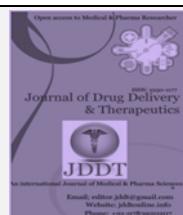


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Research Article

Formulation and Evaluation of Transdermal Topical Gel of Ibuprofen

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ABSTRACT

The present research work is based on the formulation and evaluation of topical gel of Ibuprofen where Carbopol 940 is used as the polymer. Gels were prepared by dispersing the polymers in a mixture of water and glycerol with methyl paraben as the preservative and the varying amount of ibuprofen, being kept under magnetic stirring until the homogeneous dispersion was formed. The dispersion was then neutralized and made viscous by the addition of triethanolamine. The Carbopol gels of Ibuprofen were found to be homogenous with good drug loading. The pH of all the gel formulations was found within the neutral pH range which is compatible with skin. And the viscosity of the formulations was found to be feasible for topical drug delivery. The drug content of the three formulations was found in the range of 87.56% to 90.45% which shows efficient drug loading. Results of *In vitro* drug release study showed that F5 formulation has better diffusion of drug through egg membrane and hence further permeation studies were carried out through rat epidermis. The compatibility study showed that the major peaks in FTIR spectra of the pure drug were found to be intact in their physical mixture. Hence there is no interaction between drug and Carbopol in their physical mixture. Carbopol can be effectively used as the polymer for topical gel preparation. And F5 formulation containing 0.5 % w/w Carbopol 940 may be effectively used as topical transdermal delivery for Ibuprofen.

Keywords: Ibuprofen, Transdermal Gel, Drug release, Compatibility study

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INTRODUCTION

The dosage forms, whether a tablet, an injection or a patch, to deliver the right amount of medicine at the right time to the right target site becomes complicated if each medicine is to be delivered in an optimal and preferred manner to the individual patient. The medication may not be absorbed if it is released too slowly or too rapidly, or the patient may suffer adverse effects and as because it's desired effects may not last as long as it needed. These limitations are being overcome by transdermal drug delivery systems as they achieve several advantages over conventional dosage forms. Transdermal drug delivery is a route which can deliver medicines via the skin portal to systemic circulation at a predetermined rate and maintain clinically effective concentrations over a prolonged period of time. Transdermal route of drug administration avoids discomfort associated with parenteral therapy and improves patient compliance. This route of administration also eliminates the side effects that are caused by the conventional drug forms and also provide controlled release of drugs directly into the bloodstream through the intact skin. Transdermal delivery can provide a

number of advantages over the conventional method of drug administration like-enhanced efficacy, increased safety, greater convenience, improved patient compliance. The various advantages of Transdermal Drug Delivery System are - It avoids significant presystemic metabolism and therefore the need for the daily requirement is low. It reduces inter and intrapatient variability. Drug levels can be maintained in the systemic circulation within the therapeutic limit. The duration of drug action following a single administration of the drug can be extended and the frequency of dosing is reduced. It improves patient compliance and acceptability of the drug therapy. Drug input can be terminated simply by removal of the patch.[1,2,3] Taking into account several advantages associated with Transdermal drug delivery route, we have decided to utilize 'Ibuprofen', which is a non-steroidal anti-inflammatory drug (NSAID) used for pain relief, fever reduction, and against swelling.[4] Carbopol 940 is used as the polymer, which is ideal for applications such as clear gels, hydroalcoholic gels, creams.[5,6]

Objective

The objective is to prepare transdermal topical gel of Ibuprofen using Carbopol 940 which can be effectively used for transdermal topical delivery.

MATERIALS AND METHODS

Materials

Chemicals

Ibuprofen (Hi Media, Mumbai, India), Triethanolamine (Merck, Mumbai, India), Methyl Paraben (Hi Media, Mumbai, India), Glycerol (Merck, Mumbai, India), Carbopol (Balaji Drugs, India) were procured and used in the investigation. All other reagents used were of analytical grade.

Animals

Wistar albino rats (male) were used of 250-500 gm were used which were supplied by animal house of Girijananda Chowdhury Institute of Pharmaceutical Science which were kept under proper laboratory condition. The animals were

received only after the proposed study was approved by the Institute Animal Ethics committee bearing the number GIPS/IAEC/BPH/2013/4.

