"THE THERAPEUTIC COMPONENTS IN ALOE VERA"

BY DR. IVAN DANHOF, M.D., Ph.D.

INTRODUCTION:

The following lecture is presented by Dr. Ivan E. Danhof on the scientifically proven therapeutic components in Aloe vera. Dr. Danhof attended the University of North Texas, where he received a bachelor's degree in biology and chemistry, and a master's degree in microbiology. He continued graduate studies at the University of Illinois, where he earned a master's degree in nutrition and a Ph.D. in physiology. He then attended the University of Texas Health Science Center Southwest Medical School, earning a Doctor of Medicine degree with clinical specialties in internal medicine and gastroenterology. He has published more than 80 research papers and served as a consultant to several pharmaceutical research institutes. He served as a consultant to the Food and Drug Administration, serving on review panels and committees dealing primarily with the approval of gastrointestinal drugs. Dr. Danhof also served on the faculty of Southwestern Medical School and retired after 30 years of teaching. In 1969 and 1970, Dr. Danhof served as a Fulbright Scholar at the Medical Facility, Nagahar University, Jahalabad, Afghanistan, where he studied herbal medicines. As a result of his unique training and background, Dr. Danhof has become recognized as one of the world's foremost experts on medically active plant molecules, in particular the functional component in Aloe vera and Aloe arborescens. As a consultant to the Aloe vera industry and author of the book "Remarkable Aloe," Dr. Danhof is a highly sought speaker on the discovery of the unique molecule in Aloe vera that earned it the global reputation of "the potted physician."

Dr. Ivan Danhof:

I am so pleased to have this opportunity to speak with you about a remarkable plant, Aloe barbadensis, more commonly known as Aloe vera. We are learning more and more about the Aloe plant and its constituents every day, and the more we learn the more remarkable this plant becomes. Now, as you probably know, the leaves are about 95 or more percent water, so that the plant does not really contain very many materials, if you look at the leaf. And amongst these materials are over 200 different constituents, so many of these constituents are present in very, very tiny amounts. But the major component of the solids is the polysaccharide fraction, which represents about 20-25 % of the total solids, and these are the constituents which have been demonstrated to have the major beneficial activities, so we are going to talk really about the polysaccharides of Aloe.

Now you've probably heard about polysaccharides, but many people have only a very vague idea of what they really are. Now, what they really are simply—simple sugar molecules linked together like beads in a necklace, and just as the string of beads may have different colors and lengths, so the simple sugars of the polysaccharides may be of different sugars and lengths. Now these simple sugars

are also called hexoses, because they consist of six carbon atoms, or sometimes they are call monosaccharides, meaning a single sugar. Examples of these would be glucose, also known as dextrose, which is really blood sugar. A second simple sugar is fructose, or fruit sugar, found in many fruits and in honey. A third simple sugar would be galactose, which is part of milk sugar molecule, and it's another simple sugar found in gums and seeds of many plants.

And another one is mannose, which is found in not only plants but also in the cell walls of yeast and fungal organisms. So these are examples of simple sugars: glucose, fructose, galactose, mannose. You'll notice that they all end in—'ose', which represents the name which tells us that they are simple sugars.

If we begin putting these sugars together, we can put two simple sugars together and we then have disaccharides, simply meaning "two sugars," and we also have some examples in everyday materials of these disaccharides. The first one is known to everyone, and it is sucrose, which is the same material as table, cane, or beet sugar, and it consists of a glucose molecule linked with a fructose molecule. So sucrose consists of two sugars linked together and therefore it is a disaccharide. A second example of a disaccharide would be lactose, which is milk sugar. Now it consists of two sugars, two beads, as well. One of these is a glucose and the other is a galactose. So here again is the second example of a disaccharide, namely lactose, or milk sugar. A third one is maltose, which is very commonly found, and it consists of two glucose molecules linked together. And so here we have three examples of two simple sugars linked together to make disaccharides.

Well, then, what is a polysaccharide? Well, generally polysaccharides, since the term means "many sugars" "poly-" "-saccharides"—we would think of them as having five or more simple sugars linked together. A common example of a polysaccharide would be starch, which has many, many glucose molecules linked together. So corn starch or potato starch would be examples of polysaccharides where we have more than five simple sugars linked together.

