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Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Review Article

Diverse Therapeutic Applications of Aloe vera

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ABSTRACT

Many of the health benefits associated with *Aloe vera* have been attributed to the polysaccharides contained in the gel of the leaves. These biological activities include effects promotion of wound healing, antifungal activity, hypoglycemic or antidiabetic effects, antiinflammatory, anticancer, immunomodulatory and gastroprotective properties. While the known biological activities of *A. vera* will be briefly discussed, aim of this review is to highlight recently discovered effects and applications of the leaf gel. These effects include the potential of whole leaf or inner fillet gel liquid preparations of *A.vera* to enhance the intestinal absorption and bioavailability of co-administered compounds as well as enhancement of skin permeation. In addition, important pharmaceutical applications such as the use of the dried *A. vera* gel powder as an excipient in sustained release pharmaceutical dosage forms will be outlined.

Keywords: Aloe vera, Biological activities, Absorption enhancement, Skin permeation, Excipient.

1. INTRODUCTION

Aloe vera is the colourless mucilaginous gel obtained from the parenchymatous cells in the fresh leaves of aloe vera (L) burm. f. (liliaceae) also known as aloe barbadensis. *Aloe vera* is a cactus like plant with green, dagger- shaped leaves that are fleshy, tapering, spiny, marginated and filled with a clear viscous gel [1].

The name was derived from the aeabic "alloeh" meaning "bitter" because of bitter liquid found in the leaves.It is also known as 'lily of the desert ' the plant of immortality and the medicine plant with qualities to serve as alternate medicine. *Aloe vera* is as old civilisation and throughout history it has been used as a popular folk medicine. It is present in the arid regions of India and is believed to be effective in treating stomach ailments, gastrointestinal problems, skin diseases, constipation for radiation injury, for its antiinflammatory effect, for wound healing and burns, asan antiulcer and diabetes. Currently the plant is widely used in skin care, cosmetics and as nutraceuticals [2].

Aloe vera has been used to treat various skin conditions such as cuts, burns and eczema. It is alleged that sap from *Aloe vera* eases pain and reduces inflammation evidence on the effects of *Aloe vera* sap in wound healinghowever is contradictory.

The leaf of *Aloe vera* is rubbery and smooth in touching from outside and inside the plant is the *Aloe vera* gel. It is available in a variety of products such as medicated cream, hand and body lotion, heat rub, pure aloe vera juice, mini lift mask, medicated jelly, moisturizer etc. Commercially aloe can be found in pills, sprays,ointments, lotions, liquids, drinks, jellies and creams to name a few of the thousands of products available [3].

2. ALOE VERA LEAF COMPOSITION

The aloe leaf can be divided into two major parts, namely the outer green rind, including the vascular bundles,and the inner colourless parenchyma containing the aloe gel. Description of the inner central part of the aloe leafmay sometimes be confusing, due to the different terms that are used interchangeably such as inner pulp,mucilage tissue, mucilaginous gel, mucilaginous jelly, inner gel and leaf parenchyma tissue. Technically, the term 'pulp' or 'parenchyma tissue' refers to the intact fleshy inner part of the leaf including the cell walls and organelles, while 'gel' or 'mucilage' refers to the viscous clear liquid within the parenchyma cells [4].

The three structural components of the *Aloe vera* pulp are the cell walls, the degenerated organelles and the viscous liquid contained within the cells. These three components of the

inner leaf pulp have been shown to bedistinctive from each other both in terms of morphology and sugar composition as shown in Figure:1 [5]. The raw pulp of *A. vera* contains approximately 98.5% water, while the mucilage or gel consists of about 99.5% water [6]. The remaining 0.5 – 1% solid material consists of a range of compounds including water-soluble and fat-soluble vitamins, minerals, enzymes, polysaccharides, phenolic compounds and organic acids [7]. It has beenhypothesized that this heterogenous composition of the *Aloe vera* pulp may contribute to the diverse pharmacological and therapeutic activities which have been observed for aloe gel products.

