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Original Article

FORMULATION AND CHARACTERISATION OF MELOXICAM LOADED EMULGEL FOR TOPICAL APPLICATION

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ABSTRACT

Objective: The aim of the research work is to formulate emulgel of Meloxicam for topical application.

Methods: The method used for preparation of microemulsion was water titration method with Oleic acid as oil phase, Tween 20 as surfactant and PEG 400 as co-surfactant and its concentrations were fixed based on Pseudoternary phase diagrams. The optimized emulsion formulation was incorporated into the gel matrix that is Carbopol981 NF and Carbopol 974 P NF.

Results: The prepared emulsions were characterized for globule size, drug content, zeta potential and the emulgel for physical appearance, drug content, pH, viscosity, spreadability, extrudability and *in vitro* drug release studies. The optimized emulsion formulations E1 and F1 showed globule size of 176 nm and 128 nm respectively and the emulgel formulation M2F1 with 1.5% Carbopol 981 and optimized F1 emulsion formulation showed *in vitro* drug release of 89.934% at the end of 8 h. The optimized formulation showed no skin irritation when compared with standard irritant 0.8% of Formalin. The optimized formulation showed better anti-inflammatory effect when compared with marketed formulation.

Conclusion: Meloxicam was proven to be a suitable candidate for formulating emulgel for topical delivery to achieve better patient compliance.

Keywords: Meloxicam, Emulgel, Topical application, Carbopol 981NF, Carbopol 974 P NF, Oleic acid, Tween 20 and PEG 400.

INTRODUCTION

Meloxicam is a non-steroidal anti-inflammatory agent with analgesic and anti-inflammatory effect, used for the treatment of rheumatoid arthritis and osteoarthritis. Meloxicam belongs to the class of preferential COX-2 inhibitors. It is a newer congener of Piroxicam. Meloxicam is a poorly water soluble drug having solubility of 7.15 mg/l and protein binding of 99.4% and it exhibits gastrointestinal side effects like gastric bleeding, ulceration and perforation of stomach, small and large intestine when given orally [1].

Topical delivery can be defined as the application of drug containing formulation to skin to directly treat the cutaneous disorders or the cutaneous manifestation of general disease with the intent of confining the pharmacological or other effect of the drug to the surface of skin or within the skin. Most widely used semisolid preparations includes gel, creams, ointments etc

The U. S. P defines gel as a semisolid system consisting of dispersions made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by liquid. The gel contains the larger amount of aqueous or hydroalcoholic liquid in a network of colloidal solid particles which may consist of inorganic or organic substances. Inspite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to over this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels.

When emulsions and gels are used in combined form, the dosage form is referred to as "Emulgel". The presence of gelling agent in the water phase converts the classical emulsion into an emulgel. The Emulgel are hydrogel containing randomly distributed oil micro droplets.

Emulsions are biphasic systems in which one immiscible liquid is dispersed into other due to which the system becomes unstable and so stabilized by adding an emulsifying agent. Emulsion itself is a controlled release system where entrapped drug particles in internal phase passes through the external phase and then slowly gets absorbed into the skin. The gel forms a cross linked network where it captures small drug particles and provides its release in a control manner.

Emulgel are emulsions either oil-in-water or water-in-oil type which are gelled by mixing with a gelling agent. They have high patient acceptability because of its favorable properties such as being thixotropic, grease less, easily spreadable, easily removable, emollient, nonstaining, long shelf life, biofriendly, transparent and pleasing appearance [2, 3].

Microemulsions are homogeneous, transparent, thermodynamically stable dispersions of water and oil stabilized by addition of surfactant, usually in combination with co-surfactant and whose droplet size is in the range of 20-200 nm. Since microemulsions have large surface area, they can incorporate in their core larger quantities of molecules which are insoluble in the continuous phase. The main difference between emulsion and microemulsion is the size and the shape of the droplets and since the size of the droplets in microemulsion is much smaller than the wavelength of visible light the microemulsions are transparent. The microemulsions are prepared with high concentration of surfactant which is useful in the greater stabilization of hydrophobic drugs and also requires lesser amount of energy.

To overcome the disadvantages of Meloxicam in the oral delivery an attempt has been made in the present study to formulate emulgel of Meloxicam by incorporating microemulsion of Meloxicam in the gel base.

MATERIALS AND METHODS

Materials used

Meloxicam was obtained as a gift sample from Unichem Laboratories Pvt limited Goa India. Carbopol 981NF and 974 P NF were obtained as the gift sample from Lubrizol Mumbai India. Oleic acid was obtained from Merck Specialist Mumbai India. Tween 20 and PEG 400 were obtained from Hi-media Mumbai India. All the other chemicals and reagents used were of analytical grade.

