Aloe vera: a systematic review of its clinical effectiveness

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SUMMARY

Background. *The use of aloe vera is being promoted for a large variety of conditions. Often general practitioners seem to know less than their patients about its alleged benefits.*

Aim. *To define the clinical effectiveness of aloe vera, a popular herbal remedy in the United Kingdom.*

Method. *Four independent literature searches were conducted in MEDLINE, EMBASE, Biosis, and the Cochrane Library. Only controlled clinical trials (on any indication) were included. There were no restrictions on the language of publication. All trials were read by both authors and data were extracted in a standardized, pre-defined manner.*

Results. *Ten studies were located. They suggest that oral administration of aloe vera might be a useful adjunct for lowering blood glucose in diabetic patients as well as for reducing blood lipid levels in patients with hyperlipidaemia. Topical application of aloe vera is not an effective preventative for radiation-induced injuries. It might be effective for genital herpes and psoriasis. Whether it promotes wound healing is unclear. There are major caveats associated with all of these statements.*

Conclusion. *Even though there are some promising results, clinical effectiveness of oral or topical aloe vera is not sufficiently defined at present.*

Keywords: complementary medicine; aloe vera; review.

Introduction

THE use of aloe vera is being promoted for a large variety of conditions. Often general practitioners (GPs) seem to know less than their patients about its alleged benefits. The Department of Complementary Medicine at the University of Exeter receives more enquiries from colleagues related to aloe vera than for any other herbal remedy. Considering this high level of interest, it is relevant to review systematically the evidence for or against its clinical effectiveness.

Aloe vera (synonym: *Aloe barbadensis* Miller) belongs to the Liliaceal family, of which there are about 360 species. *Aloe capensis* (Cape aloes) belongs to a different species. Aloe vera is a cactus-like plant that grows readily in hot, dry climates and currently, because of demand, is cultivated in large quantities. Cosmetic and some medicinal products are made from the mucilaginous tissue in the centre of the aloe vera leaf and called aloe vera gel. The peripheral bundle sheath cells of aloe vera produce an intensely bitter, yellow latex, commonly termed aloe juice, or sap, or aloes. Aloe vera sap and aloe vera gel are often confused. Unlike aloes, aloe vera gel contains no anthraquinones, which are responsible for the strong laxative effects of aloes. However, total leaf extracts may contain anthraquinones.[1]

Although most commercially-available products are based on the gel, the British Pharmacopoeia does not contain an entry for aloe vera gel but it does describe aloes.[2] The pharmacological actions of aloe vera, as studied *in vitro* or in animals (in most cases the total leaf extract was used), include anti-inflammatory and anti-arthritic activity, and antibacterial and hypoglycaemic effects.[1]

Aloe vera has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan, and China.[2] The therapeutic claims made for aloe vera range over a broad list of conditions, as do the pharmacological activities associated with it[3] (Table 1). Most of these claims are based on historical use rather than hard evidence.

Aloe vera contains 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids.[4] Box 1 summarizes its most important constituents.[5]

The clinical use of aloe vera is supported mostly by anecdotal data.[6] While such reports are interesting and relevant for formulating hypotheses, controlled trials are essential for defining its effectiveness more conclusively.[7] The aim of this systematic review was to summarize all controlled clinical trials on aloe vera preparations with a view to providing evidence for or against its clinical effectiveness.

Method

Computerized literature searches were performed to identify all published articles on the subject. The following databases were used: MEDLINE, EMBASE, Biosis, and the Cochrane Library — all from their inception to May 1998. In addition, other experts working in this area were asked for further papers and our own files were searched. Furthermore, major manufacturers of aloe vera products were contacted in writing and asked for published and unpublished controlled clinical trials. The bibliographies of all investigations thus located were searched for further relevant articles.

Only controlled clinical trials of aloe vera (for any indication) were included. Studies were excluded if not performed on aloe vera mono-preparations or if they were designed only on a certain pharmacological constituent of the plant. There were no restrictions regarding publication language.

All articles (or abstracts if only available as abstracts) were read in full. Data were extracted in a predefined fashion. Methodological quality was assessed using the Jadad score[8] (Box 2).

