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Original article

Formulation and in Vitro Evaluation of Emulgel Topical Drug Delivery of Aceclofenac

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ABSTRACT:
One of the most intriguing topical delivery techniques is emulgel, which has two regulated releasing mechanism, such as gel and emulsion. The main goal of this formulation is to improve aceclofenac's topical formulation by forming aceclofenac emulgel by utilising the gelling agent carbopol 934. The market offers a variety of topical formulations for analgesic medications. There is no topical formulation that is sold. The topical preparations are preferred for the local effects at the site of their application by penetration of drug into the skin or mucous membranes. The emulsion was prepared, the gelling agent was added and the desired emulgel loaded with the active drug was formulated The prepared emulgel's physical characteristics, pH measurement, viscosity, spreadability, and in-vitro testing were assessed,drug release. All prepared emulgel displayed respectable physical characteristics. F5 is the formulation that performs the best Relative to all formulations, medication release So, it can be concluded that topical emulgel of aceclofenac possesses an effective anti-inflammatory and analgesic activity.
Keywords: Emulgel, Carbopol 934, Topical formulation, Aceclofenac, Analgesic.

1. INTRODUCTION

A number of analgesic preparations are existing in the market as topical preparations. Aceclofenac, an effective NSAID has always been used as an anti-inflammatory and analgesic agent. Typically it is existing in the tablets and suspensions dosage forms. There is no topical formulation that is sold. The topical preparations are preferred for the local effects at the site of their application by penetration of drug into the skin or mucous membranes [1]. Topical drug delivery is defined as local use of formulation within the body through skin and other routes which extend its bioavailability and reduce its side effects. Emulgel are the combination of emulsions and gels [2]. Emulgels are emulsions of oil/water or water/oil type, which then mixed with a gelling agent to get gel constistency. They increase the patient acceptability as they have the benifits of both emulsions and gels. Therefore, they have been recently used as vehicles to deliver various drugs to the skin [3-5]. Emulgel are extensively used for skin delivery of drug . Its compatible in skin is due to the advantages such as easy incorporation of lipophilic drugs, viscosity, spreadability, easily removable, non-staining , biocompatibility due to appearance with increased shelf life [6].

2. MATERIALS AND METHODS

Materials

Aceclofenac was obtained as a gift sample from Mankind pharma, Carbopol 934 was obtained from Loba chemicals Mumbai., Mumbai. All the analytical grade chemicals used were used in the formulation.

Methods

Preformulation study:

Organoleptic characterization of drug:

Melting point:

Melting point was determined to indicate of purity of the sample since the presence of impurity in small amount of can be detected by a lowering in the melting point. Melting point of the Aceclofenac was determined by Capillary fusion method; one side of the capillary tube is closed and it was filled with drug, and then put into the Melting Point Apparatus. Observation was noted at which temperature drug drug converts into liquid and compared the data with standard value.

Log P Value

Log p value was the index by of Partition Coefficient Phenomenon. In which The 1 gm of drug is added in separating funnel containing equal portion of 25 ml of benzene and 25 ml of Water. The separating funnel was

shaken 20 – 25 min. and stabilized the mixture. After stabilization of the mixture water phase is removed from separating funnel and filter it. Absorbance of Filtrate was taken and log p value was calculated.

Solubility:

Solubility is defined as at specified temperature and Specific Pressure, maximum amount of solid substance that can be dissolved in a given amount of solvent to form a homogenous mixture to form a Saturated Solution. Solubility of Aceclofenac is determined in the solutions like Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, pH 7.4 Phosphate Buffer.

UV spectroscopy:

Calibration curve of Aceclofenac in phosphate buffer pH 5.5

UV Spectrophotometric techniques are used to prepare the calibration curve. To prepare the calibration curve 10 mg of drug was added in 100 ml of phosphate buffer (100 µg/ml Solution). From this different dilution of 5, 10, 15, 20, 25, 30, 35, and 40 µg/ml were prepared of the aforementioned 100 µg/ml solution. Considering the absorbance maxima at 256 nm.

FORMULATION OF EMUGEL

Preparation of emulsion:

The oil phase of emulsion was prepared by dissolving span 20 in light liquid paraffin and Aceclofenac was mixed in oil phase. While the aqueous phase of emulsion was prepared by dissolving in tween-80 in distilled water. Methyl paraben was added in propylene glycol then it was mixed with aqueous phase. Both the oily and aqueous phases were separately heated at 70°C-80°C, then the oily phase was added to the aqueous phase with continuous stirring until it was cooled to room temperature. The emulsion was obtained, which is stored in well closed air tight container [7].

