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## Phytochemistry, health benefits and toxicological profile of aloe

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### Abstract

Aloe is a perennial succulent of Liliaceae family and long been recognised for diverse medicinal preparations, extraction of drug and flavouring liquors. The exact origin of *Aloe* is uncertain, but is mainly grown in relatively warm and dry climate. Two major products derived from the leaves are the yellow bitter juice consisting of aloin and the gel rich in polysaccharides. It also includes vitamins, enzymes, anthraquinones/anthrones, chromones and many other primary as well as secondary metabolites. These are extensively used as active ingredients in laxative and in anti-obesity medicines, as emollient or wound healer in various cosmetic and pharmaceutical formulations. Many tribals have their own indigenous formulations from Aloe species to manage various ailments since ages. However, in spite of scores of beneficial role, sometimes a few chemicals present in Aloe make the products toxic which, of course, depends on the source, locality, person to be used, etc. The present study extensively reviews the phytochemistry, multi-dimensional health benefits and toxicological profile of Aloe species.

**Keywords:** Aloe sp, phytochemistry, pharmaceuticals, human health, toxicology

### 1. Introduction

Aloes are perennial succulents or xerophytes; they can adapt to habitats with low or erratic water availability, are characterized by the capacity to store large volumes of water in their tissue, and are able to use crassulacean acid metabolism, an adaptation to the photosynthetic pathway that involves the formation of malic acid (Boudreau *et al.*, 2013; Davis *et al.*, 2006) [9, 14]. Many species of Aloe appear to be stemless, with the rosette, thick, fleshy leaves growing directly at ground level. Aloe flowers are yellow, orange, pink, or red coloured, tubular and are borne densely clustered and pendant, at the apex of simple or branched, leafless stems. They vary in colour from grey to bright-green and are sometimes striped or mottled. Some aloes, native to South Africa, are tree-like (Arborescent).

### 2. Systematic Position

Kingdom	:	Plantae
Clade	:	Angiosperms
Clade	:	Monocots
Order	:	Asparagales
Family	:	Asphodelaceae
Subfamily	:	Asphodeloideae
Tribe	:	Aloeeae
Genus	:	<i>Aloe</i>

### 3. Habitat

The exact origin of *Aloe vera* is uncertain. It is mainly grown in relatively warm and dry climate (Raphael, 2012) [38]. Naturalized stands of Aloe occur through North Africa in Algeria, Morocco, and Tunisia, along with the Canary and Madeira Islands. Habitats described that it was spread throughout the mediterranean region by man including the area surrounding the Mediterranean Sea in Europe, some parts of the southwestern United States, Southern Australia, and the eastern and southern parts of Africa. Its closest relatives, however, occur in Arabia, and this is its most probable area of origin. During the 17th century, the species was introduced to China, India, Pakistan and various parts of southern Europe.

### 4. Phytochemistry

The aloe parenchyma tissue or pulp has been shown to contain (Hamman, 2008) [21] proteins, chromones lipids, anthraquinones, amino acids, vitamins, enzymes, inorganic compounds, small organic compounds and different types of carbohydrates. (Table 1)

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**4.1 Anthraquinones/anthrones:** Rajeswari *et al.* (2012) [37] reported that Aloe contains two classes of Aloins: (1) nataloins, which yield picric and oxalic acids with nitric acid, and do not give a red coloration with nitric acid; and (2) barbaloins, which yield aloetic acid (C<sub>7</sub>H<sub>2</sub>N<sub>3</sub>O<sub>5</sub>), chrysammic acid (C<sub>7</sub>H<sub>2</sub>N<sub>2</sub>O<sub>6</sub>), picric and oxalic acids with nitric acid, being reddened by the acid. This second group may be divided into a-barbaloins, obtained from Barbados aloes, and reddened in the cold, and barbaloins, obtained from Socotrine and Zanzibar aloes, reddened by ordinary nitric acid when warmed or by fuming acid in the cold. Nataloin forms bright yellow scales. Barbaloin forms yellow prismatic crystals. It provides 12 anthraquinones, which are phenolic compounds known as laxatives. Aloin and emodin act as analgesics, antibacterials and antivirals (Surjushe *et al.*, 2008) [50]. Lupeol and salicylic acid, two very effective pain-killers, are present in the juice.  $\beta$ -sitosterol is also a powerful anti-cholesterol which helps to lower harmful cholesterol levels, helping to explain its many benefits for heart patients.

**4.2 Chromones:** 8-C-glucosyl-(2'-O-cinnamoyl)-7-O-methylaloediol A, 8-C-glucosyl-7-O-methylaloediol, 8-C-glucosyl-noreugenin, isoaloeresin D, isorabaichromone, neoaloesin A.