Methods

Saturation solubility in oils, surfactant and co-surfactant

Excess amount of drug was added to 10 ml vials containing 10 ml of oil (Castor oil, sunflower oil, olive oil and oleic acid), Surfactants (Tween 20,Tween 60, Tween 80, Span 20 and Span 80) and co-

surfactants (PEG 400, PEG 600 and Propylene Glycol) respectively and then it was kept on a mechanical shaker for 72 h. After 72 h solution were centrifuged for 10 min at 3000 rpm and then the supernatant was filtered and UV absorbance was taken at 341 nm by suitable dilution with Chloroform [4, 5].

Construction of pseudoternary phase diagrams

Pseudoternary phase diagrams were constructed using Chemix school 3.60 software. The method used for the study was water titration method and it helps to determine the concentration range of components for the existing range of microemulsion. Three phase diagrams were prepared with 1:1, 2:1 and 3:1 ratio of Tween 20 to PEG 400 respectively. The mixture of oil, surfactant and co-surfactant at certain weight ratios was diluted with water drop-wise, by vortexing with vortex mixture after being equilibrated, the mixtures were assessed visually and determined as being micro emulsion, crude emulsions or gel [6].

Preparation of emulsion

Meloxicam was dissolved in the mixture of oil, surfactant, and co-surfactant with varying component ratio as shown in the table 1 and then an appropriate amount of water was added to the mixture drop by drop while continuous stirring with magnetic stirrer at ambient temperature, until a clear phase was obtained [7].

Table 1: Formulation table of Meloxicam emulsion preparation

S. No.	Formulation code	S: Cos ratio [S_{mix}]	Oil: Smix ratio	Amount of drug added (mg)	Approx. theoretical drug content (mg)	Total volume of mixture (ml)	Amount of water (ml)
1	E1	1:1	1:9	200	217.209	10	5
2	E2	1:1	2:8	200	199.39	10	2.3
F	E3	1:1	3:7	200	181.55	10	1.3
4	F1	2:1	1:9	200	202.24	10	10
5	F2	2:1	2:8	200	219.723	10	2.5
6	F3	2:1	3:7	200	201.37	10	1.8
7	G1	3:1	1:9	200	220.96	10	35
8	G2	3:1	2:8	200	154.032	10	5
9	G3	3:1	3:7	200	195.63	10	1.4

Characterization of emulsion

The prepared emulsion formulations of emulsions were evaluated for drug content, Globule size and Zeta potential.

Drug content of emulsion

1 ml of emulsion was taken and added to 10 ml volumetric flask, with making up its volume and further dilutions with chloroform and UV absorbance was taken at 341 nm. The microemulsion without drug was used as a blank. The values obtained were used to calculate the concentration of drug in emulsion [8].

Globule size determination

The globule size distribution of the formulations was measured by Nanotrac particle size analyzer [Microtrac/Nanotrac A150, Korea]. 0.1 ml of the emulsion was taken and it was diluted to 250 ml with distilled water and then the readings were taken.

Zeta potential

Zeta potential of all the formulations was measured by using Zeta meter instrument [UNITRON FSB (4X) Japan]

Formulation of emulgel

The Carbopol 981 NF and 974 P NF in the concentration of 1.5% and 2% were swelled in distilled water and the optimized emulsion formulation was added to the gel base. The emulsion equivalent to 0.5% of Meloxicam was added to the gel base. The pH was adjusted using Triethanolamine; glycerin was added as humectant and Methyl paraben, Propyl paraben as the preservatives.

Table 2: Formulation table of emulgel containing Meloxicam

Ingredients	M1E1	M2F1	M'1E1	M'2F1	NIE1	N2F1	N'1E1	N'2F1
Meloxicam emulsion equivalent to	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
Carbopol 981	1.5%	1.5%	2%	2%				
Carbopol 974					1.5%	1.5%	2%	2%
Glycerin	1%	1%	1%	1%	1%	1%	1%	1%
Triethanol amine	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%
Methyl Paraben	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
Propyl Paraben	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
Distilled water q. s	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml

Characterisation of emulgel

Physical examination

The prepared Emulgel formulations were inspected visually for their color, homogeneity and consistency.

Drug content

1 gm of emulgel was accurately weighed and dissolved in 100 ml of chloroform and it was kept for sonication for 2 h. The solution was passed through filter paper and filtered. The absorbance was measured spectrophotometrically at 341 nm against corresponding Emulgel without drug as blank. Drug content was calculated using the slope and the intercept obtained by linear regression analysis of the standard calibration curve. All the measurements were carried out in triplicates [9].

pH

The pH of various emulgel formulations was determined by using digital pH meter. 1 gm of emulgel was dissolved in 100 ml of distilled water and stored for 2 h. The measurements were carried out in triplicates.

