

WHO
*monographs
on selected
medicinal plants*

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Contents

Acknowledgements	v
Introduction	1

Monographs (*in alphabetical order of plant name*)

Bulbus Allii Cepae	5
Bulbus Allii Sativi	16
Aloe	33
Aloe Vera Gel	43
Radix Astragali	50
Fructus Bruceae	59
Radix Bupleuri	67
Herba Centellae	77
Flos Chamomillae	86
Cortex Cinnamomi	95
Rhizoma Coptidis	105
Rhizoma Curcumae Longae	115
Radix Echinaceae	125
Herba Echinaceae Purpureae	136
Herba Ephedrae	145
Folium Ginkgo	154
Radix Ginseng	168
Radix Glycyrrhizae	183
Radix Paeoniae	195
Semen Plantaginis	202
Radix Platycodi	213
Radix Rauwolfiae	221
Rhizoma Rhei	231
Folium Sennae	241
Fructus Sennae	250
Herba Thymi	259

Aloe

Definition

Aloe is the dried juice of the leaves of *Aloe vera* (L.) Burm. f. or of *A. ferox* Mill. and its hybrids with *A. africana* Mill. and *A. spicata* Baker (Liliaceae) (1-6).

Synonyms

Aloe vera (L.) Burm. f.

Aloe barbadensis Mill., *Aloe 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. (7).

In most formularies and reference books, *Aloe barbadensis* Mill. is regarded as the correct species name, and *Aloe vera* (L.) Burm. f. is considered a synonym. However, according to the International Rules of Botanical Nomenclature, *Aloe vera* (L.) Burm. f. is the legitimate name for this species (8-10). The genus *Aloe* has also been placed taxonomically in a family called Aloaceae.

Aloe ferox Mill.

Aloe horrida Haw., *A. perfoliata* Thunberg., *A. pseudoferox* Salm. Dyck, *A. socotrina* Masson., *A. supralaevis* Haw., *Pachydendron ferox* Humb. & Bonpl., *P. supralaeve* Haw. (7).

Selected vernacular names

Aloe capensis, aloe curacao, aloe vera, aloes, aloès, aloès du Cape, aloès féroce, aloes vrai, aloès vulgaire, alovis, Barbadoes aloe, Barbadoes aloes, Barbados aloe, Bergaalwyn, Bitteraalwyn, Cape aloe, chirukattali, Curacao aloe, Curacao aloes, Curacao alos, Echte Aloe, ghai kunwar, ghai kunwar, gheekuar, ghikanvar, ghikuar, ghikumar, ghikumari, ghikwar, ghiu kumari, ghrita kumari, ghritakumari, grahakanya, gwar-patha, haang takhe, hlaba, Indian aloe, jadam, korphad, kumari, kumaro, kunvar pata, kunwar, laloi, laluwe, lo-hoei, lo-hoi, lou-houey, lu wei, luchuy, manjikattali, Mediterranean aloe, murr sbarr, musabar, rokai, sabbara, saber, sábila, sabilla, sabr, saibr, savila, savilla, semper vivum, shubiri, sibr, siang-tan, star cactus, tuna, umhlaba, waan haang charakhe, wan-hangchorakhe, yaa dam, yadam, zábila, zambila (1, 7, 11).

Description

Aloe vera (L.) Burm. f.

Succulent, almost sessile perennial herb; leaves 30–50 cm long and 10 cm broad at the base; colour pea-green (when young spotted with white); bright yellow tubular flowers 25–35 cm in length arranged in a slender loose spike; stamens frequently project beyond the perianth tube (12).

Aloe ferox Mill.

Arborescent perennial shrub with a single stem of 2–3 m in height, crowned by a large rosette of numerous leaves which are glaucous, oval-lanceolate, 40–60 cm in length, thorny on the ridge and the edges; inflorescence an erect raceme 60 cm in height; flowers with perianth 2.5 cm in length, red, yellow, or orange (2).

Plant material of interest: dried juice

Solidified juice originating in the cells of the pericycle and adjacent leaf parenchyma, and flowing spontaneously from the cut leaf, allowed to dry with or without the aid of heat.

It is not to be confused with Aloe Vera Gel, which is the colourless mucilaginous gel obtained from the parenchymatous cells in the leaves of *Aloe vera* (L.) Burm. f. (13).

General appearance

Curacao or Barbados Aloe, derived from *Aloe vera* (L.) Burm. f.

The dried juice occurs in dark chocolate-brown usually opaque masses; fracture, dull waxy, uneven, and frequently conchoidal (2, 6).

Cape Aloe, derived from *A. ferox* Mill. and its hybrids with *A. africana* Mill. and *A. spicata* Baker

The dried juice occurs in dark brown or greenish brown glassy masses, often covered with a yellowish powder; in thin fragments it is transparent and exhibits a yellowish, reddish brown or greenish tinge; fracture, smooth, even, and glassy (2, 6).

