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Design of Medicated Cream for Scalp Infections

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ABSTRACT

Psoriasis is most frequently affects the skin of the elbows, knees, scalp, lumbosacral areas. It is the typical lesion well-demarcated, pink to salmon-colored plaque covered by loosely adherent scales that are characteristically silver white in color. Several topical therapies are available for the treatments of Scalp psoriasis like emollients, keratolytics, corticosteroids, tar, anthralin, vitamin D analogues and retinoids. .Currently available medications such as ointments and solutions are often greasy, sticky, odorous, difficult to apply, require frequent application, and are expensive causes poor patients compliance. In proposed work it is planned to prepare cream formulations of non-greasy and water removable, and improve patient's compliance. This cream is o/w emulsion based formulation contain suitable combination of oil phase and aqueous phase along with preservatives, was prepared and subjected to various physiochemical parameters like drug content, pH, spreadability, tube extrudability, viscosity and IR studies. *In-vitro* drug release was carried out in phosphate buffer (pH 7.4) and compared with marketed formulation. Stability studies of formulation were also done at ambient temperature (30^{o}C&40^{o}C) for the period of six months as per ICH guidelines. The formulations were subjected for primary skin irritation test in rabbits, guinea pigs, and healthy human volunteers for 72 hours and observed for any skin rashes, inflammation, itching, or redness. Drug content, pH, Spreadability, Tube extrudability of the formulation was found to be 95.47%, 7.2, 12.28gm.cm/sec, 96.14% respectively. From rheogram it is concluded that formulation shows pseudoplastic flow property. From our study it is revealed that salicylic acid cream formulation should be useful for treatment of scalp psoriasis.

Keywords: Psoriasis, salicylic acid cream

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INTRODUCTION

Patients with psoriasis experience itching, scaly, painful and disfiguring skin lesions[2] and is a genetically determined disorder of the skin[3] where the scalp is frequently involved. In children and young adults it is sometimes the first site to be affected and some patients it remains the only one[3]. A special variant of scalp psoriasis is known as sebopsoriasis or seborrhiasis. In this condition, psoriasis mostly predominates, with associated facial involvement showing a greasy scaling with a yellowish color[4]. Salicylic acid is one of the oldest known keratolytics and a well-established treatment for many dermatologic conditions, including psoriasis[5,6]. Salicylic acid appears to be a safe choice for the control of localized psoriasis in pregnancy; however, because of a greater risk of systemic absorption and toxicity, salicylic acid should be avoided in the treatment of children[2]. Patient compliance is often poor as currently available medications are often greasy, sticky, odorous, difficult to apply, require frequent application, and are expensive. In proposed work it is planned to prepare cream formulations which are non-greasy and water removable, increasing patient's compliance. These preparations are stearic acid based and part of stearic acid is saponified with an alkali and rest of the stearic acid is emulsified with this soap in a large quantity of water. The high quality stearic acid provides an oil phase, which melts above body temperature and crystallizes in suitable form, provides an invisible and non-greasy film and can produce a very attractive appearance [7, 8].

MATERIALS AND METHODS:

Salicylic acid, Cetyl alcohol (S.D. Fine Chemicals Ltd., Mumbai), Stearic acid, Methyl paraben, Propyl Paraben (Loba Chemie Pvt. Ltd., Mumbai), Glycerin, sodium Hydroxide, triethanolamine (Qualigens Fine Chemicals, Mumbai),

Preparation of cream formulation containing Salicylic acid:

These creams are o/w emulsion based preparations containing aqueous phase and oil phase. Ingredients of oil phase (A) mixed together by melting on constant stirring. Components of aqueous phase (B) mixed together and warmed to about same temperature of oil phase. Aqueous phase was added to oil phase drop by drop on constant stirring. The therapeutically active insoluble ingredient salicylic acid incorporated when the formulation begins to solidification by levigation method. The preservative propyl paraben and methyl paraben were added after cooling to 40^{o}C.(Table-1).

Evaluation of cream:

The cream was evaluated for pH, Drug content, viscosity, spreadability, tube extrudability, Drug

diffusion, Stability and primary skin irritation test on experimental animals and healthy human volunteers.

