ALOE VERA: A PLANT OF VITAL SIGNIFICANCE

M.A. Saeed, Ishtiaq Ahmad**, Uzma Yaqub***, Shazia Akbar*, Amran Waheed*, M. Saleem****, and Nasir-ud-Din***

ABSTRACT

This research shows the vital significance and importance of Aloe Vera. It is a descriptive research. Aloe Vera is a vitally important plant that has been used for different oilments i.e. geotron testinal, gont boils, etc. It has several other properties or charactertics incluidng antibacterial, anti-inflamatory and antiseptic attributes. Easy growth, maintenance and multiple uses of aloe plant's constituents have promoted several elaborated investigations in public and private sector.

Key words: Aloe vera, Glycoproteins, Aloein, Aloe-gel, and Aloe-sap.

INTRODUCTION

Herbs have been used for different remedies in all cultures. In Asia, plant products and plant-derived drugs have been used therapeutically for centuries. More recently, people have become more interested and better informed about the use of herbs [1]. The use of herbal remedies reached its zenith in late 1800s and early 1900s [2]. In early part of 20th century a dramatic decline in use of herbal remedies began in USA, due to isolation and chemical synthesis of structural analogs and so herbal remedies disappeared from pharmacy shelves. Fifty years later, trend towards herbal remedies reverted and pharmacy shelves started to fill again. A survey in 1997 showed that nearly sixty million people were using herbs and a 75% increase in sales occurred over the past years [2]. In fact, herbal medicines played an important role in treating and preventing people from debilitating diseases since long. The role of plant-derived medicine in treating diseases will ever increase. Thousands of plants have been claimed to possess medicinal properties. Throughout the world, today, extensive investments have occurred for the therapeutic applications of herbal plant-resources, which are of unlimited abundance around us, to improve the quality of life. Aloe vera is a vitally important plant that has been used in folklore for different purposes, such as for healing boils, wounds, burns and treatment of different ailments. Ancient Egyptians papyrus, Mesopotamian clay tablets contained Aloe as an active ingredient used in curing infections, treating skin problems and as a laxative [3,4].

The word Aloe vera appears to be derived from Arabic word "Alloeh", which means "a shining bitter substance." We still refer to "bitter Aloes" describing the laxative drug still listed in U.S. pharmacopoeia today. There are many romantic tales about Aloe, suggesting that Egyptian queens, Nerfertiti and Cleopatra, used it as part of their regular beauty regimen [5]. Supposedly Alexander the Great in 333 B.C occupied the island of Socotra in the Indian ocean for its famed Aloe supplies, needed to treat his wounded soldiers [3,6]. Aloe was used by Hippocrates and Arab physicians, and was introduced to Western Hemisphere by Spanish explorers.

Aloe is also common in both traditional Chinese and Ayurvedic medicine. The Chinese describe Aloe's skin and the inner lining of its leaves as a cold, bitter remedy which is downward draining and used to cure constipation due to accumulation of heat [7], the gel is considered cool and moist. In Ayurvedic medicine, the traditional medicine of India, Aloe has multiple uses inclusive of laxative, antihelminthic, hemorrhoid remedy, and uterine stimulant. It is used topically, often in combination with licorice root, to treat eczema or psoriasis. In Arabian medicine, the fresh gel is used on the forehead as a headache remedy or rubbed on the body to cool it in case of fever, as well as being used for wound-healing, conjunctivitis, and as a disinfectant and laxative [4]. The aloe gel has been extensively used in gastrointestinal disorders, including peptic ulcer, and its clinical efficacy has been documented [8-12].

In recent times, Aloe vera gel has been used as an active ingredient in hundreds of skin lotions, sun blocks and cosmetics [13]. The gel's use in cosmetics has been increased by claims that it has anti-aging effects similar to vitamin A derivatives [13]. Aloe gained popularity in the United States in the 1930's with reports of its success in treating X-ray burns [14]. Recently, Aloe extracts have been used to treat canker sores

* PCSIR Laboratories Complex, Lahore. **IMMBS, The University of Lahore, Lahore. *** Lady Willingdon Hospital, Lahore.
**** Department of Botany, Govt. College, Lahore.

Table - 1: Significant Clinical Developments in the Use of *Aloe vera*

Date	Origin	Clinical Applications
50 B.C.	Celsius, a Greek physician introduced Aloe into western medicine.	Sap as laxative [20].
41-68 A.D.	*Aloe vera* plant described in the book "Greek Herbal" of Dioscorides.	Sap as healing agent. Additionally, induces sleep, cleanses stomach, treatment for boils, ulcerated genitals, stops hair loss, heals tonsil, diseases of mouth and eyes [20].
200 A.D.	Galen, Antyllus, Aretaces, and many other Southern European physicians used Aloe as medicine.	For different clinical purposes [20].
700-800 A.D.	For the first time Chinese used *Aloe vera.*	For the of treatment of sinus, fever and Convulsions in children by Aloe [20].
1300-1500 A.D.	Aloe (dried sap) was introduced to English medicine.	For the treatment of external wounds and diseases and as purgative [20].
1700-1900 A.D.	Carl Von Linne, 1720, described the plant as Aloe Vera. In 1820 Aloe vera was officially listed in United States pharmacopoeia (U.S.P.) [20]. Aloin, The sap prepared as a purified product for commercial use.	As purgative and skin protectant [20]. For the treatment for radiation injuries, ulcers, burns, dermatitis and other skin injuries and diseases [20].
1950 A.D.	A Russian scientist discovered the utility of Aloe vera juice for various diseases.	For the treatment of parasitic diseases and several lung disorders.
1975 A.D.	Robert discovered that the plant has other multiple applications in animals [20].	For ringworm, skin allergies, abscess, hot spots, lacerations, inflamed cyst [20].
1979 A.D	Suzuki et al., (1979) isolated two lectins from leaves. of Aloe arborescence Miller [21].	Hemagglutinating and mitogenic activity [21].
1985A.D.	Bland discovered *Aloe vera* juice as a clinical drink.	Helps digestive processes, controls infections and has no toxic effects [7].
1987 A.D.	Burn described that the disease shingles (Herpes Zoster) is caused by the same virus that also causes chicken pox and common herpes.	*Aloe vera* as remedy for shingles [20].
1991 A.D.	Davis et al., reported in two different publications about inhibitory and stimulatory systems from Aloe vera.	The Aloe extract acts as modulator-system towards wounds, inflammation and is valuable for managing lower extremity conditions [22,23].
1994 A.D	Davis *et al.,* described mannose 6-phosphate from Aloe gel.	It improves wound healing and inhibits inflammation [24].
1997 A.D	A glycoprotein was isolated from *Aloe Barbadensis Miller.*	The glycoprotein promoted cell growth [25] and proliferation of human normal dermal cells and baby hamster kidney cells.
2000 A.D.	Pecere and co-workers [27] reported Aloe emodin.	Emodin (hydroxyanthraquinones) from Aloe vera leaves has antineuroectodermal tumor activity both in vitro and vivo.
2001 A.D	A glycoprotein, G1G1M1DI2, was isolated from Aloe vera.	Wound-healing via cell proliferation and migration [28].
2002 A.D	Choi *et al.* [29] isolated beta- sitosterol from *Aloe Vera*.	Beta-sitosterol has an angiogenic effect in chorioallantoic membrane.