**4.3 Enzymes:** certain enzymes present are alkaline phosphatase, amylase, carboxypeptidase, catalase, cyclooxygenase, lipase, cyclooxygenase, oxidase, phosphoenolpyruvate carboxylase, superoxide dismutase, Bradykinase (It helps to reduce excessive inflammation when applied to the skin topically, while others help in the breakdown of sugars and fats).

**4.4 Inorganic substances:** Calcium, chlorine, chromium, copper, iron, magnesium, manganese, potassium, phosphorous, sodium, zinc. They are essential for proper enzyme system functioning in different metabolic pathways and few are antioxidants.

**4.5 Hormones:** Auxins and gibberellins that help in wound healing and have anti-inflammatory action.

**4.6 Organic compounds and lipids:** Arachidonic acid,  $\gamma$ -linolenic acid, steroids (campesterol, cholesterol,  $\beta$ -sitosterol),

triglycerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, uric acid

**4.7 Carbohydrates:** Pure mannan, acetylated mannan, galactan, galactogalacturan, pectic substance, arabinogalactan, xylan, cellulose, galactoglucoarabinomannan, acetylated glucomannan, glucogalactomannan are sugars found in *Aloe vera* (Hutter *et al.*, 1996) [23].

**4.8 Non-essential and essential amino acids:** Alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tyrosine, valine

**4.9 Proteins:** Lectins, lectin-like substance.

Aloe juice contains about 23 polypeptides which improves immune system. The polypeptides plus the anti-tumor agents, Aloe emodin and Aloe lectins, are now also used in treatment of cancer.

**4.10 Saccharides:** Mannose, glucose, aldopentose

**4.11 Vitamins:** A ( $\beta$ -carotene), C and E, B1, B2, B6, C,  $\beta$ -carotene, choline, folic acid,  $\alpha$ -tocopherol. Vitamins are antioxidant which neutralizes free radicals.

**4.12 Fatty acids:** It provides 4 plant steroids; cholesterol, campesterol,  $\beta$ -sitosterol and lupeol.

**4.13 Fatty acids:** present are highly effective in treatment of burns, cuts, scrapes, abrasions, allergic reactions, rheumatoid arthritis, rheumatic fever, acid indigestion, ulcers, plus many inflammatory conditions of the digestive system and other internal organs, including the stomach, small intestine, colon, liver, kidney and pancreas.

### 5. Active Ingredients of *Aloe vera* Leaf Pulp and Exudates

*Aloe vera* contains mixture of glucosides collectively called aloin which is the active constituent of various drugs. It also contains 200 potentially active constituents viz., vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids, which are responsible for the multifunctional activity of Aloe. Vitamins include Vitamin A (beta-carotene), C and E, which are antioxidants.

**Table 1:** Major components of *Aloe* with specific compounds present

Class	Compounds
Vitamins	B1, B2, B6, C, A( $\beta$ -carotene), choline, folic acid, $\alpha$ -tocopherol
Enzymes	Alkaline phosphatase, amylase, carboxypeptidase, catalase, bradikininase, cyclooxygenase, peroxidase, carboxypeptidase.
Anthraquinones/anthrones inorganic compounds	Aloe-emodin, aloetic-acid, anthranol, aloin A and B (or collectively known as barbaloin), isobarbaloin, anthrones emodin, ester of cinnamic acid
Carbohydrates	Pure mannan, acetylated mannan, acetylated glucannan (acemannan), galactan, glucogalactomannan, galactogalacturan, galactoglucoarabinomannan, arabinogalactan, pectic substance, xylan, cellulose
Saccharides	Mannose, glucose, L-rhamnose, aldopentose
Organic compounds and lipids	Arachidonic acid, $\omega$ -linolenic acid, steroids (campesterol, cholesterol, $\beta$ -sitosterol), triglycerides, Arachidonic acid, $\omega$ -linolenic acid, steroids (campesterol, cholesterol, $\beta$ -sitosterol), triglycerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, uric acid
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-methylaloediol, 8-C-glucosyl-noreugenin, isoaloeresin D, isorabaichromone
Non-essential and essential amino acids:	Alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tyrosine, valine

(Source: Gupta and Malhotra, 2012)



in hyper lipidemic patients, but also with acute hepatitis (liver disease).

**6.9 Anti-stress properties:** Aloe juice is helpful in smooth functioning of the body machinery. It reduces cell-damaging process during stress condition and minimizes biochemical and physio-logical changes in the body. *Aloe vera* is an excellent example of a functional food that plays a significant role in protection from oxidative stress (Joseph *et al.*, 2010) [25].