Many compounds with diverse structures have been isolated from both the central parenchyma tissue of *A. vera* leaves and the exudate arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1,8 dihydroxyanthraquinone derivatives and their glycosides, which are mainlyused for their cathartic effects [8]. The aloe parenchyma tissue or pulp has been shown to contain proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and small organiccompounds in addition to the different carbohydrates. Some evidence of chemotaxonomic variation in thepolysaccharide composition of aloes exists [4, 9, 10].

The large fluctuations in polysaccharide composition of *A. vera* fillet as found in the literature has been explained by the fact that the mannosyl residues are contained in a reserve polysaccharide with a significant seasonal influence, as well as large variations between cultivars in terms of the quantities ofmannose-containingpolysaccharides within the parenchyma cells [11]. The chemical constituents of *A.vera* leaves including the pulp and exudate are given below [4, 10, 12].

2.1. Class/ Compounds

Anthraquinones/anthrones: Aloe-emodin, aloetic-acid, anthranol, aloin A and B (or collectively known as barbaloin), isobarbaloin, emodin.

Carbohydrates: Pure mannan, acetylated mannan, acetylated glucomannan, glucogalactomannan, galactan galactogalacturan, arabinogalactan, Galacto glucoarabinomannan, pectic substance, xylan, cellulose, Mannose, glucose, *L*-rhamnose, aldopentose.

Enzymes: Alkaline phosphatase, amylase, sscarboxy- peptidase, cyclooxidase, cyclooxygenase, lipase,oxidase, phosphoenol-pyruvate carboxylase, superoxide dismutase

Inorganic constituents: Calcium, chlorine, chromium, copper, iron, magnesium,manganese potassium, phosphorous, sodium, zinc.

Miscellaneous: Arachidonic acid,γ-linolenic acid,steroids (campestrol, cholesterol, sitosterol), triglicerides, triterpe-noid, gibberillin, lignins, potassium sorbate, salicylic acid, uric acid.

Proteins: Lectins, lectin-like substance.

Vitamins: B1, B2, B6, C, β-carotene, choline, folic acid,α-tocopherol.

2.2. Polysaccharide composition

Polysaccharides make up most of the dry matter of the *A. vera* parenchyma. A storage polysaccharide, acetylated glucomannan, is located within the protoplast of the parenchyma cells and a variety of polysaccharides are present in the cell wall matrix. An overall carbohydrate analysis of the alcohol insoluble residues showed that the cell walls in the fillet of the aloe leaf hold mainly mannosecontaining polysaccharides, cellulose and pectic polysaccharides whereas the skin of the leaf contains in addition significant quantities of xylose-containing polysaccharides [11, 13].

Many investigators have identified partially acetylated mannan (or acemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. As mentioned before, this discrepancy in polysaccharide composition was initially explained by differences in geographical locations of the plants and seasonal changes but later it was found that extraction and processing of the parenchyma tissue are also very important variables that contribute to the differences in the results. Other polysaccharides such asarabinan, arabinorhamnogalactan, galactan, galactogalacturan, lucogalactomannan, galacto glucoarabinomannan and glucuronic acidcontaining polysaccharides have been isolated from the *Aloe vera* inner leaf gel part [5, 12].

2.3. Mannan

In general, mannans play a structural role in plants by acting as hemicelluloses that bind cellulose. They also fulfil a storage function as non-starch carbohydrate reserves in seeds and vegetative tissues. In addition, evidence was found that it may act as a signalling molecule in plant growth and development. Linear mannans arehomopolysaccharides that are composed of linear chains of β-(1→4)-D-mannopyranosyl residues with less than 5% galactose [14].

