

ANTIOXIDANT AND ANTI-PSORIATIC ACTIVITY OF *ADENIUM OBESUM* AGAINST IMIQUIMOD INDUCED PSORIASIS

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ABSTRACT

This research focuses on pharmacological screening of anti-oxidant and anti-psoriatic potential of *Adenium Obesum* in Imiquimod induced psoriasis in rats. The *Hydroalcoholic flower extract of Adenium obesum* (FEAO), Imiquimod (API) was obtained from Glenmark Pvt Ltd Mumbai. Carbopol 934 was purchased from Sigma Aldrich Pvt Ltd. India. The fresh flowers of *Adenium obesum* were collected from the UP-West region and were authenticated by the botanist at CSIR New Delhi with reference no. NIScPR/RHMD/Consult/2022/4047-48. Animal House, Hygia Institute of Pharmaceutical Education & Research, Lucknow has provided rats (either sex) weighing 130-160g. The animals are kept in good health with room temp. of 25°C and 12hr light & dark cycle. Rats were divided 5 groups: Negative control- animals were applied gel base once a day, up to 15 days, Positive control- animals were applied IMQ (3.20mg) on saved dorsal skin once a day, up to 7 days, Test 1- animals were applied IMQ (3.20mg) (for 7 days) + Retino- A on saved dorsal skin once a day, up to 15 days, Test 2- animals were applied IMQ (3.20mg) (for 7 days) + FEAO gel on saved dorsal skin once a day, up to 15 days & Std.- animals were applied IMQ (3.20mg) (for 7 days) + FEAO gel on saved dorsal skin orally once a day, up to 15 days. Anti-psoriatic activity was evaluated in parameters i.e., body weight, weight of organs, determination of anti-oxidant activity, scoring of severity score PASI score (erythema, desquamation, epidermal, thickness) in Imiquimod-induced psoriatic model. In all the parameters, FEAO gel significantly demonstrated anti-psoriatic activity when compared with positive & negative control groups. In conclusion, FEAO predominantly showed anti-psoriatic potential when observed in animal studies.

KEYWORDS: anti-psoriatic, Imiquimod, *Adenium obesum*, antioxidant, PASI & rats.

INTRODUCTION

Skin refers largest organ in body having surface area of 1.5-2m² serves as the most complicated barrier b/w the biological system and the outside world (Maranduca et al. 2019; Someya & Amagai, 2019).

Blepharitis is the most prevalent eye condition, which may lead to cicatricial ectropion, madarosis & trichiasis (Yang et al. 2018; Caiazzo et al. 2018). Psoriasis can affect people of any age. Age of 17 is considered avg. age for onset of initial appearance of psoriasis and reaches to its peak appearing at age 55-60 years (Larsabal et al. 2019).

The occurrence of psoriasis varies b/w 0.2 percent to 4.8 percent (Gamret et al. 2008). Summer generally improves psoriasis, but winter aggravates it. The pathogenesis of psoriasis involves activated T lymphocytes infiltrating the skin and stimulating keratinocyte growth. The production of thick plaques is caused by a disruption in keratinocyte turnover (Kahn et

al. 2018; NHS, 2012). The Psoriasis Area Severity Index is the most extensively used assessment instrument for determining the severity of psoriasis and determining therapy efficacy (Perez-Chada et al. 2018; Schadler et al. 2019).

Adenium obesum species originated in African countries, but they can now be found in almost every tropical and subtropical country. The selected plant species are found throughout Africa- Ethiopia, Kenya, Senegal, Somalia, Sudan, & Tanzania and Asia. In Oman, there are several species of the chosen plant. The desert rose, for example, can be found in the Sultanate of Oman. For the treatment of various ailments, all parts of the specific species are employed as medicine. As a result of their therapeutic properties, the selected plant species are commercially farmed all over the world (Akhtar et al. 2017).

