FORMULATION AND EVALUATION OF POLYHERBAL ANTIPSORIATIC CREAM

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Summary

In the present research an attempt has been made to develop antipsoriatic cream using combination of herbs like neem, sarsaparilla, bakuchi and daruhaldi. Psoriasis is an inflammatory disease of skin characterized by well defined erythematous plaque with large adherent silvery scales. Colonization and infection with *S. aureus* has been reported to exacerbate Psoriasis. The conventional medical treatment of psoriasis relies upon combination of treatment like using coal tar preparations, dithranol, calsipotriol, topical corticosteroids and controlled UV radiations. However, serious side effects are associated with them. Shortcomings of these conventional treatments of psoriasis encouraged us to develop effective polyherbal formulation. Experimental findings indicated that formulation F3 was most stable and efficacious and showed good antimicrobial and anti inflammatory results. Formulation F3 containing Bakuchi 1.2%, Daruhaldi 2%, Neem 1% and Sarsaparilla 1.2% offers a valuable alternative to the conventional psoriasis treatment.

Keywords: Anti psoriatic, Polyherbal, *Azadirachta indica*, inflammation

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Introduction

The skin forms body's defensive perimeter. Skin suffers more physical and chemical insult compared to any other area of the body. Psoriasis is an inflammatory disorder of the skin. The main abnormality in the psoriasis is increased epidermal proliferation due to excessive division of cells in the basal layer and shorter cell cycle time. The transit time of keratocyte through epidermis is shortened and epidermal turnover time falls from 28 days to 5 or 6 days. Psoriasis alters the pH of the skin and lead to alkalinity of diseased area (1). The course of disease is unpredictable and is usually chronic with exacerbations and remission. Colonization and infection with *S. aureus* reported to exacerbate psoriasis and thus psoriasis remains to be a serious health problem.

Course of treatment available for treating psoriasis is use of the combinations of conventional methods. Coal tar preparations have been used for many years. They act probably by inhibiting DNA synthesis.

Dithranol also inhibits DNA synthesis however is skin irritant and stains normal skin purple brown. Calcipotriol is vitamin D analog and it reduces epidermal proliferation however skin irritation remains its main side effect. Topical corticosteroids are effective initially however on their withdrawal after prolong use psoriasis relapses rapidly. UV radiations are used for psoriasis treatment in combination with coal tar and dithranol.

Systemic treatment is considered if extensive psoriasis fails to respond to local measures. Most common are oral psoralens followed by exposure to long wave UV light. This treatment is called PUVA. Methotrexate and Cyclosporine-A are also given however all these treatments have potential side effects and toxicity.

Azadirachta indica (Neem) has powerful antibacterial activity due to its histamine, kinin and prostaglandin inhibitory activity. Berberine found in *Berberis aristata* (Dauhaldi) affects cell DNA putting break on cellular proliferation and have significant antibacterial activity against *S. pyrogens. Hemidesmus indicus* (Sarsaparilla) induces perspiration eliminating waste products and acts as blood purifier. *Psoralea corylifolia* (Bakuchi) is known to decrease cellular proliferation. Yet no work has been done using all these four herbs together and this prompted us to make an attempt to prepare O/W antipsoriatic cream using combination of above mentioned herbs in the present research.

Materials and Methods

Materials-

Azadirachta indica leaf extract, *Bereris aristata* root extract, *Psoralia corylifolia* seed extract and *Hemidesmus indicus* root extract were obtained from Chemiloids, Vijaywada. Other chemicals used were of analytical grade.

Methods-

Raw material analysis:

All aqueous extracts obtained from Chemiloids were analysed on the basis of Loss on drying, determination of water soluble extractives (2), determination of pH (3) and HPTLC fingerprints (4).

Preparation of O/W cream:

The emulsifier, antioxidant and other oil soluble components were dissolved in oil phase while the preservative and other water soluble components were dissolved in aqueous phase. Both the phases were heated to 75 ^{0}C and then oil phase was added to the portion of aqueous phase with continuous stirring (5). Five formulation designated as F1 to F5 were prepared with varying amounts of extracts (Table 1).

Physicochemical evaluation of prepared formulations:

All the prepared formulations F1 to F5 were then subjected for following physicochemical tests-

Viscosity:- Viscosities of the formulations were determined using Brookefield synchroelectric viscometer (RTV model) at 100rpm with spindle no 7.

pH:- 0.5 gm of the formulation was dissolved in 50 ml water and ph was noted using digital ph meter (Toshniwal pH meter, India).

