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Coleus forskohlii shows anti-psoriatic activity in imiquimod-induced psoriasis ratsSagarika Majhi[✉], Iti Chauhan¹, Deepak Kumar¹, Md. Niyaz Alam², Md. Sarfaraj Hussain², Muzaffar Iqbal³¹Faculty of Pharmacy, I. T. S College of Pharmacy, Muradnagar, Ghaziabad, U.P. India²Lord Buddha Koshi Pharmacy College of Pharmacy, Baijanathpur, NH 107, Saharsa (Bihar) 852201, India³Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

ABSTRACT

Objective: To evaluate anti-psoriatic activity of *Coleus forskohlii* in rats with imiquimod-induced psoriasis.

Methods: Imiquimod was used to induce psoriasis in rats. Body weight, skin thickness, erythema, scaling, spleen weight, and histological alternations were measured to assess the effect of *Coleus forskohlii*. Furthermore, an emulgel formulation containing *Coleus forskohlii* 10% was prepared and characterized along with its *ex vivo* permeation studies.

Results: The emulgel formulation containing *Coleus forskohlii* 10% had a pH of 5.40±0.36, with optimum spreadability of (31.67±2.08) g/(cm·s) and viscosity of (15966.67±1274.10) cps, and enhanced both the rate and the extent of drug permeation through psoriatic skin. In an *ex vivo* study, the quantity of drug permeated (19.18%), deposited (52.38%), and drug remaining in the donor compartments (28.31%) was satisfactory. *Coleus forskohlii* significantly alleviated imiquimod-induced psoriasis by increasing glutathione and superoxide dismutase activity, decreasing malondialdehyde and nitric oxide levels, and alleviating histological alternations in rat skin.

Conclusions: *Coleus forskohlii* can alleviate imiquimod-induced psoriasis, which may be used as a therapeutic candidate for the treatment of psoriasis.

KEYWORDS: Psoriasis; *Coleus forskohlii*; Emulgel; *Ex vivo*; Imiquimod; Carbopol

1. Introduction

A widespread T-cell-mediated immune condition called psoriasis is characterized by confined, reddened, thicker plaques that are covered

in a silver-white scale. As an autoimmune condition, psoriasis is thought to be significantly influenced by both hereditary and environmental factors[1]. The term ‘psora’ in Greek which means itch is the source of the disease’s name. Psoriasis is a non-contagious, dry, inflammatory, and unsightly skin condition that can affect a person’s entire body. Sharply marginated, scaly, erythematous plaques that form in a reasonably symmetrical distribution and are primarily hereditary are its principal symptoms. The head, tips of fingers and toes, palms and soles, umbilicus, gluteus, under the breasts and genitals, elbows, knees, shins, and sacrum are the areas most frequently afflicted by psoriasis[2]. The innate TLR7/8 immune activator imiquimod (IMQ) can cause and aggravate psoriasis on the skin of animals and people. The quick and easy IMQ-induced psoriasis-like mouse model has been used more often since 2009

Significance

Allopathic medications are usually used to treat psoriasis. These treatments can be helpful, but they are sometimes expensive with adverse effects and limited long-term success. New treatments are required in order to control diseases in a safer and longer-lasting manner. This study shows that *Coleus forskohlii* can mitigate imiquimod-induced psoriasis, as evidenced by enhanced antioxidants, reduced oxidative stress, and improved erythema and scaling symptoms and skin structure.

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in several recent researches to assess psoriasis and its treatment *in vivo*[3,4].

A well-known medicinal plant from the Lamiaceae family, sometimes referred to as the mint family, is *Coleus forskohlii* (*C. forskohlii*). Forskolin is a significant metabolite that is only present in the cork cells of the root of *C. forskohlii*. It can be used to treat asthma, heart, gastrointestinal, and glaucoma conditions[5]. Forskolin is the first main labdane diterpenoid isolated from the roots and one of the most extensively studied constituents of this plant. It has a special ability to stimulate adenylyl cyclase quickly, directly, and reversibly. This not only underlies its wide range of pharmacological effects but also renders it a valuable tool for the study of role of cyclic adenosine monophosphate (cAMP) in various diseases[6].

Psoriasis is a chronic autoimmune skin condition characterized by rapid and excessive skin cell proliferation. Psoriasis is characterized by decreased levels of cAMP in the skin relative to another regulating substance, cyclic guanosine monophosphate (cGMP). The decreased levels of cAMP relative to cGMP in psoriatic skin lead to dysregulation of cell growth and differentiation. This imbalance results in a significantly higher rate of cell division, with cells dividing up to 1 000 times faster than normal. This rapid cell turnover contributes to the formation of the characteristic thick, scaly plaques seen in psoriasis. Forskolin, a diterpene present in *C. forskohlii*, shows its therapeutic benefits through the stimulation of adenylate cyclase, elevating cAMP's cellular production. Elevated cAMP levels can suppress the release of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-17, potentially reducing inflammation in psoriasis. This may also reduce the hyperproliferation of keratinocytes, addressing one of the primary issues in psoriasis. By normalizing the growth and differentiation of these skin cells, forskolin may contribute to a reduction in the rapid cell turnover that leads to plaque formation. Forskolin's ability to modulate cAMP levels can also influence the activity of various immune cells, potentially leading to a reduction in the hyperproliferative and inflammatory processes characteristic of psoriasis.