Taxonomy

Kingdom- Plantae

Subkingdom- Tracheobionta

Subdivision- Spermatophyta

Division- Magnoliophyta
 Class- Magnoliopsida
 Subclass- Asteridae
 Order- Gentianales
 Family- Apocynaceae
 Genus- Adenium
 Species- obesum

Different sorts of chemicals were discovered in a locally grown entire AO plant, with the number of compounds increasing with the plant's age (Malebo et al., 2009). The phytochemical analysis revealed that the chosen plant included several chemical substances i.e., carbohydrates, flavonoids, cardiac glycoside, flavonoid, terpenoids, and pregnanes among others. The majority of the selected plant's extracted individual chemical components were physiologically active. A total of 53 chemicals were extracted and identified in previous research of the chosen plant by various authors. Some are poisonous, while others have biological activity such as antiviral, anticancer, and cytotoxic effects (Amin et al. 2013).

On the basis of above literature survey, I found that pharmacological screening of anti-psoriatic potential of *Adenium Obesum* has not been evaluated yet by any means and methods.

Therefore, this research focuses on pharmacological screening of anti-oxidant and anti-psoriatic potential of *Adenium Obesum* in Imquimod induced psoriasis in rats.

MATERIALS AND METHODS

Experimental requirements

Hydroalcoholic flower extract of *Adenium obesum* (FEAO), Imquimod (API) was obtained from Glenmark Pvt Ltd Mumbai. Carbopol 934 was purchased from Sigma Aldrich Pvt Ltd. India. Whereas, other chemicals like methyl paraben, distilled water, Wistar albino rats (either sex), rotatory evaporator, weighing machine and ethanol were obtained from certified supplier only.

Plant collection and authentication

The fresh flowers of *Adenium obesum* were collected from the UP-West region and were authenticated by the botanist at CSIR New Delhi with reference no. NIScPR/RHMD/Consult/2022/4047-48. After the flowers were left to dry then crushed into coarse powder. The powder was weighed and extracted through Soxhlet Extraction apparatus using ethanol+ water (1:1). After, it was filtered cotton plug to get the extract in homogenous manner. A rotating evaporator was used to dry the brownish, semisolid extract obtained under partial vacuum.

Preparation of animals

Animal House, Hygia Institute of Pharmaceutical Education & Research (HIPER), Lucknow has provided rats (either sex) weighing 130-160g. The animals are kept in good health with room temp. of 25°C and 12hr light & dark cycle. The relative humidity was kept at

50±2% and the rats were provided a regular rodent diet with free access to water. The rodents were continuing to fast but have free access to water until 1 hour before the ulcers are induced.

Group design

All the rats are divided into 5 groups (n=6) as followings-

Negative control: Animals are applied gel base once a day, up to 15 days.

Positive control: Animals were applied IMQ (3.20mg) on saved dorsal skin once a day, up to 7 days.

Test 1: Animals are applied IMQ (3.20mg) (for 7 days) + Retino- A on saved dorsal skin once a day, up to 15 days.

Test 2: Animals are applied IMQ (3.20mg) (for 7 days) + FEAO gel on saved dorsal skin once a day, up to 15 days.

Std.: Animals are applied IMQ (3.20mg) (for 7 days) + FEAO gel on saved dorsal skin orally once a day, up to 15 days.

Formulation of FEAO gel

A precisely weighed amount of the gelling agent Carbopol 934 was dissolved in distilled water and stirred continuously for 30 minutes at a temperature of 37 °C until a mass that resembled gel was noticed. Methyl parabens were dissolved in propylene glycol until they reached the appropriate gel-like consistency, whereas FEAO (500mg) was dissolved in ethanol. Both solutions were then combined with the aqueous phase while being continuously stirred until a homogenous gel was created. Triethanolamine (TEA) was used to further alkalize the gel, and 0.5 ml of glycerin was added as a humectant after that.

