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# FORMULATION AND EVALUATION STUDIES OF EMULGEL CONTAINING MEFENAMIC ACID

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## ABSTRACT

The objective of the present investigation was formulate & characterize the emulgel containing mefenamic acid.Mefenamic acid emulgel using HPMC and NaCMC as gelling agent were successfully developed. The developed formulations were then characterized for their physical appearance, pH, viscosity, spreadability, extrudability, drug content and *in vitro* release. The emulgel (CF1) prepared using HPMC as gelling agent, propylene glycol as co- surfactant and clove oil as penetration enhancer was found to show better result when compared to emulgel (CF2) prepared using NaCMC as gelling agent. In CF1, correlation coefficient of zero order kinetics was found to be $R^2$ = 0.995 and that of first order kinetics was to be $R^2$=0.771.Higuchi plot was found to be linear with regression coefficient $R^2$=0.902. Hence it shows that the drug release follows zero order kinectics.To confirm exact mechanism of drug permeation from the emulgel, the data was fitted according to the Korsmeyer-Peppas model.The value of slope of the plot n gives an indication of the release mechanism. When n=1, the release is independent of time i.e., zero order, if n=0.5 then the release is by Fickian diffusion. When n= 0.5-1, diffusion is non-fickian and when n>1.0 then it is super case II transport. The 'n' exponent value of optimized batch was found to be 0.651. Hence it shows non-fickian diffusion.

**KEYWORDS:** Mefenamic acid, emulgel, release kinetics.

## INTRODUCTION

New drug delivery systems development in largely based on promoting the therapeutic effect of a drug and minimizing its toxic effects by increasing the amount and persistence of drug in the vicinity of target cell and reducing the exposure of non target cells. Emulgels are emulsion, either of the oil- in-water or water-in-oil type, which are gelled by mixing with a gelling agent. Emulsified gel is the stable one and superior vehicle for hydrophobic or poorly water soluble drugs. Thus an emulgel is a combination of emulsion and gel. In recent years, there has been great interest in the use of novel polymers which can function as emulsifiers and thickeners because the gelling capacity of these compounds allows the formulations of stable emulsions and creams by decreasing surface and interfacial tension and the same time increasing the viscosity of aqueous phase. In fact, the presence of a gelling agent in water converts a classical emulsion into an emulgel.

Mefenamic acid is a non- steroidal anti-inflammatory drug which is widely used to treat pain, inflammation and in rheumatoid arthritis. Currently topical preparation of mefenamic acid is not available in the market. Emulgel is a emulsion either of oil-in-water or water-in-oil type which are gelled by mixing with a gelling agent; having favorable properties such as being removable emollient, non- staining, water soluble, greater shelf life, bio- friendly, clear and pleasant appearance. The main aim of this project was to formulate an emulgel of mefenamic acid using different gelling agents like HPMC and NaCMC; thereby reducing side effects like ulceration, gastro intestinal disturbances, liver problems and kidney failure associated with its oral administration and to increase its patient acceptability.[1,5,8]

## MATERIALS AND METHODS

Mefenamic acid pure drug was generously gifted by Camarin Pharmaceutical, kannur. sodium CMC & E was gifted by Degussa India Pvt. Ltd, Mumbai. Ethyl cellulose was purchased from Lobachemei Mumbai. All other excipients used in our work were of Analytical grade.

### Determination of ƛ max

Dissolve accurately weighed 100mg of mefenamic acid in 100ml of methanol in 100ml standard flask to get 1000µg/ml**.** From the stock solution of mefenamic acid, 1ml is pipette out and diluted to 100ml with methanol to get 10µg/ml. The absorption maximum of the standard solutions of mefenamic acid was scanned between 200-400nm regions on UV-visible spectrophotometer. The absorption maxima obtained with the substance being

examined corresponds in position and relative intensity to those in the reference spectrum.

**Preformulation Studies**[5]

Pre-formulation testing was an investigation of physical and chemical properties of a drug substance alone. It is the first step in rational development of dosage form.

**Solubility studies**

Solubility of mefenamic acid was observed in different solvent such as distilled water in acetone, methanol, 95%ethanol, sodium hydroxide, Potassium hydroxide**,** diethyl ether, chloroform, acetic acid.

**Identification by melting point**

Melting point of drug was determined using Melting point apparatus.

**Organoleptic properties**

Physical appearance of drug was observed and compared with the official monographs.

**Partition Coefficient (Kp)**

The partition coefficient of the drug was determined by shaking equal volumes of organic phase (n-octanol) and the aqueous phase in a separating funnel. A drug solution of 1 mg/ml was prepared in phosphate buffer pH7.4 and 50 ml of this solution was taken in a separating funnel and shaken with an equal volume of n-octanol for 10 minutes and allowed to stand for 24 hours with intermittent shaking. Then, the concentration was determined by U V Spectra.

**Drug-ExcipientInteractionStudies**[6]in order to find out the possible interactions between mefenamic acid and the polymers used in the formulation of the Emulgel, Fourier transform infra-red spectroscopy (FT-IR) analysis was carried out on the pure substances and their physical mixtures.