Another question that frequently comes up is, what is the difference between a polysaccharide and a mucopolysaccharide? Well, the mucopolysaccharides are very long chains of beads of simple sugars put together. If you take short polysaccharides which, say, have maybe fifty sugars linked together in water, and you make a solution of them, the solution will be clear, and the substance will look and appear like water; in other words, it has the same fluidity as water.

On the other hand, if you take very long polysaccharide chains, where you have many, many, many sugars linked together, these particular long polysaccharide chains may, again, make a matrix; that is, they sort of make a meshwork, which then forms a jelly-like appearance, and frequently then the solution will be thicker, and the solution will have a cloudiness to it, some pacification, and because these are characteristics of mucus, these long sugar polysaccharides are called mucopolysaccharides; that is, they look thick and cloudy, like mucus does. So

mucopolysaccharides are simply one of the group of polysaccharides which have these very long chains of simple sugars linked together.

Now, this simply represents a background, but now what about our polysaccharides from Aloe? Well, just as we found that the polysaccharides may have different kinds of sugars, the simple sugars found in Aloe polysaccharides are glucose and mannose. And, because they contain glucose and mannose molecules linked together, one of the terms we use is "glucomannans." So we can say Aloe glucomannans are a form of polysaccharide defined by the constituents of the sugars glucose and mannose. On the other hand, if we count the number of glucose beads and the number of mannose beads, we will see that the mannose beads are far more numerous than the glucose beads, and so we frequently refer to Aloe polysaccharides as "Aloe polymannoses," or "Aloe polymannans," reflecting the fact that the majority of these simple sugars in these chains of Aloe polysaccharides are mannose molecules.

Just as beads can come in different lengths, so these polysaccharides in Aloe can be of different lengths. Now this becomes very important because demonstrated beneficial actions of Aloe vera are due to these various length Aloe polysaccharides, or glucomannans or polymannans, whichever you prefer to call them. Now, there has been a concept, which has been prevalently talked about in the Aloe industry, and that is that Aloe is only effective when you have a complete juice; that you can't just take one of the particular portions of Aloe and have effectiveness. This concept is called "synergism." Now, the problem is that there have been no "scientific" articles which confirm this synergistic concept. In fact, all of the (scientific) studies which have used specific lengths of polysaccharides from Aloe have demonstrated remarkable beneficial actions and, in fact, these polysaccharides have some enviable properties.

The first thing about these polysaccharides from Aloe is that they are very, very safe. In fact, in studies in which we try to see if they could have any toxicity at all, they come up absolutely clean. They are non-toxic. And they are very efficacious. And, just as we have different lengths of beads, different lengths of Aloe polysaccharides have very, very different potential beneficial effects.

So, one of the things we need to know is, how many of these polysaccharides, how much of the glucomannans or polymannans is going to be present in a given product. Now, we really need very, very significant quality control, because Aloe leaves vary leaf by leaf, field by field, and even one part of the field from another part of the field, or season by season. All of these variants are present in Aloe, which we get from the field. Now this is not something that is only present with Aloe leaves; obviously, all botanicals vary this way. So, in addition to knowing how much of polysaccharides, Aloe polysaccharides, are in a product, we need to have standardization so that we have a consistent product which tells us exactly how much of the Aloe polysaccharides are present. Now, the process of isolating these Aloe polysaccharides from the leaves also is of critical importance, and one of the

major things that we need to keep in mind is that the process will determine the quality of the Aloe polysaccharides. These very, very long polysaccharides are very delicate. So, if the product and the leaf are not handled appropriately, we can break down these long polysaccharides and obviously then their beneficial activities would no longer be available in the product.

One of the best ways [without using preservatives] in which we can protect all of these various lengths in the Aloe polysaccharides is a process whereby the material is exposed to cold and vacuum, a process called lyophilization-freeze-drying, and it is the ideal mechanism for preventing any kind of change in these naturally-occurring polysaccharides. [Editor's note: This is how they scientifically studied the polysaccharides, but it is a prohibitively expensive procedure and there is no complete freeze-dried Aloe on the market today.]

