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Research Article

Investigation of Hydrogel Thickened Microemulsion for Topical Administration of Meloxicam

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ABSTRACT

The present study was conducted to investigate the microemulsion based gel of meloxicam in order to bypass gastrointestinal side effects with more patient compliance. Microemulsion existence range was defined by pseudo ternary phase diagram. Pseudoternary phase diagrams were developed for combination of Isopropyl Myristate (oily phase), Tween80:PEG400 (surfactant : cosurfactant) and water (aqueous phase) with Aqueous phase titration method. Various microemulsion formulations were prepared and further evaluated for various parameters like pH, conductance, transmittance, drug release, etc. Optimized formulation of Microemulsion was thickened with gelling agent Carbopol 940 to yield a gel with desirable properties facilitating the topical application. Safety of formulation was evaluated using skin irritancy test. Simple Meloxicam gel and optimized microemulsion gel then subjected to in vitro drug release comparison study. Drug exhibited maximum solubility in Iso propyl Myristate as oily phase among all selected oils and maximum solubility in Tween80 and Polyethylene Glycol 400(PEG400) as surfactant and cosurfactant. The pseudoternary phase diagram has been delineated at surfactant : cosurfactant ratio 2:1. Microemulsion showed -0.5 zeta potential which is desirable for its stability and average particle size was obtained less than 200nm. Microemulsion based gel afford better drug release when compared to simple gel. Present work concluded that microemulsion based gel can be promising formulation for application of Meloxicam with good patient compliance too in treatment of rheumatoid arthritis, osteo arthritis and ankylosing spondylitis.

Keywords: Meloxicam, Microemulsion, Hydrogel, Topical Administration

INTRODUCTION

INTRODUCTION TO TRANSDERMAL DRUG DELIVERY SYSTEM

Transdermal drug delivery systems are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. In order to deliver therapeutic agents through the human skin, the comprehensive morphologi -cal, biophysical and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectable and oral routes by increasing patient compliance. So transdermal drug delivery - an approach used to deliver drugs through the skin for therapeutic use as an alternative to oral, intravascular, subcutaneous and transmucosal routes. The human skin is a readily accessible surface for drug delivery [1,2]. Subcutaneous layer is the principle barrier layer of skin. Any topical dosage form has to cross it to penetrate inside the skin.

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The microemulsion concept was introduced as early as the 1940s by Hoar and Schulman[3]who generated a clear single-phase solution by titrating a milky emulsion with hexanol. Subsequently the term microemulsion defined and indeed redefined on many occasions. Thus it defined as "a system of water, oil and amphiphile which is a clear and thermodynamically stable liquid solution."

There are three types of microemulsions which are most likely to be formed depending on composition [4,5]. O/W type, W/O type and Bicontinuous.

The miscibility of oil, water and amphiphile (surfactant plus co-surfactant) depends on the overall composition, which is system specific. Ternary (water/amphiphile/oil) and quaternary (water/surfactant/co-surfactant/oil) phase diagrams can describe the phase manifestations and are essential in the study of microemulsion. Phase diagram is the vital step to know the existence of microemulsion. Such characteristics textures are commonly referred as Winsor phases [5,6] and the classification is distinguished as below.

Winsor I: with two phases, the lower or single phase region of common micelles (o/w) microemulsion phase in equilibrium with the upper excess oil;

Winsor II: with two phases, the upper microemulsion phase or a reverse micelle phase (w/o) in equilibrium with lower excess water;

Winsor III: with three phases, middle microemulsion phase so called bicontinuous phase (o/w plus w/o) in equilibrium with upper excess oil and lower excess water;

Winsor IV: in single phase, with oil, water and surfactant homogeneously mixed.

Much attention has been focused on the topical delivery of many drugs through microemulsions. Microemulsions are well known to improve the absorption and bioavailability of many compounds so their topical application is widespread, especially in the case of anti-inflammatory drugs or hormones. Skin is very big barrier in transportation of drug. So from microemulsion lipophilic domain of emulsion interact with stratum corneum so increase permeability while hydrophilic domain hydrate stratumcorneum and this will increase lamellar volume of lipid bilayer and thus interfacial structure disrupt and so facilitation of drug transport through skin.

Meloxicam is a potent non-steroidal anti-inflammatory (NSAID) drug [7,8] used orally to alleviate the symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. NSAID inhibits cyclooxygenase (COX), the enzyme responsible for converting arachidonic acid into prostaglandin H_2-which are mediators of inflammation. Meloxicam is enolic acid class of oxicam derivatives which shows preferential inhibition of cyclo-oxygenase-2 (COX-2) over COX-1. It is believed that local accumulation of the drug in target tissues could occur either by direct penetration or via redistribution through systemic circulation. It has been suggested that drugs passing through the stratum corneum, epidermis, and dermis can be effectively removed by cutaneous microcirculation, which can act as a "sink" (Yue Y et al,2012).Meloxicam is practically insoluble in water and soluble at higher pH. As being NSAID it is having gastric side effects. So to overcome problems like side effects and water solubility microemulsion based gal can be the best dosage form. It is locally acting dosage form so will give fast relief in symptoms and also better patient compliance due to less side effects. Aim of present study was to overcome drug side effects and to enhance patient compliance with suitable dosage form.

MATERIALS AND METHODS

MATERIALS

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Meloxicam was gifted by Apex Healthcare, Gujarat, India. IPM, PEG 400, Triethanolamine and Tween 80 were obtained from Qualikem Fine Chemicals Pvt. Ltd., New Delhi, India. Carbopol 940 was obtained from Loba chem., Vadodara, India.

