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PREPARATION AND EVALUATION O/W CREAM FOR SKIN PSORIASIS

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ABSTRACT

Skin psoriasis which is a common chronic inflammatory dermatosis affecting 1% to 2% of people in the general. Keratolytic agents are helpful in reducing scale and hyperkeratosis by causing softening and desquamation of the stratum corneum and most beneficial in extremely thick or scaly psoriatic plaques. In the present study Salicylic acid chosen as model drug which is the most effective keratolytic agent. In present work o/w emulsion based cream formulation contain suitable combination of oil phase and aqueous phase along with preservatives, prepared and subjected to various physiochemical parameters like drug content, pH, spread ability, tube extrude ability, 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 selected formulation were also done at ambient temperature (30^{o} C & 40^{o} C) for the period of six months as per ICH guidelines. The selected formulation 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 on applied portions. Drug content, pH, Spread ability, Tube extrude ability of the formulation was found to be 95.00%, 6.1, 11.32gm.cm/sec, 94.96% respectively. From rheogram it is concluded that formulation shows pseudo plastic flow property.

KEY WORDS

Psoriasis, salicylic acid formulations, o/w cream

INTRODUCTION

Skin diseases, however, are very common in developing countries like India[1]. Psoriasis is a common, chronic, inflammatory, multi-system disease with predominantly skin and joint manifestations affecting approximately 2% of the population[2]. Psoriasis exhibits unsightly red, scaly areas and can be a life long disease. Like eczema, it affects all age groups and is often

extremely itchy. Psoriasis arthropathy is a rare condition but it can be so serve that the patient is bound to a wheelchair and the disease is occasionally life-threatening[1]. Patients with psoriasis experience itching, scaly, painful and disfiguring skin lesions[3]. Salicylic acid is one of the oldest known keratolytics and a well-established treatment for many dermatologic conditions, including psoriasis[4]. While the precise mechanism of keratolysis is not fully understood, it is thought that salicylic acid may reduce keratinocyte-to-keratinocyte binding as well as reduce the pH of the stratum corneum; these effects lead to reduced scaling and softening of psoriatic plaques[2]. 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 o/w cream formulations to treat skin psoriasis which is 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[5]. 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.

MATERIALS AND METHODS

Materials:

Salicylic acid, Cetyl alcohol (S.D. Fine Chemicals Ltd., Mumbai), Stearic acid, Methyl paraben, Propyl Paraben (Loba Chemie Pvt. Ltd., Mumbai), Glycerin, Potassium Hydroxide, Sodium hydroxide (Qualigens Fine Chemicals, Mumbai), Propylene glycol (Ranbaxy Lab ltd.SAS Nagar)

Preparation of o/w cream formulation:

These o/w emulsion based preparations containing aqueous phase and oil phase. Ingredients of oil phase (A) mixed together by melting in a china dish 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 was added after cooling to 40^{o}C.(Table-1).

Table-1 Formulation code (F)

Sl.No.		Ingredients	Quantity in gms.
A.	1.	Salicylic acid	6.00
	2.	Stearic acid	15.00
	3.	Potasssium hydroxide	0.50
	4.	Sodium hydroxide	0.18
	5.	Cetyl alcohol	0.50
	6.	Propylene glycol	3.00
B.	7.	Glycerin	5.00
	8.	Propyl paraben	0.05
	9.	Methyl paraben	0.10
	10.	Purified water	69.67
		Total	**100.00**

Evaluation of o/w cream:

The o/w cream was evaluated for pH, Drug content, viscosity, spread ability, tube extrude ability, Drug diffusion, Stability and primary skin irritation test on experimental animals and healthy human volunteers.

Determination of pH[7]:

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 pH meter.

Drug content uniformity[8,9]:

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[10,11,12,13,14]:

The viscosity of formulated o/w 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}.**

Spread ability [9,15]

Spread ability 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 spread ability is very important in evaluating topical application characteristics.

For the determination of spread ability, 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 spread ability.