Table-1: Formulation code (F)

SI.No.	Ingredients	Quantity in gms.
A. 1.	Salicylic acid	6.00
2.	Stearic acid	20.00
3.	Cetyl alcohol	0.50
4.	Triethanolamine	1.20
B. 5.	Sodium hydroxide	0.36
6.	Glycerin	8.00
7.	Propyl paraben	0.05
8.	Methyl paraben	0.10
9.	Purified water	63.79
	Total	**100.00**

Determination of pH[9]:

Weigh accurately 5± 0.01gm of the cream in 100ml beaker. Add 45 ml of water and disperse the cream in it. Determine the pH of suspension at 27^0C using the Elico digital pH meter.

Drug content uniformity[10, 11]:

The formulation equivalent to 50 mg of drug was taken and dissolved in small quantity of methanol. Then the formulation is warmed on the water bath so that the drug present in the formulation was completely dissolved. Then the solution is filtered through Whattman filter paper in to 50ml vol.flask. The volume is made up to the mark which gives concentration of 1000mcg/ml. From this different concentration of solution was taken in 10ml volumetric flask and volume was made upto 10ml with methanol and absorbance was measured by UV spectrophotometer at 231.6nm against blank.

Viscosity [12,13,14,15,16]:

The viscosity of formulated cream was measured by Brook field Viscometer (LVDV-III ultra programmable Rheometer) using spindle CP-52 at varying speed and shear rates. The measurements were made over the range of speed setting from 0.10, 0.20, 0.30, 0.40 and 0.50 rpm with 60sec between two successive speeds as equilibration with shear rate ranging from 0.20 sec^{-1} to 1.0 sec^{-1}. Viscosity determinations were performed at room temperature. The viscosity data was plotted for Rheogram- **Viscosity in cps v/s shear rate in sec^{-1}.**

Spreadability [10,17] :

Spreadability is a term expressed to denote the extent of area to which the topical application spreads on application to skin on the affected parts. The therapeutic efficiency of the formulation also depends upon its spreading value. Hence, determination of spreadability is very important in

evaluating topical application characteristics. excess of sample (3gm) was applied in between two glass slides and was compressed to uniform thickness by placing 1000 gm weight for 5 minute. Thereafter weight (50gm) was added to the pan and the top plate was subjected to pull with the help of string attached to the hook. The time in which the upper glass slide moves the lower plate to cover a distance of 10cm is noted. A shorter interval indicates better spreadability. The spreadability (S) can be calculated using the formula.

S = m.l/t.

Where, S – spreadability' m- weight tied to upper glass slide. l- Length moved on glass slide, t- time taken.

Tube extrudability[18]:

In the present study, the method adopted for evaluating cream formulation for extrudability was based upon the quantity in percentage cream extruded from tube on application of finger pressure. More quantity extruded better was extrudability. The formulation under study was filled in a clean, lacquered aluminium collapsible one- ounce tube with a nasal tip of 5mm opening and apply the pressure on the tube by the help of finger. Tube extrudability was then determined by measuring the amount of cream extruded through the tip when a pressure was applied on tube.

***In-vitro* Drug diffusion[19, 20, 21, 22]:**

A glass cylinder with both ends open, 10 cm height, 3.7 cm outer diameter and 3.1 cm inner diameter was used as permeation cell. A cellophane membrane pre hydrated in distilled water (24 hrs. before use) was fixed to the one end of the cylinder with the aid of an adhesive to result in permeation cell. One gram of semisolid formulation was taken in the cell (donor compartment) and the cell was immersed in beaker containing 100ml of drug free pH 7.4 phosphate buffers as receptor compartment. The cell was immersed to a depth of 1 cm below the surface of receptor fluid. The medium in the receptor compartment was agitated using a magnetic stirrer and temperature of $37^{o}C\pm 1^{o}C$ was maintained. Samples (5ml) of the receptor compartment were taken at various intervals over a period of 3 hours with replacement of equal amount of free receptor fluid. The samples were estimated by measuring the absorbance at 230.6 nm in a 1700 UV Shimadzu spectrophotometer.

Stability studies:

The prepared 6% salicylic acid cream formulations were filled in the collapsible tubes and stored at ambient temperature ($30^{o}C\&40^{o}C$) for the span of six months. 1gm of cream formulation was

taken out at different time intervals (one month interval) and analyzed for drug content, physical appearance, pH and rheological properties.

