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ORIGINAL RESEARCH ARTICLE

Formulation and Evaluation of Topical Gel of Ketoprofen Using Different Polymers

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ABSTRACT

A wide choice of vehicles ranging from solids to semisolids form has been used for skin care and topical treatment of dermatological disease, High molecular weight water soluble polymers of Hydroxypropyl methylcellulose (HPMC), Carbopol 934, Carbopol 940, Sodium CMC that possess very high viscosity, transparency, film forming properties at low concentration, are reported to useful in formation of gel. In the present investigation Ketoprofen gels were prepared for topical drug delivery by using HPMC, Sodium CMC, Carbopol 934, Carbopol 940 alone and in different combination. From the study it was concluded that F4 & F2 are better formulation among all the prepared formulation and marketed gel.

Key words: Topical drug delivery, Ketoprofen, HPMC, Carbopol 934, carbopol 940, Sodium CMC.

INTRODUCTION

For topical treatment of dermatological disease as well as skin care, a wide variety of vehicles ranging from solids to semisolids and liquid preparations is available to clinicians and patients. Within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% wt liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelating substance present. NSAID's are nonsteroidal drugs having excellent anti-inflammatory and analgesic activity but NSAID produces GIT ulceration, liver and kidney trouble especially in case of oral administration [1].

Ketoprofen is an effective non-steroidal anti-inflammatory drug, used as analgesic, anti-inflammatory, antipyretic, in the treatment of rheumatoid arthritis and osteoarthritis. Oral therapy of ketoprofen is very effective, but the clinical use is often limited because of adverse effect such as irritation and ulceration of the gastrointestinal tract. This drug has a relatively short half-life (1-3 hr) in plasma and has the potential to be delivered topically [2].

Hydroxypropyl methylcellulose (HPMC), Carbopol 934, Carbopol 940, Sodium CMC has been used as hydrophilic polymers topically in gel drug delivery system. Due to their non greasy properties, they can provide easily washable film on the skin and are non toxic in nature [1].

MATERIAL AND METHODS

Ketoprofen was procured from Ranbaxy Lab Ltd. India. All other ingredients used were of analytical grade.

Procedeure for gel preparation [3]

Different gels were formulated by cold mechanical method as per the composition given in (**Table 1**). The required quantities of polymer sodium carboxy methyl cellulose or hydroxyl propyl methyl cellulose or carbopol 934, 940, were weighed. Weighed polymers were added slowly in the beaker containing distilled water (40ml) with continuous stirring at 400-600 rpm. The mixture was stirred continuously for 1h until it forms a clear gel. Accurately weighed ketoprofen was dissolved in 30 ml of ethanol & the ethanolic solution of drug was added slowly with stirring (400-600 rpm) in the previously prepared polymer gel. Triethanolamine (0.5%) was added to bring the pH neutral. Penetration enhancer oleic acid and propylene glycol was added with stirring. The final quantity was made up to 100gm with distilled water. The prepared gel was kept for 24h for complete polymer desolvation.

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EVALUATION OF GEL

a) Measurement of pH [4]

The pH of various gel formulations was determined by using digital pH meter. The measurement of pH of each formulation was done in triplicate and average values were calculated (**Table 2**).

b) Drug content [5,6]

1 gm of the prepared gel was dissolved in 50 ml of methanol. 1 ml of this solution was further diluted to 100 ml. Then absorbance was measured at 258 nm. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve (Table 2).

c) Rheological studies

i) Viscosity study [3,4]

Brookfield digital viscometer (model DV-I+, Brookfield Engineering Laboratory, INC., USA) was used to measure the viscosity (in cps) of the prepared gel formulation. The spindle (T-D) was rotated at 6 rpm. The viscosity of formulations was more correct which was near to 100% torque. Samples were measured at 30 ± 1^0 C. Reading was detected 30 sec after measurement was made, when the level was stabilized. (Table 2)

ii) Spreadability [7]

Concentric circles of different radii were drawn on graph paper & a glass plate was fixed onto it. Gel (5.0 gm) was transferred to the centre of the lower plate & spread over an area of 2 cm diameter. The glass plate of 100±5 gm was placed gently on the gel & the spread diameter was recorded after 1 minute of each addition. Results were presented as the spreading area being a function of the applied mass. (**Table 3**).

d) In vitro release studies of ketoprofen transdermal gel [3,8]

Phosphate buffer of pH 7.4 was used for in-vitro release as a receptor medium. The pretreated membrane was used in Franz diffusion cell. The gel sample was applied on the membrane and then fixed in between donor & receptor compartment of diffusion cell. The receptor compartment contained phosphate buffer of pH 7.4. The temperature of diffusion medium was thermostatically controlled at 37 ± 1^0C & stirred by magnetic stirrer at 100 rpm. The sample at predetermined intervals was spectrophotometrically estimated using phosphate buffer pH 7.4 as a blank at 261nm (**Table 4**).

e) Stability studies [9]

Formulation were kept at 40^0C, 25^0C & room temperature for 45 days & evaluated for following parameters (**Table 5**).

i) Physical stability: The gel formulations were evaluated in terms of physical character like phase separation & change in colour, odour & rheological parameters.

ii) Chemical stability: The gel formulations were evaluated for drug content, separation of liquid exudates.

