloin" fraction, which was not wanted because of its purgative action, which would have been unwanted and unhelpful in a product being taken mainly for anti-inflammatory, immunostimulant and healing effects. The fact that Aloe leaf was composed of separate Gel and rind provided a fortuitous way in which to furnish Aloe material which was virtually "aloin-free," simply by dissecting out the central Gel section of the leaf.

However, this fiddly dissection had originally to be hand done and was expensive, and discarding the rind was always an expensive option too, since the discarded rind undoubtedly contained further quantities of the same active principles which the Gel contained, made unusable only by the presence of the "aloin." Recently the development of the technology required to produce a good quality Whole Leaf Extract almost free from the purgative "aloin" components, has changed the picture, and certainly has changed the choice of options available to the user of Aloe. This technology has consisted of (a) the addition of cellulose enzyme to the disintegrated whole leaf prior to expressing the juice and (b) carbon filtration for efficient removal of the "aloin" fraction and so avoid making a product with an unwanted purgative action.

Whole Leaf Extract manufactured in this way contains a higher concentration of total solids than any Gel extract. This is no surprise because the Gel is a specialized water-storage tissue and one would expect its water content to be very high and its solids content very low. The Whole Leaf Extract contains juice made from all the cells of the leaf, including the functional palisade layers and mesophyll layers of photosynthetic tissues, which have their place within the rind. Because these cell layers are highly active in metabolism they are bound to be rich in enzyme systems and all the other biochemicals which are prerequisites for an active metabolism. Any plant biochemist would therefore expect the content of soluble solids in the juice from these layers to be correspondingly much higher than in juice made solely from Gel.

This proves to be the case in practice. The total solids level is from 1.6 to 3 times higher in the Whole Leaf Extract than in the extract made just from Gel. Total solids is one of the measures used by The International Aloe Science Council in assessing the genuineness of Aloe products. **It is hard, therefore, to avoid the conclusion at this stage, that the Whole Leaf products are more concentrated than pure Gel extracts and that they are therefore better also with regard to physiological activity.**

This is where the subject rests at present, and it makes it necessary to recommend here that **the best source of Aloe for most purposes will be the Whole Leaf Extract**.

There is little doubt that this subject will be investigated more fully in the coming years and more information about the direct measurement of the biological activities of Whole Leaf Extract compared with the Gel will be very welcome. Detailed work to be done in the future is very likely to reveal that there are at least some important qualitative differences between the biological activities of Whole Leaf Extract and Gel. It is by no means impossible that Gel will be shown to be preferable in some particular applications.

Dosage And Usage Of Whole Leaf Extract

It should be noted here that manufacturers produce Whole Leaf Extract (a) at its natural strength (b) at various levels of concentrate produced by evaporation - typically from twice the natural strength to ten times or more and (c) dried powders produced from Whole Leaf Extract by evaporation followed by freeze-drying. Clearly all these products are active when manufacture is in good hands and the processes of evaporation and drying are conducted in ways sensitive to the known susceptibilities of the active ingredients of Aloe. This author considers that the natural strength of the product is too dilute for perfect convenience and it is certainly rather uneconomic for transport across the Atlantic. On the other hand very high levels of concentration are likely to show some significant losses in activity in processing. Hence, moderate concentrates designated from 2X to 10X, and varying according to trade terminology and jargon, can be well recommended. Some of the most suitable products for general use are likely to contain between 10,000 and 15,000mg per litre of methanol precipitable solids, MPS.

Whole Leaf Aloe Vera - Ancient Herb In New Form Delivers Proven Effects

By Keisuke Fujita, M.D., Ph.D.; Hidehiko Beppu, Ph.D.; Kaoru Kawai, Ph.D. & Kan Shinpo, Ph.D.
Institute of Pharmacognosy, School of Medicine, Fujita Health University - 1992

Originating along the Mediterranean coast, Aloe (Aloe arborescens Mill var. natalensis Berger) has served mankind through the ages, preventing disease in Alexander the Great's soldiers during military expeditions, curing the obstinate eczema of Chinese Tang dynasty poet, Liu Yu Xi, and treating some latter-day ills like gastric ulcers, cancer, as well as burns.

In ancient Greece Aristotle taught Alexander the Great about the efficacy of Aloe. The hero gave it to his soldiers to maintain their health on campaigns.

Liu Yu Xi recorded his experience with Aloe or "rokai" as it was known in Chinese medicine: "When I was a child, I suffered from obstinate eczema. I used various medicines, but they were ineffective. However, when I used Aloe, which a drug merchant recommended me, the eczema healed rapidly."

Our team recently assessed the effects of Aloe scientifically, using modern medical methods, and recorded its findings of Aloe's effects as an anti-inflammatory agent, gastric ulcer suppressant, blood glucose normalizer, anti-cancer treatment and Aloe's anti-inflammatory suppressant action on burn and injury aggravation.

The most common use of Aloe is to apply it to cuts and burns. Some readers may recall their grandmother picking Aloe, growing along the veranda, and applying its juice to a cut or burn, and feeling the rapid relief of pain.

In vitro demonstrations show that extracts from Aloe degrade bradykinin, a substance responsible for pain and inflammation after injury. Carboxypeptidase is the active ingredient of Aloe which produces the anti-inflammatory action.

Figure 1 *(not shown)* shows the back of rabbits with experimentally induced burns. The left picture shows a cross-section of the rabbit's back without Aloe treatment, while the right shows the back treated with Aloe. The untreated back tissue showed progression of inflammation into the subcutaneous lipid layer. The Aloe-treated back showed inflammation only in part of the epidermis.

Burns are known to progress along the following course: pain, redness and fever, edema, necrosis and dysfunction. Aloe suppressed the burn's aggravation by suppressing the pain and edema.

Figure 2
Suppression of edema
The size of edema is larger in Group A (without oral Aloe treatment) than in Groups B and C (orally treated with Aloe).

Aloe is effective not only when applied topically, but also when taken orally. Oral treatment is more effective because it acts on the affected tissue via blood vessels.

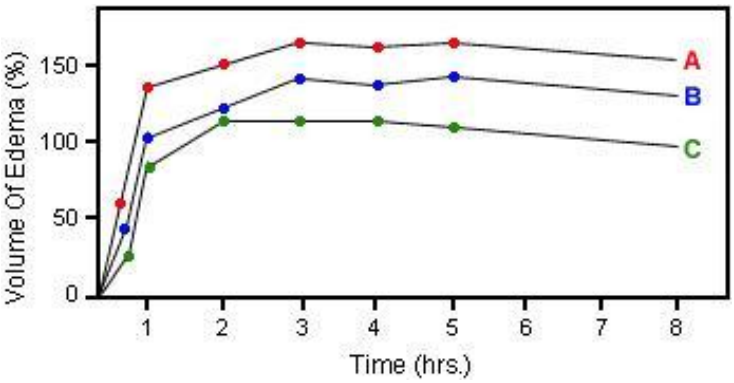


Figure 2 shows the effect of oral Aloe treatment on rats with experimentally induced foot burns. The rats were divided into three groups: Group A (rats without oral Aloe treatment) and Groups B and C (rats orally treated with Aloe). The size of edema was smaller in Groups B and C than in Group A. If grandmother had said "chew on this piece of Aloe," your wound would have healed more rapidly than with a topical application.

Group A: no oral Aloe treatment
Group B: oral treatment with Aloe extracts rich in ingredients of moderate molecular weights (10,000 to 50,000)
Group C: oral treatment with Aloe extracts rich in ingredients of higher molecular weights (over 50,000)

Effect On Gastric Ulcers

Aloe is also known to favorably affect the stomach and intestinal track. Gastric ulcers is a very common disease in our modern stress filled world. Aloe, which suppresses gastric ulcers, can be regarded as a household medicine for people who suffer from this disease.

Simply speaking, gastric ulcers is a condition where one's own gastric juice has digested the stomach. Gastric juice, primarily containing pepsin, is secreted from the stomach to digest food. Normally, gastric juice does not digest the stomach because of a protective layer of superficial membrane composed of neutral mucous cells shielding the gastric wall.

However, once a hole is created in this membrane due to stress or other causes, the pepsin digests the gastric wall, resulting in an ulceration.

Aloe first suppresses the action of pepsin itself, and then, a polysaccharide contained in Aloe promotes the repair of the protec-tive membrane.

Figure 3 *(not shown)* shows this effect. Gastric ulcers were experimentally induced in rats by occluding the pylorus (the exit of the stomach). If the pylorus is occluded, gastric juice cannot be eliminated from the stomach, and results in the onset of gastric ulcers. However, rats treated with Aloe did not develop gastric ulcers. Rats without oral Aloe treatment showed many gastric ulcers.

The lower two pictures show the cross section of the gastric wall. The surface of the gastric wall without oral Aloe treatment has been destroyed, and shows ulceration. The right picture shows the gastric wall in rats orally treated with Aloe.

Reduction Of Blood Glucose In Obese, Middle-Aged Diabetics

At the present time, people tend to eat excessively and get little exercise, factors that can be attributed to an increasing prevalence of diabetes mellitus. Aloe has been shown to be a highly effective treatment for diabetes.

There are two of diabetes mellitus: insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM).

In patients with IDDM, insulin is deficient, requiring daily insulin injection. On the other hand, NIDDM can be controlled with diet therapy without requiring insulin injections.

Obesity triggers NIDDM among people in age groups susceptible to adult diseases. Some strains of mice used to test Aloe's effect also developed NIDDM in the presence of obesity. We examined two such strains.

Figure 4 shows that in both strains of mice, Aloe injection reduced blood glucose level to a normal range (120 mg/dl) 8-12 hours after injection.

Additional studies focussed on testing Aloe's effects on IDDM induced mice.

Insulin is secreted from the beta cells of the islet of the pancreas. Treatment with streptozotocin (Sz) is known to destroy the beta cells causing diabetes mellitus. We experimentally induced IDDM in mice by Sz treatment, and then administered Aloe.

In this experiment, Aloe was given in two forms: Aloe A (superficial green-colored portion of Aloe leaf) and Aloe B (the inner white-colored fleshy portion of Aloe leaf). Both Aloe A and Aloe B reduced blood glucose level to a normal range.

Figure 4
Normalization of blood glucose level
Blood glucose level normalized in diabetic rats 8-12 hours after Aloe treatment.

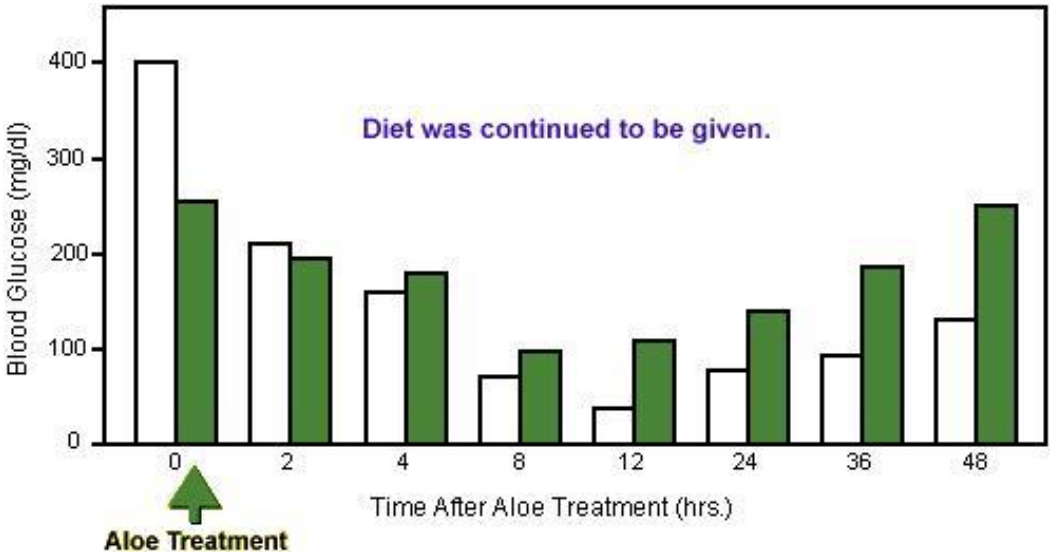


Figure 5 *(not shown)* shows micrographys of the islet. In mice treated with Aloe A, the islet remained intact, and beta cells were preserved. This is probably because the active ingredient derived from the superficial Aloe leaf, protected beta cells from Sz or promoted the normalization of degenerated beta cells.

In mice treated with Aloe B, the islet and the beta cells were destroyed, resulted in the insulin-secreting dysfunction. However, these mice also showed normalization of blood glucose level. This is probably because Aloe B contains a substance which reduces blood glucose level, like insulin.

At the present time, the leading cause for blindness is diabetic retinopathy. In view of this fact, the effects of Aloe are highly promising.

Suppression Of Precancerous Lesion

The greatest theme of 21st century medicine is to overcome cancers. Allegorically speaking, it is a military expedition, led by Alexander the Great, that continues toward the goal of defeating cancers, with Aloe a potent soldier in the expedition.

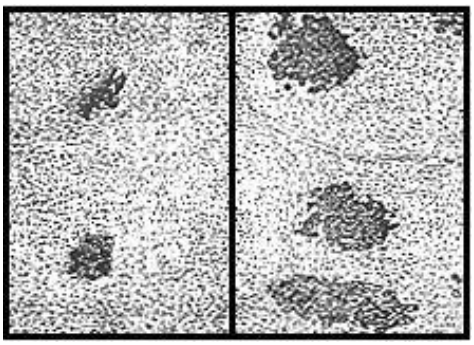
Canceration is known to involve two steps. First, an initiator acts in the genes of cells, causing mutation (precancerous lesion). Subsequently a promoter enhances the proliferation of these cells, leading to the onset of tumors. Tests showed that Aloe suppressed the formation of precancerous lesions by initiators.

If an agent called DEN is administered to rats, their liver develops precancerous lesions, the size of which was reduced by oral Aloe treatment.

Figure 6 compares the size of precancerous liver lesions (black areas) between Aloe-treated rats and untreated rats. The difference is clear.

When the effect of Aloe in preventing canceration was examined by administering it before DEN treatment, Aloe appeared to have some potential for preventing canceration.

Figure 6
Suppression of precancerous lesions
The size of precancerous lesions was reduced in the Aloe-treated group (left), when compared to the untreated group (right).



In daily life, initiators and promoters of cancer are contained in tobacco, food additives, air pollutants, scorched fish, etc. However, it is impossible to completely avoid such foods or factors. It is, therefore, reasonable to utilize the effect of Aloe, etc., in parallel to the efforts of avoiding ingestion of such factors, for the goal of preventing cancers.

Although it is ideal to ingest raw Aloe, its bitter taste makes it difficult to take daily doses in such a form. For this reason, Aloe is often ingested in the form of heat-dried powder. However, if Aloe is heated, its active ingredients (anti-inflammatory carboxylpeptidase, and anti-ulcer glycoprotein and enzymes such as protease inhibitors) can be impaired, and be accompanied by an increase in aloin due to exposure to heat and oxygen.

Aloin is a potent laxative, but its excessive increase can aggravate gastric ulcers and diabetes. To avoid such problems, it is desirable to freeze-dry Aloe into a powder form. Freeze-dried Aloe powder was used in examining the anti-cancer effects of Aloe in rats.

Whole Leaf Aloe Vera
The External Use Of Aloes

By J. E. Crewe, M.D.
Minnesota Journal Of Medicine, October 1937

In 1935, Collins reported treating roentgen burns with the leaf of Aloe vera. About that time, I was interested in a case of palmar eczema. The lesions had been of long duration, had resisted every type of treatment and were painful and annoying. I obtained enough of the leaf for four applications, which I made on four successive nights. The leaves were split, the gelatinous surface applied to the palms and the material retained with bandages. At the end of the four treatments the lesions were healed and the patient had had no further trouble up to the time of the writing of this communication on December 20, 1936.

Further Clinical Experiences

Ointments are not generally used as surgical dressings but, in my experience, the results obtained and the ease with which the Aloes dressings were removed, without adhering or causing pain, seem to be points in favor of their use. As will appear, I used not only an ointment of Aloes, but also powdered Aloes. These preparations were applied in the routine of a general practice and on empiric grounds only. The reports of results will be faithfully, if briefly, recorded.