Viscosity

The measurement of the viscosity of the prepared emulgel was done with a Brookfield Rheometer. The emulgel was rotated at 1rpm and the corresponding dial reading was noted. The viscosity of the gel

was obtained by that reading. The viscosity was measured in cPs. The measurements were carried out in triplicates [10].

Spreadability

It indicates the extent of the area to which emulgel readily spreads on application to skin or affected part. The spreadability was performed by taking two slides of 5 cm each. The down slide which was kept fixed, 1 gm of emulgel was placed on it and the other slide was kept on top of it and weight of 5 gms was placed on top of upper slide and it was kept in the same position for 5 min. The weight was removed and the time required to remove the upper slide was noted down. Lesser the time taken for the separation of two slides, better the spreadability. It is calculated by using the formula:

$$S = \frac{MXL}{T}$$

Where, M = weight tied to upper slide

L = length of glass slide

T = time taken to separate the slides [11]

Extrudability

Extrudability test is based upon the determination of weight required to extrude 0.5 cm ribbon of emulgel in 10 sec from lacquered collapsible aluminum tube. The test was performed in triplicate and the average values were calculated. The extrudability was then calculated by using the following formula. [12]

$$\text{Extrudability} = \frac{\text{weight applied to extrude emulgel from tube(gm)}}{\text{Area(cm}^2\text{)}}$$

***In vitro* release study**

The *in vitro* drug release studies of the Emulgel were carried out in modified Franz Diffusion cell using the dialysis membrane. Emulgel (1 gm) was spread uniformly on the dialysis membrane. 50 ml of the Phosphate buffer of pH 6.8 was used as dissolution media which were added to the receptor compartment. This whole assembly was kept on a magnetic stirrer and the solution on the receptor side was stirred continuously using a magnetic bead and temperature of the cell was maintained at 37±0.5 °C Sample (1 ml) was withdrawn at suitable time intervals and replaced with the equal amounts of fresh dissolution media. Samples were analyzed spectrophotometrically at 361 nm and the cumulative % drug release was calculated. The study was carried out in triplicates. The graph is plotted of % cumulative drug releases versus time [11].

Drug release kinetics

To analyze the mechanism for the release and release rate kinetics of the dosage form, the data obtained from the *in vitro* diffusion study were fitted in to Zero order, First order, Higuchi matrix and Korsmeyer-Peppas model. By comparing the R^2 values obtained, the best fit model was selected.

Skin irritation test

The skin irritation test was performed on the male Wistar rat. Prior to the experiment ethical clearance was obtained from institutional ethical committee [Resolution no KLECOP/IAEC/Re.20-09/08/ 2014]. The animals were divided in three groups i.e. control, standard and test. The back skin of the rat of 5 cm^2 was shaven one day prior to the starting of the study. After 24 h of shaving the skin of rat, the standard group was applied with 0.8% of Formalin which is the standard irritant and the test group was applied with the optimized formulation M2F1 and the rats were observed for any irritation at the end of 24 h the animals were observed for erythema or edema and score were given accordingly. If the formulation produces score of 2 or less than 2 no irritation persists [13].

***In vivo* anti-inflammatory study**

In vivo anti-inflammatory study was carried out on Wistar rats as animal model weighing approximately 200-250 gms each. For the study animals were divided into three groups i.e. the Control, Standard and test. Each group containing 6 animals each.

GROUP I (Control Group): Carragenan (1%) was administered in the plantar surface of rat.

GROUP II (Standard group): Topical marketed Piroxicam gel (Pirox gel)+Carragenan.

GROUP III (Test Group): Optimized formulation M2F1+Carragenan

Edema was induced on the left hind paw of the rats by subplantar injection of 1% Carragenan. The test formulation i.e. M2F1 and Standard i.e. Pirox gel were applied 30 min before carrageenan administration. The paw volume was measured at intervals of 30, 60, 90, 120, 150 and 180 min by mercury displacement method using Plethysmometer.

The percentage inhibition of paw edema in drug treated group was compared with Carragenan control group and calculated according to the formula:

$$\%\ Inhibition\ of\ the\ drug = \left(\frac{Vc - Vt}{Vc}\right) x\ 100$$

Vc = inflammatory increase in paw volume of control group

Vt= inflammatory increase in paw volume in (drug+Carragenan) treated animals [14].

Stability studies

Short term stability study was performed on the optimized formulation. The formulation was subjected to different conditions of temperature and relative humidity i.e. 25°C/60% RH and 40 °C/ 65% RH for a period of 2 mo. Samples were withdrawn at the interval of 1 mo and were evaluated for rheological properties, drug content and %CDR [15].