Although different results on the composition of polysaccharides in aloe pulp have been described in the literature, the consensus among most authors is that acetylated glucomannan molecules are mainly responsible for the thick,

mucilage like properties of the raw aloe gel. Acemannan found in *A.vera* gel is also known as carrysin and has a backbone of β-(1→4)-D-mannosyl residues acetylated at the C-2 and C-3 positions that exhibit a mannose monomer:acetyl ratio of approximately 1:1 and contains some side chains of mainly galactose attached to C-6. The molecular weights of these polysaccharides range from 30-40 kDa or greater and is usually as high as 1000 kDa in fresh aloe leaf material [11, 14, 15]. The repeating units of glucose and mannose exist in a ratio of 1:3, but other ratios of 1:6, 1:15 and 1:22 have also been reported. These discrepancies in glucose to mannose ratios have been explained by differences between species as well as due to sample processing and treatment [6, 7]. In a study where the linkages between monomers in acemannan were analysed, the acemannan was treated with the enzyme endo-β-D-mannanase and the C-4 and C-6 resonances of the fractions were scrutinised using ^{13}C-NMR.

The β -(1→4)-glycosidic bond configuration of acemannan is an important consideration in terms of the therapeutic effects of *A. vera* gel, since humans lack the ability to enzymatically break down these bonds [7].

The acemannan found in aloe is structurally unique that makes it a characteristic compound of aloe species amongst other well known plant mannans (which have distinct side-chains or are unacetylated and insoluble). Plant galactomannans are made up of β-(1→4)-D-mannopyranosyl residues containing side chains of single α-(1→6)-D-galactopyranosyl groups. True galactomannans are represented by those mannans that contain more than 5% by weight of D-galactose residues. The physiological function of plant galactomannans is to retain water by solvation, especially to prevent complete drying of seeds in regions with high temperatures. Glucomannans are polysaccharides that contain chains of randomly arranged β-(1→4)-D-manose and β-(1→4)-D-glucose residues in a ratio of 3:1. The backbone of galactoglucomannans consists of β -(1→4)-D-mannopyranosyl and β-((1→4)-D-glucopyranosyl residues with a α-(1→6)-D-galactopyranosyl and *O*-acetyl groups [14].

2.4. Maloyl glucans

Three malic acid acylated carbohydrates were isolated from *A. vera* gel and characterised as 6-*O*- (1-L-maloyl)-α-, β -D-Glc*p*(termed veracylglucan A), α-d-Glcp-(1→4)-6-*O*-(1-L-maloyl)-α-, β -D-Glc*p*termedveracylglucon α-D.Glcp-(1→4)-tetra-[6-*O*-(1-L-maloyl)-α-D-Glc*p*-(1→4)]-6-*O*-(1-Lmaloyl)-α-, β -D-Glc*p* (termed veracylglucan C).

Veracylglucan A (C10H16O10), with a molecular weight of 296 Da was only detected in very small quantities in the *A. vera* gel and was very unstable with hydrolysis of the ester group [6-*O*-(1-Lmaloyl)- Glc*p*-] that occurred after only one week at a temperature of 7 °C. Veracylglucan B (C16H26O15) has a molecular weight of 458 Da andpH of 3.8, while veracylglucan (C56H18O51) molecular weight of 1570 Da and a pH of 4.7 [16].

2.5. Pectic substance

Pectic substance is a term that refers to a group of closely related polysaccharides including pectin, pectic acid and arabinogalactan. Pectin is a polysaccharide consisting of α-(1→4) linked poly galacturonic acid with intra-chain rhamnose insertion, neutral sugar side-chains and methyl esterification [3].

2.6. Arabinan and arabinogalactan

Arabinogalactan contains mainly arabinose and galactose, but also other sugars including glucuronic acid and/or galacturonic acid. Certain arabinans and arabinogalactans sometimes form the neutral side chains of pectins. Arabinogalactan is present in a much lower concentration in aloe gel compared to acemannan [3].