Ulcers On Amputation Stumps

I received a supply of the leaves from the Island of Aruba in the Dutch West Indies, and these I used in the treatment of several ulcers which had appeared, after amputation, on the stumps of the legs of a single individual. Because lymphedema had developed and the condition that was present resembled elephantiasis, amputation had been performed a second time, together with removal of some of the veins. The circulation in the stumps was poor, and in 1932 several large ulcers had developed. These had shown no inclination to heal under various kinds of treatment. On the left stump were three ulcers, one of which measured 5 by 13 cm.; the other two were about 3 cm. in diameter. On the right stump was a single, deep ulcer, also about 3 cm. in diameter. Within twenty-four hours after application of the leaf of Aloe vera, pain had practically disappeared and the edema was much reduced. The smaller ulcers healed in about two weeks, leaving practically no scar. The large ulcer made good progress but my supply of leaves became exhausted.

I had become much interested in the drug, and finding that the ordinary commercial powdered Aloes was prepared mostly by natives, who dried the pulp of the leaves in the sun, I thought this sun-dried product might retain the properties of the fresh leaf. I obtained a supply of Socotrine Aloes, the best grade of powdered Aloes. This I made into an ointment with a lanolin base and applied it to the large ulcer. The relief from pain and healing continued about as it had done when the fresh leaf had been applied. However, after several months there appeared to be little progress. I then discontinued this treatment and used hot packs, scarlet red ointment, balsam of Peru, calamine ointment and zinc oxide ointment, one after another. Healing not only stopped but the size of the ulcer seemed to be increasing. I returned to the Aloes ointment and also applied powdered Aloes; the latter seemed to be a little more effective than the ointment. At the present time* the large ulcer remains unhealed, and in the past few months has made little progress. It is now 5 cm. long and 3 cm. wide. Because of the bad circulatory condition, surgical treatment seems inadvisable.

**Note - August 11, 1937. The large ulcer has been completely healed for two months.*

Pruritus Vulvae

Seven cases of pruritus vulvae have been treated and in all but two the results have been satisfactory and prompt. Of the two cases in which the results were less satisfactory, in one the condition was of long standing and an obstinate vaginal discharge was present. Also, in this case there was persistent perspiration of the groins; the perspiration appeared to be irritating and was difficult to control. This patient, although much improved after two months, is still under treatment. She has had much relief from the itching and the skin has a much better appearance than before. Nevertheless, the irritating vaginal discharge is refractory. In the other of these two cases progress has been slow, but the condition has improved and the patient is still under treatment.

Of the cases of pruritus vulvae, the following one was particularly encouraging. The patient was sixty-four years of age. The condition was very severe and the skin about the vulva and down the inner aspects of the thighs was thick-ened and purplish. Considerable treatment had been ineffective. The woman was in a highly nervous state and was unable to sleep. When treatment was begun with the Aloes ointment, administration of sedatives was continued. The intense itching and burning was almost immediately lessened; in two weeks the skin had become practically normal in appearance and the irritation had been completely relieved.

Ulcers Of Advanced Mammary Carcinoma

A woman, eighty-six years of age, had a carcinoma of the left breast of one year's duration. Because of her age and for other reasons, the condition was considered inoperable. In March, 1936, a crater-like ulcer developed and became a little more than 3 cm. in diameter. The discharge was profuse and very foul-smelling. After various applications had been tried without effect, Aloes ointment was applied. In a few days both the discharge and the odor were controlled. Odor could not be detected more than a few centimeters anway from the lesion after removal of the dressing. The application was made on gauze and this was easily applied and easily removed twice daily. Granulation developed promptly and the crater-like ulcer became level with the surrounding tissue. This treatment was continued from the latter part of March until the patient died, December 11, of abdominal metastasis. During this time the tumor became larger and more nodular, but after the depression filled there was little change in the size or appearance of the ulcer.

Ivy Poisoning

A pregnant woman twenty-two years of age had small lesions on the wrists caused by poison ivy. However, almost the entire inner aspects of both thighs were equally involved as to area and degree. The irritation in these areas was violent and inflammation and blebs caused much distress. A solution of potassium permanganate was applied to the right thigh and the woman was given some of the solution with which to continue treatment at home. To the left thigh Aloes ointment was applied liberally and the area was covered with gauze. The patient lived in the country, but she returned as directed on the second day. The lesions on the thigh that had been treated with potassium permanganate had somewhat dried but were still inflamed and very uncomfortable. The left thigh, to which Aloes ointment had been applied only once, had caused but little discomfort and the skin was normal in appearance, with the exception of a little remaining moisture and redness where the blebs had been. The patient was given ointment for the right leg also and was not seen again until her confinement two weeks later. She stated that the condition of both thighs had cleared up promptly.

Burns

A man, aged twenty-six years, had stepped into a pit containing boiling water emptied from a cooker in a canning factory. The injured foot and leg were scalded to within 8 cm. of the patella. Most of the outer layers of skin came off when the stocking was removed. Over the malleoli, burns extended through the entire integument. In a first aid station a proprietary ointment had been applied. In an effort to remove the ointment and dead skin, I applied, at first, warm, moist packs of solution of boric acid. On the following day, and thereafter, liberal applications of Aloes ointment were made. The patient had little pain and the dressings were easily removed. There was no evidence of infection. In ten days there were no raw areas, although the skin looked thin, red and shiny. The patient was dismissed and returned to work on the nineteenth day after the accident.

In another case, in which a large area had been scalded, and in several cases of moderate burn, treatment and results were similar.

Other Conditions

In addition to the cases cited, the ointment or powder was used in place of ordinary antiseptic substances in treatment of carbuncle, small infections and abrasions. In one case of "winter itch" also, a very dilute alcoholic solution was employed.

Unfavorable Effects In Three Cases

In one case of ulcer of the leg in which Aloes ointment was employed catharsis was present for one day. This may have been attributable to the Aloes. Because of possible absorption, therefore, Aloes probably should not be used on mucous surfaces, such as those of the vagina, except with caution.

Moreover, in two cases of psoriasis, there developed what appeared to be allergic erythema bordering the original patches. With the exception of these cases, I have not seen any untoward results from the use of the ointment or the powder.

Ancient And Modern Uses Of Aloes

(Please note: this was written in 1937)

The drug has maintained a place in the history of medicine since the time of King Tutankhamen, 4,000 years ago. It was known to the ancient Egyptians, is mentioned in Arabian medicine, and was employed down through biblical times and the dark ages to modern times. Aloes is used but little at present in the United States, except by veterinarians; nevertheless in the Twenty-second United States Dispensatory six pages are devoted to it. In former times Aloes was said to be useful in amenorrhea and as an abortifacient. It has long been used as a stimulant to the lower bowel in constipation and as a general tonic. It is mentioned as being useful in the treatment of abrasions, fissures, and so forth, and is a component in the official compound tincture of benzoin. Aloes was formerly used as an embalming agent and perhaps was one of the substances used by the ancient Egyptians in their now lost art of embalming. In the Bible, John 19, verses 39 and 40, is the following passage: "And there came also Nicodemus, and brought a mixture of myrrh and Aloes, about an hundred pounds. Then they took the body of Jesus and wound it in linen clothes and the spices, as the manner of the Jews is to bury."

The fresh leaf of the plant is still used by the natives of various countries. The Seminole Indians in the Everglades of Florida use it for treatment of wounds and burns. A friend from South Africa reported to me that the natives there used the leaf for treatment of sores and wounds. Another friend has told me that he has often seen it used by the peasants in southern Italy for treatment of ulcers, wounds, and so forth, and that he himself has used it for severe sunburn with great relief.

The Plant And Its Preparations

The genus Aloe embraces about a hundred species, which grow from a few centimeters in height to plants 6 meters high. The leaves of Aloe vera somewhat resemble the leaves of the century plant. They are about 40 cm. long and are dark green; sometimes they are mottled with brownish spots. The leaves are flat on the upper surface and convex on the under surface and the margins are armed with reddish thorns. The base of the leaf is about 1.5 cm. thick. The integument is thin and fibrous and the interior of the leaf is filled with a gelatinous substance resembling lemon gelatin.

The plant grows widely in warm countries. It is found wild and is cultivated in countries bordering the Mediterranean Sea and in India, Africa, China, and the Islands of the Indian Ocean. It is cultivated in many of the Islands of the West Indies, especially in Barbados, Curaqao and Aruba, and it is found in Mexico and Florida. I have not seen mention of its cultivation in any of the Pacific regions.

The various commercial products are named principally from the localities where they are produced. Socotrine Aloes, made principally from the species Aloe perryi, but also from Aloe vera, comes from the Island of Socotra in the Indian ocean. Barbados and Curacao Aloes are produced mostly from the species Aloe vera, which is grown on various islands in the West Indies. There are many other kinds of Aloes which are known by the following descriptive adjectives: “Cape,” “Natal,” “Zanzibar,” “Aganda” and “Crown.” Besides the preparation from Aloe vera and Aloe perryi, a number of preparations, mostly inferior, are made from other species and are official in the United States Pharmacopeia.

Because commercial Aloes, it is said, is prepared principally by natives, who remove the jelly-like interior of the leaves and dry it in troughs or other containers in the sun, it often contains much foreign matter. For this reason, in the United States Pharmacopeia it is advised that a purified Aloes be made by dissolving the powder in alcohol and then straining and drying the filtrate. I have used the crude powder, as I said before, because I thought some of the properties might be impaired by the alcoholic treatment.

Owing to the fact that there are so many varieties of commercial Aloes, it seems possible that the results may not always be uniform. The material I have used has been the best grade of Socotrine Aloes, and the results have been fairly uniform. The ointment which I made contains 1 drachm (4 gm.) of powdered Aloes and 1 drachm of calamine to the ounce (30 gm.) of white petrolatum. The calamine forms a sort of paste and makes the ointment more adherent. The dusting powder which I also have said that I used in some cases, has not caused any irritation or other undesirable effects.

Summary

The fresh leaves and the Aloes ointment and the powder appear to have the following properties:

1. They relieve pain, burning and itching.
2. They have some sort of antiseptic action. Infected lesions quickly become clean and exude little or no pus.
3. They seem to stimulate rapid granulation and formation of new tissue so that denuded areas appear to heal more rapidly than with other agents. They are effective in eliminating the foul odors that accompany infection of broken down carcinomas, ulcers and so forth.

Whole Leaf Aloe Vera
Aloes In The Treatment Of Burns And Scalds

By J. E. Crewe, M.D.

Minnesota Journal Of Medicine, August 1939

**Read before the Olmsted-Houston-Fillmore-Dodge County Medical Society, January 6, 1938.*

Recent medical literature contains many excellent articles on the treatment of burns. While numerous methods have been mentioned, in those most generally accepted, tannic acid is employed. In Bettman's treatment, tannic acid is applied in a spray, and this is followed by application of 10 per cent silver nitrate. Apparently, this sequence has distinct advantages over the use of tannic acid alone. Good as these methods are, I have experienced annoyance from infection, and from the long period required for separation and removal of the coagulum in some cases in which I have used tannic acid. It has been a relief to me, therefore, to find a treatment which has eliminated these disadvantages. This method has proved so simple and the results have been so satisfactory, that I have not used any other treatment for burns since the spring of 1935.

Author's Method

I employ an ointment of which the active ingredient is Socotrine or Barbados Aloes. The ointment is made by mixing 2 drams of the powdered Aloes and about 2 drams of mineral oil in an ounce of white vaseline. If mineral oil is not used the ointment is a little too stiff.

The usual precautions in regard to contamination and infection are taken. The affected area is cleaned as thoroughly as possible and, in some instances when the area is badly soiled, a preliminary application consists of warm moist dressings. These dressings are saturated in a solution composed of a teaspoonful each of borax and sodium chloride dissolved in a quart of water. If the burned area is fairly clean and a greasy substance has been used in first aid treatment, it is not necessary to remove all the grease as it will mix with the ointment that is to be applied.

Blisters are carefully protected and the serum is evacuated with a hypodermic needle, after which a small amount of Mercurochrome is injected into each collapsed vesicle. Mercurochrome is used because of its color, and only enough is injected to cover the floor of the emptied vesicle. If the blisters are torn or the burn is deep, Mercurochrome is applied with a cotton swab. Mercurochrome has been omitted in treatment of small burns, and they have remained as free of infection as those in which it has been employed. Perhaps the added precaution of its use is unnecessary.

When this preliminary treatment has been completed, sterile gauze is folded in about four thicknesses, to make an area large enough to cover the burn. If the burn is too large to be covered by one piece of gauze, or if it is in an area where a single piece would not fit snugly, more than one piece can be applied. The gauze is laid on a smooth, sterile towel and is covered with a layer of ointment at least 1/8 inch thick. This dressing is laid, ointment side down, on the burned area. More gauze may be placed on this dressing and the whole held in place with bandages or other material. No attempt should be made to spread the ointment on the burn, because it will not adhere readily to the raw surface.

Ordinarily, this dressing is not removed for two days. At the end of that time, the entire dressing can be removed as easily as a piece of wet writing paper is lifted from the top of a table. There is no sticking from dried serum or dried blood. The surface of the wound does not bleed but has a clean, glazed appearance, as if the area were covered with a thin, transparent film. Unless new blisters have formed, another dressing, prepared as before, is applied and each dressing is left in place for two days. Usually, only from four to six dressings of Aloes ointment will be required. Then zinc stearate or some other bland dressing may be applied.

Illustrative Cases

It must be stated that, in the period that has elapsed since I have been using the treatment that has been described, I have not encountered any burns of sufficient severity to endanger life. There is no reason to believe, however, that good results might not be obtained by this method in treatment of more extensive burns.

Case 1 A man stepped into a pit containing boiling water which had just been released from a pressure cooker in a canning factory. The leg, as high as the knee, was immersed in the water. Few blisters were encountered because most of the epidermis adhered to the patient's underclothing and stockings when they were removed. In areas the size of a silver dollar, over the maleoli, the burn completely penetrated the integument. Treatment such as has been described was applied and the patient returned to work on the nineteenth day after the injury.

Case 2 A girl, sixteen years of age, spilled boiling water over her feet. The very severe scald involved most of the surface, except the soles, of both feet to above the ankles. This patient lived in the country and came to the office for treatment only four times, on alternate days. The feet were coated with lard when she first was seen. Results from the treatment which has been outlined were satisfactory.

Other Cases Two infants suffered smaller burns on the face, arms and chest, by falling against heating stoves. Dressings were easily applied because their application and removal were painless.

Two patients, with severe sunburn involving the shoulders and most of the back above the waist, both complained bitterly of pain when they came for treatment but they suffered practically no pain after the first dressing was applied. Only two dressings with the ointment were required. Then zinc stearate was applied.

Comment

My interest in Aloes for the treatment of cutaneous conditions began some years ago. I have reported some experiences with this substance. Originally, I treated chronic ulcers and some skin diseases with the fresh leaf of Aloe vera, obtained from Florida and the island of Aruba in the Dutch West Indies. However, it was difficult to obtain and preserve the fresh leaves and, after trial of ointments made in various ways, the two ointments that have been described were adopted. That made from Socotrine Aloes is dark brown, and that made from Barbados Aloes, nearly black. The dark color of Aloes ointment is a disadvantage because it soils the dressings and unbroken skin, but not more so than the various dyes and other colored substances which are used in treatment. Surfaces where the ointment has been applied can be cleaned with benzine and the residue can be removed with rubbing alcohol.

Aloes, used either as the leaf or ointment, possesses distinct analgesic qualities. Removal of ointment dressings, as has been said, is painless. Dense, white scar tissue is not seen after healing of burns but the

burned areas are reddish at first and remain smooth and pliable. Healing is rapid. Aloes possesses some enzymotic action; pus is apparently digested for purulent surfaces become clean. The drug is astringent, possibly because of the tannin it contains. It has styptic properties in fresh cuts, when applied as a powder. Antiseptic properties are indicated by the rapid clearing up of infected surfaces. When burns are treated by the method that has been outlined, infection is negligible.

It might be feared that absorption would give rise to unpleasant effects but I have noted no evidence of absorption. Stools have not been loose in any case. No undesirable effect was seen when powdered Aloes was dusted in full strength, daily for a number of days, over the entire surface of large, chronic ulcers. Aloes is reputed to have abortifacient action but in treatment of one woman, eight months pregnant, the ointment was used for severe and extensive dermatitis caused by poison ivy and there was no evident effect on the uterus. Another woman four months pregnant, was treated with Aloes ointment for severe pruritus vulvae, without any untoward effect.

