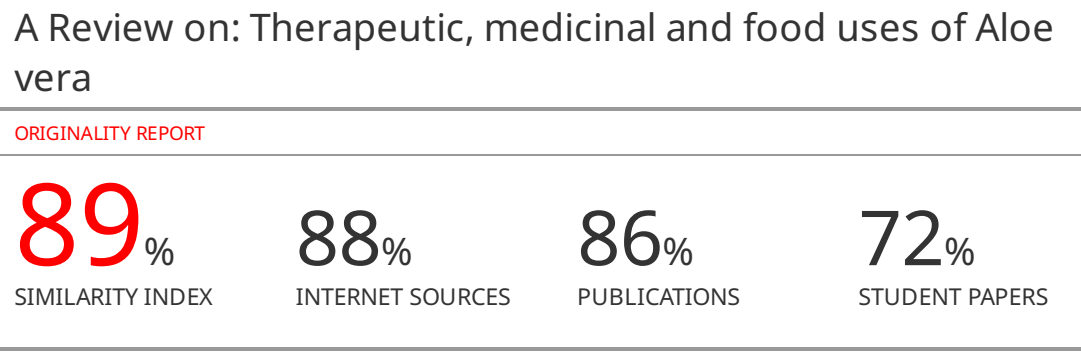
**Reviewer’s Comments**

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**A Review on: Therapeutic, medicinal and food uses of *Aloe vera***

**Abstract:**

The history for the use of *Aloe vera* for medicinal purposes starts from about 3000 years. Medicinally, this plant has potential to cure sunburns, burns and minor cuts, and even skin cancer.Scientific reports on the phytochemical analysis of this plant has so far revealed more than 104 compounds from different parts, including vitamins, minerals, enzymes, amino acids, terpenoids, anthraquinones, flavonoids, coumarins, sterols, sugars, polysaccharides, and polyphenols, have been isolated. Various biological activities have been exhibited by these compounds, such as antimicrobial, antidiabetic, antiviral, antitumor, anti-inflammatory, antioxidant, antiseptic, anthelmintic, diuretic, hepatoprotective, immunomodulatory, and cosmetic values for health care. In this article, we mainly emphasize therapeutic, medicinal and food uses of *A. vera*.

**Introduction:**

Aloe belongs to the family of Xanthorrhoeaceae, which consists of about 420 species, and has been used as a traditional medicine for about 3000 years. The genus Aloe is a succulent herb of 80 - 100 cm in height which matures in 4-6 years and survive for nearly 50 years under favorable conditions. *Aloe vera* (L.) Burm. f. syn. *Aloe barbadensis* Miller, is most biologically active among Aloe species [1-2]**.** According to World Health Organization, medicinal plants would be the best source for obtaining a variety of drugs [3]**.** The plant is native to southern and eastern Africa along the upper Nile in the Sudan, and it subsequently introduced into northern Africa and naturalized in the Mediterranean region and other countries across the globe. The plant is commercially cultivated in Aruba, Bonaire, Haiti, India, South Africa, the United States of America, and Venezuela [4] while the finest quality of Aloe is grown in desert of Southern California. The plant can survive in hot temperatures of 104˚F and with stand in below freezing temperatures until root is not damaged.

*Aloe vera* (L.) Burm.f. is a perennial succulent xerophyte, which develops water storage tissue in the leaves to survive in dry areas of low or erratic rainfall. Also, which is a well-known pharmaceutical herb that has long been used in traditional Chinese medicine for the treatment of various diseases.Plant extracts represent a continuous effort to find new compounds against pathogens. Approximately 20% of the plants are found in the world have been submitted to pharmacological or biological test, and a substantial number of new antibiotics introduced on the market are obtained from natural or semi synthetic resources [5]**.**The purpose of this review is to provide a comprehensive update on the therapeutic, medicinal and food uses of *A. vera*.

**Taxonomy**

The taxonomic classification of *A. vera*is as follows [6]:

Kingdom: Plantae

Subkingdom: Viridiplantae

Division: Tracheophyta

Class: Magnoliopsida

Order: Asparagales

Family: Xanthorrhoeaceae

Genus: *Aloe*

Species: *vera*

Binomial name: *Aloe vera*L.

**Synonym:**

*Aloe vera*is also known as (synonyms):*Aloe barbadensis* Miller, *A. chinensis* Bak., *A. elongata* Murray, *A. indica* Royle, *A.officinalis* Forsk., *A. perfoliata* L., *A. rubescens* DC, *A. vera* L. var. *littoralis* König ex Bak., *A. vera* L. var. *chinensis* Berger, *A. vulgaris* Lam. Most formularies and reference books regard *A. barbadensis* Mill. as the correct species name, and *A. vera* (L.) Burm. f. as a synonym. According to International Rules of Botanical Nomenclature (IRBN), *A. vera* (L.) Burm. f. is the legitimate name for this species[7]**.**

**Botanical Description:**

This succulent perennial herb has triangular, sessile stem, shallow root system, fleshy serrated leaves arranged in rosette having 30-50 cm length and 10 cm breadth at the base; colour pea-green. The bright yellow tubular flowers, length 25-35 cm, axillary spike and stamens are frequently projected beyond the perianth tube and fruits contain many seeds [4]**.**

**Active Ingredients:**

The active components of *A. vera*contains more than one hundred potentially active constituents from six different classes: chromone and its glycoside derivatives; anthraquinone and its glycoside derivatives; flavonoids; phenylpropanoids and coumarins; phenylpyrone and phenol derivatives; and phytosterols and others [8-9]**.**The transverse section of the leaf exhibiting three cells’ layers, the protective layer, middle layer and colorless inner layer leaf [10]**.**

***Outer Protective Layers of Leaf:***

The bitter yellow latex of pericyclic tubules in the outer layer of the leaves contain derivatives of hydroxyanthracene, anthraquinone and glycosides aloin A and B from 15-40% in different investigations[11]**.**Chemical investigation of the major constituents in *A. vera* leaves revealed moisture, ash, fiber, protein, lipids, minerals, organic acids, free sugars, and polysaccharides. Glucose, fructose, andsucrose were the main free sugars. Oxalic, L-malic, isocitric, lactic, acetic, lactone, citric, and fumaric acid were the main organic acids**.** Approximately 29 chromones, 32 anthraquinones, 13 flavonoids, 12 phenylpropanoid acids, 4 coumarins, 3 phenylpyrone, 1 triglucosylated naphthalene (aloveroside A), one 1-methyltetralin (feroxidin) and their derivatives were isolated and identified from *A. vera*[9].

