

Phytotherapeutic effects of Aloe vera (*Aloe barbadensis* Miller): A mini-review

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ABSTRACT

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Objective: Despite several modern pharmacological treatments, there is still an increasing demand for traditional, accessible and affordable natural treatments with less adverse effects such as medicinal plants. The aim of this review was to summarize the published data on several therapeutic effects of aloe vera.

Methods: A literature search was carried out using Google scholar, PubMed and Science direct with keywords such as bioactive compound, hyperlipidemia, hyperglycemia, antioxidant, inflammation, body immune system, cancer, wound healing, and antimicrobial activity, in combination with *Aloe vera* and *Aloe barbadensis* Miller. The search was limited to studies published in English.

Results: A total of 54 papers out of 63 randomized controlled trials and review articles were finally selected. *Aloe vera* (*Aloe barbadensis* Miller) is one of the most well-known herbal medicines with considerable medicinal properties such as hypolipidemic, hypoglycemic, antioxidant, anti-inflammatory, and immunomodulatory, anticancer, wound healing, antibacterial and antiviral activities. Many of the health benefits associated with aloe vera have been attributed to its various bioactive natural components such as vitamins, anthraquinones and polysaccharides.

Conclusion: Chemical compounds contained naturally in *A. vera* are expanding our disease treatment choices and benefit us with their wide range of properties for the management of diverse disorders. Therefore, it would be worthwhile to conduct further intensive scientific studies on this multipurpose medicinal plant to promote its large-scale utilization.

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Introduction

Plants have been considered as an important source of medicines since ancient times. According to the recent estimates by the World Health Organization (WHO), globally up to 80%

of the people still rely mainly on traditional medicines [1]. Compared to modern pharmaceutical treatments, traditional plant medicines are less costly and lead to relatively lower incidences of adverse effects [2].

Aloe vera (*Aloe barbadensis* Miller, *A. vera*) is one of the nearly 420 species of genus *Aloe*, from the Liliaceae family. It is among the most common well-known medicinal plants originated in North and East Africa, now quite widespread [3, 4]. *Aloe vera* is a cactus-like evergreen plant

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with dagger-shaped and jagged edges and sharp points with a high content of a viscous gel. This plant has other common names, such as burn plant, lily of the desert and elephant's gall, and is being used as a traditional medicinal plant in different countries including China, Japan, India and some African countries [1]. The major phytochemical and bioactive compounds and nutrients in *A. vera* are explained below [1, 5-7]:

Vitamins: The vitamins contained in *A. vera* are vitamins C and E, as well as beta-carotene, the provitamin A, all being antioxidants protecting the body against the destructive effects of free radicals. *A. vera* also contains vitamin B12, folic acid and the vitamin-like choline.

Minerals: *A. vera* contains minerals such as calcium, chromium, copper, selenium, magnesium, potassium, sodium and zinc, all essential as cofactors for the proper functioning of various enzymes in different metabolic pathways.

Carbohydrates: Mannose-6-phosphate and glucomannan (mainly acemannan) are the most well-known monosaccharides and polysaccharides in *A. vera*, respectively. These components play an important role in wound healing.

Amino acids: *A. vera* is known as a good source of some of the amino acids. It contains several amino acids required by man such as arginine, asparagine, glutamic acid, serine and aspartic acid.

Phytosterols: Campesterol, β -sitosterol and lupeol are common phytosterols with anti-inflammatory effects found in *A. vera*.

Anthraquinones: These are phenolic compounds (such as aloin and emodin) in *A. vera* with antioxidant, anti-inflammatory, analgesic, laxative, antibacterial and antiviral properties.

Enzymes: *A. vera* contains various enzymes such as amylase, catalase, cellulase, lipase and peroxidase, all essential for normal metabolism.

Other chemical compounds: *A. vera* is also used as a functional food, especially in the food industry, and as a main ingredient of several kinds of drugs in the pharmaceutical industry [7]. No report has been published on the side effects of this plant until now [5]. This review aims at summarizing published information about *A. vera* as a traditional medicinal plant with multiple biological activities.

Methods

A literature search was carried out in Google

scholar, PubMed and Science direct databases using keywords such as bioactive compound, hyperlipidemia, hyperglycemia, antioxidant, inflammation, body immune system, cancer, wound healing, and antimicrobial activity, in combination with *Aloe vera* and *Aloe barbadensis* Miller. For the sake of completeness, we also included references cited in all the relevant papers selected. A total of 54 papers out of 63 randomized controlled trials and review articles were finally selected. The search was limited to studies published in English.