2.7. Other polysaccharides

Aloeride is a polysaccharide that comprises only 0.015% of the crude *A. vera* juice material (dry weight). It has a molecular weight between 4 and 7 million Da with its glycosyl components containing glucose (37.2%), galactose (23.9%), mannose (19.5%) and arabinose (10.3%). Polyuronide has a molecular weight between 275 and 374 kDa, while that of aloeferon is 70 kDa. Another biologically active polysaccharide with a molecular weight between 420 and 520 kDa was isolated from aloe gel that comprises equal amounts of glucose and mannose [17].

2.8. Skin penetration enhancement

Although there is a high interest in transdermal drug delivery, the poor penetration of drugs into the skin and low permeation across the skin severely hamper the use of this route of drug administration. Techniques for improving the transdermal delivery of drugs are based on the use of chemical penetration enhancers, novel vehicle systems and physical enhancement strategies such as iontophoresis, sonophoresis, ultrasound, microneedles, and velocity based techniques and electroporation [17]. *A. vera* gel increased the *in vitro* skin penetration of compounds depending on their molecular weights, with an apparent inverse correlation between enhancement ratio and molecular weight of the compound [18]. This penetration enhancement effect of the aloe gel was explained by a probable pull effect of complexes formed between the compound and the enhancing agent within the

aloe gel, but it was stated that the proposed mechanism of action has to be further investigated and confirmed. Some constituents of the *A. vera* gel itself also penetrated the skin and this was interestingly dependent on the molecular weight of the co-applied compounds [19-20]. The higher the molecular weight of the co-applied compound, the less of the gel components were transported across the skin. This was explained by the probable displacement of *A. vera* components from the penetration pathways and thereby it inhibits permeation of the gel components more effectively than the smaller compounds [21]. Similar to the discussion for intestinal drug absorption enhancement, *A. vera* gel could potentially be used as a penetration enhancement agent for the transdermal delivery of drugs if proven to be effective and safe.

Aloe vera leaf gel as an excipient in modified release dosage forms:

Gums and mucilages from natural origin that contain complex polysaccharides have found a wide range ofpharmaceutical applications such as functional excipients in dosage forms, which include binders, disintegrants, emulsifiers, suspending agents, gelling agents and sustaining agents in modified release tablets. Furthermore, some natural gums and mucilages have been reported to modify the release of drugs from modified release dosage forms such as matrix type tablets [22].

Dried *A. vera* leaf gel (acetone precipitated component of the pulp) was directly compressed in different ratios with a model drug to form matrix type tablets, including ratios of 1:0.5; 1:1; 1:1.5; and 1:2. These matrix systems showed good swelling properties that increased with an increase of aloe gel concentration in the formulation. The directly compressed matrix type tablets also showed modified release behaviour with 35.45% and 30.70% of the dose released during the first hour and the remaining of the dose was released over a 6 hour period for those formulations containing the lower ratios of gel to drug, namely 1:0.5 and 1:1. The formulation that contained the highest ratio of gel to drug, namely 1:2 exhibited only a 23.25% drug release during the first hour with the remaining of the dose being released over an 8 hour period. The dried *A. vera* gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained-release matrix type tablets [23].

3. BIOLOGICAL ACTIVITIES OF ALOE VERA LEAF GEL

It has been claimed that the polysaccharides in *A. vera* gel have therapeutic properties such as immunostimulation, anti-inflammatory effects, wound healing, promotion of radiation damage repair, antibacterial, anti-viral, anti-fungal, anti-diabetic and anti-neoplastic activities, stimulation of hematopoiesis and anti-oxidant effects [4, 24]. On the other hand, there are a number of clinical reports that have found *A. vera* gel not effective in terms of the above mentioned therapeutic activities or even to cause undesirable effects such as retardation of wound healing. As mentioned before, these conflicting results could be due to the use of plants from different locations with variations in their chemical composition and also because of different isolation techniques that were used to extract compounds from the aloe leaf pulp. The importance of why the specific compounds that were isolated from a plant and then tested in a particular bioassay should be known can be demonstrated by the potential antagonistic and competitive activities between constituents. When the two maloyl glucans, namely veracylglucan B and C, were each individually evaluated for biological activities it was found that veracylglucan B demonstrated high anti-inflammatory and anti-proliferation effects, while veracylglucan C exhibited significant cell proliferative and anti-inflammatory activities. Therefore, if *A. vera* gel is tested in a wound healing experiment and it contains high amounts of veracylglucan B and is perhaps also contaminated with anthraquinones from the exudate, it will most probably result in retardation of wound healing. If the gel is obtained from a plant with higher concentrations of veracylglucan C, it would probably end in positive wound healing results [13].