[15,16], stomach ulcers [10] etc. Many homes keep a plant handy in the kitchen where it readily thrives in bright sunlight with little care. In case of a minor burn, a fresh leaf can be cut and the gel of the inner leaf applied directly to the burn immediately after the injury. The inner leaf lining of the plant is often used as a natural laxative. In a quite recent survey (1990) of members of a health-maintenance organization, Aloe vera was used by 64%; of these, 91% believed it had been helpful [17]. Aloe is also an ingredient in Compound Benzoin tincture [18].

Although, Aloe has remained stalwart over the aeons of time since the Biblical era to the 20th century, but it has never achieved a true notoriety as other products i.e. foxglove, digitalis, cinchona (quinine), or willow bark (acetyl salicylic acid). This position of "poor relative" across the tracks has been the fate of Aloe, partially because of the failure of industry to fund scientific investigations and because of the slow progress of science in developing models to test Aloe. The first real investigation, which provided scientific enlightenment concerning Aloe's therapeutic efficacy started early in twentieth century [19]. That was the age when the medicinal chemists traveled extensively and bought back plants, reputed for medical applications including cathartics, in order to isolate and characterize active substances using the chemistry of the day. The significant clinical developments in the applications of Aloe vera are listed in Table-1.

The precise and comprehensive isolation and analytical techniques have made it relatively easier to provide more information about the active principles of this wondrous and magical Aloe plant [30,31]. Thus a large number of chemical substances have been identified, which act as cathartic, emollients, accelerator of wound-healing [28] and modulator of immune response [32,33]. These include inorganic ions (Na, K, Ca, Mg, Zn, etc.) [34] and small and large organic chemicals of quinone family [35-38], free sugars [39], carbohydrates (polysaccharides) [40-45], enzymes [46,47], lectins [48,49], proteins and the products of their breakdowns i.e. peptides and amino acids), vitamins [50] and many more.

THE ALOE PLANT AND ITS CONSTITUENTS

Aloe (urdu name ghigwar, local name kawar gandal), is genus of shrubby, scattered, succulent plant of the Lily family (Liliaceae). There are over 250 species of Aloe grown around the world and are native to Africa. Most of them have rosette of leaves at the stem, but no stem. Several species are cultivated as ornamentals due to their sharp pointed spiny leaves and colorful clusters of yellow or red flowers. Today two species are grown commercially, namely Aloe barbadensis Miller, also called Aloe vera, and Aloe arborescence [51]. Tubular yellow flowers are produced annually in the spring. The Aloe plant is grown in warm tropical areas and cannot survive freezing temperature. Mature plant grows as tall as two and a half inches to four feet, with the average being around 28-36 inches in length. Each plant has 12-16 leaves that, when mature, may weigh up to 3 pounds. The plant can be harvested every 6 to 8 weeks by removing 3 to 4 leaves per plant. The Aloe barbadensis and Aloe arborescence are grown in the United States in the Rio Grande valley of South Texas, Florida and Southern California. Internationally the plants can be found in Mexico, the Pacific rim countries, India, South America, the Caribbean, Australia and Africa.

Chemistry of Aloe

There are more than 200 compounds found in Aloe barbadensis, about 75 of which have biological activity [46, 47, 50, 52-58]. The prominent components are anthraquinones [35-38], Aloin [44], Aloe emodine polysaccharides [48-53], enzymes [46,47], reducing sugars [39], organic acids, metallic cations [34]. The Aloe gel or fillet, which is stored in the inner portion of the leave, contains 99.5% water and 0.5% solid matter. Table-2 shows the chemical constituents of Aloe vera with their activity.

Biochemistry

The solid ingredients in Aloe gel are divided into large molecules (0.1 %) and small molecules (0.4 %). Large molecules are polysaccharides and the minor constituents include a mixture of proteins (glycoproteins), and compounds of lower molecular weights, such as sterols, terpenes and other molecules.

Aloe vera: Potentially Active Chemical Constituents

- High molecular-weight constituents e.g.

Table 2: Constituents of *Aloe vera* and their Activity

Constituents	Number Identified	Activity
Amino Acids	Twenty amino acids required by humans have been found, including 7 of the 8 essential ones, which the body cannot synthesise.	Component of proteins that are required for the functional proteins, such as muscle tissues, enzymes, hormones etc.
Anthraquinones	*Aloe vera* provides 12 Anthraquinones, including aloe emodin, aloetic acid, aloin, anthracine, anthranon, barbaloin, chrysophanic acid, emodin, ethereal oil, ester of cinnemonic acid, isobarbaloin, and resistannol.	In small quantities, anthraquinones act as potent antimicrobial [59] and antiviral 60] agents. In high concentration, these compounds exert a powerful purgative effect. Topically they can absorb ultraviolet light, inhibit tyronase activity, reduce the formation of melanin [57, 61].
Enzymes	There are 8 Enzymes isolated from *Aloe vera,* including aliiase, alkaline phosphotase, amylase, carboxypeptidase, catalase, cellulase, lipase, peroxidase.	Most of the enzymes help in the break-down of food-sugars and fats. Some of the enzymes may be involved in other functions, such as carboxypeptidase, inactivates bradykinins, produces anti-inflammatory effect [46, 47].
Hormones	Two Hormones are known from *Aloe vera* , which are auxins and gibberllins.	Both of these play an important role in wound-healing and anti-inflammatory effect.
Lignin	Cellulose-based substance.	This woody substance provides penetrating power in *Aloe vera* skin-penetrations, so having the ability to carry other active ingredients deep into the skin to nourish the dermis [62].
Minerals	Aloe Vera provides 9 minerals: Calcium, Chromium, Copper, Iron, Magnesium, Manganese, Potasium, Sodium and Zinc.	These are essential for good health and known to work in certain combination with each other, vitamins and other trace-elements. Magnesium lactate inhibits histidine decarboxylase and prevents the formation of histamine from amino acid, histadine [47]. Histamine is released in many allergic conditions and causes intense itching and pain.
Salicylic Acid	Aspirin-like compound.	Acts as analgesic.
Saponins	Glycosides	These soapy substances form 3% of the gel and are general cleansers, having antiseptic properties [63].
Sterols	The plant provides 4 main plant-steroids: Cholesterol, Campesterol, Lupeol, Beta Sitosterol.	Sterols are anti-inflammatory agents, whereas lupeol also possesses antiseptic and analgesic properties.
Sugars	*Aloe vera* provides both monosaccharides, (glucose and fructose) and polysaccharides (glucomannans and polymanose).	Monosaccharides have anti-inflammatory action and polysaccharides posses antiviral, immune-modulating activity [64-67, 68] such as Acemannan [66-68].
Vitamins	*Aloe vera* contains many vitamins, except vitamin D. The vitamins found include vitamins A,C,E,B (the thiamine, Niacin, Riboflavin, B_{12}), F, Choline and Folic acid.	Vitamin B's and Choline are involved in amino-acid metabolism, B_{12} plays an important role in production of RBCs, Folic acid is involved in the development of red cells.

a) Polysaccharides: glucomannan [42,45] and acemannan [44]
b) Glycoproteins
c) Lectins

- Low molecular weight constituents e.g. anthaquinones, vitamins, saponins, sterols, etc.