**FT-IR Spectra** of the pure drug, NaCMC and HPMC and the physical mixture of the drug with polymers were taken individually by KBr pellet technique between 600 to4000 $cm^{-1.}$ This is to ensure that there is no incompatibility between the drug and the polymers. Once spectra were recorded, the peaks of the pure drug, the polymers and the physical mixture of drug and polymers were compared for any incompatibility.[18.16.9]

**Emulgel Formation**

**Effect of concentration of polymer**

**Gel Formation**

The gels were prepared by dispersing gelling agent (HPMC or NaCMC) in different concentration in purified water with continuous stirring at moderate speed. Then the pH was adjusted to 6-6.5 using Triethanolamine

**Emulsion Formation**

- The oil phase of emulsion were prepared by dissolving span 20 in light liquid paraffin while aqueous phase were prepared by dissolving Tween 20 in purified water.
- Methyl paraben and propyl paraben was added and mefanamic acid was mixed in ethanol and was mixed with aqueous phase.
- Oil phase and aqueous phase were then separately heated to 70-80°c.
- Oil phase were added to the aqueous phase with continuous stirring until cool to room temperature.

**Emulgel Formation**

- The emulgel were obtained by mixing gel and emulsion in the ratio 1:1.

**Effect of co- surfactant**

- To the selected formulations, different concentrations of co- surfactant was incorporated.

**Effect of penetration enhancer**

- To the formulations showing best consistency, viscosity and release properties with presence of co-surfactant, 2 ml of penetration enhancer was added and further studies were done.[10,11]

The formulation component of microsponge emulgel is mentioned in table no: 1

**Table 1: Formulation of emulgel.**

| Sl. No. | Ingredients | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|---|
| 1 | Mefenamic acid | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| 2 | HPMC | 2.0 | 2.5 | 3.0 | - | - | - |
| 3 | Sodium CMC | - | - | - | 1.5 | 2.0 | 2.5 |
| 4 | Light liquid paraffin | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 | 7.5 |
| 5 | Span 20 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| 6 | Tween 20 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 |
| 7 | Methyl paraben | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |
| 8 | Propyl paraben | 0.003 | 0.003 | 0.003 | 0.003 | 0.003 | 0.003 |
| 9 | Ethanol | 5 | 5 | 5 | 5 | 5 | 5 |
| 10 | Purified water | q.s | q.s | q.s | q.s | q.s | q.s |

**Charecterization of Mefenamic Acid Emulgel[8,15,21]**

**Physical Appearance**

The prepared emulgel formulations were inspected visually for their color, homogeneity, consistency, grittiness and phase separation.

**pH Determination**

1g of gel was accurately weighed and dispersed in 100 ml of distilled water. The pH of dispersion was measured by using digital pH meter

**Rheological studies**

Brookfield digital viscometer was used to measure the viscosity (in cps) of the prepared emulgel formulations. The spindle number 62 was rotated at 50 rpm for the viscosity measurement.

**Spreadability**

Spreadability of the formulation was determined by using an apparatus designed and developed in the laboratory especially for the project and diagram of the apparatus is shown in fig.5.Two rectangular glass plates of standard dimension were selected.500mg of the sample was placed on one of the glass plate. Second plate was placed over the other one to sandwich sample between plates. A 20gm weight was placed on the top of upper plate to provide a uniform thin film of the sample between the plates. Weight was removed; excess of the gel sample was scrapped off from the edges. The top plate was then subjected to pull by using string to which 50gm weight was applied. The time required by the upper plate to travel a distance of 6cm and separate from the lower plate was noted. A shorter interval indicates better spreadability. Experiment was repeated and averages of three attempts were calculated for each formulation using following formula

$$\text{Spredabiliy} = \frac{(M \times L)}{T}$$

M = weight tied to the upper side
L = length of the glassslide
T = time in seconds**.**

**Extrudability**

The developed formulations were filled in collapsible metal tubes and crimped at one end. After removing the cap tube is pressed to extrude the product from the tube

**Drug content**

Drug content of the emulgel was determined by dissolving an accurately weighed quantity of 1g gel in about 100 ml of methanol. 2ml of this solution was diluted to 10ml with methanol Solutions were then filtered and spectrophotometrically analyzed for drug content at 285nm. Drug content was determined from the standard curve of mefenamic acid.

***In vitro* drug release of Mefenamic acid Emulgel**

**i) Activation of Egg membrane**

Activation of egg membrane was carried out by soaking the membrane sodium chloride saline solution to use. It was then mounted on the diffusion cell and equilibrated with receptor fluid for 15 minutes and used for drug release studies.

**ii) Drug Release studies[20]**

The *in vitro* release of mefenamic acid from the formulations were studied using modified Keshary-Chien apparatus which was fabricated in our laboratory and used for the release study .The dissolution medium used was Phosphate buffer 7.4 $P^H$.1 gm of the formulated emulgel was accurately weighed, and placed on membrane a and placed in membrane and attached to this assembly. The donor compartment was suspended in 50 ml of dissolution medium maintained at 37± 1°C so that the membrane just touched the receptor medium surface. The medium was stirred at 50 rpm using magnetic stirrer. Aliquots, each of 1ml volume, were withdrawn at hourly intervals and replaced by an equal volume of the receptor medium. The aliquots were diluted to 10ml with the receptor medium and analyzed by UV-Visible spectrophotometer at 285 nm and % cumulative drug release was calculated.