RESULTS AND DISCUSSION

Saturation solubility in oils, surfactants and co-surfactants

Inorder to screen appropriate solvents for the preparation of emulsion, the solubility of Meloxicam in various oils, surfactants and co-surfactants was carried out and the obtained results were summarized in fig. no: 1-3. The solubility in oleic acid was found to be 5.664 mg/ml and that in surfactant i.e. Tween 20 is 24.336 mg/ml and in case of co-surfactants i.e. PEG 400 is 22.68 mg/ml. Among the various oils used the highest solubility was found in case of Oleic acid, Tween 20 has the highest solubility among surfactant and PEG 400 among the co-surfactant. So based on the solubility the oil i.e. oleic acid, Tween 20 and PEG 400 were selected for the preparation of emulsion.

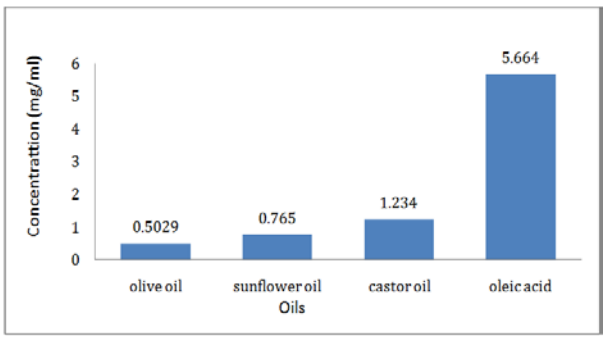


Fig. 1: Saturation solubility of Meloxicam in oils

Construction of Pseudoternary phase diagram

The region shaded yellow showed the transparent microemulsion region in the phase diagram. The microemulsion region for the surfactant: co-surfactant ratio 3:1 was found to be the largest and lowest for the 1:1 ratio. The results were shown in fig. no 4. The area of microemulsion increased as the concentration of surfactant increases possibly because Tween 20 is a non-ionic solvent that forms clear solution in water, so the area of o/w microemulsion was increased. The largest microemulsion region was obtained for the surfactant: co-surfactant ratio of 3:1 and smallest microemulsion

area was obtained for the ratio 1:1 and it was observed that as the concentration of surfactant increases the quantity of water required to obtain turbidity also increases and as more the water quantity required the solubility of drug also decreases. On the basis of stability the first three ratios of oil: Smix was selected from each ratio of surfactant: co-surfactant [8].

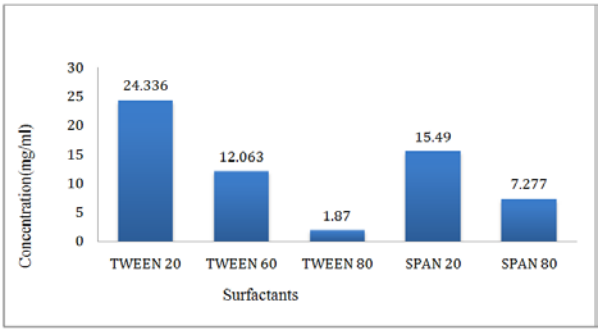


Fig. 2: Saturation solubility of Meloxicam in surfactants

Drug content

The drug content varied from 75.48% to 93.31%. The formulation E1 showed drug content of 93.31%, F1 was 92.34% and G1 was 91.76%. The highest drug content was found in case of E1 formulation due to greater solubilization of drug as compared to others and even as the quantity of water required to form the microemulsion was less in case of 1:1 ratio of surfactant: co-surfactant and 1:9 ratio of oil: Smix.

Globule size determination

The globule size of all the prepared microemulsion was evaluated on Nanotrac. The globule size obtained was reported in the table no: 3.

On the basis of result obtained it was found that the globule size decreased as the surfactant concentration increased. The lowest globule size was obtained for the microemulsion formulation G1i.e. 17.93 nm and the globule size of the formulations E1 and F1 were found to be 176.8 nm and 128 nm respectively. The formulation E1 and F1 was selected as optimized microemulsion formulation based on globule size as it was ranging in microemulsion region and there was not much difference in the drug content of the two formulations. The formulation G1 though had lowest particle size was not selected as optimized as it was falling in nanoemulsion range and since nanoemulsions are thermodynamically unstable compared to the microemulsions.