Infrared spectral analysis:

IR spectral analysis is one of the most powerful analytical technique which offer the possible chemical identification. In the present work, IR spectrum of salicylic acid pure drug and salicylic acid with other excipients in formulation was studied for their interactions.

Primary skin irritation test:

1) Laboratory experimental animals[23] :

The animals selected were rabbits and guinea pigs. These animals were kept in different cages and supplied with fresh food and water during the test period, 24 hours prior to test, and the hair from the neck and thigh region was shaved to expose sufficient large test area. The test site was cleaned with surgical spirit then cream is applied to test area. The test site was observed for erythema and edema for 24 hrs; 48 hrs; and 72 hrs after application. This test was conducted to evaluate the irritancy of the prepared cream on the intact skin of animals. None of the prepared cream showed any erythema or edema, indicating that the prepared formulation was non-irritant on the skin of animals. These studies were carried out in the animal house M.R. Medical College.

2) Healthy Human Volunteers Studies:

The prepared formulation showed high compliance in animal studies, thereby prompting to carry out skin irritation studies on healthy human volunteers. The study was conducted under the supervision of staff, Dept. Dermatalogy, M.R. Medical and general Hospital, Gulbarga, with the permission of medical college ethical committee. The skin irritation test was performed on three healthy human volunteers for each formulation (2 male and 1 female) by applying cream formulations. The volunteers were of age group between 22-28 years and weighing 50-70 Kgs. The test was performed primarily by examining each volunteer for any change of skin after application of formulations. Then photographic imaging of skin of forehead and dorsal part of ears of human volunteers was taken out after subsequent application for 72 hrs i.e. at completion of study period and these images were compared determining the difference with the images taken at 0^{th} hr of study i.e. prior to first application of formulation. moreover, skin irritation was evaluated by questioning the human volunteers at regular interval of time about the feeling of irritancy, which appears to be highly subjective for the study.

RESULTS AND DISCUSSION:

The percentage drug content of prepared cream formulation was found to be 95.47%. pH of the

formulation was nearly neutral pH range (7.2). The spreadability and tube extrudability of formulation is 12.28gm.cm/sec & 96.14% respectively. At the end of 180 min the percentage amount of drug released from F was found to be 45.22% with respective to the marketed product (MP) having 44.19% drug release in 180 min.(Table-2). The release of drug from these formulations were found to be governed by diffusion process since the plot of percentage cumulative drug release Vs square root of time were found to be linear. IR study concluded that all the peaks of the pure drugs are also observed in different formulation with slight modification. The results shown that the formulation was devoid of any primary skin irritation or sensation or erythema, or edema even after 72 hrs of application.(figure-2,3,4). Salicylic acid is a drug of choice for the treatment of scalp psoriasis due to its keratolytic effect, in the present study an attempt has been made to prepare cream preparation of salicylic acid. Results showed that the prepared cream formulation showed good spreadability and tube extrudability property. The viscosities of the formulations were measured at varying speed and shear rates. Apparent viscosity and rheological behavior of the formulation lead to consistency. The data of cream formulation has shown shear thinning/ pseudoplastic behavior at ambient temperature where there is decrease in viscosity by increasing shear rate (graph of viscosity Vs shear rate/figure-1). This shear thinning behavior is a desirable property for topical preparations, as they should be thin during application and thick otherwise. that there is no drug-excipients interaction.

Table-2 Comparative *in-vitro* drug release profile of salicylic acid (6%) vanishing cream (F) with Marketed Product (MP)(Salicylix.SF6)

Sl. No	Time (min)	Square root time	Cumulative percent drug released		Cumulative percent drug remaining		Log Cumulative percent drug remaining	
			F	MP	F	MP	F	MP
1	0	0.0000	00.00±0.000	00.00±0.000	100	100	2	2
2	30	5.4772	11.70±0.3987	9.34±0.3950	83.30	90.66	1.9459	1.9574
3	60	7.7459	18.81±0.2715	17.16±0.5772	81.19	82.84	1.9095	1.9182
4	90	9.4868	26.52±0.4214	26.86±0.6113	73.48	73.14	1.8660	1.8641
5	120	10.9544	34.98±0.7254	33.70±0.7171	65.02	66.30	1.8130	1.8215
6	150	12.2474	39.60±0.8432	39.23±0.4997	63.40	60.77	1.8020	1.7836
7	180	13.4164	45.22±0.3153	44.19±0.5412	54.78	55.87	1.7326	1.7467

Each reading is a mean of three replicates.

