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Formulation Development and Physico Chemiical Evaluation of Topical Formulation of Aceclofenac Using Pemulen

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Abstract

The present research work was aimed to formulate and optimize Aceclofenac gel employing Pemulen as a novel gel base. Pemulen is a polymeric emulsifier composed of a block copolymer consisting of a poly acrylic acid similar to the Carbopol resins presently used to make aqueous and solvent gels.The formulations were prepared by using different proportions of Pemulen. The formulated gels were evaluated for several physicochemical parameters like drug-polymer interaction, pH, Viscosity, Spredability, Drug content uniformity, In vitro drug release. Fourier Transfer Infrared Spectroscopy (FT-IR) study revealed no chemical interaction between drug and polymers. The formulation F_2 showed rapid and maximum drug diffusion rate.

Key Words: Pemulen, Aceclofenac, gel, diffusion rate, Spreadability

INTRODUCTION

Aceclofenac exhibits potent Anti-Inflammatory Analgesic activity and is widely prescribe for the treatment of osteoarthritis, rheumatoid arthritis, acute lumbago, and dental pain condition . Aceclofenac is well tolerated, with most adverse events being minor and reversible and affecting mainly the G.I system (1,2).

Non-steroidal anti inflammatory drugs (NSAID's) have been designed to deliver the drug in the form of topical gels, to avoid gastrointestinal irritation, to overcome "first pass" effect and to maximize the drug concentration at the site of action. Gels proved as potential vehicle to be administered topically in comparison to ointment, because of their non-sticky nature and requires low energy during the formulation (3,4,5).

Pemulen is a polymeric emulsifier composed of a block copolymer consisting of a poly acrylic acid similar to the Carbopol resins presently used to make aqueous and solvent gels. Pemulen is part of a class of copolymers, referred to as acrylate/C10-30 alkyl acrylate cross polymers which is crosslinked with a long-chained methacrylate having a lipophilic regions as the methacrylate as well as hydrophilic regions composed of the acrylic acid (6,7).

Pemulens are produced from primary polymer particles of about 0.2 µm diameter. Each primary particle can be viewed as a network structure of polymer chains interconnected by cross-links0. Cross-linked polymers can swell in water up to 1,000 times their original volume to form a ge (8).

Pemulen polymers deposit an occlusive layer on the skin, delivering the topical medication in the form of low-irritancy formulation with elegant skin feel. Pemulen polymer can also be used for high-clarity topical gels. So in the present work an attempt was made to formulate Pemulen gel with an effective non steroidal agent acecclofenac (9,10).

Formulation of Aceclofenac Pemulen gel

Pemulen at different concentration (0.5%,1%,1.5%,2% and 2.5% w/w) were used to formulate different topical formulation. Pemulen was dispersed in water containing preservatives methyl paraben and propyl paraben which were dissolved in freshly boiled and cooled water. Aceclofenac was dissolved in propylene glycol and glycerin mixture and it was added to the preservative mixture and stirred well. Then aqueous solution was added to the Pemulen dispersion followed by the addition of triethanolamine to obtain a gel pH was adjusted within the range of 6.8 – 7.2. The uniform dispersion was packed in collapsible tubes for further studies Three batches of Pemulen gels were prepared and subject to physical and chemical analysis (9,10).

	AG_1	**AG_2**	**AG_3**	**AG_4**	**AG_5**
Aceclofenac	1%	1%	1%	1%	1%
Pemulen (%W\W)	**0.5**	**1**	**1.5**	**2**	**2.5**
Tri ethanolamine	0.05	0.05	0.05	0.05	0.05
Propylene glycol (ml)	1.5	1.5	1.5	1.5	1.5
glycerin(ml)	1.5	1.5	1.5	1.5	1.5
Methyl paraben	0.04	0.04	0.04	0.04	0.04
Propyl paraben	0.01	0.01	0.01	0.01	0.01
Purified water q.s up to (gm)	10	10	10	10	10

Table-1 Aceclofenac gel formulation with different proportions of Pemulen

Physical analysis

To assess the influence of Pemulen physical analysis was carried out for all the topical formulations of Aceclofenac. The organoleptic features of the samples were examined at the same temperature, lighting and packaging condition to assess variation in appearance, phase separation and color.

pH measurements

One gram of each formulation was weighed and dispersed with 25 ml of distilled water. After homogenization, the pH of the sample was measured with pH meter. The test was conducted as triplicate.

