ALOE VERA

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A FAVORABLE RESPONSE OF HIV-1-INFECTED PATIENTS TO ORAL ACEMANNAN AND DEVELOPMENT OF PROGNOSTIC CRITERIA FOR CLINICAL RESPONSIVENESS

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INTRODUCTION

In 1985 and 1986 several anecdotal reports were received from AIDS patients claiming that after drinking a particular brand of commercially available aloe juice their clinical symptoms were eliminated or markedly reduced. As a result of these reports, an Initial Clinical Pilot study was performed under a Texas and Federal IND, FDA #27840 (McDaniel study).[1] Fourteen AIDS patients were treated by oral administration of aloe juice or a freeze-dried powder extracted from the juice. The purified aloe extract, acemannan (Carrisyn™), is described chemically as polydispersed b-(1,4)-acetylated mannan.[2] Acemannan has been shown in vitro to be biologically active.[3-9] Clinical improvement in this group of AIDS patients was indicated by reduction of MWR and, in selectively studied patients, by reduction or elimination of ability to culture the HIV-1 virus from blood and by lowering of the P-24 core antigen level. No side effects or toxicity were reported.

Wilcoxon paired-sample statistical evaluation (one-tail), by an independent academic mathematician revealed that improvement was significantly attributable to treatment in the less advanced patients ($p=0.005$). In more advanced patients statistical evaluation showed less significance that improvement was attributable to treatment ($p=0.25$). Both groups together, however, showed a significance of $p=0.01$.

A multi-disciplinary evaluation of this clinical pilot resulted in the recommendation that, to substantiate or disprove the clinical impression that the original small sample of AIDS patients had improved due to administration of acemannan, additional HIV-1 patients should receive the biologic at a fixed dose of 800 mg/day. The two studies reported herein were conducted to further explore the efficacy of treatment with acemannan.

demonstrate a favorable response, a patient was required to exhibit improvement in three parameters. The MWR had to improve, the absolute T-4 count had to increase and the P-24 core antigen had to decrease. A mixed-response was defined as improvement in two of these three criteria, a minor response was improvement in only one, and a poor response was lack of improvement in any.

The score (Fig. 6) of the 16 patients who were predicted to respond favorably was reduced from a mean of 2.6 to 1.1. The score of the patients who were predicted to do poorly averaged 3.5 prior to acemannan therapy and decreased to 2.6 at 90 days. The slopes of the lines for the comparative groups indicate that the rate of improvement was less in the group that was initially more symptomatic. Individual patients fulfilled the criteria for improvement, mixed response or poor response as indicated (Fig. 9).

Fig. 10 provides results of selected laboratory tests performed to evaluate if long-term ingestion of acemannan as oral aloe juice produces liver, kidney, metabolic or bone marrow toxicity. No evidence of functional suppression or toxicity was demonstrated. Minimal reductions in mean cholesterol and triglyceride concentrations were noted. Patients with higher and lower values tended to move to the mid-zone of normal for these lipid assays; this arithmetically canceled out the observed shifts. The most significant laboratory changes were increases in absolute T-4 helper and T-8 suppressor lymphocyte counts. The average T-4 lymphocyte count increased 48% and that for T-8 rose 34%.

Four patients in Study I who had previously been anergic to a battery of skin-test antigens became reactive to tetanus antigen after approximately 1 year of acemannan intake. The reactivity of one patient increased from one antigen to three. The remaining patients demonstrated no increase in skin reactivity to

intradermal antigens (mumps, Histoplasmosis, Candida, Trichophyton, tuberculin, tetanus) or saline control or remained totally non-reactive. The five patients who demonstrated a change, (either increased antigen reactivity or loss of anergy), averaged 325 cells/mm^3 absolute T-4 cells prior to therapy (range 221-391). At 350 days these same patients averaged 559/mm^3 absolute T-4 cells (range 456-664). These five patients had an average MWR of 6.2 (range 5.5-8.0) before treatment and 2.0 (range 0-3.5) at 350 days.

Patients in Study I are still being followed clinically, although their compliance for taking acemannan varies. Twelve of the original 15 have survived for over 2 years while including acemannan in their therapy. Results from ten patients in this follow-up screening are shown in Fig. 11.

DISCUSSION

Reports from AIDS patients who claimed their symptoms abated after taking a certain brand of uniquely processed aloe juice prompted a 1985-86 exploratory study in 14 HIV-1 patients. These patients received up to 800 mg/day acemannan under an individual physician investigational new drug exemption. The results of this study, verifiable by laboratory evidence, indicated that acemannan could improve the clinical condition of HIV-1 infected patients.

Such results prompted the two studies reported in this paper. The objective of the first study was to assess response of HIV-1 patients to acemannan therapy; the objective of the second was to determine if a response to acemannan treatment could be predicted based on certain pre-therapy laboratory values.