Since the middle of the 1980s, emulsion gels have become more significant in topical semisolid pharmaceutical dosage compositions. The extensive application of emulsion systems, particularly for dermatological formulas, contributes to their widespread usage as medicinal dosage forms. Either water-in-oil or oil-in-water emulsions can be turned into emulgel by combining them with a gelling agent[7]. The topical application of drug approach provides several benefits, including the capacity to administer the medication more precisely to a particular region and minimizing the risks of metabolic degradation and gastrointestinal incompatibility that are linked to oral administration[8]. Moreover, topical deliveries provide increased bioavailability by avoiding first-pass metabolism by the liver and consistent delivery for an extended period[9,10]. Emulgels now have been used for the treatment of various kinds of

skin disorders such as those infected by viral, bacterial, and fungal species (eczema, herpes simplex, acne)[11]. In this study, *C. forskohlii* was studied for its potent anti-psoriatic efficacy using the IMQ-induced psoriatic animal model. Carbopol 934 was used to formulate an herbal gel that included an extract of *C. forskohlii*. The produced emulgel formulation's pH, viscosity, and spreadability were also examined. Moreover, the *ex vivo* skin penetration model was used to examine the emulgel penetration behavior.

2. Materials and methods

2.1. Materials

C. forskohlii fresh powder was purchased from Kshipra Biotech Pvt. Ltd. in Indore, M.P, India. Commercially procured IMQ cream (5%) (Imiquad; Glenmark) is supplied in single-use packets with 12 per box and contains 250 mg of cream, which is equivalent to 12.5 mg of IMQ. Carbopol 934 was supplied by Loba Chemie Pvt. Ltd. (Mumbai, India). All other chemicals used in this study were of analytical grade.

2.2. Experimental animals

Thirty adult healthy Wistar albino rats (male) weighing about 180-200 g with no apparent skin lesions were used in this study. The animals received normal laboratory food and water while being housed in an environment with proper ventilation and temperature. They were acclimated to the lab environment for two weeks before the commencement of the experiment.

2.3. Psoriasis induction and *in vivo* study design

An IMQ-induced psoriasis-like dermatitis rat model was established by topical administration of 5% IMQ cream (62.5 mg/day for 7 d) on the back skin (1.5 cm $\times$ 1.5 cm area) that had been previously depilated. Control rats were given vaseline cream and scaling and erythema of the skin were observed on days 0, 3, and 7. Skin thickness was also measured on each of these days. Standard 2% salicylic acid cream, *C. forskohlii* 5% and 10% were topically applied (daily for 7 d) 4 h after IMQ application[4]. The animals were divided into five groups ($n=6$) randomly: Group I : Control group (vehicle vaseline); Group II : IMQ-induced psoriasis group; Group III: IMQ + 2% salicylic acid treatment group; Group IV: IMQ + *C. forskohlii* 5%; Group V : IMQ + *C. forskohlii* 10%.

The primary and foremost objective of the study was to evaluate the anti-psoriatic potency of *C. forskohlii* in rats. After establishing the pharmacological activity, a topical formulation was designed for *ex vivo* permeation studies. Vaseline has been widely used in

dermatological studies as a control due to its inert nature, minimal interaction with the skin beyond its occlusive properties and no bactericidal activity. It is not hydrophilic and will not be absorbed. When applied to the skin, it can form a film on its surface, so that moisture is not easy to evaporate and disperse. It can keep the skin moist and prevent bacteria from coming into contact with the skin from the air, thus reducing the possibility of infection. Further, biochemical and histopathological studies of excised skin were performed. Body weight and spleen weight were also measured.

2.3.1. Severity scoring of skin inflammation

The anti-psoriatic activity was evaluated based on psoriasis area and severity index (PASI) which is graded as zero, moderate, very marked score for redness and scaling along with the thickness of the skin with the help of a Vernier caliper[12].

2.3.2. Biochemical estimations

On the seventh day, rats were euthanized by administering thiopental sodium (65 mg/kg, *i.p.*). Psoriatic skin tissues were then excised and promptly washed with tyrode solution. A portion of the tissue samples that were collected were homogenized in phosphate buffer and the resulting supernatant was used to measure nitric oxide (NO)[13]. The malondialdehyde (MDA), glutathione (GSH), and superoxide dismutase (SOD) levels were also measured in tissue samples to evaluate the antioxidants potentials of *C. forskohlii*[14].

2.3.3. Histopathological study

Histopathology of psoriatic skin was carried out according to the studies reported previously. After euthanasia, rat skin was removed on day 7. Using hematoxylin and eosin, the sections (5 µm thick) of specimens were stained and then examined under a microscope (Leica DM 2000) and photographs were recorded[15].

2.4. Dose selection of *C. forskohlii* and formulation of emulgel

After the successful establishment of the activity of *C. forskohlii* in psoriasis, a suitable formulation was formulated (anti-psoriatic emulgel of *C. forskohlii*, knowing its hydrophobic nature). As per *in vivo* studies, the *C. forskohlii* 10% group showed better results as compared to the *C. forskohlii* 5%. Thus, multiple formulations were developed using various constituents with the core ingredient *C. forskohlii* 10% (Supplementary Table 1).

2.4.1. Optimization of carbopol concentration for gel preparation

Carbopol 934 was dissolved and its quantity varied (0.25%, 0.50%, and 0.75% *w/v*), based on consistency and gel-forming ability.

To make a homogeneous mixture, it was dissolved in cold water while being continually swirled at a reasonable pace. After that, triethanolamine was added to lower the pH to 6-6.5. Based on the optimized viscosity of gel base, 0.50% *w/v* was selected for emulgel formulation.

2.4.2. Preparation of emulsion

C. forskohlii and methylparaben were dissolved in ethanol and propylene glycol, respectively, to maintain the emulsion. The aqueous phase was then combined with both solutions. The oil phase and the aqueous phase were each heated to 70 °C in a separate water bath. After a homogenizer was used to continuously swirl the oil phase into the aqueous phase for 10 min at a speed of 3000 rpm, the mixture was cooled to room temperature. The oil portion was subsequently added by drops while the aqueous phase was continually agitated[16].

