



Review Article

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

Vinay K. Gupta, Seema Malhotra¹

Assistant Professor, Department of Public Health Dentistry, Faculty of Dental Sciences, Chhatrapati Shahuji Maharaj Medical University (upgrade KGMC), ¹Senior Lecturer, Department of Pedodontic, Saraswati Dental College and Research Center, Lucknow, Uttar Pradesh, India

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-Ghratakumari, Kumara;^[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.

Address for correspondence: Dr. Vinay K. Gupta,
Flat no 606, TG Campus, Khadara, Lucknow - 226025,
Uttar Pradesh, India.
E-mail: vinaycommunity@gmail.com

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 ($\beta\beta$ -carotene), choline, folic acid, $\alpha\alpha$ -tocopherol
Enzymes	Alkaline phosphatase, amylase, carboxypeptidase, catalase, bradikininase, cyclooxygenase, peroxidase, carboxy-peptidase, cyclooxygenase, lipase, oxidase, phosphoenolpyruvate carboxylase, superoxide dismutase
Anthraquinones/ anthrones	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, galactogalacturan, galactoglucoarabinomannan, arabinogalactan, pectic substance, xylan, cellulose
Saccharides	Mannose, glucose, <i>L</i> -rhamnose, aldopentose
Organic compounds and lipids	Arachidonic acid, $\gamma\gamma$ -linolenic acid, steroids (campesterol, cholesterol, $\beta\beta$ -sitosterol), triglycerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, uric acid
Chromones	8- <i>C</i> -glucosyl-(2'- <i>O</i> -cinnamoyl)-7- <i>O</i> -methylaloeidin A, 8- <i>C</i> -glucosyl-(<i>S</i>)-aloesol, 8- <i>C</i> -glucosyl-7- <i>O</i> -methyl-(<i>S</i>)-aloesol, 8- <i>C</i> -glucosyl-7- <i>O</i> -methylaloeidin, 8- <i>C</i> -glucosyl-noreugenin, isoaloesol, isorabaichromone
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 chromone 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*.^[14]

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 peroxidase 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.^[26]

The 46 patients with OLP were randomly divided into 2 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.^[30,31] 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 pulpal biocompatibility and promotes soft tissue organization.^[32]

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. mitis*.^[33]

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.^[34]

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.^[35]

Conclusions

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

References

1. Ayurveda-Recipes.com/Aloe_vera. [Homepage on the Internet]. Accessed on 2011 July 4. Available from: http://www.ayurveda-recipes.com/aloe_vera.html.
2. Josias H. Hamman composition and applications of aloe vera leaf gel. *Molecules* 2008;13:1599-616.
3. Reynolds T, Dweck AC. Aloe vera leaf gel: A review update. *J Ethnopharmacol* 1999;68:3-37.
4. Chithra R, Sajithlal GB, Chandrakasan G. Influence of aloe vera on collagen characteristic in healing dermal wound in rats. *Mol Cell Biochem* 1998;181:71-6.
5. Chithra R, Sajithlal GB, Chandrakasan G. Influence of aloe vera on the glycosaminoglycan in the matrix of healing dermal wound in rat. *J Ethnopharmacol* 1998;59:179-86.
6. Yagi A, Egusa T, Arase M, Tanabe M, Tsuji H. Isolation and characterization of the glycoprotein fraction with a proliferation-promoting activity on human and hamster cells *in vitro* from aloe vera gel. *Planta Med* 1997;63:18-21.
7. Davis RH, Leitner MG, Russo JM, Byrne ME. Anti-inflammatory activity of aloe vera against a spectrum of irritants. *J Am Podiatr Med Assoc* 1989;79:263-76.
8. Thompson JE. Topical use of aloe vera derived allantoin gel in otolaryngology. *Ear Nose Throat J* 1991;70:56.
9. Dal'Belo SE, Gaspar LR, Maia Campos PM. Moisturising effect of cosmetic formulations containing Aloe vera extract in different concentrations assessed by skin bioengineering techniques. *Skin Res Technol* 2006;12:241-6.
10. Davis RH. Biological activity of aloe vera. *SOFW Journal*; 1993;119:646-49.
11. Hutter JA, Salmon M, Stavinoha WB, Satsangi N, Williams RF, Streeper RT, et al. Anti-inflammatory C-glycosyl chromone from aloe barbadensis. *J Nat Prod* 1996;59:541-3.
12. Ito S, Teradaira R, Beppu H, Obata M, Nagatsu T, Fujita K. Properties and pharmacological activity of carboxypeptidase in *Aloe arborescens* Mill var. *natalensis* Berger. *Phytother Res* 1993;7:S26-9.
13. Habeeb F, Shakir E, Bradbury F, Cameron P, Taravati MR, Drummond AJ, et al. Screening methods used to determine the anti-microbial properties of *Aloe vera* inner gel. *Methods* 2007;42:315-20.
14. Hegggers JP, Pineless GR, Robson MC. Dermaide aloe/aloe vera gel: Comparison of the antimicrobial effects. *J Am Med Technol* 1979;41:293-4.
15. Azghani AO, Williams I, Holiday DB, Johnson AR. A beta-linked mannan inhibits adherence of *Pseudomonas aeruginosa* to human lung epithelial cells. *Glycobiology* 1995;5:39-44.
16. Sydiskis RJ, Owen DG, Lohr J, Rosler KH, Blomster RN. Inactivation of enveloped viruses by anthraquinones extracted from plant. *Antimicrob Agent Chemother* 1991;35:2463-6.
17. Tai-Nin Chow J, Williamson DA, Yates KM, Goux WJ. Chemical

