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Research Article

Formulation and Evaluation Gel from Extract of *Plumbago indica* for Acne

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ABSTRACT
In current study, an attempt has been taken for formulation and evaluation acetone extract of *Plumbago indica* for antiacne activity. The gel containing acetone extract of *Plumbago indica* was prepared by adding gel-forming material in sterile distilled water while the mixture was stirred and allowed to stand to hydrate. Extract was added in PEG 400 and polyethylene glycol mixture. Methyl paraben and propyl paraben were added as the preservative and triethanolamine was added as the neutralizer. The anti-acne activity was investigated against two causative bacteria, i.e., *Propionibacterium acnes* and *Staphylococcus epidermidis* and yeast (*Malassezia furfur)* by the well diffusion method. The result showed that gel passes all test of evaluation and was found to be active against acne causing microorganisms. *Plumbago indica* extract based gel has potential activity against acne-causing microorganism.

Keywords: Acne gel, Herbal gel, *Plumbago indica*, *Propionibacterium. acnes*

INTRODUCTION

Current treatment of acne consists of use of topical or systemic antibiotics, retinoids etc. The major problem associated with use of antibiotic is resistance and its uncommon side effects. Oral isotretinoin causes teratogenicity[1]. Medicinal plants could be a choice due to its efficacy and devoid of side effect[2]. In skin diseases medicaments are mainly applied topically. Herbal medicine is very effective in curing various dermatological diseases and there are many herbal drugs which have been mentioned to be useful in the treatment of acne. One of them is *Plumbago indica* (PI). "In our previous research it was found that acetone extract of PI could be choice of alternative for curing acne"[3]. In this context, acetone extract of root of *Plumbago indica* (AEPI) has been screened for formulation of topical gel for the aforesaid anti-acne activity.

MATERIALS AND METHODS

Materials

Carbopol 934 (Qualikems Pvt. Ltd., Mumbai, India), PEG 400 (Loba Chemie, Mumbai, India), propylene glycol), methyl paraben(Central Drug House Pvt. Ltd., New Delhi), propyl paraben (Central Drug House Pvt. Ltd., New Delhi), triethanolamine (Titan Biotech Ltd., Rajasthan, India), methanol (Jiangsu Huaxi International Trade Company Ltd., China), Plumbagin (sigma Aldrich), BHI agar (HiMedia Pvt. Ltd., Laboratories, Mumbai, India), MH agar (HiMedia Pvt. Ltd., Laboratories, Mumbai, India), PDA (HiMedia Pvt. Ltd., Laboratories, Mumbai, India) etc.

Methods

Plant materials and extract preparation

Dried roots of PI were procured from the local commercial suppliers of Jalandhar, Punjab. Authentication of PI was done by Thukral, Professor, "Department of Botanical and Environmental Sciences", GNDU, Amritsar, Punjab, and the voucher specimens have been deposited at the school of pharmaceutical sciences, Lovely professional University. The crude plant material was pulverized in coarse powder form for the purpose of extraction. Coarsely powdered dried plant drug material was extracted by Soxhlet's apparatus using acetone as solvent[4].

Collection of microbial strains

Staphylococcus epidermidis (Aerobic bacteria, MTCC 3382), *Propionibacterium acnes* (Anaerobic bacteria MTCC 1951) and fungal strain *Malassezia furfur* (MTCC 1765) were collected from the "Microbial Type Culture Collection Centre", "Institute of Microbial Technology", Chandigarh.

Preparation of anti-acne gel

The gel containing AE PI was prepared by adding gel-forming material in sterile distilled water while the mixture was stirred and allowed to stand to hydrate. Extract was added in PEG 400 and polyethylene glycol mixture. Methyl paraben and propyl paraben were added as the preservative and triethanolamine was added as the

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Table 1: Various prepared formulation of AEPI

Ingredients	I					II				III		
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
P. indica extract	0.5	0.5	1	1	1	1	1	1	1.5	2	1.5	2
Carbopol 934	1	1.5	1	1.5	1.5	1.5	2	2	2	1.5	1.5	2
PEG 400	20	20	20	20	20	30	20	30	20	20	20	20
Propylene glycol	10	10	10	10	10	10	10	10	10	10	10	10
Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Propyl paraben	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
Triethanolamine	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Purified water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

a b

Figure 1: Preparation of gels (a) 1% gel of P. indica (b) 2% gel of P. indica Evaluation of gels

