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Preparation and Evaluation of Tropical Gel of Diclofenac Sodium

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ABSTRACT

Topical gel preparations are intended for skin application or to certain mucosal surfaces for local action or transdermal penetration of medicament or for their emollient or protective action. Topical delivery of drugs can be achieved by incorporating drug into the gel matrix for effective delivery of drugs, thus avoiding first pass metabolism and for increased local action in pain management and skin diseases. NSAID's are non-steroidal drugs having excellent anti-inflammatory and analgesic activity but NSAID's produces GIT ulceration, liver and kidney trouble especially in case of oral administration. In view of adverse drug reaction associated with oral formulations, many NSAID's are increasingly administered by topical route. It is phynyl acitic acid derivative developed as anti-inflammatory agent. It has analgesic anti-inflammatory antipyretic like actions like other NSAIDS. It is recommended in long term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. It is also useful acute mescuskelatal disorder post operative pain and dysmenorrhoea Diclofenac sodium gel were developed in five different formulations (F1 to F5) by employing different grades of polymers. This research paper is to prepare and evaluate Propylene glycol 400 containing tropcal gel of Diclofenac Sodium. The gel was prepared and evaluated for pH, Spreadability, Spreadability, Homogeneity. The carbopol is high molecular weight water soluble homo polymer which posses high viscoty in low concentrations, transparency, and film Forming properties these are useful for gel formation. These results suggest the feasibility of the topical gel formulation of diclofenac sodium and suggests that the Diclofenac sodium effectively act as in vitro anti-inflammatory activity.

Keywords: Topical Drug Delivery, Anti-inflammatory, Water Soluble Polymer, Carbopol-934, Carbopol 940

Introduction

Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semi-solid formulation in all their diversity dominates the system for topical delivery. There have been concerns related to the conventional topical dosage forms such as lotions, creams, ointment and powder in terms of drug

diffusion or release from the vehicle and delivery through the skin. Creams and lotions often provide poor bioavailability of the drug because they are rapidly cleared from the skin and poorly release the drug from the base. Non-hydrophilic ointments are oleaginous, greasy and are not convenient to patients, and also medicated powders for topical application have short residence time on the skin. Gels are semisolid systems in which the movement of the dispersion medium is restricted by interlacing three-dimensional network of particles or solvated macromolecules of dispersed phase. The increased viscosity caused by interlacing and consequential internal friction is responsible for the semisolid state. Also, a gel may consist of twisted matted strands often tied together by stronger types of Vander Waals Forces to form crystalline and amorphous regions throughout the system [1]. For the topical treatment of dermatological diseases, a wide choice of vehicles ranging from solids to semisolids and liquid preparations are available to clinicians and patients. Within the semisolid preparations transparent gels are widely used in cosmetic pharmaceuticals [2,3]. Out of various semisolid dosage forms, gels are becoming more popular due to ease of application and better percutaneous absorption. Typical three-dimensional structures, characteristics of the gels, come from the links among the polymer chains. Gels can resist the physiological stress caused by the skin flexion, blinking and mucociliary movement, adopting the shape of the applied area and controlling drug release [4,5]. Effectiveness of the topical application mainly depends upon its rate and extent of drug release from the base. Gel is an excellent formulation for several route of administration such as oral, topical, nasal, gel can be a clear formulation when all of particles are Dissolve in dispersing medium but this cant occurs in all gels some are therefore turbid. Diclofenac sodium (DS) is a nonsteroidal anti – inflammatory drug (NSAIDs) widely used clinically to reduce inflammation and pain in conditions such as rheumatoid arthritis, menstrual pain, dysmenorrheal, fever, osteoarthritis or acute injury [6]. It has a short half-life in plazma (2 hrs) and only 50% of the drug reaches the circulation. Oral dose of diclofenac potassium causes an increased risk of serious gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or the intestines which could be fatal. Transdermal delivery of the drug can improve its bioactivity with reduction of the side effects and enhance the therapeutic efficacy [6, 7]. DS has a potent anti-inflammatory effect, but it does not penetrate well through skin and cannot reach the effective concentration at the site of action after transdermal application. For this reason, we wanted to suggest new, alternative dosage forms for transdermal application of DS.

Materials and methods

Materials

Diclofenac Sodium was obtained as a gift sample from Macleods Pharmaceuticals, Mumbai. Carbopol-934, Triethanolamine, Propylene glycol-400 were purchased from Qualigens Fine chemicals, New Delhi. Methenol, Glycerine, Menthol were purchased from CDH New Delhi. All other chemical used were purchased from S.D Fine Chemical Limited, Mumbai. Double distilled water was prepared freshly and used whenever required. All other chemicals used in this study including those stated were of analytical reagent (A.R.) grade.