Results

Ten trials met the above criteria and were included in this review. Three clinical studies had to be excluded. They were either not performed on aloe vera mono-preparation[9] or only designed on a pharmacologically active constituent of the plant.[10,11] Studies assessing the effects of aloes (including anthraquinones) as mono-preparations were not found. No unpublished study was located.

Two trials investigated the effects of aloe vera gel on wound healing after surgery.[12,13] One study tested its efficacy in patients

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Table 1. Aloe vera: therapeutic claims (A) and alleged pharmacological activities (B).

(A) Therapeutic claims	(B) Alleged pharmacological properties
Arthritis	'Adaptogenic'
Asthma	Non-toxic — no known side-effects
Candida	Provides essential nutrients
Chronic fatigue syndrome	Breaks down and digests dead tissue
Digestive and bowel disorders (e.g. atonic constipation, irritable bowel syndrome, Crohn's disease, ulcerative colitis)	Anti-inflammatory
Lupus erythematodes	Reduces swelling
Skin problems (e.g. eczema, psoriasis, acne, burns, athlete's foot, cold sores, frostbite)	Moisturises
Sports injuries	Penetrates tissue
Ulcers (external and internal)	Antifungal
	Relieves itching
	Antimicrobial — prevents infections
	Anaesthetises — relieves pain
	Cleanses and detoxifies
	Stimulates cell growth

Modified from Townsend (1998).[3]

Anthraquinones	*Inorganic compounds*
Aloin	Calcium
Barbaloin	Sodium
Isobarbaloin	Chlorine
Anthranol	Manganese
Aloetic acid	Zinc
Ester of cinnamic acid	Chromium
Aloe-emodin	Potassium sorbate
Emodin	Copper
Chrysophanic acid	Magnesium
Resistannol	Iron
Saccarides	*Enzymes*
Cellulose	Cyclooxygenase
Glucose	Oxidase
Mannose	Amylase
L-rhamnose	Catalase
Aldopentose	Lipase
	Alkaline phosphatase
	Carboxypeptidase
Vitamins	*Essential amino acids*
B_1	Lysine
B_2	Threonine
B_6	Valine
Choline	Leucine
Folic acid	Isoleucine
C	Phenylalanine
α-tocopherol	Methionine
β-carotene	
Nonessential amino acids	*Miscellaneous*
Histidine	Cholesterol
Arginine	Triglycerides
Hydroxyproline	Steroids
Aspartic acid	β-sitosterol
Glutamic acid	Lignins
Proline	Uric acid
Glycine	Gibberellin
Alanine	Lectin-like substance
Tyrosine	Salicylic acid
	Arachidonic acid

Box 1. Constituents of aloe vera/aloes.

Each 'yes' = 1 point; each 'no' = 0 points

A. Study described as randomized (this includes the use of words such as random, randomly, and randomization)?
B. Study described as double-blind?
C. Description of withdrawals and dropouts?
D. Method to generate the sequence of randomization described and appropriate (table of random numbers, computer generated, etc.)?
E. Method of double-blinding described and appropriate (identical placebo, active placebo, dummy, etc.)?

Deduct 1 point if:

F. Method to generate the sequence of randomization described and inappropriate (patients were allocated alternately or according to their date of birth, hospital number, etc.)
G. Method of double-blinding described and inappropriate (e.g. comparison of tablet versus injection with no double dummy).

Box 2. Jadad scoring system to measure methodological quality.[8]

suffering from psoriasis.[14] The prevention of radiation-induced skin injuries with an aloe vera gel was examined in two trials.[15] The two most recent studies were performed on men suffering from genital herpes.[16,17] One further trial examined the effectiveness of aloe vera in hyperlipidaemic patients.[18] Finally, two studies assessed the plant's hypoglycaemic and antidiabetic potential.[19,20] Key data from these studies are summarized in Table 2. All studies included are briefly described in the following section.

Topical use

Fulton[12] documented the effects of two different dressings for wound-healing management on full-faced dermabrasion patients. Eighteen patients suffering from acne vulgaris completed the study. Their abraded faces were divided in half. One side was treated with a standard polyethylene oxide gel wound dressing, while the other side was treated with a polyethylene oxide dressing saturated with aloe vera. After 48 hours with the aloe vera dressing, intense vasoconstriction and a reduction in oedema was noted; less exudate and crusting were evident by the fourth day. By the fifth day, reepithelialization was complete to 90% on the aloe side compared with 40–50% on the control side. Overall, wound healing was approximately 72 hours faster at the aloe side.