(a) Polysaccharides: The polysaccharides make up approximately 20 percent of the solid content and comprise mostly a mixture of polysaccharides of a linear, highly acetylated β 1-4 Mannan, branched dextrans, pectic acids and other polysaccharides with negative charge. Polysaccharides hexose makes up 5 to < 10 % of the total solids. Associated closely with these polysaccharides are small molecules, primary charged ions. The gel or mucilage obtained from the leaf flesh contains quite different compounds from the bitter latex extracted from the leaf-lining. Aloe gel is 99% water with a pH of 4.5 and is a common ingredient in many non-prescriptional skin conditioners. The gel contains an emollient polysaccharide, glucomannan [42,45]. It is a good moisturizer, which accounts for its use in many cosmetics. Acemannan [44], the main carbohydrate in the gel, is a water-soluble long-chain mannose polymer, which accelerates wound-healing, modulates immune function (particularly macrophage activation and production of cytokines) and demonstrates antineoplastic and antiviral effects.

(b) Proteins: Proteins in the gel, on the other hand, make up 1 % of the solid content of the gel extract. The predominant proteins in gel-extracts are lower molecular-weight (11,000 and 14,000 kDa respectively, for the two peptide chains). They are probably associated with lectin and may account for the mitogenic activity [49].

(c) Glycoproteins: Glycoproteins have been isolated from Aloe. The homogeneous glycoprotein [69] having 34% carbohydrates, of molecular weight 40 kDa, stimulates DNA synthesis in baby hamster kidney-cells and exhibits lectin properties by reacting with sheep cells. The glycopreotein fraction from Aloe vera gel exhibits proliferation-promoting activity in human and hamster cells and enhances wound-healing with significant cell- proliferation and migration. Another glycoprotein fraction (protein 82%, carbohydrate 11%) with a molecular weight 29 kD from Aloe vera gel was found to have a proliferation-promoting activity on human and hamster- cells in vitro [25].

(d) Lectins: Lectins [48,49,70,71] with different haemagglutinating activities have been isolated. Aloctin I and Aloctin II were isolated from leaf pulp [70]. The Aloctin II activity was inhibited by N-acetyl-D-galactosamine, whereas the Aloctin I was not inhibited by different sugars (twenty) tested for specificity. Two lectins [48] had also been isolated from leaves of Aloe arborescence, the P-2 with molecular weight 18000 and S-1 with molecular weight 24 kDa. The P-2 and S-1 contain more than 18% and 50% neutral carbohydrates by weight, respectively. Both of these exhibit haemagglutinating activity, whereas P-2 also exhibits mitogenic activity on lymphocytes. Interestingly, both of them contain a high proportion of acidic amino acids (i.e. Asp and Glu), and low proportion of Met and His. A lectin with a molecular weight 35 kDa was isolated from leaf-skin of Kidachi Aloe [71] that showed Haemagglunating and mitogenic activity. The sequence of this protein is highly homologous to that of mannose-binding lectin from snowdrop bulb.

(e) Anthraquinones: The leaf lining (latex, resin or sap) contains anthraquinone glycosides [35-38] (aloin, Aloe-emodin and barbaloin) that are potent stimulant laxatives. These water-soluble glycosides are split by intestinal bacteria into a glycones which effect the laxative action. The laxative effect from Aloe is stronger than from any other herb, including senna, cascara or rhubarb root; it also has more severe side-effects, such as cramping, diarrhea, and nausea [72]. For medicinal use, the leaf-lining is dried and the residue is used as herbal laxative. The products are usually taken at bedtime. They are poorly absorbed after oral administration, but moderately well-absorbed after bacterial hydrolysis. They are eliminated in the urine, bile, feces and breast milk. They turn alkaline urine red. Most of herbalists recommend that they should be avoided during pregnancy, due to the risk of stimulating uterine contractions and also avoided during lactation, due to the risk of excretion in breast milk. Aloe is seldom recommended as a first choice among laxative preparations, due to the severe cramping and nausea associated with its use.

ALOE VERA IN HEALTH AND DISEASE

The Aloe had been used for the treatment of many ailments i.e. gastrointestinal, gout boils, etc. by folks of many nations since long. However, real scientific research into Aloe vera resulted in the isolation of Aloin in 1900s, which was used as laxative until World War II. In the 1930s research began focusing in Aloe's benefits. Aloe has been used to cure X-ray dermatitis [73]. It was concluded that results as a whole had been satisfactory when the treatment of Aloe vera leaf was given to more than 50 cases of X-Ray dermatitis. Further research confirmed these findings for Aloe, helping to relieve eczema, thermal burns, scalding, sunburn, minor injuries, and certain allergies, including poison ivy.

Detailed studies explored Aloe's several other characteristics, including that of antibacterial, anti-inflammatory, and antiseptic properties of Aloe vera. Aloe may penetrate injured tissue, relieve pain, dilate capillaries, and work as an anti-inflammatory agent. It has also been shown by Davis and co-workers [22,23,74-76] that certain amino acids, vitamins, RNA act as anti-inflammatory. These and other compounds are grouped together to form the inhibitory systems [22,74]. Glycoproteins (enzymes) form a part of this system [5]. Immune stimulators, growth-factors and muco-polysaccharides heal wounds and are grouped together to form stimulatory system [23,75,76]. Many active components in both systems synergize, so that the final total activity in each system is greater than the sum of the active compounds.

Diabetics exhibit poor wound-healing, due to poor collagen formation and reduced wound-healing and reduced wound-tensile strength. The diabetic fibroblast suffers from premature aging. Aloe vera reduced inflammation and improved wound-healing in both the normal and diabetic states, in a dose dependent-response fashion [77]. Aloe vera activates enzymes found in the pancreas; it helps the blood sugar-content in individuals suffering from hypoglycemia and diabetes [78,79].

A mixture of Aloe vera and Aloe arborescence was studied for its therapeutic effects on the cirrhosis patients by a Japanese research team [80]. The liver-function tests have shown that AST, ALT and total bilirubine values were significantly reduced and normal values were completely restored after six month. It is also suggested that the mucopolysaccharides, one of the ingredients in Aloe, play an important role, by acting as a growth factor. This growth-factor contributes to wound-healing by stimulating fibroblasts (connective-tissue cells) to produce more collagen, which in turn increases the remodeling of the wound and fills in the wound area. Acting synergestically, Aloe may keep the wound moist and at the same time allow oxygen to penetrate the wound, adding to regeneration. Grindlay and Reynolds [81] revealed that Aloe seems to promote healthy-cell growth: if a cell is cancerous, growth is not stimulated. Winters [82] found that fresh Aloe vera leaves contained lectin-like compound, which enhanced the growth of normal human cells in tissue-culture, but not tumor cells. This was further confirmed in case-reports of El Zawarhy et al., [83] in which it is pointed out that Aloe vera gel promotes the regeneration of normal tissue but does not have the similar growth-patterns in carcinogenic tissue. Jeffrey Bland [7] studied the effects of Aloe vera juice-consumption on urinary indican, stool specific-gravity, gastric and bowel motility. Urinary indican values decreased, indicating lowered conversion of tryptophan by bowel bacteria, an improved protein-digestion and absorption, as well as reduced bowel putrefaction. This change, by itself, could help in preventing colon cancer.

The biological and biochemical research has delineated various properties and mechanisms leading to clinical implications of Aloe. Attributes, such as moisturizing and penetrating properties, are well known, but its healing abilities and analgesic action as well as bacterial activity need to be further elaborated.