Organoleptic properties

Aloe is marketed as opaque masses that range from reddish black to brownish black to dark brown in colour. Odour, characteristic and disagreeable; taste, somewhat sour, nauseating and very bitter (2, 7, 12).

Microscopic characteristics

See "Powdered plant material" below.

Powdered plant material

Powdered aloes are yellowish brown to dark reddish brown. Microscopically, Cape Aloe appears as transparent brown or greenish brown irregular and angular fragments; Curacao Aloe shows fragments with numerous minute acicular crystals embedded in an amorphous matrix (1-3, 12, 14).

Geographical distribution

Native to southern and eastern Africa, and subsequently introduced into northern Africa, the Arabian peninsula, China, Gibraltar, the Mediterranean countries, and the West Indies (15). It is commercially cultivated in Aruba, Bonaire, Haiti, India, South Africa, the United States of America, and Venezuela (2, 7, 12, 14, 15).

General identity tests

Macroscopic and microscopic examinations (1-3, 7, 12, 14); solvent solubility (hot alcohol, boiling water, and ether) determination (2, 4-6); chemical reactions (1-6, 8, 12-14); and thin-layer chromatographic analysis employing barbaloin as the reference standard (4-7).

Purity tests

Microbiology

The test for *Salmonella* spp. in aloe products should be negative. The maximum acceptable limits of other microorganisms are as follows (16-18). For preparation of decoction: aerobic bacteria—not more than 10^7 /g; fungi—not more than 10^5 /g; *Escherichia coli*—not more than 10^2 /g. Preparations for internal use: aerobic bacteria—not more than 10^5 /g or ml; fungi—not more than 10^4 /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^5 /g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter

Adulterants: Aloe in commerce may sometimes be adulterated with black catechu, pieces of iron, and stones. These can be detected by examining alcohol-soluble extracts under ultraviolet light which gives a deep brown colour with aloe and a black colour with catechu (14).

Total ash

Not more than 2% (3-5).

Water-soluble extracts

Not less than 50% (1, 2, 14).

Alcohol-insoluble extracts

Not more than 10% (1-3, 14).

Moisture

Not more than 10% for Cape Aloe (6), and not more than 12% for Curacao or Barbados Aloe (2-6, 14).

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Aloe is not more than 0.05 mg/kg (18). For other pesticides, see the WHO guidelines on quality control methods for medicinal plants (16) and guidelines for predicting dietary intake of pesticide residues (19).

Heavy metals

Recommended lead and cadmium levels are not more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (16).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (16).

Other tests

Acid-insoluble ash and chemical tests to be established in accordance with national requirements.

Chemical assays

Thin-layer chromatography and microchemical analyses are employed for the qualitative analysis for the presence of anthracene glycosides (4-7, 12, 14). Quantitative analysis of total anthracene glycosides, calculated as barbaloin, is performed by spectrophotometry (4, 5).

Curacao or Barbados Aloe, derived from Aloe vera (L.) Burm. f.

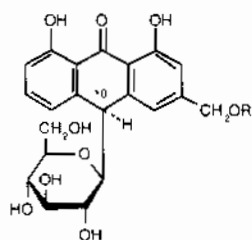
Contains not less than 28% of hydroxyanthracene derivatives, expressed as barbaloin (4-6).

Cape Aloe, derived from *A. ferox* Miller and its hybrids with *A. africana* Mill. and *A. spicata* Baker

Contains not less than 18% of hydroxyanthracene derivatives, expressed as barbaloin (4, 5).

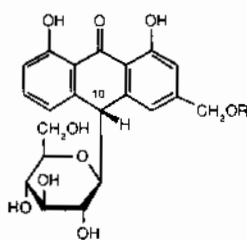
Major chemical constituents

Aloe contains as its major and active principles hydroxyanthrone derivatives, mainly of the aloe-emodin-anthrone 10-C-glucoside type. The major constituent is known as barbaloin (aloin) (15–40%) (8, 13). It also contains hydroxyaloin (about 3%). Barbaloin (=aloin) is in fact a mixture of aloin A (10S) [1] and B (10R) [2]. *A. ferox* also contains aloinoside A [3] and B [4]. Aloin A and B interconvert through the anthranol form as do aloinoside A and B (13).



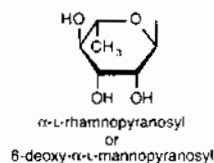
[1] R = H

[3] R = α -L-rhamnopyranosyl



[2] R = H

[4] R = α -L-rhamnopyranosyl



Dosage forms

Powdered, dried juice and preparations thereof for oral use.

