Review Article

Pharmacological attribute of Aloe vera: Revalidation through experimental and clinical studies

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Abstract

Aloe vera has long been used as a traditional medicine for inducing wound healing. It is a natural product that now a days is used in cosmetic industry. Benefits associated with Aloe vera have been attributed to the polysaccharides contained in the gel of the leaves though there are various indications for its use. Biological activities include promotion of wound healing, antifungal activity, anti-inflammatory, anticancer and immunomodulatory. Gingival fibroblasts play an important role in oral wound healing. Double blind-controlled trials are needed to determine its real efficacy in oral health.

Key words: Aloe vera, oral health, polysaccharides, wound healing

Introduction

Aloe vera (Sanskrit-Ghrítakumári, Kumára;[1] Botanical-Aloe barbadensis Miller; Hindi-Guarpatha, Ghikanvar) is perennial succulent xerophyte, which develops water-storage tissue in the leaves to survive in dry areas of low or erratic rainfall. The plant has stiff grey-green lance-shaped leaves containing clear gel in a central mucilaginous pulp. Benefits associated with Aloe vera have been attributed to the polysaccharides contained in the gel of the leaves.

Historically, it has been used for a variety of medicinal purposes. Aloe vera has long been used as a traditional medicine for inducing wound healing. Over the years, this plant has been known by a number of names such as ‘the wand of heaven’, ‘heaven’s blessing’ and ‘the silent healer’. It is a natural product that now a days is used very much in cosmetic industry.

Active ingredient of Aloe vera

More than 75 active ingredients from inner gel have been identified including vitamins, minerals, enzymes, sugars, anthraquinones or phenolic compounds, lignin, saponins, sterols, amino acids and salicylic acid.

Active ingredients of Aloe vera leaf pulp and exudates[2] were depicted in Table 1.

Biological activity of Aloe vera gel

A number of investigations have attempted to relate the chemical constituents in the gel to specific biological effects.

Wound-healing effects

Different mechanisms have been proposed for the wound-healing effects of aloe gel, which include keeping the wound moist, increase epithelial cell migration, more rapid maturation of collagen and reduction in inflammation.[3]

Glucomannan, a mannose-rich polysaccharide and gibberellin, a growth hormone, interacts with growth factor receptor on the fibroblast, thereby stimulating its activity and proliferation, which in turn increases collagen synthesis after topical and oral application.[4]

An increase in synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound is seen following oral and topical treatment.[5]

Aloe vera gel contains a glycoprotein with cell proliferating-promoting activity,[6] while in one research it is found that Aloe vera gel improved wound healing by increasing blood supply, which increased oxygenation as a result.[7] Topical application of the Aloe vera derived allantoin gel stimulated fibroblast activity and collagen proliferation.[8]

Skin hydration actions

Mucopolysaccharides help in binding moisture into the skin. It was proposed that the Aloe vera gel containing products improved skin hydration possibly by means of a humectant mechanism.[9]

Anti-aging effect

Aloe stimulates fibroblast which produces the collagen and elastin fibres making the skin more elastic and less wrinkled.[10]
Table 1: Active ingredients of Aloe vera leaf pulp and exudates

| Class                      | Compounds                                                                 |
|----------------------------|----------------------------------------------------------------------------|
| Vitamins                   | B1, B2, B6, C, A (ββ-carotene), choline, folic acid, αα-tocopherol          |
| Enzymes                    | Alkaline phosphatase, amyrase, carboxypeptidase, catalase, bradikinase, cyclooxygenase, lipase, oxidase, phosphoenolpyruvate carboxylase, superoxide dismutase |
| Anthraquinones/antihydrates| Aloe-emodin, aloetic-acid, anthranol, aloin A and B (or collectively known as barbaloin), isobarbaloin, emodin, ester of cinnamic acid |
| Inorganic compounds        | Calcium, chlorine, chromium, copper, iron, magnesium, manganese, selenium, zinc, potassium, phosphorous, sodium |
| Carbohydrates              | Pure mannan, acetylated mannan, acetylated glucomannan (acemannan), galactan, glucogalactomannan, galactogalacturactan, galactoglucoarabinomannan, arabinogalactan, pectic substance, xylan, cellulose |
| Saccharides                | Mannose, glucose, L-rhamnose, aldopentose                                    |
| Organic compounds and lipids| Arachidonic acid, γγ-linolenic acid, steroids (campesterol, cholesterol, ββ-sitosterol), triglycerides, triterpenoid, gibberelin, lignins, potassium sorbate, salicylic acid, uric acid, cholesterol, triglycerides, fatty acids, steroids |
| Chromones                  | 8-C-glucosyl-(2'-O-cinnamoyl)-7'-O-methylaloediol A, 8-C-glucosyl-(S')-aloesol, 8-C-glucosyl-7'-O-methyl-(S')-aloesol, 8-C-glucosyl-7'-O-methylalloediol, 8-C-glucosyl-noreugenin, isoaloeresin D, isoraibaichromone |
| Nonessential and essential amino acids | Alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tyrosine, valine |