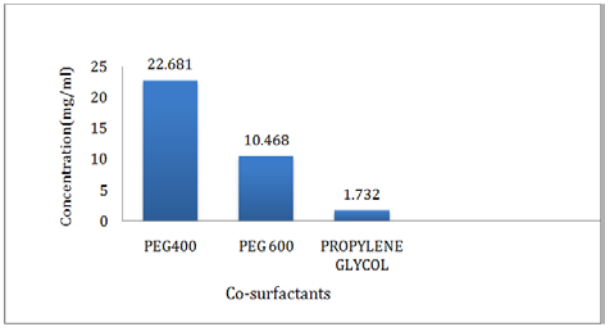


Fig. 3: Saturation solubility of Meloxicam in co-surfactants.

Characterisation of Emulsion

Zeta potential determination

The Zeta potential of all formulations was found to be in the range of-27.6 to-53.73. Based on the result of the zeta potential the formulations were found to show moderate to good stability [16].

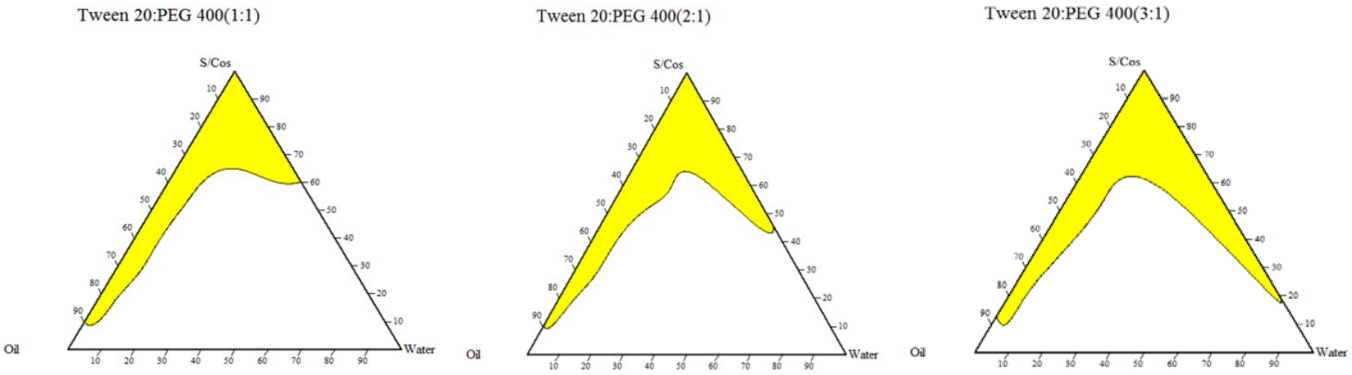


Fig. 4: Pseudoternary Phase diagram of surfactant: co-surfactant ratio of 1:1, 2:1 and 3:1 with oil: Smix in the ratios ranging from 1:9 to 9:1

Table 3: Evaluation parameters of Meloxicam emulsion

Formulation code	Drug content (%)*	Globule size (nm)	Zeta potential*
E1	93.31±1.22	176.8	-53.73±1.28
E2	90.40±0.77	399	-41.2±1.35
E3	88.6±2.34	504	-34.5±3.76
F1	92.34±4.08	128	-50.6±0.46
F2	87.6±1.94	338	-38.3±0.96
F3	87.2±4.37	454	-27.6±0.44
G1	91.76±1.59	17.93	-43.28±1.62
G2	75.48±4.19	202.4	-31.65±0.55
G3	86.8±2.26	347	-28.56±0.88

*All values are expressed as mean±SD(n=3)

Characterization of Emulgel

Appearance, Drug content and pH: All the prepared formulations were pale yellow in appearance and they showed good homogeneity and consistency. The percentage drug content of prepared emulgel was found in the range of 90.51 to 94.98%. The results were depicted in the table 4. The highest drug content i.e. 94.98% was obtained for the formulation M2F1 containing optimized F1

formulation of emulsion and gelling agent present in the concentration of 1.5% of Carbopol 981. The pH of all the formulation was found to be ranging from 6.54 to 6.94 which were found to be acceptable to avoid any skin irritation as shown in fig. 5. All the formulations were free of any lumps and grittiness. The highest drug content i.e. 94.98% was obtained for the formulation M2F1 containing optimized F1 formulation of emulsion and gelling agent present in the concentration of 1.5% of Carbopol 981.