**iii) Kinetics of drug release**

To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order, first, Higuchi's plot and Korsmeyer- Peppas plot respectively.

**RESULT**

**Determination of ƛ max:** Scanned in between 200-400 nm methanol as solvent maximum absorbance at 285 nm.

**Standard curve of mefenamic acid**

**Table 2: Standard curve of mefenamic acid.**

| Concentration(µg/ml) | Absorbance |
|---|---|
| 5 | 0.128±0.0015 |
| 10 | 0.253±0.0010 |
| 15 | 0.378±0.0021 |
| 20 | 0.496±0.0020 |
| 25 | 0.620±0.00208 |
| 30 | 0.735±0.00152 |

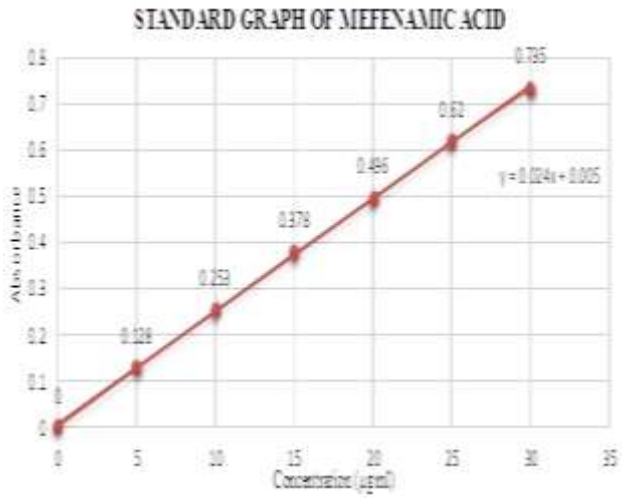



**Figure no: 1 Calibration curve of mefenamic acid.**

**Preformulation Studies**

**- Solubility profile**

Solubility of drug has been carried out in different solvents and it is practically insoluble in water, slightly soluble in ethanol (95%) and soluble in alkali hydroxide.

**- Determination of melting point**

Melting point was determined using melting point apparatus. Temperature was noted at which solid drug changes in to a liquid and it was found to be 230-231°c.

**Physical appearance**

It occurs as white powder and it is odourless.