Preparation of standard curve:

0.1mg of ibuprofen was weighed accurately and was dissolved in 10 ml of ethanol and the volume was adjusted to 100 ml by pH 7.4 and various dilutions were made to obtain concentration 2-50 mcg/ml and the absorbance was measured in the Ultra Violet (UV) Spectrophotometer at λ_{max} 267 nm, and a standard curve was obtained by plotting concentration against the absorbance.[7]

Preparation of transdermal gel:

Gels were prepared by dispersing the polymers (Carbopol 940) in a mixture of water and glycerol with methylparaben as the preservative and the varying amount of ibuprofen, being kept under magnetic stirring until the homogeneous dispersion was formed. The dispersion was then neutralized and made viscous by the addition of triethanolamine [8,9] as shown in Table 1.

Table 1: Gel Formulation

Formulation Code	Drug (mg)	Carbopol 940 (gm)	Methyl Paraben (mg)	Glycerin (ml)	Triethanolamine (ml)
F1	10	1	200	1	0.1
F2	10	0.5	200	1	0.1
F3	10	0.75	200	1	0.1
F4	20	0.5	200	1	0.1
F5	50	0.5	200	1	0.1

Preparation of pH 7.4:

2.38 gm of Disodium Hydrogen Phosphate, 0.19 gm of Potassium Dihydrogen Phosphate and 8 gm of Sodium Chloride were weighed accurately and it was diluted up to 1000 ml.[10]

Evaluation Of Transdermal Gel:

Determination of gel pH

The pH of the three gel formulations was determined by using digital pH meter after calibration with standard buffer pH 4.0, and 9.0 by inserting the electrode system into the gel.[11]

Spreadability

One of the criteria for a gel to meet the ideal quantities is that it should possess good spreadability. It is the term expressed to denote the extent of the area to which gel readily spreads on application to the skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from the gel and placed in between the slides under the direction of certain load. Lesser the time is taken for separation of two slides, better the spreadability. It is calculated by using the formula: $S = M \cdot L / T$ Where M = weight tied to upper slide, L = length of the glass slide, T = time taken to separate the slides.[12]

Viscosity

Brookfield (DV-E Viscometer) attached with spindle was used for determination of viscosity. Gels were filled in jar and spindle was lowered perpendicularly taking care that spindle does not touch the bottom of the jar. The spindle number 63 was rotated in the gel at 20 rpm. At each speed, the corresponding dial reading was noted. The reverse reading was also noted and average was taken for these two readings. The viscosity of the gel was obtained by the multiplication of the dial readings with the factors given in the Brookfield viscometer catalogs. The spindle size used is 64.[13]

Drug content

1 gm of the prepared gel was weighed accurately and dissolved in 10 ml of ethanol and was then filtered. 1ml of the filtrate was taken and was diluted up to 100 ml by pH 7.4 and was observed in the Ultra violet (UV) spectrophotometer at 267 nm.[14,15,16]

In-vitro drug release/permeation study

The drug release/ permeation studies of the prepared gels were carried out in Keshary-Chien diffusion cell for studying the drug release from the gels through an egg membrane. Gel sample (0.5g) was placed on the membrane and the diffusion studies were carried out at $37 \pm 0.5^\circ\text{C}$ using 250 ml of phosphate buffer (pH 7.4) as the receptor medium. Five milliliters of each sample was withdrawn periodically at 15,

30, 60, 120 and 240 minutes. Each sample was replaced with equal volume of fresh receptor medium. Then the samples were analyzed by UV spectrophotometer at 267 nm for the drug content by using phosphate buffer as blank.[17,18,19]

Compatibility study

The Fourier- transform infrared spectroscopy (FTIR) spectra of pure drug, Carbopol, and physical mixture of drug Carbopol (1:3) were taken and studied for any interaction using FTIR, Bruker Alpha instrument.[20,21,22]

RESULT AND DISCUSSION

Standard calibration curve of Ibuprofen:

The standard calibration curve of Ibuprofen was plotted in phosphate buffer, pH 7.4. The scanning of standard solution has resulted maximum absorption peak at the wavelength of 267 nm. It was observed that Beer-Lambert's law was obeyed within the concentration range of 2.0 μ g/ml to 50.0 μ g/ml, in phosphate buffer, pH 7.4 as shown in Table 2 and Fig. 1.

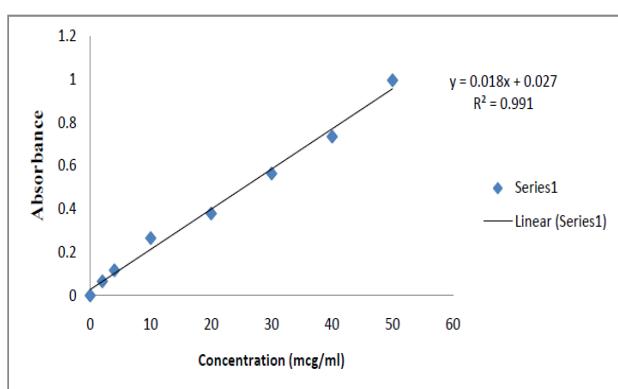


Fig 1: Standard Curve of Ibuprofen

pH of Ibuprofen Gel:

The pH of the gel formulations was found as 7.0 to 7.5 and a comparison study was done with a standard gel as shown in Table 2.