Preformulation Studies

Physical Characteristics

By visual examination, the drug was identified for physical characters like colour, texture, odour etc.

Melting point

A small quantity of powder was placed into a fusion tube. That tube was placed in the melting point determining apparatus (Chemline) containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted.

Solubility

Solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, chloroform and 7.4 pH buffer) Shake vigorously and kept for some time. Note the solubility of the drug in various solvents (at room temperature).

Determination of λ_{max} of diclofenac sodium

Accurately weighed 10 mg of drug was dissolved in 10 ml of methanol in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 1 ml pipette out and transfer into 10 ml volumetric flask and volume make up with methanol prepare suitable dilution to make it to a concentration range of 2-14µg/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). A graph of concentration Vs absorbance was plotted.

Preparation of gel formulations

All gel formulation were prepared by using simple mixing method, firstly required quantity of gelling agent (Carbopol-934/Carbopol-940/HPMC) was weighted and soaked in a small quantity of water for 24 hrs to form a homogenous dispersion. In a other beaker required quantity of propylene glycol was dissolved in small quantity of water with continuous stirring at 75°C. In a Volumetric flask required amount of drug were dissolved by using Methanol solution, other excipients are also added in a above solution with continuous stirring for 60 minutes by magnetic stirrer, pH was obtained topical delivery (pH 6.5-7.4) by using triethanolamine. The volume was made up with water and stirring until homogeneous gel is formed [8].

Table 1: Preparation of gel at variable concentration of Carbopol-934

Ingredients % (w/w)	F1	F2	F3	F4	F5
Diclofenac sod	2.5	2.5	2.5	2.5	2.5
Carbopol-934/ Carbopol 940/	3	2.5	2	1.5	1
Propylene glycol 400	14	14	15	15	16
Methanol	20	20	20	20	20
Glycerine	10	10.5	10	10.5	10.5
Rose water	0.5	0.5	0.5	0.5	0.5
Menthol	q.s	q.s	q.s	q.s	q.s
Triethanolamine	0.5	0.5	0.5	0.5	0.5
Distilled water	q.s	q.s	q.s	q.s	q.s

Table 2: Optimization of gelling agent

Gelling Agent	Mean viscosity (CPS)
Carbopol 940	4120 ± 6.77
Carbopol 934	**4445 ± 4.5**

Optimization was done on the basis of viscosity. Viscosity od standard formulation (VOLINI) was found to be 4445 ±4.5 CPS and formulation F2 using 3% w/w Carbopol 934 resembled standard formulation viscosity. Table 5 shows mean viscosity of formulation with various gelling agent.

Evaluation of Gel [9-11]

Gel formulations were visually checked for color, odour, consistency, and homogeneity.

- Color :- The color of the formulations were checked out against white background.
- Odor :- The odor of the gels was checked by mixing small quantity of gel with water and taking the smell.
- Consistency :- The consistency was checked by applying small quantity of gel on skin.
- Homogeneity :- A small quantity of gel was pressed between the thumb and the index finger in order to notice the consistency and any aggregates or coarse particles being attached or detached on the finger.

pH measurement

The pH of prepared gels was determined using a digital pH meter, which was calibrated before each use with standard pH 4 and pH 7 buffer solutions. A solution containing 1 g of prepared gel in 30 mL of neutralized distilled water was prepared and subjected to pH measurement

Viscosity

Viscosity of all formulated gels were determined by using Brookfield viscometer. Test were performed at 100 rpm, using spindle number 64 and viscosities were recorded at room temperature.

Results and discussions

Diclofenac was found to be white, crystalline powder in appearance, odorless and Bitter taste. The melting point of Diclofenac (pure drug) was found to be 147°C; it matches with the standard (145-148°C). Diclofenac was freely soluble in ethanol, methanol and phosphate buffer pH 7.4.and insoluble in water. The calibration curve of Diclofenac was found to be linear in the concentration range of 2-14 µg/ml at 278 nm. Evaluation Parameters of all formulation of was given in table 3- 5 was found with acceptable limits. Spreadability of standard formulation (Diclospin) was for 222.142g optimized the by using simple method. As spreadability increases viscosity decreases.