Spreadability of gel

For gel dosage form good spredability value is one of the important properties.Spredability means gel ability to spread on skin part. Spreading value decide the therapeutic efficiency of gel.

Spredability apparatus contains wooden block having two glass plates. Initially gel sample wasplaced between the two glass plates. Weight near about 300 g was putted on top plate which expelled the air and to form uniform gel layer. Afterwards 100 g weight was put to drag top plate by 10 cm using stringe attached to hook. Time required to move upper plate by 10 cm distance was noted, lesser the time required for dragging the upper plate better is the spredability value. Speradability value was determined with the help of formula

$S = M \times L / T$

Where, S is the Spreadability value, L is the Length of the glass slide, M is the Weight tied to the upper plate, and T is the Time taken to separate the glass slides (9,10).

Determination of Extrudability

For a good gel formulation, it should extrude easily from the container. In this test, sample was extruded from the tube by usual procedure. A closed collapsible tube containing gel was passed firmly at crimped end. When the cap was removed, gel extrudes until pressure was dissipates. The weight in grams required to extrude 0.5 cm ribbon of gel in 10 seconds was determined. The results for each formulation were recorded as extrusion pressure in grams.

***In-vitro* drug diffusion study**

The diffusion study of the Pemulen based Aceclofenac gel were carried out in Franz diffusion cell. Gel sample (1 g) was taken on the semi-permeable dialysis membrane presoaked overnight in the freshly prepared diffusion medium. Diffusion studies were carried out at 37±1 0C using 30 ml phosphate buffer (pH 6.8) as the dissolution medium. At time intervals of 10, 20, 30, 40, 50,60 minutes 2 ml sample were withdrawn and and replaced by fresh medium. The drug content was determined by measuring the absorbance at 275 nm using shimadzu UV-visible spectrophotometer (10).

Fourier transform infra-red spectroscopy

About 5 to 10 mg of finely ground sample was then placed onto the face of a KBr plate, a small drop of mineral oil was added and the second window was placed on top. The cells were rubbed with gentle circular and back-and-forth motion of the two windows, to distribute the mixture between the plates. Adequate precaution was taken so as to obtain a sample mixture that was nearly translucent, with no bubbles. The resultant disc was mounted in a suitable holder in a Schimadzu model 8033 IR spectrophotometer and the IR spectrum was recorded from 4000 cm^{-1} to 625 cm^{-1} in a scan time of 12 minutes. The resultant spectra were compared for any spectral changes.

RESULTS AND DISCUSSIONS

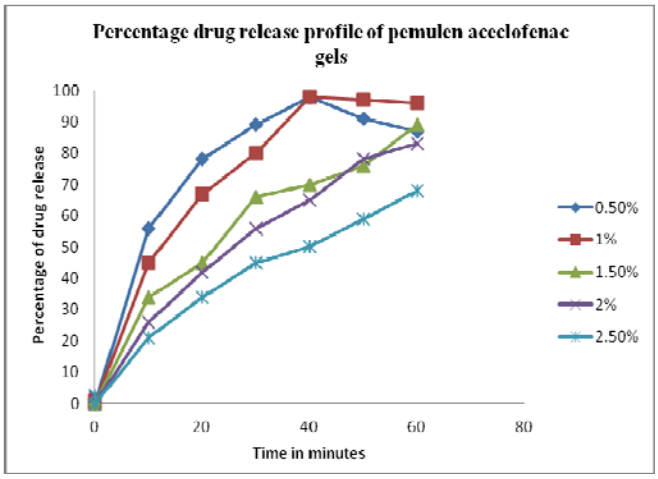
All topical formulation Pemulen based Aceclofenac gels were clear, homogenous with out any phase separation. The results for pH, spreadability, viscosity, consistency, homogeneity and drug content are shown in Table -2. Spreadability data indicate that the gel is easily spreadable by a small amount of shear. Consistency reflects the capacity of the gel to get ejected in uniform and desired quantity when the tube is squeezed. The gel formulations were homogeneous in texture and fell within a pH range of 6.8 to 7.4 which is within the normal skin pH in healthy people.