Parameters used to measure response and to serve as prognostic indicators were changes in modified Walter Reed clinical scores, absolute T-4 lymphocyte counts and serum P-24 core antigen levels.

The 1986-87 confirmatory study, Study I included 15 patients and lasted 350 days, during which the average MWR decreased from 5.6 to 1.8 and the average absolute T-4 count increased from 322/mm^3 to 478/mm^3. Serum core antigen was detected in five of the original 15 patients and was present but lower in three of the surviving 13 patients at the conclusion fo the study. One-third of the patients showed dramatic improvement.

The second study consisted of 26 patients and lasted 90 days. The average MWR in this group decreased from 3.0 to 1.8 and the average T-4 count rose from 217/mm^3 to 259/mm^3. P-24 antigen level reduction was not statistically significant.

The hypothesis applied in Study II was that those patients with a pre-therapy absolute T-4 count of greater than 150/mm^3 and a P-24 core antigen of

less than 300 pg/dl would exhibit a higher incidence of response to acemannan administration. Patients with greater than 250/mm^3 absolute T-4 should be even more likely to respond. Those patients with values reflecting greater immune system damage or greater virus load were projected to respond poorly to the immune-modulating agent. Twenty of 26 patients (77%) who ingested acemannan responded as predicted. Fifteen of 26 patients (58%) fulfilled all three assessment criteria for clinical improvement; improved MWR, increased absolute T-4 count and decreased P-24 core antigen.

Three patients predicted to improve in all three criteria failed to do so, although they did improve in two parameters. Thus, none predicted to respond favorably failed to show some improvement. Three patients predicted to show no improvement did improve in at least one category with two of the patients improving in all three.

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BIBLIOGRAPHY

1. McDaniel HR, McAnalley BH. Evaluation of Polymannoacetate (Carrisyn®) in the Treatment of AIDS. Presented at the American Federation for Clinical Research. May 1987; San Diego, California. Abstract.

2. Eberendu A, McAnalley BH, Carpenter RH, McDaniel HR. Isolation and Characterization of a New Antiviral Polysaccharide Extracted from Aloe barbadensis Miller. Presented at the Texas Society of Pathologists' Scientific Poster Presentation. January 1988; Galveston, Texas. Abstract 001.

3. Womble D, Helderman JH. Enhancement of Allo-Responsiveness of Human Lymphocytes by Acemannan (Carrisyn®). Int J Immunopharmacol. 1988:10:967-974.

4. Helderman JH, Womble D. The Impact of Acemannan on the Generation and Function of Cytotoxic T-Lymphocytes. Carrington Document # 6010.

5. McDaniel HR, McAnalley BH, Carpenter RH. In Vitro Studies on Polymannoacetate (Carrisyn) for Antiviral Effect. Presented at the American Society for Clinical Pathologists Scientific Assembly; October 1987; New Orleans, Louisiana. Abstract 121.

6. McDaniel HR, White A., McAnalley BH, Carpenter, RH In Vitro Antiviral Effect of Acemannan on Feline Rhinotracheitis . Presented at the Texas Society of Pathologists Scientific Poster Presentation. January 1988; Galveston, Texas. Abstract 003.

7. McAnalley BH, McDaniel HR, Carpenter RH. Demonstration of In Vitro Antiviral Action of Acemannan against multiple viruses including the HIV Virus. Presented at the Fourth International Conference on AIDS; June 1988; Stockholm, Sweden. Vol.II Abstract 3567.

The Truth About Aloe Vera

How to Select the Best Aloe Vera Beverage

by George Klabin

Aloe vera is a very complex plant containing thousands of healing substances. Many products sold for internal consumption contain only a small part of the leaf. This article will present little-known facts that many of the Aloe processors would rather not reveal, to allow an informed decision when purchasing Aloe products. This discussion will be confined to Aloe beverages, though much of what is said here applies to topical products as well.

The Aloe genus belongs to the Lily family (Liliaceae). There are many species in existence. All of them are perennial evergreen xerophytic (drought-resistant) plants which grow in subtropical and tropical areas. Aloe leaves are fleshy, succulent, and coated with a protective waxy deposit, and retain water for a great length of time, which is why the leaf is composed of about 99% water.

This plant grows only in climates where the temperature does not go below freezing, and is able to withstand direct sunlight for prolonged periods, being a succulent. The ideal growing climate for the plant is a warm climate, where the leaves will contain more of the healing substances than when exposed to extremes of temperature. In extremes of heat the plant will use up its store of energizing nutrients in the gel, and in cases where the ground freezes the plant will often die. Almost the entire Aloe vera crop in the Rio Grande Valley was wiped out twice in the past decade from unusually severe frost. Much of the Aloe now being processed comes from Mexico, or other countries with warmer climates. One US producer who suffered no crop loss during the freezes grows its Aloe plants hydroponically and organically in a huge greenhouse. These plants mature in half the time of plants grown outdoors (1.5 years instead of 3), and are protected from temperature extremes, which means the harvested leaves will have more consistent content of healing components.

