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Original Article

Evaluation of Anti-psoriatic Activity of *Aloe sinkatana* Extract on Imiquimod Induced Psoriatic-like Dermatitis in Mice

Azza Dawoud Hussien Dawoud[1, 2*], Mohammed Abdalbagi[3]

1. Department of Drug Formulation, Medicinal and Aromatic Plants & Traditional Medicine Research Institute, National Center of Research, Khartoum, Sudan.
2. Department of Pharmaceutics, Faculty of Pharmacy, National Ribat University, Khartoum, Sudan.
3. Department of Microbiology & Parasitology, Medicinal and Aromatic Plants & Traditional Medicine Research Institute, National Center of Research, Khartoum, Sudan.

*** Corresponding Author:**
Azza Dawoud Hussien Dawoud, Assistant Professor
Address: Department of Pharmaceutics, Faculty of Pharmacy, National Ribat University, Khartoum, Sudan.
Phone: +249 (926) 862873
E-mail: azzadawoudhussien@gmail.com

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ABSTRACT

Background: One of the most significant Sudanese medicinal plants is *Aloe sinkatana*, which has considerable pharmacological activity and has been historically used to treat psoriasis and other skin conditions.

Objectives: This study aims to evaluate the *A. sinkatana* plant's anti-psoriatic properties.

Methods: The imiquimod (IMQ)-induced psoriasis mice model was used to evaluate the anti-psoriatic effect of the *A. sinkatana* plant. So, the effects of 0.1% and 0.2% extracts of *A. sinkatana* extract on five groups of mice were assessed and compared with the conventional medication, i.e. dexamethasone. Differences between treatment groups were evaluated by a one-way analysis of variance, followed by a post hoc Fisher least significant difference test using the SPSS software, version 20. At $P<0.05$, differences were deemed significant. A minimum of three replicates were used in each duplicate experiment. For all values, Mean±SD was used.

Results: The extracts showed a significant and remarkably strong anti-psoriatic effect since the percentages of psoriasis-like symptoms were reduced in groups treated with 0.2% Aloe extract (A.E), 0.1% A.E, and dexamethasone 86%, 84%, and 68%, respectively. Both extract concentrations improved the psoriatic lesions and decreased the grading of the treated groups' psoriasis area and severity index (PASI) scale.

Conclusion: Due to the constant research to develop a safe and effective topical preparation for the treatment of psoriasis, the current study provided an enhanced anti-psoriatic treatment, represented by *A. sinkatana* extract. This herb may be beneficial in the pharmaceutical formulation of new safe and effective medication for treating psoriasis.

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Introduction

Psoriasis is recognized as the most common autoimmune disease caused by the inappropriate activation of the cellular immune system. The National Psoriasis Foundation states (NPF) that around 125 million individuals globally are affected by this condition, representing 2% to 3% of the entire population [1].

About 60% of psoriasis patients reported their disease as a significant problem in their everyday lives, declining their quality of life [2]. The total costs of psoriasis for patients are $11.25 billion annually, and approximately 60% of psoriasis patients miss an average of 26 days of work a year due to their illnesses [3]. Psoriasis is a common skin disorder characterized by severe skin inflammation, epidermal hyperproliferation, disappearance of the granular layer, and persistence of the keratinocyte's nuclei in the stratum corneum of the epidermis, vascular hyperplasia and infiltration of immune cells in dermis and epidermis. It is assessed clinically using the psoriasis area and severity index (PASI) scale, which ranks the severity of erythema (redness), induration (thickness), and desquamation (scale) [4].

Even though mouse skin differs from human skin, a new study discovered many similarities between human psoriasis and mouse models across thousands of genes, thus supporting the use of mouse preclinical models to screen anti-psoriatic compounds.

This comparative study confirmed a relationship between psoriatic gene expression in human psoriatic skin samples compared to transgenic mouse keratinocyte models and the mouse imiquimod (IMQ) induced psoriasis model. The mouse IMQ model represents an easy, fast, and inexpensive method of inducing psoriasis in mice, which avoids the expense of labor-intensive breeding programs required for producing the keratinocyte transgenic mouse lines. Furthermore, some of these transgenic mouse lines also suffer from a shortened lifespan due to stunted growth and severe psoriatic skin lesions as a result of the genetic modification. Moreover, the lesions that develop in the mouse IMQ model are similar to those of human psoriatic lesions and depend on interleukin (IL)-23 and IL-17 [5].