**Partition coefficient**

The partition coefficient was found to be 1.87

**Identification & compatibility by FTIR**

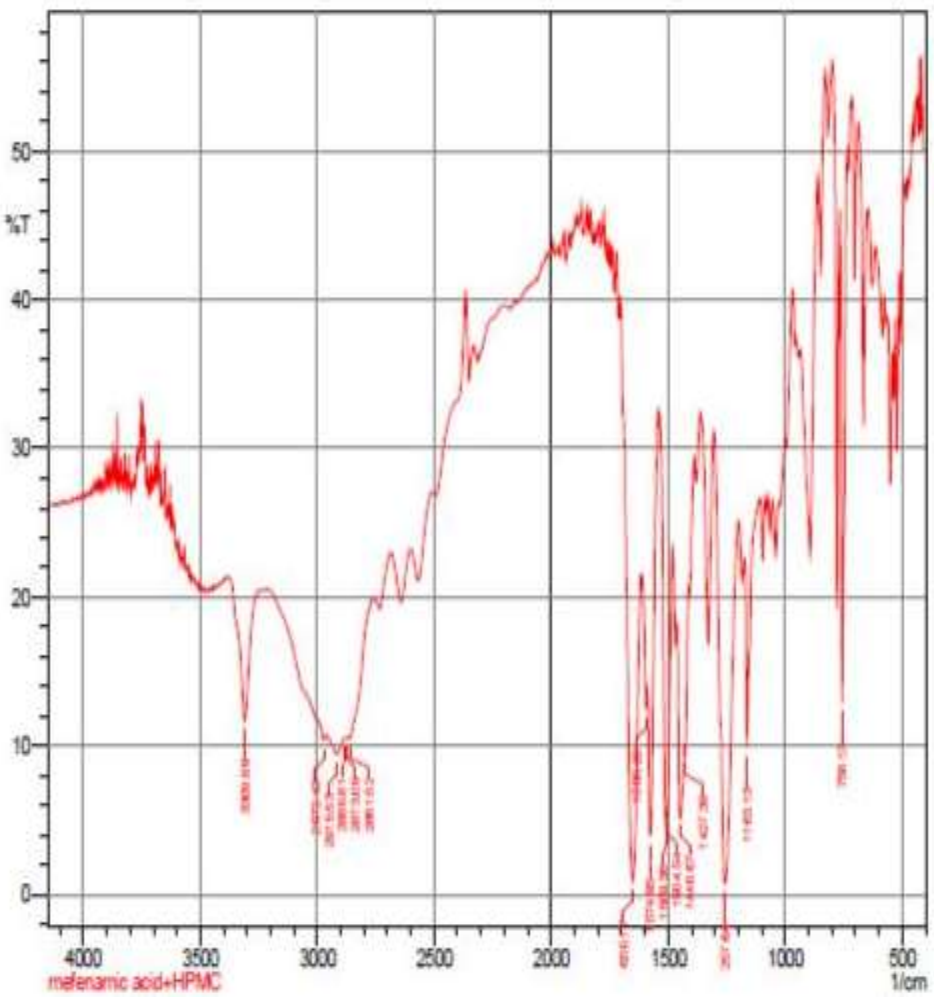



**Figure 2: FTIR mefenamic acid-**

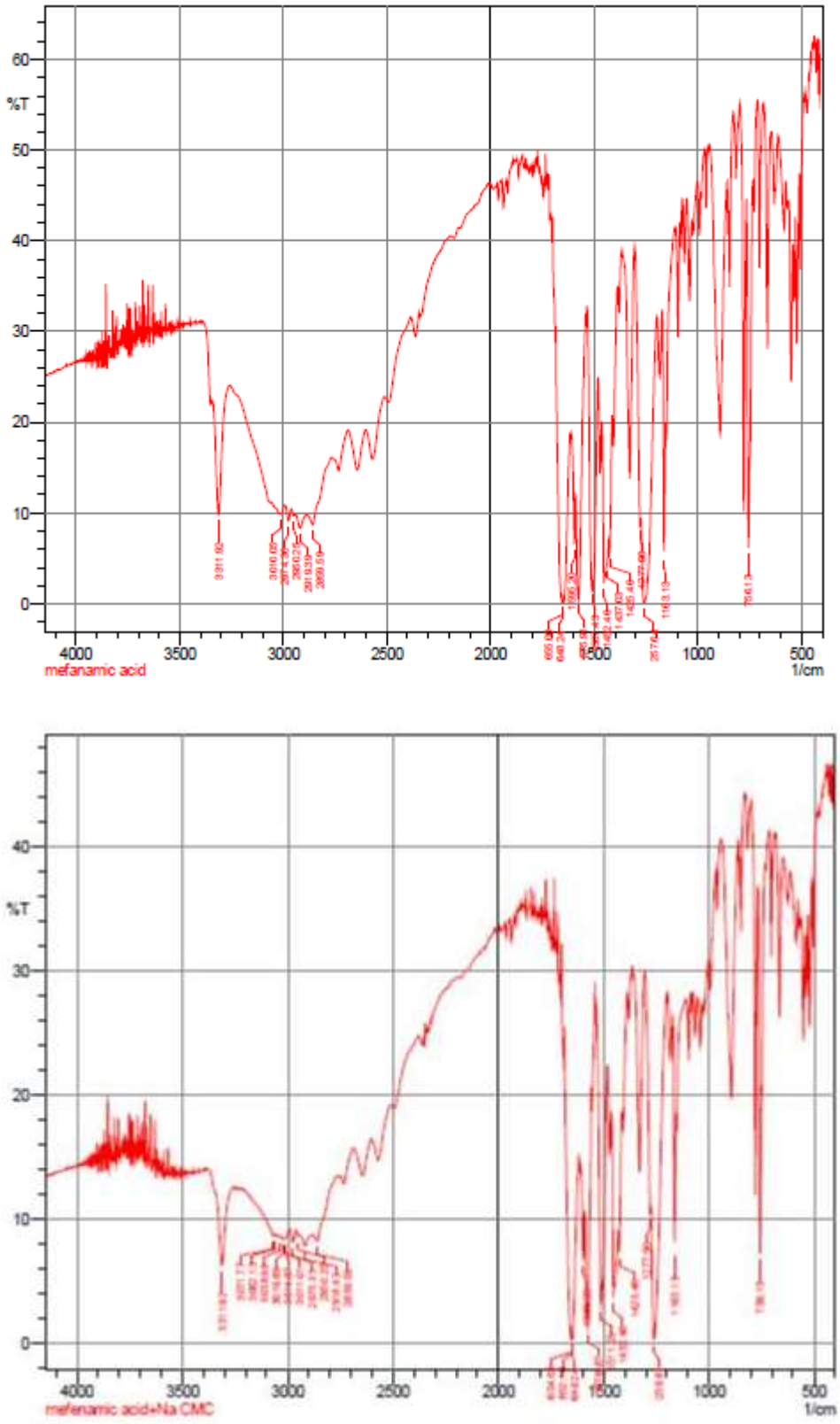



**Figure 3: FTIR mefenamic acid-sod. CMC.**

The peaks obtained in the FTIR of pure drug were found to be similar with that of reference. In order to investigate the possible interaction between drug and excipients, FT-IR studies of physical mixture of drug and excipients were carried out. After spectral comparison it was confirmed that there is no incompatibility reaction took place between drug and excipients.

**Effect of Polymer Concentration On Emulgel**

**Characterization of formulated emulgels**

**1. Physical evaluation**

**Table 3: Physical evaluation of formulations.**

| Formulation code | Color | Phase separation | Homogeneity | pH |
|---|---|---|---|---|
| F1 | White | no | Excellent | 6.0±1.25 |
| F2 | White | no | Excellent | 6.4±1.47 |
| F3 | White | no | Excellent | 6.5±0.98 |
| F4 | White | no | Excellent | 6.4±1.14 |
| F5 | White | no | Excellent | 6.7±1.37 |
| F6 | White | no | Excellent | 6.5±1.47 |