Medicinal uses

Uses supported by clinical data

Short-term treatment of occasional constipation (2, 12, 13, 15).

Uses described in pharmacopoeias and in traditional systems of medicine

None.

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of seborrhoeic dermatitis, peptic ulcers, tuberculosis, and fungal infections, and for reduction of blood sugar (glucose) levels (11, 20).

Pharmacology

Experimental pharmacology

As shown for senna, Aloe's mechanism of action is twofold. It stimulates colonic motility, augmenting propulsion and accelerating colonic transit, which reduces fluid absorption from the faecal mass. It also increases paracellular permeability across the colonic mucosa probably owing to an inhibition of Na^+ , K^+ -adenosine triphosphatase or to an inhibition of chloride channels (8, 21, 22), which results in an increase in the water content in the large intestine (21).

Clinical pharmacology

The laxative effects of Aloe are due primarily to the 1, 8-dihydroxyanthracene glycosides, aloin A and B (formerly designated barbaloin) (23, 24). 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) (25, 26), which like senna acts as a stimulant and irritant to the gastrointestinal tract (27). The laxative effect of Aloe is not generally observed before 6 hours after oral administration, and sometimes not until 24 or more hours after.

Toxicity

The major symptoms of overdose are griping and severe diarrhoea with consequent losses of fluid and electrolytes. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored in all recipients, especially in children and the elderly (28).

Contraindications

As with other stimulant laxatives, products containing Aloe should not be used in patients with intestinal obstruction or stenosis, atony, severe dehydration with electrolyte depletion, or chronic constipation (28). 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 under 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, haemorrhoids, nephritis, or any undiagnosed abdominal symptoms such as pain, nausea, or vomiting (28, 29).

Warnings

Aloe-containing products should be used only if no effect can be obtained through a change of diet or use of bulk-forming products. Stimulant laxative products should not be used when abdominal pain, nausea, or vomiting are present. Rectal bleeding or failure to have a bowel movement within 24 hours

after use of a laxative may indicate a serious condition. Chronic use may cause dependence and need for increased dosages, disturbances of water and electrolyte balance (e.g. hypokalaemia), and an atonic colon with impaired function (28).

The use of stimulant laxatives for more than 2 weeks requires medical supervision.

Chronic abuse with diarrhoea and consequent fluid and electrolyte losses (mainly hypokalaemia) may cause albuminuria and haematuria, and may result in cardiac and neuromuscular dysfunction, the latter particularly in the case of concomitant use of cardiac glycosides (digoxin), diuretics, corticosteroids, or liquorice root (see Precautions below).

Precautions

General

Laxatives containing anthraquinone glycosides should not be used continuously for longer than 1–2 weeks, owing to the danger of electrolyte imbalance.

Drug interactions

Decreased intestinal transit time may reduce absorption of orally administered drugs (30).

Existing hypokalaemia resulting from long-term laxative abuse can potentiate the effects of cardiotoxic glycosides (digitalis, strophanthus) and antiarrhythmic drugs such as quinidine (30). The induction of hypokalaemia by drugs such as thiazide diuretics, adrenocorticosteroids, and liquorice root may be enhanced, and electrolyte imbalance may be aggravated (31).

Drug and laboratory test interactions

Standard methods may not detect anthranoid metabolites, so measurements of faecal excretion may not be reliable (26).

Urinary excretion of certain anthranoid metabolites may discolour the urine, which is not clinically relevant but which may cause false positive results for urinary urobilinogen, and for estrogens when measured by the Kober procedure (30).

Carcinogenesis, mutagenesis, impairment of fertility

Data on the carcinogenicity of Aloe are not available. While chronic abuse of anthranoid-containing laxatives was hypothesized to play a role in colorectal cancer, no causal relationship between anthranoid laxative abuse and colorectal cancer has been demonstrated (32–35).

In vitro (gene mutation and chromosome aberration tests) and *in vivo* (micro-nucleus test in murine bone marrow) genotoxicity studies, as well as human and animal pharmacokinetic data, indicate no genotoxic risk from Cape Aloe (36–38).

Pregnancy: teratogenic effects

No teratogenic or fetotoxic effects were seen in rats after oral treatment with aloe extract (up to 1000 mg/kg) or aloin A (up to 200 mg/kg) (39).

Pregnancy: non-teratogenic effects

Aloe should not be used during pregnancy except under medical supervision after benefits and risks have been evaluated (40).

Nursing mothers

Anthranoid metabolites appear in breast milk. Aloe should not be used during lactation except under medical supervision, as there are insufficient data available to assess the potential for pharmacological effects in the breast-fed infant (30, 40).

Paediatric use

Oral use of Aloe in children under 10 years old is contraindicated.