***Middle Layer of Leaf:***

The juice that is originated from cells of the pericycle and adjacent leaf parenchyma, flowing spontaneously from the cut leaf get dried with or without the aid of heat and get solidified should not be confused with *Aloe vera* gel which is also the colourless mucilaginous gel that is obtained from the parenchymatous leaf cells**.**Regarding its chemical composition*, A. vera* gel consists mainly of water (>98%), polysaccharides (pectins, cellulose, hemicellulose, glucomannan, acemannan), proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and phytosterols (cycloartanol, 24-methylene-cycloartanol, lophenol, 24-methyl-lophenol, and 24-ethyl-lophenol) [12]. The main active components of Aloe juice are hydroxyanthracenic derivatives, which represent between 15 and 40% of the total components, and among them are anthraquinone glycosides aloin A and B along with Aloe emodin [13]. The elements Al, B, Ba, Ca, Fe, Mg, Na, P, Si *etc.* has also been reported to be present in *A. vera* gel [14-15]**.**

***Inner Layers of Leaf:***

The innermost part of the leaf is a clear, soft, moist and slippery tissue that consists of large thin-walled parenchyma cells in which water is held in the form of a viscous mucilage [16-17]**.**The innermost layer of leaf gel contains water up to 99%, with glucomannans, amino acids, lipids, sterols [18]**,** vitamins (B1, B2, B6, and C) [19]**,** numerous monosaccharides and polysaccharides, several inorganic ingredients, enzymes (acid and alkaline phosphatase, amylase, lactate dehydrogenase, lipase) and organic compounds (aloin, barbaloin, and emodin) [20]**.** The main functional component of *A. vera* is a long chain of acetylated mannose [21-22]**.**

Many of the medicinal effects of aloe leaf extracts have been attributed to the polysaccharides found in the inner leaf parenchymatous tissue [23-24], is believed that these biological activities should be assigned to a synergistic action of the compounds contained therein rather than a single chemical substance[25]**.**

***Root of Aloe vera:***

In the case of *A. vera*root, some phenolic compounds, especially naphthoquinones and anthraquinones, have also been identified [26-28]**.**



**Figure 1:** Potentially active anthraquinone constituents from *Aloe vera*

**Ethnopharmacology uses:**

Traditionally, *A. vera* gel is used both, topically (treatment of wounds, minor burns, and skin irritations) and internally to treat constipation, coughs, ulcers, diabetes, headaches, arthritis, immune-system deficiencies [29]. *Aloe vera* has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan, and China [30]. The Egyptians used the *A. vera* to make papyrus like scrolls as well as for treatment of tuberculosis [31]. Nadkerni,[32] stated various preparations of *A. barbadensis* like confection, lotion and juice, useful remedies for curing various diseases. Aloe contains mixture of glucosides collectively called aloin which is the active constituent of various drugs. The Elio, a product made by juice of this plant, is used for helminthiasis in children and is a purgative, anthelmintic and emmenagogue. Gel is useful in ulcerative colitis and pressure ulcers, respectively [33]. *Aloe vera* is anthelmintic, aperients, carminative, deobstruent, depurative, diuretic, stomachic and emmenagogue. Edible coating gels developed from the *A. vera* plant have been used as a traditional medicine for about 3000 years [9].

**Medicinal and Therapeutic Uses:**

The known biological activities of *A. vera* will be briefly discussed, it is the aim of this review to further highlight recently discovered effects and applications of the 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, antiviral, antifungal, antidiabetic and antineoplastic activities, stimulation of hematopoiesis and antioxidant effects**.** 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 [34-35]**.**

***Anti-Aging Agent:***

Muco-polysaccharides help in binding moisture into the skin. The amino acids also soften hardened skin cells and zinc acts as an astringent to tighten pores. Its moisturizing effects have also been studied in treatment of dry skin associated with occupational exposure where *A. vera* gel gloves improved the skin integrity, decrease appearance of acne wrinkle and decrease erythema**.** The Aloe gel gives cooling effect and acts as a moisturizing agent. It also has role in gerontology and rejuvenation of aging skin. This property of Aloe is because it’s biogenic material. *A. vera* is used as skin tonic in cosmetic industry [1].

***Antibacterial Activity:***

Previous studies have shown that the use of *A. vera* gel as an edible coating has positive effects on the prevention of fruit decay and microbial spoilage. The inhibitory effects of *A. vera* gel on the growth of mycelium (*Penicillium digitatum* and *Aspergillus niger*) was reported by Nabigol and Asghari[36], who performed a range of laboratory tests. They suggested that the inhibition of the mycelium growth rate increased with gel concentration. The 500 mL/L dose of *A. vera* gel was found to cause 100% inhibition of *P. digitatum* and 64% of *A. niger*. In a different study [37], *A. vera* leaf gel was found to inhibit the growth of *Shigella flexneri* and *Streptococcus progenies, P. aeruginosa, E. coli, S. aureus* and *S. typhi*. The antibacterial activities of *A. vera* gel against *Heliobacter pylori*was also reported[38]. Agarry et al., [39] reported that the Aloe gel inhibited the growth of *Trichophyton mentagrophytes* (20.0 mm). In contrast, *A. vera* extracts failed to show antibiotic properties against Xanthomonas species [40].

Benitez et al.,[41] reported that *A. vera* gel provides higher efficacy for the prevention of mesophilic bacteria and yeasts and molds than alginate and chitosan for kiwifruit slices. In another study, the shelf life of guava was reported to be increased by about one more week with the application of an *A. vera* gel coating, due to the fact that the edible coating prevents microbial growth [42]. The specific mechanism of action is still unknown, but it is known that saponins, acemannan and anthraquinone derivatives, which are found in *A. vera*, have antibacterial activity [43].*Streptoccocus pyogenes* and *S. faecalis* are two microorganisms that have been inhibited by *A. vera* gel [44].

***Antidiabetic Effects:***

The beneficial effects of medicinal plants such as *A. vera* were reviewedand emphasize on the role of active biomolecules which possess antidiabetic activity. The phytosterols and polysaccharides of *A. vera* showed antidiabetic effects in type-2 diabetic in mice through increase the insulin level [45-47]**.***A. vera* sap taken for 4 - 14 weeks has shown a significant hypoglycaemic effect both clinically and experimentally [48]**.**

Several preclinical (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 indicated that 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 from the exudate anthraquinones. Furthermore, it is not always clear what constituent of the aloe leaf was tested in some studies, which makes it difficult to correlate the effect (or lack of effect) with the product tested**.** In a study on streptozotocin-induced diabetic rats, oral administration of *A. vera* gel (alcohol insoluble residue extract) significantly reduced the fasting blood glucose, hepatic transaminases, plasma and tissue cholesterol, triglycerides, 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 **[49].**

***Antifungal Activity:***

Antifungal activity of *A. vera* were conducted on the mycellium development of *Rhizoctonia solani, Fusarium oxysporum,* and *Colletotrichum coccodes.* The pulp showed an inhibitory effect on *F. oxysporum* at 104 μl L-1 and the liquid fraction reduced the rate of colony growth at a concentration of 105 μl L-1 in *R. solani, F. oxysporum,* and *C. coccodes* [50]**.Sitara et al., [51]**conducted a comprehensive study regarding the antifungal activity of *A. vera* gel at three different doses against five plant pathogenic fungi: *Aspergillus niger*, *Aspergillus flavus*, *Alternaria alternata*, *Drechslera hawaiensis*, and *Penicilliumdigitatum*. The highest test dose (0.35%) of *A. vera* gel was reported to completely inhibit the growth of *D. hawaiensis* and *A. alternata*. In another study, the minimum fungicidal concentrations of *A. vera* against *Botrytis gladiolorum*, *Fusarium oxysporum*, *Heterosporium pruneti*, and *Penicillium gladioli* were reported to vary between 80 and 100 µL/mL, depending on the fungal species **[52].**

Previous studies have also shown that the combination of *A. vera* gel with some homogenizers, such as glycerol starch (0.15 g), improves the efficacy in controlling fungal decay and weight loss in cherry tomatoes [53]. Navarro et al., [54] performed a study with *A. vera* gel alone or in combination with thymol on nectarines and reported that the *A. vera* gel alone is more efficient in prevention of the decay caused by *Rhizopus stolonifer*, *Botrytis cinerea*, and *Penicillium digitatum*. *Aloe vera* gel coatings were previously tested against decay and found to significantly lower counts for molds, yeast, and mesophilic aerobics in different fruits and vegetables, including tomatoes [55-56], citrus fruits [57], raspberry fruits [58], blueberries [59], strawberries [60], and ready-to-eat pomegranate arils [61]. A processed *Aloe vera* gel preparation inhibited the growth of fungus *Candida albicans* [62].

