FORMULATION AND EVALUATION OF TOPICAL GEL OF DICLOFENAC DIETHYLAMINE

Faizan Ainee[1], Gulsan Kumar[2], Gufran Khan[3], Gulshan Dhakad[4]
Hariom Parihar[5], Gaurav Kumar Rajak[6], Asst Prof. Prateek Jain[7], Dr. Jagdish C Rathi[8]

[1]*Scholar, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[2]*Scholar, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[3]*Scholar NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[4]*Scholar, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[5]*Scholar, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[6]*Scholar, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[7]*Assistant Professor, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*
[8]*Director and Principal, NRI Institute of Pharmaceutical Sciences Bhopal, Madhya Pradesh, India*

ABSTRACT

In order for the pharmacological action of a topical dermal drug product to occur, the drug must first be released from the vehicle to be available to penetrate the skin layer and reach the site of action. Drug release is mainly dependent on the characteristics of the formulation. It is phenylacetic acid derivatives 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 musculoskeletal disorder post operative pain and dysmenorrhea. Diclofenac di-ethylamine gel was developed in five different formulation(F1 to F5) by employing different grades of polymers such as Carbopol 934 and Carbopol 1940.The gel was prepared and evaluated for pH, spreadability, consistency, homogeneity and viscosity. The Carbopol is high molecular weight water soluble homo polymer which posses high viscosity in low concentrations, transparency, and film forming properties these are useful for gel formation. The present study suggests that the Diclofenac di-ethylamine effectively act as invitro anti-inflammatory activity. Finally the gel formulations found to be economical and may overcome the draw backs associated with the drug during its absorption.

Keyword: - *Formulation1, Diclofenac diethylamine2, Topical drug delivery3, Anti-inflammatory4, and Carbopol1934, etc..*

1. 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. Semisolid 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. 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. 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. Effectiveness of the topical application mainly depends upon its rate and extent of drug release from the base. Gel are 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 occur in all gels some are therefore turbid. The ideal of present study was conducted to develop a topical gel formulation of diclofenac di-ethylamine using Carbopol 934 gelatinizing agent for enhancing the skin penetration. Effect of penetration enhancer (propylene glycol) on the release has been studied.

2. MATERIAL AND METHODS

Materials: Diclofenac di-ethylamine was purchased from Yarrow Chem. Products, Mumbai, India. Carbopol 934, 940 was purchased from CDH Laboratories New Delhi, India. Propylene glycol and triethanolamine extra pure were purchased from Hi-Media laboratories Mumbai, India. All other chemicals used were of analytical grade and were used without any further chemical modification.

2.1 Pre-formulation 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

The solubility is the maximum quantity of a solute that can be dissolved in certain quantity of a solution at a specified temperature. Diclofenac di-ethylamine (10mg) was dissolved in a 10ml of different solvents (i.e. chloroform.0.1N NaOH, ethanol, ether, 1-2 dichloromethane, water, PBS (7.4)) and phosphate buffer (6.0) at room temperature and kept for 3 days for equilibrium in separating funnel. Funnel was regularly shaken. Equilibrium solubility was determined by taking supernatant and analyzing it on the U.V. spectrophotometer (Thermo scientific Evolution 201, Mumbai).

Determination of λ max of Diclofenac di-ethylamine

Accurately weighed 10 mg of drug was dissolved in 10 ml of methanol solution 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 solution 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 (Thermo scientific). A graph of concentration Vs absorbance was plotted.

2.2 METHODS

Preparation of gel formulations

For the preparation of different gel formulations, the drugs Diclofenac di-ethylamine as an active ingredients Carbopol-934 as a gelling agent and other ingredients were used and total five formulation were prepared.

Procedure

All gel formulation were prepared by using simple mixing method, firstly required quantity of gelling agent (Carbopol-934/Carbopol-940) was weighted and soaked in a small quantity of water for 24 hrs to form a homogenous dispersion. In an 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. The composition of different formulation was given in table 1.

Ingredients% (w/w)	F1	F2	F3	F4	F5
Diclofenac di-ethylamine	2.5	2.5	2.5	2.5	2.5
Carbopol-934	3	2.5	2	1.5	1
Propylene glycol 400	14	14	15	15	16
Methanol	20	20	20	20	20
Glycerin	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 1: Preparation of gel at variable concentration of Carbopol-934

Optimization was done on the basis of viscosity. Viscosity of standard formulation (VOLINI) was found to be 4515±4.5 CPS and formulation F2 using 2.5% w/w

Carbopol 934 resembled standard formulation viscosity. Table 2 shows mean viscosity of formulation with various gelling agent.

Gelling Agent	Mean viscosity (CPS)
Carbopol940	4120 ± 6.77
Carbopol934	4445 ± 4.5

Table 2: Optimization of gelling agent.

Different gel formulations with variable concentration of Carbopol-934

3. Evaluation parameters

The prepared gel was characterized by following parameters.

Physical evaluation

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

- **Color: -** The color of the formulations was checked out against white background.
- **Odor: -** The odor of the gels was checked by mixingsmall 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 pressedbetween 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 were 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 pHmeasurement.

Viscosity

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

4. RESULT AND DISCUSSION

Diclofenac di-ethylamine was found to be white crystalline powder in appearance, odorless and bitter in taste. The melting point of Diclofenac di-ethylamine (pure drug) was found to be 145-148℃, it matches with the standard (147°C). Diclofenac di-ethylamine was soluble in methanol, ethanol and phosphate buffer pH 7.4 practically insoluble in water. The calibration curve of Diclofenac di-ethylamine was found to be linear in the concentration range of 2-

14µg/ml at 278nm table 3. The results of physical evaluation of prepared formulations were given in table 4. The pH of different formulation was found to be in range of 6.75± 0.12 to 7.11± 0.15 which was near about marketed formulation. Viscosity of all formulated gels was measured by using brook field viscometer. Test was performed at 100 rpm for all formulations, using spindle number 64 at room temperature. Viscosity values for all prepared formulation were found in a range of 3390± 3.66- 4880± 4.62 cps and for Diclofenac di-ethylamine gel (standard), it was found to be 4515 cp. The proportion increase in viscosity can be attributed to be evidence of more cross linking in polymer with increase in polymer concentration. The results are shown in a table 6.

Concentration in (µg/ml)	Absorbance at 278nm
2	0.103
4	0.152
6	0.198
8	0.249
10	0.31
12	0.355
14	0.412

Table 3: Calibration table of standard Diclofenac di-ethylamine at 278 nm.

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

Table 4: Physical evaluation of prepared formulations.

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 di-ethylamine gel (VOLINI)	6.09± 18

Table 5: pH of different formulation

S. No	Formulation code	Viscosity(cP)Mean ±SD	Temp(^{o}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 di-ethylamine gel (Diclospin)**	**4515± 4.5**	**25 ^{0}◦C**

Table 6: Viscosities of formulated gels and standard.

5. CONCLUSSION

In this present study it can be concluded that topical gel formulations containing drugs Diclofenac di-ethylamine were prepared with different concentration of gelling agents (carbopol-934), which have shown an acceptable results in various studies. From the present studies, it could be concluded that Carbopol-934 can be used as gelling agent for the development of gel formulations, because of its good release profile, water-soluble nature and good spreadability.

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