2.4.3. Preparation of emulgel

To formulate the emulgel, the gel and emulsion components were ultimately blended in a 1:1 ratio with light stirring (Supplementary Table 1).

2.5. Characterization of emulgel

Various pharmaceutical parameters of the formulated emulgel were evaluated including physical appearance, pH, viscosity, and spreadability[17].

2.5.1. Spreadability study

Spreadability equipment was used to measure spreading capacity of emulgel. It consisted of a block of wood with a pulley attached to one end of it. The 'drag and sleep' techniques were used to calculate spreadability. On this block, a ground glass slide was mounted. On this slide, test emulgel (2 g) was applied. Then, a glass slide with the same diameter as the fixed ground side and a hook were placed between these slides and the emulgel. The top of this slide was then loaded with weight (40 g). The top slide's time (in seconds) to travel a distance of 6 cm was recorded[16]. The spreadability was then determined using the formula below.

$$S = (M \times L)/T$$

Where S = spreadability, M = weight tied to the upper slide, L = length of glass slides, and T = time taken to separate the slides from each other.

2.5.2. pH

By assessing pH employing a glass electrode-based digital pH meter (ELICO) at room temperature and recording the results in triplicate, the skin biocompatibility of the emulgel was determined.

2.5.3. Viscosity

The viscosities of three freshly made formulations (CF1-CF3) were measured at room temperature using a Brookfield viscometer and using RV/HA/HB-4 spindle. The spindle was lowered into a beaker so that it was perpendicular to the center of the emulgel formulation. It was set there with care to ensure that the spindle did not contact the beaker's bottom, and revolved for 5 min at a speed of 5 rpm (optimized by hit and trial). The reading of viscosity in centipoise was noted in triplicate[18].

2.6. *Ex vivo* skin permeation analysis

Excised psoriatic rat skin was used in Franz diffusion cells for *ex vivo* drug permeation of emulgel. The receiver section had a pH 6.0 phosphate buffer while the donor compartment was filled with emulgel. The receiver chamber received the magnetic bar, which was rotating at 75 rpm. Through the use of hot water circulation in the outer jacket, the system's temperature was maintained at 37 °C. At pre-defined intervals, samples were taken at 30, 60, 90, 120, 150, 180, 210, 240, 270, and 1440 min. Fresh buffer was added to the recipient compartment each time the sample was withdrawn from it. The percentage of *C. forskohlii* permeated, deposited, and remained in the donor compartment was calculated. The absorbance was then measured at 320 nm with a UV-visible spectrophotometer[19].

2.7. Statistical analysis

The data are shown as mean $\pm$ SD and analyzed by one-way analysis of variance (ANOVA) followed by Tukey's test. The program Graph Pad Prism 5 was used to conduct all of the statistical analyses. *P* values under 0.05 were deemed significant.

2.8. Ethical statement

The Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), an Indian government body that sets standards for animal procedures, approved the study and ensured that it was conducted in accordance with its protocols. The I.T.S. College of Pharmacy's Institutional Animal Ethical Committee (IAEC) granted clearance for all experimental procedures (1044/PO/Re/S/07/CPCSEA) in order to conduct animal experimentation. In accordance with CPCSEA, all animals were given humane treatment.

3. Results

3.1. Effect of *C. forskohlii* on body weight and spleen weight

In rats with IMQ-caused psoriatic skin, body weight was considerably reduced. Significant increases in body weight were seen in *C. forskohlii* 5% and 10% treatment groups on day 7 (Figure 1A). In addition, spleen weight was noticeably increased by IMQ administration. *C. forskohlii* 10% markedly inhibited IMQ-induced increase in spleen weight while *C. forskohlii* 5% showed no significant effect (Figure 1B).

3.2. Effect of *C. forskohlii* on erythema and scaling in IMQ-induced psoriatic rats

The erythema and scaling of the PASI were used to grade the severity of the psoriasis-like skin disease during the 7-day experiment. From day 2 forward, the skin disorders that resembled psoriasis were evident. On days 3 and 7, erythema and scaling were markedly increased in IMQ-administered rats. On day 7, these symptoms were

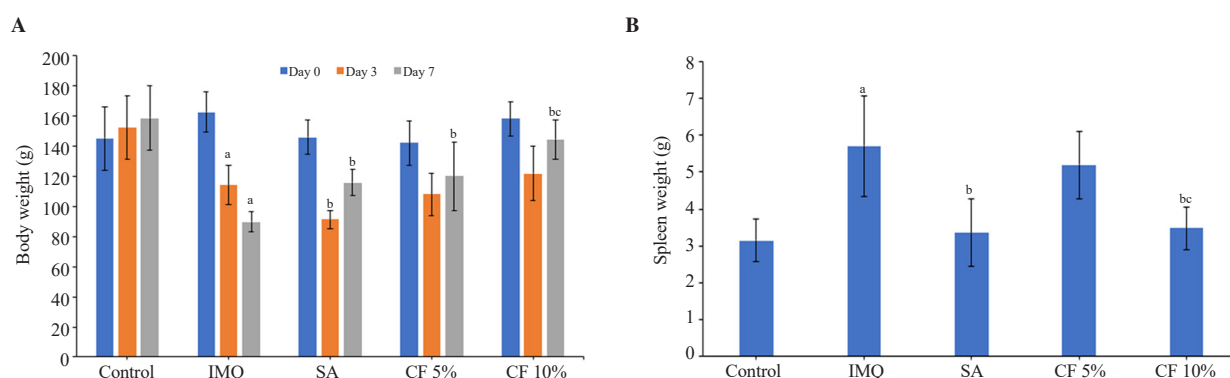


Figure 1. Effect of *Coleus forskohlii* on (A) body weight and (B) spleen weight. Spleen weight was measured on day 7 post treatment. Data are represented as mean $\pm$ SD ($n=6$) and analyzed by one-way ANOVA followed by Tukey's test. ^a $P<0.05$ compared with the normal control, ^b $P<0.05$ compared with the IMQ group, and ^c $P<0.05$ compared with the CF 5% group. IMQ: imiquimod; SA: salicylic acid; CF: *Coleus forskohlii*.

significantly alleviated in rats treated with *C. forskohlii* 5% and 10%. The mean scores of erythema and scaling on days 0, 3, and 7 are displayed in Figure 2.

