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Formulation and Evaluation of Salicylic Acid and Urea Gel for Treatment of Psoriasis

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ABSTRACT

Gel containing salicylic acid and urea with five different proportions of carbopol polymer were prepared. These formulations were studied for pH, drug content, viscosity, spreadability, extrudability, skin irritation studies, *in-vitro* studies and stability studies. The formulated gel F3 shows pH 7.0, drug content 85 % and 89 % of salicylic acid and urea respectively, viscosity 10000 cps, spreadability 24.6 gm.cm/sec, extrudability 75.1 %, no skin irritation, *in-vitro* drug release of salicylic acid and urea were found to be 71 % and 81 % respectively. After stability studies of formulation F3, all the above datas comes in acceptable range.

Key words: Psoriasis, gels, keratolytic.

1. INTRODUCTION

Psoriasis is a chronic inflammatory skin disease involving accelerated proliferation of the epidermis layer of the skin. It generally consists of erythematous, well-demarcated papules and rounded plaques, covered by silver-colored scales. It is a common T-cell-mediated immune disorder characterized by circumscribed, red, thickened plaques with an overlying silver-white scale [1]. In present investigation the formulation of salicylic acid and urea gel with different concentration of carbopol 934 were used to treat psoriasis disorders.

2. MATERIALS AND METHODS

Salicylic acid was supplied from S D Fine Chem (Mumbai). Urea was supplied from Loba Chemie (Mumbai). Carbopol 934 and Polyethylene glycol was from Oxford lab (Mumbai). Ethanol was from Changshu Yangyuan Chemical (China). Triethanolamine was from Rankem (New Dehli).

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Preparation of gel

Accurately weighed amount of carbopol 934 was taken and dissolved in water by propeller. In another beaker, drug dissolved in ethanol and added in carbopol solution by stirring, followed by addition of PEG 400. Neutralized the carbopol solution by slowly adding triethanolamine solution with stirring until the gel is formed [2].

Evaluation of gel formulations

pH

The pH of various gel formulations was determined by using digital pH meter. 1 g of gel was dissolved in 100 ml freshly prepared distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values were calculated [3].

Drug content

A specific quantity (100 mg) of developed gel was taken and dissolved in 100 ml of Neutralizing Phthalate Buffer pH 5.4. The volumetric flask containing gel solution was shaken for 2 hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 305 nm and 208 nm for salicylic acid and urea using Neutralizing Phthalate Buffer pH 5.4 as blank [4].

Viscosity

Viscosity of gel preparation was determined by Brookfield viscometer [5].

Spreadability

The spreadability of the gel formulation was determined by, measuring diameter of 1 g of gel between horizontal plates (20x20 cm^2) after 1 min. The standardized weight tied on the upper plate was 125 gm. The spreadability was calculated by using the formula [6].

$$S = \frac{ml}{t}$$

Where, S= spreadability
m= weight tied to upper plate
l= length of glass slide
t= time taken

Extrudability

For evaluation of gel formulations extrudability was determined. It was based upon the quantity in % of gel extruded from lacquered aluminium collapsible tube containing gel which was pressed and firmly crimped at the end. When the cap was removed, gel extruded until pressure dissipated. Weight in grams extruded by 0.5 cm ribbon of gel in 10 seconds was determined. The percentage of gel extruded was calculated and grades were allotted.

$$E = (W_e / W_t) X 100$$

Where, E = extrudability (%), W_e = Amount of formulation extruded (g) and W_t = Total amount of formulation in tube (g) [7].

Skin irritation studies

Test for irritation was performed on human volunteers. For each gel, five volunteers were selected and 1.0 g of formulated gel was applied on an area of 2 square inch to the back of hand. The volunteers were observed for lesions or irritation [8].

In-vitro release

The *in vitro* release of formulations was studied using cellophane membrane using modified apparatus. The dissolution medium used was neutralizing phthalate buffer pH 5.4, freshly prepared. Cellophane membrane previously soaked overnight in the dissolution medium, was tied to one end of a specifically designed glass cylinder (open at both end). One gram of formulation was accurately placed into this glass cylinder. The cylinder was attached to stand and suspended in 200 ml dissolution medium maintained at 37$\pm$ 1^o C, the membrane just touching the receptor medium surface. The dissolution medium was stirred at 100 rpm speed using Teflon coated magnetic bead. Aliquots, each of 5 ml volume were withdrawn periodically at predetermined time interval of 60, 120, 180, 240, 300, 360 min and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium and analyzed by UV spectrophotometer at 305 nm and 208 nm for Salicylic Acid and Urea respectively using neutralizing phthalate buffer as blank [9].

Stability studies

The stability study was performed as per ICH guidelines. The formulated gel were filled in the collapsible tubes and stored at different temperatures and humidity conditions, viz. 25ºC ± 2ºC / 60% ± 5% RH, 30º C ± 2ºC / 65% ± 5% RH and 40ºC ± 2ºC / 75% ± 5% RH for a period of three months and studied for appearance, pH, viscosity, spreadability, extrudability, drug content, skin irritation studies and i*n-vitro* release [10].

3. RESULTS AND DISCUSSION

Physical parameters of gel

The formulation F3 showed the pH 7.0, drug content 85 % and 89 % of salicylic acid and urea respectively, the drug content of formulation shows uniform distribution in gel. Viscosity of F3 was found to be 10000 cps, spreadability of 24.6 gm.cm/sec, extrudability of 75.1 %, and there was no skin irritation found on human volunteers.