Table 4: Appearance and drug content of Meloxicam Emulgel

Formulation code	Appearance	Drug content (%)*
M1E1(1.5% Carbopol 981)	Pale yellow	94.18±3.713
M2F1(1.5% Carbopol 981)	Pale yellow	94.98±5.074
M'1E1(2%Carbopol 981)	Pale yellow	92.38±2.153
M'2F1(2% Carbopol 981)	Pale yellow	92.78±2.645
P1E1(1.5% Carbopol 974)	Pale yellow	90.51±1.43
P2F1(1.5% Carbopol 974)	Pale yellow	93.59±5.256
P'1E1(2% Carbopol 974)	Pale yellow	91.18±1.707
P'2F1(2% Carbopol 974)	Pale yellow	91.98±1.361

*All values are expressed as mean±SD(n=3)

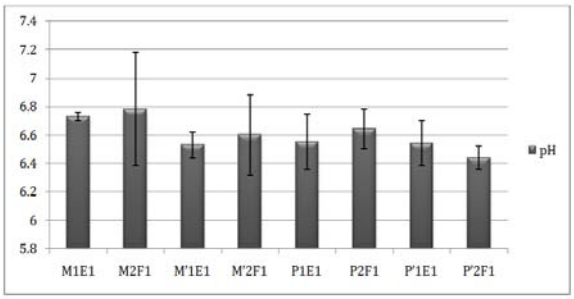


Fig. 5: pH of emu gel formulations M1E1 to P'2F1

Viscosity determination

Viscosities of all the prepared emu gel formulations are shown in fig. 6 the results showed that the emu gel formulation M2F1 showed the lowest viscosity of 12420 cPs and highest viscosity was obtained for P'1E1 i.e. of 37550 cPs. The P'2F1 showed viscosity of 35420, P1E1 and P2F1 showed 31450 and 30100 cPs respectively. The same way M1E1, M'1E1 and M2F1 showed viscosity of 13450, 20105 and 18430 cPs respectively. The emu gel formulation M2F1 containing 1.5 % of Carbopol 981 and optimized emulsion formulation F1 showed the lowest viscosity. It was found that as polymer concentration increases viscosity also increases. The F1 microemulsion formulation contains the larger surfactant concentration as compared to the E1 so its viscosity decreases as mentioned by Ghodekar *et al.* in his work antifungal activity of microemulsion based fluconazole gel. So higher the concentration of surfactant and lower the concentration of gelling agent lower the viscosity. As the concentration of polymer increases to 2% the viscosity also increases. The viscosity of formulation containing Carbopol 974 was more than the one containing Carbopol 981 [13, 15].

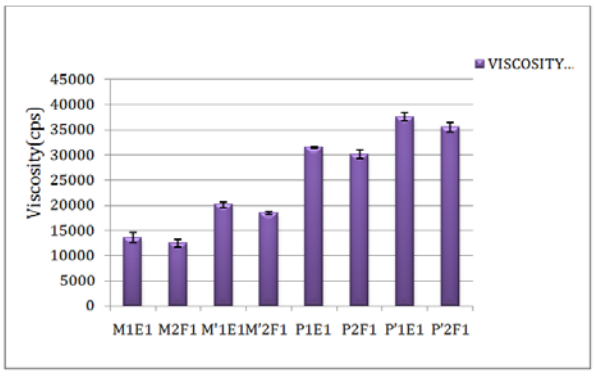


Fig. 6: Viscosity of emulgel formulations M1E1 to P'2F1

Spreadability

The spreadability value of all the prepared emu gel was depicted in the fig. 7. The formulation M2F1 having viscosity 12420 cPs has high spreading coefficient of 14.13. The other formulations showed M1E1, M'1E1, M'2F1, P1E1, P2F1, P'1E1 and P'2F1 showed spreadability of 13.24, 11.75, 12.18, 10.25, 10.75, 8.21 and 8.84 gm. cm/sec respectively. The spreadability is dependent on the concentration of polymer and viscosity of the formulation. The formulation M2F1 having viscosity 12420 cPs showed high spreading coefficient of 14.13. The viscosity increases as the concentration of polymer increases and as the spreadability is dependent on the viscosity so it increases as the viscosity decreases concluding that the formulation spreads well. The spreadability of formulation containing 2% concentration was found to be lower than the one containing 1.5% concentration of polymer. The spreadability of the formulations containing differs from polymer to polymer so the one containing Carbopol 974 spreads less than the one containing Carbopol 981.

Extrudability

The extrudability of the prepared emulgel is depicted in fig. 7. The formulation M2F1 has extrudability value of 15.52 gm/cm^2 as its viscosity was 12420 cPs. The other formulations M1E1, M'1E1, M'2F1, P1E1, P2F1, P'1E1, P'2F1 showed extrudability value of 13.53, 9.95, 10.75, 7.96, 7.16, 7.56 gm/cm^2 respectively. The extrudability is dependent on the viscosity of the polymer so as the viscosity increases extrudability decreases. As the viscosity depends on the type of polymer and its concentration and even on the surfactant concentration so the extrudability value of the formulation containing M1F1 was higher as compared to other formulations and the extrudability was found to be less for the formulation P'2E1 containing Carbopol 974 and E1 emulsion formulation.

