

Absence of contact sensitization to *Aloe vera* (L.) Burm. f.

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Aloe vera has been used as a cosmetic and medical remedy since ancient times and has gained increasing popularity in recent years. Despite its widespread use, reports of allergic reactions are rare. We patch tested 702 consecutive patients with an oily extract from the leaves, *Aloe pulvis* from the entire plant and concentrated *Aloe vera* gel. A specially designed questionnaire was used for the use of *Aloe vera*, reasons and location of application, adverse reactions, occupation, hobbies and atopy. None of the subjects showed any reaction to one of the preparations. 2 components of the plant have to be distinguished: the bark of the leaves contains anthrachinones with pro-peristaltic and potential antibiotic and anticancer properties. Constraints have been imposed due to their considerable toxic potential. Today, mostly the *Aloe* gel from the center of the leaves is processed. It almost exclusively consists of carbohydrates to which also many medical effects have been attributed. Carbohydrates are not likely to induce contact sensitization, which might explain the outcome of our study. However, this does not justify unrestrained promotion of *Aloe* products, as scientific studies investigating the claims on its constitutional effects are few in number, and the majority of them have been unable to diminish the intuitive scepticism against miracle cures, like *Aloe* seems to be.

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Aloe vera (*Aloe barbadensis* Miller) belongs to the family of Liliaceae. The name is derived from the Arabic word 'alloeh' which means 'bitter', referring to the taste of the liquid contained in the leaves. *Aloe vera* has been used as a cosmetic and medicinal remedy for several 1000 years. It was first mentioned in the Egyptian Papyrus Eber dating back to 1500 B.C., which described both systemic and topical application of the substance. Leonhart Fuchs, in his 'Neues Kräuterbuch von 1543' (New Book of Herbs 1543), summarized the beneficial effects of *Aloe vera* on gastroenteritis, headache, alopecia and wounds. Old-fashioned natural medicines and cosmetics such as arnica (1), propolis (2–4), marigold (1) and tea tree oil (5) have well-known sensitizing properties. *Aloe vera*, the new favourite since the 1990s, satisfies the increasing public demand for medical remedies of plant origin as alternatives to orthodox academic medicine. *Aloe vera* is used in cosmetics, drinks, detergents, as well as in stockings, diet foods, toothpaste and clothing. It is marketed as

a remedy for atherosclerosis, allergies, AIDS, prevention of radiation-induced dermatitis, wound healing, psoriasis, insomnia, cancer, pulpitis and several other diseases. Scientific studies investigating these claims are few in number, and the majority of them have been unable to diminish the intuitive scepticism against miracle cures, like *Aloe* seems to be (6–13).

Reports on allergic reactions resulting from the application or intake of *Aloe vera* are rare, although the substance is widely used. We performed a multicenter prospective trial to investigate the prevalence of contact sensitization of different preparations of *Aloe vera*. Several commonly used preservatives and other popular natural cosmetics were also tested.

Patients and Methods

Patch testing was performed at the Departments of Dermatology in Innsbruck, Salzburg, Graz, the Allergy Outpatient Clinic in Hall in Tirol

from September 2003 to February 2004. All study subjects were patients who had visited the centers for suspected allergic contact dermatitis and were therefore being tested for other substances as well. In most cases, at least the European standard series (from Hermal, Germany) was performed. Informed consent was obtained from all patients. Pure *Aloe* gel (concentrated 10-fold), oil (from the leaves macerated in soja oil) and *Aloe pulvis* (from the whole plant) were purchased from Caelo (Hilden, Germany). Prior to testing, the extracts were applied on 20 volunteer staff members; none of them experienced an irritative or allergic reaction.

As the oil was stabilized with vitamin E (tocopherol acetate) and the gel with citric acid, both substances were tested. Sorbic acid, which is frequently contained in commercial *Aloe* products, was also tested. In a subsequent test series, *Aloe*-positive patients were tested with commercially available substances such as emodin, anthracene, anthrone, chrysophanol and cumaric acid. Arnica and marigold were prepared as described previously (1, 14) and used as ether extracts in a concentration of 0.5% and 10%, respectively. Compositae mix and sesquiterpene lactone mix were obtained from Hermal, Germany. The testing agents were applied to Finn Chambers[®] (Epitest, Helsinki, Finland) that were fixed to the subjects' upper back with Scanpore tape (Norgesplaster Aksjeselskap, Vennesla, Norway). The patches were removed after 48 hr and read 15 min and 24 hr later, apart from Buxtehude, where patches were removed already after 24 hr. Positive reactions were graded from + to + + +, as recommended by the International Contact Dermatitis Research Group (15). A specially designed questionnaire was used to interview patients for the use of *Aloe vera* and other Liliaceae, their reasons for use and location of application, adverse reactions, occupation, hobbies and atopy.