FORMULATION	Drug content	Spreadability	pH	Homogenicity and consistency
AG_1	99.8	8.5	7.3	Good
AG_2	97.5	8.6	7.1	Very good
AG_3	94.89	7.9	7.0	Good
AG_4	96.90	6.8	7.4	Good
AG_5	97.90	5.4	6.8	Poor
AG_6	96.89	4.4	6.9	Poor

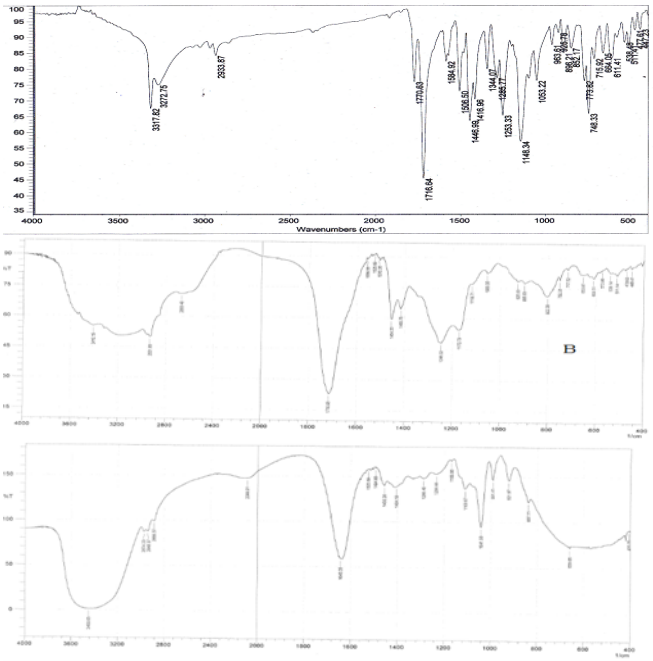
The extrusion of gel from the tube is important during application and for the patient compliance. Extrudibility of gel formulations with high concentration of gelling agent was found satisfactory while with low concentration of gelling agents good extrudability was observed. Spreadibility plays an important role in patient compliance and help in uniform application of gel to the skin. Good geltakes less time to spreads and will have high spreadibility. The spreadibility of formulation was decreased as concentration of Pemulen was increased.

In vitro drug release studies

The in vitro drug release studies of the Aceclofenac gel containing different proportions of Pemulen is shown in figure-1. As the concentration of Pemulen in the dispersion increased, the dissolution rate also decreased. Among all the formulation containing 1% of Pemulen showed complete release of drug in 30minutes wheres as increased proportions of Pemulen showed slower and incomplete drug release. This could be attributed to the fact that very high quantity in the dispersion may be responsible for impeding the drug diffusion through the dispersion matrix thus bringing about a reduction in drug release profile from the formulated system (11,12).



The FTIR spectra of Aceclofenac (figure -3) showed distinct sharp peaks at 3317 and 3272 indicate the presence of a primary amine and a broad peaks near 2937 including 1921 may be due to CH stretching of CH2 groups, carbonyl group vibration at 1770 and 1716. Peaks at1589, 1577 and 1508 indicates the presence of C=C ring stretching. All these principal IR peaks of Aceclofenac were also observed in FTIR spectrum of Aceclofenac gel. No extra peaks were found in spectrum of Aceclofenac gels indicating absence of interaction or instability in gel formation



CONCLUSION

The in vitro diffusion study of Aceclofenac incorporated Pemulen based gels were clear elegant. From over all formulations the gel containing 1% Pemulen was found to be the best formulations. From the above results, it may be concluded that Pemulen gels were better for improvement of dissolution and diffusion of Aceclofenac and also to overcome gastric side effect of the drug.

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