Homogeneity:- creams were evaluated for homogeneity by visual inspection.

Spreadability:- glass slide apparatus was used to determine the spreadability (6). An excess of cream was placed in between two glass slides and 1000gm weight was kept on the slide for 5min to compress the sample to uniform thickness.

Bottom slide was anchored to the apparatus whereas pan was attached with the help of string to the upper movable slide as shown in fig.1. Weights were placed in the pan and time in seconds needed to separate two slides was taken as measure of spreadability.

Skin irritation test:-Test was performed on healthy human volunteer. For each formulation five volunteers were selected and 1 gm of weighed formulation was applied on area of 2 sq. inch to the back of the hand and covered with cotton. Volunteers were asked to report after 24hrs to observe for any reaction or irritation.

Stability studies:
All the developed formulations were subjected to accelerated stability testing for 8weeks. The temperatures were 45 ^{0}C, room temperature and 4 ^{0}C. Effect of temperature on developed formulations was studied after every 15days. Formulations were analyzed for change in viscosity and pH.

Determination of *In vitro* antimicrobial activity by cup plate method (7**):**
In vitro antimicrobial study was conducted using cup plate method or agar diffusion method. Study was carried out in aseptic area to establish the efficacy of the formulations against *S. aureus*. *S. aureus* is most common pathogen causing psoriasis.

***In vivo* evaluation of anti-inflammatory activity:**
Among *in vivo* methods, carragenan induced rat paw edema assay is believed to be the most reliable and widely used method (8). Plethysmometer (UGO, Basile, Italy) was used for screening the anti-inflammatory activity. Normal left hind paw volume of each albino rat was measured by Plethysmometer. 50 mg of respective formulation were weighed and applied to left hind paw of each rat prior to 1 hr before carragenan injection. Marketed Beclomethasone dipropionate was used as standard anti-inflammatory cream. Control group was treated with cream developed without any active ingredient. Paw volume after 1 hr and 3 hr was noted and activity was calculated using formula-

$$\% \text{ Inhibition of oedema} = (1-Vt/Vc) \times 100.$$

Where, Vt= mean inflammation of test
Vc=mean inflammation of control.

Results and Discussion

Present study was aimed at preparing best polyherbal cream for the treatment of Psoriasis, a dreaded skin disease. The analysis of raw material revealed that the results obtained were within the limits. The pH of all the aqueous extracts was found to be acidic. HPTLC fingerprints confirmed the quality and purity of the extracts.
Five different formulations designated as F1 to F5 were prepared using ingredients in varying proportions. Formulation F1 was prepared without Neem extract. Formulation F2, F3 and F5 contains all the ingredients in different concentrations as shown in Table 1. Formulation F4 was prepared using coconut oil instead of sesame oil. As all formulations were O/W type cream and there were chances of microbial growth in the formulations, methyl paraben and propyl paraben were added to the preparations as preservatives. Oil soluble antioxidant was added to the formulation to avoid the oxidation of sesame oil or coconut oil. All the developed creams were stored in tightly closed containers and evaluated for their physicochemical properties, antimicrobial and anti-inflammatory activity.

Physicochemical evaluation results of all the formulations are depicted in Table 2. The viscosity of the formulation ranges from 6800 to 7600 cps. The pH of formulation ranges from 5.34 to 6.56. All the developed formulations showed excellent homogeneity and there were no lumps in the formulations. Spreadability values showed that formulations spread with an ease, F5 showed maximum spreadability. Skin irritation study results revealed that all the developed creams were safe for topical application and did not induce any skin reaction.

Formulations F1-F5 were then exposed to three different temperature conditions to determine the stability of the preparations. The stability results (Table 3) indicated that all formulations were stable with slight changes in the viscosity and pH of the formulation. The pH and viscosity of the formulations found to decrease at higher temperature. There was no bad rancid smell which showed the effectiveness of the antioxidants in the formulations.

In-vitro antimicrobial activity was calculated in terms of inhibition zone diameter. The organism *S. aureus* was used as pathogen as it causes the psoriasis. Results in the Fig. 1 revealed that all the formulations have antimicrobial activity. F3 showed largest zone of inhibition whereas F1 showed less antimicrobial activity which can be attributed to the absence of neem extract in it.