Each sample of 1 gm. cream contains 60mg, of drug.

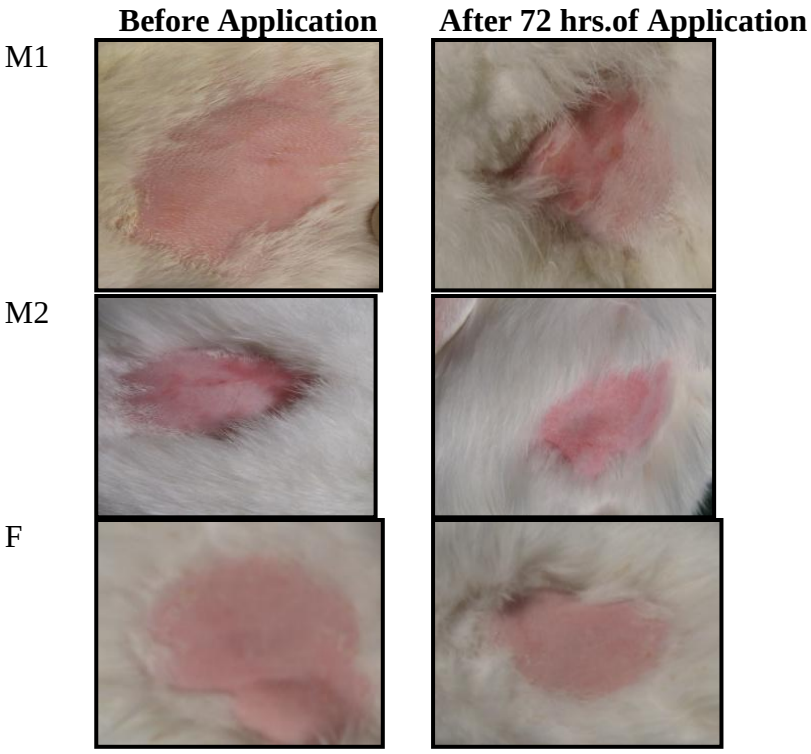

figure-2: primary skin irritation test of one of the group of rabbits

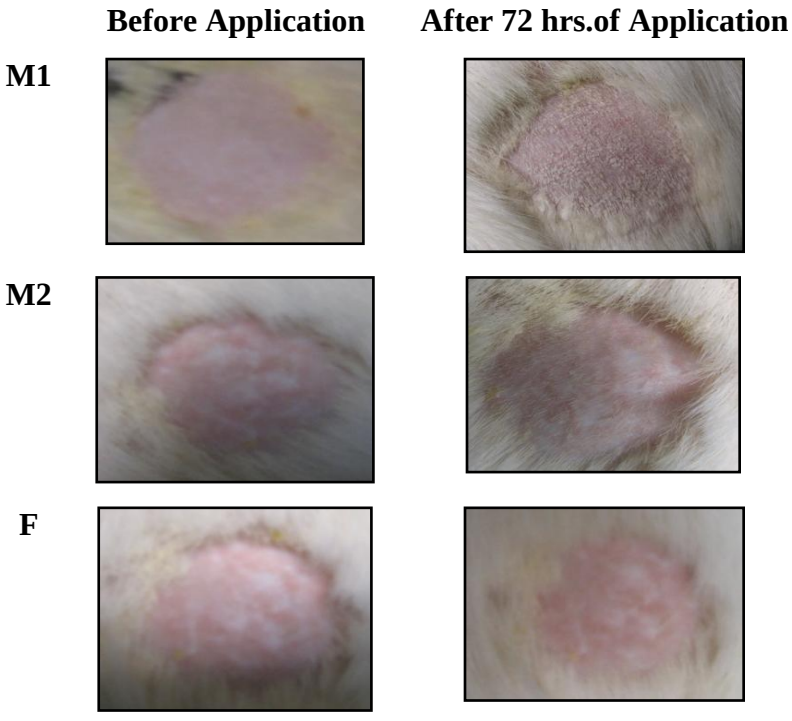

figure -3: primary skin irritation of one of the group of guinea pigs

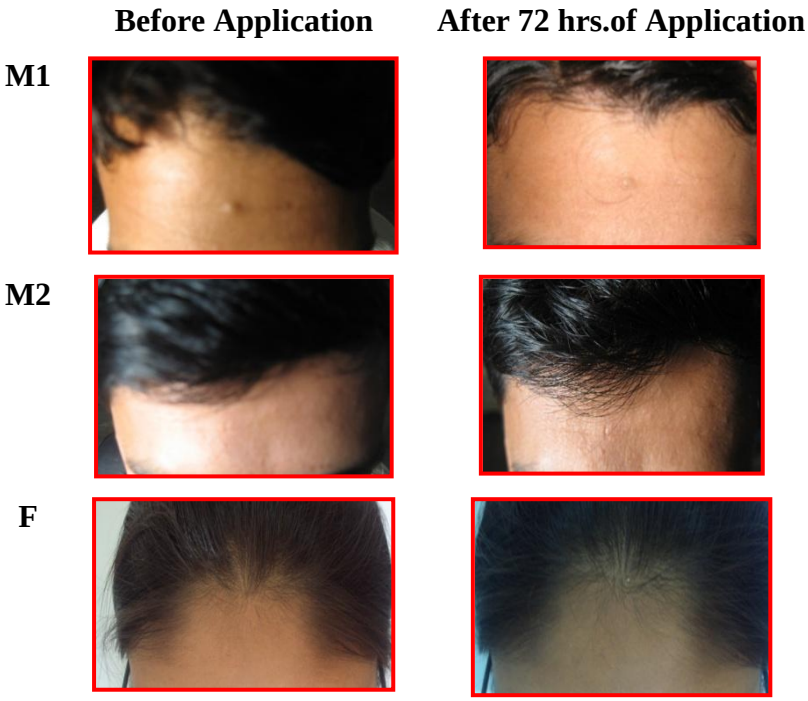

Table-3 Stability studies data of salicylic acid vanishing cream (F)

Sl. No	Storage temp.	Time interval(days)	appearance	pH	Drug content	Spreadability (gm.cm/sec)	extrudability
1.		30	White	7.2	95.47%	12.28	96.14%
2.		60	White	7.0	95.45%	12.23	96.10%
3.		90	White	7.2	95.42%	12.23	96.12%
