

**Ez a kettős-vak, placebo-kontrollált vizsgálat, arra irányult, hogy értékelje a klinikai hatékonyságát és tolerálhatóságát az 0,5%-os Aloe vera kivonatnak hidrofil krémekben a psoriasis vulgaris betegek gyógyításában.**

Tanweer A. Syed<sup>1</sup>, S. Ashfaq Ahmad<sup>2</sup>, Albert H. Holt<sup>3</sup>, Seyed Ali Ahmad<sup>4</sup>, Seyed Hamzeh Ahmad<sup>4</sup> and Mohammad Afzal<sup>5</sup>

<sup>1</sup> Department of Clinical Physiology, Malmö University Hospital, Malmö, Sweden

<sup>2</sup> Department of Chemistry, University of the Punjab, Lahore, Pakistan

<sup>3</sup> American Social Health Association, Research Triangle Park, North Carolina, USA

<sup>4</sup> Medical Faculty, University of the Punjab, Lahore, Pakistan

<sup>5</sup> PR Hospital, University of the Punjab, Lahore, Pakistan

Ez a kettős-vak, placebo-kontrollált vizsgálat, arra irányult, hogy értékelje a klinikai hatékonyságát és tolerálhatóságát az 0,5%-os Aloe vera kivonatnak hidrofil krémekben a psoriasis vulgaris betegek gyógyításában.

**Hatvan beteget** (36M/24F), melyek 18-50 évesek (átlag 25,6 év) vizsgáltak az enyhe, középsúlyos krónikus psoriasis vulgaris típusú pikkelysömörben. PASI (Psoriasis Area Severity Index) 4,8 és 16,7 közöttit (átlagos 9,3) vontak be, és random módon két párhuzamos csoportot vizsgáltak. A betegség átlagos időtartama a beválasztást megelőző 8,5 év volt (tartomány: 1-21). A betegeket ellátták 100 g-os tubusú placébóval és aktív kivonattal. (0,5% Aloe vera kivonat). Otthon 3-szor naponta 5 egymást követő napon át (maximum 4 hetes aktív kezelés) vizsgálták.

A betegeken heti rendszerességgel vizsgálták. Nézték az elváltozások fokozatos csökkentését, hámlást, majd csökkent a bőrpír, beszűrődés, és így csökkent a PASI-pontszám. A tanulmányt a tervek szerint 16 héten át 12 hónapos nyomon követéssel végezték, és havonta ellenőrizték. A kezelést jól tolerálták a betegek.

A vizsgálat végére, az Aloe vera kivonatú krém esetén 25/30 volt gyógyult betegek aránya (**83,3%**). Míg a placebo-kúra aránya 2 / 30 (**6,6%**), ( $P < 0,001$ ), ami jelentős különbség a psoriaticus (328/396 (82,8%) versus placebo 28/366 (7,7%),  $P < 0,001$ ) eredményt tekintve. E tanulmány eredményei azt sugallják, hogy a helyileg alkalmazott Aloe Vera kivonat 0,5% a hidrofil krémekben sokkal hatékonyabb, mint a placebo, és nem bizonyított, mérgező vagy bármely egyéb objektív mellékhatásokat. Ezért tekinthető biztonságosnak és alternatív kezelésnek az Aloe Vera a psoriasis vulgarisban szenvedő betegek gyógyításában.

## Management of psoriasis with *Aloe vera* extract in a hydrophilic cream: a placebo-controlled, double-blind study\*

Tanweer A. Syed<sup>1</sup>, S. Ashfaq Ahmad<sup>2</sup>, Albert H. Holt<sup>3</sup>, Seyed Ali Ahmad<sup>4</sup>, Seyed Hamzeh Ahmad<sup>4</sup> and Mohammad Afzal<sup>5</sup>

<sup>1</sup> Department of Clinical Physiology, Malmö University Hospital, Malmö, Sweden

<sup>2</sup> Department of Chemistry, University of the Punjab, Lahore, Pakistan

<sup>3</sup> American Social Health Association, Research Triangle Park, North Carolina, USA