[Aloe polysaccharides not broken down by digestion.]

Now, a second very important aspect, besides the polysaccharides themselves, is how are they handled by the digestive tract? And this becomes again a very important consideration, because it is not only the materials you put in at the top of the digestive system that's important. What's important is how much is actually absorbed into the bloodstream so that it can have activity. Now, if we take common polysaccharides consisting of glucose molecules such as starch, these materials are broken down in the digestive tract by our enzymes to their simple onosaccharide sugars, so that when we take starch into the digestive tract, the amylases in our digestive tracts will break them down completely to glucose molecules and these glucose molecules are then absorbed into the blood.

The Aloe polymannoses are not handled in this way. If they were handled in this way, the varying sizes of beads, of chain lengths, would not have any possibility of getting into the body or of doing any beneficial effects: all of these polymannoses would then be destroyed or broken down to their simple sugars.

So, very fortuitously, very fortunately, the Aloe polymannoses are handled in a totally different way, which protects the length of the chain. They are not digested by the digestive enzymes found in our digestive tracts, so that means that all of these various lengths of beads are present in the digestive tract and remain that way. The beautiful thing about that fact is that lining the gastrointestinal tract are cells, which called enterons. These enterons line the cells of the digestive tract. And each of these cells produces a very sticky substance on the surface of their cells. This sticky substance is called the glycocalyx, or sometimes it's just referred to as the "fuzz," and it is in this glycocalyx that there are special receptors, special binding sites for the Aloe polysaccharides.

Now these binding sites or receptors are of two different types. The first type is called non-specific receptors, and they bind the majority of the Aloe polysaccharide that is taken into the body. When these polysaccharides are linked to these receptors, it provides a marvelous protective action along the gastrointestinal tract

and, as a result, this protective function really is one of the major things that can prevent such things as the reflux of acid from your stomach into your esophagus and, in fact, studies are currently being done now that show that the polysaccharides of Aloe with this binding to these nonspecific receptors may protect the lining of the esophagus from acid that is refluxed from the stomach.

In addition to these non-specific binding sites, there are specific binding sites or receptors, and when these specific sites are bound to Aloe polysaccharides, a remarkable process occurs. The cell wall completely engulfs this polysaccharide, a process called pinocytosis or endocytosis. So we find then that these Aloe polysaccharides are now inside the cell, the lining cell of the intestinal tract, and they are carried to the side wall of the cell, where they are put into the lymphatic system and, from the lymphatic system, they are transported to the blood. So it means, then, by the special pinocytotic mechanism, the special cell-engulfing mechanism, the Aloe polysaccharides are able, even with very, very long chain lengths, to be transported across the lining of the intestinal tract and find their way into the bloodstream. We know this is a characteristic of polymannans, and so the polymannans are handled by the digestive tract in this very special way. This process is called pinocytosis.

[Different Sizes - Different Properties]

Now, the Aloe polysaccharides, as we've indicated before, may be of different lengths, so we've got small necklaces, and we've got medium necklaces, and large necklaces, and very long necklaces. And, as these lengths of chains of polysaccharides vary, we find that there are a significant number of different activities. One of the important things to consider, since we have these different sizes of chain lengths, is how much of these polysaccharides are actually going to be absorbed. Well, we find that, of the small polysaccharides, perhaps 12 or 14 percent are absorbed into the bloodstream by the special pinocytotic mechanism. Of the very, very large and long Aloe polysaccharides, perhaps only 4 or 5 percent are absorbed. Now, you say, "Well, this is a very small amount," and indeed it is, but the remarkable thing is that only a very small amount of these various lengths of Aloe polysaccharides are necessary for bringing about a number of beneficial actions. And, while most of the ingested polysaccharides have a protective function—protecting the delicate lining membrane of the intestinal cell—the small amounts of polysaccharides from Aloe that are absorbed have absolutely remarkable activities.

Let's consider, then, what these beneficial actions of the absorbed Aloe polysaccharides [absorbed into the bloodstream] might be. And let's again divide them into these categories of small chain lengths, medium chain lengths, large chain lengths, and very, very large chain lengths, because each of these categories has very differing beneficial actions.