1% *Plumbago indica* gel 2% *Plumbago indica* gel

Figure 2: Photographs of the developed formulations after filling in tubes

Table 2: Physical evaluations of developed gel formulations

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Appearance	+++	++	+++	+	++	++	+++	+	+	+++	+	++
pH	6.9	7.2	7.03	6.86	7.33	6.84	7.17	6.66	6.54	7.2	8.62	7.83
Viscosity	26915	43019	28260	39156	40826	31927	47186	51062	40272	34200	61420	71291
Spreadability	14. 159	25. 451	13. 093	24. 674	26. 721	22. 924	31. 972	34. 821	29. 623	24. 676	42. 715	49. 927
Gelling	++	-	+++	++	+	++	++	-	+	+++	-	++

+++ Excellent, ++ Good, + Average

neutralizer[5]. Various prepared formulation are shown in table 1

Methodology for development of formulation

I The first 22 factorial design was taken care for optimization. Two variables were the content of Carbopol 934 and AEPI. The amount of Carbopol 934 were 1% and 1.5% and those of AEPI were 0.5% and 1%. Different formulation were prepared (F1-F4).

II The second 22 factorial design taken care for optimization included the content of Carbopol 934 and Polyethylene glycol 400. The concentrations of Carbopol 934 were 1.5% and 2% and that of PEG 400 were 20% and 30%. Four formulas of anti-acne gel were prepared (F5 – F8).

III The third 22 factorial design included two variables i.e. one was concentration of plant extracts and other was concentration of carbopol polymer. The concentrations of Carbopol 934 were 1.5% and 2% and that of plant extracts were 1.5% and 2% (F9 – F12).

Evaluation of Gel

Table 3: Anti acne activity of selected formulation

Microorganism	Zone of inhibition	
	1% P	2% P
P. acnes	7.13±0.03	9.17±0.09
S. epidermidis	12.40±0.06	14.53±0.07
M. furfur	14.23±0.03	18.17±0.03

Table 4: Diffusion study of developed gels of plant extracts.

Time (min)	% Cumulative release of Plumbagin	
	1% P	2% P
0	0	0
10	6.18	14.75
20	12.87	20.31
30	17.8	22.23
40	23.19	27.39
50	31.62	32.7
60	37.9	36.31
90	41.86	41.55
120	46.57	52.14
180	52.51	55.01
240	54.14	56.04
300	54.68	55.94
360	54.86	56.73

The various gel formulations were developed containing the AEPI at different concentrations followed by their evaluation considering different parameters such as homogeneity, pH, viscosity and spreadability in order to select the best out of many prepared gels. The selected gels were to be further evaluated for their release studies.

pH measurements

pH of the gels were determined by a digital pH meter by dipping the glass electrode entirely in to the formulation to cover the electrode[5].

Homogeneity

Visual inspection in presence of light techniques was adopted for ensuring homogeneity of gel[5].

Viscosity

Brookfield viscometer (Spindle type, S-62) at 10 rpm was used to determine viscosity of gel. The spindle of brookfield viscometer was dipped beaker containing 100g of gel. Run the instrument for 5 minutes and reading was noted in cps[5].

Spreadability

The gel was transferred on a glass slide and covered with an equivalent slide. The slides are placed in such a way that gel sandwiched up to 7.5 cm. A weight of 50g was placed over upper slide which helped in forming uniform thin layer. The weight was removed and excess adhering gel was wiped. After that 20 g weight was coupled carefully to upper slide. Time taken to travel a distance of 7.5 cm by upper slide under influence of weight was recorded. The procedure was repeated thrice and the mean was calculated. The following formula was used to determine spreadability.

$S = MxL/T$

Where, S - Spreadability

M - Weight coupled to the upper slide (50 g)

L - Length of the glass slide (7.5 cm)

T- Time taken to separate the slides in seconds[6].

Extrudability

20 g of gel was filled in a closed collapsible tube and pressed safely at the crimped end. A clamp was used to check rollback. The cap was separated and the gel was extruded until the pressure was dissipated. A good quality gel extrude from collapsed tube with slight pressure applied.

In-vitro skin permeation studies

Franz diffusion cell were used for in vitro skin permeation studies with a receptor compartment capacity of 25 ml and an effective diffusion area of 2.54 cm2. The cellophane membrane of required thickness was hydrated 24 hours before use with pH 7.2 phosphate buffer saline. The donor compartment contained 1 g gel and recipient compartment consisted of phosphate buffer saline pH 7.2. At regular interval sampling was done from receptor compartment and equal amount of fresh phosphate buffer saline was added in the receptor compartment. The active constituent present in the samples withdrawn was determined by UV spectroscopy[7].