<sup>4</sup> Medical Faculty, University of the Punjab, Lahore, Pakistan

<sup>5</sup> PR Hospital, University of the Punjab, Lahore, Pakistan

### Summary

The purpose of this double-blind, placebo-controlled study was to evaluate the clinical efficacy and tolerability of topical *Aloe vera* extract 0.5% in a hydrophilic cream to cure patients with psoriasis vulgaris. Sixty patients (36M/24F) aged 18–50 years (mean 25.6) with slight to moderate chronic plaque-type psoriasis and PASI (Psoriasis Area and Severity Index) scores between 4.8 and 16.7 (mean 9.3) were enrolled and randomized to two parallel groups. The mean duration of the disease prior to enrolment was 8.5 years (range 1–21). Patients were provided with a precoded 100 g tube, placebo or active (with 0.5% *Aloe vera* extract), and they self-administered trial medication topically (without occlusion) at home 3 times daily for 5 consecutive days per week (maximum 4 weeks active treatment). Patients were examined on a weekly basis and those showing a progressive reduction of lesions, desquamation followed by decreased erythema, infiltration and lowered PASI score were considered healed. The study was scheduled for 16 weeks with 12 months of follow-up on a monthly basis. The treatment was well tolerated by all the patients, with no adverse drug-related symptoms and no dropouts. By the end of the study, the *Aloe vera* extract cream had cured 25/30 patients (83.3%) compared to the placebo cure rate of 2/30 (6.6%) ( $P < 0.001$ ) resulting in significant clearing of the psoriatic plaques (328/396 (82.8%) vs placebo 28/366 (7.7%),  $P < 0.001$ ) and a decreased PASI score to a mean of 2.2. The findings of this study suggest that topically applied *Aloe vera* extract 0.5% in a hydrophilic cream is more effective than placebo, and has not shown toxic or any other objective side-effects. Therefore, the regimen can be considered a safe and alternative treatment to cure patients suffering from psoriasis.

**keywords** psoriasis, *Aloe vera*, herbal extracts, pharmaceutical creams

**correspondence** Dr Tanweer A. Syed, The University of North Carolina at Chapel Hill, CB 7030, 547 Burnett-Womack Bldg, Chapel Hill, NC 27599–7030, USA

\*This work was presented in part in abstract (Abstract 108) at the Fourth Congress of The European Academy of Dermatology and Venereology, 10–15 October 1995, Brussels, Belgium.

### Introduction

Psoriasis is a very common, non-infectious, inflammatory skin disease characterized by well defined,

distinctive erythematous plaques yielding adherent silvery white scales, which may manifest bleeding points when removed (Auspitz's sign). Psoriasis may affect any cutaneous surface, but the commonest sites are the extensor surfaces of the elbows and knees, scalp (where scales may become extremely dense) and sacral areas. Precipitation of psoriasis may occur due to trauma (scratching, sunburn or surgical wounds), Köbner phenomenon, stress or genetic predisposition. The eruption of psoriasis may cause numerous symmetrical plaques affecting both sides of the body or may be limited to one or two patches. Men and women are equally affected, but it is more common in white people than in Asians and black people. In the majority of patients it appears for the first time between the ages of 5 and 25.

There is no satisfactory or effective cure for psoriasis. However, a variety of therapeutic modalities have yielded limited efficacy with frequent side-effects. The available treatments, both local and systemic, which have to some extent proved effective include coal tar, Dithranol (anthralin), calcipotriol, corticosteroids, photochemotherapy (PUVA, psoralens with long-wave ultraviolet radiation), retinoids, methotrexate and other cytostatic drugs such as hydroxyurea and cyclosporin.

*Aloe vera* is a stemless, perennial, drought-resisting, succulent plant and has reportedly been used since ancient times for medicinal purposes (Klein & Penneys 1988; Shelton 1991; Kent 1979). It belongs to the lily (Liliaceae) family, and has stiff grey to bright green lance-shaped leaves containing clear gel in a central mucilaginous pulp. Recent research has shown that the pharmacologically active agent is concentrated in both the gel and the rind of the *Aloe vera* leaf. The active agents have shown considerable analgesic, antipruritic, wound healing and anti-inflammatory properties (Duke 1985), thus justifying consideration of *Aloe vera* as an effective remedy for the treatment of psoriasis.

The purpose of this double-blind, placebo-controlled study was to evaluate the clinical efficacy and tolerance of *Aloe vera* extract (0.5%) in a hydrophilic cream to cure patients suffering from psoriasis vulgaris.