Herbal medicines are safer than synthetic drugs. Nowadays, herbal resources play a very important role in managing skin and inflammatory diseases.

Numerous studies have been carried out that have demonstrated and confirmed the efficacy of the Aloe plant in treating psoriasis and its safety without causing any adverse effects. One of the most important studies is the study conducted by Dhanabal et al. [6]. The effectiveness and safety of using Aloe vera extract as a cure for psoriasis were demonstrated in mice. Furthermore, there are studies in which the Aloe vera plant extract was used to treat 60 patients with psoriasis for one month. The results of the experiments were impressive in terms of patient recovery without any side effects [7-9].

With all extremes of meteorological, climatic, and topographical features resulting in varied and luxuriant flora, Sudan could supply many world countries with medicinal plants. Many drugs of established therapeutic value used in the pharmacopeias of different countries grow in many parts of Sudan. Bearing in mind all this, the main task of this study is to spotlight the anti-psoriatic effect of the very important Sudanese medicinal tropical plant known as *Aloe sinkatana* (Aloe Sudan).

A. sinkatana grows naturally in Eastern Sudan in the Red Sea Mountains, mainly in the Arkawit area, where it is popularly used extensively by region residents to treat skin diseases, specifically psoriasis.

Materials and Methods

Plant collection and authentication

The *A. sinkatana* plants were collected in August 2022, from the Sinkat area, Red Sea state, Sudan. They were authenticated by a taxonomist in the Herbarium Unit of the Department of Chemistry, Medicinal, and Aromatic Plants Research Institute and Traditional Medicine, National Research Center, Sudan.

Animals used in the screening of anti-psoriatic activity

Healthy Albino mice of either sex, 7-8 weeks of age (between 23 and 26 g), were supplied by Animal House of Medicinal and Aromatic Plants Research Institute and Traditional Medicine, National Research Center, Khartoum, Sudan.

The pathogen-free animals were maintained under standard conditions (12 h light and dark cycle at an ambient temperature of 25±1 ˚C.

They were fed with commercially available rats/mice and water ad libitum. The animals were allowed to ac-

climatize to the environment for 7 days before the commencement of experiments.

Extraction of *A. sinkatana*

Mature, healthy, and fresh leaves of *A. sinkatana*, 75 to 90 cm long, were scrapped and cut into pieces. A traditional hand filleting method of processing Aloe leaves was used. In this method, the lower leaf base, the tapering point at the leaf top, and the short spines located along the leaf margins were removed by sharp blades. The blade was then introduced into the mucilage layer below the green rind, avoiding the vascular bundles, and the top rind was removed. The epidermis of the leaves was peeled off, and the colorless, solid mucilaginous gel was cut into pieces. Then, 250 g of gel was loaded into a 1000 mL flask, and 500 mL solvent (Ethanol) was added. Ultrasound-assisted extraction was performed at 60 ˚C for 60 min. After that, the solution was filtered, and the solvent was removed under reduced pressure in a rotary evaporator until it became completely dry [10].

Method of induction of psoriasis

This method was modified from the protocol by van der Fits et al. [11].

The mice were shaved on the dorsal skin. The IMQ cream with a dose of 62.5 mg was topically administered on the shaved back except for group I (normal control). The rest of the groups were IMQ-induced psoriatic groups, and the treatment was given once daily and continued for 6 consecutive days. The control group (group 1) was topically applied a control vehicle (glycerin).

The experimental design

All the animals were treated daily with the topical application for 14 days.

IMQ was continued throughout the treatment phase to all the mice from G2-G5 groups to ensure that the recovery, if any, in the mice was due to the test extracts.

The mice were distributed into 5 groups, each consisting of 6 animals as follows:

Group 1: Control group without disease (animal's application of glycerin was continued),

Group 2: Without any treatment, served as untreated disease-induced mice,

Group 3: Psoriatic mice treated one time daily with topical dexamethasone (0.1%) (served as positive control),

Group 4: Psoriatic mice were treated once daily with topical Aloe extract (A.E), 0.1% in a glycerin vehicle,

Group 5: Psoriatic mice were treated one time daily with topical A.E, which was 0.2% in a glycerin vehicle.