Of the 200-300 species of Aloe vera in existence (200 according to Morton, 1961,[15] or 300 plus according to Klein and Penneys, 1988[5] around the world, two types most used and studied in the US, Japan, and Russia are Aloe Barbadensis Miller (also known as Aloe vera Linne or Mediterranean Aloe) and Aloe Arborescens. The papers reviewed in this article all relate primarily to these two varieties.

Despite being used medicinally for thousands of years, the chemistry of Aloe vera is still incompletely understood. Dr. Ronald Pelley in his presentation to the National Aloe Science Council in 1991 stated that Aloe contained over 10,000 proteins. Hundreds of other substances have been identified in Aloe vera, many of them useful in tissue healing. Most of the identification and quantification of these constituents was performed in the latter half of this century, and we still have much to learn about this remarkable plant.

Because it is so complex and easily misunderstood, Aloe vera has been misrepresented by many of the producers who sell products made with it, and has led to much skepticism regarding its medicinal value from the medical and scientific establishment.

Healing Substances In Aloe vera

A leaf of Aloe vera contains about 99% water, and only 1% solids. What follows is a list of well-known nutritional substances isolated from Aloe Barbadensis Miller or Aloe Arborescens, with references to the scientific studies or papers wherever possible.

Minerals (found as mineral salts, and some as inorganic): Magnesium lactate, Calcium Oxalate, Potassium, Chloride, Iron, Zinc, Manganese, Copper, Chromium, Sulfur.

Note: Magnesium lactate in Aloe was found by Hirata and Suga[4] to inhibit gastric acid secretion on male rats by 32%, which was comparable to commercially available preparations of magnesium lactate. Klein and Penneys[5] state that magnesium lactate inhibits the in-vivo conversion of histidine to histamine in mast cells by inhibiting histidine decarboxylase. In topical use, magnesium lactate as found in Aloe exhibits an antipruritic (anti-itch) effect.

Triglycerides: These supply the essential fatty acids for growth and health of tissues, and are found in high levels (Robson et al. found levels of 374 mg. per deciliter)[12]

Essential fatty acids: Hirata and Suga[4] assayed the following fatty acids in isolates of the whole leaf: Linoleic, Linolenic, Myristic, Oleic, Palmitic, and Stearic. The highest percentage was Linolenic, at 35% of the total. Caprylic acid has also been found (Stepanova et al. 1977)[11] and recent studies have shown its potent anti-yeast activity, which is why it is used in nutritional anti-Candida products.

Anti-Inflammatory: Lupeol, plant sterols such as b-sitosterol and campesterol. Brasher et al.[13] report that Aloe vera has anti-inflammatory effects similar to the drugs prednisolone and indomethacin, yet is less toxic to cells, and when tested on HeLa cells and rabbit kidney fibroblasts, the cells lived 67% longer than expected.

Antiseptic: sulfur, phenol, natural salicylic acid (derived from the breakdown of aloin in heat processing), urea nitrogen, The anti-microbial action of Aloe is dependent on the concentration. In a cream base product examined by Robson and Heggers in 1982,[12] they found concentrations of 70% were necessary for effective action against a number of gram positive and gram negative organisms, including E. coli; enterobacter sp.; Klebsiella sp; Pseudonomas aeruginosa; Staph aureus; Staph pyrogenes, group A; Bacillus subtilis, and yeast such as Candida albicans.

Analgesic (anti-pain): natural salicylic acid and magnesium. Prostaglandin/thromboxane inhibition: Robson and Heggers postulate that Aloe vera acts as an enzymatic substrate competitor. "Therefore, although Aloe vera inhibits thromboxane production by competitive inhibition through stereochemical means, it also supplies the necessary precursors to initiate the arachidonic cascade, giving the cell important constituents (PGE2 and PGF2) to maintain cellular integrity."[12]

Anti-helminthic (anti-parasite): cinnamonic acid (also known as cinnamic or hydroxycinnamic acid)

Vitamins: B1, B2, B3, B12, Folic Acid, Carotene, Choline.

Amino acids: 20 of the 22 amino acids needed for proper nutrition, including: Arginine, Aspartic acid, Cystine, Glutamic Acid, Glutamine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tyrosine, Valine. Gjerstad[16] assayed 18 amino acids in a freeze-dried Aloe juice.

Proteins: Over 10,000 are said to exist in Aloe vera. Since these components are present in relatively small amounts, it has been widely speculated that the synergistic action of many of them produce the healing attributed to Aloe.