Screening of oils, surfactants and co-surfactants for microemulsion [2,9]:

The solubility [10] of meloxicam in various oils (IPM, IPP, oleic acid, Eucalyptus Oil, Castor oil), surfactants (Tween 20 & tween 80), cosurfactants (PG and PEG 400) was determined by dissolving an excess amount of meloxicam in 2 mL of each of the selected oils, surfactants, and co-surfactants in 5 mL capacity stoppered vials separately to determination of solubility. They were stirred continuously for 72 h at 37 ± 1°C. After equilibrium was attained, the mixture was centrifuged at 3000 rpm for 10 min; the supernatant layer was carefully removed and then diluted with a solution. The concentration of drug was then measured using UV/Visible spectrophotometer by comparison with a standard calibration curve.

Construction of Pseudo-Ternary phase Diagrams [11]:

Phase Titration method:

In order to find out the concentration range of components for the existence range of microemulsions, pseudo-ternary phase diagrams were constructed using H_2O titration method at ambient temperature (25 ºC). Three phase diagrams were prepared with the weight ratios 1:1, 2:1 and 3:1 of Tween 80 to PEG 400 respectively. For each phase diagram at specific surfactant/co-surfactant weight ratio, the ratios of IPM to the mixture of surfactant and co-surfactant were varied as 1:9 to 9:1. These mixtures were titrated drop wise with water under gentle magnetic stirring. After being equilibrated the systems were visually characterized. Persistent turbidity up to 24hr considered as end point. Transparent fluid systems were characterized as microemulsion. Highly viscous systems that did not show a change in the meniscus after being tilted to an angle of 90◦ were considered as gel.

Method of preparation of meloxicam loaded microemulsion:

Meloxicam was added to the oil. Varying ratios of S_{mix} (surfactant + cosurfactant) and water was taken. Meloxicam microemulsion was obtained by adding oil and drug mixture to water phase drop by drop with moderate stirring at ambient temperature.

Method of preparation of microemulsion based gel [12,13]:

Gelling agents were evaluated for their ability to Gel meloxicam microemulsion. Briefly, meloxicam microemulsion was prepared as per section 2.4. Then gelling efficiency of gelling agents like poloxamer 407(20%) [14,15] and carbopol 940(1%) [16] were decided. After optimization plain gel of desired gelling agent i.e Carbopol 940 was prepared with 3 different concentrations to get better gel with optimum concentration.

After formation of plain gel prepared microemulsion was added to that gel upto its efficiency. Efficiency of gel for having microemulsion with desired characteristics was checked. Then amount of Meloxicam for 2gm gel was calculated. 0.4%w/w [17] gel was prepared.

Method of Preparation of Simple Meloxicam Gel [18]:

Meloxicam gel formulation was prepared by using Carbopol 940 as gelling agent. Plain carbopol gel with concentration of 2.5% was prepared with water. Meloxicam was dissolved in PEG400 and then poured into previously prepared plain gel. 0.4% Meloxicam gel was prepared and then compared with results of microemulsion gel.

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CHARACTERIZATION

CHARACTERIZATION OF MICROEMULSION:

Particle size, Size distribution and Zeta potential:

The particle size, size distribution and zeta potential were determined using a computerized inspection system with zeta sizer.

Determination of pH [19]:

The pH values of 1% aqueous solutions of the prepared microemulsions were measured by a pH meter. The glass electrode was calibrated with two standard buffers (pH of 4.00 and 9.00). The preparation was left for about 15 min for attaining equilibrium while measuring.

Viscosity:

Viscosity of microemulsion formulation was measured by Brookfield Viscometer. Apparent viscosity was measured rotating the RV spindle 2 at 2 and 5 rpm at 30ºC.

% drug Content:

1 ml microemulsion dissolved in solvent mixture (Ethanol + 0.1N NaOH) and measure drug content through UV spectrophotometer at 364 nm [20]

Percent transmittance (%T) [21]:

Transparency of microemulsion formulation was determined by measuring the percentage transmittance with purified water taken as blank through UV spectrophotometer.

Conductance [22]:

The conductive measurements were taken by a conductivity meter. The microemulsion prepared with addition of water was measured after thorough mixing and temperature equilibration at 25°C, the electrode was dipped in the microemulsion sample until equilibrium was reached, and reading becomes stable.

In-vitro drug release study [23,24[:

An essential parameter in the evaluation of drug delivery is the rate at which the drug is released from the carrier. Skin permeation study with drug-containing microemulsion formulation was carried out using modified Franz diffusion cell. Full thickness abdominal skin of male Wister albino rats weighing 140 to 200 g was used for the skin permeation. Briefly, to obtain skin, animal was sacrificed. Hair from the abdominal region was carefully removed and an excision in the skin was made. The dermal side of the skin was thoroughly cleaned of any adhering tissues. Dermis part of the skin was wiped 3 to 4 times with a wet cotton swab soaked in isopropanol to remove any adhering fat. The skin specimen was cut into appropriate size after carefully removing subcutaneous fat and washing with normal saline.

Skin was mounted in a modified Franz diffusion cell, kept at 32±0.5ºC. The known quantity of microemulsion equivalent to 8 mg of drug was put uniformly on the skin on donor side. PH 7.4 phosphate buffer [17] was used as the acceptor medium, from which samples were collected at regular intervals. Collected samples were estimated with UV spectroscopy at 364 nm. All permeation experiments were repeated three times and data were expressed as mean of three experiments ± standard deviation (SD).