That this is not one of those measures which seems effective only in the hands of the one who advocates it is evident in the results which Collins and Wright have obtained with Aloes in the treatment of roentgenologic injuries.

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Aloe's Effectiveness As An Anti-Inflammatory Agent

By Hiroko Saito, Department Of Pharmacy
Aichi Cancer Center - 1993

Aloe has long bee effective as an anti-inflammatory, so an investigation was undertaken to determine whether Aloctin A inhibits adjuvant arthritis in rats and carrageenin induced edema in rats. Aloctin A is a glycoprotein isolated by ammonium sulphate precipitation, pH dependant isolated and gel filtration from Aloe arborescens Miller.

Previous publications have demonstrated that Aloctin A inhibits the growth of methylcholanthrene-induced fibrosarcoma in vivo with the mechanism appearing to be host related. Since Aloe arborescens Miller has been used as an anti-inflammatory in folklore medicine its effect on adjuvant arthritis and carrageenin-induced edema was examined. The model used for adjuvant arthritis was developed by Newbould, and the carrageenin-induced edema used the method of Winters et al.[1, 2]

Adjuvant Arthritis Formation And Compound Treatment

Indomethacin, prednisolone carrageenin, liquid paraffin and heat killed Mycobacterium butyricum were used. The Aloctin A was prepared according to the method of Suzuki et al.[3] The arthritic syndrome was induced in Sprague Dawley rats by an intradermal injection of 0.10 ml of liquid paraffin containing 0.6 mg of heat killed Mycobacterium into the interplantar surface of the right hind foot. The compounds to be tested were administrated either orally or intraperitoneally each day for 15 days beginning one day prior to the injection of the phlogistic agent into the foot.

In the preliminary investigation, the oral administration of Aloctin A did not affect adjuvant arthritis at the doses tested in this experiment.

Aloctin A was suspended in 0.9% sodium chloride, and was administered intraperitoneally through this investigation. The Indomethacin and prednisolone in an aqueous suspension were administered by gastric gavage. The control animals received adjuvant but no drug. The body weight and foot volumes were recorded at regular intervals.

Edema Formation And Compound Treatment

Edema was induced in the hind paw of the rats by a sub-cutaneous injection of 0.05 ml of 1% carrageenin solution in 0.9% sodium chloride. The Aloctin A suspended in 0.9% sodium chloride was administered intraperitoneally 30 minutes prior to the injection of the phlogistic agent. Indomethacin in aqueous suspension was administered by gastric gavage.

The volume measurements were made immediately prior to and at one, three, four, and five hours after injection of the phlogistic agent. The volume measurement was determined by the water displacement method. The effects of the compounds were expressed in terms of percent inhibition in the swelling volume of the control animal versus the treated animals.

The results in Table 1 clearly show that Aloctin A at all dose levels effectively suppressed the swelling of adjuvant arthritis, with the optimal dose level being 5 mg/kg/day. The activity of Aloctin A given intraperitoneally appeared to be higher than that of indomethacin given p.o., and was nearly equal to prednisolone given p.o. During the course of this experiment no side reactions of Aloctin A were noted.

Table 1

Effect of Aloctin A, Indomethacin and Prednisolone on arthritis induced in rats by mycobacterial adjuvant.

Compound	Daily Dose (mg/kg)	Route	B.W. Gain Day 0-21 (g +/- S. E.)	Inhibition (%) Injected Hind Paw Day 14	Inhibition (%) Injected Hind Paw Day 21	Inhibition (%) Secondary Lesion Day 14	Inhibition (%) Secondary Lesion Day 21
	0.5	i.p.	15 +/- 12	14.4	9.3	28.4	17.4
	2.5	i.p.	35 +/- 9	39.3	27.0	23.9	30.3
Aloctin A	5.0	i.p.	45 +/- 8	57.2	56.6	43.3	72.3
	7.5	i.p.	5 +/- 1	49.4	29.5	39.3	-2.3
	10.0	i.p.	5 +/- 1	22.6	4.6	28.6	-5.3
Indomethacin	2.0	p.o.	-10 +/- 7	38.1	23.9	12.1	-1.2
Prednisolone	2.0	p.o.	0 +/- 1	58.3	43.2	82.2	35.7
Control			10 +/- 9	0	0	0	0

Six rats per group were used.
Each value of Inhibition (%) is average of six rats per group.

Aloctin A showed marked inhibition of edema in the carrageenin foot paw swelling assay (Table 2). When Aloctin A was given intraperitoneally 30 minutes prior to the injection of the carrageenin, a marked inhibition of edema was observed three hours after the injection. The effect of Aloctin A showed a dose-response relationship up to 10 mg/kg.

Table 2

Effect of Aloctin A and Indomethacin on swelling of rat hind paw induced by carrageenin.

Compound	Dose (mg/kg)	Route	Inhibition (%) 1	Inhibition (%) 3	Inhibition (%) 4	Inhibition (%) 5 (hr)
Aloctin A	0.5	i.p.	10.2	32.3	36.0	26.4
	1.0	i.p.	10.8	66.5	64.2	55.8
	5.0	i.p.	12.5	50.8	55.6	59.2
	7.5	i.p.	4.8	89.2	88.0	94.6
	10.0	i.p.	2.2	92.8	93.4	95.3
Indomethacin	0.5	p.o.	-14.4	18.8	19.2	29.5
	1.0	p.o.	-28.5	32.6	41.5	40.8
	2.0	p.o.	12.5	59.5	63.4	59.0

Each value is mean of six rats per group.

The present experiments demonstrated that Alotin A inhibits adjuvant arthritis and carrageenin-induced edema in rats. Alotin A is a new type of anti-inflammatory. Anti-inflammatory drugs reported to date are classified as steroids, non-steroids, immunosupressive drugs and antiphlogistic agents, whereas Aloctin A is a glycoprotein. Further studies are needed to construct a reasonable hypothesis for the mode of action of Aloctin A.

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Antiarthritic Activity Of Anthraquinones Found In Aloe Vera For Podiatric Medicine

By Robert H. Davis, Ph.D.; Patrick S. Agnew, B.S. & Eugene Shapiro, B.S.
Journal Of The American Podiatric Medical Assoc., Vol 76, Number 2, February 1986

Rheumatoid arthritis is a painful and crippling systemic disease for which there is no cure. The best experimental model for studying rheumatoid arthritis in humans is the adjuvant-induced arthritis in rats. One of the group of compounds found in Aloe is the anthraquinones. These substances have been recognized for their use in veterinary medicine against inflammation. The authors evaluate the anti-inflammatory and antiarthritic activity of anthraquinone, anthracene, cinnamic acid, and anthranilic acid found in the Aloe vera plant, and show what contribution each ingredient makes toward the total activity found in Aloe.

In previous studies, the authors have shown that Aloe gel extract has anti-inflammatory and antiarthritic activity.[1] Combinations of Aloe with ascorbic acid, thymus extract, and RNA significantly improved the activity.[2] The chemical makeup of Aloe holds a valuable key to antiarthritic activity that could be used by podiatrists to treat patients.[3] Elements in Aloe gel include lignin, saponins, anthraquinones, inorganic ingredients / minerals, vitamins, enzymes, and amino acids. Anthraquinones such as anthracene have been recognized for their use in veterinary medicine against inflammation. They possess anti-inflammatory, analgesic, and tissue repair properties.

No doubt anthraquinones have a bearing on the healing and pain-killing effectiveness of the fresh leaf gel. Few people understand the meaning of the anthraquinone complex in Aloe. Many studies verify the successful treatment of burns, ulcers, and dermatitis, but no one knows why Aloe has these healing qualities.[5] The authors propose to test the antiarthritic and anti-inflammatory activity of anthraquinone, anthracene, cinnamic acid, and anthranilic acid in an adjuvant arthritis model in order to determine if there are possible ingredients that can be used to treat rheumatoid arthritis. This approach will help us understand the antiarthritic activity of Aloe. The purpose of this study is to determine, in part, the active elements in Aloe so as to unlock the mystery of the gel. Many medicines in common use today, such as digitalis and quinidine, were derived in a similar way from barks and leaves.

Materials And Methods

Adult male Sprague-Dawley rats (175 to 200 gm, 12/group) were injected with heat-killed *Mycobacterium butyricum*. The bacteria were suspended in light mineral oil at 5 mg/ml. Under ether anesthesia, two groups of rats were injected in their right hind paw with 0.1 ml of oil. All the other groups were injected with the suspended bacteria. Six hours after the injections, the day 0 measurements were taken. Two experiments were conducted together. One study investigated the effect of anthraquinones on the prevention of adjuvant arthritis. The other study determined their effect on established adjuvant arthritis. Three control groups were used. The animals injected with oil alone were used to be sure that the oil, itself, did not cause swelling. One of the groups injected with adjuvant was also injected with distilled water at the same times and amounts as those groups being treated. This was done to determine whether the volume and frequency of injections affected the amount of swelling. A third group was injected with the adjuvant.

In the first experiment, prevention of adjuvant arthritis by anthraquinones was studied. The right hind paws of two control groups were injected with the adjuvant, and day 0 paw volume measurements were taken. One of the control groups was injected with 10 ml of water subcutaneously daily for 13 days beginning on day 0. Either anthraquinone, anthracene, cinnamic acid, or anthranilic acid was injected into rats in four other groups that had received *M. butyricum*. Each day the anthraquinones were injected subcutaneously at 150 mg/kg aqueous suspensions.

In the regression study, the rats were injected with *M. butyricum* suspension. The symptoms of adjuvant arthritis usually take from 14 to 21 days to develop. After 21 days, treatment was initiated with 150 mg/kg suspensions of anthraquinones subcutaneously daily from day 21 through day 33.

Adjuvant arthritis in rats manifests itself by swelling in all paws, especially the hind paws, gonads, and ears. A water plethysmograph was used to monitor the hind paw volume. The plethysmograph was at zero prior to each reading while maintaining constant sensitivity to obtain consistency. Edema in the injected (right) hind paw was considered to be inflammation caused by trauma. Prolonged inflammation in this paw was maintained by the slow release of the *M. butyricum*. Any edema in the left paw was considered to be an immunological phenomenon.[6,7]

The rats were anesthetized with ether on paw-measuring days. Their hind paw volumes were determined by dipping them into a fluid-filled cell up to the anatomical hair line. Day 0 measurements were taken 6 hours after the paws were injected with *M. butyricum* adjuvant or oil alone. This initial measurement was used as a reference from which units of edema were calculated in the prevention study. These units of edema were calculated by subtracting the day 0 volumes from those measured on days 7, 14, and 21. The base-line values for calculating units of edema in the regression study were measured on day 21. Day 21 values were viewed as 0 units of edema. The hind paws were measured on days 0, 21, 28, 35, and 38 for this study.

The animal's body weight was measured on days 0 and 2l in both studies and day 38 in the regression study. The change in weight during the experiments was calculated by subtracting from day-38 weights in the regression experiment. The change in edema was divided by the change in weight to obtain a relative change in edema. This served to rule out any gain in paw volume caused by weight gain. A CU-5 Medical Land Camera was used to photograph representative rats on days 21 (prevention study) and 38 (regression study). This was done to demonstrate the difference in paw edema between the rats receiving anthraquinones and the control rats. Mean paw volumes and body weights were recorded for all animals. Standard errors were determined by using the formula $SE = E\,d^2/N(N - 1)$. The deviation of individual values from the mean is Ed^2, and $N - 1$ represents the degrees of freedom.

Results And Discussion

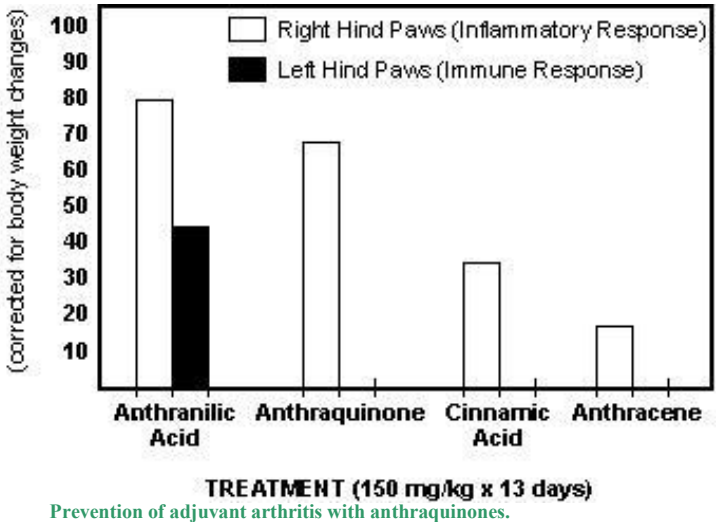
Prevention of Arthritis. Aloe has antipyretic and anti-inflammatory activity that has been used to treat burns and skin conditions over the years. Splitting the leaves of Aloe and applying the gel directly to burns produces beneficial effects.[8] The curative principle occurs within the pulp and rind of the leaf.[9] The authors have administered fresh Aloe leaf extract to prevent or regress adjuvant arthritis. Aloe extract produced a 48% inhibition of inflammation and a 72% inhibition of the immune response (the arthritis) when 150 mg/kg of Aloe extract was administered subcutaneously, daily, over 13 days as preventive measure.[1]

The anti-inflammatory and antiarthritic activity of the anthraquinones were tested to determine if they could prevent the formation of arthritis. An increase in volume of the right hind paw is an anti-inflammatory response to the presence of the adjuvant, whereas the swelling of the left hind paw is an autoimmune response, in part, against the animal's own cartilage. *Mycobacterium butyricum* is similar to cartilage so that the immune response attacks both. Swelling occurs in both hind paws injected with adjuvant. This swelling continues to increase over the entire experimental period. Aqueous controls

received equal amounts of water injections as those receiving injections of anthraquinone. Since these animals swelled somewhat more than those receiving the adjuvant, the volume or the trauma of daily injections contributed to the disease process. In order to more accurately estimate the effect of the compounds under investigation, the response of anthraquinones was compared to the aqueous injected adjuvant controls.

Forst and Davis[10] have shown that anthranilic acid has antiarthritic activity. This compound is present in Aloe and was considered as an activity internal control so that the authors could be certain that the responses recorded in the study were real and not phantoms. Edema in the right hind paw (inflammation) was 40% less than the aqueous adjuvant control animals on day 21 *(Table 1; Fig. 1)*. The left hind paw (immune) was 35.5% less than the controls. The percentage of inhibition by anthranilic acid corrected for body weight was 79.7% in the inflammatory paw and 42.4% in the immune paws. Tryptophane, an active anti-inflammatory compound, is produced from anthranilic acid. Previous work showed that tryptophane inhibited arthritis 75% in the immune paw.[10] Anthranilic acid may work through tryptophane.

Figure 1



Prevention of adjuvant arthritis with anthraquinones.