3.3. Effect of *C. forskohlii* on skin thickness

Skin thickening was observed only on the IMQ-treated dorsal skin of rats. Increased skin thickness scores were observed throughout the 7-day experiment in IMQ-administered rats, which were pronouncedly decreased by treatment with *C. forskohlii* 5% on day 7 as well as 10% on days 3 and 7 (Figure 2).

3.4. Antioxidant parameters

IMQ-induced psoriatic rats showed significantly decreased GSH and SOD activities with increased MDA and NO levels (Figure 3). Treatment with *C. forskohlii* 5% and 10% reversed IMQ-induced changes in antioxidant parameters while reducing MDA and NO levels.

3.5. Histopathological results

The epidermal layer thickening, parakeratosis, corium/fat layer immune cell infiltration, fat necrosis, and fibrous hyperplasia were among the pathological alterations that were mostly used to score the samples. The IMQ-induced psoriatic rats displayed a thicker epidermis, enhanced keratinization, and lack of granular

layer compared with the normal control. A substantial reduction in epidermal thickness was observed in rats treated with *C. forskohlii* 5% and 10%. *C. forskohlii* 10% showed a more notable effect in improving IMQ-induced skin disorder (Figure 4). Moreover, the effect of *C. forskohlii* treatment on IMQ-induced rat skin is shown in Supplementary Figure.

3.6. Emulgel characterization result

The emulgel was found to be dark brown with a characteristic odor, and smooth homogeneous appearance. The formulations were in the pH range of 5.40 to 6.03 and results are listed in Supplementary Table 2. The mean viscosity of the above formulations was found in a range of (12300.00±360.56) to (20300.00±624.50) cps. The prepared *C. forskohlii* emulgel spreadability was deemed to be good. The spreadability coefficient's value should be higher so that more easily it spreads across the skin. All formulations' spreadability values were in the following order: CF1>CF2>CF3 and remained relatively constant. After a successful physical evaluation of the above formulations, CF2 was selected for *ex vivo* drug skin permeation analysis.

3.7. Ex vivo skin permeation results

The mean cumulative quantity diffused at each sample point (30, 60, 90, 120, 150, 180, 210, 240, 270, and 1440 min) was used to compute the *ex vivo* permeation of *C. forskohlii* emulgel via rat skin

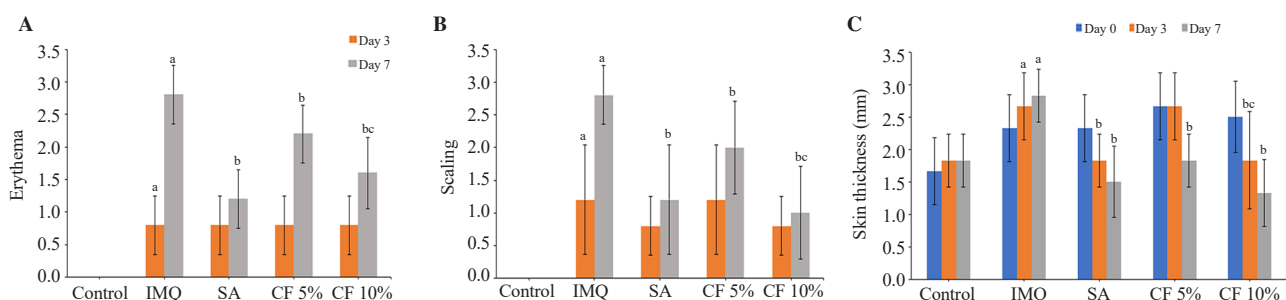


Figure 2. Effect of *Coleus forskohlii* on (A) erythema, (B) scaling and (C) skin thickness. Data are represented as mean ± SD ($n=6$) and analyzed by one-way ANOVA followed by Tukey's test. ^a $P<0.05$ compared with the normal control, ^b $P<0.05$ compared with the IMQ group, and ^c $P<0.05$ compared with the CF 5% group.

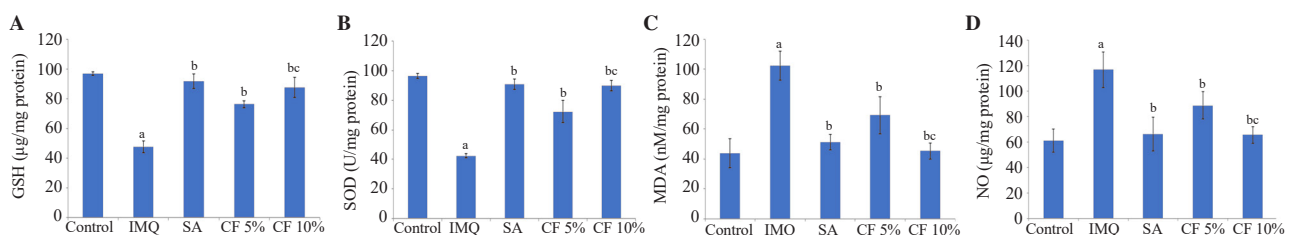


Figure 3. Effect of *Coleus forskohlii* on (A) GSH (B) SOD, (C) MDA and (D) NO level on day 7 post treatment. Data are represented as mean ± SD ($n=6$) and analyzed by one-way ANOVA followed by Tukey's test. ^a $P<0.05$ compared with the normal control, ^b $P<0.05$ compared with the IMQ group, and ^c $P<0.05$ compared with the CF 5% group. GSH: glutathione; MDA: malondialdehyde; SOD: superoxide dismutase; NO: nitric oxide.