The research conducted during the last two decades contributes further to the useful effects of Aloe biochemicals that are miraculously effective and a summary of clinical applications of Aloe vera is described in Table-3.

COMMERCIAL SIGNIFICANCE OF ALOE

The original commercial use of the plant was to grow it for the production of a latex substance called Aloin [30], which is yellow and, possess bitter and lingering taste. The latex of Aloe contains the laxative anthraquinones that have been shown to possess substantial antimicrobial activity against a wide variety of microorganism [30].

Table 3: Clinical Applications of Aloe vera

1. Antimicrobial	
a. Antibacterial	Aleo gel is bacteriostatic or bactericidal against a variety of common wound-infecting bacteria in *vitro*:*Staphylococcus auerus, Streptococcus pyogenes, Serratia marcescens, Klebsiella pheumoniae, Pseudomonas aeruginosa, E. coli, Salmonella typhosa and Mycobaterium tuberculosis*[4,59].Aloe-emodin also inhitbits the growth of *Helicobacter pylori* in a dose-dependent fashion[84].
b. Antiviral	Acemannan acts alone and synergistically with azidothymidine(AZT) [64,65,85] and acemannan hydrogel is used as treatment for persons infected with HIV relevant to CD44 [66,67]. *Aloe vera* extract (0.5%) in a hydrophilic cream had a significantly enhanced healed lesions [86].
c. Antifungal	Aloe extract treatment of guinea pig feet that had been infected with *Trichophyton mentagrophytes* resulted in a 70% growth inhibition compared with untreated animals [87].
2. Antineoplastic	Aloin A and B, aloesin and aloeresin were devoid of antitumor activity effects on human K562 leukemia cell lines [66]. Acemannan has demonstrated activity against feline leukemia virus and solid [88-93], and maligrant tumors 28 and inhibits hepatic tumor induction [94,95]. In preliminary studies it has been significantly enhanced neatly a year survival [96]
3. Endocrine	Aloe gel has been shown to lower blood sugar in diabetic mice [97,98], as well as normal mice [99]. Nearly half of diabetic patients surveyed in Texas reported using *Aloe vera* or other herbal remedies as complementary therapies for their diabetes [100]. Aloe gel to enhance the hypoglycemic effect of glibenclamide when given orally to diabetic patients [99,101].
4.Gastrointestinal	Stimulant laxative (leaf lining), gastric and duodenal ulcers (gel), inflammatory bowel disease.
a. Laxative	Barbaloin, or loin, derived from inner sheath cells of the leaves, is a bitter, yellow laxative. Affects the sodium/potassium pump and chloride channels at colonic membrane [102,103]. Aloe's Anthraquinones enhance intestinal propultion and water secretion in mice [104]. The Anthraquinones present in latex stimulate chloride and water secretion in large intestine, inhibits its reabsorption and stimulate peristalsis [105,106], and acts as a cathartic in chronically constipated adults [107].
b. Gastric and duodenal ulcers [11].	Aloe-emodim inhibits growth *Helicobactor pylori* in a dose –dependent fasion [84]. *Aloe vera* inhibits gastric acid secretion in mice and rats and has protective effects against gastric mucosal demage in rats [108], *Aloe vera* extract reduced asprin-induced gastric mucosal injury in experimental rats [109], and extracts also suppressed the ulcerogenic effects of stress in experimental rats [110].
c. Inflammatory bowel disease.	Acemannan is under consideration as an experimental remedy for inflammatory bowel disease [111,112].
5.Immune modulation	Acemannan acts as immune stimulant and anti-inflammatory [113,114], increases monocyte and macrophage activity and cytotoxicity, stimulates killer T-cells and enhances macrophage candidacidal activity in *vitro* [115-117]. Acemannan enhances macrophage release of interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and interferon gama (INF-γ) in a dose dependent fasion [115,118]. Aloe extracts also blocks prostaglandin and thromboxane production from arachidonic acid , reducing inflammation [4,119,120]. Acetylated mannans from Aloe in mice stimulated an increase in white blood counts, splenic cellularity, and absolute numbers of neutrophils, lymphocytes and monocytes [121-126]. Aloe reduced the production of interleukin-10 following exposure to ultraviolet radiation, reduces the suppression of delayed type hypersensitivity [127-129]. and blocked mast cell inflammatory responses to antigen-antibody complexes [130,131].

continue...

...continued

The other main ingredient of Aloe is called gel, which covers inner portion of the leaves. It is clear, colourless, and tasteless. Aloe Vera gel, like most natural juices in both fruits and vegetables, is unstable and subject to discoloration and spoilage from contamination by microorganisms. It is, therefore, most important to stabilize and concentrate the gel in powder natural form, for commercial use in nutritional foods and cosmetics.

Today the Aloe industry in USA and Mexico has established high ethical standards for businesses and Aloe products. Through the International Aloe Science Council of America (IASC), the Aloe Industry in America and Mexico solidified its dedication to providing the world with highest quality Aloe and Aloe products. The wide acceptance of Aloe by society in so many consumer-products suggests that the IASC is moving in the right direction. The IASC has committed professionals to the further growth of Aloe products by quality-research and marketing.

CONCLUSIONS

The ease in growth and maintenance of Aloe plant and multiple uses of its constituents have prompted several elaborate investigations in the private and public sector. Aloe Vera research based on comprehensive biological, biochemical, chemical and clinical studies have opened up new areas, and many more effective uses are likely to be developed. There is a major scope in the promotion of recombinant-DNA based studies, targeting compounds of value to be isolated and produced in stable and realistic quantities. The procedures of isolation and maintenance of Aloe-products in stable form required special care and these have been established after painstaking efforts.

REFERENCES

1. J.L. Vogelzang, "What You Need to Know About Dietry Supplements", Home Health Nurse, 19, 50-52 (2001).
2. J.S. Williamson and C.M. Wyadat, "The Herbal Generation: Legal and Regulatory Considerations", Trends in Pharmacy and Pharmaceutical Care, 19, 101-110, (1999).
3. P. Atherton, "Aloe vera: Magic or Medicine", Nurs. Stand. 12, 41-52, (1998).
4. M.C. Robson, J.P. Heggers and W.J. Hagstrom, "Myth, Magic, Witchcraft, or Fact? Aloe Vera Revisited" Journal of Burn Cure and Rehabilitation, 3, 157-163 (1982)
5. I.E. Dandhof, "Remarkable Aloe", Omnimedicus Press, Grand Prairie, Texas, (1987).
6. I.E. Dandhof , "Some External Uses of Aloe", Aloe Today Winter, 22-25 (1991/92).
7. Jeffrey Bland, "Effect of Orally Consumed Aloe Juice on Gastrointestinal Function in Normal Humans", Linus Pauling Institute of Science and Medicine, Palo Alto, Cal., Preventive Medicine, (1985).
8. A. Kandil and W. Gobran, "Protection of Gastric Mucosa by Aloe vera", J. Drug Res.(Egypt), 11, 191-196 (1979).
9. A. Kandil and W. Gobran, "Protection of Gastric Mucosa by Aloe vera", Ull Islamic Med., 2, 508-511 (1982).
10. F. Borrelli, A.A. Izzo, "The Plant Kingdom as a Source of Anti Ulcer Remedies", Phytother. Res.,14, 581-591 (2000).
11. N.S. Parmer, M.A. Teri, A.M. Angel, M.S. Asaid, "Evaluation of Aloe vera Leaf Gel and Exudate for Gastric and Duodenal Anti Ulcer Activity", Fitoterapia 57(5), 380-380 (1986).
12. J.J. Blitz, J.W. Smith and H.R. Gerad, "Aloe vera Gel in Peptic Ulcer Therapy: Preliminary Report", J. Amer. Osteopathic Assc., 62, 731-735 (1963).
13. J.E. Crew, "Aloes in the Treatment of Burns and Scalds", Minnesota Med, 22, 538-539 (1939).
14. T. Rowe, "Further Observation on the Use of Aloe vera Leaf in the Treatment of Third Degree X-Ray Reactions", J. Am. Pharm. Assoc. 30, 266 (1941).