***Anti-inflammatory Action:***

The anti-inflammatory activity of *A. vera* gel has been revealed by *in vitro* and *in vivo* studies through bradykinase activity [63]**.**The peptidase bradykinase isolated from aloe shown to break down the bradykinin, an inflammatory substance that induces pain [64-65]. The *A. vera* active ingredients such as mannose - 6-phosphate and sterol (campesterol, β-sitosterol, lupeol, and cholesterol)[65]which are anti-inflammatory in nature, helps in reducing the inflammation pain and act as a natural analgesic. Other aspirin-like compound present in Aloe is responsible for anti-inflammatory and antimicrobial properties**.***A. vera* inhibits the cyclo-oxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Fresh *A. vera* gel significantly reduced acute inflammation in rats (carrageenin-induced paw oedema), but not in chronic inflammation [66]**.**

The aqueous and chloroform extracts of *A. vera*were found to inhibit the oedema formation close to that of well-established anti-inflammatory agents (i.e. indomethacin and dexamethasone). Furthermore, the anti-oedema effects of these two extracts correlated well with their abilities to decrease the number of neutrophils migrating into the peritoneal cavity[67]**.** *A. vera* leaf extract (5.0% leaf homogenate) decreased inflammation by 48% in a rat adjuvant-induced arthritic inflammatory model [68]**.** *A. vera* show potential in the treatment of the inflammatory response of the gastric mucosa due to H. pylori infection [69]**.**

***Antioxidant effects:***

It has been reported by several authors that different fractions of *A. vera* as well as unfractionated whole gel have antioxidant 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 antioxidant 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 antioxidant effect. The cell-free techniques used in this study assessed the scavenging of both superoxide and peroxyl radicals. 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 [70].

***Antiseptic Properties:***

The antiseptic property of *A. vera* is due to presence of six antiseptic agents namely lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulphur. These compounds have inhibitory action on fungi, bacteria and viruses. Though most of these uses are interesting controlled trials are essential to determine its effectiveness in all diseases [71]**.**

***Anti-stress Effect:***

Aloe juice is helpful in smooth functioning of the body machinery [72]**.** It reduces cell-damaging process during stress condition and minimizes biochemical and physiological changes in the body [73]**.** Oxidative stress refers to chemical reactions in which compounds have their oxidative state changed. Some antioxidants are part of the body’s natural regulating machinery while other dietary antioxidants are derived from diet sources. *A. vera* is an excellent example of a functional food that plays a significant role in protection from oxidative stress [74]**.**

***Antitumor Activity:***

The *A. vera* gel play chief role in stimulation of the complement linked to polysaccharides, hydration, insulation, and protection. Application of fresh gel to normal human cells *in vitro* promoted cell growth and attachment, whereas a stabilized gel preparation was cytotoxic to both normal and tumor cells. This cytotoxicity was attributed to additional substances added to gel during processing [75].

Glycoproteins present in *A. vera* gel have been reported to have antitumor and antiulcer effects and to increase proliferation of normal human dermal cells**.** The polysaccharide fraction has shown to inhibit the binding of benzopyrene to primary rat hepatocytes, thereby preventing the formation of potentially cancer-initiating benzopyrene-DNA adducts. An induction of glutathione S-transferase and an inhibition of the tumor-promoting effects of phorbol myristic acetate has also been reported which suggest a possible benefit of using aloe gel in cancer chemoprevention [76]**.** *A. vera* emodin, an anthraquinone, can suppress or inhibit the growth of malignant cancer cells making it to have antineoplastic properties**.** However, statistically significant clinical studies on the efficacy of *A. vera* gel on human health are very limited and often inconclusive[77]**.**

***Antiviral Activity:***

Antiviral activities of *A. vera* have also been of interest to many researchers, wherein its positive influence has been reported against herpes simplex virus (HSV) type 2 strains by Keivan et al.,**[78]** and against influenza A virus replication by Li et al.,[79].Several ingredients in *A. vera*jell have been shown to be effective antiviral agent. Acemannan reduced herpes simplex infection in two cultured target cell lines [80]. Lectins, fractions of *A. vera* gel, directly inhibited the cytomegalovirus proliferation in cell culture, perhaps by interfering with protein synthesis [81]**.** A purified sample of aloe emodin was effective against infectivity of herpes simplex virus Type I and Type II and it could inactivateall viruses including varicellazoster virus, influenza virus, and pseudorabies virus**.** Electron micrograph examination of anthroquinone treated herpes simplex virus demonstrated that the envelopes were partially disrupted. Such results indicate that anthraquinones extract from variety of plants are directly virucidal to enveloped viruses. These actions may be due to indirect effect due to stimulation of the immune system. The anthraquinone aloin also inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza [82-83]**.**

***Cosmetic & Skin Protection Application:***

*Aloe vera* is widely used as cosmetics, asnutraceuticals [84], and a protective agent against radiation damage to the skin [85]**.** The administration of *A. vera* gel, an antioxidant protein, metallothionein, is generated in the skin, which scavenges hydroxyl radicals and prevents suppression of superoxide dismutase and glutathione peroxidase in the skin. It reduces the production and release of skin keratinocyte derived immunosuppressive cytokines such as interleukin-10 (IL-10) and hence prevents UV-induced suppression of delayed type hypersensitivity [86]. Some researcher has been reported the contact dermatitis and burning skin sensations following topical applications of *A. vera* gel to dermabraded skin. These reactions appeared to be associated with anthraquinone contaminants in this preparation [87]**.** Aloin and its gel are used as skin tonic against pimples. The Aloe sugars are also used in moisturizing preparations**.** Mixed with selected essential oils, it makes an excellent skin smoothening moisturizer, sun block lotion plus a whole range of beauty products. *Aloe vera* extracts have antibacterial and antifungal activities, which may help in the treatment of minor skin infections, such as boils and benign skin cysts and have been shown to inhibit the growth of fungi that cause tinea [88]**.**

***Effect on Gastric Acid Secretion and Ulcers:***

It has been claimed that *A. vera* gel can cure gastric ulcers or protect against its formation in both animals and humans. However, it was also shown that aloe gel could not prevent ethanol-induced gastric lesions in rats. The anti-ulcer activities of *A. vera* has been attributed to several possible mechanisms including its anti-inflammatory properties, healing effects, mucus stimulatory effects and regulation of gastric secretions [89]**.**

The aqueous ethanol extract of *A. vera* exhibited concentration dependent inhibition of gastric acid secretions, which was explained by direct interaction with the acid producing cells or possible interaction with H2-receptors on the parietal cells. Gastroprotective activity was only observed at the lowest dose tested. It was suggested that the *A. vera* extract possesses cytoprotection activity at this low concentration, therefore protection against mucosal injury by means of a mechanism different from gastric acid inhibition and neutralization. Several hypotheses have been given for the mechanism of cytoprotection, namely increased mucus synthesis, increased mucosal blood flow and increased phospholipid content of the mucosal coating [90].

***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 metabolising enzymes of the liver through an antioxidant activity [91]**.**

***Immunomodulatory Effects:***

A number of studies indicated immunomodulating activities of the polysaccharides such as acemannan 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 [92-94]. Several low-molecular-weight compounds are also capable of inhibiting the release of reactive oxygen free radicals from activated human neutrophils [95]. Some immunomodulation effects were shown to be linked to glycoproteins, namely lectins, found in aloe gel. Alprogen inhibit calcium influx into mast cells, thereby inhibiting the antigen-antibody-mediated release of histamine and leukotriene from mast cells [96].