Protocols

Body weight

All the animals in each are subjected to weigh-out their weight before the administration of drug starts and after the dosing is complete. Body weight, before drug administration and after drug administration is compared.

Weight of organs

All the rats of different groups are incised after sacrificing them. Organs such as Kidney, Liver, Spleen were weighed separately to confirm the impact on different organs as well.

Estimation of total antioxidant activity

The Prieto et al. method was used to calculate the total antioxidant activity of the fractions. a few of the components are 4mm ammonium molybdate, 28nm sodium phosphate and 0.3ml sulfuric acid. The reaction mixture was incubated at 95°F for 90 minutes in a water bath. The absorbance of each sample combination was calculated at 695nm (wavelength). Total antioxidant activity was calculated using the ascorbic acid equivalents in mg/g of extract.

Imiquimod-induced psoriatic model

Animals in each experimental group had their back parts cleanly and smoothly shaved. When a commercially available 5 percent IMQ cream with a dose of 62.5mg of imiquimod was topically applied for 7 consecutive days, translating to a daily dose of 3.20mg of the active compound, psoriasis was induced in rats using imiquimod-induced psoriasis. The dorsal part of rat was then shaved. A control vehicle cream was applied similarly to control rats. Skin biopsies were immediately taken after 7 days, fixed in 10% formalin, and embedded in paraffin. It was decided to use haematoxylin and eosin to stain the tissue section, which was 4µm thick. The total number of layers of keratinocytes, including the basal layer. Direct microscopy was used to count the cells.

Scoring of severity

It was determined by PASI score to assess the anti-psoriatic activity, as below-

- Zero,
- Slight,
- Moderate
- Very marked

Statistical analysis

Two-tailed t tests were used after ANOVA to assess the statistical data. Values are presented as S.E.M. Sigma Stat pro3.3 will be used to do the statistical analysis. At

the $P \leq 0.05$, the findings were deemed statistically significant.

RESULTS AND DISCUSSION**Percentage yield**

After the extraction process, the precipitate was refined and dried and weighed. When calculated, % yield was found as 65.34% (on dry basis).

Body weight determination

In order to evaluate anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day, up to 7 days.

Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

In body weight observation, negative control showed a marked decrease in body weight of rats as $162.94 \pm 0.34^{**}g$ that prior $165.31 \pm 0.19^{**}g$. Test 1 group showed an increase in body weight of rats and measured as $172.25 \pm 0.27^{***}g$ after the treatment with FEAO gel (1%) but action was much significant in the Test 2 that was applied FEAO gel (2%), as $192.40 \pm 0.42^{**}g$. Effect of 2% FEAO gel was found almost similar to standard treated rats and that was $219.16 \pm 0.17^{***}g$.

Following table depicted the body weight determination-
Table 2. Body weight determination of FEAO gel.

Treatment	Body weight (g) (Mean± SEM)	
	before	after
Gel base	$163.27 \pm 0.35^*$	$179.21 \pm 0.26^*$
IMQ (3.20mg)	$165.31 \pm 0.19^{**}$	$162.94 \pm 0.34^{**}$
IMQ (3.20mg)+ FEAO gel (1%)	$163.62 \pm 0.47^{**}$	$172.25 \pm 0.27^{***}$
IMQ (3.20mg)+ FEAO gel (2%)	$166.37 \pm 0.64^{***}$	$192.40 \pm 0.42^{**}$
IMQ (3.20mg)+ Retino- A	$166.46 \pm 0.27^{***}$	$219.16 \pm 0.17^{***}$

Significance level was represented by *; $P < 0.05$
 $n=6$; readings were given in Mean± SEM, Dennett's test

Organ weight determination

To evaluate anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day, up to 7 days. Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