Results

A total of 702 patients were tested; among them 176 were from the Buxtehude center where no questionnaire had been performed. From the remaining 526 subjects, 373 (70.9%) were females and 153 (29.1%) were males. 68 (12.9%) reported atopic dermatitis and/or inhalation allergy as a sign of atopy. 80 subjects (15.2%) were aware of having used products containing *Aloe vera* on the skin. None of them had experienced any side-effects. No patch test reactions to any of the *Aloe* preparations were observed. 2 subjects had a + reaction to sorbic acid, but none to citric

acid or tocopherol acetate. In 655 (93.3%) patients, at least the European standard series was tested additionally. Nickel (133 of 655 subjects; 20.3%), cobalt (53 subjects; 8.1%), Myroxylon pereirae resin (55 subjects; 8.3%), fragrance mix (46 subjects; 7.0%), colophonium (41 subjects; 6.3%) and propolis (30 subjects; 4.6%) were the most frequently observed positive reactions. Ten patients reacted to the compositae mix, and 14 to camomile, arnica and the sesquiterpene lactone mix.

Discussion

In a multicenter investigation, patch testing to *Aloe vera* yielded no evidence of a sensitizing potential for this herbal drug. This is remarkable in view of the fact that a large number of the tested subjects had sought medical help because of dermatitis due to other causes and were obviously at risk for skin reactions. None of them reported any side-effects after the application of *Aloe vera* on the skin. It may be assumed that an even much larger number of the patients had experienced unwitting contact to *Aloe*-containing products in the past.

A distinction must be made between 2 components of the plant. The bark of the leaves and the layer under the bark contain *Aloe*, a yellow and extremely bitter fluid containing aloin, *Aloe*-emodin and barbaloin. These are anthrachinones with pro-peristaltic properties (16) and were formerly used to treat constipation because the water-soluble glycosides are split by intestinal bacteria into aglycones which affect the laxative action. They also possess potential antibiotic and anticancer properties (6) but are also known to exert neoplastic effects (7, 8). As aloin and emodin have a considerable irritating potential and may cause cramping, bloody diarrhoea and nausea (17), constraints have been imposed on their use for a long time. This might explain why all reports in the Pubmed elicited by entering the terms 'Aloe' and 'allergy' or 'dermatitis' or 'anaphylaxis' (18–22) are older than 15 years – a time when the irritating extracts of the leaves were still in use. To our knowledge, a patch test or prick test in the case of an anaphylactic reaction was performed only in 1 instance (18). An anaphylactic reaction after injection (!) of *Aloe vera* (20) is likely to be toxic; in another report, other reasons for the reaction were not ruled out (21). Some of the published literature is in the Russian language, which the authors of the present study are not familiar with.

Today, most manufacturers of *Aloe* products process the *Aloe* gel, which is a transparent and

viscous pulp found in the center of the leaves. Light and electron microscopic studies (23) showed that it consists of large clear mesophyll cells. Cell walls, degenerated cellular organelles and liquid content accounted for 16.2%, 0.7% and 83.1% of the pulp, respectively, on a dry weight basis. Carbohydrates seem to contribute to the chemical composition almost exclusively but are distinct in each of the components (23) and may thus be functionally different. Many medical effects have been attributed to these polysaccharides (23), among them are acemannan, which is being studied for its effects on the immune system (9, 10), and glucomannan, a good moisturizer, which accounts for its use in cosmetics.

The components of *Aloe* gel itself are not likely to induce contact sensitization. This might explain the outcome of our study. As we used pure formulations, the concentration of the test substances was sufficient to reproduce sensitization. At first glance, our results indicate that *Aloe* is a herbal drug without side-effects. However, this does not justify unrestrained promotion of *Aloe* products. Recently in the USA, a physician was sentenced to approximately 4 years of imprisonment and a restitution of US\$ 222 000 for claiming that his products bolstered the immune system and could be used to treat several serious diseases such as AIDS and cancer (24).

Conclusion

The sensitizing capacity of *Aloe vera* appears to be very low. This might be because the *Aloe* pulp (*Aloe* gel) is used almost exclusively, whereas reports on eczematous or anaphylactic reactions were observed at a time when anthrachinone-containing leaf extracts were commonly used.

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