CHARACTERIZATION OF MICROEMULSIONGEL:

Determination of drug content:

For determination of drug content, about 1 g of the gel is been weighed in a 100-ml volumetric flask and dissolved in suitable solvent. It is diluted appropriately and drug content is been determined at 364 nm using Shimadzu – 1700 UV Visible spectrophotometer.

pH:

The pH value of 1% aqueous solutions of the prepared gels is measured by a pH meter. The glass electrode is calibrated with two standard buffers (pH of 4.00 and 9.00).The preparation is

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left for about 15 min for attaining equilibrium while measuring.

Viscosity:

Microemulsion based gel is evaluated for viscosity under constant temperature, RV spindle 2 and 5 rpm by using Brookfield viscometer at 30ºC.

Drug Release:

An essential parameter in the evaluation of drug delivery is the rate at which the drug is released from the carrier. Skin permeation study with drug-containing microemulsion based gel formulation was carried out using modified Franz diffusion cell. Full thickness abdominal skin of male Wister albino rats weighing 140 to 200 g was used for the skin permeation. Briefly, to obtain skin, animal was sacrificed. Hair from the abdominal region was carefully removed and an excision in the skin was made. The dermal side of the skin was thoroughly cleaned of any adhering tissues. Dermis part of the skin was wiped 3 to 4 times with a wet cotton swab soaked in isopropanol to remove any adhering fat. The skin specimen was cut into appropriate size after carefully removing subcutaneous fat and washing with normal saline.

Skin was mounted in a modified Franz diffusion cell, kept at 32±0.5ºC. The known quantity of microemulsion based gel equivalent to 4 mg of drug was put uniformly on the skin on donor side. pH 7.4 phosphate buffer was used as the acceptor medium, from which samples were collected at regular intervals. Collected samples were estimated with UV spectroscopy at 364 nm. All permeation experiments were repeated three times and data were expressed as mean of three experiments ± standard deviation (SD).

Calculation of steady state skin flux (J_{flux}) of formulation [25]:

Skin flux (mg/cm^2/h) (J_{flux}) is determined from Fick's first law of diffusion:

J_{flux}= (dM/dt) × V / A

Where,

dM/dt = amount of meloxicam penetrated per unit time

A = effective diffusion area

V= volume of receiver compartment (ml).

Steady state skin flux (J_{flux}) was determined from the slope (dM/dt) of the linear portion of a cumulative penetration time curve.

Kinetic modeling [6,19]:

In order to understand the kinetics and mechanism of drug release, the results of in vitro drug release are fitted into various kinetic equations like zero order (cumulative % release vs. time), first order (log % drug remaining vs. time), Higuchi's model (cumulative % drug release vs. square root of time), Krosmeyer peppas plot (log of cumulative % drug release vs. log time). R^2 (coefficient of correlation) were calculated for the linear curve obtained by regression analysis of the in vitro drug permeation plots.

Primary skin irritation studies [26]:

The optimized gel formulation was evaluated for skin irritation studies on healthy rats. The hairs of the dorsal portion were removed physically with the help of sharp surgical scissors and the skin was washed properly one day prior to use. Rats were divided into four groups (six rats in each group):

Group I: Normal: No treatment was given.

Group II: Blank: Blank gel (without drug) was secured.

Group III: Medicated: Medicated gel (with meloxicam) was secured.

Group IV: Formalin: 0.8%v/v aq. solution of Formalin was applied as a standard irritant

The gel was removed after each 48 hr. and the area examined for any signs of skin sensitivity or irritation and the fresh gel was secured at the same site at 2nd, 4th, 6th day. All the respective treatments were continued till 7 days and finally application sites were monitored visually.

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RESULTS

Solubility:

Solubility studies of meloxicam in oils:

Table 1: Solubility studies of meloxicam in oils

OILS	SOLUBILITY(mg/ml)
Iso propyl myristate(IPM)	2.88±0.05
Iso propyl palmitate(IPP)	1.85±0.04
Oleic acid(OA)	1.33±0.02
Castor oil	1.17±0.03
Eucalyptus oil	0.98±0.07

N=3

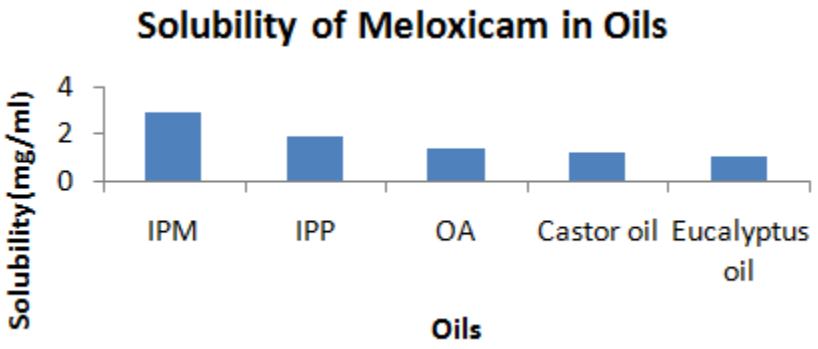

Figure 1: Solubility studies of meloxicam in oils

Solubility studies of meloxicam in surfactants:

