Possible Mechanisms of the Healing Actions of Aloe Gel

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Aloe gel appears to have not only one, but a number of active components.[1-3] Of the actives that have been identified,[4] some are lacking in mechanisms revealing how the components effectively yield their end result. In this paper some of the actives will be named, and known or theoretical mechanisms of action will be discussed.

Aloe has been claimed to be anti-inflammatory. There are three components of aloe that appear to have or suggest anti-inflammatory activities. These are: bradykininase,[1] magnesium lactate,[2] and Aloctin A.[3]

Bradykininase

Bradykininase is an enzyme that cleaves amino acid from bradykinin, angiotensin I, and other endogenous peptide chains. In order to understand the biological consequences of bradykininase, it is necessary to realize the biochemical aspects of bradykinin, angiotensin I and angiotensin II. These biochemicals fall into a category called peptides which are made up exclusively of amino acids linked together forming a chain.

The three peptides, bradykinin, angiotensin I and II, all play a role in the body's natural systemic regulation of blood pressure. Bradykinin

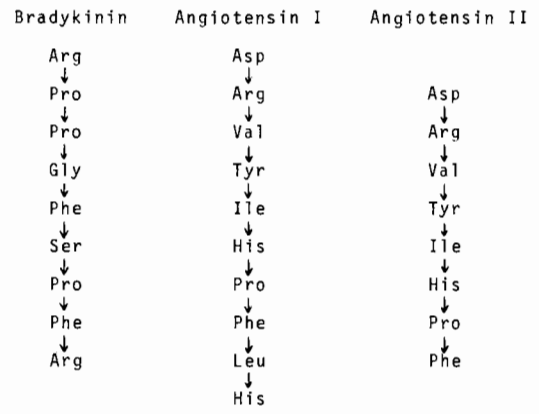

Figure 1. Arrows point from N-terminal to C-terminal ends of the peptide chains.

is a tissue hormone that consists of nine amino acids linked together (see fig. 1). This nonapeptide is a vasodilator (an agent that causes dilation of the blood vessels), and is also a potent pain-producing agent.[5] Angiotensin I is a decapeptide containing ten amino acids that is biologically inactive until two amino acids are

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removed from the C-terminal end.[6] Because of this cleavage, angiotensin I is converted to the biologically active octapeptide, angiotensin II. The octapeptide is a vasopressor (an agent that causes constriction of the blood vessels).[7,8]

Bradykininase cleaves amino acids specifically from the C-terminus of angiotensin I and bradykinin.[9] As a result, bradykinin is rendered inactive, and angiotensin I is converted to active angiotensin II. Since some of the pathological consequences of inflammation are vasodilation and pain, the degradation of bradykinin and the activation of angiotensin II by the enzymatic action of bradykininase would appear to combat inflammation. Removal of bradykinin would presumably reduce pain and decrease the stimulus responsible for dilation of the blood vessels. Activation of angiotensin II would seemingly cause the blood vessels to constrict more toward their normal size. It would be interesting to see if bradykinin is present in effective concentrations in various skin impairments. If so, then the above mechanism could be responsible for effectively reducing pain by the use of aloe.

Angiotensin II has other biological activities. The peptide acts directly on the adrenal gland to release the steroid, aldosterone.[6] This molecule is the most biologically active of a group of hormones produced by the adrenal cortex that regulate electrolyte metabolism. This is a complicated process that involves hormones from both the adrenal and pituitary glands. Generally, aldosterone acts as a diuretic, decreasing edema by antagonizing an antidiuretic hormone, ADH.[10]

Magnesium Lactate

The metabolic pathway in which magnesium lactate plays a role involves the enzyme histidine decarboxylase. This enzyme is responsible for conversion of the amino acid histidine to histamine[11] (see fig. 2). The conversion occurs in mast cells of the lungs, liver, and the gastric mucosa. Similar to bradykinin, histamine is a potent dilator of blood vessels.[12] Magnesium lactate is an inhibitor of histidine decarboxylase[2] and may prevent the production of histamine in the mast cells. Reducing the production of histamine should decrease the amount of vasodilation; and in this manner the magnesium lactate in aloe gel would apparently be effective against inflammation of the gastric mucosa and, possibly, the liver and lungs.