Table 2: pH of Gel Formulation

Formulation	pH (mean \pm SD)
F1	7.2 \pm 0.18
F2	7.5 \pm 0.20
F3	7.0 \pm 0.15
F4	7.3 \pm 0.07
F5	7.2 \pm 0.18
Nurofen (Boots Healthcare)	7.4 \pm 0.14

Drug spreadability study:

The spreadability of the different gel formulations after 1 min. was determined and was compared with a standard gel and noted in Table 3.

Table 3: Spreadability of Gel Formulation

Formulation	Spreadability (mean \pm SD)
F1	19.79
F2	22.5
F3	21.25
F4	22.29
F5	22.08
Nurofen (Boots Healthcare)	21

Viscosity:

The viscosity of the gel formulations was found between 15900 to 23230 cps. The results are shown in Table 4.

Table 4: Viscosity of Gel Formulation (20 rpm)

Formulation	Viscosity (mean \pm SD)
F1	20800 \pm 4336.828
F2	23230 \pm 4984.532
F3	27700 \pm 5981.081
F4	15900 \pm 2969.848
F5	20100 \pm 4984.532

Drug Content:

The drug content of the gel formulations was found in the range of 87.56 to 90.45 % which shows efficient drug loading. The results are shown in Table-5.

Table 5: Drug Content of Different Formulation

Formulation	Drug Content (mean \pm SD)
F1	87.56 \pm 1.11
F2	89.67 \pm 0.85
F3	88.44 \pm 1.02
F4	90.45 \pm 0.94
F5	89.12 \pm 0.85

In-vitro drug release/permeation study:

In-vitro drug release of all the formulation through egg membrane is shown in Fig-2.

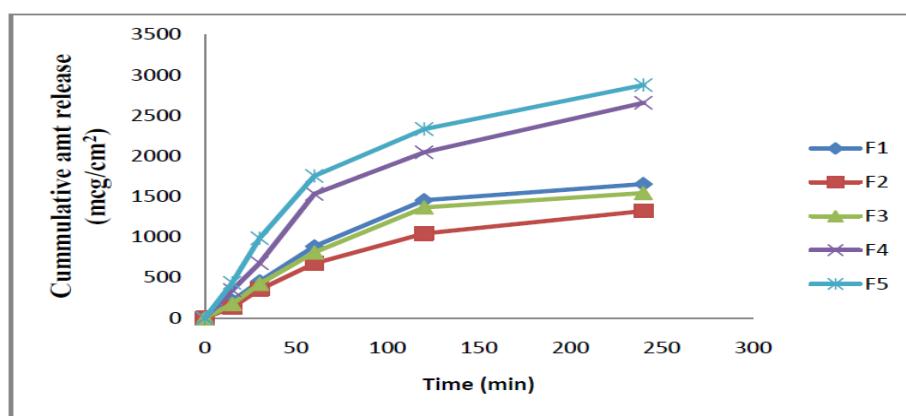


Fig 2: RELEASE PROFILE OF IBUPROFEN FROM GELS THROUGH EGG MEMBRANE Formulation F5 shows the highest release across the egg membrane chosen for permeation across rat epidermis. The result of permeation of transdermal gel across rat epidermis is shown in Fig 3.

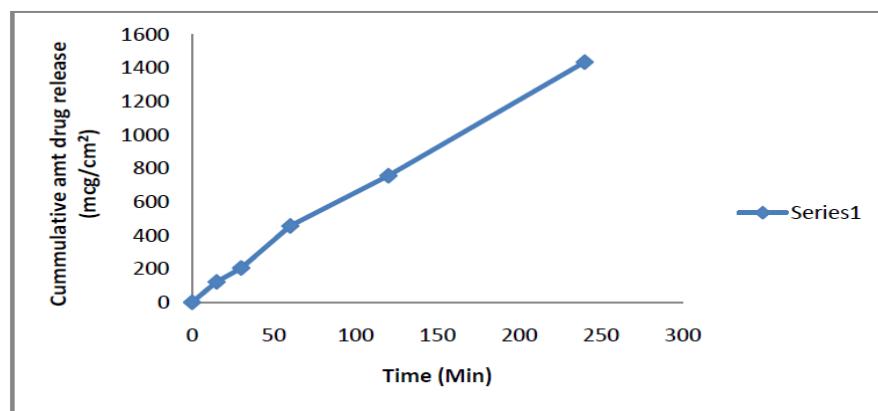


Fig 3: Permeation Profile oF Ibuprofen from Transdermal Gel through Rat Epidermis