**2. Rheological Studies**

**Table 4: Rheological studies of formulations.**

| Formulation code | Spindle number | Revolutions per minute (RPM) | Torque (%) | Viscosity (cp) |
|---|---|---|---|---|
| F1 | S63 | 50 | 88.2 | 1379±22.50 |
| F2 | S63 | 50 | 88.5 | 1425±31.1 |
| F3 | S63 | 50 | 82.8 | 1534±26.51 |
| F4 | S63 | 50 | 81.5 | 1474±33.4 |
| F5 | S63 | 50 | 86.3 | 1581±31.39 |
| F6 | S63 | 50 | 88.1 | 1612±33.4 |

**3. Extrudability**

**Table 5: Extrudability of formulations.**

| Formulation code | Weight extruded from the tube (gm) |
|---|---|
| F1 | 0.69±.128 |
| F2 | 1.02±0.20 |
| F3 | 1.1±0.096 |
| F4 | 0.73±0.121 |
| F5 | 0.81±0.15 |
| F6 | 0.89±0.151 |

**Spreadability**

**Table 6: Spreadability coefficient of formulations.**

| Formulation code | M(gm) | L(cm) | T(sec) | Spreadability |
|---|---|---|---|---|
| F1 | 50 | 6 | 10 | 30±0.54 |
| F2 | 50 | 6 | 11 | 23.07±0.47 |
| F3 | 50 | 6 | 15 | 20±0.34 |
| F4 | 50 | 6 | 10 | 30±0.46 |
| F5 | 50 | 6 | 11 | 27.27±0.65 |
| F6 | 50 | 6 | 16 | 21.42±0.24 |

**Drug content**

Drug content of the formulated emulgels were estimated by UV spectrophotometer at λmax 285 nm and the results of drug content of each formulation was given in the table below.

**Table 7: Drug content of emulgels.**

| Product | Drug content (%) |
|---|---|
| F1 | 84.21±1.35 |
| F2 | 85.21±1.16 |
| F3 | 84.29±0.98 |
| F4 | 73.45±0.87 |
| F5 | 75.88±1.31 |
| F6 | 74.88±1.10 |

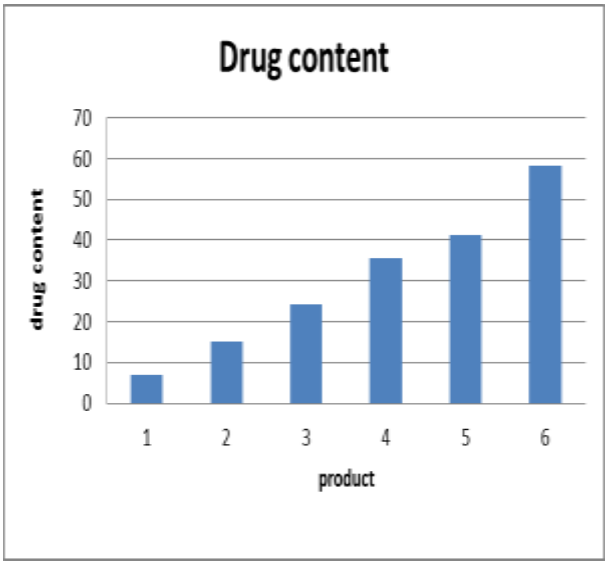
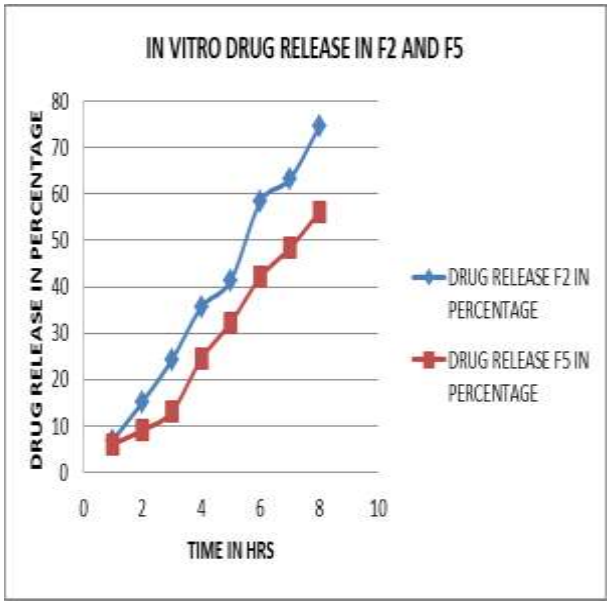



**Figure 4: Drug content of emulgel.**




***In vitro* Drug release study**

From the above studies it was seen that consistency and viscosity of formulations F2& F5 were the best and the *in vitro* studies of above formulations were conducted.

**Table 8: Cumulative percentage drug release of F2 & F5.**

| Time (hrs.) | Cumulative percentage drug release | |
|---|---|---|
| | F2 | F5 |
| 1 | 7.0 | 6.1 |
| 2 | 15.2 | 9.1 |
| 3 | 24.3 | 13.1 |
| 4 | 35.6 | 24.1 |
| 5 | 41.4 | 32.3 |
| 6 | 58.3 | 42.1 |
| 7 | 63.2 | 48.3 |
| 8 | 74.5 | 56.1 |

**Effect of Co-Surfactant Concentration**

To the selected formulations of emulgels different concentration of co- surfactant were added and further studied.