Table 2: Solubility studies of meloxicam in surfactants

SURFACTANTS	SOLUBILITY(mg/ml)
TWEEN80	5.674±0.04
TWEEN20	4.973±0.04

N=3

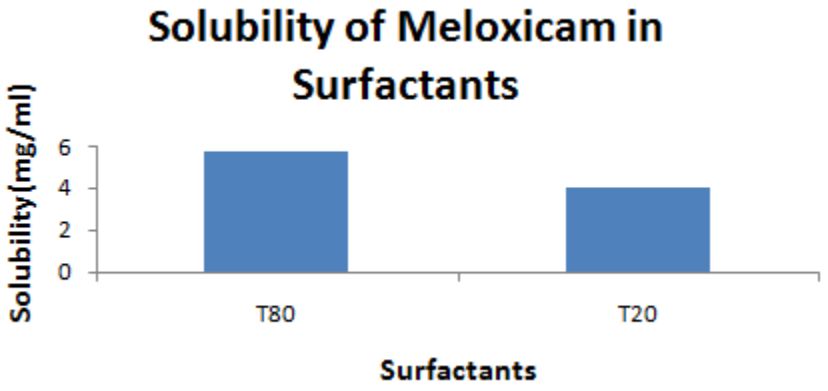

Figure 2: Solubility studies of meloxicam in surfactants

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Solubility studies of meloxicam in co-surfactants:

Table 3: Solubility studies of meloxicam in co-surfactants

COSURFACTANTS	SOLUBILITY(mg/ml)
PEG 400	10.213±0.1
PG	8.909±0.06

N=3

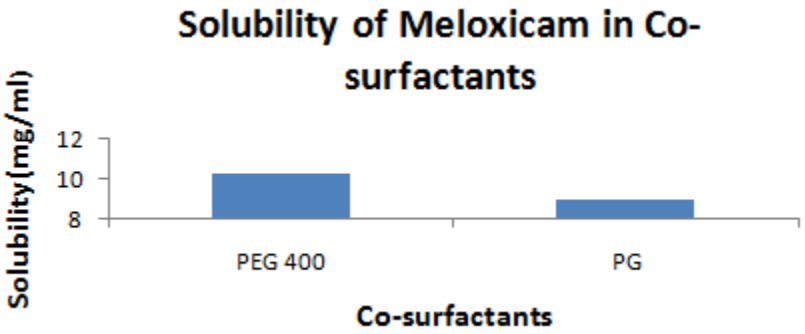

Figure 3: Solubility studies of meloxicam in co-surfactant

RESULTS OF PSEUDO TERNARY PHASE DIAGRAM:

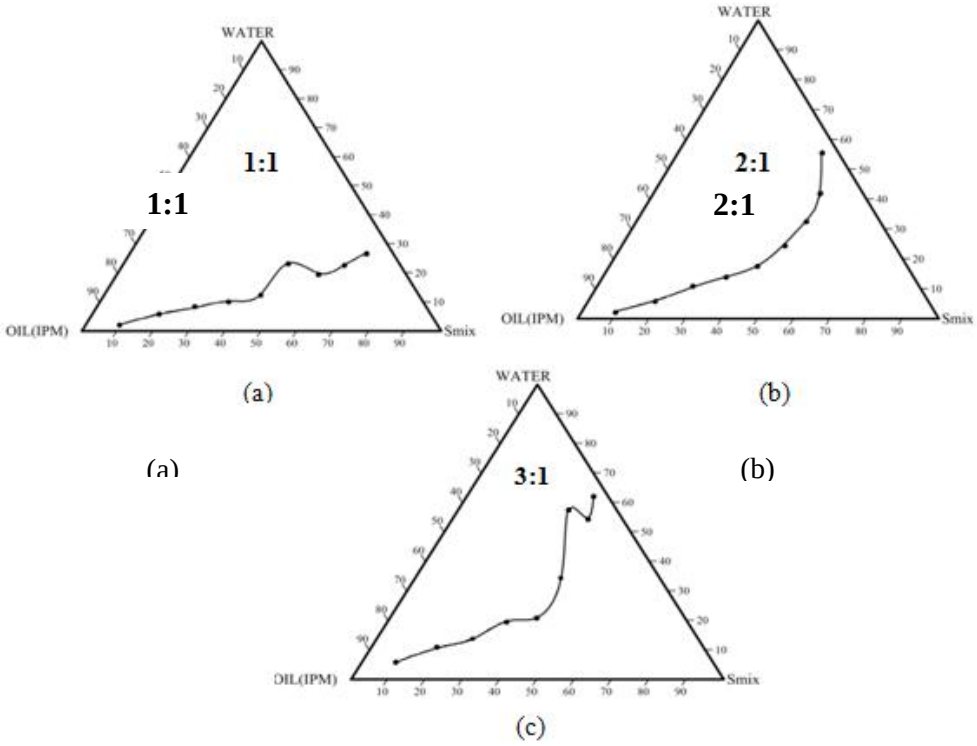

Figure 4: Pseudo ternary phase diagrams (a) 1:1, (b) 2:1, (c) 3:1 ratio of S_{mix} i.e. s:co::Tween80:PEG 400

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Table 4: Formulations of microemulsions of 2:1 ratio of Surfactant: co-surfactant

BATCH	IPM (%)	TWEEN 80: PEG400 (%) (2:1)	WATER (%)
F1	4	35	61
F2	5	40	55
F3	5	45	50
F4	6	60	34
F5	7	43	50
F6	9	55	36
F7	9	45	46
F8	9	35	56
F9	10	45	46
F10	10	55	36