Table 3: physical evaluation of prepared formulations

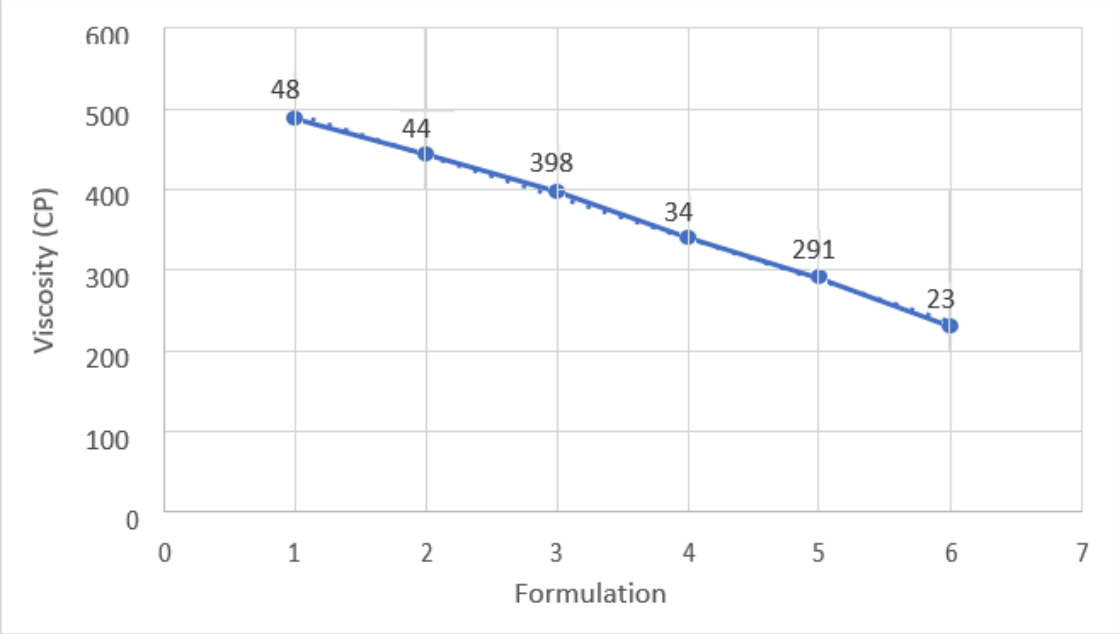
S.No	Formulation code	Color	Odor	Consistency	Homogeneity
1	F1	White	Odourless	Smooth	Homogenous
2	F2	White	Odourless	Smooth	Homogenous
3	F3	White	Odourless	Smooth	Homogenous
4	F4	White	Odourless	Smooth	Homogenous
5	F5	White	Odourless	Smooth	Homogenous

Table 4: pH of different formulation

S.No	Formulation code	pH Mean ± S.D.
1	F1	7.01± 0.2
2	F2	7.11 ± 0.15
3	F3	6.95 ± 0.13
4	F4	6.75 ± 0.12
5	F5	6.78 ± 0.12
6	Diclofenac Gel (VOLINI)	6.09 ± 18

Table 5: Viscosities of formulated gels and standard

S. No	Formulation code	Viscosity (cP) Mean ± SD	Temp (C)
1	F1	4880 ± 4.62	25 C
2	F2	4445 ± 7.12	25 C
3	F3	3680 ± 6.76	25 C
4	F4	3404 ± 6.02	25 C
5	F5	3390 ± 3.66	25 C
6	Diclofenac Diethylamine Gel (Diclospin)	4515 ± 4.5	25C



Graph No. 1: Viscosity of formulated gel

Conclusion

Diclofenac sodium is an on-steroidal anti - inflammatory medicament (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic activities. To overcome the side effects associated with oral diclofenac sodium remedy and to have the benefits associated with topical remedy; diclofenac sodium topical gels are prepared in this study. It has been observed that the formulated F2 gel produces with good consistency, homogeneity, spreadability. Since the polymer is water soluble; consequently, it forms water washable gel and has wider prospect to be used as a topical drug delivery dosage form. Protein denaturation is a process in which protein lose their tertiary structure and secondary structure by operation of external stress as strong acid, an organic solvent or heat most biological protein lose their biological function when denaturation. Denaturation of protein is a well- proved cause of inflammation. As a part of the study on the mode of the anti-inflammatory activity, ability of diclofenac sodium to inhibit protein denaturation was studied. Other anti-inflammatory drugs have showed dose dependent ability to inhibit thermally induced protein denaturation. Denaturation of protein is a well document cause of inflammation.

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