Furthermore, the polysaccharides found in aloe gel are not stable, especially under stress conditions such as heat, the presence of acid and enzymatic activities. It has been suggested that a standardised method is necessary for production of aloe gel products to avoid degradation of the polysaccharides and thereby preventing the removal of high molecular weight molecules. This standardised and consistent production process is vital for preserving the natural biological activity of the aloe gel [25]. Some of the biological activities of *A. vera* gel will only be briefly described in this review as it has been comprehensively discussed elsewhere [12, 15, 24].

3.1. Anti-diabetic effects

Several pre-clinical (in animals) and clinical (in humans) trials showed a blood glucose lowering effect for *A.vera* gel preparations in different forms (e.g. juice or as constituents in bread etc.), while other studies indicatedthat no change in glucose levels could be obtained. The differences in results of these *in vivo* studies can possibly be explained by differences in the way that the aloe mucilaginous gel was isolated and separated fromthe exudate anthraquinones. Furthermore, it is not always clear what constituent of the aloe leaf was tested insome studies, which makes it difficult to correlate the effect (or lack of effect) with the product tested [10, 24]. In a study on streptozotocin-induced diabetic rats, oral administration of *A. vera* gel (alcohol insoluble residueextract) significantly reduced the fasting blood glucose, hepatic transaminases, plasma and tissue cholesterol, triglicerides, free fatty acids and

phospholipids and in addition also significantly increased plasma insulin levels.

The decreased plasma levels of high density lipoprotein cholesterol and increased levels of low density lipoprotein cholesterol in the streptozotocin-induced rats were restored to normal after treatment with gel extract [26]. From the findings of another study on streptozotocin-induced diabetic rats, it was suggested that the mechanism of action of *A. vera* extracts to reduce blood glucose levels is by enhancing glucose metabolism. It was further proposed that the glucose lowering effect could be explained by an antioxidant mechanism because it attenuated oxidative damage in the brains of streptozotocin-inducedmice and reduced peroxidation levels in the kidneys of streptozotocin-induced diabetic rats [7].

3.2. Immunomodulatory effects

A number of studies indicated immunomodulating activities of the polysaccharides in *A. vera* gel, and suggested that these effects occur via activation of macrophage cells to generate nitric oxide, secrete cytokines (e.g. tumour necrosis factor-alpha or TNF-α, interleukin-1 or IL-1, interleukin-6 or IL-6 and interferon-γ or INF-γ) and present cell surface markers [27-29]. Some immune reactions that seem to be specific for acemannan as compared to other polysaccharides include stimulation of the antigenic response of human lymphocytes as well as the formation of all types of leucocytes from both spleen and bone marrow in irradiated mice. However, some other immunomodulation effects were shown to be linked to glycoproteins, namely lectins, found in aloe gel [24].

In a study on the immunomodulatory properties of *A. vera*, it was shown that relatively high concentrations of acemannan are required to achieve modest activation of macrophages compared to crude *A. vera* juice, whichsuggested that there is another component in the juice responsible for the macrophage activation. Further investigation revealed that although it is present only in small amounts, its potency in terms of macrophage stimulation accounted fully for the activity obtained for the crude *A. vera* juice [24]. It was found that aloe gel can prevent suppression of local and systemic immunity to haptens and delayed type hypersensitivity responses to *Candida albicans* and alloantigen when applied after UV exposure. The mechanism of this immune protection effect by the polysaccharides in the gel differs from those described for anti-oxidants, anti-inflammatories and DNA-repair enzymes. Although antiinflammatory agents have been identified in *A. vera*, the polysaccharides failed to reduce UV-induced edema and inflammation as well as to accelerate excision and repair of UV-induced cyclobutyl pyrimidine dimmers. In addition, anti-oxidants must be present in the skin before UV-irradiation to be effective while aloe polysaccharides are effective even when applied up to 24 h post UV exposure. The immune protection action therefore occurs at a step downstream from DNA damage and repair, possibly by modulating DNA-damage-activated signal transduction pathways. The mechanism of action of the polysaccharides was therefore explained by their effects on antigen presenting cells and the cytokine cascade [30].