Results and discussion

1. Antihyperlipidemic Activity:

A. vera is known for its antihyperlipidemic properties through reducing fatty acid accumulation and atherosclerosis prevention [8]. The existing reports suggest that aleo-phytosterols are the main active ingredients in *A. vera* gel with antihyperlipidemic and antiobesity effects [9, 10]. These phytosterols can bind to cholesterol and prevent its absorption resulting in decreased total serum cholesterol [11]. Several clinical trial studies have shown the lipid-lowering effects of *A. vera* gel preparations [12, 13]. In an animal study, oral administration of processed *A. vera* gel in obese mice models for 8 weeks lead to a decrease in triglyceride (TG) levels in the liver and plasma and lowered the average size of adipocytes [14]. The results of another study showed that administration of phytosterols isolated from *A. vera* gel decreased visceral fat mass in diabetic Zucker-fatty rats [10]. Maharjan et al. (2010) reported that *A. vera* gel caused significant reductions in plasma TG and low-density lipoprotein cholesterol (LDL-C) levels, with an increase in high-density lipoprotein cholesterol (HDL-C) in rats with letrozole-induced polycystic ovarian syndrome [15]. In an effort to explain the beneficial effects of *A. vera* on body fat, Misawa et al. (2012) demonstrated that a 3-month administration of dried *A. vera* gel powder in obese rats significantly reduced both subcutaneous and visceral fat contents, as well as total body fat percentage [9]. Another study by Agarwal in 1985 on heart disease patients who consumed, for a period of 90 days, breads prepared with wheat flour and *A. vera* gel (two meals a day) showed a reduction in total lipids and serum cholesterol and TG [16]. Furthermore, Iji et al. (2010) reported a

significant reduction in plasma total cholesterol, TG and LDL-C after 4 weeks in Wistar rats treated with A. vera gel [17]. Moreover, Alinejad-Mofrad et al. (2015) observed similar results in a double-blind randomized controlled trial in pre-diabetic patients treated with A. vera extract for 8 weeks [18].

2. Antioxidant, Anti-inflammatory and Immunomodulatory Activities:

Natural antioxidants in A. vera, such as vitamin C, vitamin E, beta-carotene, phytosterols and anthraquinones have recently attracted the attention of researchers due to their roles in reducing the risk of different diseases associated with oxidative stress [19-21]. According to the results of in-vitro studies, A. vera gel in a dose-dependent manner can scavenge free radicals (2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and nitric oxide) [22]. As regards the antioxidant activities of aloe-anthraquinones, "aloin" was found to possess a strong antioxidant activity and also inhibit the cyclooxygenase pathway which, in turn, would result in decreased production of prostaglandin E2 from arachidonic acid. The anti-inflammatory role of A. vera could also be attributed to the above-mentioned mechanisms [6, 23, 24]. Furthermore, an animal study concluded that Aloe-emodin can protect the liver against carbon tetrachloride, an important factor in the induction of lipid peroxidation and inflammatory response in a rat model [25].

A. vera gel has a potent immunomodulatory property through down-regulating the production of lipopolysaccharide-induced pro-inflammatory and inflammatory cytokines such as interleukin 8 (IL-8), tumor necrosis factor alpha (TNF α), interleukin 6 (IL-6) and interleukin 1 beta (IL-1 β) [26]. Also, A. vera could significantly increase the phagocytic activity of the reticuloendothelial system which is essential for the immune system [27]. In an animal study, Madan et al. (2008) reported a considerable increase in the concentration of the total white blood cell count and macrophages after 5 days administration with an A. vera gel extract [28].

3. Antihyperglycemic Activity:

Several clinical and experimental studies have suggested antihyperglycemic and also higher insulin-sensitivity actions for the A. vera gel in the treatment of diabetes mellitus [8, 29, 30]. Possible mechanisms for the hypoglycemic effects of A. vera are as follow:

- a. Delaying intestinal digestion and absorption of macronutrients due to its fiber-like effect [5];
- b. Reducing insulin resistance by inhibiting the secretion of pro-inflammatory cytokines in muscle, liver, and adipose tissue [31];
- c. Reducing serum free fatty acid (FFA) and TG levels, which will result in higher insulin sensitivity [10];
- d. Increasing insulin secretion by preventing damage to pancreatic β -cells [32].