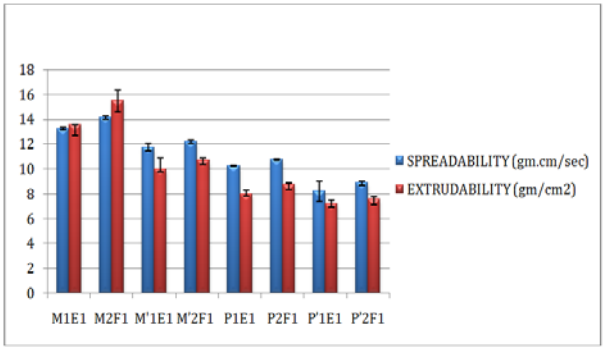


Fig. 7: Spreadability and Extrudability of emulgel formulation M1E1 to P'2F1

In vitro drug release

The percentage cumulative drug release of all the prepared emulgel formulations at the end of 8 h is represented graphically in the fig. 8 and 9. Maximum drug release was observed for the formulation M2F1 i.e. of 89.934% and minimum was obtained for P'1E1 i.e. of 74.26 %. The pure drug showed release of 52.162% at the end of 8h. It is represented graphically in fig. no 10. Maximum drug release was observed for the formulation M2F1 i.e. of 89.934%. The reason attributed for a higher release is the lower concentration of gelling agent i.e. 1.5% of Carbopol 981 employed in that formulation and the concentration of the optimized microemulsion formulation F1 which contains 2:1 ratio of surfactant and co-surfactant as the release of drug from microemulsion may be more because of the larger concentration of surfactant and even it has lower droplet size and as the release rate is inversely related to particle size i.e. smaller the droplet size higher the release.

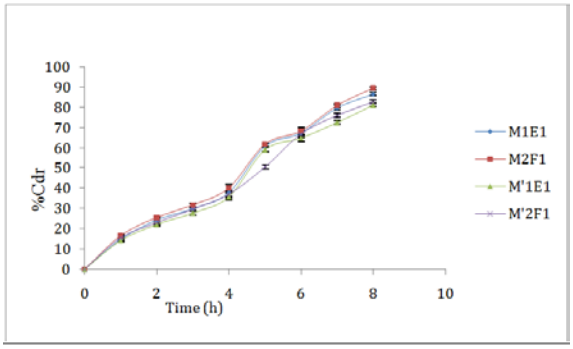


Fig. 8: *In vitro* release profile of M1E1 to M'2F1containing Carbopol 981 as gelling agent

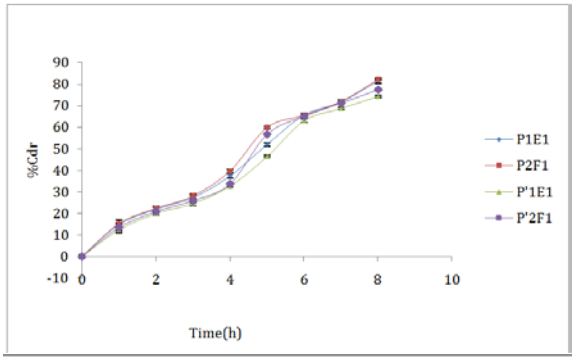


Fig. 9: *In vitro* release profile of P1E1 to P'2F1 containing Carbopol 974 as gelling agent

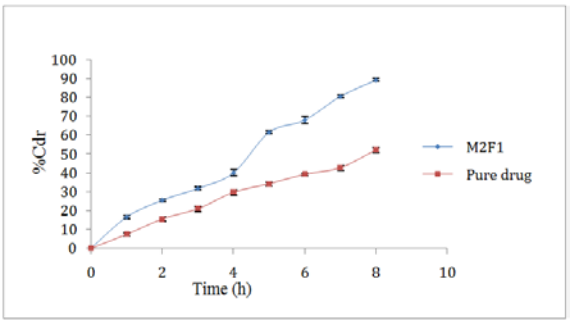


Fig. 10: *In vitro* release profile of optimized formulation and pure drug

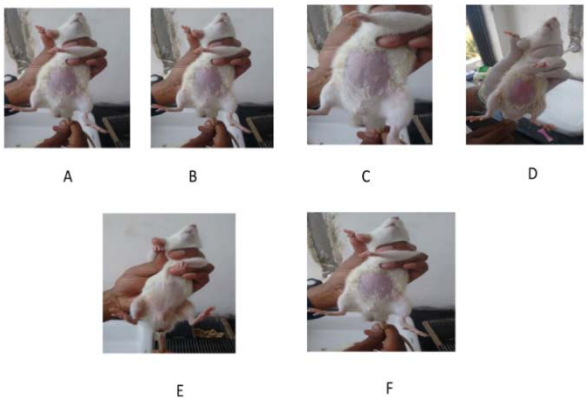
The release is dependent on the polymer concentration and the viscosity of polymer. The formulation containing higher concentration of polymer will show lower percentage cumulative release as the concentration increases viscosity increases which retards the drug release. The percentage cumulative release of optimized formulation was compared with that of the pure drug incorporated into the Carbopol 981 gel base. The pure drug showed release of 52.162% at the end of 8 h, as the drug being water insoluble it may not have been properly dispersed in the gel base and so the release is retarded [9, 11].