At the end of the experiment, the animals were sacrificed, and their shaved skins were removed and processed for subsequent histological examination.

PASI

The PASI, as described by van der, was introduced in the study to evaluate the severity of inflammation of the shaved back skin [11]. Briefly, four important parameters of skin erythema, scaling, and thickness were scored independently from 0 to 4, where 0=no signs, 1=slight signs, 2=moderate signs, 3=marked signs, and 4=marked clinical signs [12].

Histological studies

The animals were sacrificed, and the kidney fragments were fixed in 10% buffered neutral formalin and embedded in paraffin. The sections (4.0 µm) were stained with hematoxylin and eosin (H & E) for histopathological examination. Histological observations were made through an Olympus CX-21LED (Japan) optical microscope (10X and 20X lenses) coupled to an Olympus (Japan) digital camera [13].

Statistical analysis

Differences between treatment groups were assessed by one-way analysis of variance (ANOVA), followed by a post hoc Fisher least significant difference (LSD) test using the SPSS software, version 20. At $P<0.05$, differences were deemed significant. A minimum of three replicates were used in each duplicate experiment. For all values, Mean±SD was used.

Results

The composite clinical psoriasis score is the result of summing the individual erythema (0-4), thickness (0-4), and scale (0-4) score on each assessment day. Mean±SEM values were reported for all treatment groups.

Table 1. Cumulative score of the IMQ-induced psoriasis model of *A. sinkatana* extract

Day	Control	IMQ	IMQ+Dexamethasone	IMQ+0.1%A.E	IMQ+0.2%A.E
2	0	0	0	0	0
4	0	3.2	2.8	2.2	2.5
6	0	4.7	4.3	3.1	3.3
8	0	7	4.6	3.4	2.8
10	0	8.9	3.8	3	2.7
12	0	10.1	3.7	2.4	2
14	0	10	3.2	1.6	1.4

A.E: Aloe extract.

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Calculation

Composition clinical psoriasis score (cumulative)=

10/100×100=10%

1.6/100×100=1.6%

Percentage reduction over disease only (IMQ)=

1.6/10×100=16%

100-16= 84%

3.2%/10×100=32%

100-32=68%

For the duration of the experiment, all of the mice's characteristics and health status, including their intake of food and water, body weight, psychological signs, breathing patterns, and circulatory, were within normal limits. There were signs of erythema, scaling, and thickening on the mice's dorsal skin two or three days after the IMQ application began. Following that, G2 mice's psoriasis-like symptoms gradually worsened until day 14, the end of the treatment protocol.

Figure 1 presents the effect of topical treatment of *A. sinkatana* extract (A.E) and dexamethasone standard drug on PASI grading on IMQ-induced psoriatic mice.

In the present study, the application of IMQ to the mice showed the development of an apparent psoriasis phenotype, including erythema, scaling, and skin thickness.

On treatment with two concentrations of A.Es and dexamethasone, the results demonstrated a marked recovery from psoriasis in the treated groups as there was a gradual reduction in the thickness and scaling of the skin, which was also evident through reduced grading of the PASI scale of treated groups.

A.Es inhibited the IMQ-induced increased thickness of the epidermal and subcutaneous tissue. In addition, 0.2% A.E showed a remarkable reduction in psoriasis-like symptoms which was followed by the 0.1% Aloe and dexamethasone standard drug (Table 1 and Figure 1).

