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Research Article

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Formulation development and evaluation of aceclofenac sodium gel

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ABSTRACT

The continue use of aceclofenac through oral route causes ulcerogenic effect, flatulence, indigestion (dyspepsia), vertigo, dizziness, dyspnoea, stomatitis, itching (pruritis) . When a drug system is applied topically, drug diffuses passively out of its carrier or vehicle. A unique feature of aceclofenac's pharmacology is that it stimulates glycosaminoglycans (GAG) synthesis, which in turns enhances skin permeation of NSAIDs. Aceclofenac when presented in the form of topical gel can reduce local inflammations. Hence for local inflammation or pain in the body, the topical application of aceclofenac may be useful which also avoids the side effects associated with the oral therapy. Hence, a topical gel containing aceclofenac sodium was prepared. The aim of this study was to formulate topical gel containing carbopol934, glycerin, water, triethylamine, aceclofenac and evaluate the same. The gels were evaluated for physical appearance, rheological behavior, drug release and stability. All gels showed acceptable physical properties concerning color, homogeneity, consistency, spreadability and pH value. Among all the gel formulations, formulation F3 containing maximum quantity of carbopol showed superior drug release than formulations F1 and F2 which shows lesser drug release. Stability studies showed that the physical appearance, rheological properties, and drug release remained unchanged upon storage for three months at ambient conditions. Hence it is established that gel formulations are superior topical formulation over any other topical formulations, because these system have better application property in comparison to creams and ointments.

Key words: Aceclofenac Gel, Carbopol934, Glycerin, Triethylamine, NSAIDs.

INTRODUCTION

Acelofenac Sodium is a potent member of the nonsteroidal anti-inflammatory drugs (NSAIDs), for topical treatment of skin care and dermatological disease, 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% wet 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.[1, 2]

The use of non-steroidal anti-inflammatory drug is well recognized for regional inflammatory disorders such as muscle pain, osteoarhtritis and rheumatoid arthritis [3, 4]. The Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) possess anti-inflammatory, analgesic and antipyretic activities. The Indian drug industry is always ready to cater to the needs of medical professionals by developing combinations of various kinds of drugs that are capturing substantial market share. Aceclofenac is a Diclofenac derivative of the Non–Steroidal Anti-Inflammatory Drug[5,6,7] which is chemically,(2-[2-[2-(2,6- dichlorophenyl)aminophenyl]acetyl]oxyaceticacid)[8,9].Aceclofenac exhibited potent Anti-Inflammatory Analgesic activity and is widely prescribe for the treatment of osteoarthritis, rheumatoid

arthritis, acute lumbago, and dental pain condition[10]. Aceclofenac is well tolerated, with most adverse events being minor and reversible and affecting mainly the G.I system. In the present study is the development a formulation of Aceclofenac gel and to evaluate the same for drug content, pH and viscosity.

Methods of preparation of Aceclofenac Gel:
About 1g of Acelofenac was weighed and dissolved in ethanol, to this solution; specified quantity of glycerin was added and dissolved (solution A). Stir the solution by mechanical stirrer at 1000rpm. Weighed quantity of carbopol was added to the 100ml of distilled water and stirred to dissolve the same (solution B). Solution A and B were mixed thoroughly and finally trimethyl-amine was added to this solution. In carbopol gels, pH of the gel was brought to skin pH by Trimethylamine. Final weight of the gel was adjusted with distilled water. The gels were stored in wide mouthed bottles. Entrapped air bubbles were removed. The prepared Aceclofenac gels were inspected visually for their color. The pH was measured using a pH meter reading at room temperature.

Table 1. Composition and concentration of Aceclofenac Sodium gel

Batch	Drug(g)	Carbopol934(g)	Glycerine(ml)	Trimethylamine(ml)	Water(ml)
F1	1	1	1	1	Up to 100ml
F2	1	2	5	1	Up to 100ml
F3	1	3	10	1	Up to 100ml

Evaluation of Acelofenac gel:
The above formulated gel containing Acelofenac were subjected to evaluation for the following parameters:

A. pH: [11]
The pH of the various gel formulations was determined by using digital pH meter. (Table 2)

B. Spreadability: [12]
It was determined by wooden block and glass slide apparatus. Weights about 20g were added to the pan and the time was noted for upper slide (movable) to separate completely from the Fixed slides. (Table2)

