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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF TOPICAL GEL OF ACECLOFENAC

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ABSTRACT

Topical gel formulations of Aceclofenac were prepared using these polymers such as Carbopol-934, Carbopol-940, HPMC, Poloxamer 407 in different concentration for the treatment of rheumatoid arthritis. The gels were evaluated for various parameters such as homogeneity, grittiness, skin irritancy, extrudability, *in vitro* drug release, viscosity(Brooke field viscometer), pH, drug content, stability studies. The *in vitro* release rate of gel was evaluated using Franz diffusion cell containing cellophane membrane with phosphate buffer pH 7.4 as the receptor medium. The release rate of the gel was found to obey Higuchi model. The percentage of drug release follow following order Poloxamer-407> HPMC> Carbopol-940>Carbopol-934.

Keywords: Aceclofenac, carbopol, poloxamer hydroxyl propyl methyl cellulose, anti inflammatory activity.

INTRODUCTION

Topical gel preparation has remains one of the most popular and important pharmaceutical dosage forms. As a result, the therapeutics effects of the drugs are achieved effectively whereas the systemic side effects can be avoided or minimized. The Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have been widely used in the treatment of rheumatoid arthritis and other related condition .However, they carry the risk of undesirable systemic side effect and gastrointestinal irritation at the usual dose of oral administration[1] .Considering the fact that most inflammatory diseases occur locally and near the surface of the body ,topical application of NSAID on the inflamed site can offer the advantage of delivering a drug directly to the disease site and producing its local effect .This occurs by avoiding gastric irritation and also reduced adverse systemic effect[2,3] .However the barrier properties of intact skin limit the permeability of wide variety of substance including pharmaceutical active agent. Aceclofenac is largely based on the inhibition of prostaglandin synthesis. It is potent inhibitor of the enzyme cyclooxygenase, which is involved in the production of prostaglandins and has analgesic and anti-inflammatory activity, widely used in the treatment of rheumatoid arthritis, osteoarthritis and other joint disease. Aceclofenac was similar to that comparator NSAID in individual clinical trial withdrawal rate due to these events were significantly lower Aceclofenac than with Ketoprofen and Temoxicam.Other adverse effects which are not common such as dizziness (1%), vertigo (0.3%) and tremor[4, 5]. The objective of present study was conducted to develop a gel formulation of aceclofenac using four types of gelling agents: carbopol-934, carbopol-940 hydroxypropylmethylcellulose (HPMC) and poloxamer-407. Effect of penetration enhancer (propylene glycol) on the release has been studied. The gels were evaluated for physical appearance, rheological behavior, drug release and stability. The drug release from all gelling agents through standard cellophane membrane was evaluated using Franz diffusion cell.

MATERIALS AND METHODS

Aceclofenac (Mecleods pharmaceutical, Baddi), Carbopol-934 and Carbopol-940 (ultratech pharmaceutical Baddi), Poloxamer 407 (Signet Chemicals), HPMC (Qualikem chemicals,Delhi) Propylene glycol (S.D Fine chemical, Mumbai) and other ingredients used were of analytical grade.

Preparation of carbopol & HPMC gel

Required amount of Aceclofenac was dissolved in solvent mixture and then the required quantity of polymer was added to the solution with constant stirring at 500 rpm for about 2 hours. Later the speed was reduced to avoid air entrapment. Then the solution was neutralized with triethanolamine.

Preparation of poloxamer gel

The gels were prepared by modification of the "Cold dispersion" method described by Schmolka. The weighed amount of drug and poloxamer were placed in beaker and left in an oven at 110^0C for 15 minutes to obtain a homogeneous liquefied mixture. After the solution was cooled to room temperature, the other ingredient was added with continuous agitation. The beaker was left in a refrigerator until a clear solution was obtained. The gel was formed when the solution was brought back to room temperature and stored at ambient temperature prior use.

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Table 1: Different gel formulations

S.N.	Ingredients (%w/w)	Formulation Code															
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
1	Aceclofenac	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	Carbopol-934	0. 5	1.0	1.5	2.0	-	-	-	-	-	-	-	-	-	-	-	-
3	Carbopol-940	-	-	-	-	0.5	1.0	1.5	2.0	-	-	-	-	-	-	-	-
4	HPMC	-	-	-	-	-	-	-	-	2.0	4.0	6.0	8.0	-	-	-	-
5	Poloxamer-407	-	-	-	-	-	-	-	-	-	-	-	-	15	20	25	30
6	Propylene Glycol	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15
7	Triethanolamine	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
8	Acetone	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
9	Propyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
10	Water up to	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation

Following parameters were used for the evaluation of gels:

Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

Grittiness

All the formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation.

Extrudability study

A good gel extrude optimally from the gel with slight pressure applied. The extrudability of formulations from aluminium collapsible tubes was determined using universal tube filling machine. Aluminium collapsible tubes filled with 10g gels were held between two clamps. A tube was compressed and extrudibility of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 seconds[6].

Measurement of pH

The pH of Aceclofenac gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml of distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values were calculated.