**Table 9: Formulation of emulgels containing co-surfactants.**

| Sl. No | Ingredients | F7 | F8 | F9 | F10 |
|---|---|---|---|---|---|
| 1 | Mefenamic acid | 0.1 | 0.1 | 0.1 | 0.1 |
| 2 | HPMC | 2.5 | 2.5 | - | - |
| 3 | Sodium CMC | - | - | 2.0 | 2.0 |
| 4 | Light liquid paraffin | 7.5 | 7.5 | 7.5 | 7.5 |
| 5 | Span 20 | 0.5 | 0.5 | 0.5 | 0.5 |
| 6 | Tween 20 | 1.3 | 1.3 | 1.3 | 1.3 |
| 7 | Propylene glycol | 2.5 | 5.0 | 2.5 | 5.0 |
| 7 | Methyl paraben | 0.001 | 0.001 | 0.001 | 0.001 |
| 8 | Propyl paraben | 0.003 | 0.003 | 0.003 | 0.003 |
| 9 | Ethanol | 5 | 5 | 5 | 5 |
| 10 | Purified water | q.s | q.s | q.s | q.s |

**Characterizations of emulgels**

**Table 10: evaluation of formulations (F7, F8, F9& F10).**

| Formulation code | Color | Phase seperation | homogenity | pH | Viscosity | Weight extruded from the tube (gm) |
|---|---|---|---|---|---|---|
| F7 | white | no | Excellent | 6.4±0.98 | 1420± 21.10 | 1.15±0.20 |
| F8 | white | no | Excellent | 6.5±0.78 | 1415± 31.10 | 1.03±0.79 |
| F9 | white | no | Excellent | 6.5±0.65 | 1538 ±27.5 | 0.93±0.09 |

| | | | | | | |
|---|---|---|---|---|---|---|
| F10 | white | no | Excellent | 6.8±0.71 | 1520± 21.10 | 1.2±0.114 |

**Spreadability**

**Table 11: Spreadability of formulations (F7, F8, F9& F10).**

| Formulation code | M(gm) | L(cm) | T(sec) | MLT |
|---|---|---|---|---|
| F7 | 50 | 6 | 13 | 23.07±1.82 |
| F8 | 50 | 6 | 12 | 25.0±1.43 |
| F9 | 50 | 6 | 14 | 21.42±1.28 |
| F10 | 50 | 6 | 13 | 23.07±1.12 |

**5. Drug content**

**Table 12: Drug content of formulations (F7, F8, F9& F10).**

| Formulation code | Drug content (%) |
|---|---|
| F7 | 86.71±2.86 |
| F8 | 87.90±3.13 |
| F9 | 76.45±3.46 |
| F10 | 76.72±2.35 |

***6. In vitro* Drug release study**

**Table 13: Cumulative percentage drug release of F7, F8, F9, & F10.**

| Time (hrs) | | Cumulative percentage drug release | | |
|---|---|---|---|---|
| | F7 | F8 | F9 | F10 |
| 0 | 0 | 0 | 0 | 0 |
| 1 | 7.9 | 8.4 | 6.1 | 6.34 |
| 2 | 15.5 | 16.8 | 9.2 | 10.7 |
| 3 | 24.6 | 25.1 | 16.1 | 18.93 |
| 4 | 38.4 | 40.5 | 29.6 | 33.2 |
| 5 | 43.1 | 47.3 | 32.3 | 41.6 |
| 6 | 58.5 | 60.7 | 44.5 | 51.5 |
| 7 | 67.5 | 68.21 | 54.1 | 58.4 |
| 8 | 76.5 | 79.6 | 61.3 | 63.4 |

**Effect of Penetration Enhancers**

From the above studies, formulations F8 and F10 were found to show better result, so to this formulations 2ml of penetration enhancer (clove oil) were incorporated and evaluations were done**.**

**Characterizations of emulgels**

**Table 14: Evaluation of CF1& CF.**

| Formulation code | Color | Phase seperation | homogenity | pH | Viscosity | Weight extruded from the tube (gm) |
|---|---|---|---|---|---|---|
| CF1 | Whitish Yellow | no | Excellent | 6.5±0.98 | 1414±31.10 | 1.1±0.096 |
| CF2 | Whitish Yellow | no | Excellent | 6.4±0.78 | 1519±21.10 | 1.02±0.20 |

**Spreadability**

**Table 15: Spreadability of CF1& CF.**

| Formulation code | M(gm) | L(cm) | T(sec) | Spreada bility |
|---|---|---|---|---|
| CF1 | 50 | 6 | 12 | 25.0±1.54 |
| CF2 | 50 | 6 | 13 | 23.07±1.31 |

**Drug content**

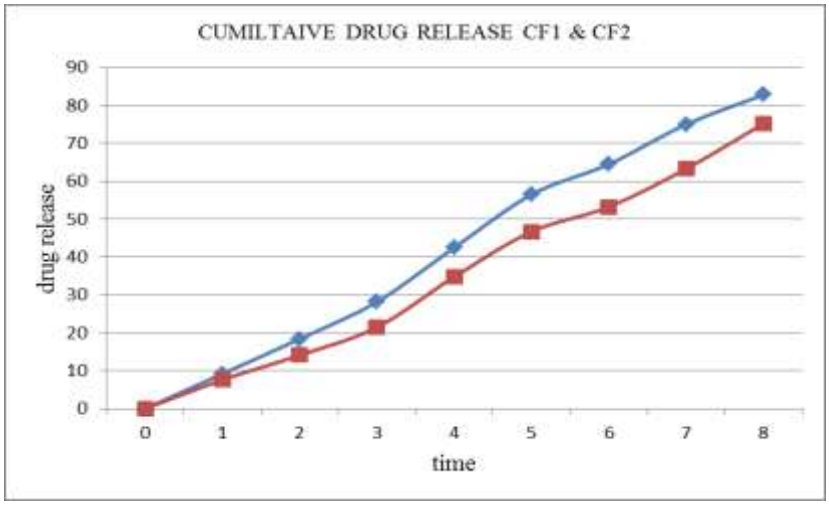
**Table 16: Drug content of CF1 and CF2.**