**6.10 Antiviral properties:** Several ingredients in *Aloe vera* gel have been shown to be effective antiviral agent. Lectins present in *Aloe vera* gel, directly inhibits the cytomegalovirus proliferation in cell culture, perhaps by interfering with protein synthesis. A purified sample of aloe emodin is effective against infectivity of herpes simplex virus Type I and Type II. It is responsible for the inactivation of all of the viruses, including varicella- zoster virus, influenza virus, and pseudorabies virus. The findings of Rezazadeh *et al*(2016) [40] suggested that *Aloe vera* gel can be a useful topical treatment for oral HSV-1 infections.

**6.11 Antifungal properties:** A study on the mycellium development of *Rhizoctonia solani*, *Fusarium oxysporum*, and *Colletotrichum coccodes* showed an inhibitory effect of the pulp of *A. vera* 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*. For bacteria, inner leaf gel from *Aloe vera* was shown to inhibit growth of *Streptococcus* and *Shigella* species in vitro. Agarry *et al.*, (2005) [2] reported that the Aloe gel inhibited the growth of *Trichophyton mentagrophytes* (20.0 mm), while the leaf possesses inhibitory effects on both *Pseudomonas aeruginosa* and *Candida albicans*.

**6.12 Anti-bacterial properties:** *Aloe vera* gel is an excellent bactericidal agent. It can prevent human lung epithelial cells from adhering in a monolayer culture. The aloe extract was particularly potent against three strains of Mycobacterium (*M. fortuitum*, *M. smegmatis* and *M. kansasii*) and a strong antimycobacterial activity against *M. tuberculosis* as well as antibacterial activity against *P. aeruginosa*, *E. coli*, *S. aureus* and *S. typhi*. *Aloe vera* was shown to inhibit microbes like *Staphylococcus aureus*, *Candida albicans* *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. It has indirect antimicrobial property through self-ability to stimulate the phagocytic leukocytes. Jain *et al.* (2016) [24] studied on antibacterial effect of *Aloe vera* gel against oral pathogens and found that higher concentrations (100%, 50%) of AVG had comparable zone of inhibition with Ofloxacin (5mcg) and Ciprofloxacin (30mcg).

**6.13 Cosmetic and Skin protection:** *Aloe vera* is used as skin tonic in cosmetic industry (Kaushik *et al.*, 2016) [30]. It is extensively used to heal skin wounds, burn and helps in speeding post-surgery recovery. The *Aloe* gels are applied on dry skins to give them glowing effect, reducing acne, pimples, sunburn, screening out x-ray radiation. It has been reported to have a protective effect against radiation damage to the skin. Following the administration of *Aloe 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. Adding sap or other derivatives from *Aloe vera* is essential for cosmetic producers to products such as make up, tissues, moisturizers, soaps, sunscreens, incense, razors and shampoos.

**6.14 Moisturizing and Anti-aging agent:** *Aloe vera* helps to fight against the dry skin and shingles; reduce psoriasis, warts and ageing, wrinkles and eczema. Muco-polysaccharides present in *Aloe* help in binding moisture into the skin. On the other hand, hardened skin cells are softened by the amino acids and zinc acts as an astringent to tighten pores. *Aloe vera* gel improved the skin integrity, decrease appearance of acne wrinkle and decrease erythema (Rajeswari *et al.*,2012) [37]. The gel gives a cooling effect and acts as a moisturizing agent. It also has a significant role in gerontology and rejuvenation of aging skin.

**6.15 Anti-tumour properties:** A number of glycoproteins present in *Aloe vera* gel have been reported to have antitumor and antiulcer effects and to increase proliferation of normal human dermal cells (Sahu *et al.*, 2013) [41]. In recent studies, a 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.

**6.16 Laxative effects:** 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. Anthraquinones present in latex are a potent laxative. It stimulates mucus secretion, increase intestinal water content and intestinal peristalsis (Sahu *et al.*, 2013) [41]. These are due primarily to the 1, 8-dihydroxyanthracene glycosides, aloin A and B (formerly designated barbaloin). 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, which acts as a stimulant and irritant to the gastrointestinal tract.

**6.17 Biomedical applications:** *Aloe vera*, being non-toxic, having no known side effects, and having the powerful aloin content with diverse positive roles, has a long association with herbal medicine, As such it is used widely in the traditional herbal medicine of China, Japan, Russia, South Africa, The United States, Jamaica and India. Gao *et al.*, (2018) [18] reported that over the last centuries, *Aloe vera* have been extensively studied for various therapeutic activities including anti-bacterial, antiviral, anti-cancer activity, as well as immunoregulative and hepatoprotective properties. Qadir (2009) [34] reported about the scientific evidence for the cosmetic and therapeutic effectiveness of *Aloe vera*.