It was found that aloe gel can prevent suppression of local and systemic immunity to happens 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 antioxidants, anti-inflammatories, and DNA-repair enzymes. Although anti-inflammatory 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 cyclo-butyl pyrimidine dimmers. In addition, antioxidants 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 [97]**.**

***Laxative Effects:***

Anthraquinones present in latex are a potent laxative; it’s stimulating mucus secretion, increase intestinal water content and intestinal peristalsis [98]**.** The Aloe are due primarily to the 1, 8-dihydroxyanthracene glycosides, aloin A and B (formerly designated barbaloin) [63]**.** After oral administration aloin A and B, which are not absorbed in the upper intestine, are hydrolysed in the colon by intestinal bacteria and then reduced to the active metabolites (the main active metabolite is aloe-emodin 9-anthrone) [66]**,** which like senna acts as a stimulant and irritant to the gastrointestinal tract**.** Aloe latex is known for its laxative properties. The laxative effect of Aloe is not generally observed before 6 hours after oral administration, and sometimes not until 24 or more hours after.

***Moisturizing and Skin Hydration Effects:***

Moisturizing effects of *A. vera* gel 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 [99]**.**

***Wound Healing Effects:***

Wound healing is a dynamic process, occurring in 3 phases. The first phase is inflammation, hyperaemia and leukocyte infiltration. The second phase consists of removal of dead tissue. The third phase of proliferation consisting of epithelial regeneration and formation of fibrous tissue [100]. A more recent review concludes that the cumulative evidence supports the use of *A. vera* for the healing of first to second degree burns [101]**.**

Acemannan [21-22], mannose-6-phosphate**,** glucomannan, glycoprotein [102]and plant growth harmone gibberellins are considered the main functional component of *A. vera,* accelerates wound healing, interacts with growth factor receptors of fibrobroblast, reduces radiation induced skin reactions [103]**,** stimulate the release of fibrogenic cytokines [98], andpromote prolong stimulation of granulation tissue**.**The Aloe administration influence collagen composition (more type III) and increased collagen cross linking for wound contraction and improving breaking strength [18]**.** It also increases synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound [104]**.**

The Aloe gel has been used for the treatment of radiation burns and radiation ulcers**,** and complete healing has been observed in two radiation burns patients**.** The fresh gel was more effective than the cream as Aloe gel-treated lesions healed faster (11.8 days) compared to burns treated with petroleum jelly gauze (18.2 days) [105-106].Aloe gel is often commercialized as powdered concentrate. The therapeutically, Aloe gel is used to prevent progressive dermal ischemia due to burns, frostbite, electrical injury and intra-arterial drug abuse. *In vivo* analysis of these injuries demonstrates that this gel acts as an inhibitor of thromboxane A2, a mediator of progressive tissue damage [107]**.**

**Adverse Reactions:**

Abdominal spasms and pain may occur after even a single dose and overdose can lead to colicky abdominal spasms and pain, as well as the formation of thin, watery stools. Chronic abuse of anthraquinone stimulant laxatives can lead to hepatitis [108]and electrolyte disturbances (hypokalaemia, hypocalcaemia), metabolic acidosis, malabsorption, weight loss, albuminuria, and haematuria [109] Weakness and orthostatic hypotension may be exacerbated in elderly patients when stimulant laxatives are repeatedly used**.** Secondary aldosteronism may occur owing to renal tubular damage after aggravated use. Steatorrhoea and protein-losing gastroenteropathy with hypoalbuminaemia have also been observed, as have excessive excretion of calcium in the stools and osteomalacia of the vertebral column. Melanotic pigmentation of the colonic mucosa (*Pseudomelanosis coli*) has been observed in individuals taking anthraquinone laxatives for extended time periods. The pigmentation is clinically harmless and usually reversible within 4 to 12 months after the drug is discontinued [110]**.**

**Uses in the Food Industries:**

In the food industry, it has been used as a source of functional foods and as an ingredient in other food products, to produce gel-containing health drinks and beverages [35]**.** Aloe gels have an important role in food preservation as edible coatings. Edible coatings generally provide a thin layer on the fruit surface, which acts as a barrier to atmospheric gases and moisture [111-112]**.** Aloe gels help to reduce the respiration and transpiration of fresh produce and delay postharvest deterioration of foods, promoting food preservation [113]**.** To date, numerous studies have been conducted on the postharvest use of *A. vera* gel [9]**.**

**Uses in the Pharmaceutical Industries:**

In the pharmaceutical industry, *A. vera* has been used for the manufacture of topical products such as ointments and gel preparations, as well as in the production of tablets and capsules [114]**.** Important pharmaceutical properties that have recently been discovered for both the *A. vera* gel and whole leaf extract include the ability to improve the bioavailability of co-administered vitamins in human subjects [115]**.** Due to its absorption enhancing effects, *A. vera* gel may be employed to effectively deliver poorly absorbable drugs through the oral route of drug administration. Furthermore, the dried powder obtained from *A. vera* gel was successfully used to manufacture directly compressible matrix type tablets. These matrix type tablets slowly released a model compound over an extended period of time and thereby showing potential to be used as an excipient in modified release dosage forms [116]**.**

**Other Uses:**

Other uses for *A. vera* extracts include the dilution of semen for the artificial fertilization of sheep, used as fresh food preservative [43] and used in water conservation in small farms**.** The soapy saponins substances from the *A. vera* gel are capable of cleansing and having antiseptic properties. The saponins perform strongly as anti-microbial against bacteria, viruses, fungi, and yeasts [117].

**Usage Risks:**

Aloe should not be administered to patients with inflammatory intestinal diseases, such as appendicitis, Crohn disease, ulcerative colitis, irritable bowel syndrome, or diverticulitis or to children less than 10 years of age. Aloe should not be used during pregnancy or lactation except under medical supervision after evaluating benefits and risks. Aloe is also contraindicated in patients with cramps, colic, hemorrhoids’, nephritis, or any undiagnosed abdominal symptoms such as pain, nausea, or vomiting [118]].

**Conclusion:**

*Aloe vera* has importance in everyday life to soothes a variety of skin ailments such as mild cuts, antidote for insect stings, bruises, poison ivy and eczema along with skin moisturizing and anti-ageing, digestive tract health, blood and lymphatic circulation and functioning of kidney, liver and gall bladder makes it a boon to humankind. *Aloe vera* as the “wonder plant” are multiple from being an antiseptic, anti-inflammatory agent, helps in relieving like cancer and diabetes, and being a cosmetic field. The plant is in need to a greater research emphasis for better utilization of this plant for humankind. *Aloe vera* is undoubtedly, the nature’s gift to humanity for cosmetic, burn and medicinal application and it remains for us to introduce it to ourselves and thank the nature for its never-ending gift.