Table 5: Evaluation of microemulsion formulation

BATCH	pH	%DRUG CONTENT	%TRANSMITTANCE
F1	6.10±0.01	69.25±0.04	81.3±0.14
F2	6.56±0.01	74.34±0.05	85.7±0.14
F3	6.12±0.00	75.23±0.02	82.3±0.14
F4	7.12±0.01	79.17±0.03	83.9±0.00
F5	7.01±0.02	85.16±0.03	92.3±0.14
F6	6.71±0.01	97.99±0.04	99.8±0.07
F7	6.39±0.01	92.64±0.04	99.6±0.14
F8	6.52±0.01	90.94±0.02	94.2±0.14
F9	6.22±0.01	84.33±0.03	89.7±0.14
F10	6.28±0.02	85.51±0.04	99.6±0.07

N=3

Table 6: Evaluation of microemulsion formulation

BATCH	CONDUCTANCE (µs/cm)	%CUMULATIVE DRUG RELEASE IN 240min.	VISCOSITY (Spindle 5)	
			2 RPM	5 RPM
F1	145.5±0.85	47.45±0.55	61±1.41	56±2.45
F2	170.2±1.13	59.87±0.29	54 ±5.66	50±2.56
F3	168.3±0.99	73.49±0.71	48±3.54	45±0.12
F4	165±2.33	91.54±1.13	72±2.12	68±4.67
F5	147.4±2.47	91.84±0.35	58±2.83	53±1.32
F6	165.6±1.27	95.91±0.64	67±0.71	59±2.45
F7	140.4±1.56	93.34±1.27	62±1.41	56±1.78
F8	132.3±0.64	74.89±0.55	78±0.00	71±1.41
F9	173.7±1.48	79.41±0.04	81±1.41	73±5.66
F10	178.2±1.7	81.21±1.32	75±4.24	63±2.83

N=3

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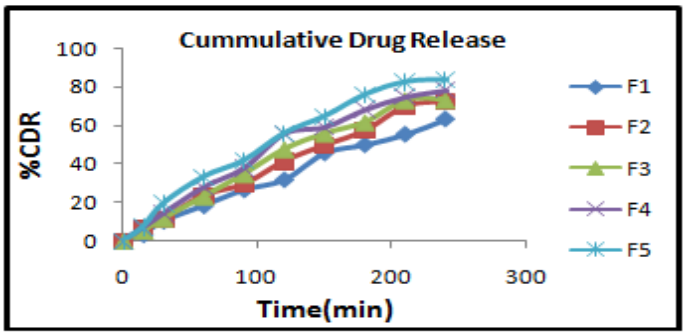


Figure 5: Cumulative Drug release of batches F1-F5

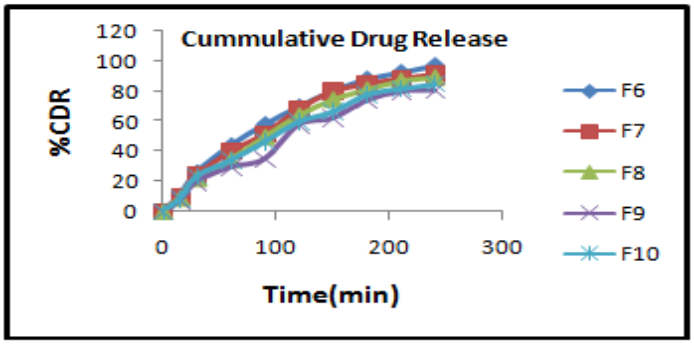
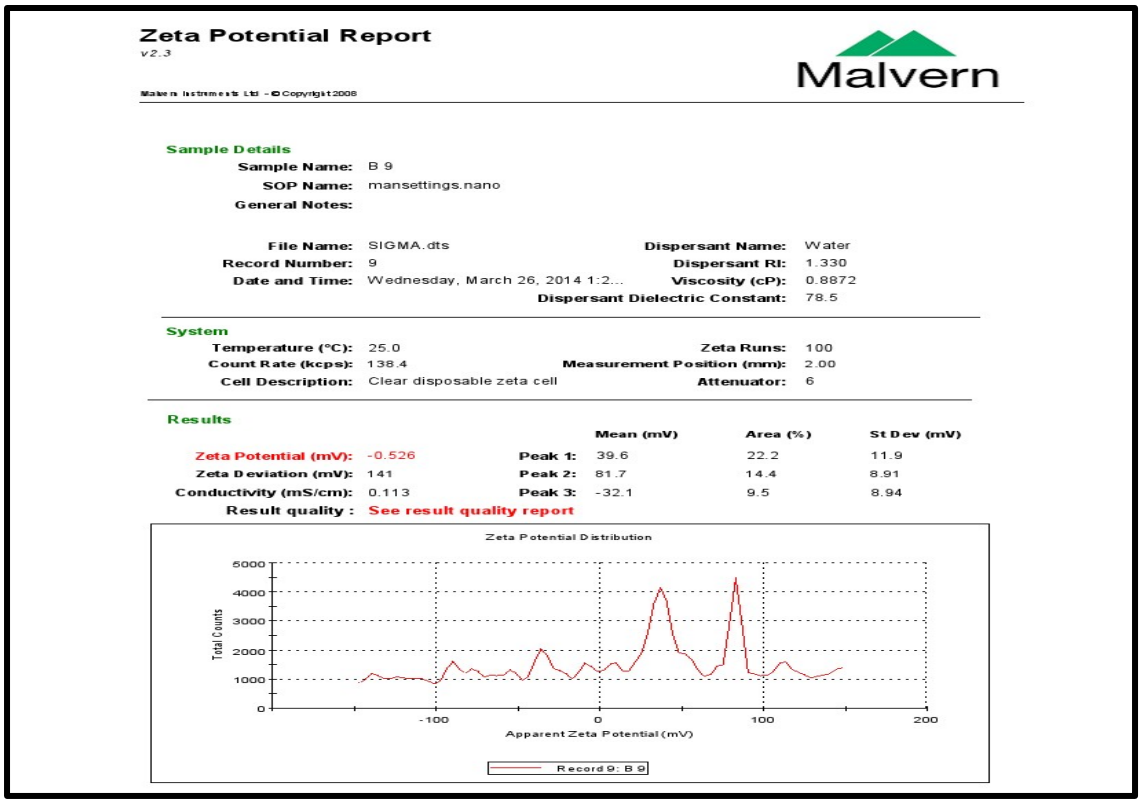