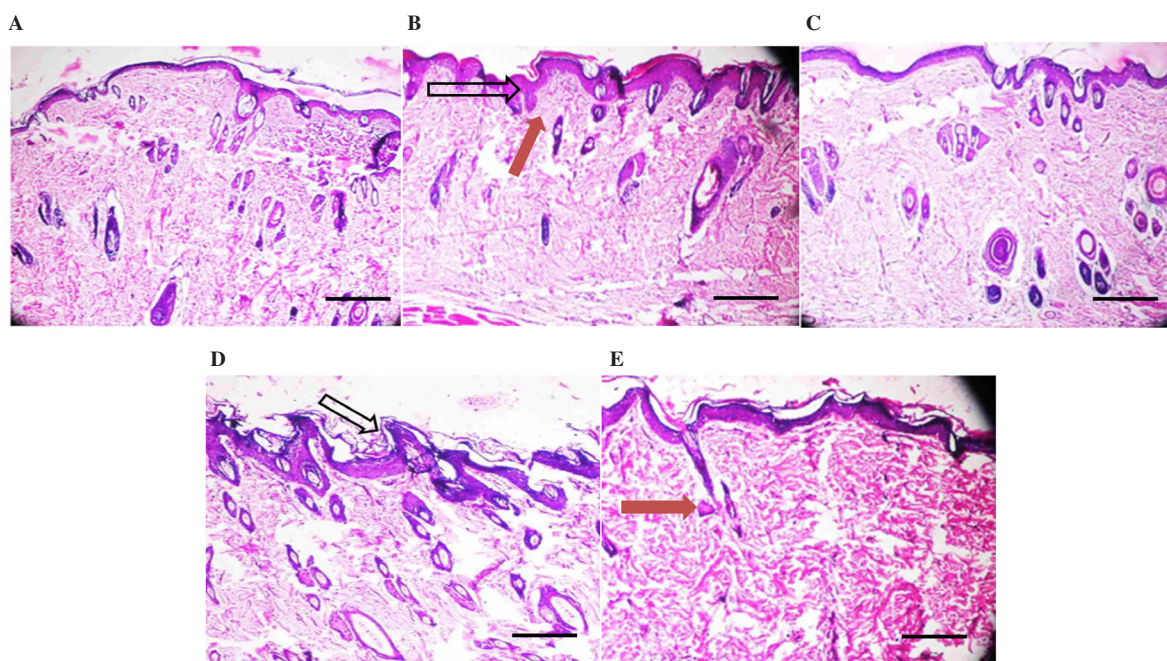


Figure 4. Effect of *Coleus forskohlii* on IMQ-induced histological alternations in rat skin (scale bar = 20 μ m, H&E staining, 40 $\times$). (A) The normal control group shows normal skin structure. (B) A lack of epidermal thickness is seen (black arrow) with obvious inflammatory cell infiltration (red arrow) in the IMQ group. (C) Epidermal thickness is nearly normal, and no inflammatory cells are observed in the positive control group. (D) The flaky epidermal layer is observed (black arrow) in the group treated with *Coleus forskohlii* 5%. (E) The group treated with *Coleus forskohlii* 10% demonstrates intact and normal epidermal layer but with very few inflammatory cells (red arrow).

(Figure 5). A plot of *C. forskohlii* penetrated as a function of time up to 240 min revealed a linear relationship ($R^2 = 0.966$). The flux value of the *C. forskohlii* emulgel after 24 h was determined to be 0.075 mg/cm²/min. The findings showed that the quantity of drug permeated through psoriatic skin was 19.18%, drug deposited in the skin was 52.38%, and the percentage of drug remaining in the donor compartment was 28.31%. The permeation parameters were found to be satisfactory with Flux Jss of 0.0753 (mg/cm²/min), 11.77 min Lag time, 0.0753 (cm/min $\times 10^{-3}$) permeability coefficient, and diffusion coefficient of 0.0674 (cm²/min $\times 10^{-3}$).

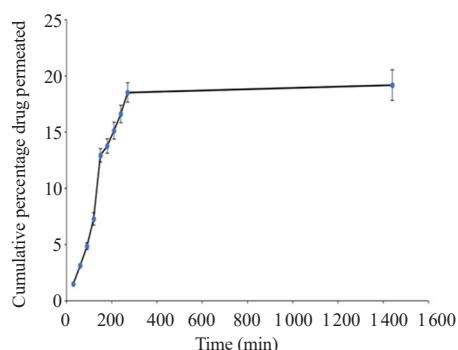


Figure 5. *Ex vivo* skin permeation results of *Coleus forskohlii* emulgel. Data are represented as mean $\pm$ SD and performed in triplicate.

4. Discussion

In this study, the psoriasis-like skin inflammation was developed by daily topical application of IMQ cream (5%) on the shaved skin for 7 d. IMQ-induced psoriasis is a commonly used model in experimental animals, as it displays similarities to human psoriatic lesions, such as erythema, epidermal thickness, scaling, an abundance of inflammatory cells (T cells, neutrophils, and dendritic cells), and vascular growth. Topical treatment with IMQ stimulates the innate immune system followed by the induction of adaptive immunity, leading to psoriasis[20,21]. During the development of psoriasis, epidermal keratinocyte proliferation may be a kind of cellular infiltration. Numerous inflammatory pathways, such as IL-12/Th1, IL-23/Th17, and IL-22/Th22, have an impact on the progression of psoriasis[20,21].