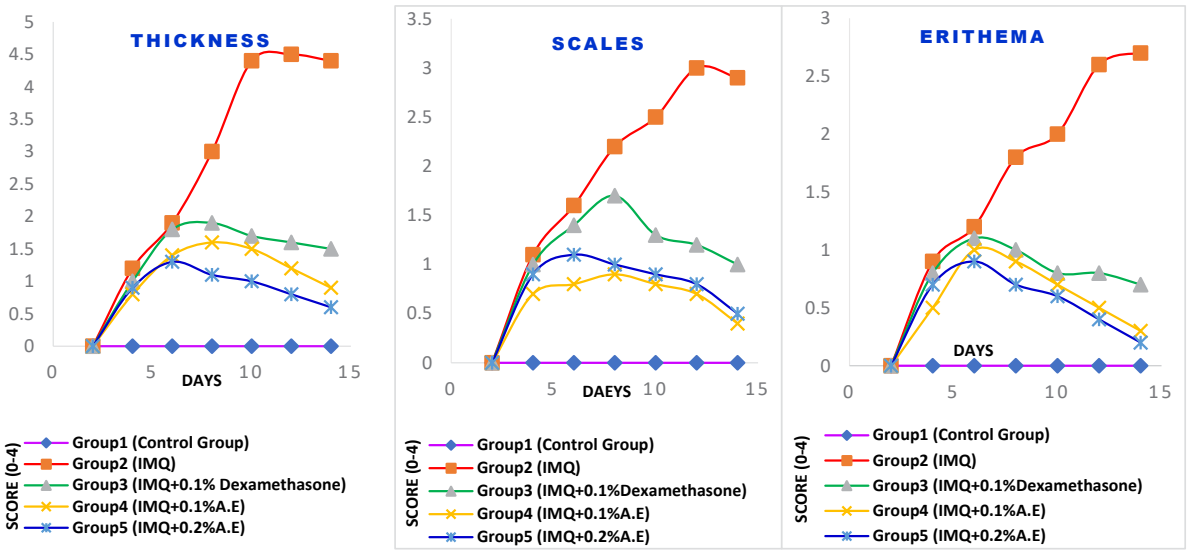
The percentages of the reduction in the PASI scale for G3, G4, and G5 were 68%, 84%, and 86%, respectively (Table 2).

From the overall observation, a maximum effect (86%) was observed at 0.2% concentration of A.E.

Table 2. The percentage of psoriasis reduction of *A. sinkatana* extract

Variables	%			
	IMQ	IMQ+ Dexamethasone	IMQ+0.1% A.E	IMQ+0.2% A.E
Composition clinical psoriasis score (cumulative)	10	3.2	1.6	1.4
Percent reduction over disease only (IMQ)	--	68	84	86

IMQ: Imiquimod; A.E: Aloe extract.