Antiacne assay of different formulations

Screening of selected formulations of plant extracts individually

The antiacne activity of selected formulations was determined by disc diffusion method. In this method, MH and BHI agar plates were seeded with 24 hr broth culture of S. epidermidis and P. acnes also PDA plates were seeded with 7 days broth culture of M. furfur. A sterilized borer was used to make wells in each of plates; 100µg of gel and erythromycin disc (15µg) were introduced into the plates along with 100µg of marketed erythromycin gel (2% w/w). The plates were incubated at 37oC for 24 hours in case of S. epidermidis and for 24-48 hours in case of P. acnes and M. furfur. Diameter of zones of inhibition (in mm) was measured for evaluation of anti acne activity.

Stability study

Accelerated stability study was conducted for optimized gels at 40oC and 75% RH for one month using Navyug India Ltd. stability chamber.

RESULTS AND DISCUSSION

Preparation of gels

All the developed gels were examined visually for appearance, nature and homogeneity matching the desired characteristics of gel and the following gels were selected.

The various gel formulations were optimized on the basis of different physical parameters. On the basis of the results obtained of all the batches, the best formulations meeting the characteristics of gel were selected.

It was observed that F3 and F10 batches comply with the desired characteristics of gel and was selected for further evaluation of antimicrobial assay.

Antimicrobial assay of selected formulations

The antibacterial activity of developed formulations was evaluated by measuring the diameter of zones of

In-vitro skin permeation studies for developed gels

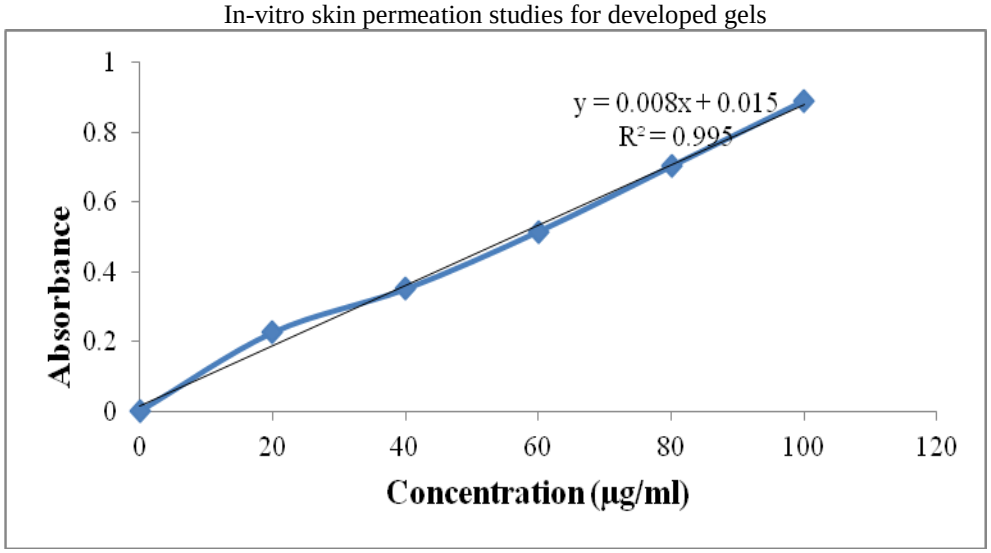

Figure 3: Standard plot (UV absorptions of different concentrations of Plumbagin)

inhibition (in mm). The results of this investigation showed that the selected formulations F3 and F10 of P. indica showed inhibitory effect on the test bacterium which is comparable to marketed preparation. However, the activity of the standard erythromycin gel was more than that of all developed formulations. The zones of inhibition are given in table 3.

On the other hand, the activity of selected formulations against M. furfur showed remarkable inhibitory effect as compared to standard drug i.e. fluconazole. Comparative study of antiacne activity of formulations as separate entity and in combination against *P. acnes, S. epidermidis* and *M. furfur*.

Drug diffusion study of the herbal gel was essential to confirm that the extract would partition from the vehicle and permeate through the semi permeable membrane which symbolizes the stratum corneum. The study was carried out for a period of 6 hours in which the gel demonstrated % Cumulative drug release of 71.74% and 56.73% for the 2% ethanolic extract of B. aristata and P. indica and 61.76% and 54.86% for the 1% ethanolic extract of B. aristata and P. indica.

Stability study

Stability study which was conducted for optimized batches stored at 40°C/75%RH for one month do not shows any stability issues after evaluation (appearance, feel on application, pH, viscosity.

CONCLUSION

Plumbago indica extract based gel has potential activity against acne-causing microorganism.

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