Adverse reactions

Abdominal spasms and pain may occur after even a single dose. Overdose can lead to colicky abdominal spasms and pain, as well as the formation of thin, watery stools (28).

Chronic abuse of anthraquinone stimulant laxatives can lead to hepatitis (41). Long-term laxative abuse may lead to electrolyte disturbances (hypokalaemia, hypocalcaemia), metabolic acidosis, malabsorption, weight loss, albuminuria, and haematuria (30, 42, 43). Weakness and orthostatic hypotension may be exacerbated in elderly patients when stimulant laxatives are repeatedly used (31). 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 (44, 45). Melanotic pigmentation of the colonic mucosa (pseudomelanosis coli) has been observed in individuals taking anthraquinone laxatives for extended time periods (29, 42). The pigmentation is clinically harmless and usually reversible within 4 to 12 months after the drug is discontinued (29, 42). Conflicting data exist on other toxic effects such as intestinal-neuronal damage after long-term use (42, 46).

Posology

The correct individual dose is the smallest amount required to produce a soft-formed stool (26). As a laxative for adults and children over 10 years old, 0.04–0.11 g (Curacao or Barbados Aloe) or 0.06–0.17 g (Cape Aloe) of the dried juice (6, 14), corresponding to 10–30 mg hydroxyanthraquinones per day, or 0.1 g as a single dose in the evening.

References

1. *The United States pharmacopeia XXIII*. Rockville, MD, US Pharmacopeial Convention, 1996.
2. *African pharmacopoeia, Vol. 1*, 1st ed. Lagos, Organization of African Unity, Scientific, Technical & Research Commission, 1985.
3. *The Japanese pharmacopoeia XIII*. Tokyo, The Society of Japanese Pharmacopoeia, 1996.
4. *Pharmacopée française*. Paris, Adrapharm, 1996.
5. *European pharmacopoeia*, 2nd ed. Strasbourg, Council of Europe, 1995.
6. *British pharmacopoeia*. London, Her Majesty's Stationery Office, 1993.
7. Hänsel R et al., eds. *Hagers Handbuch der Pharmazeutischen Praxis, Vol. 6*, 5th ed. Berlin, Springer, 1994.
8. Bradley PR, ed. *British herbal compendium, Vol. 1*. Bournemouth, British Herbal Medicine Association, 1992:199-203.
9. Newton LE. In defence of the name *Aloe vera*. *The cactus and succulent journal of Great Britain*, 1979, 41:29-30.
10. Tucker AO, Duke JA, Foster S. Botanical nomenclature of medicinal plants. In: Cracker LE, Simon JE, eds. *Herbs, spices and medicinal plants, Vol. 4*. Phoenix, AR, Oryx Press, 1989:169-242.
11. Farnsworth NR, ed. *NAPRALERT database*. Chicago, University of Illinois at Chicago, IL, August 8, 1995 production (an on-line database available directly through the University of Illinois at Chicago or through the Scientific and Technical Network (STN) of Chemical Abstracts Services).
12. Youngken HW. *Textbook of pharmacognosy*, 6th ed. Philadelphia, Blakiston, 1950.
13. Bruneton J. *Pharmacognosy, phytochemistry, medicinal plants*. Paris, Lavoisier, 1995.
14. *The Indian pharmaceutical codex. Vol. I. Indigenous drugs*. New Delhi, Council of Scientific & Industrial Research, 1953.
15. Haller JS. A drug for all seasons, medical and pharmacological history of aloe. *Bulletin of the New York Academy of Medicine*, 1990, 66:647-659.
16. *Quality control methods for medicinal plant materials*. Geneva, World Health Organization, 1998.
17. *Deutsches Arzneibuch 1996. Vol. 2. Methoden der Biologie*. Stuttgart, Deutscher Apotheker Verlag, 1996.
18. *European pharmacopoeia*, 3rd ed. Strasbourg, Council of Europe, 1997.
19. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (unpublished document WHO/FSF/FOS/97.7; available from Food Safety, WHO, 1211 Geneva 27, Switzerland).
20. Castleman M. *The healing herbs*. Emmaus, PA, Rodale Press, 1991:42-44.
21. de Witte P. Metabolism and pharmacokinetics of anthranoids. *Pharmacology*, 1993, 47(Suppl. 1):86-97.
22. Ishii O, Tanizawa H, Takino Y. Studies of *Aloe* III. Mechanism of laxative effect. *Chemical and pharmaceutical bulletin*, 1990, 38:197-200.
23. Tyler VE, Bradley LR, Robbers JE, eds. *Pharmacognosy*, 9th ed. Philadelphia, Lea & Febiger, 1988:62-63.
24. Tyler VE. *Herbs of choice*. New York, Pharmaceutical Products Press, 1994:155-157.
25. Che QM et al. Isolation of human intestinal bacteria capable of transforming barbaloin to aloe-emodin anthrone. *Planta medica*, 1991, 57:15-19.
26. *Aloe capensis, Cape Aloes: proposal for the summary of product characteristics*. Elburg, Netherlands, European Scientific Committee of Phytotherapy, 1995.
27. Reynolds JEF, ed. *Martindale, the extra pharmacopoeia*, 30th ed. London. Pharmaceutical Press, 1993:903.

