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Research Article

FORMULATION AND *IN -VITR0* EVALUATION OF NSAID's GEL

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ABSTRACT

The aim of this study was to improve the transdermal permeation of Diclofenac Soduim. Permeation studies were carried out *in -vitro* using Cellophane Membrane. Topical gel formulations of diclofenac sodium were prepared by using Carbopol 934, Carbopol 940, sodium carboxymethylcellulose (NaCMC), polymer as a gel-forming material that is biocompatible and biodegradable. The skin permeation enhancer on release characteristics of the diclofenac sodium from the prepared gels through a standard cellophane membrane was studied in comparison with commercially available gel formulations of diclofenac sodium. *In-vitro* Permeability study showed that permeation studies of Carbopol 934 and marketed gel were comparable. Tne *in-vitro* permeation studies by using cellophane membrane in Diffusion cell revealed good improvement of permeation characteristics of diclofenac sodium using Carbopol 940 gels as compared to the commercial gels. The permeation study enhancers such as isopropyl alcohol (IPA), Polyethylene glycol exhibited little or no effect on the permeation characteristics of diclofenac sodium. The samples withdrawn were spectrophotometrically estimated at 256nm against their respective blank. These types of topical dosage forms could give sustained delivery of drug onto the skin, so they are interesting promises to improve skin absorption of nonsteroidal anti-inflammatory drugs and to prevent side effects associated. The gel preparation is excellent in the percutaneous absorption of diclofenac or its salts and provides good properties upon use and superior medical effects of diclofenac or its salts.

Keywords: Diclofenac sodium gel, Formulation and Evaluation, Diffusion Cell.

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. Examples of drug commonly prepared in topical gel form include gastrointestinal (GI)-irritating nonsteroidal antiinflammatory drugs (NSAID) and antibacterials, antifungal, local anaesthetic and antihistaminic agents.The formulation of an effective gel requires the use of an appropriate gelling agent, usually a polymer. The preferred characteristics of such polymer include the inertness, safety, and biocompatibility with other ingredients, good adhesion to mucous membrane, and permission of drug permeation while not being absorbed into the body, irritation-free and preferably biodegradable. When in the formulation, the polymer should exhibit good swelling, syneresis and rheological properties suitable for solidifying stiffening the system. A number of gelling agents have been commercially employed in the preparation of topical gels, including the synthetic carbomers and the semi-synthetic cellulose, cellulose derivatives. As the number of newly formulated topical gel products containing drugs and chemicals continue to increase in recent years and expand into products containing natural compounds or extracts, coupled with concerned over the safety of totally synthetic materials, the development of new gelling agents from natural source has regained the attention. E.g. Of biopolymer reported as gelling agent for topical preparation are carrageen, xanthan gum and chitosan. Different types of polymers may undergo gelation through different mechanisms. For e.g. CP solution gelatinized upon addition of alkaline molecules like Triethanolamine (TEA) to nullify the acidic group, allowing the polymer chain to align closer together forming network[1,2,3].

Diclofenac sodium is a derivative of phenyl acetic acid. Diclofenac sodium is a non-steroid drug soluble in water and alcohols, and having excellent anti-inflammatory and analgesic effects. At the present time, it is used only in the form of oral preparations or suppositories exhibiting excellent anti-inflammatory and analgetic effects when so administered. However, side effects such as stomach and intestine problems, liver problems and kidney problems may occur, especially upon oral administration. Therefore, anti-inflammatory and analgesic preparations which are absorbed cutaneous without showing such side effects are desired.

Drug permeation through semi-solid dosage form, commonly occurs through process of diffusion, in order to make the rate & extend measurement by various type diffusion cell have been prescribed

- Franz and modified Franz diffusion cell
- European Pharmacopoeia diffusion cell[4,5]

MATERIALS AND METHODS

Equipment

Instruments used were Ultraviolet spectrophotometer, Franz diffusion cell, pH meter.