Figure 6: Cumulative Drug release of batches F6-F10



Zeta Potential Report
v2.3

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Sample Details

Sample Name:	B 9		
SOP Name:	mansettings.nano		
General Notes:			
File Name:	SIGMA.dts	Dispersant Name:	Water
Record Number:	9	Dispersant RI:	1.330
Date and Time:	Wednesday, March 26, 2014 1:2...	Viscosity (cP):	0.8872
		Dispersant Dielectric Constant:	78.5

System

Temperature (°C):	25.0	Zeta Runs:	100
Count Rate (kcps):	138.4	Measurement Position (mm):	2.00
Cell Description:	Clear disposable zeta cell	Attenuator:	6

Results

		Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV):	-0.526	Peak 1:	39.6	22.2	11.9
Zeta Deviation (mV):	141	Peak 2:	81.7	14.4	8.91
Conductivity (mS/cm):	0.113	Peak 3:	-32.1	9.5	8.94
Result quality :	See result quality report				

Figure 7: Zeta potential of Microemulsion Batch F6

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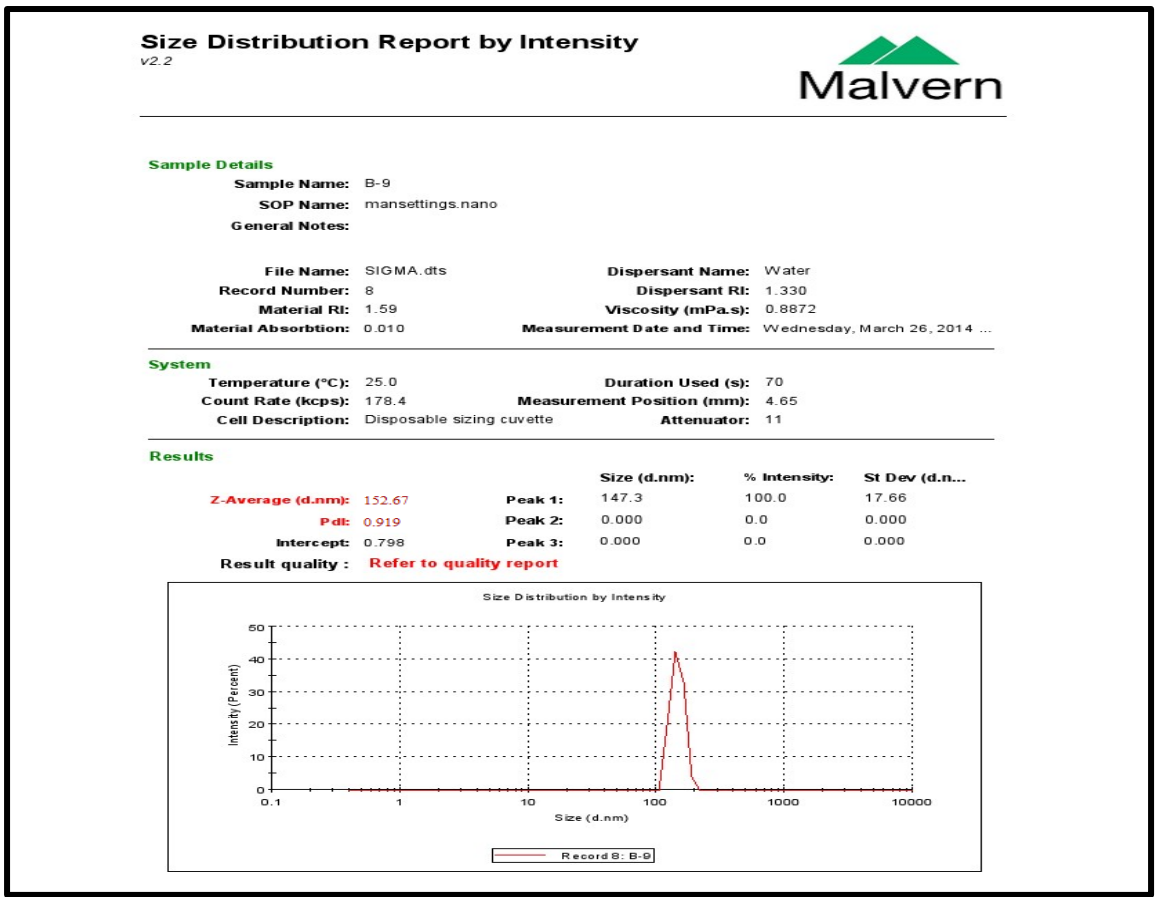