Best Aloe Vera

New Discoveries:
Polysaccharides In Aloe

The importance of plant polysaccharides in healing is only beginning to be understood. Aloe contains several plant sugars, also known as mucco-polysaccharides. The most important one consists mostly of glucose, mannose, and (hexo)uronic acid, and is produced in the leaf rind. Discovered in the 1950's, it was named Polyuronide in a 1963 patent by Drs. Farkas and Mayer.[4] The polysaccharide was later renamed Acemannan by Carrington Labs of Texas, which has been granted a patent on extraction using methyl alcohol and freeze-drying to produce a powdered form, under the brand name of Carrisyn.[24]

It is speculated that Acemannan works as an anti-viral by "change in glycosylation and subsequent processing of viral glycoproteins."[1] It has potential uses against many types of viruses, including HIV, retroviruses, and very common viruses such as measles. While its method of action has not yet been pinpointed, it appears to prevent viruses from entering healthy T-cells and infecting them. The immune system can thus rebuild itself with fresh uninfected cells. This could be a very important treatment in illnesses which slowly disable the immune system by killing off the cells which attack foreign bodies.

There also appears to be no toxicity even when administered to animals in doses equivalent to 100 times the maximal dose in human studies.[2]

Carrington has spent millions of dollars to research and develop this single substance from Aloe, with the aim of receiving a drug patent on the extracted powder. The reference section lists several papers on Acemannan published in the past few years.

In "Antiviral Action of Acemannan (Ace-M) in a Measles Infected Cell Line,"[21] the conclusion is "A low concentration of Acemannan in vero cultures well-infected with measles virus demonstrated antiviral action by protecting new cells from virus infection, thus restoring the cytoprotective free monolayer of vero cells."

In "Inhibition of Human T-Cell Lymphotrophic (HIV) Virus in vitro by Acemannan," the conclusion was "Acemannan, in a concentration attainable in blood of human subjects, produced anti-HIV virus activity in vitro cultures composed of target human T-cells of proven HIV susceptibility."

Recently, in 1991, researchers at Texas A&M University published preliminary findings showing that use of Acemannan could reduce the need for AZT in those taking it by up to 90%. One would expect a large decrease in toxicity at those lower dosages. In the fall of 1991 the USDA approved Acemannan as a treatment for fibrosarcoma (cancer) of dogs and cats.

The extracted, freeze-dried Acemannan produced by Carrington Labs is chemically identical to Acemannan naturally occurring in Aloe. Since it is a plant sugar, Acemannan is quite stable and can be retained in commercial products, if proper processing methods are used. Only recently, a handful of Aloe beverages have been developed which are made from the whole leaf of the plant, and thus have the potential to contain measurable amounts of Acemannan. The producers of these products face a new problem when dealing with the sap and rind: the removal of undesirable aloin.

Fortunately, it is relatively easy and reproducible to measure the amount of Acemannan in any Aloe product. Dr. Ivan Danhof, a researcher and publisher on Aloe, uses a technique developed several decades ago, which precipitates the polysaccharides in a solution of methyl alcohol. A known amount of the product in question is placed in a known amount of alcohol, and allowed to stand for 72 hours. The extract which precipitates out can be weighed and quantified, and related to the total product by milligrams per liter (parts per million). Danhof stated that approximately 98% of the precipitate is the polysaccharide Acemannan, the rest being preservatives or other substances. Several hundred Aloe products were tested in this manner over the past few years, and very few had any measurable amounts of Acemannan. This is due to the fact that most of the products measured used only the gel portion, and many may also have been diluted, or improperly processed or handled.

Undesirable Components of Aloe

Aloin is an anthraquinone glucoside found primarily in the sap (latex). It is a potent cathartic (laxative). In commercial Aloe beverages not designed as laxatives, the aloin must be removed. Federal specifications state that Aloe beverages contain no more than 50 ppm aloin. The presence of aloin in fresh whole leaves limits their usefulness to topical application. That is why one rarely hears of people grinding up whole Aloe leaves and drinking the collected juice., except for laxative purposes.

Due to this undesirable component, most producers of Aloe beverages have discarded the sap and rind, where the aloin resides, to use the central gel, which, if carefully separated from the rest of the leaf, will be aloin-free.

The NASC (National Aloe Science Council) has developed specific standards which must be met for a product to receive its seal of approval and to be considered "real" Aloe vera. The problem is that the standards are merely a listing of a few chemicals in certain minimal amounts which must be present in the product, and which can be measured. In addition, the standard was developed for Aloe gel products, which make up the vast majority of products sold. Acemannan is not one of the chemicals listed in the standard.

The weakness in this NASC standard is the fact that it is easy to produce a fake Aloe that will pass their test by making a cocktail of chemicals purchased from supply houses.

At this time, it seems to be impossible to prove, by testing alone, that a given product is Aloe vera or not. Certain components can be measured, but the complex structure has yet to be fully unravelled.