Materials

All chemicals used were of either analytical or pharmaceutical grade, such as

- Diclofenac sodium,(Danish Lab. Ujjain)
- Carbopol 940,(Central Drug House Ltd. New Delhi)
- Carbopol 934, (Central Drug House Ltd. New Delhi)
- Xanthan Gum,(LOBA Chemie Pvt. Ltd.)
- Sodium CMC,(Pure Chem Lab. Mumbai)
- Ethanol, (Changshu Yanguan Chemical, China)
- Propylene Glycol, (RFCL Ltd,New Delhi)
- Triethanolamine(TEA), (Qualigens Fine Chemicals)
- Cellophane membrane,(Jinendra Scientific)
- Marketed gel preparation was purchased from the market.

Methods

Procedure of gel preparation [6(34)]

Diclofenac sodium (1 g) was dissolved in 95% ethanol (30 g) while stirring. On the other hand, propylene glycol (10 g),2%,3% and 4% aqueous solution (25 g) of a carboxyvinyl polymer (Carbopol 940, Carbopol 934 , Xanthan Gum) and distilled water (20 g) were mixed uniformly by stirring, and triethanolamine (1.5 g) was added to the mixture while continuing the stirring. To the gel base thus prepared, the alcoholic solution of diclofenac sodium previously prepared was added and the whole was adjusted to 100 g by further adding purified water shown in table1s. After stirring well, a gel preparation having a pH of 7.15 was obtained.The formulation of diclofenac gel by NaCMC as polymer (Batch A8&A9) was not prepared. As alcohol have less potency in Water. Batch A8&A9 was failed.

Evaluation of gel containing diclofenac sodium and marketed gel

A. pH: The pH of the various gel formulations was determined by using digital pH meter.

B. Appearance: -The prepared gel bases were inspected visually for clarity, colour and presence of any particles.

C. 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. (Table 2)

D. Skin irritation test: 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)

E. Drug content [7(36)]

A specific quantity (100mg) of developed gel and marketed gel were 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 256.0nm using phosphate buffer (pH 6.8) as blank. (Table 2)

F. Permeability studies: (diffusion cell)[8(37)]

Phosphate buffer of pH 6.8 was used for in vitro release as a receptor medium. The pretreated skin of albino mice(or cellophane membrane) was used in diffusion cell. The gel sample was applied on the skin(Or cellophane membrane) and then fixed in between donor and receptor compartment of diffusion cell. The receptor compartment contained phosphate buffer 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.The sample at predetermined intervals were withdrawn and replaced by equal volume of fresh fluid. The samples withdrawn were spectrophotometrically estimated at 256nm against their respective blank.(Table 3 and Fig.1)

RESULTS AND DISCUSSION

- The pH values of all developed (A1, A2 A3, A4, A5,A6 and A7) and marketed gel was 6-8.
- All developed and marketed gel showed good homogeneity with absence of lumps. The developed preparations were much clear and transparent as compared to marketed gel.
- 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.
- In vitro Permeability study showed that permeation studies of A3 and marketed gel were comparable.
- It was observed that diclofenac sodium gel (batch A3) showed good homogeneity, no skin irritation and in vitro permeability was comparable with marketed gel. The gel has wider prospects to be used as a topical drug delivery system.

Table 1: Composition and concentration of diclofenac sodium gel

Carbopol 940

Batch no.	Drug (g)	Ethanol (g)	Polymer (Carbopol 940) (g)	Carbopol gel (g)	Propylene glycol (g)	TEA (g)	Distilled Water (g)
A1	1	30	2	25	10	1.5	20
A2	1	30	3	25	10	1.5	20
A3	**1**	**30**	**4**	**25**	**10**	**1.5**	**20**

Carbopol 934

Batch no.	Drug (g)	Ethanol (g)	Polymer (Carbopol 934) (g)	Carbopol gel (g)	Propylene glycol (g)	TEA (g)	Distilled Water (g)
A4	1	30	2	25	10	1.5	20
A5	**1**	**10**	**4**	**25**	**10**	**1.5**	**20**