The spread ability (S) can be calculated using the formula

$$S = m.l/t$$

Where,

S – spread ability

m- weight tied to upper glass slide.

l- length moved on glass slide

t- time taken.

Tube extrudability[16]

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

***In- vitro* Drug diffusion[17,18,19,20]**

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 prehydrated 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 buffer 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 o/w cream formulation 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 exciepients in formulation was studied for their interactions.

Primary skin irritation test:

1) Laboratory experimental animals[21]

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, 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 o/w cream was 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. Dermatology, M.R. Medical and general Hospital, Gulbarga.

Test procedure

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:

Salicylic acid is a drug of choice for the treatment of psoriasis due to its keratolytic effect, In the present study an attempt has been made to prepare o/w cream preparation of salicylic acid.

The percentage drug content of prepared cream formulation was found to be 95.00%. pH of the formulation was shown nearly neutral pH range (6.1). The spread ability and tube extrude ability of formulation is 11.32gm.cm/sec & 94.96% respectively.

Fig-1: Viscosity vs. Shear rate graph for (F)

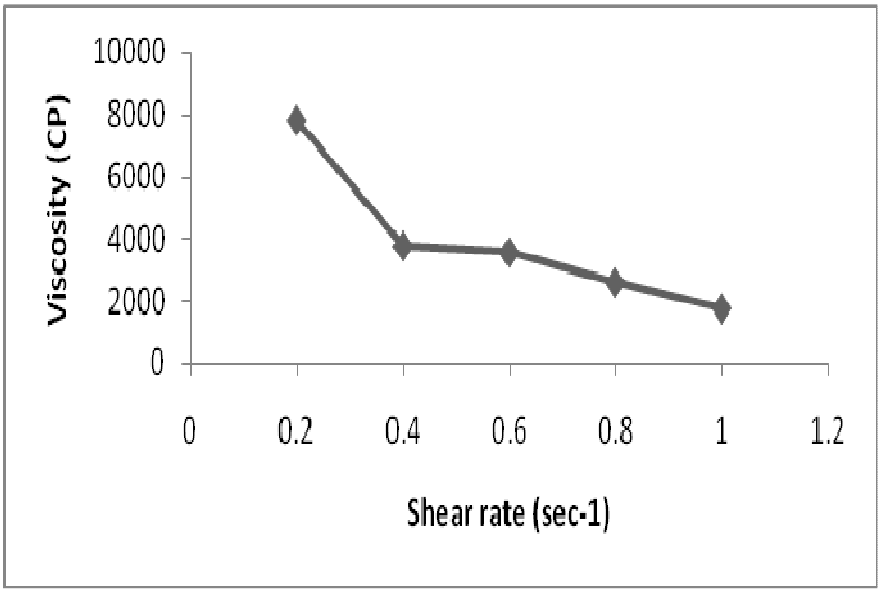

Table-2
Comparative *in-vitro* drug release profile of salicylic acid (6%) o/w cream (F) with Marketed Product (MP)

Each reading is a mean of three replicates.

Sl. No	Time (min)	Square root of 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±0000	00.00±0000	100	100	2	2
2	30	5.4772	10.71±0413	9.34±0.3950	89.29	90.66	1.9508	1.9574
3	60	7.7459	18.52±0.6034	17.16±0.5772	81.48	82.84	1.9110	1.9182
4	90	9.4868	25.22±0.8586	26.86±0.6113	73.78	73.14	1.8737	1.8641
5	120	10.9544	31.48±0.8681	33.70±0.7171	68.52	66.30	1.8358	1.8215
6	150	12.2474	38.20±0.5902	39.23±0.4997	61.80	60.77	1.7909	1.7836
7	180	13.4164	44.08±0.6471	44.19±0.5412	55.87	55.87	1.7475	1.7467

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

Table-3
Stability studies data of salicylic acid o/w cream (F)