PASI is calculated to have an insight into the prevalence of the disease and the pattern of cure. More than 50% recovery in PASI scores is considered a significant improvement in psoriasis and >75% recovery in PASI is considered a highly significant improvement in psoriatic conditions[22]. A frequently used way for determining the severity of the psoriatic disease is the PASI grading system[23–25]. The differentiation and proliferation of keratinocytes as well as post-inflammatory pigmentation, which enhance skin thickness, scaling, and erythema, are known as PASI parameters[26].

These three parameters collectively express the severity of psoriasis and hence cumulative PASI scores are useful in accessing the disease conditions[23]. Our preliminary study found that the psoriasis-like symptoms tended to spontaneously decline after treatment with *C. forskohlii* 5% and 10%.

The pathogenesis of psoriasis is not completely understood. An insufficient antioxidant system together with increased levels of reactive oxygen species (ROS) has been suggested in the pathogenesis of psoriasis. It is well-known that there is a polymorphonuclear infiltrate in the dermis in psoriatic lesions[24]. Recent studies have shown that the ROS discharged by keratinocytes, fibroblasts, and endothelial cells have chemotactic effects on neutrophils[25], and neutrophil accumulation in psoriatic lesions may cause abundant superoxide production during the phagocytic reaction[26]. ROS may be produced during the inflammatory process in psoriasis, affecting primarily lipid metabolism, DNA, protein, and carbohydrate metabolism of cells. The lipid peroxidation that starts in the membrane may cause cell death by continuing in a chain reaction. As a result of lipid peroxidation, adenyl cyclase is deactivated and guanyl cyclase is activated, thus the cAMP/cGMP ratio decreases, which is responsible for epidermal hyperproliferation in psoriasis[27]. Glutathione peroxidase is an antioxidant enzyme that turns H_2O_2 and other peroxides into water[28]. SOD accelerates the reaction in which superoxides are converted to H_2O_2 . In our study, we found significantly lower SOD and GSH activity in the psoriatic group. Oxidative stress may be related to lipid peroxidation products. High MDA levels occur in cases of psoriasis, suggesting a correlation between the severity of psoriasis and serum MDA levels[28–33]. Our results support the concept that an imbalance between oxidants and antioxidants may play an important role in the pathogenesis of psoriasis[34,35].

The biggest secondary lymphoid organ in the immune system is the spleen. In this study, splenomegaly was induced by IMQ through systemic effects, whereas *C. forskohlii* 5% and 10% significantly reduced spleen weight. It may be indicative of a deficiency in T-independent humoral immune responses as the spleen weight decreased following treatment in the IMQ-induced psoriasis-like dermatitis rats[36]. Histopathological research demonstrates that when *C. forskohlii* 5% and 10% were applied topically, tissue integrity was significantly improved with higher levels of keratinization, and cell proliferation with a declined number of inflammatory cells as compared to the negative control groups[37]. When creating topical preparations like gels, it is necessary to consider the skin's pH to ensure compatibility and reduce the risk of irritation. In the current study, the emulgel of *C. forskohlii* was prepared for topical application on psoriatic skin. Emulgels can offer controlled drug delivery, enhanced skin hydration, and easy spreadability over psoriatic lesions. They can be easily spread and removed from the surface of the skin. Emulgels are non-staining, bio-friendly, and well-

tolerated by patients. They are simple to prepare and economical. People affected by skin diseases prefer to use gels rather than sticky and fatty formulations. Moreover, due to their non-greasy nature, they can be conveniently applied to the skin of both the body and the scalp. Therefore, after *in vivo* studies, an emulgel prepared using *C. forskohlii* was formulated and studied. The formulation of emulgel for psoriatic treatment has been reported in the literature as well. It was observed that psoriatic patients have a skin pH of 5.2 ± 0.5 . The CF2 formulation showed an acceptable pH of 5.40 ± 0.36 which is close to the pH of psoriatic skin. This formula is psoriatic skin-friendly and is less likely to cause any irritation. On the other hand, formulations CF1 and CF3 had higher pH levels, which could lead to skin irritation. A gel with superior spreadability is more likely to be evenly spread and absorbed effectively into the skin. The CF2 formula showed essential spreadability, making it comfortable and convenient to apply on psoriatic skin. Even spreadability ensures that the active ingredient in the gel is evenly distributed over the surface. Although formulation CF1 displayed a high value of spreadability, it had a runny consistency and was not able to retain over skin properly. Viscosity affects how the gel spreads and adheres to the skin during application. Formulation CF2 showed optimized viscosity, ensuring localized application and better adherence over psoriatic skin. The low viscosity of CF1 led to a runny and messy application, while CF3 with high viscosity tended to be lumpy and may contribute to a negative user experience. The optimum viscosity will also contribute to controlled delivery, improving therapeutic efficacy and patient compliance[38]. The prepared gel was evaluated for its pH, spreadability, drug content, and % drug diffusion. The permeation kinetics parameters were found to be satisfactory and capable of giving reproducible results[39]. The data of % drug diffusion indicated that the emulgel formulation can control the release of drug for a longer period. Thus, emulgel was found to significantly enhance both the rate and the extent of drug permeation through psoriatic skin.

There are some study limitations: The response to treatments in Wistar albino rats may not accurately reflect the response in humans due to species-specific differences in skin structure, immune response, and metabolism. Determining the appropriate dose for rats that accurately corresponds to an effective and safe dose in humans is challenging, which can affect the translatability of the results to clinical settings. Anti-psoriatic potency is often evaluated over relatively short periods in animal models, which may not reflect the long-term efficacy and safety required for chronic conditions like psoriasis in humans. Differences in skin permeability between rats and humans can affect the absorption and efficacy of topically applied treatments, potentially leading to misleading conclusions about a compound's potency. Therefore, further studies are needed to verify the efficacy of *C. forskohlii*.