Figure 8: Size Distribution of Microemulsion Batch F6

Formulation Table of Microemulsion Gel:

Table 7: Formulation table microemulsion based gel of optimized microemulsion batch F6

INGREDIENTS	G1	G2	G3
MELOXICAM (%)	0.4	0.4	0.4
IPM (%)	9	9	9
TWEEN80:PEG400 (%)	55	55	55
Water (%)	36	36	36
Carbopol 940	1.5	2	2.5
Triethanolamine	q.s	q.s	q.s

Results of Evaluation of microemulsion based gel:

Table 8: Evaluation of Microemulsion Based Gel

Sr.No	Viscosity(Cps)(2 RPM)	Drug Content (%)	Drug Release (%)
1	4500±124.72	94.89±1.13	76.10±0.12
2	5200±124.72	95.34±0.8	78.28±0.9
3	6100±169.97	97.75±0.65	100±0.1

N=3

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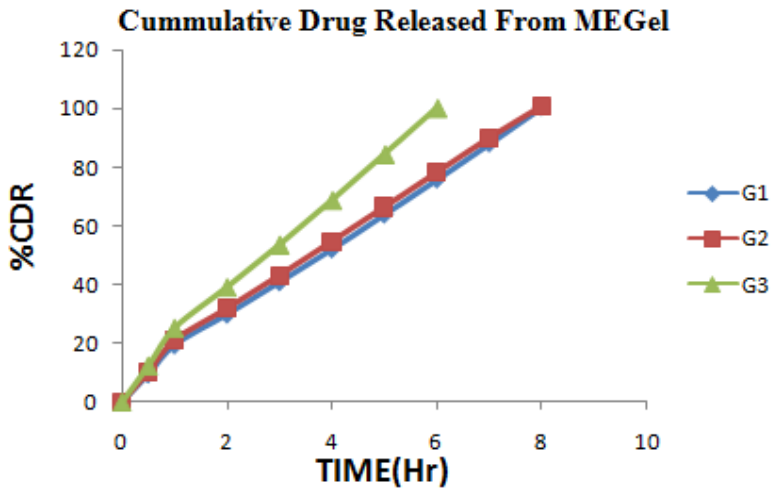

Figure 9: Cumulative Drug Release of batches G1-G3

Table 9: Kinetic fitting results of Meloxicam released from microemulsion

Formulation Code	Correlation coefficient (R^2)				Release mechanism
	Zero order	First order	Higuchi	Peppas	
G3	0.9038	0.7403	0.8495	0.8782	Zero order

Comparison between Permeation of Simple Meloxicam gel and Microemulsion based meloxicam gel (G3)

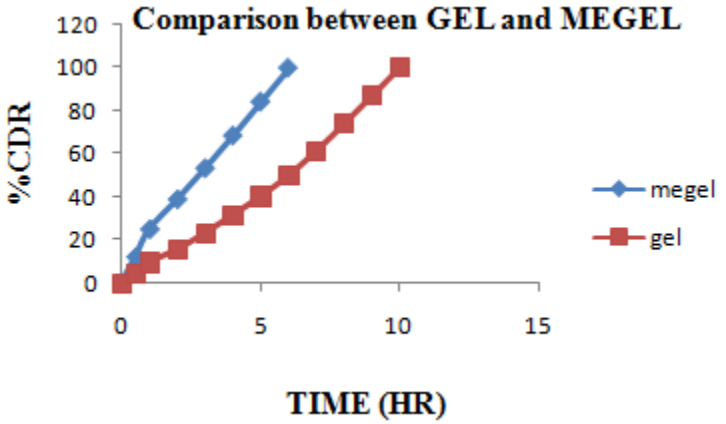

Figure 10: Comparison between Release from GEL and MEGEL (G3)

J_{flux} of formulation:

The J_{flux} of optimized microemulsiongel formulation G3 and Plain gel of Meloxicam were found to be 309.72 and 193.54 µg/cm^2/hr. respectively which areshowed in table 10.

Table 10: J_{flux} of various formulations

FORMULATION	J_{flux} (µg/cm^2/hr)
Meloxicam Microemulsion Gel	309.72
Meloxicam Plain Gel	193.54

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Skin Irritancy Study:

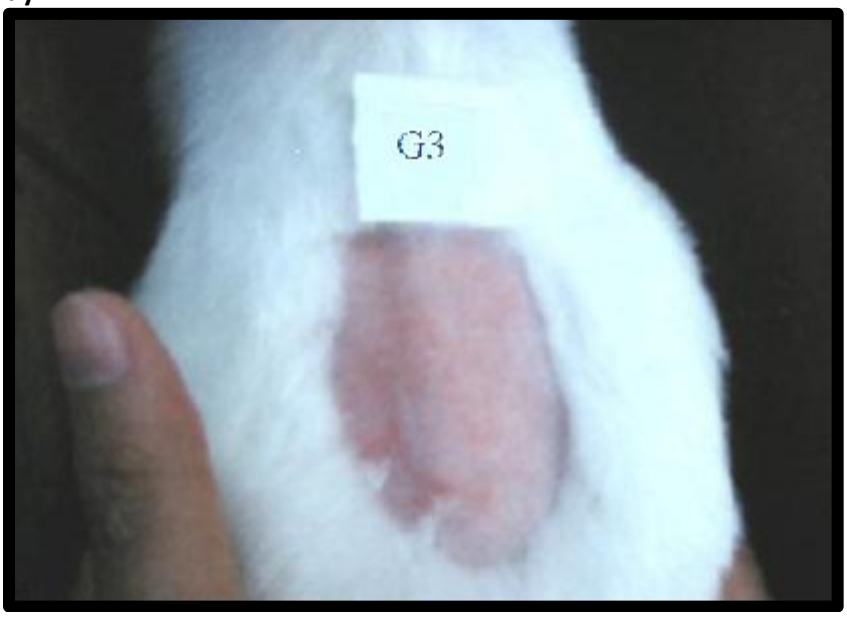

Figure 11: Skin irritation study on rat skin

On application of final formulation on excised skin of rat no any edema was foundupto 7 days. This meant that formulation is non-irritant to skin.