Sl. No	Storage temp.	Time interval (days)	appearance	pH	Drug content	Spreadability (gm.cm/sec)	extrudability
1.	$30^{o}C$	30	White	6.1	95.00%	11.32	94.96%
2.		60	White	6.1	95.00%	11.29	94.90%
3.		90	White	6.2	94.97%	11.21	94.92%
4.		120	White	6.1	95.04%	11.21	94.98%
5.		150	White	6.3	95.07%	11.14	94.96%
6.		180	White	6.2	94.86%	11.09	94.90%

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

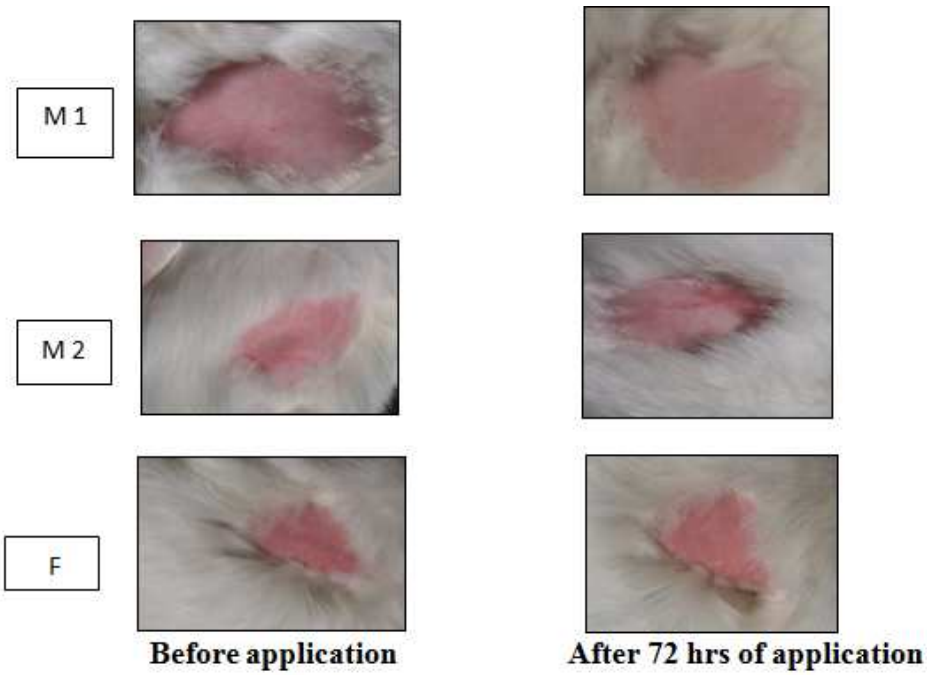

Fig-2: Primary skin irritation test of one of the group of rabbits

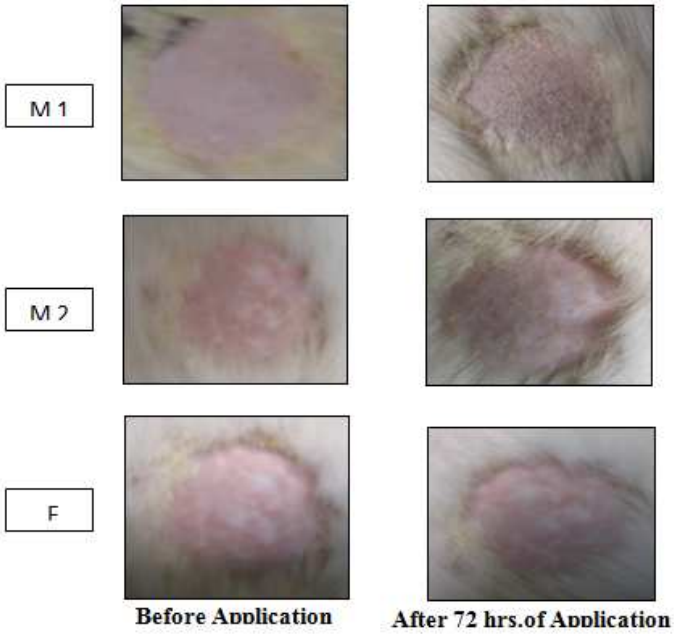

Fig-3: primary skin irritation test of one of the groups of guinea pigs

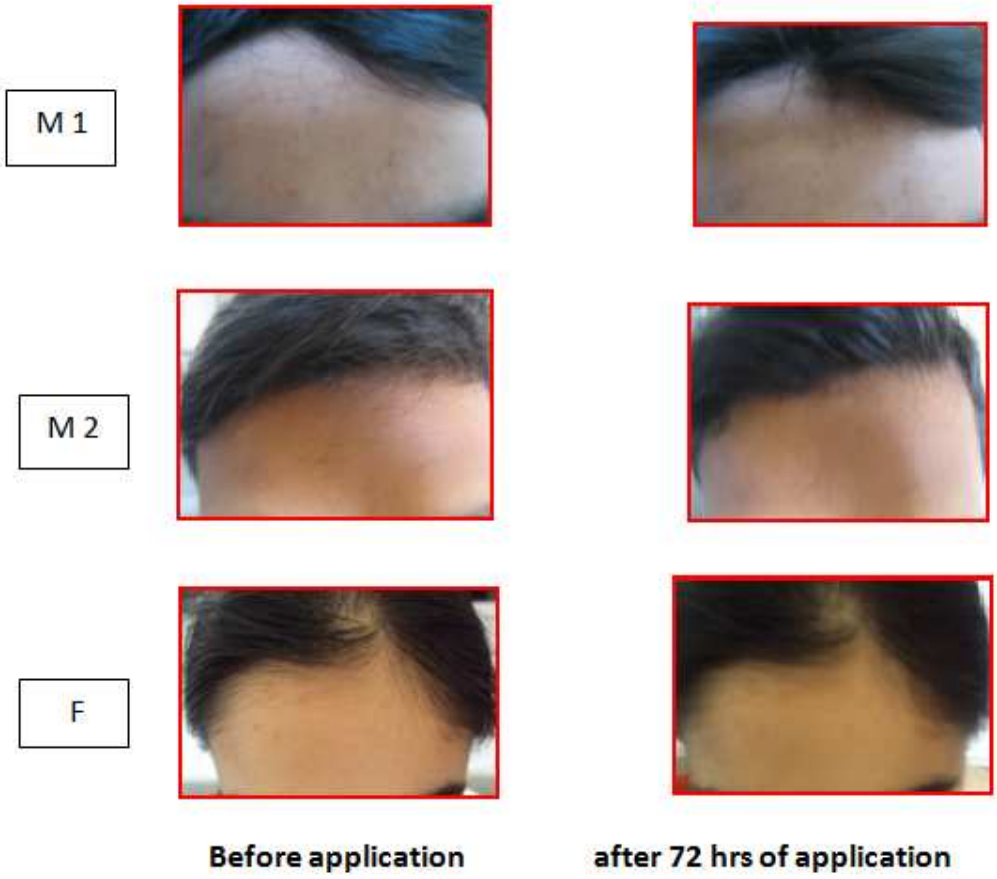

Fig-4: Primary Skin irritation test of one of the groups of healthy human volunteers

Results showed that the formulation showed good spread ability and tube extrude ability 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 formulations 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/fig-1) this shear thinning behavior is a desirable property for topical preparations, as they should be thin during application and thick otherwise. At the end of 180 min the percentage amount of drug released from F was found to be 44.08% with respective to the marketed product (MP) having 44.19% drug release in 180 min.(Table-2). No significant difference has found in drug release in 180 min between F and MP. 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. The prepared o/w cream formulation passed stability studies with no much significant changes in physical appearance, pH, drug content, spread ability and tube extrude ability.(Table-3). IR study concluded that all the peaks of the pure drugs

are also observed in different formulation with slight modification. The result concludes that there is no drug-excipients interaction. 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.(Fig-2,3,4).

CONCLUSIONS:

From our study it is revealed that salicylic acid o/w cream formulation should be useful for treatment of skin psoriasis. In contrast with ointments which are greasy and messy in nature and may causes staining of cloths, o/w cream is pleasant, easily washed by water with increase patient compliance.

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