Preparation of gel:

The quantity of carbopol 934 were taken accurately and it was mixed with distilled water 75°C by u magnetic stirrer with stirring speed is 1000 RPM for 10 min to form an even dispersion. Entrapped air was removed by keeping the gel stationary. Then the pH was adjusted to 6-7 by using triethanolamine [8].

Preparation of emulgel:

Emulsion was added into gel base in the ratio of 1:1 and it was mixed continuously using mechanical stirrer at 4000-5000 RPM for 15-20 minutes to get emulgel.

Evaluation of emulgel:

Physical examination:

The colour of formulation was checked against white and black background. The odour of emulgel was checked by mixing it in water and by smelling it [9].

pH:

1% solution of emulgel were prepared and subjected to measure pH by digital pH meter [10].

Rheological study

The viscosity of the emulgels was determined by using Brookfield viscometer at temperature of 25±2°C and the viscosity was determined in cps [11].

Spreadability:

A lower glass slide was fixed on a block in which excess amount of of prepared emulgel (1gm) was ket on lower slide. Emulgel preparation was then pressed between the two slides having the dimension of fixed lower slide which was attached by hook. To expel air a weight of 100gm was placed on top of two slides for 10 min so it provides uniform film of gel between the slides. Excess of emulgel was removed from the edges. Upper slide was then pulled with 20g weight by using string which was attached to the hook and the time required was measured by upper slide to cover distance. Shorter time interval indicated superior spreadability [12].

Spreadability (S) was calculated as follow:

$S=M.L/T$

where M is the weight tied to upper slide, L is the length of glass slide, and T is the time taken to separate slides.

Centrifugation study

The emulgel formulations were selected for centrifugation test. It was carried out by using a centrifuge at different temperatures (8^0C, 25^0C, and 40^0C). All the formulations were centrifuged by placing 2 g of a sample in a 15-mL centrifuge tube and rotating the tube at 3000 rpm for 30 min [13].

Temperature swing test

A temperature swing test gives us an understanding of the stability of all emulgels at high and low temperatures .All formulations were subjected to a freeze-and-thaw cycle for two days. One cycle was -4^0C for 8 h and 40^0C for 16 h. The stability was checked visually. Freeze-and-thaw cycle is used to know stability by the effect of temperature on an emulgel, this method accelerate the changes. It also mimics potential outdoor storage conditions of final emulgel formulations [13].

Drug content:

Drug content in emulgel was determined. To get drug content 1gm of emulgel was dissolved in 100ml of solvent. A clear solution is obtained after filtering the solution which was then spectrophotometrically analyed by making dilution.

In-vitro drug diffusion study:

Dialysis membrane was used to find out drug release of Aceclofenac from the emulgel formulations which was measured through by using Franz diffusion cell. The dialysate membrane is immersed in diffusion medium overnight and then placed on the supporting screen of the diffusion cell assembly. Phosphate buffer at pH 7.4 was used as the receiving medium and 1 g of gel was placed on the donor side. At a predetermined time interval, 2 ml of sample was withdrawn from the receiving cell and replaced with the same volume of phosphate buffer at pH 7.4. The fractions were analyzed by UV spectrophotometer at 256 nm [14].

3. RESULT AND DISCUSSION

Preformulation study:

Organoleptic characterization of drug:

Melting Point

Melting point of the Aceclofenac was determined by Capillary fusion method and Melting Point of Aceclofenac is found to be 151^{0}C

Log P Value

Log P Value is determined by Partition Coefficient Phenomenon and Log P Value of Aceclofenac is is found to be 2.18

Solubility Studies

The Solubility of Aceclofenac in Given Solution. (Water, 0.1N HCL PH 1.2, PH 7.4 Phosphate Buffer) is Reported in Table 1.

Calibration Curve of Aceclofenac

The Calibration Curve of Aceclofenac was determined by using U.V. Spectroscopic Method as seen in Table 2. In which the Absorbance of Aceclofenac in Different Concentration (0, 5, 10, 15, 20, 25,30,35 and 40 µg/ml) is reported in Table 5. And The Calibration Curve is shown in Figure 1.