Table 1

Prevention of Adjuvant Arthritis with Anthraquinones in Rats[a,b]

	Protocol	Aqueous Adjuvant Control[c]	Anthraquinone	Anthracene	Cinnamic Acid	Anthranilic Acid
	Treatment (mg/kg x 13)					
	Days 0 to 12		150	150	150	150
	Number of rats	12	12	12	12	12
	Final body weight (g)	254 +/- 12	249 +/- 12	271 +/- 13	261 +/- 9	275 +/- 5
	Edema of hind paws (volume units +/- SE)					
Day 7	Left	1.59 +/- 0.05	1.59 +/- 0.08	1.49 +/- 0.04	1.50 +/- 0.04	1.40 +/- 0.04
	Right	2.59 +/- 0.10	2.28 +/- 0.16	2.41 +/- 0.12	2.41 +/- 0.08	2.41 +/- 0.09
Day 14	Left	1.62 +/- 0.19	1.54 +/- 0.06	1.61 +/- 0.11	1.72 +/- 0.09	1.52 +/- 0.05
	Right	2.38 +/- 0.21	2.53 +/- 0.22	2.43 +/- 0.18	2.41 +/- 0.09	2.22 +/- 0.08
Day 21	Left	0.53 +/- 0.12	1.11 +/- 0.16	0.80 +/- 0.06	0.66 +/- 0.08	0.34 +/- 0.11
	Right	1.56 +/- 0.32	1.42 +/- 0.19	1.82 +/- 0.19	1.26 +/- 0.13	0.93 +/- 0.12
	Percent inhibition[d]					
Day 21	Left		-10.90	-50.90	-23.80	35.50
	Right		9.00	-16.70	19.20	40.20
	Relative weight ratio of hind paws					
	Relative change in volume[e]					
	Left	0.700	-0.214	-0.178	-0.146	0.297
	Right	1.142	0.802	0.021	0.381	0.950

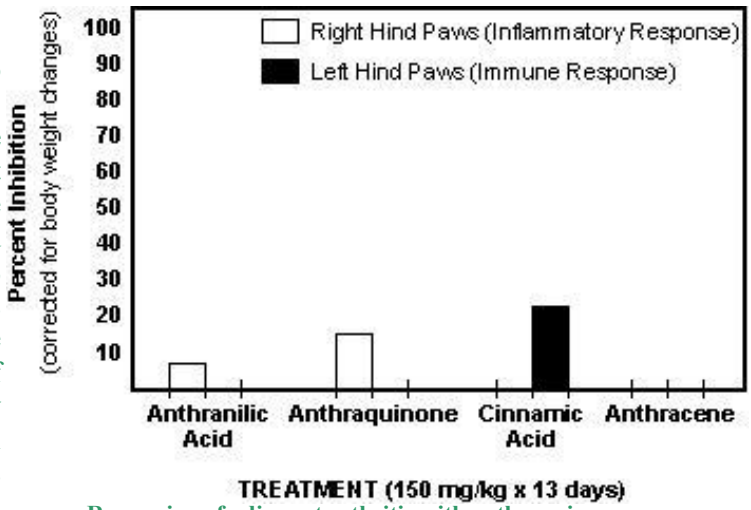
Percent inhibition[d]					
Left	-30.6		-25.4	-20.9	42.4
Right	67.3		17.6	32.0	79.7

a Initial body weight, 170-185 g.
b Symbols: +/-, standard error; and the negative value (-, minus) means swelling. *c* Adjuvant arthritis with 0.1 mg/kg H_2O x 13, day 0-12.
d Percent difference from aqueous adjuvant controls.
e $\frac{\text{Change in hind paw vol. aqueous adjuvant}}{\text{Change in body weight}} - \frac{\text{Change in test paw vol.}}{\text{Change in body weight}}$ = Relative change in volume.

Anthraquinone had the most preventive antiarthritic activity recorded of the three Aloe compounds tested. Anthraquinone inhibited inflammation 67.3%, which was the largest response next to anthranilic acid. Anthracene had no antiarthritic activity, but a 17.6% inhibition of inflammation was obtained in the inflammatory paws. This is about one third the effect seen with anthraquinone and anthranilic acid. A good positive anti-inflammatory response was also obtained with cinnamic acid (32.0%).

Regression of Arthritis. Anthranilic acid had no antiarthritic activity in the regressive phase, unlike its ability to prevent the onset of the disease *(Table 2; Fig. 2)*. On the other hand, anthraquinone showed anti-inflammatory activity, but exhibited no anti-immune response in the regression phase. Cinnamic acid exhibited no anti-inflammatory effect, but a 17.3% regression of the immune response was recorded. This is somewhat opposite to the effect measured against prevention of arthritis. Since the anthraquinones show activity that helps to explain the overall response seen with Aloe, future studies should evaluate other ingredients such as amino acids, enzymes, vitamins, and saponins.

Figure 2



Regression of adjuvant arthritis with anthraquinones.

Table 2

Regression of Adjuvant Arthritis with Anthraquinones in Rats[a,b]

Protocol		Aqueous Adjuvant Control[c]	Anthraquinone	Anthracene	Cinnamic Acid	Anthranilic Acid
Treatment (mg/kg x 13)						
Days 0 to 12			150	150	150	150
Number of rats		12	12	12	12	12
Final body weight (g)		333 +/- 12	315 +/- 8	320 +/- 14	329 +/- 16	336 +/- 9
Edema of hind paws (volume units +/- SE)						
Day 28	Left	1.67 +/- 0.13	1.71 +/- 0.14	1.80 +/- 0.12	1.62 +/- 0.09	1.67 +/- 0.05
	Right	3.07 +/- 0.78	2.61 +/- 0.25	3.38 +/- 0.26	3.13 +/- 0.30	3.00 +/- 0.29
Day 35	Left	1.76 +/- 0.14	1.84 +/- 0.18	1.89 +/- 0.12	1.74 +/- 0.11	1.77 +/- 0.11
	Right	3.41 +/- 0.27	3.00 +/- 0.25	3.69 +/- 0.29	3.91 +/- 0.44	3.52 +/- 0.32
Day 38	Left	0.65 +/- 0.09	0.80 +/- 0.10	0.87 +/- 0.36	0.52 +/- 0.06	1.53 +/- 0.12
	Right	1.63 +/- 0.15	1.26 +/- 0.13	1.96 +/- 0.16	1.82 +/- 0.17	1.65 +/- 0.19
Percent inhibition[d]						
Day 21	Left		-22.9	-34.4	-20.0	-135.0

Right	22.7		-22.2	-11.7	-1.2
Relative weight ratio of hind paws					
Relative change in volume[e]					
Left	-0.157	-0.193	0.072	-0.530	0.297
Right	1.038	0.138	-0.323	-0.159	0.020
Percent inhibition[a]					
Left		-37.0	-46.5	17.3	-127.7
Right		13.3	-31.1	-15.3	1.9

a Initial body weight, 170-185 g.

b Symbols: +/-, standard error; and the negative value (-, minus) means swelling.

c Adjuvant arthritis with 0.1 mg/kg H_2O x 13, day 0-12.

d Percent difference from aqueous adjuvant controls.

e $\frac{\text{Change in hind paw vol. aqueous adjuvant}}{\text{Change in body weight}} - \frac{\text{Change in test paw vol.}}{\text{Change in body weight}}$ = Relative change in volume.

Summary

Anthraquinones found in Aloe may be responsible for the healing properties and anti-inflammatory activity recorded. This study has shown both anti-inflammatory and antiarthritic activity that can be improved by combining Aloe with ascorbic acid, thymus extract, and RNA. Since the chemical composition of Aloe holds a valuable key to its activity, the antiarthritic and anti-inflammatory activity of the anthraquinone complex in the adjuvant arthritis rat were tested. Anthraquinone and cinnamic acid exhibited anti-inflammatory activity in the prevention study. Anthranilic acid prevented inflammation as well as arthritis. Both anthraquinone and cinnamic acid exhibited activity in the regression phase. This work proves that the anthraquinone complex contributes to the healing properties of Aloe.

References

Aloe Vera And Gibberellin Anti-Inflammatory Activity In Diabetes

By Robert H. Davis, Ph.D. & Nicholas P. Maro
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Abstract

Aloe vera inhibits inflammation and adjuvant-induced arthritis. The authors' laboratory has shown that Aloe vera improves wound healing, which suggests that it does not act like an adrenal steroid. Diabetic animals were used in this study because of their poor wound healing and anti-inflammatory capabilities. The anti-inflammatory activity of Aloe vera and gibberellin was measured in streptozotocin-induced diabetic mice by measuring the inhibition of polymorphonuclear leukocyte infiltration into a site of gelatin-induced inflammation over a dose range of 2 to 100 mg/kg. Both Aloe and gibberellin similarly inhibited inflammation in a dose-response manner. These data tend to suggest that gibberellin or a gibberellin-like substance is an active anti-inflammatory component in Aloe vera.

Aloe vera inhibits inflammation and adjuvant-induced arthritis.

Aloe vera inhibits inflammation and adjuvant-induced arthritis. The authors' laboratory has demonstrated that Aloe vera improves wound healing in a dose-response fashion, reduces edema and pain, but does not decrease the granuloma tissue around a foreign substance under the skin.[1-3] This suggests that Aloe acts on an acute anti-inflammatory basis and does not act like a steroid.

Aloe vera is a clear mucilaginous gel within the leaf of the spiney Aloe barbadensis plant. Investigation of the chemical composition of the gel indicates that it includes minerals, vitamins, monosaccharides, polysaccharides, and enzymes. Other ingredients believed to be responsible for Aloe's healing powers are lignins, which, with cellulose, penetrate human skin; saponins, with antiseptic capabilities; and anthraquinones, which are believed to be a pain-related component.[4] The authors focus on the carbohydrate fraction of Aloe vera. Based on evidence in the literature and the authors' studies, the authors wondered if a main, active component in Aloe is glycoside. Corbin et al[5] found that indole acetic acid, a plant auxin, appears to have anti-inflammatory properties.

Diabetic animals were used in the study because of their poor healing and anti-inflammatory capabilities. Biochemical alterations in the microvasculature of diabetics make them vulnerable to injections and prolong the healing response.

The authors determine if gibberellin, a glycolic and growth hormone found in plants, could account for some of the anti-inflammatory activity Aloe vera possesses. The antiphlogistic activity of colorized (with anthraquinones) Aloe vera and gibberellin in streptozotocin-induced diabetic mice at 2, 20, and 100 mg/kg subcutaneously was determined by measuring the inhibition of polymorphonuclear leukocyte infiltration into a 2% gelatin-induced inflammation. The reduction of polymorphonuclear leukocyte cells at the site of inflammation is a standard technique to measure acute inflammatory activity.

Materials And Methods

Adult male ICR mice (20 to 30 g, eight animals group) were injected intraperitoneally with 200 mg/kg streptozotocin to induce diabetes. The streptozotocin (powder basis) was mixed into a solution with 0.9% saline. The control animas received injections. Five days later, two animals from each group, with the exception of the control groups, were randomly chosen to test for diabetes. Blood sugars were determined to certify that the animals were diabetic. Under ether anesthesia, all mice were shaven on one side. A marking pencil was used to outline an area the size of a nickel. Each animal was injected subcutaneously within this area with 0.2 cc of 2% gelatin (0.4% NaCl, 1% ethanol) solution to form a bleb. This was immediately followed by a second subcutaneous injection of 2, 20, and 100 mg/kg colorized Aloe vera or gibberellic acid A. The Aloe vera and gibberellin were injected into an area outside the designated circle. A nondiabetic and a diabetic control group each received saline injections in place of the gelatin irritant, as well as the Aloe vera or gibberellin. A third nondiabetic control group received the gelatin injection and saline in place of the Aloe vera or gibberellin.

The animals were killed 3 hr. following the second injection. Incisions were made along the indicated circumscribed area so that subdermal tissue could be removed and stained. Polymorphonuclear leukocyte infiltration in the circumscribed inflamed area was determined by staining the subdermal tissue with Wright stain. Three separate sections of each excised tissue were randomly chosen for viewing under a light microscope, high power. Mean and standard errors were calculated for polymorphonuclear leukocyte cell counts. The Student t-test was used to determine p values.[6]

Table 1
Comparison of Aloe vera & Gibberellin on Polymorphonuclear Leukocyte Infiltrationin Diabetic Mice[a]

Treatment	PMN Count Number/HPF[b]	p Value	Reduction (%)
Saline control	17.4 +/- 0.6		
Saline diabetic	10.8 +/- 0.5	<0.001	
2% Gelatin	28.4 +/- 0.8	<0.001	
+ Aloe vera 2 mg/kg	28.2 +/- 0.7	>0.5	0.7
+ Aloe vera 20 mg/kg	17.0 +/- 0.6	<0.001	40.1
+ Aloe vera 100 mg/kg	9.1 +/- 0.5	<0.001	68.0
Saline control	18.1 +/- 0.7		
Saline diabetic	9.5 +/- 0.6	<0.001	
2% Gelatin	28.3 +/- 0.5	<0.001	
+ Gibberellin 2 mg/kg	28.8 +/- 0.8	>0.5	0.0
+ Gibberellin 20 mg/kg	21.2 +/- 0.8	<0.001	25.1
+ Gibberellin 100 mg/kg	11.3 +/- 0.7	<0.001	60.1

[a] Eight animals/group.
[b] PMN, polymorphonuclear; HPF, high power field.

Results And Discussion

Gibberellin may be an active anti-inflammatory ingredient in Aloe vera. Two percent gelatin caused an increase in polymorphonuclear leukocyte infiltration in inflammation. This response was reduced by Aloe vera in a dose-response fashion to 68% and as much as 60.1% with the maximum dose of gibberellin in diabetic animals. These responses were significant at $p<0.001$ *(Table 1)*. By substituting gibberellin, a growth hormone glycoside, for Aloe vera, virtually identical results were obtained. Gelatin-treated diabetic mice receiving 2 mg/kg of gibberellin had a polymorphonuclear leukocyte count of 28.8 +/- 0.8 ($p>0.05$) neutrophils, showing no significant effect at this dosage relative to the diabetic 2% gelatin control group that received no gibberellin injection. The experimental animals receiving 20 mg/kg of gibberellin showed a significant decrease in polymorphonuclear leukocyte infiltration. The neutrophil cell count was 21.2 +/- 0.8 ($p<0.001$), which is a 25.1% reduction in neutrophil infiltration, while Aloe vera showed a similar count of 17.0 +/- 0.6 ($p<0.001$) at the same dosage. At 100 mg/kg, Aloe vera reduced the polymorphonuclear leukocyte cell count 68% below the 2% gelatin control, showing a mean value of

9.1 +/- 0.5 ($p<0.001$) neutrophils/high power field. At this same dose, gibberellin reduced the count 60.1%, with a mean count of 11.3 +/- 0.7 ($p<0.001$). These data show that Aloe vera and gibberellin are parallel in activity and possibly could suggest that the activity of each has similar origin.

The growth of root tips has demonstrated the dependence of the root on the shoot for carbohydrates, vitamins, and enzymes. The chemical determinant for growth and differentiation depends on plant growth hormones called auxins. These are essential for growth. Gibberellin was first isolated from mass cultures of fungus by Japanese investigators[7] who observed an increase in elongation growth in dwarfed plants. This hormone is universally distributed in taller plants. Gibberellic acid (GA_3) tends to be the most active of all the chemically identified gibberellins.[8, 9] Key[10] indicates that the auxin-like substance, gibberellic acid, is a significant mediator in plant tissue growth because it enhances cell enlargement. The ability of gibberellic acid to enhance the rate of cell elongation is dependent on new RNA and protein synthesis.[11, 12] These data would tend to suggest a wound-healing property. Since gibberellin stimulates protein synthesis as well as the DNA-RNA system in cells, it may have a value in healing wounds as it reduces inflammation.[13-16]

Infiltration of polymorphonuclear leukocyte cells into the wound area is an important cellular response to injury. Polymorphonuclear leukocyte activity might be a chemotactic response to hydrolysis products from the protein of the injured tissues.[17] These cells first marginate to the walls of the microcirculation in the injured area, then emigrate between the endothelial cells of the vessel wall, and, finally, migrate from the vessel through the ground substance to the site of the injury. Phagocytes, found in acutely traumatized tissue, are responsible for release of tissue-damaging lysosomal enzymes.[18] The auxins present in certain plant extracts are probably related to steroid-like compounds. This would account for the anti-inflammatory effect gibberellin has on gelatin-induced edema. Unlike steroids, which are antianabolic, gibberellins increase protein synthesis.[19] They would, therefore tend to heal wounds. Microsomes from auxin-treated tissue incorporate amino acid into protein at a higher rate than untreated tissue.

Aloe vera and gibberellin have similar anti-inflammatory activity in diabetic animals. The activity of gibberellin-like substances possibly plays a major role in the wound healing and anti-inflammatory activity of Aloe vera. Unlike steroids, Aloe vera and gibberellin inhibit inflammation but do not retard wound healing. This study helps redefine inflammation as it relates to wound healing.

References

Aloe Vera Gel In Peptic Ulcer Therapy: Preliminary Report

Excerpts By Julian J. Blitz, D.O.; James W. Smith, D.O. & Jack R. Gerard, D.O.

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At this time both the medical and surgical procedures employed in the management of peptic ulcer are directed principally to the control of the peripheral gastric secretory mechanism. Satisfactory clinical methods are available for achieving such control, but the very variety of these methods suggests to some degree that scientific certainty is still lacking. As Allen[1] puts it, "Present therapy is directed primarily at the physiologic sequela and not the physiologic stimulus."

Some interesting work from the Ukraine[2] has been directed to a "wound hormone" present in plant tissues, whose function it is to accelerate the healing of injured plant surfaces. In experimental studies, artificially induced skin lesions in rats and rabbits responded as favorably as injured plants to this substance. In either plants or animals the reparative response was effected systemically by injection of the wound hormone, but the effect was much more rapid and complete by topical application. Co-factors, particularly glutamic acid, aid substantially in the more vigorous and prompt repair of a wound or sore. Possibilities for the therapeutic application of these substances in medicine are stressed by the researchers; they include mention of ulcers of such diverse pathogenesis as cutaneous leishmaniasis (protozoan), dendritic keratitis (viral), and peptic (acid-pepsin secretory imbalance).