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**Author’s Contribution**

**References:**

1. West DP, Zhu YF. Evaluation of Aloe vera Gel Gloves in the Treatment of Dry Skin Associated with Occupational Exposure. Am J Infect Control. **2003;31(1):40-42.**
2. Yagi A, Kabash A, Mizuno K, Moustafa SM, Khalifa TI, Tsuji H. Radical Scavenging Glycoprotein Inhibiting Cyclooxygenase-2 and Thromboxane A2 Synthase from Aloe vera Gel. Planta Med. **2003;69(3):269-271.**
3. **Lanka S. A Review on Aloe vera-the Wonder Medicinal Plant. J Drug Deliv Ther. 2018;8(5-s):94-99.4.** Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic Review of Herbs and Dietary Supplements for Glycemic Control in Diabetes. Diabetes Care. **2003;26(4):1277-1294.**
4. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic Review of Herbs and Dietary Supplements for Glycemic Control in Diabetes. Diabetes Care. 2003;26(4):1277-1294.
5. **Mothana RA, Linclequist U. Antimicrobial Activity of Some Medicinal Plants of the Island Soqotra. J Ethnopharmacol. 2005;96(1-2):177-181.**
6. **Hossain M, MamunOrRashid A, Towfique N, Sen M. A Review on Ethnopharmacological Potential of Aloe vera L. J Intercult Ethnopharmacol. 2013;2(2):113.**
7. **African Pharmacopoeia. Vol. 1, 1st ed. Organization of African Unity, Scientific, Technical & Research Commission, Lagos, 1985.8.** Choi SW, Son BW, Son YS, Park YI, Lee SK, Chung MH. The Wound-Healing Effect of a Glycoprotein Fraction Isolated from Aloe vera. Br J Dermatol. 2001;145(4):535-545.
8. Choi SW, Son BW, Son YS, Park YI, Lee SK, Chung MH. The Wound-Healing Effect of a Glycoprotein Fraction Isolated from *Aloe vera*. British Journal of Dermatology. 2001; 145(4): 535-545
9. **Kahramanoğlu İ, Chen C, Chen J, Wan C. Chemical Constituents, Antimicrobial Activity, and Food Preservative Characteristics of Aloe vera Gel. Agronomy. 2019;9(12):831.10.** Brown JP. A Review of the Genetic Effects of Naturally Occurring Flavonoids, Anthraquinones and Related Compounds. Mutat Res. 1980;75(3):243-277.
10. Brown JP. A Review of the Genetic Effects of Naturally Occurring Flavonoids, Anthraquinones and Related Compounds. Mutation Research. 1980; 75(3): 243-277.
11. **Saccu D, Bogoni P, Procida G. Aloe Exudate: Characterization by Reversed Phase HPLC and Headspace GC-MS. J Agric Food Chem. 2001;49(10):4526-4530.**
12. **Tanaka M, Misawa E, Ito Y, Habara N, Nomaguchi K, Yamada M, Toida T, Hayasawa H, Takase M, Inagaki M,** et al. Identification of five phytosterols from Aloe vera gel as anti-diabetic compounds. Biol Pharm Bull. 2006;29(7):1418-1422.
13. **Bozzi A, Perrin C, Austin S, Arce Vera F. Quality and authenticity of commercial aloe vera gel powders. Food Chem. 2007;103(1):22-30.14. Yamaguchi T, Takamura H, Matoba T, Terao J. HPLC Method for Evaluation of the Free RadicalScavenging Activity of Foods by Using 1,1-Diphenyl-2- Picrylhydrazyl. Bioscience, Biotechnology and Biochemistry. 1998;62(6):1201-1204.**
14. Yamaguchi T, Takamura H, Matoba T, and Terao J. HPLC Method for Evaluation of the Free Radical Scavenging Activity of Foods by Using 1,1-Diphenyl-2- Picrylhydrazyl. Bioscience, Biotechnology and Biochemistry. 1998; 62(6): 1201-1204.
15. Femenia A, Sanchez ES, Simal S, Rossello C. Compositional Features of Polysaccharides from Aloe vera (Aloe barbadensis Miller) Plant Tissues. Carbohydrate **Polymers. 1999;39(2):109-117.**
16. **Newton LE. Aloes in habitat. In: Reynolds T, ed. Aloes: the genus Aloe. CRC Press: Boca Raton; 2004. pp. 3-36.**
17. López A, de Tangil M, Vega-Orellana O, Ramírez A, Rico M. Phenolic Constituents, Antioxidant and Preliminary Antimycoplasmic Activities of Leaf Skin and Flowers of Aloe vera (L.) Burm. f. (syn. A. barbadensis Mill.) from the Canary Islands (Spain).
18. Reynolds T, Dweck AC. *Aloe vera* Leaf Gel: A Review Update,” Journal of Ethnopharmacology.1999; 68(1-3): 3-37.
19. Vogler BK, Ernst E. *Aloe vera*: A Systematic Review of Its Clinical Effectiveness, The British Journal of General Practice.1999; 49(447): 823-828.
20. Hayes SM. Lichen Planus: Report of Successful Treatment with *Aloe vera*,” General Dentistry.1999; 47(3): 268-272.
21. Djeraba A, Quere P. In Vivo Macrophage Activation in Chickens with Acemannan, a Complex Carbohydrate Extracted from *Aloe vera*. International Journal of Immunopharmacology.2000; 22(5): 365-372.
22. Lee JK, Lee, MK, Yun, YP, Kim Y, KimJS, Kim YS, KimK, Han SS, Lee CK. Acemannan purified from Aloe vera induces phenotypic and functional maturation of immature dendritic cells. International Immunopharmacology.2001; 1(7): 1275–1284.
23. Habeeb F, Shakir E, Bradbury F, Cameron P, Taravati MR, DrummondAJ, Gray AI, Ferro VA. Screening methods used to determine the anti-microbial properties of Aloe vera inner gel. Methods.2007; 42(4): 315–320.
24. Ni Y, Turner D, Yates KM, Tizard I. Isolation and characterization of structural components of Aloe vera L. leaf pulp. International Immunopharmacology. 2004; 4(14): 1745–1755.
25. Dagne E, Bisrat D, Viljoen A, Van WykBE. Chemistry of Aloe Species. Current Organic Chemistry.2000; 4(10): 1055–1078.
26. Lobo R, Prabhu KS, Shirwaikar A, Ballal M, Balachandran C, Shirwaikar A. A HPTLC densitometric method for the determination of aloeverose in Aloe vera gel. Fitoterapia, 2010; 81(4): 231–233.
27. Induli M, Cheloti M, Wasuna A, Wekesa I, Wanjohi JM, Byamukama R, Heydenrich M, Makayoto M, Yenesew A. Naphthoquinones from the roots of Aloe secundiflora. Phytochemistry Letters.2012; 5(3): 506–509.
28. Quispe C, Villalobos M, Bórquez J, Simirgiotis M. Chemical Composition and Antioxidant Activity of Aloe vera from the Pica Oasis (Tarapacá, Chile) by UHPLC-Q/Orbitrap/MS/MS. Journal of Chemistry. 2018; 1–12. <https://doi.org/10.1155/2018/6123850>
29. Eshun K, He Q.*Aloe vera*: A Valuable Ingredient for the Food, Pharmaceutical and Cosmetic Industries-A Review. Critical Reviews in Food Science and Nutrition.2004; 44(2): 91-96. <http://dx.doi.org/10.1080/10408690490424694>
30. Marshall JM. *Aloe vera* Gel: What Is the Evidence?” The Pharmaceutical Journal.1990; 24: 360-362.
31. Baker OT. The Amazing Ancient to Modern Useful Plant *Aloe vera*: Amazing Plant of the Magic Valley, R. Prevost, Lemon Grove, 1975.
32. Nadkerni KM. Indian Meteria Medica, 3rd Edition, Bombay Popular Prakashan Private Limited, Mumbai, 1976.