FEAO gel significantly modulated those weights of different organs taken into study. Negative control exhibited increase in organs weight as $0.65 \pm 0.23^{**}g$, $2.26 \pm 0.43^{**}g$ and $11.50 \pm 0.23^{**}g$ of spleen, kidney and liver, respectively. IMQ (3.20mg)+ FEAO gel (1%)

treated rats showed a moderate balance b/w the organs weight as $0.36 \pm 0.13^{**}g$, $1.79 \pm 0.24^{**}g$ and $9.47 \pm 0.53^*g$ respectively. Whereas, Test 2 rats demonstrated a much significant role in balancing the organ weights as $0.51 \pm 0.12^{**}g$, $2.37 \pm 0.29^{**}$ and $9.37 \pm 0.42^{**}$, respectively. Effect of FEAO gel was predominant when compared with the control & standard rats. It might be due to decreased level of accumulation of fat, triglycerides etc.

Table 3. Organ weight determination.

Treatment	Organ weight (g) (Mean± SEM)		
	Spleen	Kidney	Liver
Gel base	0.34±0.19**	1.86±0.42**	9.05±0.52**
IMQ (3.20mg)	0.65±0.23**	2.26±0.43**	11.50±0.23**
IMQ (3.20mg)+ FEAO gel (1%)	0.36±0.13**	1.79±0.24**	9.47±0.53*
IMQ (3.20mg)+ FEAO gel (2%)	0.51±0.12**	2.37±0.29**	9.37±0.42**
IMQ (3.20mg)+ Retino- A	0.48±0.13***	1.86±0.12**	9.14±0.64**

Significance level was represented by *; P<0.05
n=6; readings were given in Mean± SEM, Dennett's test

Estimation of SOD, CAT & LPO levels

In ref. to evaluate anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day, up to 7 days.

Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

In estimation of total antioxidant activity, SOD, CAT & LPO parameters were determined. IMQ (3.20mg)+

FEAO gel (2%) treated rats showed SOD level as 15.52± 0.71** unit/mg, whereas, IMQ (3.20mg) treated rat showed SOD as 9.21± 0.37* unit/mg.

IMQ (3.20mg)+ FEAO gel (2%) treated rats showed CAT level as 4.26± 0.72* unit/mg, whereas, IMQ (3.20mg) treated rat showed CAT level as 2.39± 0.21** unit/mg. IMQ (3.20mg)+ FEAO gel (2%) treated rats showed LPO level as 3.12± 0.24* unit/mg, whereas, IMQ (3.20mg) treated rat showed LPO level as 16.57± 0.25** unit/mg. FEAO significantly demonstrated anti-oxidant potential that indicates for its anti-psoriatic effect when compared with positive control.

The following table 4.4 depicts the anti-oxidant activity of FEAO gel-

Table 4. Estimation of anti-oxidant activity of FEAO gel.

Treatment	Anti-oxidant activity (Units/mg)		
	SOD	CAT	LPO
Gel base	21.34± 0.60*	7.47± 0.17**	3.16± 0.38*
IMQ (3.20mg)	9.21± 0.37*	2.39± 0.21**	16.57± 0.25
IMQ (3.20mg)+ FEAO gel (1%)	12.32± 0.54**	3.19± 0.39*	4.19± 0.13*
IMQ (3.20mg)+ FEAO gel (2%)	15.52± 0.71**	4.26± 0.72*	3.12± 0.24*
IMQ (3.20mg)+ Retino- A	18.42±0.13*	5.36± 0.28**	5.34± 0.49**

Significance level was represented by *; P<0.05
n=6; readings were given in Mean± SEM

Imiquimod-induced psoriatic model

Anti-psoriatic activity was determined, in terms of decreased levels of erythema, Desquamation & epidermal thickness and depicted as below in figures & tables.



a. Negative Control



b. Positive Control



c. Test 1



d. Test 2



e. Std.

Fig. 4.5: Depiction of anti-psoriatic potential of FEAO (a-e).