In-vivo anti-inflammatory activity studied by carragenan induced rat paw oedema method showed that formulation F3 has maximum anti-inflammatory activity amongst the five developed formulations (Table 5). Formulation F5 containing proportionately less concentration of extracts than other formulations showed lowest anti-inflammatory activity. The anti-inflammatory activity of F3 was comparable with that of Beclomethasone dipropionate.

Clinical evaluation of the developed formulation was carried out in order to find the effectiveness of the creams in the psoriasis. Clinical evaluation was carried out in six patients. One was treated with marketed beclomethasone dipropionate and referred as standard while remaining five used developed formulation F1-F5. The study was conducted under strict observation of private medical practitioner. The results were seen after 20 days (Table 6).

Marketed Beclomethasone dipropionate showed complete disappearance of redness. The psoriatic area was reduced to about 0.6 cm^2. The scaling was also decreased. Formulation F3 showed comparable results. The patients did not complain of any skin irritation, itching or burning sensation on the applications of the formulations. It was well tolerated by all the patients used in the clinical study. The psoriatic area was decreased by 75% and inflammation was remarkably decreased. There was no scale formation and no other side effect was observed during the course of treatment.

Conclusion

From the results obtained above in the study, it can be concluded that Formulation F3 is stable and efficacious. It showed good antimicrobial as well as anti-inflammatory activity. F3 produced encouraging clinical results and was well tolerated by the patient. Hence formulation F3 containing Bakuchi 1.2%, Daruhaldi 2%, Neem 1% and Sarsaparilla 1.2% offers a valuable alternative to the conventional psoriasis treatment.

Table 1. Formulation Chart of the developed O/W cream formulations:

a. Oil Phase

Ingredients	Control	F1	F2	F3	F4	F5
Sesame oil	10	10	10	10	10*	10
GMS	4	4	4	4	4	4
Cetosteryl alcohol	10	10	8	10	10	10
Stearic acid	4	4	4	4	4	4
B.H.T.	0.05	0.05	0.05	0.05	0.05	0.05
Propyl paraben	0.1	0.1	0.1	0.1	0.1	0.1
Beeswax	0.5	0.5	0.5	0.5	0.5	0.5
Liquid paraffin	5	5	5	5	5	5

*Coconut oil

b. Water Phase

Ingrendients	Control	F1	F2	F3	F4	F5
KOH	0.25	0.25	0.25	0.25	0.25	0.25
Methyl paraben	0.15	0.15	0.15	0.15	0.15	0.15
Psoralea corylifolia	-----	1.2	1.0	1.2	1.2	0.8
Berberis aristata	-----	2.6	1.8	2.0	2.0	1.6
Azadirachta indica	-----	-----	0.8	1.0	1.0	0.6
Hemidesmus indicus	-----	1.2	1.0	1.2	1.2	0.8
Distilled water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table 2. Physicochemical evaluation of the developed creams:

Formulation	pH	Viscosity (cps)	Homogeneity	Spreadability gm.cm/sec	Skin irritation
F1	5.34	7400	Excellent	10.55	No
F2	6.39	7000	Excellent	11.17	No
F3	6.48	7200	Excellent	11.87	No
F4	6.40	7600	Excellent	10.85	No
F5	6.56	6800	Excellent	12.66	No

Table 3. Stability studies of the developed creams:

a. Effect of temperature on viscosity of the creams-

DAYS	F1			F2			F3			F4			F5		
	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0
0	7400	7400	7400	7000	7000	7000	7200	7200	7200	7600	7600	7600	6800	6800	6800
15	7300	7100	7000	6900	6700	6400	7000	6800	6500	7400	7000	6700	6600	6300	5900
30	7200	6900	6500	6800	6500	6000	6900	6600	6100	7200	6800	6500	6400	6000	5500
45	7000	6500	6200	6400	6100	5800	6500	6300	5700	6900	6600	6300	6100	5700	5000
60	6900	6400	6000	6200	5900	5000	6100	6000	5400	6500	6400	6000	5800	5000	4400

b. Effect of temperature on pH of the creams-

DAYS	F1			F2			F3			F4			F5		
	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0	4^0	R.T.	45^0
0	5.3	5.3	5.3	6.2	6.2	6.2	6.4	6.4	6.4	6.4	6.4	6.4	6.5	6.5	6.5
15	4.6	5.0	5.1	5.9	5.5	5.0	6.0	5.9	5.7	6.2	6.1	5.8	6.3	6.1	5.8
30	5.0	5.1	4.5	5.7	5.6	4.9	5.8	5.6	5.5	6.0	5.9	5.6	6.1	5.9	5.7
45	4.8	4.7	4.1	5.6	5.4	4.8	5.7	5.5	5.3	5.9	5.7	5.4	5.8	5.8	5.5
60	4.7	4.4	3.9	5.4	5.3	4.6	5.5	5.3	4.9	5.8	5.4	5.0	5.6	5.7	5.1