33. Langmead L, Feakins RM, and Goldthorpe S. Randomized, Doubleblind, Placebo-Controlled Trial of Oral *Aloe vera* Gel for Active Ulcerative Colitis. Alimentary Pharmacology & Therapeutics, 2004; 19(7): 739-747. <http://dx.doi.org/10.1111/j.1365-2036.2004.01902.x>
34. Boudreau MD, Beland FA. An Evaluation of the Biological and Toxicological Properties ofAloe Barbadensis(Miller), *Aloe Vera*. Journal of Environmental Science and Health, Part C,2006; 24(1): 103–154. <https://doi.org/10.1080/10590500600614303>
35. Hamman J. Composition and Applications of Aloe vera Leaf Gel. Molecules.2008;13(8): 1599–1616. <https://doi.org/10.3390/molecules13081599>
36. Nabigol A, Asghari A. Antifungal activity of Aloe vera gel on quality of minimally processed pomegranate arils. International journal of Agronomy and plant production. 2013; 4(4): 833-838.
37. Ferro VA, Bradlbury F, Cameron P, Shakir E, Rahman SR, Stimson WH. In vitro suscepitibilities of Shigella flexneri and Streptococcus pyogenes to inner gel of Aloe barbadensis Miller. Antimicrobial Agents and Chemotherapy. 2003; 47: 1137–1139. <http://dx.doi.org/10.1128/AAC.47.3.1137-1139.2003>
38. Cellini L, Di Bartolomeo S, Di Campli E, GenoveseS, Locatelli M, Di Giulio M. *In vitro* activity of *Aloe vera* inner gel against Helicobacter pylori strains. Letters in Applied Microbiology. 2014; 59(1): 43–48. <https://doi.org/10.1111/lam.12241>
39. AgarryOO, Olaleye MT, Bello-MichaelCO. Comparative Antimicrobial Activities of *Aloe vera* Gel and Leaf. African Journal of Biotechnology.2005; 4(12): 1413-1414.
40. SatishS, Raveesha KA,JanardhanaGR. Antibacterial Activity of Plant Extracts on Phytopathogenic Xanthomonas Campestris Pathovars. Letters in Applied Microbiology.1999; (28)2: 145-147. <http://dx.doi.org/10.1046/j.1365-2672.1999.00479.x>
41. Benítez S, Achaerandio I, Pujolà M, Sepulcre F. Aloe vera as an alternative to traditional edible coatings used in fresh-cut fruits: A case of study with kiwifruit slices. LWT - Food Science and Technology.2015;61(1): 184–193. <https://doi.org/10.1016/j.lwt.2014.11.036>
42. Krishnan SA, Ullas A, Sagarika N, Oommen TE, Sunaila K. Development of Aloe vera Based Edible Coating. Int. J. Pure App. Biosci. 2017; 5: 796–801.
43. Serrano M, Miguel J, GuillenF, Castillo S, Martinez-Romero D, Valero D. Use of *Aloe vera* gel coating preserves the functional properties of table grapes. J. Agri. Food Chem. 2006; 54(11): 3882–3886. <http://dx.doi.org/10.1021/jf060168p>
44. RobsonMC, Heggers JP,HagstromWJ. Myth, Magic, Witchcraft or Fact? Aloe vera Revisited, Journal of Burn Care & Research.1982; 3(3): 157- 163. <http://dx.doi.org/10.1097/00004630-198205000-00005>
45. YagiA, SatoY, MiwaY, A. Kabbash S, Moustafa K. Shimomura A, El-Bassuony. Ribosomal DNA Sequence Analysis of Different Geographically Distributed *Aloe vera* Plants: Comparison with Clonally Regenerated Plants, Saudi Pharmaceutical Journal. 2006; 14( 3-4): 208-211.
46. NoorA, GunasekaranS, Manickam AS,VijayalakshmiMA. Antidiabetic Activity of *Aloe vera* and Histology of Organs in Streptozotocin-Induced Diabetic Rats. Current Science. 2008;94(8):1070- 1076.
47. ArokiyarajS, RadhaRS, Martin S, PerinbamK. Phytochemical Analysis and anti-diabetic Activity of Cadaba Fruticosa. R. Br.. Indian Journal of Science and Technology. 2008; 1(6): 1-4.
48. GhannamN, KingstonM, Al-MeshaalIA, TariqM., Parman NS,WoodhouseN. The Antidiabetic Activity of Aloes: Preliminary Clinical and Experimental Observations. Hormone Research. 1986;24(4): 286-294. <http://dx.doi.org/10.1159/000180569>
49. Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S. Beneficial effects of *Aloe vera* leaf gel extract on lipid profile status in rats with streptozotocin diabetes. Clin. Exp. Pharmacol. Physiol. 2006; 33: 232-237.
50. de RodríguezDJ, Hernández-CastilloD, RodríguezGarcía R,Angulo-SanchezJL. Antifungal Activity in Vitro of *Aloe vera* Pulp and Liquid Fraction against Plant Pathogenic Fungi, Industrial Crops and Products. 2005;21(1): 81-87.<http://dx.doi.org/10.1016/j.indcrop.2004.01.002>
51. Sitara U, Hassan N, Naseem J. Antifungal activity of *Aloe vera* gel against plant pathogenic fungi. Pak. J. Bot. 2011; 43: 2231–2233.
52. Rosca-CasianO, Parvu M, Vlase L, Tamas M. Antifungal activity of Aloe vera leaves. Fitoterapia. 2007; 78(3): 219–222. <https://doi.org/10.1016/j.fitote.2006.11.008>
53. Ortega-Toro R, Collazo-Bigliardi S, Roselló J, Santamarina P, ChiraltA. Antifungal starch-based edible films containing Aloe vera. Food Hydrocolloids. 2017; 72: 1–10. <https://doi.org/10.1016/j.foodhyd.2017.05.023>
54. Navarro D, Díaz-Mula HM, Guillén F, Zapata PJ, Castillo S, Serrano M, Valero D, Martínez-Romero D. Reduction of nectarine decay caused by Rhizopus stolonifer, Botrytis cinerea and Penicillium digitatum with Aloe vera gel alone or with the addition of thymol. International Journal of Food Microbiology.2011; 151(2): 241–246. <https://doi.org/10.1016/j.ijfoodmicro.2011.09.009>
55. García MA, Ventosa M, Díaz R, Falco S, CasariegoA. Effects of Aloe vera coating on postharvest quality of tomato. Fruits. 2014; 69(2): 117–126. <https://doi.org/10.1051/fruits/2014001>
56. Chrysargyris A, Nikou A, Tzortzakis N. Effectiveness of Aloe vera gel coating for maintaining tomato fruit quality. New Zealand Journal of Crop and Horticultural Science. 2016; 44(3): 203–217. <https://doi.org/10.1080/01140671.2016.1181661>
57. JhalegarMd, , SharmaJ, SinghD. Antifungal efficacy of botanicals against major postharvest pathogens of Kinnow mandarin and their use to maintain postharvest quality. Fruits. 2014; 69(3): 223–237. <https://doi.org/10.1051/fruits/2014012>
58. HassanpourH. Effect of Aloe vera gel coating on antioxidant capacity, antioxidant enzyme activities and decay in raspberry fruit. LWT - Food Science and Technology,2015; 60(1): 495–501. <https://doi.org/10.1016/j.lwt.2014.07.049>
59. Vieira MJ, Flores-López ML, de Rodríguez DJ, Sousa MC, Vicente AA, Martins JT. Effect of chitosan– Aloe vera coating on postharvest quality of blueberry (*Vaccinium corymbosum*) fruit. Postharvest Biology and Technology. 2016; 116: 88–97. <https://doi.org/10.1016/j.postharvbio.2016.01.011>