15. L.M. Cera, J.P. Heggers, M.C. Robson and W.J. Hagstrom, "The Therapeutical Efficacy of Aloe vera Cream (Dermaid Aloe) in Thermal Injuries: Two Case Reports", Journal of the American Animal Hospital Association, 16, 786-772 (1988).
16. M. Egawa, K. Ishida, M. Maekawa and Y. Sato, "Anti-inflammatory and Wound Healing Topical Skin Preparations Containing Aloe Extract and Elagic Acids", Patent-Japan Kokai Tokkyo Koho-02 231,408 10PP-(1990), CA 114:129142.
17. J.S. Brown, S. A. Marky, " The Use of Botanicals for Health Purposes by Members of a Prepaid Health Plan", Res. Nurs. Health, 14, 399-350 (1991).
18. R.H. Davis, J.M. Kabbani and N.P. Maro, "Aloe vera and Inflammation", Proc. Penn. Acad. Sci., 60, 67-70 (1986).
19. T.D. Rowe and L.M. Parks, "A Phytochemical Study of Aloe vera Leaf", J. Amer, Pharm Ass. Sci Ed., 30, 262-266 (1941).
20. M.H. Odus, B.R. Cook, "Aloe Myth-Magic Medicine" 2nd Edition,Universal Graphics, (1989).
21. I. Suzuki, H. Siato, S. Inove, S. Mijita, T. Takahashi, "Purification and Characterization of Two Lectins from Aloe arborescense Miller", J. Biochem. (Tokyo) 85, 163-171 (1979).
22. R.H. Davis, W.L. Parker, R.T. Samson and D.P. Murdoch, "The Isolation of an Active Inhibitory System from an Extract of Aloe vera", J.Amer Podiatr. Med. Assoc., 81(5), 258-261 (1991).
23. R.H. Davis, "Isolation of a Stimulatory System in an Aloe vera Extract", J. Amer. Podiatric Med. Assoc., 81(9), (1991).
24. R.H. Davis, J.J. Donato, G.M. Hartman, R.C. Hass, "Anti-Inflammatory and Wound Healing Activity of a Growth Substance in Aloe vera", Am. Poddiatr. Med. Assoc. 84,77-81 (1994).
25. A.Yagi, T. Egusa, M. Arase, M. Tanabe, H. Tsugi, "Isolation and characterization of Glycoprotein Fraction with a Proliferation-Promoting Activity on Human and Hamster Cells in Vitro form Aloe vera Gel", Planta Med., 63, 18-21 (1997).
26. M.I. Ali, N.M. Shalaby, M.H. Algamal, A.S. Mousa, "Antifungal effects of different Plant Extracts and their major components of selected Aloe Species", Phytother. Res.,13, 401-407 (1999).
27. T. Pecere, M.V. Gazzola, C. Mucignat, C. Parolin, F.D. Vacchia, A. Cavagioni, G.Basso, A. Diaspro, B.Salvato, M.Carli, G.Palu, "Aloe Emodin is a New Type of Anti-Cancer Agent with Selective Activity Against Neuroactodermal Tumors", Cancer Res., 60, 2800-2804 (2000).
28. S.W. Choi, B.W. Son, Y.S. Son, Y.I. Park, S.K. Lee, M.H. Chung, "The Wound-Healing Effect of a Glycoprotein Fraction Isolated from Aloe vera", Br. J.Dermatol., 145, 535-545 (2001).
29. S.W. Choi, K.W. Kim, J.S. Choi, S.T. Han, Y.I. Park, S.K. Lee, M.H. Chung "Angiogenic Activity of beta-Sitosterol in The ischemia/reperfusion-demaged brain of Mangolian Gerbil," Planta Med., 68, 330-335 (2002).
30. T.A. Waller, "Comparative Studies of Aloe from Commercial Sources", Aloe Today Spring, 22-26 (1993).
31. G.R. Waller, S. Mangiofico and C.R. Ritchey, "A Chemical Investigation of Aloe barbadensis", Proc.Okla. Acad. Sci., 59-69 (1978).
32. N. Paugh, S.A Ross, M.A. Elsohly, D.S. Pasco, "Characterisaton of Aloeride, a New High Molecular Weight Polysaccharide from Aloe vera with Potent Immunostimulatory Activity", J. Agric. Food Chem., 49,1030-1034 (2001).
33. T. Reynolds, A.C. Dweek, "Aloe vera Leaf Gel: A Review Update", J. Ethnopharmacol., 15, 3-37 (1999).
34. G.D. Bouchey and G. Gjerstad, "Chemical Studies of Aloe (barabadensis) Juice.II: Inorganic Ingredients", J. Crude Drug Res., 9, 1445-1453 (1969).
35. J.P. Brown, "A Review of the Genetic Effects of Naturally Occuring Flavanoids, Anthraquinones and Related Compounds", Mutat. Res., 75, 243-277 (1980).
36. L.E. Sandelbach, "A Review of the Toxicity and Carcinogenicity of Anthraquinone Derivatives", Toxicology, 57, 227-240 (1989).
37. J. Westendorf, H. Marquardt, B. Poginnsky, M. Dominiak, and J. Schmidt, "Genotoxicity of Naturally Occurring Hydroxy-anthraquinones", Mutat. Res., 240, 1- 12 (1990).
38. D.Wolfe, C. Schumatte, J. Westendorf, and H. Marquardt, "Hydroxy-anthraquinines as Tumor Promoters, Enhancement of Malignant Transformation of C3H Mouse Fibroblasts and Growth Simulation of Primary Rat Heptocytes", Cancer Res., 50, 6540-6544 (1990).
39. J.E. Hodge, and B.T. Hofrieter, "Determination of Reducing Sugars and Carbohydrates", Methods of Carbohydrate Chemistry, 1, 380-394 (1962).
40. D.C. Gowda, B. Neelisiddaiah and Y.V. Anjaneyalu, "Structural Studies of Polysaccharides from Aloe vera", Car. Res., 72, 201-205 (1979).
41. G. Mendal, and A. Das, "Characterisation of the Polysaccharides of Aloe barbadensis, Part I: Structure of D-Galactan Isolated from Aloe barbadensis Miller", Carb. Res., 86, 247-257 (1980).
42. G. Mendal and A. Das, "Characterisation of the Polysaccharides from Aloe barbadensis, PartII, Structure of the Glucomannan Isolated from the Leaves of Aloe barbadensis Miller", Carb. Res., 87, 249-256 (1980).
43. G. Mendal, , R. Ghosh and A. Das, "Characterisation of the Polysaccharides of Aloe Barbadensis, Part III, Structure of Acidic Oligosaccharide", Indian J. Chem.,