**6.18 Healing properties:** *Aloe vera* plants are helpful in healing insect bites, rashes, sores, herpes, urticaria, fungal infections, vaginal infections, conjunctivitis, and allergic reactions (Surjushe *et al.*,2008) [50]. The cumulative evidence supports the use of *Aloe vera* for the healing of first to second degree burns (Reddy *et al.*, 2011) [39]. The effective components for wound healing may be tannic acid and a type of polysaccharide. It may also be due to glucomannan, a mannose-rich polysaccharide and gibberellin a growth hormone interacts with growth factor receptors on the

fibroblast thereby stimulating its activity and proliferation which in turn significantly increase collagen synthesis after topical and oral *Aloe vera*. Aloe gel not only increased collagen content of the wound but also changed collagen composition and increased the degree of collagen cross linking.

Apart from the above, *Aloe vera* is being traditionally used by indigenous tribes of different areas since prehistoric times. The following table (Table 2) highlights the indigenous technical knowledge of the tribal as well as rural people used in crude or refined formulations from the plant alone or in combination with other ingredients.

**Table 2:** Use of *Aloe vera* as ITK medicine:

S. No	Major ITK Uses of <i>Aloe vera</i>	Preparation of the formulation
1.	for sunstroke	<i>Aloe vera</i> leaf is mixed with sugar, water and few drops of essence prepared naturally from roots of herbs. It is to be consumed 2 to 3 times a day.
2.	for improving digestive system	Tribal people uses both the dried leaf powdered form and gel form.
3.	for teeth and gums	The tribal people mix <i>Aloe vera</i> leaf gel with wood ash or wood charcoal and use it to clean the teeth.
4.	for dysmenorrhea	The tribal people prepares fresh <i>Aloe vera</i> leaf juice by adding little honey to it and taking 3 times a day so that it will smooth the flow of blood, relaxes uterine muscles and reduce excessive pain.
5.	for eye problems	<i>Aloe vera</i> gel mixed with a pinch of alum (potassium aluminum sulfate) in a cloth and ultimately to put it on the eyes. This is to be done as many times as possible so that it reduces redness, eye rashes and watering.
6.	for ear and nose infections	Dried <i>Aloe vera</i> leaf gel powder mixed with raw turmeric juice put few drops into ear and nose 3 to 4 times a day to reduce infections.
7.	for spleen enlargement	<i>Aloe vera</i> leaf gel mixed with pinch of dried turmeric powder and pinch of powdered dried seeds of bitter gourd, add little sugar to make it sweet and taken 2 times a day.
8.	for diarrhea	<i>Aloe vera</i> leaf gel mixed with few drops of raw garlic juice, and a pinch of dried turmeric powder, mix them to make a homogeneous paste and taken 2 to 3 spoons three times a day.
9.	for uterine and cervical cancer	<i>Aloe vera</i> leaf gel mixed with few drops of fresh tuberous root juice of asparagus racemose and taken for 2 to 3 times a day.
10.	for constipation	<i>Aloe vera</i> leaf gel mixed with milk and water make it as a thick milk shake and drink it before going to bed every day.
11.	for rectal infection and ulcers	Dried <i>Aloe vera</i> leaf gel powder mixed with few drops of coconut oil and mix it completely until it becomes homogeneous thick paste, applied at the affected area, also apply inside the rectum with the help of a finger.
12.	for lowering cholesterol in the blood	daily intake of 10 ml or 20 ml of aloe for 3 months is helpful.
13.	for miscarriage and anti-Abortive	<i>Aloe vera</i> leaf gel mixed with homemade jaggery (Indian traditional sugar) and few drops of Ghee (Indian butter) taken at bed time, at the time of ovulation every month.
14.	for arthritis, joint pain, body pain, muscle pain, etc	Young <i>Aloe vera</i> leaf gel mix with pinch of white pepper and few drops of garlic juice, add some sugar to make it sweet and eat two spoons three times a day.
15.	for increasing potentiality and sperm count	Young <i>Aloe vera</i> leaf gel mixed with 2 to 3 dried cloves of garlic and onion taken 2 to 3 times a day
16.	for heart disease	<i>Aloe vera</i> leaf gel mixed with few drops of garlic juice, and pinch of black salt taken 3 times a day.
17.	For depression, stress release, anger management, stability management etc	<i>Aloe vera</i> leaf gel mixed with little amount of old tamarind (fruit in black color) boil to make a soup, mix pinch of salt and taken as a soup two times a day, it will stabilize the brain cells by initiating the adrenal gland to release hormones that can control stress, depression, anxiety and make stable etc.
18.	for cuts and wounds	<i>Aloe vera</i> leaf gel mixed with pinch of dried turmeric powder and mix it properly for few minutes until it become homogeneous mixture and applied it on the affected areas as well as taking <i>Aloe vera</i> leaf gel orally enhances wound healing.
19.	for white hair reduction, hair fall, ticks, mites, dandruff, baldness, grey hair, dry split hair etc.	<i>Aloe vera</i> leaf gel mixed with traditionally prepared double distilled alcohol and few drops of sesame oil mix it properly for homogeneous mixture and applied to the head before going to bed.
20.	for piles	Half tea spoon of dried <i>Aloe vera</i> leaf gel powder mixed with pinch of hing (Asafoetida) powder and few drops of sesame make it a homogeneous mixture and apply at the affected area before bed.
21.	for lower abdomen pain	Half tea spoon of dried <i>Aloe vera</i> leaf gel powder mixed with water and warm to make a homogeneous paste, apply to the lower part of the abdomen to relieve pain.
22.	for migraine	Dried <i>Aloe vera</i> leaf gel powder mixed with neem ( <i>Azadirachta indica</i> ) seed oil and applied to the head for a period of three months which effectively stabilizes the migraine
23.	for breast pain	The application of <i>Aloe vera</i> leaf gel to the breast will give the best results for breast pain. <i>Aloe vera</i> leaf gel dried powder mixed with small amount of coconut oil and a pinch of camphour is applied on the area where the pain is more
24.	for tuberculosis	Pinch of Dried leaf gel powder mix with pinch of venugaram (Borax) ( $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ ) in a glass of milk and taken two times a day.
25.	for stomach ulcers, heart burn, indigestion	Pinch of Dried leaf gel powder mix with milk and ghee (Indian homemade butter) and taken at bed time daily which will reduce steadily heart burns and stomach ulcers.
26.	for dysentery	Dried <i>Aloe vera</i> leaf gel powder mixed with sulphate of iron in three table spoons of freshly prepared curd and taken 2 to 3 times a day until the infection completely decreases.
27.	for sexually transmitted infections, endometriosis and presence of fibroids in uterus, gonorrhoea etc.	<i>Aloe vera</i> gel mixed with two spoons of milk and water applied in the affected areas, and at the same time <i>Aloe vera</i> gel mixed with pinch of dried garlic powder is taken orally 3 times a day.
28.	for pimples and achiness	<i>Aloe vera</i> leaf gel can be directly applied to the face or mixed with a pinch of dried facial turmeric powder and a pinch of sandal wood powder until it become homogeneous mixture and applied on the affected areas or complete face