Table 2. Controlled clinical trials of aloe vera (a.v.).

First author (year)	Jadad score (max. = 5)	Condition treated	Design	Sample	Interventions	Primary endpoint	Main results
Fulton (1990)[12]	0	Facial postdermabrasion wound healing in acne vulgaris patients	Controlled clinical trial	17 patients	Comparison between half face treated with standard polyethylene oxide wound gel vs half face treated with wound gel saturated with a.v.	Time of wound healing (reepithelialization)	Wound healing was 72 hours faster at a.v. site
Schmidt et al (1991)[13]	3	Wound healing complications after gynaecologic surgery	RCT	40 women	Standard wound care vs additional a.v. dermal gel every 8–12 hours	Time to completely epithelialized wound	Mean healing time: standard + a.v. = 83 days standard = 53 days
Syed et al (1996)[14]	4	Slight to moderate chronic plaque-type psoriasis	RCT, double-blind, placebo-controlled, two parallel groups	60 men and women	Topical administration of 0.5% hydrophilic a.v. cream vs placebo cream, both for four weeks	Skin lesions (Psoriasis Area and Severity Index)	Number of patients cured: a.v. = 83.3%; placebo = 6.6%; no adverse effects, no
Williams et al (1996)[15]	4	Prevention of radiation-induced skin injury	RCT, double-blind, placebo-controlled, two parallel groups	194 women receiving radiation therapy for breast cancer	Topical a.v. gel (98% pure) vs placebo gel (both with usual care in addition) twice daily	Maximum dermatitis severity judged by (a) patient (b) healthcare provider	No significant inter-group differences
Williams et al (1996)[15]	1	Prevention of radiation-induced skin injury	RCT, two parallel groups	108 women receiving radiation therapy for breast cancer	Topical a.v. gel (98% pure) vs no treatment (both with usual care in addition)	Maximum dermatitis severity judged by (a) patient (b) healthcare provider	No significant inter-group differences
Syed et al (1996)[16]	3	Treatment of first genital herpes episode	RCT, double-blind, placebo-controlled, three parallel groups	120 men	Topical application of a.v. cream, a.v. gel or placebo three times daily for maximum two weeks	Number of cured patients, mean healing time	a.v. cream: 70%, cured at 4.8 days a.v. gel: 45%, cured at 7.0 days Placebo: 7.5%, cured at 14.0 days
Syed et al (1997)[17]	4	Treatment of first genital herpes episode	RCT, double-blind, placebo-controlled, two parallel groups	60 men	Topical application of 0.5% hydrophilic a.v. cream vs placebothree times daily for maximum two weeks	As above	a.v. cream: 67%, cured at 4.9 days Placebo: 7%, cured at 12 days
Nasiff et al (1993)[18]	Abstract	Hyperlipidaemia in patients with negative response to diet	Controlled clinical trial, three parallel groups	60 patients	Oral administration of 10ml a.v. vs 20ml placebo daily for 12 weeks	Blood lipid levels	Decrease in blood cholesterol, LDL, triglycerides in both treatment groups
Yongchaiyudha et al (1996)[19]	1	Diabetes mellitus, not on oral antidiabetic drugs	Placebo-controlled, single-blind, clinical trial	72 women	Oral administration of 1 tablespoon of a.v. twice daily for 42 days vs placebo	Blood glucose	No change in control group, blood glucose 250 to 141 mg % in actively treated group
Bunyapraphatsara et al (1996)[20]	1	Diabetes mellitus treated with oral glibenclamide	Placebo-controlled, single-blind, clinical trial	72 men and women (all on oral anti-diabetic med-ication already)	Aloe vera as above or placebo + 2 x 5 mg glibenclamide/day for 42 days	Blood glucose	No change in control group, blood glucose 250 to 141 mg % in actively treated group

RCT = randomized controlled trial; vs = versus.