4.	30°C	120	White	7.1	95.42%	12.19	96.13%
5.		150	White	7.2	95.37%	12.15	96.08%
6.		180	White	7.2	95.33%	12.04	96.06%

- Each reading is a mean of three replicates.
- Each sample of 1 gm. cream contains 60mg, of drug.

Figure-4:Primary Skin irritation test of one of the group of healthy human volunteers

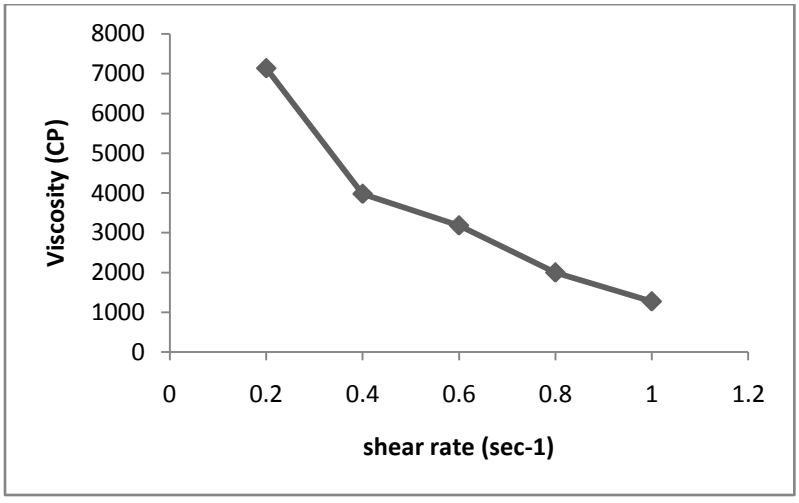

Figure-1 Viscosity Vs. Shear rate graph for (F)

CONCLUSIONS

From our study it is revealed that salicylic acid cream formulation will be helpful for the treatment of scalp infections.

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