3.3. Anti-inflammatory effects

Inflammation is a reaction by the body due to injury and is characterised by swelling, pain, redness, heat and loss of function. This natural response can delay healing, but it may also be detrimental to suppress inflammation before its purpose is accomplished. The anti-inflammatory activity of mannose-phosphate is believed to resemble the effects observed for acetylated mannan in aloe gel. Aloe gel reduces inflammation that is induced by agents via promotion of prostaglandin synthesis as well as increased infiltration of leucocytes, but is less effective against inflammation caused by agents that produce allergic reactions [24]. The effects of aqueous, chloroform and ethanol extracts of *A. vera* gel were investigated on oedema in the rat paw as well as neutrophil migration into the peritoneal cavity induced by carrageenan. Both the aqueous and chloroform extracts were found to inhibit the oedema formation close to that of well established anti-inflammatory agents (i.e. indomethacin and dexamethasone). Furthermore, the antioedema effects of these two extracts correlated well with their abilities to decrease the number of neutrophils migrating into the peritoneal cavity. The ethanol extract did not show an effect on the oedema, but reduced the number of migrating neutrophils. Further experimentation on the mechanism of action suggested that the anti-inflammatory activity of the extracts of *A. vera* gel probably occurs via an inhibitory action on the arachidonic acid pathway through cyclooxygenase [8]. A study on *Helicobacter pylori*-infected rats showed that treatment with *A. vera* significantly reduced leukocyte adhesion and tumour necrosis factor α (TNF-α) levels. The results therefore suggest that *A. vera* show potential in the treatment of the inflammatory response of the gastric mucosa due to *H. pylori* infection [31].

3.4. Anti-oxidant effects

It has been reported by several authors that different fractions of *A. vera* as well as unfractionated whole gel have anti-oxidant effects. Glutathione peroxidise activity, superoxide dismutase enzymes and a phenolic antioxidant were found to be present in *A. vera* gel, which may be responsible for these anti-oxidant effects. It was shown in two cell-free *in vitro* systems and by incubation with inflamed colorectal mucosal biopsies that *A. vera* gel has a dose-dependent anti-oxidant effect. The cell-free techniques used in this study assessed the scavenging of both superoxide and peroxyl. The *A. vera* gel in a concentration of 1 in 50 also inhibited prostaglandin E2

production from inflamed colorectal biopsies, but had no effect on thromboxane B2 release [32].

3.5. Anti-cancer effects

The two fractions from aloes that are claimed to have anti-cancer effects include glycoproteins (lectins) and polysaccharides [24]. The anti-tumour activity of polysaccharides isolated from *A. vera* and specifically acemannan has been investigated in many *in vitro* models as well as in different animal species. Different studies indicated anti-tumour activity for *A. vera* gel in terms of reduced tumour burden, tumour shrinkage, tumour necrosis and prolonged survival rates. In addition to these effects, *A. vera* gel has also shown chemopreventative and anti-genotoxic effects on benzo[α]pyrene- DNA adducts [7]. One mechanism of action that was proposed for these anti-cancer effects of aloe polysaccharides is stimulation of the immune response [15].