60. Nasrin TAA, RahmanMA, HossainMA, Islam MN, Arfin MS. Postharvest quality response of strawberries with aloe vera coating during refrigerated storage. The Journal of Horticultural Science and Biotechnology.2017;92(6): 598–605. <https://doi.org/10.1080/14620316.2017.1324326>
61. Martínez-Romero D, Castillo S, Guillén F, Díaz-Mula HM, ZapataPJ, Valero D, Serrano M. *Aloe vera* gel coating maintains quality and safety of ready-to-eat pomegranate arils. Postharvest Biology and Technology. 2013; 86: 107–112. <https://doi.org/10.1016/j.postharvbio.2013.06.022>
62. HeggersJP, Pineless GR,RobsonMC. Dermaide Aloe/*Aloe vera* Gel: Comparison of the Antimicrobial Effects. The American Journal of Medical Technology.1979; 41: 293-294.
63. TylerVE, Herbs of Choice. Pharmaceutical Products Press, New York, 1994.
64. ItoS, TeradairaR, BeppuH, ObataM, Nagatsu T.and FujitaK. Properties and Pharmacological Activity of Carboxypeptidase in Aloe arborescens Mill. var. Natalensis Berger. Phytotherapy Research.1993; 7(7): S26-S29. <http://dx.doi.org/10.1002/ptr.2650070710>
65. HallerJS. A Drug for All Seasons, Medical and Pharmacological History of Aloe. Bulletin of the New York Academy of Medicine. 1990; 66: 647-659.
66. CheQM, AkaoT, HattoriM, Kobashi K, NambaT. Isolation of Human Intestinal Bacteria Capable of Transforming Barbaloin to Aloe-Emodin Anthrone. Planta Medica. 1991;57(1): 15-19. <http://dx.doi.org/10.1055/s-2006-960007>
67. Vázquez B, Avila G, Segura D, Escalante B. Antiinflammatory activity of extracts from Aloe vera gel. Journal of Ethnopharmacology. 1996; 55(1): 69–75. <https://doi.org/10.1016/s0378-8741(96)01476-6>
68. DavisRH, ParkerWL, Samson RT,MurdochDP. Isolation of a stimulatory system in an Aloe extract. Journal of the American Podiatric Medical Association. 1991; 81(9): 473–478. <https://doi.org/10.7547/87507315-81-9-473>
69. Prabjone R, Thong-Ngam D, Wisedopas N, Chatsuwan T, Patumraj S. Anti-inflammatory effects of *Aloe vera* on leukocyte-endothelium interaction in the gastric microcirculation of Helicobacter pylori-infected rats. Clin. Hemorheol. Microcirc. 2006; 35: 359-366.
70. Langmead L, Makins RJ, Rampton DS. Anti-inflammatory effects of aloe vera gel in human colorectal mucosa in vitro. Alimentary Pharmacology &amp. Therapeutics. 2004; 19(5): 521–527. Portico. <https://doi.org/10.1111/j.1365-2036.2004.01874.x>
71. ZawahryME, Hegazy MR,and HelalM. Use of Aloe in Treating Leg Ulcers and Dermatoses. International Journal of Dermatology.1973; 12(1): 68-73. <http://dx.doi.org/10.1111/j.1365-4362.1973.tb00215.x>
72. SarojPL, Dhandar DG,SinghRS. Indian Aloe Central Institute for Arid Horticulture, Bikaner, 2004.
73. FosterS.*Aloe vera*: The Succulent with Skin Soothing Cell Protecting Properties, Herbs for Health Magazine, 1999. <http://www.healthy.net/library/articles/hfh/Aloe.htm>
74. El-ShemyHA, Aboul-SoudMA, Nassr-AllahAA, Aboul-EneinKM, Kabash A, YagiA.Antitumor Properties and Modulation of Antioxidant Enzymes’ Activity by *Aloe vera* Leaf Active Principles Isolated via Supercritical Carbon Dioxide Extraction. Current Medicinal Chemistry. 2010; 17(2): 129-138. <http://dx.doi.org/10.2174/092986710790112620>
75. DavisRH, Di DonatoJJ, Hartman GM,HassRC. Anti-inflammatory and wound healing activity of a growth substance in Aloe vera. Journal of the American Podiatric Medical Association, 1994; 84(2): 77–81. <https://doi.org/10.7547/87507315-84-2-77>
76. SteenkampV, Stewart MJ. Medicinal Applications and Toxicological Activities of Aloe. Products. Pharmaceutical Biology.2007;45(5): 411–420. <https://doi.org/10.1080/13880200701215307>
77. Fenig E, Nordenberg J, Beery E, Sulkes J, Wasserman L. Combined effect of aloe-emodin and chemotherapeutic agents on the proliferation of an adherent variant cell line of Merkel cell carcinoma. Oncology Reports. 2004; 11(1): 213-217. <https://doi.org/10.3892/or.11.1.213>
78. Keivan Z, isup Moloud AZ, Kohzad S, Zahra R. Antiviral activity of Aloe vera against herpes simplex virus type 2: An in vitro study. African Journal of Biotechnology. 2007; 6(15): 1770–1773. <https://doi.org/10.5897/ajb2007.000-2276>
79. SWLi, Yang TC, Lai CC, Huang SH, Liao JM, Wan L, Lin YJ, Lin CW. Antiviral activity of aloe-emodin against influenza A virus via galectin-3 up-regulation. European Journal of Pharmacology. 2014; 738: 125–132. <https://doi.org/10.1016/j.ejphar.2014.05.028>
80. KempMC, KahlonJB, ChinnahAD, CarpenterRH, McAnalleyBH, McDaniel HR, ShannonWM. 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 Glycoprotein Precursors. Antiviral Res. 1990;13(1): 83-96. <http://dx.doi.org/10.1016/0166-3542(90)90156-2>
81. SaooK, MikiH, Ohmori M, WintersWD. Antiviral Activity of Aloe Extracts against Cytomegalovirus. Phytotherapy Research. 1990; 10(4): 348- 350. <https://doi.org/10.1002/(SICI)1099-1573(199606)10:4%3C348::AID-PTR836%3E3.0.CO;2-2>
82. SydiskisRJ, OwenDG, LohrJL, Rosler KH,BlomsterRN. Inactivation of Enveloped Viruses by Anthraquinones Extracted from Plants. Antimicrobial Agents and Chemotherapy. 1991; 35(12): 2463-2466. <http://dx.doi.org/10.1128/AAC.35.12.2463>
83. Alves DS, Pérez-Fons L, Estepa A, Micol V. Membrane-related effects underlying the biological activity of the anthraquinones emodin and barbaloin. Biochemical Pharmacology.2004; 68(3): 549–561. <https://doi.org/10.1016/j.bcp.2004.04.012>
84. Cragg GM, Newman DJ. Natural Product Drug Discovery in the Next Millennium. Pharmaceutical Biology. 2001;39(sup1): 8–17. <https://doi.org/10.1076/phbi.39.s1.8.0009>
85. Roberts DB,TravisEL. Acemannan-Containing Wound Dressing Gels Reduce Radiation-Induced Skin Reactions in C3H Mice. International Journal of Radiation Oncology, Biology and Physiology.1995; 32(4): 1047-1052. <http://dx.doi.org/10.1016/0360-3016(94)00467-Y>
86. BosleyC, Smith J,BarattiP. A Phase III Trial Comparing an Anionic Phospholipidbased (APP) Cream and *Aloe vera*-Based Gel in the Prevention and Treatment of Radiation Dermatitis. International Journal of Radiation Oncology Biology Physics. 2003; 57 (2): 34-38. <http://dx.doi.org/10.1016/S0360-3016(03)01404-4>
87. SiegersCP. Anthranoid Laxative Abuse—A Risk for Colorectal Cancer. Gut.1993; 34(8): 1099- 1101. <http://dx.doi.org/10.1136/gut.34.8.1099>
88. SumbulS, Ahmed SW, AzharI. Anti Fungal Activity of Allium, Aloe, and Solanum Species. Pharmaceutical Biology.2004;42(7), 491-498. <http://dx.doi.org/10.3109/13880200490891845>