Table 2. Values of evaluation parameters of developed gel

Batch No	pH	Viscosity Cps	Spreadability (g.cm/sec)	Consistency (60 sec)	Homogeneity	Skin irritation test	Drug content (%)	Extrudability
F1	6.8	3405.82	5	7mm	Good	Nil	99.0	14.23
F2	6.8	2962.73	6	7mm	Good	Nil	99.5	15.43
F3	6.8	3469.65	6.5	7mm	Good	Nil	99.8	17.65

Spreadability was then calculated by using the formula:

$S = M.L / T$
Where,
S = Spreadability
M = Weight tide to upper slide
L = Length of glass slide
T = Time taken to separate the slide completely from each other

C. Extrudability: [13]
In the present study, the method adopted for evaluating gel formulation for extrudability was based upon the quantity in percentage of gel extruded from aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of gel in 10 seconds. More quantity extruded better was extrudability. The measurement of extrudability of each formulation was in triplicate and the average values are presented. The extrudability was then calculated by using the following formula:

Extrudability = Applied weight to extrude gel from tube (in gm) / Area (in cm2)

D. Consistency: [14]
The measurement of consistency of the prepared gels was done by dropping a cone attached to a holding rod from a fix distance of 10cm in such way that it should fall on the centre of the glass cup filled with the gel. The penetration by the cone was measured from the surface of the gel to the tip of the cone inside the gel. The distance traveled by cone was noted down after 10sec. (Table 2)

E. Homogeneity: [15]
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. (Table 2)

F. Skin irritation test: [16]
Test for irritation was performed on human volunteers. For each gel, five volunteers were selected and 1.0g 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. (Table 2)

G. Drug content: [17]
A specific quantity (100mg) of developed gel was taken and dissolved in 100ml of phosphate buffer of pH 6.8. The volumetric flask containing gel solution was shaken for 2hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 280.0nm using phosphate buffer (pH 6.8) as blank. (Table 2)

H. Accelerated stability studies: [18]
All the selected formulations were subjected to a stability testing for three months as per ICH norms at a temperature of 40º ± 2º. All selected formulations were analyzed for the change in appearance, pH or drug content by procedure stated earlier. (Table 3)

Table 3. Stability study of various developed gel

Sr No	Batches	Months	Appearance	pH	Drug Content
1	F1	0	Clear	6.7	99.95
		1	Clear	6.8	99.08
		2	Clear	6.7	98.58
		3	Clear	6.7	99.50
2	F2	0	Clear	6.6	99.76
		1	Clear	6.5	98.62
		2	Clear	6.8	97.60
		3	Clear	6.8	98.20
3	F3	0	Clear	6.6	99.70
		1	Clear	6.5	99.85
		2	Clear	6.7	99.66
		3	Clear	6.8	99.89

I. Permeability studies: [19]
Phosphate buffer of pH 6.8 was used for *in vitro* release as a receptor medium. The pretreated skin of albino mice was used in franz diffusion cell. The gel sample was applied on the skin and then fixed in between donor and receptor compartment of diffusion cell. The receptor compartment contained phosphate buffer (100ml) of pH 6.8. The temperature of diffusion medium was thermostatically controlled at 37º ± 1º by surrounding water in jacket and the medium was stirred by magnetic stirrer at 500 rpm. The sample at predetermined intervals were withdrawn and replaced by equal volume of fresh fluid. The samples withdrawn were spectrophotometrically estimated at 280nm against their respective blank. (Table 4 and Figure 1)

Table 4. Permeability studies of all formulations

Time (hrs.)	F1	F2	F3
0.5	26.5	39.5	45.59
1	40.5	60.7	65.86
1.5	50.3	71.5	90.63
2	70.6	80.95	99.2