WHO monographs on selected medicinal plants

28. Goodman and Gilman's the pharmacological basis of therapeutics, 8th ed. New York, McGraw Hill, 1990.
29. Bisset NG. *Sennae folium*. In: Max Wichtl's herbal drugs & phytopharmaceuticals. Boca Raton, FL, CRC Press, 1994:463-469.
30. American Hospital Formulary Service. Bethesda, MD, American Society of Hospital Pharmacists, 1990.
31. United States pharmacopeia, drug information. Rockville, MD, United States Pharmacopeial Convention, 1992.
32. Siegers CP et al. Anthranoid laxative abuse—a risk for colorectal cancer. *Gut*, 1993, 34:1099-1101.
33. Siegers CP. Anthranoid laxatives and colorectal cancer. *Trends in pharmacological sciences*, 1992, 13:229-231.
34. Patel PM et al. Anthraquinone laxatives and human cancer. *Postgraduate medical journal*, 1989, 65:216-217.
35. Loew D. Pseudomelanosis coli durch Anthranoiden. *Zeitschrift für Phytotherapie*, 1994, 16:312-318.
36. Lang W. Pharmacokinetic-metabolic studies with ¹⁴C-aloe emodin after oral administration to male and female rats. *Pharmacology*, 1993, 47(Suppl. 1):73-77.
37. Brown JP. A review of the genetic effects of naturally occurring flavonoids, anthraquinones and related compounds. *Mutation research*, 1980, 75:243-277.
38. Westendorf J et al. Genotoxicity of naturally occurring hydroxyanthraquinones. *Mutation research*, 1990, 240:1-12.
39. Bangel E et al. Tierexperimentelle pharmakologische Untersuchungen zur Frage der abortiven und teratogenen Wirkung sowie zur Hyperämie von Aloe. *Stein-Informationsdienst*, 1975, 4:1-25.
40. Lewis JH, Weingold AB. The use of gastrointestinal drugs during pregnancy and lactation. *American journal of gastroenterology*, 1985, 80:912-923.
41. Beuers U, Spengler U, Pape GR. Hepatitis after chronic abuse of senna. *Lancet*, 1991, 337:472.
42. Muller-Lissner SA. Adverse effects of laxatives: facts and fiction. *Pharmacology*, 47, 1993, (Suppl. 1):138-145.
43. Godding EW. Therapeutics of laxative agents with special reference to the anthraquinones. *Pharmacology*, 1976, 14(Suppl. 1):78-101.
44. Heizer WD et al. Protein-losing gastroenteropathy and malabsorption associated with factitious diarrhoea. *Annals of internal medicine*, 1968, 68:839-852.
45. Goodman and Gilman's the pharmacological basis of therapeutics, 9th ed. New York, McGraw Hill, 1996.
46. Kune GA. Laxative use not a risk for colorectal cancer: data from the Melbourne colorectal cancer study. *Zeitschrift für Gastroenterologie*, 1993, 31:140-143.

Aloe Vera Gel

Definition

Aloe Vera Gel is the colourless mucilaginous gel obtained from the parenchymatous cells in the fresh leaves of *Aloe vera* (L.) Burm. f. (Liliaceae) (1, 2).

Synonyms

Aloe barbadensis Mill., *Aloe 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. (2-5). Most formularies and reference books regard *Aloe barbadensis* Mill. as the correct species name, and *Aloe vera* (L.) Burm. f. as a synonym. However, according to the International Rules of Botanical Nomenclature, *Aloe vera* (L.) Burm. f. is the legitimate name for this species (2-4). The genus *Aloe* has also been placed taxonomically in a family called Aloaceae.

Selected vernacular names

Aloe vera gel, aloe gel.

Description

Succulent, almost sessile perennial herb; leaves 30-50 cm long and 10 cm broad at the base; colour pea-green (when young spotted with white); bright yellow tubular flowers 25-35 cm in length arranged in a slender loose spike; stamens frequently project beyond the perianth tube (6).

Plant material of interest: liquid gel from the fresh leaf

Aloe Vera Gel is not to be confused with the juice, which is the bitter yellow exudate originating from the bundle sheath cells of the leaf. The drug Aloe consists of the dried juice, as defined on page 33.

General appearance

The gel is a viscous, colourless, transparent liquid.

Organoleptic properties

Viscous, colourless, odourless, taste slightly bitter.