Prostaglandins

Although bradykinin and histamine are metabolic intermediates of inflammation it is the group of chemicals, the prostaglandins, that

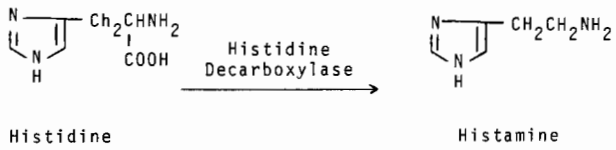

Figure 2. The conversion of histidine to histamine catalyzed by the enzyme histidine decarboxylase.

seem to be associated with long-term inflammation.[13] When injected into the skin, they cause well-marked vasodilation that lasts for several hours.[14] The prostaglandins are synthesized from the 20 carbon straight chain, arachidonic acid. In the conversion to the prostaglandins, a five member ring is formed from the mid-section of arachidonic acid (see fig. 3). The cyclic ring with its tailing straight chains is the basis for the prostaglandin structures. This group of molecules can be synthesized in human platelets.[13] The action can be inhibited by the common, but powerful, anti-inflammatory drug, aspirin.[15,16] In fact, many anti-inflammatory drugs act by inhibiting the conversion of arachidonic acid to prostaglandins.[17] Aloe gel inhibits the synthesis of prostaglandins from arachidonic acid.[18] This is possibly a factor that would be helpful in preventing long-term inflammation.

Aloctin A

Although some prostaglandins are associated with prolonged inflammation, paradoxically they

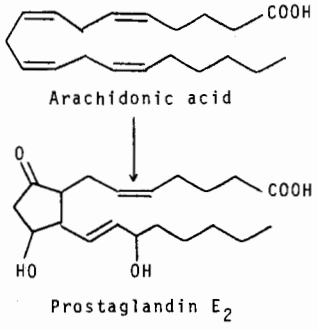

Figure 3. The production of Prostaglandin E_2 occurs via a biochemical pathway.

are also suspected of having a role in wound healing by increasing adenylate cyclase activity in T-lymphocytes. Cyclic AMP, the product of adenylate cyclase and ATP, is believed to stimulate mitosis and post-injury cell proliferation.[21a] It could be that what the body needs is a substance that induces mitosis to promote wound healing without causing a prolonged inflammatory response.

Aloe gel may be this substance because it inhibits prostaglandin synthesis thereby reducing the effect of its stimulus for inflammation and mitosis. But aloe gel contains a glycoprotein, Aloctin A, shown by Suzuki to have mitogenic activity.[20] In this manner aloe gel may take the advantages of prostaglandins while leaving the disadvantages, i.e., it appears to promote healing through mitosis while preventing inflammation.

Aloctin A was also shown to restrict the amount of edema in laboratory rats. This was demonstrated in tests reported by Suzuki. In the tests, two groups of laboratory white rats were injected with an agent that causes edema (swelling). The test group was innoculated with Aloctin A; while into the control group only the agent that caused edema was injected. The difference in the amount of swelling showed Aloctin A to be effective against edema. As a result, Suzuki suggests that Aloctin A is an anti-inflammatory agent.[3,19]

The enzymatic, mitogenic, and anti-inflammatory activities previously discussed may help to explain the healing of wounds observed with the use of aloe gel. When a wound occurs, a certain amount of tissue is either damaged or destroyed. In order for a wound to heal damaged tissue must be repaired, dead tissue must be removed, and tissue must be regenerated.

One aspect in which aloe gel would appear to aid in the repair of tissue is the biosynthesis of proteins. When tissues become damaged, especially by heat, proteins are often denatured. Bradykininase has a proteolytic action[9] which may break down these biologically inactive polypeptides. This would make available the free building block amino acids which can then be used for protein synthesis.