Determination of erythema

In evaluation of anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day, up to 7 days. Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

The erythema is a factor that is evaluated in the anti-psoriatic potential from the score 0-4. This was observed

on the day 5, 10 and 15. IMQ (3.20mg) treated rats showed the erythema as $4.14 \pm 0.41^{**}$, $5.27 \pm 0.38^{**}$ & $5.63 \pm 0.21^{**}$ on the day 5, 10 & 15, respectively. Rodents treated with IMQ (3.20mg) + FEAO gel (1%) exhibited the erythema as $3.35 \pm 0.16^{**}$, $2.79 \pm 0.24^{**}$ & $1.47 \pm 0.53^*$ on day 5, 10 & 15 respectively but Test 2 exhibited more satisfactory response in modulation of erythema as $2.59 \pm 0.12^{**}$, $2.12 \pm 0.29^{**}$ & $1.15 \pm 0.42^{**}$ on day 5th, 10th & 15th that was highest when compared with control.

Table 5. Determination of erythema of FEAO gel.

Treatment	Erythema (Mean± SEM)		
	5 th day	10 th day	15 th day
Gel base	$1.30 \pm 0.29^{**}$	$1.47 \pm 0.42^{**}$	$1.83 \pm 0.31^{**}$
IMQ (3.20mg)	$4.14 \pm 0.41^{**}$	$5.27 \pm 0.38^{**}$	$5.63 \pm 0.21^{**}$
IMQ (3.20mg)+ FEAO gel (1%)	$3.35 \pm 0.16^{**}$	$2.79 \pm 0.24^{**}$	$1.47 \pm 0.53^*$
IMQ (3.20mg)+ FEAO gel (2%)	$2.59 \pm 0.12^{**}$	$2.12 \pm 0.29^{**}$	$1.15 \pm 0.42^{**}$
IMQ (3.20mg)+ Retino- A	$1.72 \pm 0.13^{***}$	$1.53 \pm 0.12^{**}$	$0.61 \pm 0.64^{**}$

Significance level was represented by *; P<0.05
n=6; readings were given in Mean± SEM

Determination of Desquamation

In screening of anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day, up to 7 days. Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

The Desquamation is a factor that is evaluated in the anti-psoriatic potential from the score 0-4 (0- none, 1-slight,

2-moderate, 3-marked, 4-highly marked). This was observed on the day 5, 10 and 15. IMQ (3.20mg) treated rats showed the desquamation as $4.14 \pm 0.41^{**}$, $5.27 \pm 0.38^*$ & $5.63 \pm 0.21^*$ on the day 5, 10 & 15, respectively. Rats treated with IMQ (3.20mg) + FEAO gel (1%) exhibited the desquamation as $3.35 \pm 0.16^{**}$, $2.79 \pm 0.24^{**}$ & $1.47 \pm 0.53^{**}$ on day 5, 10 & 15 respectively but Test 2 exhibited more satisfactory response in modulation of desquamation as $2.59 \pm 0.12^{**}$, $2.12 \pm 0.29^*$ & $1.15 \pm 0.42^{**}$ on day 5th, 10th & 15th that was highest when compared with control.

Table 4.5.2 represents the depiction of the same-

Table 6. Determination of Desquamation of FEAO gel.

Treatment	Desquamation (Mean± SEM)		
	5 th day	10 th day	15 th day
Gel base	$1.30 \pm 0.29^*$	$1.47 \pm 0.42^*$	$1.83 \pm 0.31^{**}$
IMQ (3.20mg)	$4.14 \pm 0.41^{**}$	$5.27 \pm 0.38^*$	$5.63 \pm 0.21^*$
IMQ (3.20mg)+ FEAO gel (1%)	$3.35 \pm 0.16^{**}$	$2.79 \pm 0.24^{**}$	$1.47 \pm 0.53^{**}$
IMQ (3.20mg)+ FEAO gel (2%)	$2.59 \pm 0.18^{**}$	$2.12 \pm 0.29^*$	$1.15 \pm 0.42^{**}$
IMQ (3.20mg)+ Retino- A	$1.72 \pm 0.13^{**}$	$1.53 \pm 0.12^{**}$	$0.61 \pm 0.64^*$