[Small polysaccharides-diabetes, anti-inflammation-arthritis, ulcerative colitis]

The first group we want to talk about are the small polysaccharides. Now, when we say "small", how long is our necklace? Well, our necklace may be as limited as seventy beads, or it might have as many as six hundred beads in our chain length. Remember these are glucose and mannose molecules linked together. So, we range from about seventy molecules to, let's say, six-hundred fifty or so molecules linked together in the "small" category. We find that these molecules have a very remarkable effect on patients and individuals who have diabetes.

You are all familiar with the fact that diabetes is a deficiency of insulin. In the pancreas, scattered throughout the pancreas, are little islets, "islets of Langerhans," and each of these islets contains four different kinds of cells, and one of these cells obviously makes insulin. And we find that, if there is a problem with insulin, it may divide into two different types. So we have type 1 diabetes, which is sometimes called juvenile type of diabetes, in which the cells in these little islands are selectively destroyed by antigens and antibody reactions; these are self-destructing processes. And so, in the person with type 1 diabetes mellitus, they cannot make insulin because their cells that have secreted and synthesized the insulin have been destroyed, so it's obviously necessary for these people to have insulin daily for survival.

The second type, called type 2 (sometimes it's called "adult" or "maturity onset diabetes") usually occurs in older ages. Here, the problem is not that the cells producing insulin are destroyed—they still can make insulin—but the sensors that detect an increase in blood sugar no longer work. Obviously, as your blood sugar increases following a meal, that should be the signal for these cells to release their insulin to control the blood sugar, and what the insulin does, literally, is it permits the blood sugar, which is absorbed after a meal, to enter fat and muscle so it can be used for energy or for storage. Now, the problem then in the second type, as we've indicated, is the fact that there is a problem with the sensing mechanism, so that when the blood sugar rises, there is a defect in the sensor, so insulin is not released. In order to help this release mechanism, many individuals are given oral hypoglycemic drugs that tend to restore this mechanism.

Now, the Aloe polysaccharides have been shown to lower blood sugar levels in both types of diabetes, in both animal and human studies. This is a profound action, because we are now lowering blood sugar even in the absence of insulin. And this mechanism, while it is now poorly understood, is obviously going to receive a great deal more investigative work, because it is a totally different concept than we have ever encountered before. Let me say that again: that Aloe polysaccharides have been shown to lower the blood sugar levels in both type 1 and type 2 diabetics in animal studies and in human studies. A profound action.

Another example of "small polysaccharide" action is in the category of anti-inflammation. All of us are familiar with inflammation, and the normal inflammation occurs with injury or irritation, and it can be either external or internal. The process is the same and is characterized by five different findings: The first is "rubor,"

which is Latin for "redness"; the second characteristic is "kalor," or heat; the third is "tumor," or swelling, so when are talking about a tumor we are simply indicating that there is a swelling; the fourth characteristic of inflammation is "dolor," or pain; and the last and fifth characteristic of inflammation is "functualese," which means disuse of the part because of the inflammatory changes.

Now just think back the last time you had a cut, or you had an abrasion, or you had an irritation that was really sore. You were very careful with that part of your anatomy, and rightly so. Now, a couple of the very, very serious inflammations that we have in the body are arthritis and ulcerative colitis, and I want to say just a word about these two. Arthritis, obviously, is an inflammation of the linings of the joint, and these inflammatory reactions are brought about by the release of a specific material, a specific mediator called leukotriene B4. The beautiful thing about this mechanism is the fact that Aloe polysaccharides specifically inhibit the action of leukotriene B4, and therefore these polysaccharides, taken on a consistent basis, have the possibility of controlling the arthritic inflammatory reaction.

In ulcerative colitis, this is a serious inflammation of the lining of the colon associated with ulceration and infection, and it is a very, very serious condition. It has been shown that Aloe polysaccharides have a profound anti-inflammatory effect in ulcerative colitis as well. [Editor's note: please see R. Davis' article about other anti-inflammatory actions as well as tissue regenerating properties—helpful in these conditions]

So here we have two examples where the Aloe polysaccharides, polymannans, glucomannans, through their anti-inflammatory activity, may protect and indeed may reverse serious conditions such as arthritis and ulcerative colitis.