22B-890-893 (1983).
44. A.H. McAnalley, "Identification of Polysaccharides (the Acetylated B1-4 Mannan)", U.S. Patents, 4, 735, 935, 4, 851, 22, 4, 959, 214 and 4, 966, 892 (1988).
45. Q.N. Haq and A. Hannan, "Studies of Glucogalactomannan from the Leaves of Aloe Vera Tourn. (Ex.linn)", Bangaldesh J.Sci. and Ind. Res., 16, 68-72 (1981).
46. M. Obata, "Mechanism of Anti-Inflammatory and Anti-Thermal Burn Action of Carboxypeptidase Aloe arborescence Miller, Netalensis Berger in Rats and Mice", Phsiotherapy Research, 7, Special Issues, 530-533. (1993).
47. M.S. Shelton, "Aloe vera, Its Chemical and Therapeutic Properties", International Journel of Dermatology, 30, 679-683.
48. I. Suzuki, H. Saito, S. Inueo, and Takahashi, "Purification and Characterisation of Two Lectins from Aloe barbadensis Miller", Jap. Biochem., 85, 163-171 (1979).
49. D. Winters Wendal, "Immunoreactive Lectin-Mitogenes From Aloe Barbadensis Mill" International Congress of Phytotherapy, organised by The Pharmaceutical Society of Korea and Aloe Research Foundation, U.S.A., October abstract SB1(1991).
50. B.C. Coats, The Silent Healer, "A Modern Study of Aloe vera, Texas", Garland (1998).
51. Wang Yin-Tung, "Long- term Monitoring of Field-grown Aloe vera, IASC. 12th Annual Aloe Scientific Seminar", Irving TX, 3, July 17th (1993).
52. P. Atherton, "The Essentials of Aloe vera, The Actions and The Evidence", 2nd Eddition, (1997).
53. G.P. Lawrence, "The Health and Medical Use of Aloe vera" {ISBN: 0-943685-21-4}, (1998).
54. R.H. Davis, "Aloe vera: A Scientific Approach" {ISBN: 0533-12137-x}, (1997).
55. B.C. Coats And R. Ahola, "The Silent Healer, a Modern Study of Aloe vera" 3rd Eddition, (1996).
56. D. Gage, "Aloe Vera: Nature's soothing Healer" {ISBN: 0-89281-627-9}, (1997).
57. E. Mckeon, "Anthraquinones and Anthracenic Derivatives Absorb UV light", Cosmetics and Toiletries, 102, 64-65 (1987).
58. F. M. Strickland, R.P. Pelly, M.L. Kripke, "Prevention of Ultraviolet Radiation and Induced Supperssion of Contact and Delayed Hypersensitivity by Aloe barbadensis Gel Extrect", Journel of Investigative Dermatology, 9, 197-204, (1994).
59. L. Lorenzetti, R. Salisbury, J. Beal, J. Baldwin, "Bacteriostatic Property of Aloe vera", J. Pharmacol. Sci., 3, 1287(1964).
60. P.Sims, M. Ruth., E.R. Zimmerman., "Effect of Aloe vera on Herps Simplex and Herps virus (strain Zoster)", Aloe vera of American Archives, 1, 239-240, (1971).
61. F.M. Strickland et al., "Prevention of ultraviolet raditions and induced suppression of contact and delayed hypersensitivity by Aloe barbadensis gel extract", Journal of Investigative Dermatology, 9, 197-204, (1993).
62. B.C. Coats, "The silent healer, a modern study of Aloe vera", Texas Garland, (1979).
63. T.Hirat and T. Suga, "The efficiency of aloe plants, chemical constituents and Biological activities", Cosmetics and toiletries, 98, 105-108, (1983).
64. J.B. Kahlon, M.C. Kemp, N. Yawei, R.H. Carpenter, W.M. Shannon, B.H. McAnalley, "In Vitro Evaluation of the Synergistic Antiviral Effects of Acemannan in Combination with Azidothymidine and Acyclovir", Mol. Biother., 3, 214-23 (1991a).
65. J.B. Kahlon, M.C. Kemp, R.H. Carpenter, B.H. McAnalley, H.R. McDaniel, W.M. Shannon, "Inhibition of AIDS Virus Replication by Acemannan in Vitro", Mol. Biother., 3, 127-35 (1991b).
66. J.S. Montaner, J. Gill, J. Singer, "Double-Blind Placebo-Controlled Pilot Trial of Acemannan in Advanced Human Immunodeficiency Virus Disease", J. Acquir. Immune Defic. Syndr. Hum. Retrovirol., 12, 153-7 (1996).
67. J. Singer, J. Gill, R. Arseneau, B. McLean, "A Randomized, Placebo-Controlled Trial of Oral Acemannan as an Adjunctive to Antiretroviral Therapy in Advanced Disease", Int. Conf. AIDS, 9, 494 (1993).
68. M.A. Sheets, B.A. Unger, G.F. Giggleman Jr., Tizard IR. "Studies of the Effect of Acemannan on Retrovirus Infections: Clinical Stabilization of Feline Leukemia Virus-Infected Cats", Mol. Biother., 3, 41-5 (1991).
69. A. Yagi, K. Machi, H. Nishimura, T. Shida, I. Nishioka, "Effect of Aloe Lectin on Deoxyriboneuclic Acid Synthesis in Baby Hamster Kidney Cells", Experientia 41, 669-671 (1985).
70. N. Akev, A. Can, "Seperation and Some Properties of Aloe vera Pulp Lectins", Phytother. Res., 13, 489-493 (1999).
71. T. Koike, H. Beppu, H. Kuzuya, K. Maurata, K. Shimpo, M. Suzuki, K. Titani, K. Fujita, "A 35 kDa Mannose-Binding Lectin with Hemaglutinating and Mitogenic Activities from 'Kidachi Aloe' (Aloe brborescence Miller Var. Natalensis Berger)", J. Biochem. (Tokyo), 118, 1205-1210 (1995).
72. F.M. Strickland, R.P. Pelly, D. Hill and M.I. Kripke, "The Effect of Topical Administration of Aloe barbadensis Gel Extract Upon UVB-Induced Suppression of Contact Hepersensitivity in C3H Mice", J. Invest. Dermatology, 98, 120s, (1992).
73. C.E. Collins and C. Collins, J. Amer, "Roentgen Dermatitis Treated with Fresh Whole Leave of Aloe vera", Roentgen, 33, 396-397 (1937).
74. R.H. Davis, "Inhibitory and Stimulatory Systems in Aloe vera", Aloe Today Winter, 6-8 (1991/1992).
75. R.H. Davis, M.G. Leitner, J.M. Russo and M.E. Barne,