There are many topical psoriasis treatments, but there is an

increasing need for its prescription to address symptoms and issues brought on by other channels. Due to their excellent safety and lipophilic characteristics, topical herbal formulations may be helpful for those who are elderly, young, or intolerant to conventional medicines. In our study, *C. forskohlii* can significantly relieve IMQ-induced psoriasis by enhancing antioxidant activity and improving skin histological structure. An emulgel formulation that contains *C. forskohlii* 10% shows good results in *ex vivo* skin permeation analysis with good viscosity and spreadability. Therefore, *C. forskohlii* 10% emulgel may be a potential and effective therapy for psoriasis.

Conflict of interest statement

The authors declare no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

Both SM and MSH developed the concept and methodology. SM and MI performed data analysis. IC, DK, MNA and MSH contributed to writing, reviewing, editing, and investigation. MSH contributed to funding acquisition.

References

- [1] Hu M, Sun L, Zhao Q, Li Y, Wang Z, Liu H, et al. COVID-19 exacerbates psoriasis progression through inducing IFN- α expression. *Asian Pac J Trop Med* 2024; **17**(8): 379-380.
- [2] Zhang M, Hong S, Sun X, Zhou Y, Luo Y, Liu L, et al. Exploration of and insights into advanced topical nanocarrier systems for the treatment of psoriasis. *Front Med* 2022; **9**. doi: 10.3389/fmed.2022.1017126.
- [3] Gao J, Chen F, Fang H, Mi J, Qi Q, Yang M. Daphnetin inhibits proliferation and inflammatory response in human HaCaT keratinocytes and ameliorates imiquimod-induced psoriasis-like skin lesion in mice. *Biol Res* 2020; **53**(1). doi: 10.1186/s40659-020-00316-0.
- [4] Fereig SA, El-Zaafarany GM, Arafa MG, Abdel-Mottaleb MMA. Tackling the various classes of nano-therapeutics employed in topical therapy of psoriasis. *Drug Deliv* 2020; **27**(1): 662-680.
- [5] Mitra M, Gantait S, Mandal N. *Coleus forskohlii*: Advancements and prospects of *in vitro* biotechnology. *Appl Microbiol Biotechnol* 2020; **104**(6): 2359-2371.
- [6] Roshni PT, Rekha PD. Biotechnological interventions for the production of forskolin, an active compound from the medicinal plant, *Coleus forskohlii*. *Physiol Mol Biol Plants* 2024; **30**(2): 213-226.
- [7] Badruddoza AZM, Zahid MI, Walsh T, Shah J, Gates D, Yeoh T, et al. Topical drug delivery by Sepineo P600 emulgel: Relationship between rheology, physical stability, and formulation performance. *Int J Pharm* 2024; **658**. doi: 10.1016/j.ijpharm.2024.124210.
- [8] Jagdale SC, Kothekar PV. Development of emulgel delivery of mupirocin for treatment of skin infection. *Recent Pat Antiinfect Drug Discov* 2020; **15**(2): 137-156.
- [9] Roberts MS, Cheruvu HS, Mangion SE, Alinaghi A, Benson HAE, Mohammed Y, et al. Topical drug delivery: History, percutaneous absorption, and product development. *Adv Drug Deliv Rev* 2021; **177**. doi: 10.1016/j.addr.2021.113929.
- [10] Cheruvu HS, Liu X, Grice JE, Roberts MS. Modeling percutaneous absorption for successful drug discovery and development. *Expert Opin Drug Discov* 2020; **15**(10): 1181-1198.
- [11] Raszewska-Famielec M, Flieger J. Nanoparticles for topical application in the treatment of skin dysfunctions-An overview of dermo-cosmetic and dermatological products. *Int J Mol Sci* 2022; **23**(24). doi: 10.3390/ijms232415980.
- [12] Thirumal D, Sindhu RK, Goyal S, Sehgal A, Kumar A, Babu MA, et al. Pathology and treatment of psoriasis using nanoformulations. *Biomedicines* 2023; **11**(6). doi: 10.3390/biomedicines11061589.
- [13] Katari O, Jain S. Solid lipid nanoparticles and nanostructured lipid carrier-based nanotherapeutics for the treatment of psoriasis. *Expert Opin Drug Deliv* 2021; **18**(12): 1857-1872.
- [14] Mohd Nordin UU, Ahmad N, Salim N, Mohd Yusof NS. Lipid-based nanoparticles for psoriasis treatment: A review on conventional treatments, recent works, and future prospects. *RSC Adv* 2021; **11**(46): 29080-29101.