What seems to make Aloe work best is synergism. Modern medicine is oriented to breaking things down to find single substances, which can then be extracted and synthesized. Aloe is loaded with healing elements, but in relatively small amounts. It seems logical that many Aloe products work by a synergistic relationship of the parts. While most Aloe juice products have had significant portions of beneficial substances removed by processing, they still perform some healing functions, such as soothing inflamed mucous membranes. To get the most benefit, one should look for the most complete Aloe juice, one which is closest to the fresh whole leaves, only with the cathartic aloin removed.

The Aloe leaf consists of three main sections: the thick green outer rind; the sap contained inside large pericylic tubules forming part of the vascular bundles just beneath the rind; and the inner portion, the gel fillet, also called mesophyll.

The central gel is mostly water, containing only about 1/2% solids, and thus obviously much less healing compounds than the other parts of the leaf. Aloe products stating they are made from "gel" use only this portion of the leaf, and thus avoid the presence of the laxative aloin. Over 95% c Aloe beverages for sale today are made only from the gel portion.

This gel portion contains only some stored carbohydrates and minerals, and varies with exposure to heat and cold, as the plant will use these nutrients for itself and deplete them in the gel. In combination products which use the whole leaf, the gel acts as a buffering agent.

Researchers who used only the gel portion did not find many ingredients in it.

then created a freeze-dried extract. While he did not refer to the method of extraction, he did measure the water content of it and found it to be only 1/2% solids, which corresponds to the gel portion alone. If he had used the sap or rind, he would have found a higher portion of solids. Gjerstad confirmed the presence of many amino acids, in small concentrations of 3 to 17 parts per million (milligrams per liter). In addition he found a-D-glucose as the only free sugar, an unidentified aldopentose (a carbohydrate with 5 atoms of carbon, containing an aldehyde group), and a tiny protein content of 0.013 percent. From this he concluded that it was "difficult to visualize Aloe vera as a panacea." He did also state that infrared spectra showed peaks corresponding to hydroxy, amino, ether, carboxyl, and peptide linkages, which are expected in most natural products.

A second paper by Gjerstad and Bouchey[17] examined inorganic substances in the same preparation of freeze-dried gel extract, and found only small amounts of Calcium, Chlorine, Sodium, Potassium and Manganese. Once again the conclusion was that these were too small to be of much medicinal use.

These studies illustrate the complexity of aloe and point out the need for further chemical analyses of finished products with today's sophisticated equipment. They also support the fact that, while the gel portion probably contains more healing substances than Gjerstad found, it does not contain many that are in the other portions of the leaf. It should be noted that some beneficial substances in the gel may have been lost Gjerstad, since this process breaks the electrolyte bonding of water in the solution.

The sap or latex of the Aloe plant is yellow colored, and high in anthraquinone glucosides, especially aloin. The anthraquinones absorb the sun's ultraviolet rays and prevent overheating of the central portion of the leaf, where the water is stored. The sap contains about 6% solids. No sap is found in the gel portion of the leaf. However, depending on how the leaf was processed, it is possible for some sap to mix in with gel and be present in certain gel-only Aloe products. Producers of gel-only products supposedly take care to remove the gel fillet from the leaf in a manner that does not break any of the tubules in the outer area, and allow the sap with its bitter aloin to leak out. The practice of hand filleting, by which each leaf is individually opened and the gel removed, is the best method to assure pure gel. However, many processing plants employ rolling equipment. The leaf is passed between two rollers and the juice squeezed out. The rind remains behind. In this common process, some sap may leak into the gel. Gel products made by this method may actually contain more healing ingredients in the final beverage than those made with hand filleting, but may also contain some aloin.

The rind is the thick green outer portion of the leaf, and contains over 12% solids and minerals. The rind manufacturers all the polysaccharides and enzymes. These carbohydrates (polysaccharides) not needed for energy metabolism are transported to and stored in the gel, where they can be used if the plant becomes "stressed" by

extremes of temperature or poor nutrition.

Which is the best part of the leaf? Aloe producers readily state that Aloe vera was used for thousands of years for healing, but often omit the fact that most of the serious writings on Aloe vera mention the bitter, yellow or red sap as the main medicinal part. There are documents which show that the whole leaf was ground and either used as a poultice or eaten as treatment for internal disorders.

Dioscorides, a first Century Greek physician, stated that the healing properties were found in this bitter juice, referring to the sap, not the gel. He adds that this bitter Aloe is a treatment for boils, ulcerated genitals, hair loss, tonsils, gums, mouth pain, and works as an eye medicine when roasted in a hot vessel and mixed with water.

The Chinese Materia Medica called Aloe "Lu-hui" (meaning black deposit, a reference to is dark color), or "Hsiang-tqan" (elephant gall, referring to its bitter taste). These writings show Aloe was used for sinusitis, worm fever and convulsions in children, all by internal administration.