- characterisation of the immunomodulating polysaccharide of Aloe vera L. Carbohydr Res 2005;340:1131-42.
18. Im SA, Oh ST, Song S, Kim MR, Kim DS, Woo SS, et al. Identification of optimal molecular size of modified Aloe polysaccharides with maximum immunomodulatory activity. Int Immunopharmacol 2005;5:271-9.
 19. Khan MA, Tania M, Zhang D, Chen H. Antioxidant enzyme and cancer. Chin J Cancer Res 2010;22:87-92.
 20. Kim HS, Lee BM. Inhibition of benzo (a) pyrene-DNA adduct formation by aloe barbedebis miller. Carcinogenesis 1997;18:771-6.
 21. Steenkamp V, Stewart MJ. Medicinal applications and toxicological activities of Aloe products. Pharm Biol 2007;45:411-20.
 22. Ishii Y, Tanizawa H, Takino Y. Mechanism of cathartic effect. Biol Pharm Bull 1994;17:651-3.
 23. Surjusha A, Vasani R, Saple DG. Aloe vera: A short review. Indian J Dermatol 2008;53:163-6.
 24. Oral ulcers remedy gets FDA clearance. J Am Dent Assoc 1994;125:1308-10.
 25. Garnick JJ, Singh B, Winkley G. Effectiveness of a medicament containing silicon dioxide, aloe, and allantoin on aphthous ulcers. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;86:550-6.
 26. Hayes SM. Lichen planus—Report of successful treatment with aloe vera. Gen Dent 1999;47:268-72.
 27. Mansourian A, Momen-Heravi F, Saheb-Jamee M. Comparison of treatment efficacy of daily use of aloe vera mouthwash with triamcinolone acetonide 0.1% on oral lichen planus: A randomized double-blinded clinical trial. Am J Med Sci 2011;342:447-51.
 28. Choonhakarn C, Busaracome P, Sripanidkulchai B, Sarakarn P. The efficacy of aloe vera gel in the treatment of oral lichen planus: A randomized controlled trial. Br J Dermatol 2008;158:573-7.
 29. Salazar-Sanchez N, Lopez-Jornet P, Camacho-Alonso F, Sanchez-Siles M. Efficacy of topical Aloe vera in patients with oral lichen planus: A randomized double-blind study. J Oral Pathol Med 2010;39:735-40.
 30. PDR for herbal medicines. 1st ed. Montvale, NJ: Medical Economics Company; 1998. p. 631.
 31. Krinsky DL, Hawkins EB, Pelton R, Willis NA, La-valle JB. Natural therapeutics pocket guide, 2nd ed. Cleveland: Lexi-Comp, Inc.; 2003. p. 379.
 32. Jittapiromsak N, Sahawat D, Banlunara W, Sangvanich P, Thunyakitpisal P. Acemannan, an extracted product from Aloe vera, stimulates dental pulp cell proliferation, differentiation, mineralization, and dentin formation. Tissue Eng Part A 2010;16:1997-2006.
 33. George D, Bhat SS, Antony B. Comparative evaluation of the antimicrobial efficacy of aloe vera tooth gel and two popular commercial toothpastes: An *in vitro* study. Gen Dent 2009;57:238-41.
 34. Poor MR, Hall JE, Poor AS. Reduction in the incidence of alveolar osteitis in patients treated with the SaliCept patch, containing Acemannan hydrogel. J Oral Maxillofac Surg 2002;60:374-9.
 35. Tello CG, Ford P, Iacopino AM. *In vitro* evaluation of complex carbohydrate denture adhesive formulations. Quintessence Int 1998;29:585-93.

हिन्दी सारांश

घृतकुमारी की कार्मुकता का प्रायोगिक एवम् चिकित्सकीय सत्यापन

विनय के. गुप्ता, सीमा मल्होत्रा

घृतकुमारी या अलोवेरा को घाव भरने के लिये पारम्परिक औषधि के रूप में लम्बे समय से प्रयोग किया जाता रहा है। यह एक प्राकृतिक उत्पाद है जो कि आज कल सौन्दर्य प्रसाधन उद्योगों में प्रयोग किया जाता है। अलोवेरा के लाभ इसकी पत्तियों में पाये जाने वाले जैल में उपस्थित पौलीसैकेराइड के कारण होते हैं। यद्यपि इसके अतिरिक्त इसके अन्य भी प्रयोग हैं। जैविक क्रिया के अन्तर्गत घाव भरने को बढ़ावा देना, एंटीफंगल क्रिया, शोथहर, एन्टी कैंसर तथा प्रतिरक्षा तंत्र को बढ़ावा देने वाली क्रियाएँ आती हैं। मसूड़ों में पायी जाने वाली फाइब्रोब्लास्ट कोशिकाएँ इसके घाव भरने की प्रक्रिया में एक महत्वपूर्ण योगदान प्रदान करती हैं। अलोवेरा की वास्तविक क्षमता को मुख के स्वास्थ्य में निर्धारित करने के लिये डबल ब्लाइन्ड नियंत्रित प्रयोग आवश्यक है।