89. Suvitayavat W, SumrongkitC, Thirawarapan SS, Bunyapraphatsara N. Effects of Aloe preparation on the histamine-induced gastric secretion in rats. Journal of Ethnopharmacology, 2004; 90(2–3): 239–247. <https://doi.org/10.1016/j.jep.2003.09.044>
90. Yusuf S, Agunu A, Diana M. The effect of *Aloe vera* A. berger (Liliaceae) on gastric acid secretion and acute gastric mucosal injury in rats. Journal of Ethnopharmacology. 2004; 93: 33-37. <https://doi.org/10.1016/s0378-8741(04)00119-9>
91. Chandan BK, Saxena AK, Shukla S, Sharma N, Gupta DK, SuriKA, Suri J, Bhadauria M, Singh B. Hepatoprotective potential of Aloe barbadensis Mill. against carbon tetrachloride induced hepatotoxicity. Journal of Ethnopharmacology. 2007; 111(3): 560–566. <https://doi.org/10.1016/j.jep.2007.01.008>
92. Chow JTN, WilliamsonDA, Yates KM, Goux WJ. Chemical characterization of the immunomodulating polysaccharide of Aloe vera L. Carbohydrate Research.2005;340(6): 1131–1142. <https://doi.org/10.1016/j.carres.2005.02.016>
93. Im SA, Oh ST, Song S, Kim MR, Kim DS, Woo SS, Jo TH, Park YI, Lee CK. Identification of optimal molecular size of modified Aloe polysaccharides with maximum immunomodulatory activity. International Immunopharmacology.2005; 5(2): 271–279. <https://doi.org/10.1016/j.intimp.2004.09.031>
94. PughN, RossSA, ElSohly MA,PascoDS. Characterization of Aloeride, a New High-MolecularWeight Polysaccharide from *Aloe vera* with Potent Immunostimulatory Activity,” Journal of Agricultural and Food Chemistry.2001; 49(2): 1030-1034. <http://dx.doi.org/10.1021/jf001036d>
95. HartLA, NibberingPH, van den BarselaarMT, van DijkHAJ, LabadieRP. Effects of Low Molecular Constituents from *Aloe vera* Gel on Oxidative Metabolism and Cytotoxic and Bactericidal Activities of Human Neutrophils. International Journal of Immunopharmacology.1990; (12)4: 427- 434. <http://dx.doi.org/10.1016/0192-0561(90)90026-J>
96. HanselR, KellerK, Rimpler H, SchneiderG. Hagers Handbuch der Pharmazeutischen Praxis. Monograph: Valeriana, 5th Edition, Springer, Berlin, 1994. <http://dx.doi.org/10.1007/978-3-642-57881-6>
97. Strickland FM. Immune regulation by polysaccharides: implications for skin cancer. Journal of Photochemistry and Photobiology B: Biology. 2001;63(1–3): 132–140. <https://doi.org/10.1016/s1011-1344(01)00210-x>
98. IshiiY, Tanizawa H, TakinoY. Studies of Aloe. V. Mechanism of Cathartic Effect. (4), Biological & Pharmaceutical Bulletin, 1994; 17(5): 651-653. <http://dx.doi.org/10.1248/bpb.17.651>
99. DalBelo SE, Rigo Gaspar L, Berardo Gonçalves PM. Moisturizing effect of cosmetic formulations containing Aloe vera extract in different concentrations assessed by skin bioengineering techniques. Skin Research and Technology.2006; 12(4): 241–246. <https://doi.org/10.1111/j.0909-752x.2006.00155.x>
100. Reddy UmaCH, Reddy SK ReddyJ.*Aloe vera*—A Wound Healer,” Asian Journal of Oral Health and Allied Sciences.2011; 1: 91-92.
101. R. Maenthaisong N, Chaiyakunapruk, NiruntrapornS. The Efficacy of *Aloe vera* for Burn Wound Healing: A Systematic Review, Burns.2007; 33(6): 713-718. <http://dx.doi.org/10.1016/j.burns.2006.10.384>
102. HeggersJP. Beneficial Effect of Aloe on Wound Healing in an Excisional Wound Healing Model. Journal of Alternative and Complementary Medicine.1996; 2(2): 271-277. <http://dx.doi.org/10.1089/acm.1996.2.271>
103. de WitteP. Metabolism and Pharmacokinetics of Anthranoids. Pharmacology.1993; 47(1): 86-97. <http://dx.doi.org/10.1159/000139847>
104. ChithraP, Sajithal GB,ChandrakasanG.Influence of Aloe vera on Glycosaminoglycans in the Matrix of Healing Dermal Wounds in Rats. Journal of Ethanopharmacology. 1998; 59(3): 179-186. <http://dx.doi.org/10.1016/S0378-8741(97)00112-8>
105. SyedTA, Afzal M, AshfaqAS. Management of Genital Herpe in Men with 0.5% *Aloe vera* Extracts in a Hydrophilic Cream: A Placebo-Controlled Double-Blind Study. Journal of Dermatological Treatment. 1997; 8(2): 99-102. [http://dx.doi.org/10.3109/095466397091602](http://dx.doi.org/10.3109/09546639709160279)
106. JiaY, ZhaoG, JiaJ. Preliminary evaluation: the effects of Aloe ferox Miller and Aloe arborescens Miller on wound healing. Journal of Ethnopharmacology. 2008; 120(2): 181–189.<https://doi.org/10.1016/j.jep.2008.08.008>
107. AnthertonP.*Aloe vera*: Magic or Medicine?. Nursing Standard.1998; 12(41): 49-54.
108. BeuersU, Spengler U,PapeGR. Hepatitis after Chronic Abuse of Senna. Lancet.1991; 337 (8737): 472. <http://dx.doi.org/10.1016/0140-6736(91)91012-J>
109. Muller-LissnerSA.Adverse Effects of Laxatives: Facts and Fiction. Pharmacology.1993; 47(1): 138-145. <http://dx.doi.org/10.1159/000139853>
110. HeizerWD, et al. Protein-Losing Gastroenteropathy and Malabsorption Associated with Factitious Diarrhea. Annals of Internal Medicine. 1968; 68(4): 839-852. <http://dx.doi.org/10.7326/0003-4819-68-4-839>
111. McHughTH, SenesiE. Apple Wraps: A Novel Method to Improve the Quality and Extend the Shelf Life of Fresh-cut Apples. Journal of Food Science, 2000;65(3): 480–485. <https://doi.org/10.1111/j.1365-2621.2000.tb16032.x>
112. Michailides TJ, Manganaris GA. Harvesting and handling effects on postharvest decay. Stewart Postharvest Review. 2009; 5(2): 1–7. <https://doi.org/10.2212/spr.2009.2.3>
113. Kahramanoğlu I. Introductory chapter: Postharvest physiology and technology of horticultural crops. In Postharvest Handling; Kahramanoğlu, I., Ed.; InTech Open: London, UK, 2017; 1–5.
114. HeQ, Changhong L, KojoE, TianZ. Quality and safety assurance in the processing of Aloe vera gel juice. Food Control. 2005; 16(2): 95–104. <https://doi.org/10.1016/j.foodcont.2003.12.001>
115. VinsonJA, Al Kharrat H, Andreoli L. Effect of Aloe vera preparations on the human bioavailability of vitamins C and E. Phytomedicine.2005; 12(10): 760–765. <https://doi.org/10.1016/j.phymed.2003.12.013>
116. Jani GK, Shah DP, Jain VC, Patel MJ, Vithalan DA. Evaluating mucilage from Aloe Barbadensis Miller as a pharmaceutical excipient for sustained-release matrix tablets. Pharm. Technol. 2007; 31: 90-98.
117. PeterA.*Aloe vera* Myth or Medicine?” Positive Health Publications, 2002. http://www.positivehealth.com/permit/Articles/Aloe%20 Vera/atherton.htm
118. BissetNG. Sennae folium. Max Wichtl’s Herbal Drugs & Phytopharmaceuticals,” CRC Press, Boca Raton, 1994.