3.6. Skin hydration effects

In a study where the moisturising effects of cosmetic formulations containing different concentrations of lyophilised *A. vera* gel were studied, showed that only formulations with higher concentrations (0.25 % w/w and 0.5 % w/w) increased the water content of the stratum corneum after a single application. When the formulations were applied twice daily for a period of 2 weeks, all the formulations (containing concentrations of 0.1 % w/w, 0.25 % w/w and 0.5 % w/w of *A. vera* gel powder) had the same effect. However, the transepidermal water loss was not changed by inclusion of the *A. vera* gel in the formulations compared to the vehicle used in the formulations. It was proposed that the *A. vera* gel containing products improved skin hydration possibly by means of a humectant mechanism [33].

3.7. Hepatoprotective activities

An aqueous extract of dried aerial parts of *A. vera* significantly reduced hepatic damage induced by carbon tetrachloride in mice and reversed certain biochemical parameters. Histopathological studies confirmed the curative efficacy of the water extract of *A. vera* against carbon tetrachloride induced liver damage as indicated by reversal of centrilobular necrosis, macro-vascular fatty changes and scattered lymphomononuclear cell infiltrate in hepatic parenchyma. Furthermore, an increase in bile flow and bile solids as a result of treatment with the extract suggests stimulation of the secretary activity of the liver cells. The hepatoprotective action was also attributed to preserving the metabolizing enzymes of the liver through an antioxidant activity [34].

3.8. Antimicrobial activities

The activity of *A. vera* inner gel against both Gram-positive and Gram-negative bacteria has been demonstrated by several different methods [6]. Anthraquinones isolated from the exudate of *A. vera* have shown wide antimicrobial activity. The antibacterial activity of emodin against *Escherichia coli* was proposed to be mediated through inhibition of solute transport in membranes. Many anthraquinones have shown antiviral and/or virucidal effects on enveloped viruses [35].

3.9. Wound healing activity

The effect of *Aloe vera* on skin fibroblasts was measured by Danhof in 1983 [36]. He found that tritated thymidine uptake by skin fibroblasts were increased in a dose response fashion by *Aloe vera*. He also found that the anthroquinones in the yellow sap killed the fibroblasts has potential as an anti-inflammatory assay if *Aloe vera* was protect against this killing effect. However, we found that dry wounds drop, and prevent the migration of cells and the influence wound healing growth factors.With *Aloe vera* acting as a cover , the wound remains most and there is excellent migration of epidermal and fibroblasts cells. So there is an increase in covered wound healing over that of uncovered wounds. *Aloevera* increased the wound healing over a dosage range of 1 to100mg/kg in a dose response fashion. This was the first study that demonstrated that *Aloe vera* was effective in animals. *Aloe vera* is a modulator. It has an inhibitor system capable blocking the immune system observed in the adjuvant arthritic animal, and it can block the mediators responsible for inflammation. Similarly, if the aloe gel was given after the ulcers were formed, healing was three times as fast compared to the healing in the control animals [37].

In a second laboratory investigation, aloe gel pretreatment was 85% effective in preventing stomach lesions, & 50% better than the controls in healing the gastric ulcerations [38].

Additional studies should that a common group of plant constituents, the triterpenes, including lupeol, possess ulceroprotective in albino rats induced by immobilization restraint [39]. Other investigations have shown that aloe gel preparations contain lupeol as well as other triterpeniods [40]. Aloe gel mixed with heavy liquid petrolafum (2:1) was given to 12 patients, 7 males & 5 females ages 24 to 84 years , with definitive X- ray evidence of duodenal ulcers. All 12 patients should complete recovery with no recurrence for at least a year after ulcer healing. This study suffers, however from the fact that; duodenal ulcers are often self healing without any treatment; Aloe vera also has a stimulatory system in which it can increase production and stimulate wound healing by means of growth factors such as gibberllin, auxin and mannose phosphate. The isolation of the wound healing and

antiinflammatory activities using the 50% ethanol extraction of aloe vera revealed that supernatant contained 78% precipitate had only 32%.On the otherhand, the supernatant had 0% wound healing activity whereas the precipitate had only 160% value likely due to the fact that the antiinflammatory activity is masking some of the wound healing effect seen in the original Aloe vera.