Aloe gel may also assist the body's natural means for the removal of dead tissue. Two types of leukocytes, macrophages and monocytes, serve a common function of scavenging for various kinds of dead tissue.[21b] In many cases an increaes in the number of these leukocytes caused possibly by the mitogenic activity of Aloctin A[20,22] would increase the rate of dead tissue removal. Besides making macrophages more available by inducing one free macrophage to split into two daughter cells, Aloctin A may proliferate this leukocyte in another fashion. A characteristic of macrophages is that some of them are fixed and not free to move about. Upon undergoing mitosis, an immobile macrophage may produce two daughter cells, one fixed and the other free. A liberated macrophage would be capable of moving to a site where the need is the greatest, which is typical of this type of leukocyte.[23]

While dead tissue is being removed from an injury site, the mitogenic activity of the lectin in aloe gel, Aloctin A, may play a crucial role in the rate of replacement of the destroyed tissue. When tissue is destroyed, a number of new replacements equaling the volume of all the destroyed cells are needed to restore the region. Many of the replacement cells are regenerated from the surrounding healthy tissue.[24] How quickly and what quantity of the healthy cells divide are factors that are involved in determining the rate of replacement. The mitogenic activity of Aloctin A[20] induces cells to divide earlier than when they normally would; consequently there is a potential for a greater rate of replacement.

Experiments reported by Winters demonstrated the increase in growth rate.[22] In the experiments, monolayer tissue cultures were scratched in a streaking fashion to produce regions of healthy and dead or damaged cells. In the control, tissue cultures were kept in Dulbecco's Minimum Essential Medium supplemented with 10% heat inactivated fetal bovin serum and antibiotics. The test tissue cultures contained, along with a similar solution to that described above, a fraction of aloe gel that would have contained Aloctin A. The tissues with the aloe gel fraction had a marked enhancement of attachment and growth in comparison to the tissue cultures without aloe gel fractions.

Another important factor in healing, besides the mere replacement of cells lost, is the reinstatement of the function(s) in the cells lost due to destruction of tissue. This is done by the process of differentiation.[22] Since mitosis is a primary step of regeneration,[25] it would be interesting to investigate differentiation influenced by Aloctin A.

Aloctin A induces certain cells to divide which is a potential for rapid growth. When this power was applied to tumor cells where rapid growth is harmful or malignant, interesting results have been observed. Winters found that when influenced by a lectin in aloe gel the rate of tumor cell growth does not increase, but is either unchanged or diminished.[22]

Earlier experiments reported by Suzuki show that Aloctin A has a strong anti-tumor activity. Two groups of Douryu inbred rats were implanted with AH-130 tumor cells. The test group

was intraperitoneally injected with a fraction of aloe gel that contained Aloctin A. This was done for seven days before the implantation of the tumor cells. The control group was not injected with any aloe gel preparation. After 27 days, there were no survivors of the control group. The test group which had been given Aloctin A injections had 60 percent of the original population surviving at the 27th day following tumor implantation. The rats that survived lived for the duration of the reported experiment which was 150 days.[20]

Later experiments by Suzuki revealed evidence on the inhibition mechanism of methylcholanthrene induced fibrosarcoma in which Aloctin A plays a part. These experiments support the contention that there is a host mediated immune response influenced by Aloctin A but not a direct toxic effect on the tumor cell.[26]

Aloe gel, which is a bacteriostatic agent in itself,[27,28] has been noted to help clear up infectious tissue.[29,30,31] (An infection is a condition in which the body or parts of the body itself are invaded by a pathogenic agent; e.g., virus, bacteria, fungi.) Under favorable conditions these pathogens multiply and produce effects which are injurious to the body and usually are accompanied by inflammation. One of the body's defenses against infection involves an increase of macrophages and microphages at the site of the impairment.[23] As previously discussed, macrophages are responsible for carrying away all kinds of dead tissue and matter from the injury site.[21] The microphages, which are also leukocytes, engulf and destroy many of the pathogens responsible for infections. It is plausible that the mitogenic effect of Aloctin A aids the body in the increase of the leukocytes necessary to fight infectious pathogens, alleviate inflammation, and contribute to the removal of dead tissue and pus.

Indeed, aloe gel does contain, not one, but many active components; not all of which have been mentioned here. The basic lesions discussed in this paper which appear to be influenced by the components of aloe gel are involved in many kinds of ailments. In this light, the potential for aloe gel may be great.

Much research is yet to be done to investigate these proposed mechanisms. Perhaps this paper will inspire the others to undertake the required research.

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