Xanthan Gum

Batch no.	Drug (g)	Ethanol (g)	Polymer (XanthanGum) (g)	Carbopol gel (g)	Propylene glycol (g)	TEA (g)	Distilled Water (g)
A6	1	30	1	25	10	1.5	20
A7	**1**	**30**	**2**	**25**	**10**	**1.5**	**20**

Sodium Corboxymethyl Cellulose (NaCMC)

Batch no.	Drug (g)	Ethanol (g)	Polymer (NaCMC) (g)	Carbopol gel (g)	Propylene glycol (g)	TEA (g)	Distilled Water (g)
A8	1	30	1	25	10	1.5	20
A9	**1**	**20**	**2**	**25**	**10**	**1.5**	**20**

Table 2: Values of evaluation parameters of developed gel and marketed gel

Batch No	pH	Homogeneity	Skin irritation test	Drug content
A1	7.2	Fair	-	99.30
A2	6.8	Good	Nil	102.10
A3	7.3	Good	Nil	99.43
A4	6.9	Fair	-	98.42
A5	7.2	Good	Nil	97.27
A6	6.7	Good	-	96.94
A7	7.2	Good	Nil	98.12
Marketed gel	7.1	Good	Nil	99.04

Table 3: Permeability studies of batches and marketed gel

S. No.	Time Interval (min)	% Drug Release							
		A1	A2	A3	A4	A5	A6	A7	Marketed Preparation
01	30	68.7	57.1	45.6	40.4	43.4	25.3	42.8	50.8
02	60	84.6	81.9	69.6	51.7	69.0	36.5	70.3	67.4
03	90	98.6	94.7	90.2	62.0	84.1	49.3	87.6	88.2
04	120	-	100.1	99.2	78.9	97.9	69.6	99.9	104

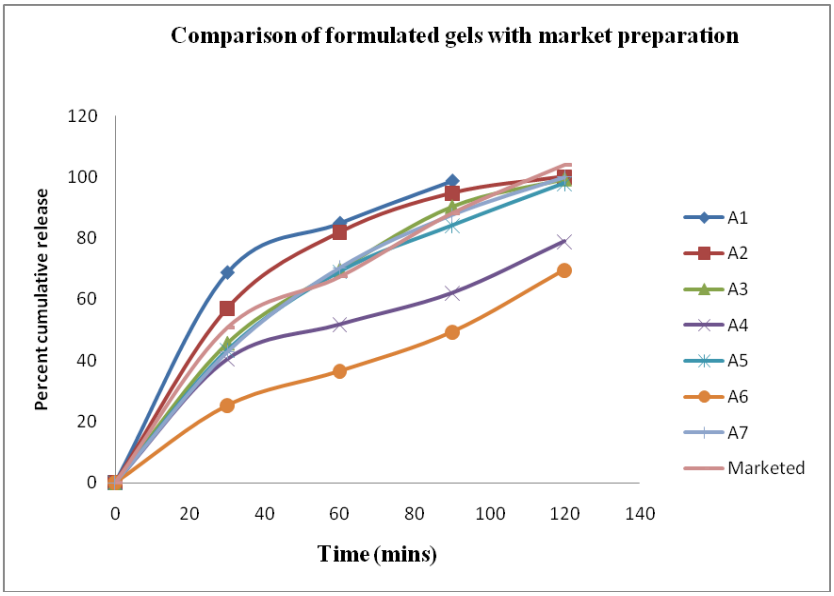

Fig. 1: Drug permeability release profile of diclofenac sodium gel formulation

CONCLUSION

It has been observed during the formulation of diclofenac gel with Carbopol 934, which does not obtain an optimized batch. Further it would be concluded that the, alcohol have a less polarity in water so the concentration of ethanol was reduced to 10%.

It has been observed that optimized batch produces the gel with good homogeneity, appearances and drug release. Gel has wider prospects to be used as a topical drug delivery dosage form.

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