Microscopic characteristics

Not applicable.

Geographical distribution

Probably native to north Africa along the upper Nile in the Sudan, and subsequently introduced and naturalized in the Mediterranean region, most of the tropics and warmer areas of the world, including Asia, the Bahamas, Central America, Mexico, the southern United States of America, south-east Asia, and the West Indies (2).

General identity tests

To be established in accordance with national requirements.

Purity tests

Microbiology

The test for *Salmonella* spp. in Aloe Vera Gel should be negative. Acceptable maximum limits of other microorganisms are as follows (7-9). For external use: aerobic bacteria—not more than 10^2 /ml; fungi—not more than 10^2 /ml; enterobacteria and certain Gram-negative bacteria—not more than 10^1 /ml; *Staphylococcus* spp.—0/ml. (Not used internally.)

Moisture

Contains 98.5% water (10).

Pesticide residues

To be established in accordance with national requirements. For guidance, see WHO guidelines on quality control methods for medicinal plants (7) and guidelines on predicting dietary intake of pesticide residues (11).

Heavy metals

Recommended lead and cadmium levels are not more than 10 and 0.3mg/kg, respectively, in the final dosage form (7).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (7).

Other tests

Chemical tests for Aloe Vera Gel and tests for total ash, acid-insoluble ash, alcohol-soluble residue, foreign organic matter, and water-soluble extracts to be established in accordance with national requirements.

Chemical assays

Carbohydrates (0.3%) (12), water (98.5%) (10). Polysaccharide composition analysis by gas-liquid chromatography (13).

Major chemical constituents

Aloe Vera Gel consists primarily of water and polysaccharides (pectins, hemicelluloses, glucomannan, acemannan, and mannose derivatives). It also contains amino acids, lipids, sterols (lupeol, campesterol, and β -sitosterol), tannins, and enzymes (1). Mannose 6-phosphate is a major sugar component (14).

Dosage forms

The clear mucilaginous gel. At present no commercial preparation has been proved to be stable. Because many of the active ingredients in the gel appear to deteriorate on storage, the use of fresh gel is recommended. Preparation of fresh gel: harvest leaves and wash them with water and a mild chlorine solution. Remove the outer layers of the leaf including the pericyclic cells, leaving a "fillet" of gel. Care should be taken not to tear the green rind which can contaminate the fillet with leaf exudate. The gel may be stabilized by pasteurization at 75–80 °C for less than 3 minutes. Higher temperatures held for longer times may alter the chemical composition of the gel (2).

Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and in traditional systems of medicine

Aloe Vera Gel is widely used for the external treatment of minor wounds and inflammatory skin disorders (1, 14–17). The gel is used in the treatment of minor skin irritations, including burns, bruises, and abrasions (1, 14, 18). The gel is further used in the cosmetics industry as a hydrating ingredient in liquids, creams, sun lotions, shaving creams, lip balms, healing ointments, and face packs (1).

Aloe Vera Gel has been traditionally used as a natural remedy for burns (18, 19). Aloe Vera Gel has been effectively used in the treatment of first- and second-degree thermal burns and radiation burns. Both thermal and radiation burns healed faster with less necrosis when treated with preparations containing Aloe Vera Gel (18, 19). In most cases the gel must be freshly prepared because of its sensitivity to enzymatic, oxidative, or microbial degradation. Aloe Vera Gel is not approved as an internal medication, and internal administration of the gel has not been shown to exert any consistent therapeutic effect.

Uses described in folk medicine, not supported by experimental or clinical data

The treatment of acne, haemorrhoids, psoriasis, anaemia, glaucoma, petit ulcer, tuberculosis, blindness, seborrhoeic dermatitis, and fungal infections (2, 6, 19).

Pharmacology

Wound healing

Clinical investigations suggest that Aloe Vera Gel preparations accelerate wound healing (14, 18). *In vivo* studies have demonstrated that Aloe Vera Gel promotes wound healing by directly stimulating the activity of macrophages and fibroblasts (14). Fibroblast activation by Aloe Vera Gel has been reported to increase both collagen and proteoglycan synthesis, thereby promoting tissue repair (14). Some of the active principles appear to be polysaccharides composed of several monosaccharides, predominantly mannose. It has been suggested that mannose 6-phosphate, the principal sugar component of Aloe Vera Gel, may be partly responsible for the wound healing properties of the gel (14). Mannose 6-phosphate can bind to the growth factor receptors on the surface of the fibroblasts and thereby enhance their activity (14, 15).

Furthermore, acemannan, a complex carbohydrate isolated from *Aloe* leaves, has been shown to accelerate wound healing and reduce radiation-induced skin reactions (20, 21). The mechanism of action of acemannan appears to be twofold. First, acemannan is a potent macrophage-activating agent and therefore may stimulate the release of fibrogenic cytokines (21, 22). Second, growth factors may directly bind to acemannan, promoting their stability and prolonging their stimulation of granulation tissue (20).