Drug compatibility study:

Fourier-transform infrared spectroscopy (FTIR) spectra of pure drug, carbopol 940 and 1:3 ratio of the physical mixture of drug- carbopol 940 is presented in Fig 7 to 9 respectively. All the major peaks such as of alkenes i.e. C-H (stretching) at 2988.29, 2949.21, 2867.97, carbonyl group i.e. C=O

(stretching) at 1707.22, aromatic C=C (stretching) at 1504.04, alkyl halide groups i.e. C=F (stretching) at 1454.85, 1266.87, 1225.51, 1179.08, are retained in the physical mixture. Thus it indicates that the drug is compatible with the polymer used in the formulations as shown in Fig.4, Fig.5, Fig.6.

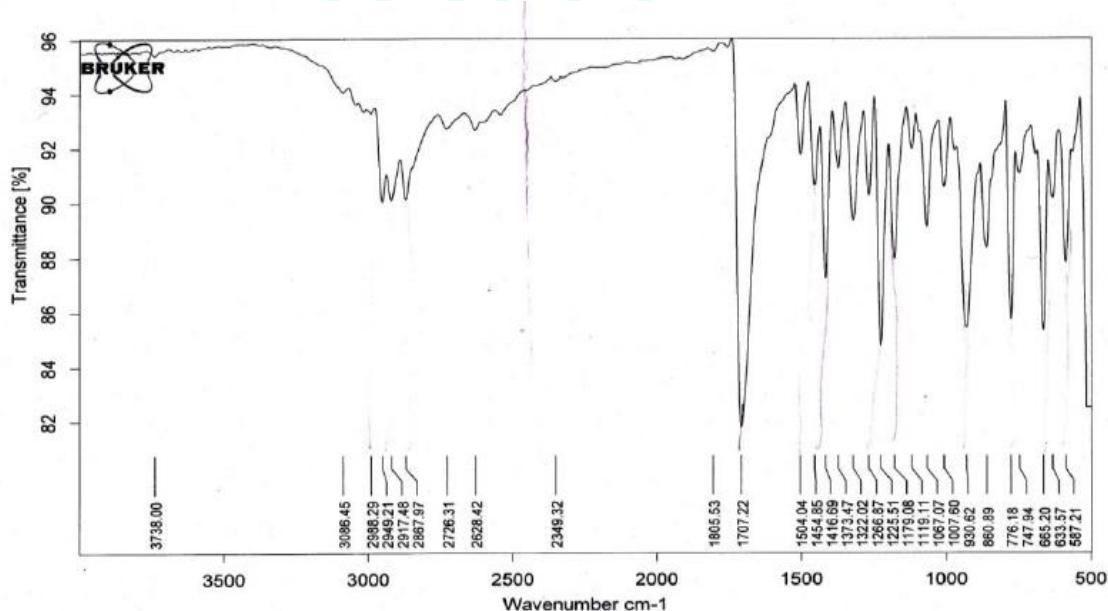


Fig-4: FTIR Spectra of Pure Drug (Ibuprofen)