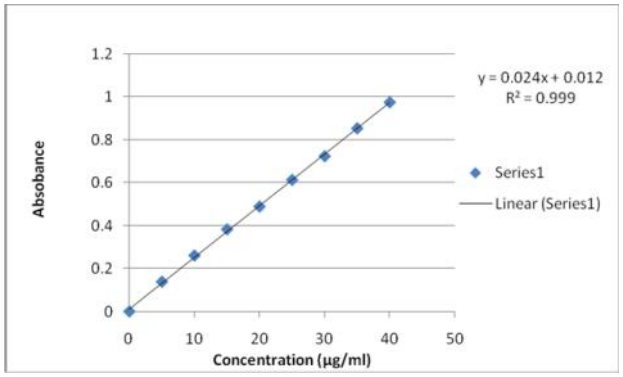

Fig1: calibration curve of Aceclonac

EVALUTION PARAMETERS

Physical examination:

The emulgels were assessed physically and visually for color (white viscous creamy), phase separation, and consistency. Nine different formulations (F1–F9) were evaluated for color, phase separation, homogeneity, and consistency (Emulsion and polymeric gels prepared as seen in Table 3 and 4). Almost all the formulations were stable. F5 was found to be the most optimized formulation having white color, good appearance, excellent consistency, and no phase separation [15].

pH

The pH of a topical formulation is considered important for the stability of a preparation and its compatibility with skin It is an important factor, as it must range between 6-7 for suitable topical application of drugs and to avoid skin irritations.

Temperature swing test and centrifugation study

The centrifugation test is very important for the determination of the stability of a topical formulation like emulgel and for the determination of the shelf life of a formulation. This test indicates the effect of physical stress on a semisolid preparation in terms of phase separation. The prepared formulations of Aceclofenac emulgels were passed through a physical test such as the freeze-and-thaw test and then centrifuged for stability. All formulations were found to be stable under different storage conditions (freeze-and-thaw cycle of -4^{0}C to 40^{0}C) and then they were centrifuged at 3000 rpm for 30 min. No signs of phase separation found throughout the study period. Additionally, other stability parameters such as color and odour were also observed and were found to be stable (Table 5).

Rheological study

The viscosity of the aceclofenac emulgels was found to be in the range of 438.6–622.4 cps. Results were reported in Figure 2. From the study, it was observed that viscosity of the formulated emulgels was dependent on the concentration of carbopol 934. As the concentration of carbopol 934 was increased, the viscosity of emulgels was also increased and reported in Table -6.

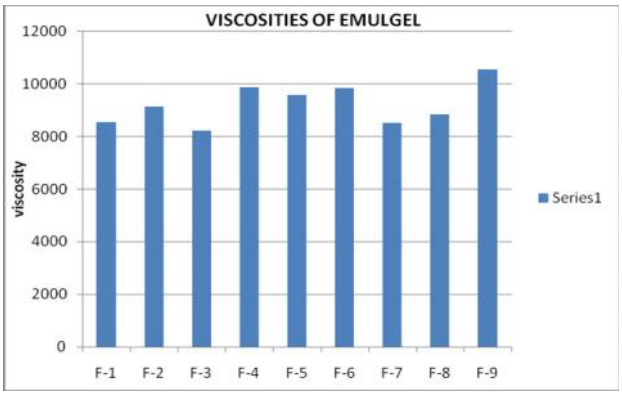

Fig 2: Viscosities of emulgel

Spreadability

The spreadability of all the emulgels was ranging from 15.22 to 45.58 g.cm/s. It was observed that formulations F-4, F-5, and F-6 showed higher spreadability, which may be due to an increased concentration of carbopol 934. The spreadability test results are interpreted in Table 6, and spreadability test for aceclofenac emulgels is depicted in Figure 2 and Figure 3.

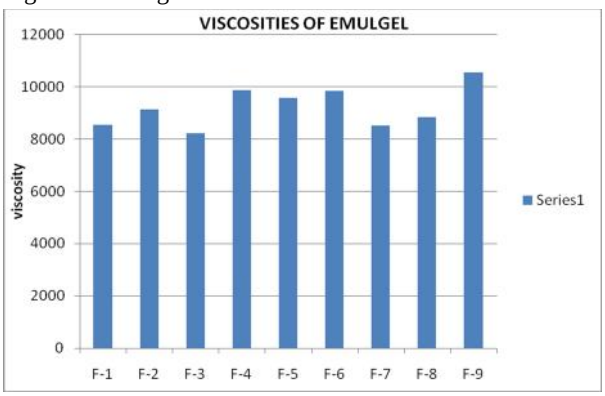

Fig 3: Spreading coefficient of emulgel

Drug content

The drug content of all the formulated emulgels was in the range of 81.6–98.5%, and formulation F5 showed the highest drug content among the other eight formulations. The results of the drug content are shown in Table -7

In vitro drug release study

The bioavailability of any drug is dependent upon the release of drug from the formulation .Drug release from topical formulation depends on various factors including gelling agents, emulsifying agents (surfactants used), spreadability, and viscosity. The results showed that the release of Aceclofenac from the emulgel was dependent on the concentration of Carbopol 934 in the formulation (i.e. the drug released decreased with an increasing concentration of the polymer).The drug release pattern of the formulations was F5>F6>F9>F8>F4>F7>F1>F2. The drug release pattern depended on the concentration of polymer; an increase in the concentration of polymer caused the drug release time to decrease and the diffusion through the membrane to decrease.