The therapeutic effects of Aloe Vera Gel also include prevention of progressive dermal ischaemia caused by burns, frostbite, electrical injury and intra-arterial drug abuse. *In vivo* analysis of these injuries demonstrates that Aloe Vera Gel acts as an inhibitor of thromboxane A₂, a mediator of progressive tissue damage (14, 17). Several other mechanisms have been proposed to explain the activity of Aloe Vera Gel, including stimulation of the complement linked to polysaccharides, as well as the hydrating, insulating, and protective properties of the gel (1).

Because many of the active ingredients appear to deteriorate on storage, the use of fresh gel is recommended. Studies of the growth of normal human cells *in vitro* demonstrated that cell growth and attachment were promoted by exposure to fresh *Aloe vera* leaves, whereas a stabilized Aloe Vera Gel preparation was shown to be cytotoxic to both normal and tumour cells. The cytotoxic effects of the stabilized gel were thought to be due to the addition of other substances to the gel during processing (23).

Anti-inflammatory

The anti-inflammatory activity of Aloe Vera Gel has been revealed by a number of *in vitro* and *in vivo* studies (14, 17, 24, 25). Fresh Aloe Vera Gel significantly

reduced acute inflammation in rats (carrageenin-induced paw oedema), although no effect on chronic inflammation was observed (25). Aloe Vera Gel appears to exert its anti-inflammatory activity through bradykinase activity (24) and thromboxane B₂ and prostaglandin F₂ inhibition (18, 26). Furthermore, three plant sterols in Aloe Vera Gel reduced inflammation by up to 37% in croton oil-induced oedema in mice (15). Lupeol, one of the sterol compounds found in *Aloe vera*, was the most active and reduced inflammation in a dose-dependent manner (15). These data suggest that specific plant sterols may also contribute to the anti-inflammatory activity of Aloe Vera Gel.

Burn treatment

Aloe Vera Gel has been used for the treatment of radiation burns (27-30). Healing of radiation ulcers was observed in two patients treated with *Aloe vera* cream (27), although the fresh gel was more effective than the cream (29, 30). Complete healing was observed, after treatment with fresh Aloe Vera Gel, in two patients with radiation burns (30). Twenty-seven patients with partial-thickness burns were treated with Aloe Vera Gel in a placebo-controlled study (31). The Aloe Vera Gel-treated lesions healed faster (11.8 days) than the burns treated with petroleum jelly gauze (18.2 days), a difference that is statistically significant (*t*-test, $P < 0.002$).

Contraindications

Aloe Vera Gel is contraindicated in cases of known allergy to plants in the Liliaceae.

Warnings

No information available.

Precautions

No information available concerning general precautions, or precautions dealing with carcinogenesis, mutagenesis, impairment of fertility; drug and laboratory test interactions; drug interactions; nursing mothers; paediatric use; or teratogenic or non-teratogenic effects on pregnancy.

Adverse reactions

There have been a few reports of contact dermatitis and burning skin sensations following topical applications of Aloe Vera Gel to dermabraded skin (18, 32). These reactions appeared to be associated with anthraquinone contaminants in this preparation (33). A case of disseminated dermatitis has been reported following application of Aloe Vera Gel to a patient with stasis dermatitis (34). An acute bullous allergic reaction and contact urticaria have also been reported to result from the use of Aloe Vera Gel (35).

Posology

Fresh gel or preparations containing 10–70% fresh gel.