3.10. Anti-ulcer Activity

For over 300 years the Curanderos and Curanderas in the northern states of Mexico have recommended internal aloe gel for the disease of stomach and intestines, but especially for ulcers. Scientific investigations have been undertaken in animal models (laboratory rats) which have shown that if aloe gel is administered prior to the ulcer–including stress (immobilization), there is an 80% decrease in the number of ulcers found compared with the control animals given saline instead other *aloe vera* gel. There was no control groups of patients treated in a similar manner without the administration of aloe. Nonetheless, the physicians who conducted the study represent trained, clinically–experienced observers, thus even those uncontrolled observations have some scientific merit [41].

3.11. Atherosclerosis and coronary heart disease

Coronary heart disease associated with the accumulation of blood fats/lipids in the lining of the arteries is still one of the major causes of death in the western wound. Several studies in animal models as well as in human have suggested that the ingestion of aloe gel may have beneficial effect by lowering serum cholesterol, serum triglycerides and serum phospholipids, which when elevated ,seem to accelerate the deposition of fatty material in the large and medium sized arteries, including the coronary arteries ,including the coronary arteries of the heart.

In one study albino laboratory rats were fed high cholesterol diets with the experimental group fed the polysaccharide (glucomannan from aloe). Compare with the control animals, the group fed the aloe fraction showed, decreased total cholesterol levels, decreased triglyceride levels, decreased phospholipid levels, decreased nonesterified fatty acid levels, increased HDL cholesterol (the"good" cholesterol level) and markedly increased HDL(total cholesterol ratios).

The evidence suggest that the ingestion of aloe gel may have a salubrious effect on fat (lipid) metabolism, which if active in human subjects would tend to decreased the risk of coronary artery disease in people [42]. Monkeys given trition, which causes marked increased in blood lipids, were divided into two groups. The first group was given aloe, while the second group received the drug, clofibrate, which is usually to low serum cholesterol and triglycerides levels. There was marked in the beneficial HDL/total cholesterol ratios [42]. A third investigation was performed studying 5,000 patients who were fed the husks of a local Indian plant, isabgol, which provided fiber, and Aloe gel as a beverage. There were some remarkable effects in three important areas:

1. Lipid metabolism

a. Decreased total cholesterol
b. Decreased triglycerides
c. Increased HDL cholesterol

2. Carbohydrate metabolism

a. Decreased fasting blood sugar levels in diabetic patients.
b. Decreased post-parandial (after a meal) elevation in blood sugar levels in diabetic patients

3. Angina pectoris

a**.** Chest pain from insufficient delivery of the oxygen in the heart.
b. Decreased frequency of anginal pectoris.
These data in the human study suggest that the benefit from the regimen, at least in part attributable to the ingested Aloe beverages, may have salubrious effects on several systems in the body.

4. CONCLUSION

A. vera has a long history as a medicinal plant with diverse therapeutic applications. Although it was claimed that some of the biological activities of this plant can be attributed to the polysaccharides found in the leaf gel, it is a daunting task to link individual polysaccharides to specific therapeutic properties. Differences in plant composition due to geographic location as well as differences in gel extraction methods and sample preparation techniques have contributed to discrepancies in the results obtained from many studies in terms of the chemical composition and biological activities of *A. vera* leaf gel. Although some indications were found that a particular polysaccharide is effective when tested for a specific biological activity, it seems as if it is rather a combination of compounds that account for the health benefits of *A. vera* leaf gel. With technological developments in the field of analytical chemistry it has become easier to isolate and characterise the chemical components of the leaf gel and it is expected that more information in this regard will become available in the future at a faster rate. Interesting pharmaceutical applications such as intestinal absorption enhancement activities and skin penetration improvement effects have recently been shown for *A. vera* gel. The dried gel has also showed potential as an excipient in modified release matrix type tablets.

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