Schmidt *et al*[13] evaluated the time interval required for wound healing using a standard wound management protocol with and without aloe vera gel in a randomized controlled trial (RCT) with 40 women. All patients had complications of wound healing after gynaecological surgery. Only 21 of them completed the study. The mean healing time in the conventional care group (53 days) was significantly shorter ($P<0.003$) than in the aloe vera gel group (83 days). This trial was not blinded. The details of the standard wound management protocol were not mentioned.

Syed *et al*[14] randomized 60 patients with mild to moderate chronic psoriasis to receive either an aloe vera or placebo cream. The cream was self-applied three times per day for four weeks. Patients were subsequently followed up for 12 months. The cure rate in the aloe vera group was 83% and only 7% in the placebo group. This inter-group difference was statistically significant ($P<0.001$). The cream was well tolerated. The authors stated that, even after the follow-up period, there were no relapses.

Williams *et al*[15] reported two RCTs in one publication. In the first study they randomized 194 women receiving radiation therapy to be treated with aloe vera gel, self-administered to the radiation-exposed skin twice per day or with placebo gel. The severity of the dermatitis was judged weekly during the 10 weeks treatment period both by the patients and by their healthcare providers. There was no difference between the treatment group and the placebo group.

Some clinicians participating in this trial felt that there were fewer skin problems than normally expected. Thus, it was speculated that the inert carrier gel might have had some beneficial effects. A second RCT was therefore performed with 108 women.[15] The only difference compared with the first study was that the control group now received no topical therapy at all. The trial was therefore not blinded. Again, the results did not suggest any benefit of the aloe vera gel in terms of prevention of radiation-induced dermatitis.

Syed *et al*[16,17] conducted two trials on the efficacy of aloe vera for first episodes of genital herpes in men. In the first study[16] they randomized 120 men into three parallel groups. Each patient applied either aloe vera cream (aloe vera extract 0.5% in hydrophilic cream), aloe vera gel, or placebo three times daily for two weeks. Aloe vera cream showed shorter mean duration of healing than aloe vera gel and placebo (4.8 days versus 7.0 and 14.0 days, respectively). The numbers of cured patients were 70%, 45%, and 7.5%, respectively ($P<0.02$). Of the 49 patients healed at the end of this trial period, six had a relapse after 21 months of follow-up.

The second study[17] included 60 men who were randomized into two groups. The trial compared aloe vera extract 0.5% in a hydrophylic cream versus placebo. The results are comparable with the above trial. The aloe vera cream group had both significantly shorter healing time (4.9 days versus 12 days, $P<0.001$) and a higher number of cured patients (66.7% versus 6.7%, $P<0.001$) compared with the placebo group. Of the 22 healed patients, three showed recurrence after 15 months.

Oral administration

Nasiff *et al*[19] conducted a controlled clinical trial on 60 patients with hyperlipidaemia who previously had not responded to dietary interventions. Patients received either 10 ml or 20 ml aloe vera or placebo daily over a period of 12 weeks. Blood lipid levels were measured before treatment and after four, eight, and 12 weeks. Total serum cholesterol decreased by 15.4% and 15.5%, triglycerides by 25.2% and 31.9%, low density lipoprotein (LDL) by 18.9% and 18.2% respectively in the two groups receiving aloe vera. Since this trial was available as an abstract only, neither intergroup comparisons nor randomization nor blinding were mentioned.

Yongchaiyudha *et al*[19] divided 72 diabetic women without drug therapy into two groups. They received one tablespoon of aloe vera gel or placebo for 42 days. Blood glucose levels subsequently decreased from 250 mg to 141 mg percentage in the experimental group, while controls showed no significant changes. In addition, cholesterol, serum triglycerides, weight, and appetite were also monitored. With the exception of triglyceride levels, which fell significantly in the actively treated group (220 mg percentage to 123 mg percentage; no change in controls), these variables remained unaltered in both groups. This study was neither randomized nor was it blinded to patient or investigator.

The same research team investigated the effects of aloe vera gel in combination with a standard oral antidiabetic therapy.[20] All diabetic patients admitted to this study were on 2 x 5 mg oral glibenclamide. In addition, for the duration of the trial (42 days) they were given either aloe vera or placebo as above. The results show similar decreases in blood glucose and serum triglyceride levels in the actively treated group as described in the first trial. The same methodological drawbacks apply as to the previous study.