"Wound Healing Oral and Topical Activity of Aloe vera", J. Amer. Podiatr. Assoc., 79, 559-562 (1989).
76. R.H. Davis, J.M. Kabbani and N.P. Maro, "Aloe vera and Wound Healing", J. Am. Podiatr. Med. Assoc., 77, 165-169,70 (1987).
77. R.H. Davis and N.P. Maro, "Aloe vera and Gibberllin Anti-Inflammatory Activity in Diabetes", J. Amer. Podiatr. Med. Assoc., 79(1), 24-26 (1989).
78. S. Yongchaiyudha, "Antidiabetic Activity of Aloe vera L. Juice. I , Clinical Trial in new cases of Diabetes mellitus", Phytomed., 3(3), 241-3 (1996).
79. N. Bunyapraphatsara, "Antidiabetic Activity of Aloe vera L. Juice. I, "Clinical Trial in diabetes mellitus patients in combination with Glibenclamide", Phytomed., 3, 245-8 (1996).
80. You-Jin, Jin Tai Hong, Loan Kim, Sin-koa and Yeo-Pyo Yun, "Effects of Aloe vera and arborescnce Mixture on Cirrhosis Patients", International Congress of Phytotherapy, Organised by The Pharm. Soc. of Korea and Aloe Research Foundation,USA., Abstract. page 42, Oct. (1991).
81. Grindlay and Reynolds, "Aloe Promotes only Healthy Cell: If a Cell is Cencerous, Growth is not Stimulated", J. Ethnopharmacology, 117-151 (1986).
82. W.D. Winters, R. Beavides and W.J. Clouse, "Effects of Aloe Extracts on Human Normal Tumor Cells in Vitro", Econ. Bot., 35, 89-95 (1981).
83. M. El Zawahry, "Ueses of Aloe in Treating Leg Ulcers and Dermatosis", Dermatology, Jan-Feb (1973).
84. H. Wang, J. Chung, C. Ho, L. Wu, S. Chang, "Aloe-Emodin Effects on Arylamin N-Acetyltransferase Activity in the Bacterium Helicobacter pylori", Planta. Medica., 64, 176-8 (1998).
85. M. Kemp, J. Kahlon, A. Chinnah, "In vitro Evaluation 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", Antiviral Res. Suppl., 1, 83 (1990).
86. T. Syed, M. Afzal, A. Ashfaq, A. Holt, A. Ali, S. Ahmad, "Management of Genital Herpes in Men with 0.5% Aloe Vera extract in a Hydrophilic Cream: a Placebo-Controlled Double Blind Study", Journal of Dermatological Treatment, 8, 99-102 (1997).
87. K. Kawai, H. Beppu, K. Shimpo, "In Vivo Effects of Aloe arborescens Miller Var. natalensis berger on Experimental Tinea Pedis in Guinea pig Feet', Phytotherapy Research, 12, 178-82 (1998).
88. S.Y. Peng, J. Norman, G. Curtin, D. Corrier, H.R. McDaniel, D. Busbee, "Decreased Mortality of Norman Murine Sarcoma in Mice Treated with the Immunomodulator, Acemannan", Mol.Biother, 3, 79-87 (1991).
89. M.M. Corsi, A.A. Bertelli, G. Gaja, A. Fulgenzi, M.E. Ferrero, "The Therapeutic Potential of Aloe vera in Tumor-Bearing Rats" Int. J. Tissue React., 20, 115-8 (1998).
90. C. Harris, K. Pierce, G. King, K.M. Yates, J. Hall, I. Tizard, "Efficacy of Acemannan in Treatment of Canine and Feline Spontaneous Neoplasms", Mol. Biother., 3, 207-13 (1991).
91. G.K. King, K.M. Yates, P.G. Greenlee, "The effect of Acemannan Immunostimulant in Combination with Surgery and Radiation Therapy on Spontaneous Canine and Feline Fibrosarcomas", J. Am. Anim. Hosp. Assoc., 31, 439-47 (1995).
92. K.M. Yates, L.J. Rosenberg, C.K. Harris, "Pilot Study of the Effect of Acemannan in Cats Infected with Feline Immunodeficiency Virus", Vet. Immunol. Immunopathol. 35, 177-89 (1992).
93. K.N. Desai, H. Wei, C.A. Lamartiniere, "The preventive and therapeutic potential of the Squalene-Containing Compound, Roidex, on Tumor Promotion and Regression", Cancer Lett., 101, 93-6 (1996).
94. H. Tsuda, K. Matsumoto, M. ITo, I. HIrono, K. Kawai, H. Beppu, "Inhibitory Effect of Aloe arborescense Miller var. natalensis Berger (Kidachi Aloe) on Induction of Preneoplastic Focal Lesions in the Rat Liver", Phytother. Res., 7, S43-S47 (1993).
95. N.A. Shamaan, K.A. Kadir, A. Rahmat, W.Z. Ngah, "Vitamin C and Aloe vera Supplementation Protects from Chemical Hepatocarcinogenesis in the Rat", Nutrition, 14, 846-52 (1998).
96. P. Lissoni, L. Giani, S. Zerbini, P. Trabattoni, F. Rovelli, "Biotherapy with the Pineal Immunomodulating Hormone Melatonin Versus Melatonin Plus Aloe vera in Untreatable Advanced Solid Neoplasms, Nat. Immun. 16, 27-33 (1998).
97. M. Ajabnoor, "Effect of Aloes on Blood Glucose Levels in Normal and Alloxan Diabetic Mice", J. Ethnopharmacology, 28, 215-20 (1990).
98. N. Ghannam, "The Antidiabetic Activity of Aloes: Preliminary Clinical and Experimental Observations", Hormone Res., 24, 288-94 (1986).
99. H. Beppu, Y. Nagamura, K. Fujita, "Hypoglycemic and Antidiabetic Effects in Mice of Aloe arborescens Miller var. natalensis Berger", Phytotherapy Research, 7, S37-S42 (1993).
100. P. Noel, J. Pugh, A. Larme, G. Marsh, "The Use of Traditional Plant Medicines for Non-Insulin Dependent Diabetes Mellitus in South Texas", Phytotherapy Research, 11, 512-17 (1997).
101. M.S. Williams, M. Burk, C.L. Loprinzi, "Phase III Double-Blind Evaluation of an Aloe vera Gel as Amprophylactic Agent for Radiation-Induced Skin Toxicity", Int. J. Radiat. Oncol. Biol. Phys. 36, 345-937 (1996).
102. Y. Ishii, H. Tanizawa, Y. Takino, "Studies of Aloe III Mechanism of Cathartic Effect (2)", Chem. Pharm. Bull (Tokyo), 38, 197-200 (1990).