Tanaka et al. (2006) reported reductions in both fasting and random blood glucose levels of diabetic mice treated with phytosterols isolated from the A. vera gel [33]. In another study by Noor et al. (2008) 3 weeks oral feeding with an ethanolic A. vera extract in diabetic rats resulted in a reduction in the fasting blood glucose levels by 50% [34]. Similarly, Maithani et al. (2011) reported a reduction of 48% in blood sugar levels in albino rats after 15 days of treatment with an A. vera aqueous extract [35]. Furthermore, an A. vera gel supplement caused a reduction in body weight, body fat mass and insulin resistance in obese prediabetic and early untreated diabetic patients [36]. In another study by Rajasekaran et al. (2006) oral administration of an A. vera gel extract to streptozotocin-induced diabetic rats for 21 days led to considerable reductions in fasting blood glucose, hepatic transaminases (aspartate transaminase (AST) and alanine transaminase (ALT)), plasma cholesterol, FFA and TG, as well as a significant improvement in the plasma insulin level [12].

4. Anticancer Activity:

Over the past few years, several studies have reported an antitumor activity for A. vera gel as regards reduced tumor burden, tumor necrosis and higher survival rates [7]. In several in vitro and in vivo studies, researchers have noted several aloe components with remarkable antitumor activity including anthraquinone molecules (aloin and emodin) and polysaccharides, particularly "acemannan" [37-39]. Aloe anthraquinones exhibit an antiproliferative action in cancer cells, which is one of the basic mechanisms for antineoplastic property [40]. Also, it has been documented that aloin possesses an inhibitory effect in tumor angiogenesis and growth via blocking the secretion of vascular endothelial growth factor (VEGF) in cancer cells. VEGF is one of the main proangiogenic cytokines characterized as an inducer of tumor neovascularization [41].

According to some studies, acemannan has antitumor effects through its immunomodulatory action. The mechanism of immunostimulating activity of acemannan may be exerted through the induction of immune effector cells, such as macrophages [4, 42]. In an in vivo study, peritoneal macrophages treated with acemannan caused activation of the host immune system and regression of the implanted tumors [43].

Niciforovic et al. (2007) studied the effects of treatment with aloe aloin on human uterine carcinoma and reported that it could block the cell cycle in the "S phase" (synthesis phase), resulting in increased apoptosis of the carcinoma cells [40]. Similarly, Lin et al. (2006) showed that aloe emodin can induce apoptosis in human bladder cancer cells [44]. Also, the antiproliferative effect of emodin has been proved in lung, glioma, and neuroectodermal cancer cells [21].

5. Wound Healing Activity:

Wound healing is a reaction to restore the integrity of an injured tissue [45]. In several studies, it has been shown that A. vera gel could improve wound healing after topical and systemic usage [7, 24]. Several mechanisms have been suggested for wound healing activity of A. vera gel such as moisturizing capability, increasing epithelial cell migration, increasing maturation of collagen and reducing inflammation [46]. Moreover, some reports attribute this activity to the A. vera mono- and polysaccharides including mannose-6-phosphate and glucomannans. These components increase the proliferation of fibroblasts and also promote the production of hyaluronic acid and hydroxyproline in these cells, which will result in faster extracellular matrix recovery during wound healing [24, 47]. In an animal study, authors reported a 62.5% reduction in wound diameter due to oral administration of 100 mg/kg/day A. vera gel [48].

6. Antibacterial and Antiviral Activities:

Anthraquinones in A. vera such as, e.g., emodin, have a structure and function similar to those of tetracycline, one of the well-known antibacterial drugs. Aloe anthraquinones can destroy bacteria by inhibiting bacterial protein synthesis which, in turn, will prevent bacterial growth [49, 50]. Furthermore, aloe polysaccharides have been shown to eliminate bacteria through stimulation of phagocytic leucocytes [51]. A recent study reported a novel

effect for A. vera gel in regard to its action against helicobacter pylori infection, which is responsible for peptic ulcer [52]. One clinical trial has suggested that the intake of A. vera might be helpful in HIV-infected individuals through enhancing the body immune system [53]. Also, there is some evidence about the inhibitory effect of aloe anthraquinones on replication of influenza A virus [54].

Conclusion

This review summarizes the available scientific evidence regarding several nutritional and medicinal properties of Aloe vera. This plant has a long history as a medicinal plant with various phytotherapeutic applications. It contains many biologically active substances with hypolipidemic, hypoglycemic, antioxidant, anti-inflammatory, immune boosting, anticancer, wound healing, antibacterial and antiviral activities. Chemical compounds contained naturally in A. vera are expanding our disease treatment choices and benefit us with their wide range of properties for the management of diverse disorders. Therefore, it would be worthwhile to conduct further intensive scientific studies on this multipurpose medicinal plant to promote its large-scale utilization.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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