The common element in many of the writings about the use of Aloe, in the past several thousand years, is the reference to dark color and bitter taste, demonstrating the use of the sap and rind.

A common myth about Aloe, passed from one Aloe promoter or producer to another, and widely quoted in writings about the plant, is that it was mentioned in the Bible, and used to annoint the body of Christ. The

Here's the bottom line: Whole leaf Aloe vera products processed by either cold or heat will not contain significant amounts of enzymes. In most of the literature which goes beyond merely listing the beneficial components in Aloe, the importance of enzymes is minor, or is merely speculated to be an additional benefit.

Enzymes are most useful in Aloe as a debriding agent for external wounds. Perhaps this is why fresh Aloe leaves, with enzymes intact, show excellent results in wound healing. In their patent paper of 1963 for Polyuronide extraction, Drs. Farkas and Mayer state "When Aloe jel (gel) is taken out of the leaves deterioration started immediately. Germs, molds, but especially the enzymes ferment the gel completely overnight.... The role of the enzymes in Aloe, and also all other plants, is to decompose the ripe fruits and plant components so their components may return to the soil under and around the plant. The enzymes will still act, even when they are incorporated in cosmetic products. Decomposition of the jel may be slowed down, but not arrested."

The Preservative Controversy

There are some Aloe products which state clearly on their label "No Preservatives." This is an attempt to gain the favor of consumers who wish to avoid added chemicals in food products. However, since Aloe vera is a vegetable juice, it must be properly preserved, or it will rot, from growth of bacteria, mold, or other organisms. The only sure, effective, and approved way to prevent this is to add small amounts of preservatives such as sodium benzoate and potassium sorbate, which keep bacterial and fungal growth in check, and anti-oxidants such as vitamin C. In addition, an acidic pH discourages microbial replication, and citric acid is usually added to lower the pH of Aloe beverages. The only alternative to these preservatives would be constant refrigeration, which is impractical.

The simple fact is that if a product states that it uses no preservatives, most likely it either does not contain any Aloe vera in it, or, though the marketing company may not add any preservatives, their supplier or processor added them. There are hundreds of brands of Aloe vera juices on the market, but only a handful of processors and growers, who do not wish to risk their reputation or a liability suit by producing a product which will rot.

With the new generation of whole leaf aloe products, the goal of choosing an effective Aloe vera beverage should be to buy the one closest in content to the fresh whole leaf, with the most healing components left in, at the best price. This seems to rule out gel only products. The choice is between whole leaf products that can prove by assay that they contain measurable amounts of acemannan. The optimal daily dose of acemannan is still not known. Carrington recommends 1000 milligrams per day. Other whole leaf products, such as Lametco, Coats, or Aloe Ace, recommend doses which would correspond to 25 to 185 milligrams per day. Acemannan is only part of the story. Those products which can show, either by assay or by the method of processing that they retain the most healing substances, are the most useful in healing. Since it is so difficult to quantify the other beneficial ingredients in Aloe products, the consumer must educate him or herself by demanding as much information as possible about a brand or product.

Good Aloe products are expensive. Aloe vera juice can be purchased at retail prices ranging from a few dollars a quart to $30 to $40 per pint! Is paying $20 a gallon for a non-concentrated product with a lot of the best parts removed, a better deal than paying more for a concentrated product that contains most of what was in the whole leaf?

Here are the choices among whole leaf products:

1. A product made by adding a reconstituted amount of extracted and freeze-dried Acemannan powder to Aloe gel liquid. Part of the process by which the Acemannan is extracted involves carbon filtering.
2. A cold-processed product made from the whole leaf, with measurable amounts of Acemannan, but with significant other portions removed by carbon filtering.
3. A heat-processed product using the Kolbe reaction, which is a low heat (about 70-80 degrees Centigrade) pasteurization, and no carbon filtering, containing measurable amounts of Acemannan, and most of the other components of the whole leaf.