In vitro drug release kinetics

The best fit model in the optimized formulation was found to be the Korsmeyer Peppas and its n value is greater than 0.89it follows super case II transport i.e. the drug release doesn't change over time and it involves polymer relaxation and chain disentanglement. The formulations P1E1 and P'1E1 follows zero order release pattern as the correlation coefficient values are higher in case of zero order and also the release rate is independent of the concentration of the drug. The other formulations showed Peppas as the best fit model. The n value of Korsmeyer Peppas is greater 0.5 so it follows the non-fickian diffusion. The n value of Korsmeyer Peppas is greater than 0.5 so it follows the non-fickian diffusion. ie drug release is both diffusion and erosion controlled mechanism [17, 18].

Skin irritation test

The score given for the standard group was 2.5 and for test group was 0. In case of standard group, there was moderate erythema with barely perceptible edema was and the test group showed no irritation. As shown in fig. 11. Since no irritation persists the optimized formulation passes the skin irritation test.



A-Control group after shaving, B-Control group after 24 h, C-Standard group (0.8% Formalin), D-Standard group after 24 h of application of formalin, E-Test group after shaving, F-Test group 24 h after application of optimized M2F1 formulation
Fig. 11: Skin irritation test on male Wistar Rats

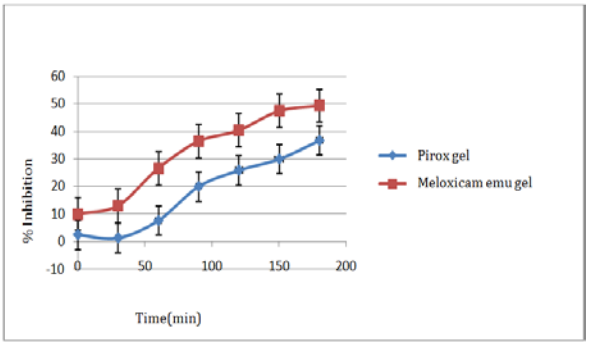


Fig. 12: Percentage inhibition of anti-inflammatory study of optimized Meloxicam loaded Emulgel formulation M2F1 and standard Pirox gel Stability studies

***In vivo* anti-inflammatory study**

The test and standard formulations exhibit anti-inflammatory effect for 3 h and the % inhibition of standard group at the end of 3 h is 36.71% and that of the test group is 49.38 %. It can be concluded from the above results that the test formulation shows better anti-inflammatory effect as compared to the standard group. The results were depicted in fig. 12. From the results, it was found that the optimized formulation has better ability to decrease the paw volume of the rat and the % inhibition was found to be more than the standard formulation. It can be concluded from the above results that the test formulation shows better anti-inflammatory effect as compared to the standard group.

Formulation M2F1 showed no change in appearance after 60 d of storage. The pH, viscosity and percentage cumulative release showed the minor difference in the values so the formulations were found to be stable at the end of 60 d. The viscosity showed slight increase after 30 d at 25 °C and slight decrease at the end of 60th day. The viscosity was found to decrease at 40 °C. The drug release was found to decrease as the temperature increases and as the day passes. The pH of the formulation was found to increase slightly [15].

CONCLUSION

Based on saturation solubility study Oleic acid, Tween 20 and PEG 400 were selected for the preparation of the emulsion. The emulsion was successfully prepared using water titration method. The optimized formulations of emulsion i.e. E1 and F1 showed globule size of 176.8 and 128 nm respectively. The emulgel formulations were prepared with Carbopol as gelling agent with concentrations of 1.5% and 2% using oleic acid as penetration enhancer enhances the ease of application onto the skin. The prepared emulgel for topical application with required viscosity, spreadability, extrudability, drug release and stability showed better results and the optimized formulation showed no irritation to skin and better anti-inflammatory result as compared to marketed one. Thus, it can be concluded that Meloxicam was proven to be a suitable candidate for formulating emulgel for topical delivery to achieve better patient compliance. The emulgel could help significantly to optimize the targeting of the drug without a concomitant increase of the systemic side effects.

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CONFLICT OF INTERESTS

Declared None

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