References

1. Bruneton J. *Pharmacognosy, phytochemistry, medicinal plants*. Paris, Lavoisier, 1995.
2. Grindlay D, Reynolds T. The *Aloe vera* phenomenon: a review of the properties and modern uses of the leaf parenchyma gel. *Journal of ethnopharmacology*, 1986, 16:117–151.
3. Newton LE. In defence of the name *Aloe vera*. *The cactus and succulent journal of Great Britain*, 1979, 41:29–30.
4. Tucker AO, Duke JA, Foster S. Botanical nomenclature of medicinal plants. In: Cracker LE, Simon JE, eds. *Herbs, spices and medicinal plants, Vol. 4*. Phoenix, AR, Oryx Press, 1989:169–242.
5. Hänsel R et al., eds. *Hagers Handbuch der Pharmazeutischen Praxis, Vol. 6*, 5th ed. Berlin, Springer, 1994.
6. Youngken HW. *Textbook of pharmacognosy*, 6th ed. Philadelphia, Blakiston, 1950.
7. *Quality control methods for medicinal plant materials*. Geneva, World Health Organization, 1998.
8. *Deutsches Arzneibuch 1996. Vol. 2. Methoden der Biologie*. Stuttgart, Deutscher Apotheker Verlag, 1996.
9. *European pharmacopoeia*, 3rd ed. Strasbourg, Council of Europe, 1997.
10. Rowe TD, Park LM. Phytochemical study of *Aloe vera* leaf. *Journal of the American Pharmaceutical Association*, 1941, 30:262–266.
11. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (unpublished document WHO/FSF/FOS/97.7; available from Food Safety, WHO, 1211 Geneva 27, Switzerland).
12. Pierce RF. Comparison between the nutritional contents of the aloe gel from conventional and hydroponically grown plants. *Erde international*, 1983, 1:37–38.
13. Hart LA et al. An anti-complementary polysaccharide with immunological adjuvant activity from the leaf of *Aloe vera*. *Planta medica*, 1989, 55:509–511.
14. Davis RH et al. Anti-inflammatory and wound healing of growth substance in *Aloe vera*. *Journal of the American Pediatric Medical Association*, 1994, 84:77–81.
15. Davis RH et al. *Aloe vera*, hydrocortisone, and sterol influence on wound tensile strength and anti-inflammation. *Journal of the American Pediatric Medical Association*, 1994, 84:614–621.
16. Heggors JP, Pelley RP, Robson MC. Beneficial effects of *Aloe* in wound healing. *Phytotherapy research*, 1993, 7:S48–S52.
17. McCauley R. Frostbite—methods to minimize tissue loss. *Postgraduate medicine*, 1990, 88:67–70.
18. Shelton RM. *Aloe vera*, its chemical and therapeutic properties. *International journal of dermatology*, 1991, 30:679–683.
19. Haller JS. A drug for all seasons, medical and pharmacological history of aloe. *Bulletin of New York Academy of Medicine*, 1990, 66:647–659.
20. Tizard AU et al. Effects of acemannan, a complex carbohydrate, on wound healing in young and aged rats. *Wounds, a compendium of clinical research and practice*, 1995, 6:201–209.
21. Roberts DB, Travis EL. Acemannan-containing wound dressing gels reduce radiation-induced skin reactions in C3H mice. *International journal of radiation oncology, biology and physiology*, 1995, 15:1047–1052.
22. Karaca K, Sharma JM, Norgren R. Nitric oxide production by chicken macrophages

- activated by acemannan, a complex carbohydrate extracted from *Aloe vera*. *International journal of immunopharmacology*, 1995, 17:183-188.
23. Winters WD, Benavides R, Clouse WJ. Effects of aloe extracts on human normal and tumor cells *in vitro*. *Economic botany*, 1981, 35:89-95.
 24. Fujita K, Teradaira R. Bradykininase activity of aloe extract. *Biochemical pharmacology*, 1976, 25:205.
 25. Udupa SI, Udupa AL, Kulkarni DR. Anti-inflammatory and wound healing properties of *Aloe vera*. *Fitoterapia*, 1994, 65:141-145.
 26. Robson MC, Heggors J, Hagstrom WJ. Myth, magic, witchcraft or fact: *Aloe vera* revisited. *Journal of burn care and rehabilitation*, 1982, 3:157-162.
 27. Collin C. Roentgen dermatitis treated with fresh whole leaf of *Aloe vera*. *American journal of roentgen*, 1935, 33:396-397.
 28. Wright CS. *Aloe vera* in the treatment of roentgen ulcers and telangiectasis. *Journal of the American Medical Association*, 1936, 106:1363-1364.
 29. Rattner H. Roentgen ray dermatitis with ulcers. *Archives of dermatology and syphilology*, 1936, 33:593-594.
 30. Loveman AB. Leaf of *Aloe vera* in treatment of roentgen ray ulcers. *Archives of dermatology and syphilology*, 1937, 36:838-843.
 31. Visuthikosol V et al. Effect of *Aloe vera* gel on healing of burn wounds: a clinical and histological study. *Journal of the Medical Association of Thailand*, 1995, 78:403-409.
 32. Hormann HP, Korting HC. Evidence for the efficacy and safety of topical herbal drugs in dermatology: Part 1: Anti-inflammatory agents. *Phytomedicine*, 1994, 1:161-171.
 33. Hunter D, Frumkin A. Adverse reactions to vitamin E and *Aloe vera* preparations after dermabrasion and chemical peel. *Cutis*, 1991, 47:193-194.
 34. Horgan DJ. Widespread dermatitis after topical treatment of chronic leg ulcers and stasis dermatitis. *Canadian Medical Association Journal*, 1988, 138:336-338.
 35. Morrow DM, Rappaport MJ, Strick RA. Hypersensitivity to aloe. *Archives of dermatology*, 1980, 116:1064-1065.