Table 1: Composition of topical gel formulation

S. No	Ingredients (%)	Batch code						
		F1	F2	F3	F4	F5	F6	F7
1	Ketoprofen	2.5	2.5	2.5	2.5	2.5	2.5	2.5
2	Sodium CMC + PEG 4000 (1:1)	2	-	-	-	-	-	-
3	Carbopol 934	-	2	-	-	-	-	-
4	Carbopol 940	-	-	2	-	-	-	-
5	Sodium CMC + Carbopol 934 (1:1)	-	-	-	2	-	-	-
6	Sodium CMC + PVP (1:1)	-	-	-	-	2	-	-
7	Sodium CMC + Carbopol 940 (1:1)	-	-	-	-	-	2	-
8	HPMC(50 cps) + Carbopol 934 (1:1)	-	-	-	-	-	-	2
9	Oleic acid	2.5	2.5	2.5	2.5	2.5	2.5	2.5
10	Ethanol	30	30	30	30	30	30	30
11	Glycerin	20	20	20	20	20	20	20
12	Distilled water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
13	Triethanolamine	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Table 2: pH, Drug content and Viscosity of different formulations

S. No	Formulations	pH	Drug content%	Viscosity (cps)
1	F1	7.14±0.12	92.82±0.15	2193±2.15
2	F2	7.11±0.06	95.44±0.20	4688±3.08
3	F3	7.20±0.08	94.36±0.35	4892±3.28
4	F4	7.05±0.18	96.58±0.20	2895±4.88
5	F5	7.16±0.16	96.72±0.67	2387±4.76
6	F6	7.20±0.21	93.93±0.54	2799±8.90
7	F7	7.17±0.19	94.89±0.80	4382±7.23
8	F8 (Marketed gel)	6.47±0.24	96.24±0.75	2854±6.87

Table 3: Spreadability of different formulations

S. No	Formulation	Spreadability (gm.cm\sec) (n=3)
1	F1	23.5±0.05
2	F 2	21.5±0.09
3	F3	32.8±0.13
4	F4	23.2±0.17
5	F5	28.23±0.10
6	F6	31.26±0.14
7	F7	30.32±0.12
8	F8	33.32±0.19

Table 4: in- vitro release study in PBS 7.4 pH

S. No	Time (hrs)	% Drug release							
		F1	F2	F3	F4	F5	F6	F7	F8
1	0	0	0	0	0	0	0	0	0
2	2	18.92±0.345	20.8±0.239	24.2±0.320	17.6±0.379	20.3±0.456	26.2±0.004	15.28±0.456	19.23±0.007
3	4	37.2±0.239	35.91±0.312	38.6±0.290	29.2±0.520	38.4±0.543	36.8±0339	32.35±0.009	32.89±0.290
4	6	65.16±0.189	48.20±0.289	46.2±0.487	39.1±0.397	41.2±0.239	48.3±0.386	52.30±0.692	47.98±0.374
5	8	73.44±0.567	60.12±0.687	58.50±0.034	47.5±0.460	53.3±0.659	57.2±0.234	60.87±0.854	62.34±0.593
6	10	79.68±1.09	78.65±0.99	75.23±1.18	58.3±0.789	67.5±0.869	69.2±0.989	72.8±0.52	70.36±0.742
7	12	84.88±1.13	89.72±1.28	90.1±1.16	77.0±0.879	88.3±0.799	86.9±0.723	85.7±1.09	87.56±0.829
8	24	92.68±1.17	93.25±1.19	92.0±1.14	90.2±0.999	91.7±1.12	90.12±0.989	90.2±1.18	90.81±1.15

Table 5: Accelerated stability studies of formulations

S. No	Parameters	F2			F4		
		40^0C	25^0C	Room Temp.	40^0C	25^0C	Room Temp.
1	pH	7.5±0.13	7.10±0.09	7.7±0.23	7.02±0.17	7.08±0.19	7.03±0.24
2	Viscosity in cps	4679±2.24	4692±4.12	4683±5.37	2880±3.25	2898±6.87	2890±6.28
3	Phase seperation	No	No	No	No	No	No
4	Spreadability	Good	Good	Good	Good	Good	Good
5	% Drug content	95.36±1.15	95.41±1.01	95.40±1.15	96.50±1.06	96.53±1.18	96.55±1.13

RESULTS AND DISCUSSION

Ketoprofen gels containing, different polymers were prepared and evaluated for different parameters. The formulations were also evaluated for pH, drug content and rheological properties like viscosity & spredability and results found for all satisfactory.

All seven formulation were evaluated for *in- vitro* release study. Study were carried for 24 hrs for all seven formulation and marketed gel results reported in table (4) shows that the highest cumulative amount permeated of Ketoprofen at 24 hr from transdermal gel of (F2) carbopol 934 i.e 93.25 %. But the linear curve was obtained from F4 formulation 90.2 % .The cumulative amount permeated of marketed gel through membrane was found to be 90.81% which was less than F1, F2, F5, F6 formulations. The addition of oleic acid & propylene glycol increased the amount of drug permeated across the membrane.

Stability study indicated that all the selected formulations were stable enough at different temperature conditions (40^0C, 25^0C, room temperature) for 45 days as there was no change in color, odor, drug content, phase separation, rheological properties, pH. Thus it may conclude that formulation were physically and chemically stable.

It is clear from above discussion that F4 & F2 are better formulation among all the prepared formulation and marketed gel.

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