## Patients and methods

Sixty preselected patients (36M/24F) aged 18–50 years (mean 25.6) with slight to moderate chronic plaque-type psoriasis were randomly allocated to two parallel groups. The diagnosis of psoriasis was established by both biopsy and the clinical manifestation of the characteristic silver-white erythematous psoriatic plaques. The mean duration of the disease was 8.5 years (range 1–21). The clinical cycle was measured using the PASI (psoriasis area and severity index) scoring method as described elsewhere (Fredriksson & Pettersson 1978). Prior to entry each patient underwent a general physical body examination including routine laboratory tests, such as haematology, complete blood cell count, urinalysis, pregnancy test and the demographic recording of the number of chronic plaques using Harpenden skin calipers. At the start and end of the study full-thickness 6-mm punch skin biopsies were taken under local anaesthesia with 1% lidocain from one lesion of each patient, and were stained with haematoxylin and eosin for the evaluation of acanthosis, parakeratosis, thinning, papillary vessel dilatation and inflammatory infiltration. Subjects also received oral and written information about the purpose of the study and, accordingly, an informed consent was obtained from all patients (Helsinki Declaration). The study was approved by the respective hospitals' ethics committees and also the district health authorities Lahore and Multan, and took place at official and private clinics and hospitals in Punjab, Pakistan, at the beginning of February 1991. Patients who had been treated with systemic steroids, cytotoxic drugs, beta-blockers, ultraviolet irradiation therapy in the preceding 3 months, as well as patients with epilepsy, other types of psoriasis, and pregnant or lactating mothers were excluded.

Patients were allowed to use water-washable emollients during the course of study. *Aloe vera* extract was prepared as described elsewhere (Davis *et al.* 1991) and incorporated 0.5% by weight into a hydrophilic cream using a combination of mineral oil and castor oil (B.P.) as vehicle. Matching placebo cream contained no *Aloe vera* extract. Both active and placebo preparations (prepared at the Department of Chemistry, University of the Punjab, Lahore), precoded, 100 g in tubes, were kept at

ambient temperature. Patients were given a precoded 100 g tube (active/placebo) for one week's use and shown how to apply the trial preparation topically on their lesions 3 times daily (without occlusion and without exposure of lesions to sunlight) for 5 consecutive days, to a maximum of 15 applications per week. The study was restricted to 4 weeks of active treatment (protocol limitation). To assess the clinical efficacy and tolerance of the trial preparation, patients were examined once a week for up to 16 weeks and thereafter followed up on a monthly basis for 8 months.

$\chi^2$  and Fisher's exact test with two-tailed values were used for significant test results.

## Results

Patient compliance was excellent, the trial preparation was well tolerated and there were no drop-outs. All 60 patients were available for efficacy analysis. Every subject had 4 weeks active treatment, and during that period progressive reduction of desquamation, followed by decreased erythema, infiltration, resulting in moderate to excellent improvement or complete resolution of psoriatic lesions was noted. The mean duration of disease prior to entry was 8.5 years (range 1–21). By the end of the 4-week active treatment, 27/60 (45%) patients (18M/9F), and 46.7% (356/762) of psoriatic plaques were cured, resulting in a substantial lowering of the PASI score from a mean 9.3 to 2.2.

The *Aloe vera* cream cured a significantly larger number of patients than the placebo (25/30 (83.3%) vs 2/30 (6.6%),  $P < 0.001$ ). The active group also showed a higher number of healed chronic plaques (328/396 (82.8%) vs 28/366 (7.7%),  $P < 0.001$ ). Periodic laboratory tests, including complete blood cell count and urinalysis, were all within normal limits. Biopsy analysis revealed that cured lesions showed a decrease in the levels of epidermal acanthosis, parakeratosis, thinning, papillary vessel dilatation, and inflammatory infiltration. Demographically, both treatment groups were comparable in age, race, marital status and duration of disease. The 60 subjects used a total of 245 tubes (100 g) in 4 weeks. Patients experienced no drug-related adverse symptoms, either local or systemic, and there was no reporting of hypersensitivity or dermatitis.

**Table 1** Patients' characteristics

	<i>Aloe vera</i> group (n=30)	Placebo group (n=30)
Sex	18M/12F	18M/12F
Mean age (years)	25.9	25.2
Plaques at baseline	396	366
Plaques cured after 4 weeks	328	28
Patients cured after 4 weeks	25 (83.3%)	2
Sex	16M/9F	M
Mean PASI at baseline	9.7	8.9
Mean PASI after 4 weeks	2.2	8.2
Locations of plaques		
Buttock	81	86
Knee	98	94
Elbow	96	89
Body surface	121	97

Table 1 summarizes the characteristics of the study population. The study was followed up on a monthly basis for 8 months and there were no relapses.