[Medium length polysaccharides—Anti-oxidant]

Let's move on very quickly to the medium-length polysaccharides. Here we have a necklace which is about 1500 beads long, and one of the major effects in this category are anti-oxidants. Now, many diseases are thought to at least be partially caused from the formation of free radicals and other kinds of very potent oxidizing materials, and these include heart disease, arteriosclerosis, emphysema, and Parkinson's disease. A number of these diseases have at least as a component of their manifestations injury from these very, very potent free radical generation material. It has been shown that these medium-size polysaccharides have a very, very potent anti-oxidant activity, but they do not interfere with the normal functions of the cell. Many drugs that we take which have antioxidant properties may interfere with the normal functions of the cell. So here we have an ideal antioxidant material that protects against the formation of the serious diseases.

[Large polysaccharides-antibacterial, tissue regeneration]

Now let's look at the large molecules. Now we're talking about maybe four to five thousand beads in our necklace. And, two of these activities—one is the fact that there has been isolated a very potent antibacterial material which is in this

category. Some of the organisms that we have are very, very smart, as you know. So, for instance, we have a staphylococcus aureus, staph infections—which are very common—and some of these organisms have been treated with different kinds of drugs, and they have become so smart that they now are tolerant to the drugs because they have developed mechanisms for protecting themselves against them. One such category would be methecillin-resistant staphylococcus aureus, and we find that the polysaccharides of Aloe vera are very potent killers of these cells in tissue culture. Now, it takes a fair amount of the polysaccharides to do this, but it is really remarkable that we have polysaccharides that work in diabetes, that work in arthritis, that work in ulcerative colitis, which also have antibacterial activities.

A second activity in this "large" category are those materials responsible for the healing properties of Aloe vera. And, as we are all aware, one of the major indications historically, used for over 350 years, is the application of Aloe and its polysaccharides to induce healing. So, again, we have some very, very interesting and diverse activities in these various fractions. It points out the fact that we really need products that contain at least some molecules of all of these categories. [This "healing property" is also known as "tissue regeneration;" please see R. Davis' article]

[Very Large Polysaccharides-Immune system]

But perhaps the most important of all of the activities is found in the very large beads—now we're talking about eight or nine thousand beads of glucose or mannose molecules [Ed. note: Aloe is known to contain the full range of these beta-linked glucomannans, including the Beta-1,3 and Beta- 1,4s that the scientific research is based on] in our necklace—because these are the ones that support and actually improve immune system function. Now, what do they do? Well, actually, they release different kinds of materials from different kinds of white cells, which then produce a remarkable array of protective effects. One of the effects is that they stimulate the lymphocytes, and these lymphocytes, obviously, are necessary for the formation of antibodies.

A second activity is that they increase natural killer cells. All of us every day are bombarded with all kinds of viruses and spoors and bacteria that potentially can cause a great deal of problems, including viral causation of cancers. And yet, these polysaccharides will increase the natural killer activity of the white cells to prevent these particular organisms from having any deleterious effect.

Another very interesting effect is that these large polysaccharides, very large polysaccharides, release a material called "tumor necrosis factor." Now, "necrosis" means to decay, to rot. When we have tumors, tumors can only exist because they produce materials that then permit blood vessels to grow into them so that their blood supply of nutrients is improved. One of these materials is called "angiogenesis factor." "Angio-" means blood vessel; "-genesis" means formation; and obviously, it's a factor. So most cancers release to the body angiogenesis factor that in turn permits blood vessels to form very rapidly in the tumo, thereby

providing the tumor with an unlimited supply of nutrients so it can grow. Tumor necrosis factor does this whole system in. It is a marvelous mechanism for protecting against not only the formation of tumors, but also reducing the size of tumors by causing the tumors to become necrosed, become rotten, and the way they do this frequently is by inhibiting the release and the formation of angiogenesis factor. These very large polysaccharides, as you can see, are of enormous importance.