29.	for stretch marks	Apply <i>Aloe vera</i> leaf gel directly on the affected area to get rid of stretch marks, and for best results apply 3 to 4 times a day.
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## 7. Toxicological effects

In spite of all the beneficial effects of *Aloe vera* gel, it can also have certain side effects that may affect overall human health as follows:

- Many people are allergic to *Aloe vera* latex, which can cause stomach issues like irritation, stomach cramps and low potassium levels. Externally, latex could be safe, if applied appropriately. However, more research is required.
- Most people can be allergic to the *Aloe vera* gel, causing skin allergies, redness in the eyes, skin rashes, irritation and burning sensation.
- Consuming *Aloe vera* juice might cause the blood sugar levels to drop.
- The laxative effects of *Aloe vera* can lead to dehydration. Laxatives are generally used to alleviate constipation; however, if taken in more quantity than recommended, they may cause dehydration.
- The irritant qualities of *Aloe vera* juice may stimulate uterine contractions in pregnant women, which may lead to birth complications.
- As the juice may lower the levels of potassium in the body causing further irregular heartbeat, weakness and fatigue, it is unsafe for elderly and sick people.
- The bio-active compounds in *Aloe vera* might interfere with liver's detoxification process, further causing health complications.
- The *Aloe vera* latex can cause excessive cramps and pain case of stomach discomfort (Sundarkar *et al.*, 2011; Kareman *et al.*, 2013; Akev *et al.*, 2015; Ahmada *et al.*, 2016) [49, 29, 5, 4].
- Allergy-sensitive individuals should avoid intake of this product as it may cause redness, burning, stinging sensation and rarely generalized dermatitis. anthraquinones, such as aloin and barbaloin are mostly responsible for this kind of allergic reactions. (Dhikav *et al.*, 2002; Sharma *et al.*, 2014; Ahluwalia *et al.*, 2016) [15, 44, 3].

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