103. J. Honig, P. Geck, H. Rauwald, "Inihibition of Cl-Channels as a Possible Base of Laxative Action of Certain Anthraquinones and Anthrones", Planta Medica, 58, 586-7 (1992).
104. T. Yagi, "The Synergistic Purgative Action of Aloe-Emodin Anthrone and Rheinanthrone in Mice: Synergism in Large Intestinal Propulsion and Water Secretion", J. Pharm. Pharmacol., 49, 22-25 (1997).
105. N.G. Bissett, "Herbal Drugs and Phytopharmaceuticals. Stuttgart: MedPharm CRC Press, 566 (1994).
106. M. Blumenthal, "The complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines", Austin: American Botanical Council, (1998).
107. H. Odes, Z. Madar, "A double-blind trial of a Celandin, Aloe Vera, and Psyllium Laxative Preparation in Adult Patients with Constipation", Digestion, 49, 65-71 (1991).
108. W. Suvitayat, N. Bunyapraphatsara, S. Thirawarapan, K. Watanabe, "Gastric Acid Secretion in Inhibitory and Gastric Lesion Protective Effects of Aloe Preparation", Thai Journal of Phytopharmacy, 4, 1-11 (1997).
109. G. Maze, R. Terpolilli, M. Lee, "Aloe vera Extract Prevents Aspirin-Induced Gastric Mucosal Injury in Rats", Medical Science Research, 25, 765-66 (1997).
110. R. Teradaira, M. SIngzato, H. Beppu, K. Fujita, "Antigastric Ulcere Effects in Rats of Aloe arborescens Miller var. natalensis Berger", Phytotherapy Research, 7 (1993).
111. M. Robinson, "Optimizing Therapy for Inflammatory Bowel Disease", Am. J. Gastroenterol, 92, 12S-17S (1997).
112. M. Robinson, "Medical Therapy of Inflammatory Bowel Disease for the 21st century", Eur. J. Surg. Suppl., 582, 90-8 (1998).
113. L.A. t'Hart, P.H. van Enckevort, H. van Dijk, R. Zaat, K.T. de Silva, R.P. Labadie, "Two Functionally and Chemically Distinct Immunomodulatory Compounds in the Gel of Aloe vera", J. Ethnopharmacol. 23, 61-71 (1988).
114. t'Hart LA, van den Berg AJ, Kuis L, van Dijk H, Labadie RP, "An Anti-Complementary Polysaccharide with Immunological Adjuvant Activity from the Leaf Parenchyma Gel of Aloe vera", Planta Med. 55, 509-12 (1989).
115. L. Zhang, I.R. Tizard, "Activation of a Mouse Macrophage Cell Line by Acemannan: the Major Carbohydrate Fraction from Aloe vera Gel", Immunopharmacology, 35, 119-28 (1996).
116. D. Womble, J.H. Helderman, "Enhancement of Allo-Responsiveness of Human Lymphocytes by Acemannan (Carrisyn)", Int. J. Immunopharmacol., 10, 967-74 (1988).
117. R.W. Stuart, D.L. Lefkowitz, J.A. Lincoln, K. Howard, M.P. Gelderman, S.S. Lefkowitz, "Upregulation of Phagocytosis and Candidicidal Activity of Macrophages Exposed to the Immunostimulant Acemannan", Int. J. Immunopharmacol., 19, 75-82 (1997).
118. Marshall, A. Gibbons, L. Parnell, "Human Cytokines Induced by Acemannan", J. Allergy Clin. Immunol., 91, 295 (1993).
119. L. Cera, J. Heggers, M. Robson, "The Therapeutic Effect of Aloe vera Cream (Dermaid Aloe) in Thermal Injuries: Two Case Reports", J. Am. Animal Hosp. Assoc., 16, 768 (1980).
120. B. Vazquez, G. Avila, D. Segura, B. Escalante, "Antiinflammatory Activity of Extracts from Aloe vera Gel", J. Ethnopharmacol., 55, 69-75 (1996).
121. S.F. Egger, G.S. Brown, L.S. Kelsey, K.M. Yates, L.J. Rosenberg, J.E. Talmadge, "Hematopoietic Augmentation by a Beta-(1,4)-Linked Mannan", Cancer Immunol. Immunother, 43, 195-205 (1996).
122. S.F. Egger, G.S. Brown, L.S. Kelsey, K.M. Yates, L.J. Rosenberg, J.E. Talmadge, "Studies on Optimal Dose and Administration Schedule of a Hematopoietic Stimulatory Beta-(1,4)-Linked Mannan", Int. J. Immunopharmacol., 18, 113-26 (1996).
123. R.H. Davis, M.G. Leitner, J.M. Russo, "Topical anti-inflammatory activity of Aloe Vera as Measured by Ear Swelling", J. Am. Podiatr Med. Assoc., 77, 610-2 (1987).
124. R.H. Davis, K.Y. Rosenthal, L.R. Cesario, G.A. Rouw, "Processed Aloe Vera Administered Topically Inhibits Inflammation", J. Am. Podiatr Med. Assoc., 79, 395-7 (1989).
125. R.H. Davis, M.G. Leitner, J.M. Russo, M.E. Byrne, "Anti-Inflammatory Activity of Aloe vera Against a Spectrum of Irritants", J. Am. Podiatr Med. Assoc., 79, 263-76 (1989).
126. R.H. Davis, G.J. Stewart, P.J. Bregman, "Aloe vera and the Inflamed Synovial Pouch Model", J. Am. Podiatr Med. Assoc., 82, 140-8 (1992).
127. S. Byeon, R. Pelley, S. Ullrich, T. Waller, C. Bucana, R. Strickland, "Aloe Barbadensis Extracts Reduce the Production of Interleukin-10 After Exposure to Ultraviolet Radiation", J. Invest. Dermatol., 110, 811-17 (1998).
128. K. Chong, S. Seong, K. Young, S. Ro, H. Myung, "Prevention of Ultraviolet Radiation-Induced Suppression of Accessory Cell Function of Langerhans Cells by Aloe vera", Immunopharmacology, 37, 153-62 (1997).
129. F. Strickland, R. Pelley, M. Kripke, "Prevention of Ultraviolet Radiation-Induced Suppression of Contact and Delayed Hypersensitivity by Aloe barbadensis Gel Extract", Journal of Investigative Dermatology, 102, 197-204 (1994).
130. J. Ro, B. Lee, M. Chung, "The Inhibitory Mechanism of Aloe Glycoprotein (NY945) on the Mediator Release in the Guinea Pig Lung Mast Cell Activated with Antigen-Antibody Complexes", Korean J. Physiol. Pharmacol., 2, 119-31 (1998).
131. M. Yamamoto, K. Sugiyama, M. Yokota, Y. Maeda, "Inhibitory Effects of Aloe Extracts on Antigen- and Compound 48/80 Induced Histamine Release from Rat Peritoneal Mast Cells", Japanese Journal of

Toxicology and Environmental Health, 39, 395-400 (1993).
132. I.A. Ross, "Medicinal Plants of the World: Chemical Constituents, Traditional, and Modern Medicinal Uses", Totowa, N.J.: Humana Press, xi, 415 (1999).
133. V.E. Tyler, "The Honest Herbal: a Sensible Guide to the Use of Herbs and Related Remedies", New York: Pharmaceutical Products Press, xviii, 375 (1992).
134. W.J. Brasher, E.R. Zimmermann, C.K. Collings, "The Effects of Prednisolone, Indomethacin, and Aloe vera Gel on Tissue Culture Cells", Oral Surg. Oral Med. Oral Pathol., 27, 122-8 (1969).
135. R.H. Davis, M.G. Leitner, J.M. Russo, "Aloe vera: A Natural Approach for Treating Wounds, Edema, and Pain in Diabetes", J. Am. Podiatr Med. Assoc., 78, 60-8 (1988).
136. P. Chithra, G.B. Sajithlal, G. Chandrakasan, "Influence of Aloe vera on the Healing of Dermal Wounds in Diabetic Rats", J. Ethnopharmacol, 59, 195-201 (1998a).
137. P. Chithra, G.B. Sajithlal, G. Chandrakasan, "Influence of Aloe vera on Collagen Characteristics in Healing Dermal Wounds in Rats", Mol. Cell Biochem., 181, 1-6 (1998b).
138. T.A. Syed, S.A. Ahmad, A.H. Holt, S.H. Ahmad, M. Afzal, "Management of Psoriasis with Aloe vera Extract in a Hydrophilic Cream: A Placebo-Controlled, Double-Blind Study", Trop. Med. Int. Health, 1, 505-9 (1996).