Now, another factor that these particular molecules bring about is a very interesting one. Obviously, if you have a site in the body of infection or injury, you would like the white cells, which are our soldiers, to get to this area. How do they know that infection or injury has occurred? Well, there is a release of "chemotactic factor," and the very large polysaccharides enhance this chemotactic factor whereby white blood cells are drawn to sites of infection and injury in the body. So you can see that these very, very large long beads, these very long necklaces, have a profound effect in conquering tumors and in protecting us from various noxious agents in the environment. [Editor's note: Please see Carrington Lab's report; more on immune enhancement and antiviral activity]

[Concentrated Aloe breaks down larger polysaccharides]

With this as a background, let's talk a little bit about a typical American approach. An American approach is that, "If a little bit is good, more should be much better" and, as a result of that, we have in the marketplace a number of concentrated Aloe products. Most of these are liquid beverages or drinks, the idea being that the more concentrated the Aloe product, the better it is for you. Well, let's take a close look at this particular concept. In the first place, how are these Aloe products concentrated? We've indicated the plant is 95 percent plus water. So if we're going to concentrate these total solids, we're going to have to have some kind of method for getting rid of the water.

The most common method, because it's the most economical, is exposing the liquid Aloe to high heat and vacuum. The problem is that the high heat breaks down the large Aloe polysaccharides. So that means that the total polysaccharides might still be there, but the big ones, which are responsible for the antibacterial activity, the healing activity, the immune modulating activity, are not there. Also, as concentration proceeds, that is as the water is removed, the natural salts are also concentrated and, as these salts become very concentrated, more of the Aloe polysaccharides are broken down. So we have two mechanisms in the concentrated product, both the heat process as well as the salt concentration. The other problem is that these increased salts may actually irritate the delicate lining of the stomach, and that is not a particularly good situation.

There is another activity associated with these concentrated materials that creates a problem. All of you know that most of these polysaccharides have to have, if they're in liquid solution, a preservative system, and the FDA limits the amount of preservatives that you can use. Now, if you have these very concentrated solutions,

this puts an enormous stress on the preservation system because of the limits imposed by the federal regulations.

But probably the most salient feature for not recommending these concentrates, besides the fact that the complement of polysaccharides is not what the plant has available, is the fact that, as we've indicated, most of these polysaccharides are going to occupy the protective receptors, and only a small amount of Aloe polysaccharide is necessary for all of the receptors, both specific and nonspecific, to be bound. So that means that most of the Aloe polysaccharides in these concentrates are going to pass by these receptors and will end up in the excrement, which is excreted from the gastrointestinal tract. As one individual put it, "That's a very expensive bowel movement." Now, this indicates to us that we have to be very careful and cautious when we look at products with respect to whether or not they do contain the full complement of polysaccharides produced by the plant.

[Mislabeling:]

One of the problems we have had in the Aloe industry is the fact that we have had a large number of products that have been misbranded and mislabeled and, in fact, this problem has been so serious that the International Aloe Science Council has undertaken a number of investigations. And, indeed, some products on the marketplace that were purported to contain Aloe vera contained no Aloe vera at all, but simply contained maltodextrins and other kinds of sugars. Indeed, they're polysaccharides, but they're not Aloe polysaccharides. So one has to be very cautious in looking at labels, because what is reflected by the label may not have any bearing or semblance of what is in the bottle. It's an unfortunate situation, but the realities of the situation are such that one frequently cannot rely on the label claims because they may be spurious.

Legislation was passed and implemented in 1996, of having a new category of materials under the survey of the Food and Drug Administration. Normally, the Food and Drug Administration has been in charge of foods, drugs, and cosmetics, and now we have another category in which we have foods that have demonstrated beneficial activities. These will then be called nutraceuticals. Not pharmaceuticals, but nutraceuticals: food materials that have demonstrated beneficial activities. So we can have available to us food-grade Aloe that is safe and non-toxic. These materials should be standardized so that they are consistent with respect to the polysaccharide content. We would prefer to have these materials in a freeze-dried form so no preservatives are necessary. And, the interesting thing is that if there have been sufficient studies, claims will be permitted for these particular new nutraceuticals. So we have with this new legislation an opportunity to have products available for which we will have permissible claims based upon studies that have been demonstrating these beneficial health-promoting activities.