Anti-inflammatory effects

It inhibits the cyclooxygenase pathway and reduces prostaglandin E2. Recently, the novel anti-inflammatory compound called C-glycosyl chrome was isolated from gel extracts.[11]

Recently, the peptidase bradykinase was isolated from aloe and shown to break down the bradykinin, an inflammatory substance that induces pain.[12]

Antibacterial

The activity of Aloe vera inner gel against both Gram-positive and Gram-negative bacteria has been demonstrated by several different methods.[13] Streptococcus pyogenes and Streptococcus faecalis are two microorganisms that have been inhibited by Aloe vera gel.[14] Aloe vera gel reportedly was bactericidal against Pseudomonas aeruginosa while acemannan prevented it from adhering to human lung epithelial cells in a monolayer culture.[15]

Antifungal

A processed Aloe vera gel preparation reportedly inhibited the growth of Candida albicans.[16]

Antiviral effects

This action may be direct and indirect. Indirect due to stimulation of immune system and direct is due to anthraquinones. The anthraquinones aloin activates various enveloped virus; herpes simplex, varicella zoster and influenza.[16]

Effect on immune system

Immunomodulating effects occur via activation of macrophage cells to generate nitric oxide, secrete cytokines (e.g., tumor necrosis factor-α, interleukin-1, interleukin-6 and interferon-γ) and present cell surface markers.[17,18]

Antioxidant property

Glutathione peroxides activity, superoxide dismutase enzymes and a phenolic antioxidant were found to be present in Aloe vera gel, which may be responsible for these antioxidant effects.[19]

Antitumor effect

The two fractions from aloe that are claimed to have anticancer effects include glycoproteins (lectins) and polysaccharides.[3] Different studies indicated antitumor activity for Aloe vera gel in terms of reduced tumor burden, tumor shrinkage, tumor necrosis and prolonged survival rates.

An induction of glutathione S-transferase and an inhibition of the tumor-promoting effect of phorbol myristic acetate has also been reported which suggest aloe gel in cancer chemoprevention.[20] Indirect action on antitumor activity is stimulation of the immune response.[21]

Laxative effect (Purgative effect)

Anthraquinones increase intestine water content, stimulate water secretion and increase intestinal peristalsis.[22]

Antiseptic Properties

Aloe vera contain six antiseptic agent; lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenol and sulfur.[23]

Use of aloe vera in dentistry

Aphthous ulcer

It has been reported that acemannan hydrogel accelerates the healing of aphthous ulcers and reduces the pain associated with them.[24]

Researchers evaluated a gel that combined allantoin, Aloe vera, and silicon dioxide and its effects on aphthous ulcers of the oral cavity.[25] Each patient used a daily diary to document the number and duration of aphthous ulcers, the interval between ulcers, ulcer size, and ulcer pain over a period of 3-4 months. The reduced duration of the lesions in one arm of the study and the increased interval between lesions in the other arm of the study both were significant statistically. The gel did not
demonstrate any consistent effectiveness on ulcers in the oral cavity.