Drug content

A 500 mg of Aceclofenac gel was taken and dissolved in 50 ml of phosphate buffer pH 7.4.The volumetric flask were kept for 2 hours and shaken well in a shaker to mix it properly. The solution was passed through the filter paper and filtered. The drug content was measured spectrophotometrically at 276 nm against corresponding gel concentration as blanks[7].

Viscosity study

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gels were rotated at 20 and 30 rpm using spindle no. 64. At each speed, the corresponding dial reading was noted.

***Invitro* diffusion studies**

The in vitro diffusion studies of prepared gel were carried out in Franz diffusion cell using through a cellophane membrane.100 ml of phosphate buffer was used as receptor compartment, then 500 mg of gel containing 10 mg of Aceclofenac was spread uniformly on the membrane. The donor compartment was kept in contact with a receptor compartment and the temperature was maintained at 37±0.50. The solution on the receptor side were stirred by externally driven Teflon coated magnetic bars at predetermined time intervals, pipette out 5ml of solution from the receptor compartment and immediately replaced with the fresh 5ml phosphate buffer. The drug concentration on the receptor fluid was determined spectrophotometrically against appropriate blank. The experiment was carried out in triplicate[8].

Stability study

For the evaluation of stability study, maintaining the formulations at an ambient condition over a period of three months on temperature 4^0c, 25^0c, and 37^0c. The physical appearance, Homogenicity, viscosity was determined periodically[9].

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Evaluation data

Table 2: Evaluation data of Aceclofenac gels

Formulation code	Homogeneity	Grittiness	Extrudability	Skin irritation	pH	Viscosity cps± S.E	Drug content (%)±SE
FI	**	--	**	--	6.33±0.48	16425.64±17.55	89.54±2.0
F2	**	--	**	--	6.42±0.39	1763.33±7.65	90.10±3.2
F3	***	--	***	--	7.21±0.26	18534.45±10.44	93.32±1.6
F4	**	--	**	--	6.72±0.14	18734.31±15.28	90.62±1.5
F5	***	--	***	--	6.81±0.32	17341.62±20.21	91.12±2.4
F6	**	--	**	--	6.52±0.35	1852.61±12.58	91.54±4.3
F7	***	--	***	--	7.26±0.41	19712.63±7.61	95.36±4.7
F8	**	--	**	--	6.67±0.13	1996.32±10.41	89.62±5.1
F9	**	--	**	--	6.46±0.15	9918.71±16.81	92.08±4.9
F10	***	--	***	--	6.41±0.17	9551.91±15.14	87.14±2.5
F11	***	--	***	--	6.68±0.11	1025.21±13.43	96.22±2.2
F12	**	--	**	--	6.61±0.24	1121.66±11.92	89.22±2.3
F13	***	--	***	--	6.85±0.21	7866.67±7.62	94.67±4.2
F14	**	--	**	--	6.87±0.31	9943.11±11.37	93.55±3.8
F15	***	--	***	--	7.12±0.16	8931.30±10.49	99.51±3.7
F16	***	--	***	--	6.75±0.33	11226.28±11.25	98.60±1.6

Excellent ***, Good **, Satisfactory *, No grittiness & skin irritation-

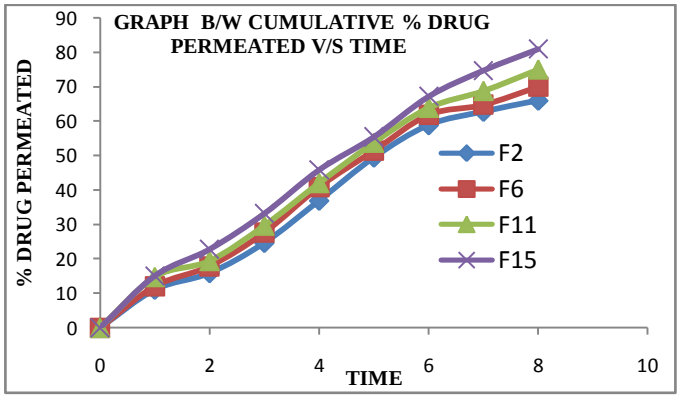

Figure 1: *In vitro* release of Aceclofenac from different gel formulations through Cellophane Membrane

RESULT AND DISCUSSION

From the experimental work finding it can be concluded that Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic activities and used for the treatment of rheumatoid arthritis. Aceclofenac by oral administration can produces stomach indigestion, so it is not suitable for the treatment of rheumatoid arthritis patient with gastric ulcer, so, to avoid gastric irritation to G.I.T, minimizing systemic toxicity. To overcome the side effects associated with oral aceclofenac therapy and to have the benefits associated with topical therapy; Aceclofenac topical gels are prepared in this study. Studies showed that drug release was decrease with increase in gelling agent concentration because polymer concentration increases; viscosity increases. The best release pattern of drug was observed F15- Poloxamer-407.

So, then release pattern order is ***Poloxamer-407> HPMC>Carbopol-940> Carbopol-934***

On the basis of physical parameters and release pattern F2, F6, F11, F15 selected as best formulations. Further stability of selected formulation had been done on different temperature such as on 4°c, 25°c and 37°c for 3 months. There were no significant changes in the viscosity, and physical appearance of the gel after storing at different temperature conditions for three months.

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