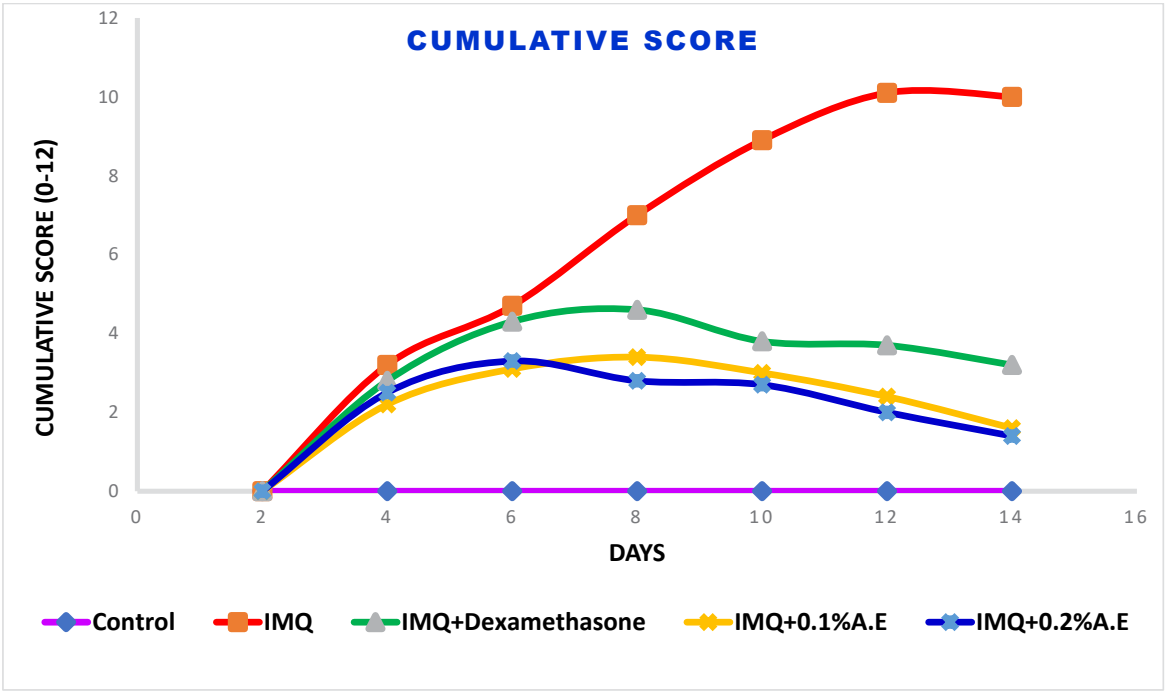


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Figure 1. The effect of topical treatment of *A. sinkatana* extract on PASI on IQM-induced psoriatic mice
Abbreviations: IMQ: Imiquimod; A.E: Aloe extract; PASI: Psoriasis area and severity index.

Results from H & E-stained IMQ-treated back skin aligned with the phenotypical observations and PASI score results. The mice treated with IMQ exhibited markedly elevated inflammatory infiltration and hyperkeratosis of the epidermis in their dorsal skin. Nevertheless, the epidermis and dermis of the control mice's dorsal skin slices were normal.

Remarkably, mice treated with dexamethasone and *A. sinkatana* extracts had significantly thinner epidermis than mice treated with IMQ alone.

Similar to mice treated with dexamethasone (group 3), animals treated with 0.1% A.E. (group 4) demonstrated significant suppression of the epidermal hyperplasia resulting from allergic dermatitis. Compared to other groups, mice treated with 0.2% A.E. (group 5) showed the highest levels of anti-psoriatic activity, recovering

nearly entirely from the IMQ-induced hyperplasia of the epidermal and subcutaneous tissue with just a mild inflammatory response.

Discussion

Since IMQ-induced psoriasis exhibits characteristics comparable to those of human psoriatic lesions, including epidermal, erythema, thickness, scaling, vascular development, an abundance of T cells, neutrophils, and dendritic cells, it is frequently employed as a model in experimental animals. When applied topically, IMQ activates the innate immune system and triggers adaptive immunity, resulting in psoriasis [14, 15]. The proliferation of epidermal keratinocytes may be a kind of cellular infiltration during psoriasis development. Psoriasis progression is influenced by several inflammatory pathways, including IL-12/T helper type 1(Th1), IL-23/Th17, and IL-22/Th22 [14, 15].

The PASI provides information on the disease's prevalence and cure pattern. Psoriasis is seen to significantly improve when PASI values recover by more than 50%, while psoriatic conditions are thought to improve significantly when PASI levels recover by more than 75% [16]. *A. sinkatana* showed a significant and remarkably strong anti-psoriatic effect since the percentage of psoriasis-like symptoms was reduced in groups treated with 0.2% A.E, 0.1% A.E, 86%, and 84%, respectively. According to this study, *A. sinkatana* plant extract is a promising therapeutic alternative for treating psoriasis. Further investigation of *A. sinkatana* biological mechanisms of action is required to verify that it may be utilized suitably and effectively to treat psoriasis in patients.

Conclusion

The in vivo evaluation of the *A. sinkatana* plant extract showed remarkable anti-psoriatic activity in mice with IMQ-induced psoriasis-like inflammation. It inhibited the IMQ-induced increased thickness of both the epidermal and subcutaneous tissue. Therefore, the *A. sinkatana* plant could be a potential drug to treat psoriasis individually or synergistically with other herbs or anti-psoriatic agents.

Ethical Considerations

Compliance with ethical guidelines

This study was performed in line with the principle of the Declaration of Helsinki and approved by the Pharmacology Department, Medicinal and Aromatic Plants, and Traditional Medicine Research Institute, National Center for Research, Khartum, Sudan (Code: 2022–0002).

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Authors' contributions

Methodology, investigation, data collection, and writing the original draft: Azza Dawoud Hussien Dawoud; Data analysis: Mohammed Abdalbagi; Review and editing: All authors.

Conflict of interest

The authors declared no conflict of interest.

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