A safe and effective source of such "wound hormone" is Aloe vera gel, according to Freytag.[3] If the gel is recovered from the fresh Aloe vera parenchyma and separated from its cellulosic matrix, it can be emulsified with heavy liquid petrolatum to produce an elegant preparation with minimum distaste to the great majority of patients. It appears that an effective dose amounts to from 2 to 2 1/2 fluid drams of the cellulose-free gel. This amount can easily be incorporated in a tablespoonful of emulsion which, therefore, becomes a single dose.

To ascertain whether or not Aloe vera gel be helpful clinically in the management of peptic ulcer, we used its emulsion in a group of patients with peptic ulcer as essentially the sole medication, except for the occasional administration of Pro-Banthine in instances in which overwhelming distress indicated the need for the immediate restraint of hydrochloric acid secretion. Twelve patients diagnosed clinically as having peptic ulcer, and having unmistakable roentgenographic evidence of duodenal cap lesions, were treated with the Aloe vera gel emulsion. Preliminary findings were most encouraging.

All these patients had recovered completely by the end of 1961, so that at this writing at least 1 year has elapsed since the last treatment, and in some instances a much longer interval has elapsed. Usually, such unmistakable lesions are accompanied by exacerbations of distress once and more often twice a year under any form of medical treatment, but no such episodes were experienced in this series of cases. If exacerbations of symptoms are interpreted as signals of attempted recurrence, it follows that over the length of time indicated the medication must have delayed reappearance of ulcer activity. This also was confirmed by roentgenographic examination, which gave evidence of complete healing.

Table I - Response Of Patients With Duodenal Ulcer To Aloe Vera Gel Emulsion

Case No.	Sex	Age	Result Of Treatment
1	Male	24	Clinical recovery; no recurrence
2	Male	28	Clinical recovery; no recurrence
3	Male	38	Clinical recovery; no recurrence
4	Male	40	Clinical recovery; no recurrence
5	Male	40	Clinical recovery; no recurrence
6	Male	54	Clinical recovery; no recurrence
7	Male	67	Clinical recovery; no recurrence
8	Female	27	Clinical recovery; no recurrence
9	Female	41	Clinical recovery; no recurrence
10	Female	56	Clinical recovery; no recurrence
11	Female	60	Clinical recovery; no recurrence
12	Female	84	Clinical recovery*

*The patient had suffered from duodenal ulcer, on and off, for 20 years. She improved on Aloe vera gel medication but subsequently died of cardiac failure without, however, ever again suffering from gastric distress.

Inflammation of the mucosa of the first and second portions of the duodenum occurs in individuals subjected to emotional upset and tension encountered in various forms of gastritis (hypertrophic, for example) and especially in peptic ulcer. Clinically, the beginning symptoms are practically indistinguishable from those of peptic ulcer, and the diagnosis rests on the roentgenographic demonstration of spasm and irritability of the duodenal cap without the ability to demonstrate an ulcer fleck. This condition appears to be increasing, especially among the younger set, although no age group is exempt. Since the treatment is the same as for peptic ulcer, Aloe vera gel emulsion was used in a series of six patients with clinically diagnosed duodenitis. Duodenal irritability and spasm were elicited roentgenographically, but there was no evidence of an ulcer fleck.

Table II - Response Of Patients With Duodenal Irritability & Spasm To Aloe Vera Gel Emulsion

Case No.	Sex	Age	Result Of Treatment
13	Male	16	Complete recovery
14	Male	22	Complete recovery
15	Female	39	Complete recovery
16	Female	39	Complete recovery
17	Female	40	Complete recovery
18	Female	49	No improvement

Although Case 18 is listed as a failure, the events were these: The patient started Aloe vera gel emulsion treatment and, after a few doses, stopped and never again returned to the clinic. Her record is therefore incomplete in our files. It is assumed that she did not respond to treatment.

Statistically, one in every ten persons may be expected to develop peptic ulcer and appeal to the physician for treatment; but in reality probably great many more persons than this are lightly afflicted, if the evidence gained through gastroscopy is valid indication. The ingestion of an aspirin, a small quantity of mustard, a strong alcoholic beverage, a hot spicy sauce, and many other irritants are known to cause local, superficial inflammation in many people, often resulting in mucosal erosion equivalent to an ulcer. Few and sometimes no symptoms are precipitated beyond a slight burning distress.

Obviously, if these complaints were initiated in individuals without the history of consuming any of a number of irritants such as those mentioned, the disorders would be looked upon clinically as incipient peptic ulcers, on finding hydrochloric acid hypersecretion in the gastric juice. This condition is also increasing in incidence at a fairly rapid rate. In our patients, **it was relieved immediately on the administration of Aloe vera gel emulsion**. So favorable was the response that it created the clinical impression that this medication can certainly delay and perhaps prevent the development of a peptic ulcer.

This evidence sustains the practice of continuing the Aloe vera gel medication in small daily doses for a year or two after the clinically acute stage of the disease has been corrected by larger and more frequent doses of the same medication. Numerous patients, completely recovered from an acute peptic ulcer episode, are now on preventive treatment, which amounts to a single tablespoonful of Aloe vera gel emulsion taken at bedtime. It is too early to record the ultimate outcome of this procedure, although no recurrences have yet appeared in our patients after 18 months of preventive management in this fashion.

Repeated and sustained satisfaction in the management of peptic ulcer by use of Aloe vera gel emulsion invited further inquiry into the properties of this gel. Every edition of the United States Dispensatory refers to the use of Aloe vera gel as early as 2,300 years ago; to this drug Hindu herbalists ascribed amazing healing powers when it was applied topically to wounds and ulcers of the skin. Until quite recently, western medicine seemingly has ignored these virtues and failed to credit any pharmacologic action to the gel. In 1935 a report appeared indicating the successful management of x-ray dermatitis with ulceration by the use of fresh Aloe vera gel.[4] Confirmatory reports sustained this original announcement.[5-12] The use of Aloe vera gel for this purpose has waned, along with the advances in radiologic technology which have lessened the incidence of dermatitic damage. Renewed interest in Aloe vera gel developed with increasing peacetime and military applications of atomic energy, prompting experimental research at the Los Alamos Scientific Laboratory.[13] Radiodermatitic injury, resulting in ulcers of the skin, responded quickly to Aloe vera gel applications; healing took place in half the time required by untreated controls.

The Ukraine research on the gel brought out new information of considerable clinical import.[14] These workers have extracted a constituent which, on injection, operates systemically to effect the healing of ulcers, presumably because of biogenic stimulation. Oral administration is even more effective. There was a suggestion that the active constituent might be traumatic acid (chemically, 1-decene-1, 10-decarboxylic acid) but this is disputable. Traumatic acid is the hormone known to accumulate at the site of injury in plants, usually accompanying the gums and mucilages that collect in the wound (acacia, cherry gum, tragacanth, and others).

Following the work of the Ukrainians, Aloe vera gel was submitted to various studies which revealed that:[2, 3, 13-15]

1. The gel coacervates pepsin in the same fashion that quince seed gel coacervates papain. Coacervated pepsin is reversible and can release its enzyme at the proper electrical charge. In coacervated form pepsin loses its proteolytic effectiveness, but regains it when released. Food reverses the coacervation so that after the administration of the gel the pepsin remains inert so long as the stomach is devoid of food, but on introducing food (particularly protein) the coacervate reverses and the pepsin is set free to digest the nutrients.
2. The gel inhibits the secretion of hydrochloric acid by the parietal cells of the stomach. There is no free hydrochloric acid within the parietal cell; the acid develops at the membrane surface through the interaction of sodium chloride and carbonic acid catalyzed, it was at one time thought, by carbonic anhydrase. Whatever the mechanism involved in the exchange of sodium and hydrogen ions whereby sodium bicarbonate and hydrochloric acid are formed, the reaction is halted by Aloe vera gel. For example: The injection of histamine (as phosphate) is followed by a prompt increase in gastric flow and acid content. However, if the histamine is dissolved in Aloe vera gel as diluent and injected in that menstruum, there is no change in the amount or acid content of the juice. Since this is true in experimental Heidenhain pouches in dogs, it is clear that the Aloe vera gel affords a systemically operative antisecretagogue capable of offsetting the well known, action of histamine.

The inhibition is more marked if the gel is fed orally and the histamine is injected subsequently.

3. The gel is an extraordinary demulcent comprised of mannuronic and glucuronic units combined to form a polymer of high molecular weight. Gastric mucin contains only glucuronic units in its carbohydrate moiety. The uronic acids are natural detoxicants and as they are released by the hydrolytic cleavage of Aloe vera gel they may take part in the healing process by stripping toxic materials of their harmful irritation. Whether or not this occurs, however, the gel is tenacious to a marked degree, in which property it excels over all other known gums including methylcellulose. Unlike methylcellulose, which is biochemically inert, Aloe vera gel is certainly reactive. It serves as a biochemical "bandage" and is protectively helpful in restraining aggravating irritants from reaching the sensitive ulcer.

To the extent that these attributes of Aloe vera gel are operable in the human being in whom peptic ulcer exists, they should meet obvious therapeutic indications with anticipated helpfulness.

In its fresh state the gel is slightly acrid and possesses a somewhat disagreeable odor. Apparently the odor is due to volatile matters which disappear if the gel is subjected to proper processing. Tartness, partly because of free uronic acid that is contained in the gel, is easily compensated by adjusting the pH to any desired level, preferably around pH 6.5 to 6.8. Like gastric mucin, it is a glairy gel that does not altogether appeal to those who have a distaste for thick, mucilaginous products; but this feature is readily overcome by emulsifying the gel with heavy mineral oil.

Almost all patients with peptic ulcer are to some degree constipated. Harsh laxatives are constraindicated. Liquid petrolatum in small doses helps this condition and at the same time protects the gel against degradation such as occurs when it is admixed with an oxidizable oil.

If there is reason to suspect a lowered tissue resistance on the part of the mucosa, it is probable that measures designed to improve the general health may be helpful. There are no known procedures that satisfactorily benefit the tone of the gastric or duodenal mucosa directly.

Diet is certainly important, though there is no evidence that relates peptic ulcer to any dietetic deficiency requiring special nutritional supplements (such as cabbage juice). Frequent feeding of bland foods; avoidance of mechanical, chemical, or thermal irritants; and the provision of nutrient balance with respect to protein, carbohydrate, fat, mineral, vitamin, and adequate caloric requirements suffice. Innumerable diet lists are available that plan menus achieving this objective.

At best, antacids can only effect neutralization of the acid; they have no control over its excessive secretion. In selecting an antacid the clinician seeks an ideal which does not exist: prolonged neutralization when administered orally in acceptable amounts; no untoward systemic derangements such as alkalosis; absence of delayed secondary stimulation of secretion; no cathartic or constipating effect; no interference with the processes of digestion or absorption; and palatability. Such an antacid has yet to be developed. In the study presented here, antacids were not used at all.

Anticholinergic restraint of acid secretion is directed to the interference with the transmission of nerve impulses mediated by acetylcholine and is based on the concept that vagal hyperactivity is chiefly responsible for the gastric hypersecretion. In some instances Pro-Banthine was prescribed in usual doses at the initiation of treatment. Emotional disturbance needs to be identified and an effort made to guide the patient into a tension-free routine.

However tempting it is scientifically to split such a series of peptic ulcer patients so as to have half on treatment and half on placebo, it is impractical to carry on such a test in private practice. Patients come in to be treated and to obtain the quickest possible relief from their distress. The doctor must dispatch this obligation. Despite this lack of "control" it is obvious that certain interpretations are entirely plausible in the fight of the experience presented. These are:

1. In such a series of chronic peptic ulcer cases it would not be expected to experience 100 per cent complete recovery if the sole medication (Aloe vera gel emulsion) were pharmacologically inert, as the indictment of Western medicine has intimated.
2. Disappearance of painful distress related to meals and feedings could not have vanished in every instance if the peptic activity had not been arrested and the corrosive attack of hydrochloric acid inhibited to an unmistakable clinical degree.
3. Some recurrences should have appeared, since treatment of the series was completed early in 1962 and several patients had had recurrences previously as frequently as 6 months apart.
4. The gratitude expressed by the patients was in each instance so sincere as to leave little doubt about the reorientation of their previously dismal outlook on life. In these cases, the emotional distress seemingly vanished as the ulcer healed, suggesting that the neurogenic facet was ushered in by the peptic disease instead of the usually assumed reverse.

Considerable further evaluation of the Aloe vera gel emulsion as a therapeutic approach to the management of peptic ulcer is certainly desirable, coincident with which the probing of the pharmacologic mechanism involved is worthy of intensive research. Meanwhile, this preliminary study develops outstanding experience. There can be little question that Aloe vera gel emulsion is clinically helpful in the following conditions:

1. Prodromal changes in the gastrointestinal mucosa that strongly suggest incipient ulceration, in which the symptoms are somewhat borderline and the x-ray evidence is noncorroborative.
2. Duodenitis, in which the clinical picture coincides with ulcerative symptomatology and is supported by x-ray evidence of motility changes characteristic of response to ulcerative irritation.
3. Frank instances of ulcers, in which the clinical diagnosis is clear and supported x-ray demonstration of a niche or crater or pathognomonic roentgenographic deformity.

It is not possible to ascribe the benefits derived from the Aloe vera gel emulsion to its excellent demulcent property alone. Other demulcents that are biochemically inert, such as methylcellulose, do not effect clinical recovery when used as the sole therapeutic agent, even if supported occasionally with Pro-Banthine.

In vitro demonstration of the ability of Aloe vera gel to coacervate solutions of pepsin in acid, such as occurs in the gastric juice, and demonstration by Heidenhain pouch of the ability of Aloe vera gel to inhibit gastric parietal cell secretion of hydrochloric acid, favor the belief that these pharmacologic properties must be operative, to a measurable clinical degree, in the successful therapeutic management of peptic ulcer. But whether these properties or other virtues yet to be recognized are responsible for the decidedly beneficial action of Aloe vera gel emulsion in peptic ulcer, there can be little doubt of its utility as a therapeutic agent in this serious disease.

Summary

Clinically, Aloe vera gel emulsion has dissipated all symptoms in patients considered to have incipient peptic ulcer. Duodenitis, probably representing duodenal ulcer but lacking x-ray demonstration of pathognomonic deformity, treated with Aloe vera gel, resulted in uniformly excellent recovery, except questionably in one patient. In cases of peptic ulcer about which there could be little clinical doubt, and in every instance confirmed by roentgenologic identification of a fleck, niche, or crater with accompanying hypermotile manifestations, Aloe vera gel emulsion provided complete recovery.

It appears that recurrence has been delayed and possibly prevented in cases normally expected to flare up after satisfactory treatment.

Recent research on Aloe vera gel suggests the presence of an active ingredient which, on ingestion or injection, is accompanied by the inhibition of excess hydrochloric acid secretion by the parietal cells of

the stomach. If the gel is mixed with artificial gastric juice, the pepsin is coacervated and becomes inert in that state; but a change of pH, as by the introduction of food (protein especially) reverses the coacervate and the pepsin once more exerts its proteolytic capacity. Finally, Aloe vera gel is a saccharide polymer, resembling gastric mucin in its carbohydrate moiety, but it is many times more tenacious than any other commonly known mucilage (methylcellulose, gastric mucin, karaya, or others).

There can be little doubt that the properties ascribed to Aloe vera gel should be therapeutically helpful in the management of peptic ulcer; but whether or not these properties occasion correction of the ulcer-producing process, it is unmistakable that Aloe vera gel, through whatever mechanism, is clinically beneficial in the treatment of this very important disease.

References

Aloe And Other Topical Antibacterial Agents In Wound Healing

By John P. Heggers, Ph.D. & Wendell Winters, Ph.D.

Unlike any other wound, the burn is a non-uniform injury in which some tissues are partially or completely damaged, while other tissues suffer minimal damage. The latter will heal without any therapeutic treatment, while the former will become permanently damaged, creating a granulating wound if not appropriately treated.