Significance level was represented by *; P<0.05
n=6; readings were given in Mean± SEM

Epidermal thickness

In determination of anti-psoriatic activity, positive control was topically applied gel base whereas negative control was applied externally IMQ (3.20mg) once a day,

up to 7 days. Test 1 was treated with IMQ (3.20mg)+ FEAO gel (1%) on saved dorsal skin & ear whereas Test 2 was treated with IMQ (3.20mg)+ FEAO gel (2%) on

saved dorsal skin & ear. All the treatment were made once a day for 15 days except negative control.

Treatment of IMQ (3.20mg)+ FEAO gel (2%) showed a marked decrease in the epidermal thickness as $4.23\pm 0.14^{**}$, $3.15\pm 0.29^*$ & $2.93\pm 0.42^{**}$ on 5th day, 10th day & 15th day, respectively. Whereas, IMQ (3.20mg)

applied mice showed increasing effect on epidermal thickness as $4.14\pm 0.41^{**}$, $4.59\pm 0.38^*$ & $5.20\pm 0.21^*$ on day 5th, day 10th & day 15th respectively.

It significantly reduced the thickness of skin thus showed anti-psoriatic potential when compared with control.

Table 7. Epidermal thickness.

Treatment	Epidermal thickness (Mean± SEM)		
	5 th day	10 th day	15 th day
Gel base	$3.83\pm 0.27^*$	$3.91\pm 0.42^*$	$4.33\pm 0.21^{**}$
IMQ (3.20mg)	$4.14\pm 0.41^{**}$	$4.59\pm 0.38^*$	$5.20\pm 0.21^*$
IMQ (3.20mg)+ FEAO gel (1%)	$4.76\pm 0.16^{**}$	$4.11\pm 0.24^{**}$	$4.04\pm 0.53^{**}$
IMQ (3.20mg)+ FEAO gel (2%)	$4.23\pm 0.14^{**}$	$3.15\pm 0.29^*$	$2.93\pm 0.42^{**}$
IMQ (3.20mg)+ Retino- A	$3.72\pm 0.13^{**}$	$2.57\pm 0.12^{**}$	$1.61\pm 0.64^*$

Significance level was represented by *; $P < 0.05$
n=6; readings were given in Mean± SEM

In all the parameters, FEAO gel significantly demonstrated anti-psoriatic activity when compared with positive & negative control groups. It modulated body weights of organs and also maintained weights of different organs i.e., kidney, spleen % & liver.

When observed anti-oxidant profile, FEAO gel showed a lowering effect on SOD & CAT. It increased LPO level when compared with positive control mice. Thus, it demonstrated a better anti-oxidant activity that might be basic mechanism behind its anti-psoriatic role.

In Imiquimod-induced psoriatic model, application of FEAO gel showed modulation on the PASI score when used once for 15 days. FEAO gel exhibited a decrease in Erythema when compared with positive control and effect was in dose dependent ratio in contrast to standard drug treated group. Similarly, pharmacological action was seen in terms of Desquamation. T1 & T2 lowered the strength of Desquamation in contrast to control group. As we know, epidermal thickness is an important factor considered in evaluation of anti-psoriatic activity.

CONCLUSION

In conclusion, FEAO predominantly showed anti-psoriatic potential when observed in animal studies. It may be used in the cure of psoriasis among human beings if proved in the clinical trials in terms of safety & efficacy. Further molecular level research is required to demonstrate its psoriasis prevention. It suggests to identify and isolate the active components for the anti-psoriatic activity and incorporate those into suitable dosage form for better availability & accessibility of the same, in the cure of psoriasis.

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Nil.

CONFLICT OF INTEREST

Authors have declared for none conflict on interest.

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