| Formulation code | Drug content (%) |
|---|---|
| CF1 | 87.90±3.14 |
| CF2 | 76.72±4.78 |

***In vitro* Drug release study**

**Table 17: Cumulative percentage drug release of CF1 & CF2.**

| Time (hrs) | Cumulative percentage drug release | |
|---|---|---|
| | CF1 | CF2 |
| 0 | 0 | 0 |
| 1 | 9.2 | 7.6 |
| 2 | 18.4 | 14.1 |
| 3 | 28.2 | 21.5 |
| 4 | 42.5 | 34.8 |
| 5 | 56.5 | 46.7 |
| 6 | 64.5 | 53.25 |
| 7 | 75.0 | 63.3 |
| 8 | 82.8 | 75.2 |




**Kinetics of drug release** was studied to examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing

- Zero order
- First order
- Higuchi's plot
- Korsemeyer Peppas model

**Drug release kinetics**

**Table 18: Drug release kinetics.**

| Formulation code | Zero order (R2) | First order (R2) | Higuchi (R2) | Korsmeyer – peppas (R2) |
|---|---|---|---|---|
| CF1 | 0.995 | 0.771 | 0.902 | 0.651 |

**DISCUSSION**

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body and then maintain the desired drug concentration. A well designed drug delivery system can overcome some of problems of conventional therapy and enhance therapeutic efficacy of the given drug. There were various approaches in delivering therapeutic substance to the target site in sustained and controlled release fashion. One such approach is emulgel. In this study mefenamic acid emulgels was formulated using two polymers HPMC and NaCMC and their evaluations are performed and the results obtained.

Drug identification was done by performing melting point determination and FT-IR studies. From the result the melting point of drug was found to be 2300C which complies with official standard indicating the purity of the sample. FT-IR studies peak of mefenamic acid obtained at 3311.92$cm^{-1}$, 2974.36$cm^{-1}$, 1648$cm^{-1}$, 1595.2 $cm^{-1}$,1575.91 $cm^{-1}$, 1507$cm^{-1}$, 1257 $cm^{-1}$, 1163 $cm^{-1}$,756.13 $cm^{-1}$ showed that the peaks are identical to reference indicating the identity of drug. The FT-IR spectrums of pure drug, polymers and physical mixture of drug and polymers. (Figure) and (table) shows that no interaction took place between drug and polymer. However, some additional peaks were observed with physical mixtures, which could be due to the presence of polymers. These results suggest that there is no interaction between the drug and polymers used in the study. Thus indicating that the drug and polymer are compatible with each other

**Formulation and Characterizations of mefenamic acid emulgel**

**Effect of polymer concentration**

Three emulgel containing HPMC and three emulgel containing NaCMC as polymer were formulated.

**Characterizations of emulgels**

**1. Physical appearance**

All the prepared emulgel formulations were white viscous creamy preparations with a smooth and homogeneous appearance.

**2. pH determination**

The pH values of all prepared formulations ranged 6.0-6.7, which lies within the normal pH range of the skin and was considered acceptable to avoid any irritation upon application to the skin.

**3. Rheological studies**

The rheological behavior of all formulated emulgels was studied using Brookfield viscometer at a speed of 50rpm and spindle no.62were used. The viscosity of the formulation increases as concentration of polymer increases.

**4. Extrudability**

The extrusion of the emulgel from the tube is important during its application. Gel with high consistency may not extruded from the tube where as low viscous gel may flow quickly and hence suitable consistency is required to extrude the gel from the tube. Extrudability of HPMC emulgels were found to be good.

**5. Spreadability**

The value of spreadability indicates that emulgels is spreadable by small amount. Spreadability of HPMC emulgels was in the range of 20-30gm.cm/sec and spreadability of NaCMC was in the range 21-30gm.cm/sec, indicating the spreadability of both type emulgel formulations were good. It was found that the spreadability increased with decreased viscosity.

**6. Drug content**

Drug content of the formulated gels was estimated by UV spectrophotometer at λmax 285nm and drug content was calculated from calibration curve. Drug content of the formulations showed that the drug was uniformly distributed in to emulgels.

**7. *In vitro* Drug release studies**

From the prepared six formulations, the formulations (F2&F5) showing good viscosity, extrudability, spreadability and drug content uniformity were selected. These formulations were then subjected to in-vitro release studies.

- For F2, in the first hour about 7.0% and at the end of 8$^{th}$ hour about 74.5% cumulative amount of drug was released.
- For F5, in the first hour about 6.1% and at the end of 8$^{th}$ hour about 56.1% cumulative amount of drug was released.