**Oral lichen planus**
A patient of lichen planus with systemic involvement placed on Aloe vera therapy. The patient’s treatment involved drinking 2.0 ounces of stabilized Aloe vera juice daily for 3 months, topical application using Aloe vera lip balm and aloe cream for itching hands. The oral lesions cleared up within 4 weeks, although the systemic lesions took longer, due in part to the fact that the patient temporarily interrupted the course of aloe therapy and sought an alternate source of treatment.[20]

The 46 patients with OLP were randomly divided into two groups. Each group was treated with Aloe vera mouthwash and triamcinolone acetonide 0.1% (TA). The treatment period for both groups was 4 weeks. Patients were evaluated on days 8, 16 and after completing the course of treatment (visit 1-3). The last follow-up was 2 months after the start of treatment (visit 4). Aloe vera mouthwash is an effective substitute for TA in the treatment of OLP.[27]

A double-blind trial on 54 patients were randomized into two groups to receive Aloe vera gel or placebo for 8 weeks. The most common site of OLP was the lower lip. 81% patients treated with Aloe vera had a good response after 8 weeks of treatment, while 4% placebo-treated patients had a similar response ($P < 0.001$). Furthermore, 7% patients treated with Aloe vera had a complete clinical remission. Burning pain completely disappeared in 33% patients treated with Aloe vera and in 4% treated with placebo ($P = 0.005$). Therefore, Aloe vera gel can be considered a safe alternative treatment for patients with OLP.[28]

Another double-blind study of 64 patients with OLP were randomized to either Aloe vera (32 patients) or placebo (32 patients), at a dose of 0.4 ml (70% concentration) three times a day. The patients were evaluated after 6 and 12 weeks. In the Aloe vera group, complete pain remission was achieved in 31.2% of the cases after 6 weeks, and in 61% after 12 weeks. In the placebo group, these percentages were 17.2% and 41.6%, respectively. Concluded that Aloe vera improves the total quality of life score in patients with OLP.[29]

**Gingival**
Aloe vera gel reportedly has been used to treat gingivitis and has been effective against herpes simplex viruses.[30] Acemannan, a prominent glucomannan-stimulate gingival fibroblast proliferation.

**Pulp**
Acemannan promotes dentin formation by stimulating primary human dental pulp cell proliferation, differentiation, extracellular matrix formation, and mineralization. Acemannan also has pulp biocompatibility and promotes soft tissue organization.[12]

**Bacteria**
Results showed that Aloe vera tooth gel and the toothpastes were equally effective against C. albicans, Streptococcus mutans, Lactobacillus acidophilus, Enterococcus faecalis, Prevotella intermedia, and Peptostreptococcus anaerobius. Aloe vera tooth gel demonstrated enhanced antibacterial effect against S. mutis.[31]

**Extracted socket**
Salicept Patch (a freeze-dried pledget that contains Acemannan Hydrogel) significantly ($P < 0.0001$) reduces the incidence of Alveolar Ostitis compared with clindamycin-soaked Gelfoam.[14]

**Denture adhesive**
Because of the sticky and viscous nature of acemannan, a prototype acemannan was formulated into a denture adhesive and evaluated for adhesive strength in both wet and dry conditions; the adhesive was also used to evaluate cytotoxicity to human gingival fibroblasts.[19]

**Conclusions**
The pharmacological attributes of Aloe vera have been revalidated in modern sciences which proves that drug has immense potential in pharmaco-therapeutics.

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हिंदी सारांश

घृतकुमारी की कार्मिकता का प्रायोगिक एवं चिकित्सकीय सत्यापन

विनय के गुरू, सीमा महोत्रा

घृतकुमारी या अलोवेरा को धार भरने के लिए पारम्परिक औषधि के रूप में लम्बे समय से प्रयोग किया जाता रहा है। यह एक प्राकृतिक उत्पाद है जो कि आज कल सोनदर्प्रशासन उद्योगों में प्रयोग किया जाता है। अलोवेरा के लहर इसकी फलियाँ में पाये जाने वाले जैल में उपस्थित पोलीसेक्रेटाइड के कारण होते हैं। यद्यपि इसके अतिरिक्त इसके अन्य भी प्रयोग हैं। जैविक क्रिया के अन्तर्गत धार भरने को बढावा देना, एंटीफैक्टर क्रिया, शोध, एंटी संसार तथा प्रतिपक्ष तंत्र को बढ़ावा देने वाले क्रियायें आती हैं। मसूदों में पाये जाने वाली फाइब्रोवस्टो कोशिकाओं के धार भरने की प्रक्रिया में एक महत्वपूर्ण योगदान प्रदान करती है। अलोवेरा की वास्तविक क्षमता को मुख्य स्वास्थ्य में निर्माण करने के लिए डबल ब्लाइंड नियंत्रित प्रयोग आवश्यक है।