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References

1. Kemp, M.C., Kahlon, A.D., et al. In vitro examination of the antiviral effects of acemannan on the replication and pathogenesis of HIV-1 and other enveloped viruses: Modification of the processing of glycoprotein precursors. Abstract #84 presented at Third Int. Conference on Antiviral Research, Brussels, Belgium, 4/22-27/1990.
2. McDaniel, H.R. and McAnalley, B.H. Evaluation of Acemannan (Carrisyn) in the Treatment of Acquired Immunodeficiency Syndrome (AIDS) Patients. *Amer. Fed. for Clinical Research*, Vol. 35, No. 3, April 1957.
3. Hemmesee, Odus, and Cook, William. *Aloe, Myth, Magic, Medicine*. Universal Graphics, 1989.
4. Farkas, A., and Mayer, R. Aloe Polyuronide The Active Healing Principle of the Aloe Plants U.S. Patent 3,362,951, 1963.
5. Klein, Alan D. and Penneys, Neal S. Aloe Vera *Journal of American Academy of Dermatology* 1988;18:714-20.
6. *Merck Index*, 11th ed. ion, 1989. Page 307 Chemical structure of Aloin and Aloe emodin.
7. Sheets, M., Unger, B. et al. Studies of the effect of acemannan on retrovirus infections: clinical stabilization of feline leukemia virus infected cats. *Journal of Molecular Biotherapy*, Vol. 3, March, 1991.
8. National Aloe Science Council, Analytical and Reporting Procedures and 1983 Program of Work, McLean, VA.
9. Filatov, V.P. Tissue Therapy in Cutaneous Leishmaniasis *American Review of Soviet Medicine*, vol. 2, August 1945.
10. Gottshall, R.Y., Lucas, E.H., Lickfeldt, A., and Roberts, J.M. The occurrence of Antibacterial Substances active against Mycobacterium Tuberculosis in Seed Plants. *Journal of Clinical Investigation*, V. 28, 1949, p. 920-923.
11. Stepanova, O.S. et al. Chemical Composition and biological activity of dry Aloe leaves. *Farol Aktivnye Vesh* 9, 94-97 (1977).
12. Robson, M.C., Heggers, J., and Hagestrom, W. Myth, Magic, Witchcraft, or Fact? Aloe Vera *Journal of Burn Care and Rehabilitation*, May/June 1982, p. 157-163.
13. Brasher, W.J., Zimmerman, E.R., and Collings, C.K. The effects of prednisolone, indomethacin, and Aloe vera gel on tissue culture cells. *Oral Surgery, Oral Medicine & Oral Pathology*, 27, 122-128 (1969).
14. Hirata, T. and Suga, T. Biologically Active Constituents of Leaves and Roots of Aloe Arborescens Var. Natalensis. *Zeitschrift Fur Naturforsch*, Vol. 32, 1977, p. 731-734.
15. Morton, Julia F. Folk Uses and Commercial Exploitation of Aloe Leaf Pulp. *Economic Botany*, Vol. 15, 1961, pages 311-319.
16. Gjerstad, G. Chemical Studies of Aloe Vera Juice - I: Amino Acid Analysis. *Advancing Frontiers of Plant Sciences*, Vol. 28, 1969.
17. Bouchey, G.D. and Gjerstad, G. Chemical Studies of Aloe Vera Juice II. Inorganic Ingredients *Quarterly Journal of Crude Drug Research*, p. 1445-1453, 1969.
18. Skousen, Max B., ed. *Aloe Vera: New Scientific Discoveries*. Aloe Vera Research Institute, 1982.
19. Gage, Diane. *Aloe Vera*. Healing Arts Press, 1988.
20. Danhof, I., Ph.D., M.D. *Remarkable Aloe; Aloe Through the Ages*. Omnimedicus Press, 1987.
21. White, A., McAnalley, B., Funderburk, N. Antiviral Action of Acemannan (Aoe-M) in a Measles Infected Cell Line from Proceedings of Texas Society of Pathologists, Jan. 29-31, 1988, Univ. of Texas at Galveston.
22. McDaniel, H. et al. Inhibition of Human T-Cell Lymphotrophic Virus (HIV) in vitro by Acemannan (Aoe-M) from Proceedings of Texas Society of Pathologists, Jan. 29-31, 1988, Univ. of Texas at Galveston.
23. McDaniel, H. and McAnalley, B. Evalution of Acemannan (Carrisyn) in the Treatment of Acquired Immunodeficiency Syndrome (AIDS) Patients. *Amer. Fed. for Clinical Research*, Abstracts, vol. 35, No. 3, April 1987.
24. Eberendu, A. et al. Isolation and characterization of a New Antiviral Polysaccharide Extracted from Aloe barbadensis Miller from Proceedings of Texas Society of Pathologists, Jan. 29-31, 1988, Univ. of Texas at Galveston.
25. NAME, *The Chemistry and Physics of Carbon*, Vol. 2, Adsorption from Solution by Graphite Surfaces. M. Dekker, 1965.

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Letter to the Editor
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Vitamin C and AIDS

In "Vitamin C Gets a Little Respect" (Research News, October 18, 1991, p. 375), I have been quoted as "admitting" that I've heard of only one anecdotal case of an AIDS patient who claimed that megadoses of vitamin C improved quantitative clinical markers such as T-cell count.

As a laboratory researcher, I don't presume or expect to be considered an authority on clinical data. Yet, the limited clinical information on vitamin C and AIDS that I have come across includes reports of patients claiming marked improvement in their clinical symptoms after ingesting large doses of the vitamin. At this Institute, our laboratory studies of this were in fact prompted by a visit here, a few years ago, of six patients diagnosed with full-blown AIDS. Four of them with Kaposi's sarcoma claimed amelioration of their skin lesions after self-medication with 15 - 20 grams/day of vitamin C for many months. I continue to receive many calls from AIDS patients who are taking large doses of vitamin C, but these are persons who are self-medicating rather than being under the care of a physician who might monitor such markers as T-cell subsets.