The percentage of drug released in all formulations was plotted against the time duration, as shown in Figure 4. The percentage of Aceclofenac released from the F-1 to F-9 formulations after 4 hours of study is shown in Table 7.

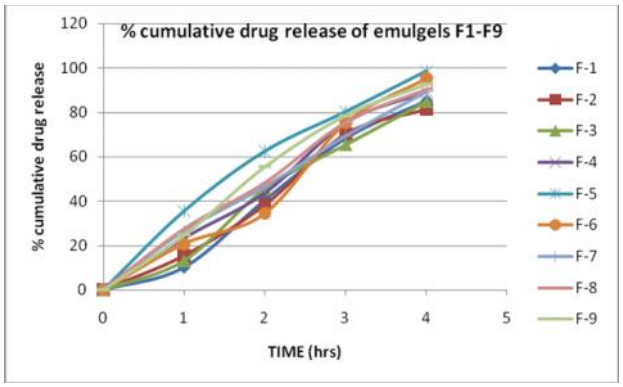

Fig 4: Cumulative drug release of emugel formulations F1-F9

Table 1: Solubility studies of aceclofenac

Solvent	Solubility(mg/ml)
Distilled water	1.85
0.1 N HCL	2.1
Phosphate buffer 7.4	5.15

Table 2: Calibration curve of Aceclofenac in phosphate buffer pH 7.4

SL.No	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.138
3	10	0.260
4	15	0.382
5	20	0.488
6	25	0.612
7	30	0.722
8	35	0.852
9	40	0.973

Table 3: Composition of various emulsion formulations (w/w)

Ingredients	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
Aceclofenac	1	1	1	1	1	1	1	1	1
Propylene Glycol(ml)	5	5	5	5	5	5	5	5	5
Liquid paraffin	6	6	6	6	6	6	6	6	6
Methyl Paraben(ml)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Propyl Paraben(ml)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Tween 80(ml)	0.5	0.4	0.5	0.3	0.6	0.7	0.5	0.5	0.4
Span-20	0.8	0.7	0.6	0.7	0.8	0.7	0.6	0.7	0.6
Distilled water to make 100%	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Triethanolamine	Q.S to adjust PH 6-7								

Table 4: Composition of polymeric gel formulations

Ingredients	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
Carbopol 934 (g)	1	1.2	0.8	1.3	1.2	1.3	0.9	1	1.4
Distilled water (mL)	100	100	100	100	100	100	100	100	100
Triethanolamine	Q.S adjusted to PH 6-7								

Table 5: Physical parameters of formulation batches

Formulation	Colour	Homogeneity	Phase separation
F-1	white	Good	No
F-2	white	Good	No
F-3	white	Good	No
F-4	white	Good	No
F-5	white	Excellent	No
F-6	white	Excellent	No
F-7	white	Good	No
F-8	white	Good	No
F-9	white	Good	No

Table 6: Rheological property and spreading coefficient of formulations

Formulation	Viscosity(cps)	spreading coefficient
F-1	8562	28.69
F-2	9145	27.56
F-3	8235	26.59
F-4	9865	32.58
F-5	9580	39.58
F-6	9845	35.56
F-7	8535	36.52
F-8	8845	31.58
F-9	10545	35.38

Table 7: percentage of drug content and percentage cumulative drug release

Formulation	% Drug content	% Cumulative Drug release
F-1	95.6	85.3
F-2	94.6	81.6
F-3	94.8	84.8
F-4	96.7	89.5
F-5	99.2	98.5
F-6	98.4	95.4
F-7	96.5	89.2
F-8	93.5	90.4
F-9	97.3	92.6

4. CONCLUSION

In the coming years, topical drug delivery will be used extensively to give better patient compliance. Since emulgel

is helpful in enhancing spreadability, adhesion, viscosity and extrusion, for this novel topical drug delivery become popular. Moreover, they will be helpful for the formulations for loading hydrophobic drugs in water soluble gel bases for the long term stability.

Topical emulgels of Aceclofenac were formulated and subjected to physicochemical studies i.e. rheological studies, spreading coefficient studies and bioadhesion strength, in vitro release studies. In vitro release of the tests formulations were performed to determine drug release from emulgel rate and duration of drug release. From the in vitro studies, formulation F5 showed maximum release of 98.5% in 4 hrs and F5 formulation have optimum constitency and good spreadability.

So Aceclofenac emulgel can be used as a topical formulation and as a novel topical drug delivery system

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