**Effect of co- surfactant concentration**

From the above studies it was seen that the consistency and viscosity of formulations F2 & F7 were the best. Hence different concentration of co-surfactant ( propylene glycol) were added to two formulation and further studied.

**Characterizations of emulgels**

**1. Physical evaluations**

All the prepared emulgel formulations were white viscous creamy preparations with a smooth and homogeneous appearance.The pH values of all prepared formulations ranged 6.0-6.7, which lies within the normal pH range of the skin and was considered acceptable to avoid any irritation upon application to the skin.

**2. Rheological studies**

The rheological behavior of all formulated emulgels was studied using Brookfield viscometer at a speed of 50rpm and spindle no.62 was used. The viscosities of the formulations were satisfactory.

**3. Extrudability**

Extrudability of emulgels containing HPMC as polymer were found to be better than that of emulgels containing NaCMC

**4. Spreadability**

The value of spreadability indicates that emulgels is spreadable by small amount. Spreadability of HPMC emulgels was in the range of 23-25gm.cm/sec and spreadability of NaCMC was in the range 21-24gm.cm/sec, indicating the spreadability of both type emulgel formulations were good.

**5. Drug content**

Drug content of the formulated gels was estimated by UV spectrophotometer at λmax 285nm and drug content was calculated from calibration curve. Drug content of the formulations showed that the drug was uniformly distributed in to emulgels.

**6. *In vitro* Drug release studies**

All the above formulations (F7, F8, F9 and F10) were then subjected to in-vitro release studies.

1. For F7, in the first hour about 7.9% and at the end of 8$^{th}$ hour about 76.5% cumulative amount of drug was released.
2. For F8, in the first hour about 8.4% and at the end of 8$^{th}$ hour about 79.6% cumulative amount of drug was released.
3. For F9, in the first hour about 6.1% and at the end of 8$^{th}$ hour about 61.3% cumulative amount of drug was released.

4. For F10, in the first hour about 6. 34% and at the end of 8$^{th}$ hour about 63.4% cumulative amount of drug was released.

**Above results indicates that**

- As the polymer concentration increases emulgel become viscous but release decreases. So an optimum concentration of polymer which gives correct consistency and maximum drug release should be selected.
- As the concentration of co-surfactant increases the drug release also increases.

**Effect of penetration enhancer**

To the best formulations (F8 and F10) from above results, clove oil as penetration enhancer was added and effect was studied.

**1. Physical evaluations**

The prepared emulgel formulations where whitish yellow creamy preparations with a smooth and homogeneous appearance. The pH values of CF1 and CF2 were 6.4 and 6.5 respectively, which lies within the normal pH range of the skin and was considered acceptable to avoid any irritation upon application to the skin.

**2. Rheological studies**

The rheological behavior of all formulated emulgels was studied using Brookfield viscometer at a speed of 50rpm and spindle no.62 was used. The viscosities of CF1 and CF2 were 1379±22.50cp and 1425±31.1cp respectively, which shows that prepared emulgels have required consistency.

**3. Spreadability**

The spreadability coefficient of CF1 and CF2 were 25.0 gm.cm/sec and 23.07 gm.cm/sec respectively. This result indicates CF1 had good spreadability than CF2.

**4. Extrudability**

Both the emulgels had good extruding property. Comparatively CF1 has good extruding property than CF2.

**5. Drug content**

Drug content of the formulated emulgels was estimated by UV spectrophotometer at λmax 285nm and drug content was calculated from calibration curve. Drug content of the formulations showed that the drug was uniformly distributed in to emulgels.

**6. *In vitro* release studies**

- For CF1, in the first hour about 9.2% and at the end of 8$^{th}$ hour about 82.8% cumulative amount of drug was released.
- For CF2, in the first hour about 7.6 % and at the end of 8$^{th}$ hour about 75.2% cumulative amount of drug was released.

From above studies it was found that CF1 was an excellent emulgel and hence the data obtained from in-vitro release studies was fitted into various kinectic models and also stability studies were conducted on the selected formulation as per ICH guidelines.

**Drug Release kinetics**

In CF1, correlation coefficient of zero order kinetics was found to be $R^2$ = 0.995 and that of first order kinetics was to be $R^2$=0.771.Higuchi plot was found to be linear with regression coefficient $R^2$=0.902 Hence it shows that the drug release follows zero order kinectics.To confirm exact mechanism of drug permeation from the emulgel, the data was fitted according to the Korsmeyer-Peppas model. The value of slope of the plot n gives an indication of the release mechanism. When n=1, the release is independent of time i.e., zero order, if n=0.5 then the release is by Fickian diffusion. When n= 0.5-1, diffusion is non-fickian and when n>1.0 then it is super case II transport. The 'n' exponent value of optimized batch was found to be 0.651. Hence it shows non-fickian diffusion.

## CONCLUSION

Mefenamic acid emulgel using HPMC and NaCMC as gelling agent were successfully developed. The developed formulations were then characterized for their physical appearance, pH, viscosity, spreadability, extrudability, drug content and *in vitro* release. The emulgel (CF1) prepared using HPMC as gelling agent, propylene glycol as co- surfactant and clove oil as penetration enhancer was found to show better result when compared to emulgel (CF2) prepared using NaCMC as gelling agent.

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