Infection also plays a major role in the conversion of this wound.[1] Many of the topical agents used are to control burn wound infections. However, there are other products that have multivaried effects on the burn wound. Some of the major properties attributed to Aloe vera include its ability to:

a. penetrate tissue
b. anesthetize the tissue
c. allay bacterial, fungal & viral growth
d. act as an anti-inflammatory
e. dilate capillaries & enhance blood flow[2]

Heggers and his co-workers[3] showed that topical application of anti-eicosanoids, more specifically anti-thromboxane agents, could reverse progressive tissue necrosis in the partially damaged tissue. Topical application of an Aloe compound resulted in healing patterns comparable to the anti-thromboxane agents. Robson and his colleagues[2] also showed that such an Aloe compound had anti-bacterial properties as well.

Therefore, topical application of anti-microbials and other chemo-therapeutic agents is essential in order to restore the normal healing process and prevent infection. Halsted has been quoted as saying, "A wound which has been irrigated with solutions of carbolic acid, corrosive sublimate, or other disinfectant labors under the disadvantage of a more less extensive area of superficial necrosis"[3]. McCauley and his colleagues[4] have show that both silver sulfadiazine and Sulfamylon® are toxic to fibroblasts in tissue culture at concentrations of 0.005% and 0.1%, respectively. Leitch, et al[5] recently presented data that silver sulfadiazine, Sulfamylon® and silver sulfadiazine with chlorohexadine significantly retarded wound healing in the acute wound model.

Since application of topical chemotherapeutic agents is essential in the prevention of infection and enhancement of wound healing, we examined Aloe's role in accelerating wound healing or reversing the wound retardant effect of silver sulfadiazine as well as the influence of Bactroban® and clindamycin on the healing process.

In order to be assured that Aloe contained active components which are essential in the healing process we employed a Polyarcylamide gel electrophoresis (PAGE) and cell growth assays to determine the presence of active components. Acrylamide-bis acrylamide 37.5:1 (Fisher Biotech Houston), tris-HCI (Sigma St. Louis), sodium lauryl sulfate (SDS), N,N,N',N'-tetramethylenediamine (TEMED), ammonium persulfate (Bio-Rad (Richmond), rainbow weight marker (Amersham Arlington Heights were purchased

from the respective vendors). Electrophoresis was performed using a 12.5% separating gel and a 4% stacking gel run in a Bio-Rad Protean II Xi vertical electrophoresis cell system at 3OmA constant current[6]. The gel was stained by silver stain kit method, and the kit was purchased from Bio-Rad.[7]

Cells were grown in Dulbecco's Minimal Medium (DMEM) supplemented with 10% heat-inactivated horse serum, 5% fetal calf serum, 50 units penicillin, 0.05% mg/ml streptomycin 1mM L-glutamine and 1mM sodium pyruvate. The rat adrenal cultured cells were prepared following incubation at 37^{o} C in 5% CO_2. Cell concentration and viability were determined by hemacytometer counts and dye exclusion with 0.04% trypan blue.

Cells at 5x10^{4} cell/well were plated into 96-well flat-bottom plates and maintained 24 hours at standard conditions in adherence studies. The media was removed before the addition of the Aloe-DMEM mixture. After 72 hours of incubation, 10ul of MTT (3-[4,5-Dimeth-ylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide) solution (5mg/ml) was added to each well. The formazan crystals, formed only in viable cells after four hours at 37^{o} C, were dissolved by addition of 100ul of acid-isopropanol solution. The plates were read by a Micro ELISA reader (MR 580 Dynatec) at 570nm (630nm reference wavelength, calibration setting of 1.99).

The acute model was used as previously described by Heggers, et al.[8] Appropriately anesthetized Sprague Dawley rats, two proximal and two distal, received four 1.5 cm^{2} dorsal defects through the skin and panniculus carnosus. This study was conducted in compliance with UTMB's Animal Care and Use Committee under ACUC protocol #92-05-026. *(Fig. 1)*

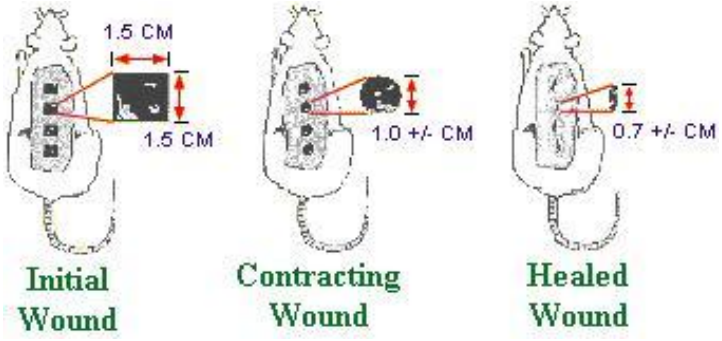

Figure 1 Schematic representation of the acute wound healing model.

The skin defects were treated three times a day for 14 days with Aloe vera gel (n=10), 2% mupirocin ointment (n=10), 1% clindamycin cream (n=10), 1% silver sulfadiazine alone (n=10), 1% silver sulfadiazine cream + Aloe (n=10). An untreated group served as control (n=10). Wound closure rate was assessed by serial planimetry. Following healing, the breaking strength of each resultant scar was determined using an Instron tensiometer model #4201 (Instron Corp, Canton, MA). Wound half-lives and overall healing rates were calculated by regressing the log of the areas of all wounds over time.

Results

The SDS PAGE analysis revealed a high molecular weight polypeptide in Aloe vera 1:1 gel #5.

The rat adrenal cultured cells in the presence of Aloe vera gel #5 showed a 26% increase in growth activity when compared to the control *(Fig. 2)*. Therefore, we utilized the Aloe vera gel #5 for our in vivo assay.

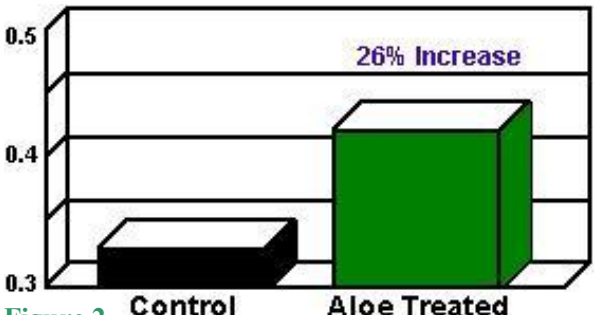

Figure 2
Tissue culture response to Aloe 1:1 gel compared to control (untreated).

Acute Wound Healing

Topical application of each therapeutic agent had a profound effect on the healing process. Overall healing rates of all the treated groups were significantly different as compared to the control group ($p<0.05$). The Aloe group had the shortest half-life, and healed faster than the control group *(Table I)*. All the other treated groups had longer half-lives compared to the control group. While silver sulfadiazine with Aloe significantly increased the breaking strength (2.000 + 0.504) of the healed wound, Aloe alone was slightly stronger than the control silver sulfadiazine.

Table I
Fractional Area & Healing Rates of Wounds Treated With Topical Antibacterials

Group	Days (n)	Fraction Of Initial Wound Area Throughout + SD	Overall Healing Rate (Slope +SD)	1/2 Life
1. Control	480	0.289 + 0.385	0.1477 (0.0027)	6.38
2. Aloe	360	0.279 + 0.364	0.1657 (0.0027)	6.14*
3. SSD	480	0.368 + 0.420	0.1800(0.0050)	8.56
4. SSD + Aloe	480	0.277 + 0.392	0.1339 (0.0030)	6.94
5. Bactroban®	480	0.332 + 0.414	0.1300 (0.0026)	8.74
6. Clindamycin	324	0.396 + 0.482	0.1711 (0.0037)	8.30

*All half-life days are significant ($p = <0.05$)

Topical Aloe significantly enhances the rate of wound healing, and, when combined with silver sulfadiazine, it apparently reverses the wound retardant effect of silver sulfadiazine. Clindamycin and mupirocin significantly delayed wound closure as did silver sulfadiazine, while the breaking strength for the three topical agents appears stronger or comparable to the control. *(Table II)*

Table II
Breaking Strength of Healed Wounds

Group	Breaking Strength (KG) + S		(n)
1. Control	1.461	+ 0.421	30
2. Aloe	1.640	+ 0.533	29
3. SSD	1.521	+ 0.432	28
4. SSD + Aloe	2.000	+ 0.504*	28
5. Bactroban®	1.845	+ 0.421	24
6. Clindamycin	1.621	+ 0.404	15

*SSD + Aloe breaking strength is significant ($p = <0.05$)

Conclusions

Topical application of a variety of cytokines to open wounds has revolutionized the process of wound healing. Hayward, et al[9] provided evidence that the basic Fibroblast Growth Factor (bFGF) reverses bacterial retardation of wound contraction in a chronic granulating wound.

Carney and his co-workers[10] showed that exogenous delivery of synthetic Thrombin Receptor-activating peptides enhanced the healing process and neovascularization of an incisional wound. In a clinical trial Bishop, et al[11] evaluated two potential wound healing agents in a blinded trial for the treatment of venous status ulcers. Contrary to previous in vitro and in vivo studies by McCauley, et al[4] and Leitch, et al[5] the Bishop study showed that silver sulfadiazine was significantly more therapeutic in healing the venous status ulcer when compared to a biologically active tripeptide copper complex or a placebo. These results suggest that a silver sulfadiazine cream may facilitate healing in wounds that heal by epitheliazation. Robson and co-workers,[12, 13] in two separate publications, reported on the efficacy and safety of platelet-derived growth factor B-B and bFGF in chronic pressure sore ulcers.

Our previous studies have provided evidence that Aloe vera may contain a growth factor like substance.[2, 3, 4] Recently, Winters[14] presented data regarding a growth stimulating as well as a growth suppressant substance in Aloe gel. PAGE analysis revealed the presence of a polypeptide species possibly responsible for these activities. By immunoblot technique, the Aloe substances were found to contain Na+/K+ATPase and Con A activities. These mitogenic lectin-like substances in Aloe have been previously described.

Therefore, with this foundation of knowledge regarding the exogenous administration of cytokines and Aloe substances in the process of wound healing, we closely examined Aloe vera gel 1:1 (#5) to provide further evidence of its wound-healing potential compared to other chemotherapeutic agents.

McCauley, et al[4] showed that silver sulfadiazine in tissue culture was toxic to fibroblasts and keratinocytes, and Leitch and his co-workers[5] showed that it retarded wound healing in vivo. We wondered if Aloe would respond as bFGF did in reversing the retardation of wound healing[9] and if the treated, healed wound was stronger or weaker than the control wound.

The Aloe-alone treated wounds healed faster and had a half-life of 6.14 days which was significantly ($p<0.05$) shorter when compared to the other groups *(Table 2)*. The silver sulfadiazine and Aloe group, while it healed significantly faster ($p = <0.05$) than the Bactroban® silver sulfadiazine, clindamycin groups, had a half-life of 6.94 which was slightly longer than the control wound (half-life 6.38).

The breaking strength of the Aloe-treated wound (1.640) was significantly less ($p<0.05$) than the silver sulfadiazine + Aloe group (2.000) *(Table II)*. The control breaking strength was 1.461, less than the Aloe-treated wounds, while the silver sulfadiazine + Aloe treated wounds were significantly ($p<0.05$) greater than all other groups. The Bactroban® -clindamycin- and silver sulfadiazine-treated wounds were apparently stronger than the controls, but the healing time was significantly ($p<0.05$) retarded. This study further substantiates the fact that Aloe contains a growth promoting factor that enhances the healing process and the breaking strength of these healed wounds. Aloe can also reverse the wound healing retardant effect of silver sulfadiazine, a topical antimicrobial used to treat and control burn wound sepsis.

References

Wound Healing, Oral And Topical Activity Of Aloe Vera

By Robert H. Davis, Ph.D.; Mark G. Leitner, R.Ph., D.P.M.; Joseph M. Russo, D.P.M. & Megan E. Byrne, B.S.

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Abstract

The influence of Aloe vera, orally and topically, on wound healing was studied. Wounds were induced on both sides of the vertebral column of ICR mice using a biopsy punch. For the oral study, experimental animals received Aloe vera in their drinking water for 2 months, whereas the control animals received only water. In the topical study, experimental animals were given 25% Aloe vera in Eucerin® cream topically. The control animals received cream only. A 62.5% reduction in wound diameter was noted in mice receiving 100 mg/kg/day oral Aloe vera and a 50.80% reduction was recorded in animals receiving topical 25% Aloe vera. These data suggest that Aloe vera is effective by both oral and topical routes of administration.

Previous studies have amply demonstrated the wound-healing influence of Aloe vera.[1, 2] Aloe vera given subcutaneously showed a dose-response relationship on improvement of wound healing. Decolorized Aloe vera (without anthraquinones) was more effective than colorized Aloe. Addition of vitamin C and RNA did not increase the wound-healing potency of Aloe vera. Aloe vera is a natural substance containing enzymes, amino acids, and other active ingredients that contain important properties needed for wound healing.[3, 4] Aloe's watery composition may increase the migration of epithelial cells so that an improvement of wound healing is recorded.[5-7]

Rowe[8] found that 50% of rats treated with Aloe vera exhibited improved wound healing. Crewe[9] reported that Aloe vera advanced healing with tissue regeneration. This response could be explained by the fact that Aloe dilated capillaries to increase blood flow to injured areas.[10] In fact, decolorized Aloe vera improved wound healing in a dose-related fashion even in the diabetic animals,[11] in which the healing of vascular tissue was impaired. Possibly, there are specific factors that Aloe vera overcomes to improve wound healing. In normal and diabetic animals, Aloe vera possesses anti-inflammatory, antiedemic, and improved healing properties. This study attempts to show the oral and topical activity of Aloe vera in improving wound healing.

Materials And Methods

In the oral study, adult male ICR mice (35 to 45 gm, 8 animals/group) received food grade Aloe vera for 2 months in their drinking water. The control animals did not receive any Aloe vera. The mice were anesthetized and shaved on both sides of the back. A 6-mm punch biopsy was used to induce two skin wounds on each side of the vertebral column. The diameters of the wounds were measured from anterior to posterior with a Vernier® caliper. Standard errors and p-values were subsequently calculated.

For the topical study, the materials and methods were as follows: adult male ICR mice (35 to 45 gm, 10 animals/group) were anesthetized and shaved on both sides of the back, and two wounds were made on either side of the vertebral columns of each animal. The wounds were induced by a 6-mm punch biopsy. Anterior-to-posterior measurements of the wounds were recorded by a Vernier caliper on days 1, 4, and 7. One group of experimental mice received 25% colorized Aloe vera topically on each wound daily for 6 days. The total application was 200 mg. A second experimental control group received topical Eucerin cream alone. Untreated mice served as a non-treatment control. The standard errors were calculated, and the p-values were obtained.[12]

Results And Discussion

Normal wound healing occurs in three stages: inflammation, proliferation, and remodeling. The wound healing process depends on a given provision of local circulation, as well as the formation and deposition of collagen. A considerable amount of evidence has shown that Aloe vera improves wound and burn healing in animals and humans.[13] Some studies found that 50% of rats showed improved wound healing over 7 days.[8, 9] Aloe given subcutaneously showed a dose-response relationship on improvement of wounds. A similar response was recorded in diabetics, whose wounds normally are characterized by poor or delayed healing.[11]

Current methods used to treat difficult wounds include debridement, irrigation, antibiotics, tissue grafts, proteolytic enzymes, and corticosteroids, which possess major drawbacks and unwanted side effects. Aloe vera contains important ingredients necessary for wound healing, such as vitamin C (ascorbic acid), amino acids, vitamin E, and zinc.[13, 14] Ascorbic acid enhances the synthesis of collagen and counterbalances collagen breakdown.[15, 16] Vitamin E is a fat-soluble vitamin found in Aloe that has proven anti-oxidant activity. It may help stabilize lysosomal enzymes needed to synthesize collagen and it prevents free radical damage (cross-linkage) that appears to be detrimental to normal wound healing.[13, 17] It was demonstrated in the authors' laboratory that zinc improved the tensile strength of wounds, thus improving healing.[18] Aloe vera penetrates, cleanses, and dilates capillaries going to an injured site, which also improves healing. Aloe vera may hasten epithelialization of wounds and reduce dehydration necrosis.

Several factors delay or reduce wound healing, including bacterial infections, necrotic tissue, interference with blood supply, lymphatic blockage, and diabetes mellitus. These conditions that inhibit wound healing can be combined under the classification, of "tissue anoxia,"[19] or reduction of oxygen in body tissue below physiologic levels. If tissue anoxia could be altered by regional superoxygenation, an increased healing rate could be achieved.