In-vitro drug release study

In-vitro drug release profile of gel formulation F3 containing salicylic acid and urea, the total amount of drug release was found to be 71% and 81% of salicylic acid and urea respectively, at different time intervals for a period of 6 hrs (Figure 1 and 2).

Stability studies

Stability studies of F3 formulation shows acceptable results shown in table no. 2 and table no. 3 respectively.

4. CONCLUSION

Salicylic acid and urea are drugs of choice for the treatment of psoriasis due to their keratolytic effect. In the present study an attempt has been made to prepare gel preparation of salicylic acid and urea. From above results, it can be concluded that salicylic acid and urea gel formulations were prepared with different concentration of carbopol 934 showed different physical properties and drug release study. The Formulation gel F3 showed acceptable physical properties concerning pH, drug content, viscosity, spreadability, extrudability, skin irritation studies, *in-vitro* drug release and stability studies values.

5. ACKNOWLEDGEMENT

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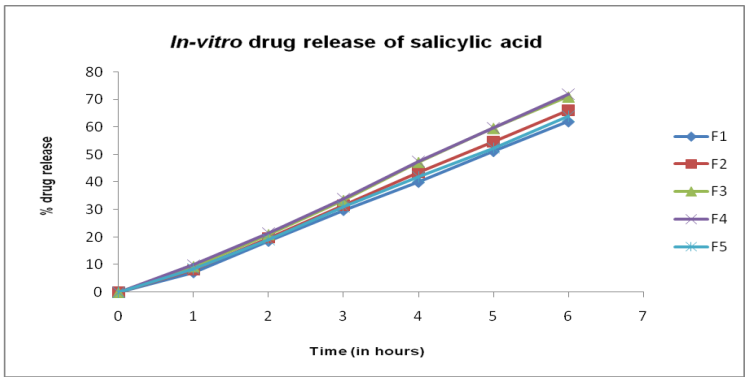

Figure 1: Salicylic acid (Drug release) release profile of gel formulations

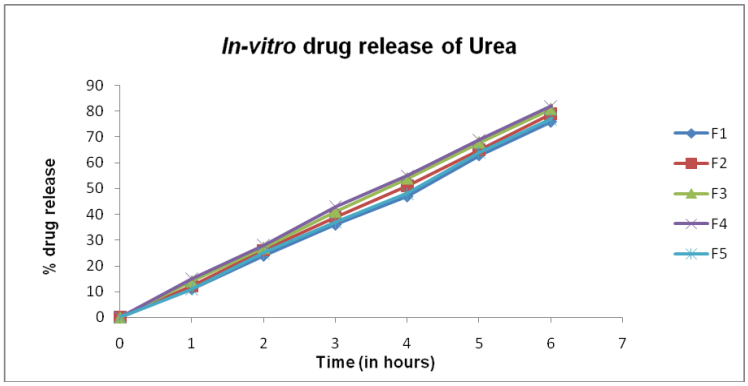

Figure 2: Urea (Drug release) release profile of gel formulations

Table No.1: Composition of gel formulations

S No	Ingredients	F1	F2	F3	F4	F5
1.	Salicylic acid	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg
2.	Urea	2000 mg	2000 mg	2000 mg	2000 mg	2000 mg
3.	Carbopol 934	450 mg	500 mg	550 mg	600 mg	650 mg
4.	Ethanol	15 ml	15 ml	15 ml	15 ml	15 ml
5.	PEG 400	15 ml	15 ml	15 ml	15 ml	15 ml
6.	Triethanolamine	5 ml	5 ml	5 ml	5 ml	5 ml
7.	Distilled water q.s.	100 ml	100 ml	100 ml	100 ml	100 ml

Table No. 2: Readings of various parameters after stability studies

Formulation code	**Parameters for stability studies**	**25ºC ± 2ºC / 60% ± 5% RH**		**30ºC ± 2ºC / 65% ± 5% RH**		**45ºC ± 2ºC / 75% ± 5% RH**	
F3	pH	7.0		6.9		6.7	
	Viscosity	12350		11200		8050	
	Spreadability	21.8		22.5		26.8	
	Extrudability	70.2		72.8		79.2	
	Skin Irritation	Nil		Nil		Nil	
	Drug Content	Salicylic Acid	Urea	Salicylic Acid	Urea	Salicylic Acid	Urea
		81	85	83	87	79	83

Table No. 3: Readings of percent drug release after stability studies

Formulation code	**Parameter for stability studies**	**25ºC ± 2ºC / 60% ± 5% RH**		**30ºC ± 2ºC / 65% ± 5% RH**		**45ºC ± 2ºC / 75% ± 5% RH**	
	***In-vitro* release (in hrs)**	**Salicylic Acid**	**Urea**	**Salicylic Acid**	**Urea**	**Salicylic Acid**	**Urea**
F3	1	8.0	9.8	8.2	10.2	7.8	9.7
	2	18.8	25.6	19.2	26.0	18.6	24.4
	3	30.4	38.0	31.0	39.2	29.2	35.6
	4	42.2	48.8	42.9	50.4	41.2	46.8
	5	54.0	63.6	54.2	64.8	50.4	62.4
	6	65.6	77.2	65.8	78.4	63.8	76.4

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