- [15] Hussain MS, Ismail H, Fareed S, Ali M. New aliphatic ester constituents from *Hygrophila auriculata* (K.Schum) Heine from the basin area of Koshi River. *Orient Pharm Exp Med* 2019; **19**(3): 251-258.
- [16] Hussain MS, Azam F, Nazeer Ahamed KFH, Ravichandiran V, Alkskas I. Anti-endotoxin effects of terpenoids fraction from *Hygrophila auriculata* in lipopolysaccharide-induced septic shock in rats. *Pharm Bio* 2016; **54**(4): 628-636.
- [17] Hussain MS, Nazeer Ahamed KFH, Ravichandiran V, Ansari MZH. Free radical scavenging capacity of natural terpenes from *Hygrophila auriculata* (Schum) Heine. *Asian J Trad Med* 2009; **4**: 179-187.
- [18] Hussain MS, Azam F, Eldarrat HA, Haque A, Khalid M, Zaheen Hassan M, et al. Structural, functional, molecular, and biological evaluation of novel triterpenoids isolated from *Helichrysum stoechas* (L.) Moench. collected from Mediterranean Sea bank: Misurata-Libya. *Arabian J Chem* 2022; **15**(6). doi: 10.1016/j.arabjc.2022.103818.
- [19] Hussain MS, Azam F, Mezogi J, Enwiz FA, Benhusein GM, Haque A, et al. A simple validated HPTLC method for analysis of flavonoid and structural analysis of novel terpenoid glycoside from ethanolic extract of *Carya illinoensis* bark with potential anti-inflammatory activity. *South African J Bot* 2022; **147**: 596-607.
- [20] Tripathi D, Srivastava M, Rathour K, Rai AK, Wal P, Sahoo J, et al. A promising approach of dermal targeting of antipsoriatic drugs via engineered nanocarriers drug delivery systems for tackling psoriasis. *Drug Metab Bioanal Lett* 2023; **16**(2): 89-104.
- [21] Shaif M, Kushwaha P, Usmani S, Pandey S. Exploring the potential of nanocarriers in antipsoriatic therapeutics. *J Dermatolog Treat* 2022; **33**(7): 2919-2930.
- [22] Bacchetti T, Simonetti O, Ricotti F, Offidani A, Ferretti G. Plasma oxidation status and antioxidant capacity in psoriatic children. *Arch Dermatol Res* 2020; **312**(1): 33-39.
- [23] Savu O, Serafinceanu C, Grajdeanu IV, Iosif L, Gaman L, Stoian I. Paraoxonase lactonase activity, inflammation and antioxidant status in plasma of patients with type 1 diabetes mellitus. *J Int Med Res* 2014; **42**(2): 523-529.
- [24] Speeckaert R, Dugardin J, Lambert J, Lapeere H, Verhaeghe E, Speeckaert MM, et al. Critical appraisal of the oxidative stress pathway in vitiligo: a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol* 2018; **32**(7): 1089-1098.
- [25] Sm F, Sarkar D, Samuel Kelechi M, AAl-Haidari R, Al Busaidi HN, Samman W, et al. Effect on ethanolic extract of sechiu medule fruits on imiquimod-induced psoriasis like dermatitis in wistar rats. *Pak J Pharm Sci* 2022; **35**(4): 1083-1088.
- [26] Bigliardi PL. Role of skin pH in psoriasis. *Curr Probl Dermatol* 2018; **54**: 108-114.
- [27] Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, et al. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pac J Trop Biomed* 2013; **3**(5): 337-352.
- [28] Asha K, Singal A, Sharma SB, Arora VK, Aggarwal A. Dyslipidaemia & oxidative stress in patients of psoriasis: Emerging cardiovascular risk factors. *Indian J Med Res* 2017; **146**(6): 708-713.
- [29] Asefi M, Vaisi-Raygani A, Bahrehmand F, Kiani A, Rahimi Z, Nomani H, et al. Paraoxonase 1 (PON1) 55 polymorphism, lipid profiles and psoriasis. *Br J Dermatol* 2012; **167**(6): 1279-1286.
- [30] Laloo D, Prasad SK, Krishnamurthy S, Hemalatha S. Gastroprotective activity of ethanolic root extract of *Potentilla fulgens* Wall. ex Hook. *J Ethnopharmacol* 2013; **146**(2): 505-514.
- [31] Khan A, Ullah MZ, Afridi R, Rasheed H, Khalid S, Ullah H, et al. Antinociceptive properties of 25-methoxy hispidol A, a triterpenoid isolated from *Poncirus trifoliata* (Rutaceae) through inhibition of NF- κ B signalling in mice. *Phytoth Res* 2019; **33**(2): 327-341.
- [32] Ali Khan, Ullah S, Khan MK. Alshahrani SM, Braga VA. Formulation and evaluation of *Ocimum basilicum*-based emulgel for wound healing using animal model. *Saudi Pharm J* 2020; **28**(12): 1842-1850.
- [33] Laxmi RJ, Karthikeyan R, Babu PS, Babu RN. Formulation and evaluation of anti-psoriatic gel using natural excipients. *J Acute Dis* 2013; **2**: 115-121.
- [34] Parmar KM, Jagtap CS, Katore NT, Dhobi M, Prasad SK. Development of a psoriatic-like skin inflammation rat model using imiquimod as an inducing agent. *Indian J Pharmacol* 2021; **53**(2): 125-131.
- [35] Hussein ZA, Shaker NS, Tahseen NJ, Al-Tuhafi AM, Mutee AF. Possible anti-psoriasis effect of the methanol extract of *Phoenix dactylifera* L. seeds. *J Herbmmed Pharmacol* 2020; **9**(4): 382-390.
- [36] Horvath S, Komlodi R, Perkecz A, Pinter E, Gyulai R, Kemény A. Methodological refinement of Aldara-induced psoriasiform dermatitis model in mice. *Sci Rep* 2019; **9**(1): 3685. doi: 10.1038/s41598-019-39903-x.
- [37] Shahrine Y, El-Aal SAA, Reda AM, Sheta E, Atia NM, Abdallah OY, et al. Diosmin nanocrystal gel alleviates imiquimod-induced psoriasis in rats via modulating TLR7,8/NF- κ B/microRNA-31, AKT/mTOR/P70S6K milieu, and Tregs/Th17 balance. *Inflammopharmacology* 2023; **31**(3): 1341-1359.
- [38] Okasha EF, Bayomy NA, Abdelaziz EZ. Effect of topical application of black seed oil on imiquimod-induced psoriasis-like lesions in the thin skin of adult male albino rats. *Anat Rec* 2018; **301**(1): 166-174.
- [39] Chauhan I, Singh L. Formulation and optimization of solid lipid nanoparticle-based gel for dermal delivery of linezolid using taguchi design. *Recent Adv Antiinfect Drug Discov* 2024; **19**(4): 322-347.

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