It was found in the authors' laboratory that Aloe vera was effective orally in promoting wound healing. Oral food-grade Aloe vera (100 mg/kg/day) improved wound healing compared to the healing of control animals receiving only water *(Table 1, Figure 1)*. The decrease in wound diameters for the control animals was 3.5 +/- 0.3 mm (51.1%), whereas the Aloe-treated mice had a decrease in wound diameters by as much as 4.8 +/- 0.5 mm (62.5%). The difference was significant at $p < 0.05$.

Table 1
Effect of oral Aloe vera on wound healing in mice over a 2-month period.

	Decrease in Wound Diameter	
	MM	% Decrease
Control	3.5 +/- 0.3	51.1 +/- 4.2
Aloe 62.5 +/- 5.4	4.8 +/- 0.5*	

100 mg/kg/day

8 Animals/Group; *p <0.05

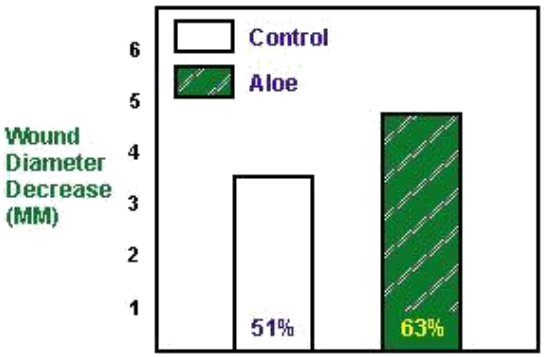

Figure 1
Effect of oral Aloe vera on wound healing in mice over a 2-month period.

Moreover, the laboratory found that Aloe vera administered topically also served to improve wound healing. Table 2 and Figure 2 depict the effect of topical, 25% colorized Aloe vera in mice over a period of 7 days. The wounds on the mice that received 25 % colorized Aloe vera demonstrated a 3.9 +/- 0.4-mm reduction in diameter, as compared to the wound diameter reduction of 1.9 +/- 0.3 mm ($p < 0.001$) for the animals that received cream alone. No significant difference was observed between the untreated wounds and the wounds treated with Eucerin cream alone ($p > 0.5$). Therefore, the percentages of decrease in wound diameters for the nontreatment control group, cream alone control group, and cream plus 25% Aloe vera group were 32.5% +/- 4.8%, 25.4% +/- 3.4%, and 50.8% +/- 3.6%, respectively. These findings clearly suggest that 25% colorized Aloe vera was a significant factor in the healing of the wounds. Since oxygen is required for the synthesis of collagen by fibroblasts,[20] Aloe vera may improve the vascular supply and make more oxygen available to improve collagen formation for wound healing.

Table 2
Topical effect of Aloe vera on wound healing in mice over a 7-day period.

	Decrease in Wound Diameter	
	MM	% Decrease
Control	2.1 +/- 0.4	32.5 +/- 4.8
Cream Alone	1.9 +/- 0.3	25.4 +/- 3.4
+25% Aloe	3.9 +/- 0.4	50.8 +/- 3.6

10 Animals/Group; *p <0.001

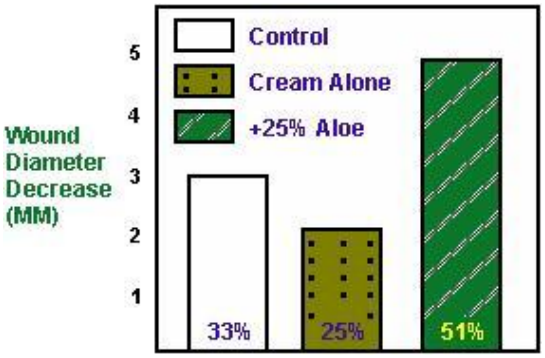

Figure 2
Topical effect of Aloe vera on wound healing in mice over a 7-day period.

It also was observed that the animals not receiving topical Aloe had hard and crusty wounds, which generally appeared unclean. However, the Aloe-treated wounds were clean, with healthy granulation tissue. The presence of Aloe seemed to reduce the amount of dead tissue at the wound site and provide better wound healing. Previous studies by the authors have shown that the wounds of mice receiving 100 mg/kg of colorized Aloe vera had better vascularity and healthier looking granulation tissue. Mice receiving decolorized Aloe vera had an even firmer connective tissue and the appearance of more vascularization.

During the wound-healing process, epithelial cells proliferate, migrate from the edges of the wound, and eventually cover the wound with skin. By lysing collagen with enzymes, the epithelial cells move across the wound and attach to viable tissue. The proliferation and migration of the epithelial cells are dependent on an adequate supply of oxygen. Therefore, the increased presence of oxygen, caused by the Aloe vera improving microcirculation, should greatly improve the wound-healing process.[21] It is hypothesized that catecholamines (epinephrine and norepinephrine) retard epithelial cell proliferation.[22] When a wound is sustained, the supply of catecholamines is interrupted, and the barrier to mitosis is removed. Thus, cells begin to grow and divide. Possibly, some constituents of Aloe vera may either block catecholamines or directly stimulate epithelialization to improve wound healing.

During early wound healing, the vascular and lymphatic systems are of primary importance. Failure or delay of vascular regeneration decreases oxygen transport to the wound, which subsequently depresses the mobilization of excessive fluids from the wound site. The wound becomes edematous, leading to further damage, infection, and eventually cell death. In wound healing, new blood vessels sprout up from platelets or macrophages to keep the wound open-ended. Hypoxia may be a stimulant to revascularization. Aloe may, thus, achieve the following effects to improve tissue healing: an increased blood supply, and, hence, an increased oxygen supply to the wound by blocking vasoconstrictive compounds (inflammation stage); greater migration of epidermal cells over moist tissue caused by factors and enzymes present in Aloe vera (proliferation stage); and extensive reorientation of collagen fibers caused by a stronger cross-linking (remodeling stage).[23] Aloe vera also provides for a clean wound free of excess exudate and contamination, making it a favorable treatment for wounds.

The authors' histologic work indicates that Aloe vera stimulates and enhances vascularity around the wound area. As a result, the general appearance of the wound is, in all respects, healthier than the untreated control wound. It may be that Aloe vera increases the supply of oxygen to the wound. This is further evidence to support the theory that an increase in oxygen availability improves wound healing. Furthermore, Aloe vera can topically reduce inflammation and depress the symptoms of adjuvant arthritis.

Summary

The authors' studies have shown that Aloe vera improves wound healing when administered either orally or topically. It not only contributes to a decrease in wound diameter, but also leads to better vascularity and healthier granulation tissue. The fact that Aloe is effective orally suggests that it is not broken down by the gastrointestinal tract and is absorbed into the blood. Aloe possibly improves wound healing by increasing the availability of oxygen and by increasing the synthesis and the strength of Collagen. Aloe vera has become a subject of scientific study concerning inflammation and wound healing. As knowledge about Aloe increases, significant benefits of a practical nature in the management of healing wounds can be expected.

References

Table 1
Effect of oral Aloe vera on wound healing in mice over a 2-month period.

Aloctin A, An Active Substance Of Aloe Arborescens Miller As An Immunomodulator

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Phytotherapy Research (1993) Vol 7, No. Special issue,
pp. S20-S22. 15 ref.

Aloe has been used as a folk medicine for centuries all over the world. Among the components of Aloe, the low-molecular weight components have been well studied and used as purgatives. In the last few decades, the clinical application of Aloe extract, probably the components of high molecular weight, in skin injury and burns, as well as an anti-inflammatory, has been reported. Aloctin A (Alo A) is a highly purified glycoprotein with molecular weight of 1.8×10^4 from the leaves of Aloe arborescens and exhibits various biological activities, such as mitogenic activity for T lymphocytes, binding reactivity for human a2-macroglobulin and activation of component 3 of complement system via the alternative pathway[1].

In this article, I would like to describe the antitumor activity of Alo A using methylcholanthrene-induced nurine fibrosarcoma (Meth A)[2] and lymphocytic leukemia (P388) (unpublished data) in syngeneic mouse systems.

One million of Meth A cells were implanted into the peritoneal cavity of BALB/c mice. Alo A were administered i.p. at an appropriate concentration in saline, once daily for 5 days, starting 24 hours after tumor implantation. Antitumor activity was evaluated by total cell packed cell volume ratio (Alo A-treated mice/control mice) calculated from collected whole ascites obtained from mice anesthetized with ether. A representative experiment is shown in table 1. Alo A obviously inhibited the growth of the tumor cells and administration at a dose of 10 mg/kg/day, for 5 days, remarkably inhibited it ($p<0.001$). It was important to determine whether this activity was due to cytotoxicity of Alo A for tumor cells or host-mediated effects of Alo A, since Alo A was administered i.p. Therefore, the effect of Alo A on the growth in vitro of Meth A and the other cell lines was examined by ^{3}H-thymidine uptake. Alo A had almost no inhibitory effect on the growth of tumor cell lines tested including Meth A up to a concentration of 200 ug/ml, the highest concentration tested (table 2). This result suggests that Alo A is not directly cytotoxic to tumor cells.

One million of P388 cells were implanted intraperitoneally in CDF1 mice. Alo A was administered i.p. at an appropriate concentration in saline, once daily on the 1st and 5th days after tumor implantation. Antitumor activity was evaluated by survival time. The antitumor activity of Alo A is also obvious in this system (table 3).

The mechanisms of antitumor activity of Alo A seemed to be host-mediated. We have reported a couple of immunomodulatory activities, such as elevation of natural killer cell activity, augmentation of cytotoxicity of peritoneal exudate cells and generation of lymphokine-activated killer cells. We consider that Alo A is a promising candidate as an immunomodulator.

Table 1
The anti-tumor activity of Aloctin A against sarcoma Meth A (ascites form) in BALB/c mice

Treatment	Dose (mg/kg/day x days)	Average TPCV[a] (ml)	T/C Ratio (%)	Complete Inhibition
None		0.61		0/10
Aloctin A	10 x 5	0.05	7.7*	4/6
Aloctin A	.2 x 5	0.37	60.4	1/6
Aloctin A	0.4 x 5	0.41	66.7	1/6

Antitumor test, 5-week-old BALB/c mice were used for this test. The tumor used was methylcholanthrene-induced fibrosarcoma (Meth A) maintained in the ascites form, 1 x 10^6 washed cells of Meth A were implanted i.p. into the mouse. Aloctin A as injected i.p. once daily for 5 days, starting 24 h after tumor implantation. Antitumor activity was evaluated by the total packed cell volume ratio (T/C %) on the 7th day.

[a]Total packed cell volume, *$p<0.001$, Significantly different from control.

Table 2
Cytotoxicity of Aloctin A in vitro

Concentration of Aloctin A (ug/ml)	^{3}H-TdR Incorporation (cpm)[a]				
	Meth A	EL 4	P815	BW5147	YAC
None	42890	68351	39865	14989	7120
0.02	43195	87497	67506	24247	8345
0.2	40512	90111	74904	24468	7648
2.0	39250	87798	68245	28597	7618
20.0	45924	80864	63572	19300	6835
200.0	45537	66979	49111	11250	818

Cytotoxicity test: Various concentrations of Aloctin A in 00ul of cell suspension, each containing 5 x 10^3 cells. The mixture was incubated at 37 ^{o}C for 28 h in a humidified atmosphere of 5% CO_2 and 95% air. After 24h, 1 uCi/well of ^{3}H-thymidine was added. After a further 4 h of incubation, radioactivity incorporated into DNA was determined.

[a]Mean cpm of 3 wells.

Table 3
The anti-tumor activity of Aloctin A against P388 in CDF_1 mice

Treatment	Dose (mg/kg/day)	No. Of Mice	Survival Time Range	Survival Time M. S. T. days	T/C %
Control		10	8-9	8.50	
Aloctin A	10	6	9-11	10.33**	121.6

Aloctin A	5	5	9-11	9.60*	112.9
Aloctin A	1	6	8-10	9.17	107.8
Aloctin A	0.2	6	8-10	8.67	102.0

M. S. T., Median Survival Time, T/C % = M. S. T. of treated group / M. S. T. of Control x 100.
Evaluation of anti-tumor activity; T/C % in life-span *, **,
Significantly different from Control * P<0.01, ** P<0.001.

References

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2 **Imanishi et al.** (1981) *Experientia* 37: 1186.

Tumor Inhibitors 114 Aloe Emodin: Antileukemic Principle Isolated From Rhamnus frangula L

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Lloydia 39(4):223-4 1976 Jul-Aug

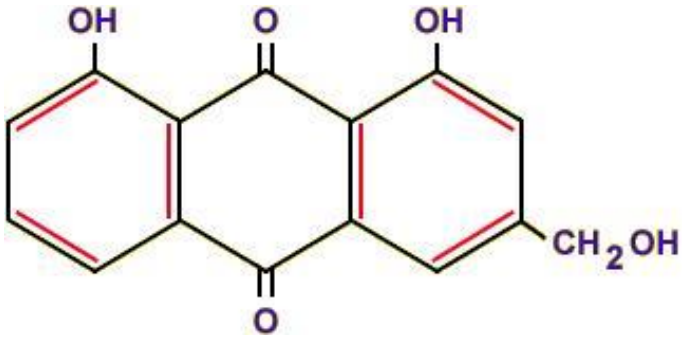
Abstract

A systematic fractionation of an ethanol-water (1:1) extract of the seeds of Rhamnus frangula L., guided by assays for tumor-inhibitory activity, led to the isolation of Aloe emodin (1). This compound was found to show significant antileukemic activity against the P-388 lymphocytic leukemia in mice. A noteworthy vehicle-dependence of the testing results is reported. In the light of this vehicle-dependence, the re-examination of other anthraquinone derivatives is recommended.

Rhamnus frangula L. (Rhamnaceae) has been used in England and the United States to treat cancers, and other Rhamnus species have been used similarly in folk medicine from at least the time of Galen (circa A.D. 150) (2).

In the course of our continuing search for tumor inhibitors of plant origin, an ethanol-water (1:1) extract of the seeds of Rhamnus frangula L.[2] showed significant inhibitory activity when tested in mice against the P-388 lymphocytic leukemia[3]. Fractionation of the extract, guided by assay against the P-388 system, revealed that the inhibitory activity was concentrated in the aqueous layer of a petroleum ether-water partition, and that the active material was extractable by chloroform from the aqueous solution. Column chromatography of the chloroform solubles on SilicAR CC-7 with 2.5% methanol in chloroform led to the isolation of Aloe emodin (1) from the active chromatographic fraction. The compound was characterized by direct comparison of its melting point, tlc, and infrared spectral characteristics with those of an authentic sample of Aloe emodin.

Aloe emodin (1) shows significant inhibitory activity against the P-388 leukemia in mice when administered as a suspension in acetone-Tween 80. Results corresponding to T/C values of 133-154% were found at the optimal dose of 20 mg/kg.



In a recent review, the results of antitumor assays of 379 anthraquinone derivatives were reported. The authors concluded that "the most noteworthy observation concerning the anthraquinones is the relative lack of activity among the numerous derivatives tested from this group" (4). None were found to inhibit the L-1210 leukemia in mice, and only five showed some activity against solid tumor systems. Aloe emodin (NSC-38628) was among the derivatives which were found to be inactive. Since the P-388 system did not number among the tumors used in the study, our discovery of the antileukemic activity of Aloe emodin may reflect only a unique sensitivity of this mouse leukemia toward the compound. We note here, however, that the antileukemic activity of Aloe emodin is particularly vehicle-dependent, and that the reproducible inhibitory activity toward the P-388 system was manifested only when the acetone-Tween 80 suspension was used. In view of this fact, a re-examination of other anthraquinones for potential antitumor activity, with particular attention to possible vehicle-dependence, may be rewarded by the discovery of new and useful structure-activity relationships.

Experimental

Extraction & Fractionation -

Ground, dried seeds of Rhamnus frangula L. (1 kg) were extracted with ethanol-water (1:1, 7 liters) at room temperature overnight. The extract was filtered, concentrated under reduced pressure to about 1.5 liters and freeze-dried, to yield 163 g of residue. The residue was partitioned between petroleum ether (2 liters) and water (2 liters), whereupon 13.5 g of solid remained undissolved and was separated by filtration. Evaporation of the petroleum ether to dryness under reduced pressure yielded 11 g of residue. The aqueous solution was extracted with chloroform (2 X 2 liters), and evaporation of the chloroform extract to dryness under reduced pressure yielded 9.5 g of residue (fraction A).