Table 4. Total microbial count of the developed creams:

Formulations	Bacterial count in CFU/ml	fungal count in CFU/ml
F1	$30x10^8$	$8x10^4$
F2	$8x10^6$	$5x10^4$
F3	$16x10^6$	No colonies observed
F4	$35x10^8$	$3x10^3$
F5	$20x10^7$	No colonies observed

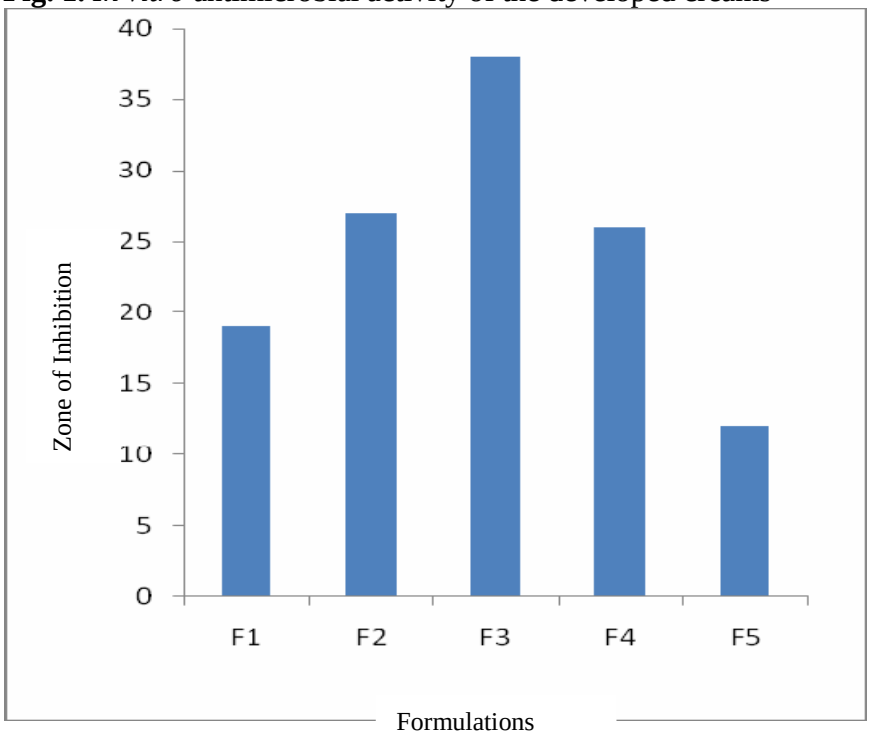
Table 5. *In vivo* anti-inflammatory activity of developed creams:

Treatment	%inhibition of oedema after 1hr	%inhibition of oedema after 3hrs
Control	---------	---------
Beclomethasone dipropionate	79.61± 0.011	72.52 ± 0.020
F1	59.97 ± 0.023	57.50 ± 0.028
F2	62.13 ± 0.045	59.81 ± 0.075
F3	74.50 ± 0.010	71.05 ± 0.072
F4	71.41 ± 0.029	68.96 ± 0.051
F5	50.80 ± 0.005	46.17 ± 0.007

Table 6. Clinical evaluation of developed creams:

Formulation	Psoriatic area		Itching	Scaling
	Before treatment	After treatment		
Beclomethasone dipropionate	3x3 cm	0.6 cm	Absent	Absent
F1	3x5 cm	0.9 cm	Absent	Decreased
F2	4x3 cm	1.0 cm	Absent	Decreased
F3	5x5 cm	1.6 cm	Decreased	Absent
F4	2x3 cm	0.5 cm	Absent	Absent
F5	3x3 cm	0.8 cm	Decreased	Absent

Fig. 1. *In vitro* antimicrobial activity of the developed creams



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