In addition, two physicians who have monitored AIDS patients on megadoses of vitamin C have independently observed [1,2] such clinical effects as *(i)* prevention and shortening of *pneumoncytis carinii pneumonia* (PCP) episodes; *(ii)* reduction or disappearance of Kaposi's sarcoma lesions; *(iii)* lessening of allergic reactions to antibiotics for PCP and other opportunistic infections, and *(iv)* reduction in HIV p24 antigen level in blood serum. Data on T-cell counts were not reported in these cases.

Maybe when vitamin C gets a little *more* respect, some clinician will take the seemingly rather obvious step of finding out — by clinical trials, not anecdotal reports — about the effects of high-dose vitamin C in HIV-infected people.

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References

1. Cathcart, R.F. Vitamin C in the treatment of AIDS, *Medical Hypotheses* 14:423-433, 1984; reprinted in O'Connor, Tom. Living with AIDS: Reaching Out, (Corwin Publishers, 1987).
2. Brighthope, I.E. AIDS: remissions using nutrient therapies and megadose intravenous ascorbate. International Clinical Nutrition Review, April 1977, pp. 53-75; referred to in his book, The AIDS Fighters (Keats Publishing, Inc., 1988).

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AIDS UPDATE

Aloe Vera Concentrate

by Ron Mealy

After completion of a two month observation period, *aloe vera concentrate* was brought to my attention by Karen Masterson-Koch, CN, a nutritionist at *Park Center for Health* in San Diego, CA who has been counseling persons with HIV and AIDS for several years. "We decided to include this unique aloe vera juice concentrate in the regimen of many of our sicker patients, ranging from Ebstein Barr to AIDS and the results have been astounding! Every single patient states that their energy has increased, and many are now sleeping through the night. We even had a patient receive the news that his tumors located in his throat were now receding after three weeks of use, where previously the chemotherapy was not creating any success," says Ms. Masterson-Koch.

One of the active ingredients in this aloe vera concentrate is a mucopolysaccaride, a natural sugar molecule, and one of its components is *Acemmannan*, also known as Carrisyn. Acemannan has previously and continues to be investigated as a potential antiviral agent for HIV. A team of scientists from Texas A & M University and three other institutions say that acemannan purified from the green, spiky aloe vera plant appears to help drugs such as Retrovir (zidovudine, a drug formerly known as AZT) and acyclovir (ACV) block the pathology associated with the human immunodeficiency virus (HIV) and herpes simplex virus (HSV). They also found that the compound interfered with HIV's ability to reproduce in infected cells. Dr. Maurice C. Kemp, a virologist at Texas A & M's College of Veterinary Medicine said the research suggests that one-tenth the AZT dose could be administered to AIDS patients if it is given with acemannan. Kemp's laboratory research uses cultures of cells to study how acemannan affects the way viruses attach to cells and spread once they have infected them. Other members of the research team are testing the compound's effect on humans infected with HIV. A related investigational new drug (IND) clinical study with AIDS patients in Canada began in December. "It's not going to be a magic bullet against AIDS," cautions Dr. Kemp. There aren't many magic bullets out there. But as an adjunctive therapy, it looks like it can be used in combination with a lot of other therapies."

Aloe is considered a food, it has no bad side effects, except for the rare occurrence of allergy, as any food substance can potentially have. However, Ms. Masterson-Koch says, "because of aloe's apparent effect on fungus, some individuals that have had acute candida or thrush, actually feel more tired for 3-7 days upon drinking this aloe, and then the individuals seem to feel better and better, perhaps due to the die off of the fungus. Because of its anti-fungal properties, gas or diarrhea could be a sporadic effect of the fungal die off." It is believed that viral and fungal activity in the body can greatly effect the individual with fatigue and clouded thinking. Patients with thrush or candida in the esophagus can gargle with the aloe before swallowing to encourage a topical application.

Lametco International, Inc. the company that produces the aloe concentrate asserts that it is pre pared by a whole-leaf, a cold process to assure maximum efficacy, and each bottle contains 7,000 - 14,000 mg per liter of the active ingredient.

Although the use of acemannan in treating HIV infection has not been widely accepted by AIDS researchers, aloe could be an important adjunct needed to strengthen the body's capacity to combat HIV infection.

Recommended dose by Karen Masterson-Koch, CN: 5 tsp two times a day on an empty stomach. Refrigerate after opening to insure freshness.

Recommended reading: The book by Ivan Danhof, MD, Ph.D., ***Remarkable Aloe - Aloe Through the Ages.***