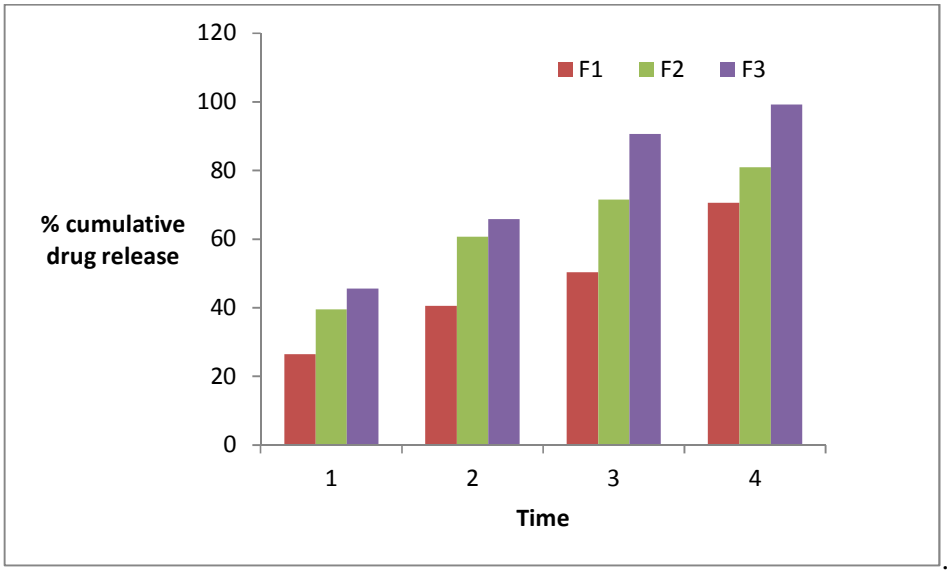

Fig 1. Drug permeability release profile of acelofenac sodium gel formulations

RESULTS AND DISCUSSION

The pH values of all developed (F1, F2, and F3) gel was 6.8. The values of spreadability indicate that the gel is easily spreadable by small amount of shear. Spreadability of gel was found to be 5(f1), 6(f2), 6.5(f3) g.cm/sec, indicating spreadability of acelofenac sodium gel was good. All developed gel showed good homogeneity with absence of lumps. The developed preparations were much clear and transparent. The skin irritation studies of developed gel were carried out on human volunteers and that confirmed the absence of any irritation on the applied surface. During the stability studies the appearance was clear and no significant variation in pH was observed. Considering the accelerated stability studies and physiochemical parameters, batch F3 was selected for *in vitro* permeability release studies. *In vitro* Permeability study showed that 99.2 % permeation occurs in 2 hours.

CONCLUSION

A Gel provides a successful approach in delivering combination products hence for the present study a Gel system has designed to deliver the drug Aceclofenac and also improve physical appearance of the gel. The most significant part is the high performance polymer Carbopol-934 was used as the gelling agent; also Glycerine as a humectant. Three trials of Gels were prepared. Among the three trials, Trial no-3 was chosen as the best and will be subjected to further studies.

REFERENCES

[1] Gupta A., Mishra AK., Singh AK., Bansal P., *Drug Invention Today*. **2010**, 2(5): 250-253.
[2] Ramchandani U. and Sangameswaran B., *International Journal of Pharmaceutical & Biological Archives*. **2013**, 4(2): 323-326
[3] Roberts M., Cross S., *Inflammopharmacology*. **1999**, 339- 350.
[4] Hadgraft J., Plessin J., Goosen C., *Int J Pharm*. **2000**, 207:31-37.
[5] Piniella J. F., Carrasco E., Ginebreda A., Julia S., *Journal of Crystallographic and Spectroscopic Research*. **1992**, 22: 3.
[6] Brogden RN., Wiseman LR., *Drugs*. **1996**, 52, 113-5.
[7] Grau M., Grauch JL., Montero A., Felipe A., Julia S., *Arzneim Forsch*, **1991**, 41: 1265-76.
[8] Mallikarjuna Setty C., Prasad D.V.K., Gupta V.R.M., Development of fast dispersible Aceclofenac tablets: Effect of functionality of superdisintegrants, **2008**, 70 (2): 180-185.
[9] Hinz B., Auge D., Rau T., Rietbrock S., Brune K., Werner U., *Biomed Chromatogr* . **2003**, 17: 268-75.
[10] G.D.Gupta., R.S. Goud., *Indian J Pharm Sci*. (**1999**), 61: 229-234

[11] Murthy., T.E.G.K., Kishore, V.S., *Indian J Pharm Educ Res.* **2008**. 42 (3): 272-276.
[12] Sara M., Nevine S., Omaima N., Abdel Aziz A., *Drug Discoveries & Therapeutics*. **2010**, 4(6):459-471.
[13] Rathore RPS., Nema RK., *Asian. J. Pharm. Clinical. Res*. **2008**,1: 12 – 16.
[14] L.William., Remington: The Science and Practice of Pharmacy. 20th edition. Mack Publishing Company. Easton, PA, (**2000**).
[15] U.V.Sera., M.V.Ramana., *The Indian Pharmacist*. (**2006**). **73:** 356-360
[16] ICH Harmonized Tripartite Guidelines. Stability Testing of New Drug Substances and Products. ICH Committee,, 8, (**2003**).
[17] Shivhare U., Jain K., Mathur V., *Digest. J. of Nanomaterials and Biostructures*. **2009**, 4: 285-290.