Adverse effects

No withdrawals owing to adverse effects of aloe vera were reported in any of the above trials. Some patients experienced burning after topical application,[12] contact dermatitis,[15] and mild itching.[16,17] All adverse effects were reversible and aloe vera was generally very well tolerated.

Discussion

To the best of our knowledge, this is the first systematic review on this subject. In view of the widespread use of aloe vera, perhaps the most surprising finding is the paucity of controlled clinical trials. Furthermore, the few studies that are available are by no means free of methodological flaws. Of all 10 trials included in this systematic review, none achieved the highest methodological score (Table 3). Lack of randomization, lack of blinding, small sample size, lack of intention-to-treat analyses, and lack of power calculation are some prevalent limitations. Furthermore, it is noteworthy that trials tend to originate from the same research groups, and independent replications are, by and large, lacking. Thus, it is problematic to draw firm conclusions from this review.

In this situation, other types of evidence may inform the debate. Results of *in vitro* studies on the effects of aloe vera on cell proliferation are contradictory. One explanation is that the sap could have cytotoxic activity while the gel might promote cell growth.[21] Various animal models have been used to study the promotion of wound healing by topical aloe vera preparations.[22-26] On balance, these investigations do seem to suggest that aloe vera does enhance wound healing, although its mechanism of action is still unclear. Several studies emphasize the anti-inflammatory properties of aloe vera in mice and rats.[27-29] A number of animal experiments suggest that oral aloe vera (juice and gel) has hypoglycaemic effects in streptozotocin-induced diabetes in rats.[30,31] Obviously, such animal experiments are not a substitute for clinical trials in the evaluation of efficacy.

The question arises whether aloe vera is safe. Studies in mice revealed no acute toxicity in therapeutic doses.[32] In high doses, however, a decrease of CNS activity was noticed. During chronic treatment, there was a decrease in red cell count and significant sperm damage.[32] No systematic investigations exist in humans. In the reviewed trials, no withdrawals or serious adverse reac-

Table 3. Methodological quality of individual trials using the Jadad scoring system[8] (Box 2).

First author	A	B	C	D	E	F	G	Total (maximum)
Fulton et al[12]	–	–	–	–	–	–	–	0
Schmidt et al[13]	1	–	1	1	–	–	–	3
Syed et al[14]	1	1	1	–	1	–	–	4
Williams et al[15]	1	1	1	–	1	–	–	4
Williams et al[15]	1	–	–	–	–	–	–	1
Syed et al[16]	1	1	1	–	–	–	–	3
Syed et al[17]	1	1	1	–	1	–	–	4
Nasiff et al[18]	–	–	–	–	–	–	–	Abstract
Yongchaiyudha et al[19]	–	–	1	–	–	–	–	1
Bunyapraphatsara et al[20]	–	–	1	–	–	–	–	1

tions were reported. Three patients experienced allergic reactions.[15] This corresponds with anecdotal reports relating to contact dermatitis and hypersensitivity.[33-38] One recent publication details the suspension of a physician by the United States Virginia Board of Medicine because of causing the death of 'several' of his patients through *injections* of aloe vera for cancer.[39] One text on herbal treatments[1] warns of oral use during pregnancy but lists no further adverse effects or contraindications.

It is concluded that there is some preliminary evidence to suggest that oral administration of aloe vera might be effective in reducing blood glucose in diabetic patients and in lowering blood lipid levels in hyperlipidaemia. The topical application of aloe vera does not seem to prevent radiation-induced skin damage. It might be useful as a treatment for genital herpes and psoriasis. The evidence regarding wound healing is contradictory. More and better trial data are needed to define the clinical effectiveness of this popular herbal remedy more precisely.

Keypoints

- Because of its popularity with consumers, it is important to determine the efficacy and safety of aloe vera products.
- Only 10 controlled clinical trials of aloe vera exist (for various indications).
- These trials suggest that oral aloe vera might be valuable for lowering cholesterol or reducing glucose levels. Topical aloe vera could be effective for genital herpes or psoriasis.
- However, for none of these indications are the existing data sufficient to draw firm conclusions.

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