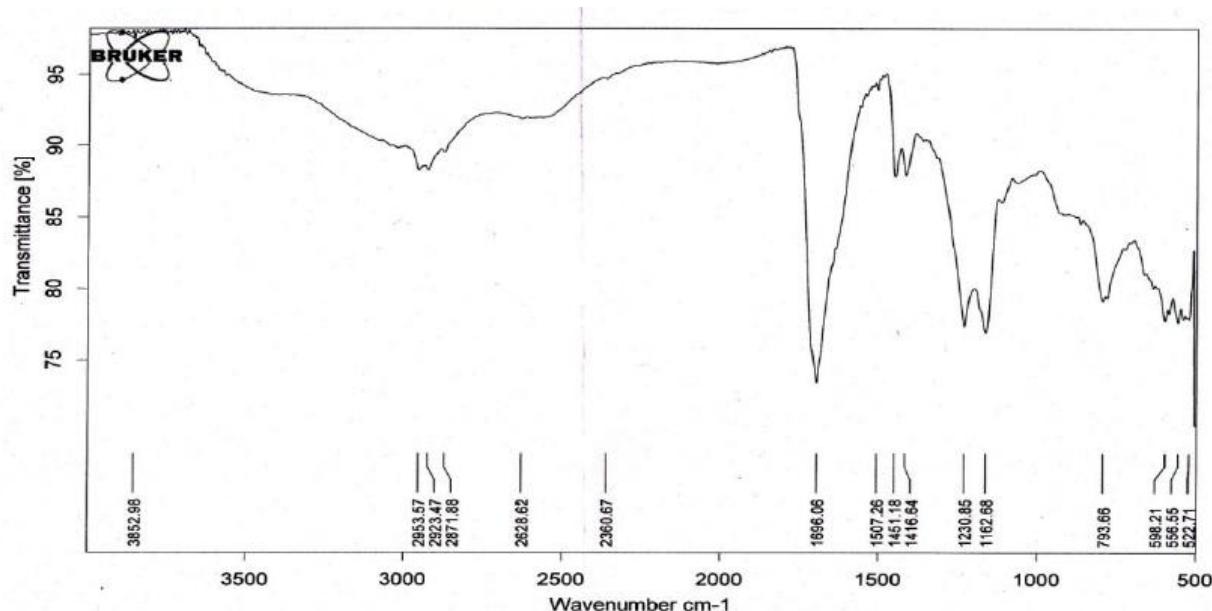


Fig-5: FTIR Spectra of Carbopol 940

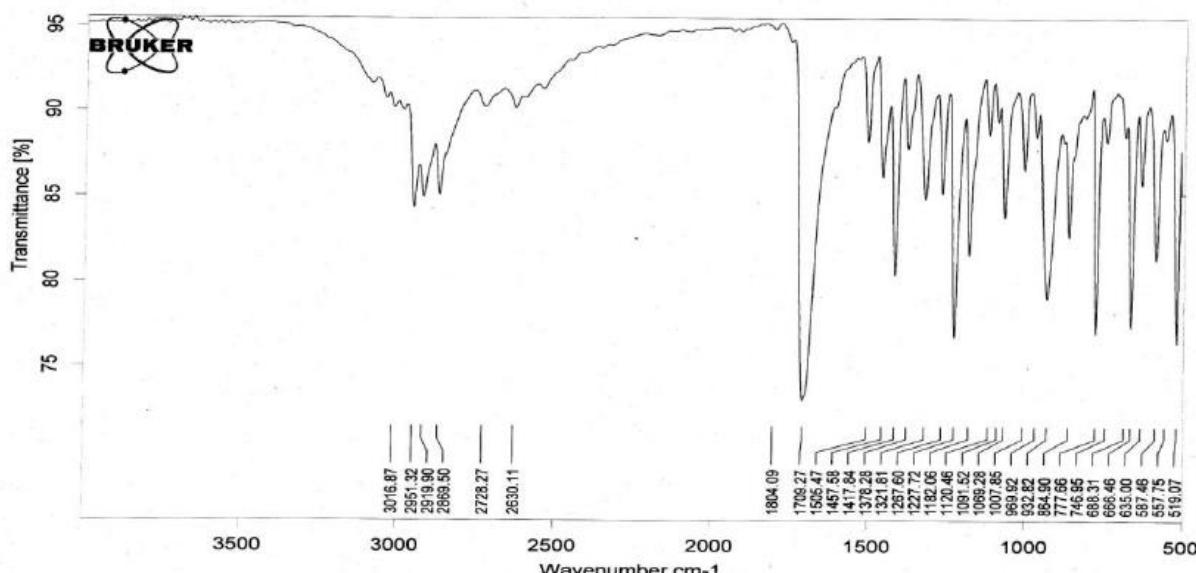


Fig-6: FTIR Spectra of Ibuprofen:Carbopol 940

DISCUSSION

The Carbopol gels of Ibuprofen were found to be homogenous with good drug loading. The pH of all the gel formulations was found within the neutral pH range which is compatible with skin. And the viscosity of all formulations was found to be feasible for topical drug delivery. The drug content of the three formulations was found in the range of 87.56 to 90.45% which shows efficient drug loading. Results of *in-vitro* drug release study showed that F5 formulation has better diffusion of drug through egg membrane and hence further permeation studies were carried out through rat epidermis. The compatibility study showed that the major peaks in Fourier-transform infrared spectroscopy (FTIR) spectra of the pure drug were found to be intact in

their physical mixture. Hence there is no interaction between drug and Carbopol in their physical mixture.

CONCLUSION

It can be concluded that Carbopol can be effectively used as the polymer for topical gel preparation. And F5 formulation containing 0.5 % w/w Carbopol 940 may be effectively used as topical transdermal delivery for Ibuprofen.

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