## Discussion

One of the major findings of this study is that topical *Aloe vera* extract 0.5% cream significantly resolved psoriatic plaques and proved to be quite effective in healing patients suffering from psoriasis vulgaris. Patients complained of no adverse symptoms or other side-effects. They were pleased to be able to maintain their normal way of life while receiving treatment. Placebo recipients showed no change, indicating lack of efficacy.

A recent review (Lebwohl *et al.* 1995) mentioned that 70% of patients preferred topical therapy for treating psoriasis. However, most of the current psoriasis treatments are suppressive and directed either at inducing a remission or relieving the patient's condition. At present, cyclosporine, calcitriol, calcipotriol, retinoids, dithranol and coal tar are among the usually accepted antipsoriatic compounds. Cyclosporin is a neutral cyclic peptide that inhibits cell-mediated immune responses with its direct antiproliferation effect on epidermal cells. In a recent study, Ellis *et al.* (1995) reported 57% of their patients as completely resolved or cleared of

psoriasis plaques with the use of 3 mg/kg per day cyclosporine (as maintenance agent) for a period of 4 months. Although cyclosporine has been shown to be very effective in the treatment of psoriasis, one cannot ignore its severe side-effects, namely gradual and progressive decline in renal function, hypertension and nephrotoxicity (Koo 1995).

Calcitriol (1,25-dihydroxyvitamin D<sub>3</sub>) also inhibits proliferation and induces differentiation in epidermis. Both Smith *et al.* (1988), in a study of 17 subjects in a 6-week trial, and Perez *et al.* (1995) in a study of 4 children for a period of 8 weeks, reported favourable results with calcitriol, but this compound is associated with the risk of hypercalcaemia, hypercalcaemia and induction of bone resorption.

Calcipotriol is a synthetic analogue of calcitriol but devoid of hypercalcaemic and hypercalcaemic side-effects. By using different concentrations of calcipotriol (topically) in an ointment on 50 patients, Kragballe (1989) reached a cure rate of 88%, accompanied by drug-related side-effects such as facial dermatitis on 5 patients during the course of treatment; 4 subjects dropped out. By using calcipotriol ointment for 6 weeks on 20 patients Mozzanica *et al.* (1994) achieved a cure rate of 85% (17/20), with 2 patients experiencing local adverse events.

Retinoids (tretinoin and acitretin) are a group of compounds derived from vitamin A, retinoic acid, and more commonly prescribed for slim thick hyperkeratotic psoriatic lesions. Associated side-effects to retinoids include teratogenicity, pruritus, general dryness of skin, lips and vagina and rise of blood lipids. Dithranol (Anthralin) inhibits granulocyte function and DNA replication. It is presumed that some of its beneficial effects may be due to the release of free-radical oxygen during therapy. Anthralin is an irritant, stains normal skin and requires medical supervision during its application, which has limited its use. Compared to these and other studies on topical treatment of psoriasis, this study demonstrates a statistically significant ( $P < 0.001$ ) healing in 4 weeks, without drug-related side-effects or dropouts.

Psoriasis is primarily a hyperproliferation of keratinocytes in the dermis. *Aloe vera* extract is a grease-free penetrant which is readily absorbed into dermal and deeper tissues. It carries analgesic, antiallergic, antipruritic, wound healing and anti-

inflammatory components such as amino acids. The results of this study may suggest that the extract acted in an occlusive manner, keeping the skin moistened and at the same time directly inhibiting the psoriatic plaques by suppressing proliferation and stimulatory differentiation of the cells in the epidermis.

We have previously reported (Syed *et al.* 1995a,b) that many parameters must be observed in incorporating biologically active compounds into hydrophilic emulsions. In order to motivate and enhance the therapeutic efficacy of a drug in semi-solids (gel, cream and lotion, etc.), one has to consider the drug's preservation, antioxidation, bio-availability of the molecules, the type and status of the skin, the choice of a proper vehicle, and the actual interaction of the drug with the target cells (pharmacodynamic phase). These criteria are crucial in maximizing the clinical response to the drug.

In conclusion, the results of this study indicate that *Aloe vera* extract 0.5% in a hydrophilic cream was well tolerated and appeared to be quite effective. It was beneficial in enhancing resolution and improvement in the majority of study patients compared to the placebo, which suggests its possible use as an alternative treatment of psoriasis vulgaris.

### Acknowledgements

The authors wish to thank Professor Per Wollmer, head of the department of Clinical Physiology, University Hospital Malmö, University of Lund, Sweden, and Miss Marianne Pickens for their encouragement.

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