Chromatography Of Fraction A -

A solution of fraction A (8 g) was treated with 25 g of SilicAR CC-7. The suspension was evaporated to dryness on a rotary evaporator, and the residue was added to a column of SilicAR CC-7 (500 g) prepared as a suspension in chloroform. The column was eluted first with chloroform (1 liter) and then with 2.5% methanol in chloroform, and 30 X 100 ml subfractions were collected. Subfractions were examined by tlc and those which were similar were combined and submitted for biological testing. The aggregate of subtractions 17-25, all rich in Aloe emodin (R_F 0.54), constituted the sole active fraction (B, 1.9 g).

Isolation Of Aloe Emodin (1) -

Active fraction B (1.5 g) was crystallized from chloroform-methanol, and recrystallization from the same solvents yielded orange-yellow needles (700 mg), mp 223-224°; lit. mp 223-225° (5). The melting point was not depressed by admixture of an authentic sample of Aloe emodin[5]. Mixture tlc and infrared spectral comparisons confirmed the identity of the two samples.

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[1] Part 113 is reference 1.

[2] Seeds of Rhamnus frangula L. were collected in Austria in November, 1966. We acknowledge with thanks receipt of the dried plant material from Dr. R. E. Perdue, Jr., U.S. Department of Agriculture, in accordance with the program developed by the National Cancer Institute. Voucher specimens are on deposit at the Medicinal Plant Resources Laboratory, Agricultural Research Service, Beltsville, Maryland.

[3] Antileukemic activity was assayed under the auspices of the National Cancer Institute, by the procedure described in reference 3.

[4] Melting points were determined with a Mettler FP2 hot-stage microscope. Infrared spectra were determined with a Perkin-Elmer Hitachi model 257 spectrophotometer as KBr pellets. Petroleum ether refers to the fraction of bp 60-68°. Thin-layer chromatography was carried out on silica gel 60 F-254 (E. Merck) precoated plates, and chromatograms were visualized by spraying with an anisaldehyde-sulfuric acid spray; the developing solvent was 5% methanol in chloroform.

[5] We thank Professor H. Wagner, Universität München, for an authentic sample of Aloe emodin.

Prevention Of Atheromatous Heart Disease

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Abstract

Five thousand patients of atheromatous heart disease, presented as angina pectoris, were studied over a period of five years. After adding the "Husk of Isabgol" and "Aloe vera" (an indigenous plant known as ghee-guar-ka-paththa) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, fasting and post parandial blood sugar level in diabetic patients, total lipids and also increase in HDL were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks and gradually, the drugs, like verapamil, nifedipine, beta-blockers and nitrates, were tapered. The patients, most benefitted, were diabetics (without adding any antidiabetic drug). The exact mechanism of the action of the above two substances is not known, but it appears, that probably they act by their high fibre contents. Both these substances need further evaluation. The most interesting aspect of the study was that no untoward side effect was noted and all the five thousand patients are surviving till date.

Introduction

Incidence of atheromatous heart disease is increasing day by day. The factors commonly responsible for atherosclerotic heart disease are diabetes mellitus, hypertension, smoking, family tendency in the form of hyperlipidemias, gout, excessive intake of saturated fatty acids, obesity, lack of exercise, etc.

For the first time, an Indian plant known as Aloe vera belonging to the Liliacee family along with the Husk of Isabgol, was tried on five thousand patients who had proved ischaemic heart disease due to atherosclerosis and the above two herbal medicines proved to be very effective when mixed with wheat flour paste before preparing the bread. This plant; Aloe vera, is used in Indian medicine as a tonic, purgative, aphrodisiac, antihelminthic, in various opthalmological disorders, enlargement of spleen, various forms of hepatitis, vomiting, fever due to bronchitis, erysipelas, skin disorders, asthma, leprosy, jaundice, strangury, as a carminative, various musculoskeletal disorders, menstrual suppression and various other nonspecific disorders.

Table I

Sex	Total Patients	Age Group	No. Of Patients	Diabetic Patients	Family History Of Diabetics	Total Hyper- tensives	Mild	Moderate
M	3489	35-40	869	612	408	115	65	50
M		41-50	1050	823	639	325	201	124
M		51-65	1570	989	805	467	301	166
Non- Diabetic Patients			1065			589	381	208
F	1511	35-40	231	85	60	25	15	10
F		41-50	589	207	189	67	49	18
F		51-65	691	451	371	210	108	102

Non- Diabetic Patients		768			353	240	113
	5000	5000	3167	2472	2151	1360	791

Table II

Age Group	No. Of Patients	Anterior Wall Ischaemia	Inferior Wall Ischaemia
Male Diabetics			
35-41	612	398	214
41-50	823	526	297
51-65	989	605	384
Male Non-Diabetics	1065	424	641
Female Diabetics			
35-40	85	31	54
41-50	207	96	111
51-65	451	302	149
Female Non-Diabetics	768	438	330
	5000	2820	2180

Table III

Fasting Blood Sugar (Normal 60-110 Mgm%)

Sex	Age Group	No. Of Patients	111-125 Mgm%	126-150 Mgm%
Males	35-40	612	398	214
	41-50	823	564	259
	51-65	989	598	391
Females	35-40	85	48	37
	41-50	207	140	67
	51-65	451	299	152
		3167	2047	1120

Post Parendial Blood Sugar (Normal 100-160 Mgm%)

Sex	Age Group	No. Of Patients	161-250 Mgm%	251-400 Mgm%
Males	35-40	612	405	207
	41-50	823	530	293
	51-65	989	611	378
Females	35-40	85	42	43
	41-50	207	131	76
	51-65	451	305	146

		3167		2024	1143

Table IV
Total Serum Cholesterol (Normal 125-285 Mgm%)

Sex	Age Group	No. Of Patients	286-350 Mgm%	351-425 Mgm%	426-500 Mgm%
Males	35-40	612	309	198	105
Diabetics	41-50	823	429	256	138
	51-65	989	547	232	210
Non-Diabetic Males		1065	219	657	189
Females	35-40	85	25	40	20
Diabetics	41-50	207	67	108	32
	51-65	451	112	298	95
Non-Diabetic Females		768	204	469	95
		5000	1912	2258	830

Table V
Serum Triglycerides (Normal Level 40-150 Mgm%)

Age Group	No. Of Patients	151-170	171-200	201-250
Male Diabetics				
35-40	612	305	203	104
41-50	823	415	301	107
51-65	989	509	249	231
Male Non-Diabetics	1065	208	701	156
Female Diabetics				
35-40	85	20	44	21
41-50	207	61	112	34
51-65	451	108	304	39
Female Non-Diabetics	768	198	502	68
	5000	1824	2416	760

Table VI
Total Lipids (Normal Value 450-850 Mgm%)

Age Group	No. Of Patients	851-1000	1001-1200	1201-1350
Male Diabetics				
35-40	612	291	180	141
41-50	823	402	281	140
51-65	989	517	241	231

Male Non-Diabetics	1065	205	670	190
Female Diabetics				
35-40	85	22	42	21
41-50	207	61	111	35
51-65	451	104	313	40
Female Non-Diabetics	768	198	480	90
	5000	1800	3118	882

Table VII
HDL Cholesterol (Normal Level 25 Mgm% to 75 Mgm%)

Age Group	No. Of Patients	20-25	26-30	31-35
Male Diabetics				
35-40	612	401	176	35
41-50	823	509	289	25
51-65	989	610	260	119
Male Non-Diabetics	1065	304	677	84
Female Diabetics				
35-40	85	15	50	20
41-50	207	101	98	8
51-65	451	156	258	37
Female Non-Diabetics	768	212	470	86
	5000	2308	2278	414

The plant has never been tried in the prevention of atherosclerotic heart disease. The other substance, Husk of Isabgol, in Indian medicine is mainly used to increase the bulk of faeces in constipation. This study is mainly based on its antiatherosclerotic properties.

Materials And Methods

Five thousand patients were selected for the study ranging from 35-65 years of age. *(Table I)* All patients had clear cut evidence of ischaemic heart disease in the form of unequivocal ECG changes apart from effort angina. *(Table II)* All patients were subjected to serum chemistry and were screened for fasting blood sugar, post parandial blood sugar *(Table III)*, total serum cholesterol *(Table IV)*, serum triglycerides *(Table V)*, total lipids *(Table VI)*, HDL cholesterol *(Table VII)*, BUN & other investigations were normal.

Out of 5'000 patients, 3167 were diabetics; 2572 patients had a history of smoking 10 to 15 cigarettes per day, for about five years; 2151 patients had evidence of hypertension which was not renal in origin. Out of these 2151 hypertensives, 1360 had mild hypertension and 791 patients had moderate hypertension. The patients, who had unstable angina, past history of myocardial infarction, severe hypertension, severe diabetics & patients on insulin therapy, history of left ventricular failure, gout, were not included in the study. Out of 1065 male non-diabetics, 912 had family history of hyperlipidemia and out of 768 female non-diabetic patients, 454 patients were having family history of hyperlipidemia. All

5000 patients were instructed not to consume alcohol in any form during the study. Smoking was also not allowed during study period.

All 5'000 patients were instructed to take 100 gms of fresh flesh gelatin of the plant Aloe vera and 20 gms of Husk of Isabgol mixed with wheat flour to prepare the bread. These breads were consumed at lunch and dinner. Apart from this, the strict dietary schedule and the drugs, which these patients were already taking, in the form of beta blockers, verapamil, nifedipine, isosorbide dinitrate, sulphonylureas, digoxin and diuretics and B-complex, were asked to continue and report weekly. All these patients were assessed clinically and biochemically.

Table VIII
Tread Mill Test Reading After One Year of Treatment

Age Group	No. Of Patients	Anterior Wall Ischaemia	No Evidence Of Ischaemia	Inferior Wall Ischaemia	No Ischaemia
Male Diabetics					
35-40	612	398	396	214	202
41-50	823	526	500	297	276
51-65	989	605	600	384	341
Male Non-Diabetics	1065	424	399	641	582
Female Diabetics					
35-40	85	31	29	54	52
41-50	207	96	93	111	107
51-65	451	302	259	149	133
Female Non-Diabetics	768	438	388	330	295
	5000	2820	2664	2180	1988

Table IX
Serum Cholesterol Levels Returned After Three Months (160-240 Mgm%)

Age Group	No. Of Patients	290-350	Normal	351-425	Normal	426-500	Normal
Male Diabetics							
35-40	612	309	306	198	192	105	100
41-50	823	429	408	256	238	138	130
51-65	989	547	504	232	231	210	206
Male Non-Diabetics	1065	219	200	657	599	189	182
Female Diabetics							
35-40	85	25	23	40	39	20	19
41-50	207	67	65	108	106	32	29
51-65	451	112	101	298	251	41	40
Female Non-Diabetics	768	204	162	469	431	95	90
	5000	1912	1769	2258	2087	830	796

Table X
Serum Trigylcerides Returned After Three Months (50-90 Mgm%)

Age Group	No. Of Patients	151-170	Normal	171-200	Normal	201-250	Normal
Male Diabetics							
35-40	612	305	300	203	200	104	98
41-50	823	415	399	301	300	107	77
51-65	989	509	489	249	229	231	223
Male Non-Diabetics	1065	208	158	701	680	156	143
Female Diabetics							
35-40	85	20	18	44	43	21	20
41-50	207	61	60	112	110	34	30
51-65	451	108	69	304	288	39	35
Female Non-Diabetics	768	198	140	502	485	66	58
	5000	1824	1633	2416	2335	760	684

Table XI
Total Lipids After Three Months of Treatment

Age Group	No. Of Patients	851-1000	Normal	1001-1200	Normal	1200-1350	Normal
Male Diabetics							
35-40	612	291	282	180	176	141	140
41-50	823	402	370	281	268	140	138
51-65	989	517	499	241	213	231	229
Male Non-Diabetics	1065	205	155	670	650	190	176
Female Diabetics							
35-40	85	22	21	42	41	21	19
41-50	207	61	60	111	109	35	31
51-65	451	104	84	313	282	34	25
Female Non-Diabetics	768	198	168	480	430	90	85
	5000	1800	1639	2318	2170	882	943

Table XII
HDL Cholesterol (Normal 50-75 Mgm) After Three Months

Age Group	No. Of Patients	20-25	Normal	26-30	Normal	31-35	Normal
Male Diabetics							
35-40	612	401	390	176	174	35	34
41-50	823	509	478	289	279	25	19
51-65	989	610	580	260	250	119	111
Male Non-Diabetics	1065	304	254	677	647	84	80
Female Diabetics							
35-40	85	15	12	50	49	20	20
41-50	207	101	97	98	96	8	7
51-65	451	156	126	258	238	37	28

Female Non-Diabetics	768	212	180	476	418	86	85
	5000	2308	2117	2278	2151	414	384

Table XIII
Blood Sugar Levels Before & After Treatmet

Age Group	No. Of Patients	Fasting 110-115	Normal	Fasting 116-150	Normal	P.P 161-250	Normal	P.P 251-400	Normal
Male Diabetics									
35-40	612	398	394	214	208	405	399	207	203
41-50	823	564	554	259	247	530	518	293	283
51-65	989	598	538	391	364	611	553	378	349
Female Diabetics									
35-40	85	48	45	37	35	42	40	43	40
41-50	207	140	136	67	65	131	126	76	75
51-65	451	299	259	152	145	305	275	146	129
	3167	2047	1926	1120	1064	2024	1911	1143	1079

Table XIV
Drug Therapy

Verapamil	Beta-Blockers	ISDN	Digoxin & Diurects
40-80 mgm in 2 divided doses (mild cases)	40-60 mgm in 2 divided doses in mild cases to non-diabetics	10 mgm 3 to 4 times per day	0.25 mgm of digoxin & dytide 1 tab./day
&	&		
80-120 mgm in 3 divided doses (moderate cases) to diabetics	80-120 mgm in 3 divided doses in moderate cases to non-diabetics		

Results

Most of the patients started responding from second week after the therapy was instituted. The improvement was noticed in the form of disappearance of angina pectoris and feeling of well being. The ECG changes also started improving and from 3 months to one year all patients, except 348, had normal tracing even after treadmill *(Table VIII)*.

None of the patients suffered fresh myocardial infarction during the study. The lipid profile also started improving after three months of institution of therapy *(Table IX)*.

Out of 5000 patients, 4652 patients had their normal levels of serum cholesterol ranging from 160 Mgm to 240 Mgm%, serum triglycerides from 50-90 Mgm% *(Table X)*.

Total lipids from 500 Mgm to 800 Mgm% *(Table XI)*, HDL cholesterol ranging from 50 Mgm to 75 Mgm% *(Table XII)*.

Out of 3167 diabetic patients, the blood sugar values, fasting and post parendial, started coming down to normal levels *(Table XIII)* except in 177 patients, and all the oral hypoglycemic agents had to be withdrawn by the end of two months of therapy. On the contrary, beta blockers, calcium channel blockers, isosorbide dinitrate and diuretics, etc., which the patients were taking for hypertension and angina control, could not be withdrawn completely *(Table XIV)* but their doses substantially reduced to half of the quantity which they were taking. Similarly the hypertensive patients did not show any significant change in their blood pressure levels. Total number of patients who did not respond to treatment were 525 (348 ischaemic and 177 diabetics out of 5000 patients).

Discussion

In the present study it has been noticed that the plant had a definite role in the prevention and management of atherosclerotic heart disease. The plant also had a definite role in controlling the blood sugar level in diabetic patients. The exact mechanism of the plant Aloe vera and Husk of Isabgol is not known but it appears that both these substances act by their high fibre contents and these substances need further evaluation. In the entire study no untoward side effect was noticed and all the patients were followed for a period of five years from July 1978 to June 1983 and all the patients turned up for regular follow up and till date all the 5000 patients are surviving. The diabetic patients, except 177 patients, are on diet control alone and none of them has ever complained about any hypoglycemic episode during the study. There is no such study available in medical literature where such a large number (5000 patients) of patients are being followed up for five years and no Indian plant has ever been tried with such success. So this is a unique study of its own type.

To conclude, the Indian plant Aloe vera, when mixed with the Husk of Isabgol, was given to the patients of atherosclerotic heart disease, there was a definite and substantial improvement (about 95%) in their clinical profile apart from biochemical changes and ECG tracings. These two substances need further evaluation to find out the exact mechanism of action on atherosclerosis.

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