DISCUSSION

The solubility of meloxicam was highest in IPM followed by IPP, castor oil, eucalyptus oil and oleic acid. Based on the solubility studies of meloxicam in oils, surfactants, and co-surfactants we found IPM, tween 80 and PEG400 could be the most appropriate combination for development of microemulsion as they are showing higher solubility.

After screening of components pseudoternary phase diagram was plotted. The aim of the construction of pseudo-ternary phase diagrams was to find out the existence range of microemulsions[17] and it helps in finding out the concentration range of the components for the formation of clear and stable microemulsion systems. From the results of the pseudo-ternary phase diagram, 2:1 ratio of S_{mix} was selected for microemulsion preparation. It was observed that as S_{mix} ratio increased microemulsion existence area also increased but problem with 3:1 ratio was that it gave much thickened solution. Optimum microemulsion formula was selected using phase studies employing IPM as oily phase, tween 80 as surfactant, PEG400 as co-surfactants and distilled water as aqueous phase. Suitable formulas were hence selected from the phase diagram.

The clarity of microemulsions was checked by transparency, measured in terms of transmittance (%T) [21]. Formulation F6, F7and F10 has % transmittance value greater than 99%.These results indicate the high clarity of microemulsion. Lower percentages of transmittance indicate higher globule size in microemulsion.

The pH of the microemulsion was found to be in the range of 6-7.The range of drug content was from 69.25% to 97.99% which is desirable.

Rheological behaviour of microemulsion systems indicated that the systems were non - Newtonian in nature showing decrease in viscosity at the increasing shear rates. W/O type

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of microemulsions shows about 50 µs/cm conductivity while of o/w reaches above 100µs/cm [17]. The Conductance of All Microemulsion Formulation was found to be 132.3 to 178.2 µs/cm. It concluded that all formulation was o/w microemulsion.

In-vitro drug release from formulations is a valuable tool to predict behaviour of a particular formulation with respect to drug transport across membrane various physicochemical parameters pertaining to formulations such as flux, partition coefficient and diffusion coefficient can be derived using in vitro evaluation techniques. The formulation F6 showed highest release rate among all the microemulsion formulations i.e. 95.91%. The cumulative drug permeation of all formulation was found in phosphate buffer in 4 hr [27]

The charge of microemulsion is another important property that should be assessed. In this study, the effect of drug on the ζ- potential is in figure 8. The negative zeta potential was obtained which is desired [17]. The zeta potential governs the stability of microemulsion, it is important to measure its value for stability samples. The high value of zeta potential indicates electrostatic repulsion between two droplets. A negative force means a negative potential between the droplets. Optimum Particle size of microemulsion should also between 10-200nm. Particle size distribution and zeta potential of optimized batch F6 was found to be 152.67nm and –0.526.
Screening of gelling agent was performed between Carbopol 940 and Poloxamer 407. Poloxamer407(20%) didn't give release upto 100% in 12 hrs. while carbopol 940(1.5%) did. So Carbopol 940 was optimized for further process of gel formation. The viscosity of microemulsion based gel was found to be 4500 to 6100 cps. Carbopol 940 1.5%, 2%, 2.5% were formed. 2.5% Carbopol 940 G3 batch which was optimized was found to be 6100 cps. The % drug content of all microemulsion based gel was found to be 94.89 to 97.75. The in vitro drug permeation of microemulsion gel G1 (1.5% Carbopol) was found to be 76.1 % in 6 hrs. , G2 (2 % Carbopol) and G3 (2.5% Carbopol) was found to be 78.28 % and 100 in 6 hrs.in 7.4 pH phosphate buffer.

The release study data of Meloxicam loaded microemulsion based gel analysed using rate constant equations such as zero order, first order, Higuchi and Krosmeyer peppas equations showed that microemulsion based gel formulations had the tendency to follow zero order diffusion pattern of release. Drug transport mechanism was found to be zero order based diffusion. Formulation proved to be safe after application on rat skin as it did not show any edema at application site.

There is no marketed gel formulation is available of Meloxicam gel. So here release of plain gel prepared in lab and microemulsion based gel has been compared. Result shows that microemulsion based gel gives good release than plain Meloxicam gel.

SUMMERY AND CONCLUSION

Aim of this research work was to formulate microemulsion gel of Meloxicam, NSAID having very low water solubility. Meloxicam an NSAID having very high side effects if given orally. Developed formulation overcomes problems like lower water solubility and gastric side effects.
From above study it can be concluded that microemulsion based gel overcomes problem of lower water solubility and gastric side effects of Meloxicam. So microemulsion based gel can be suitable formulation in various diseases like rheumatoid arthritis, ankylosing spondylitis, etc. as a carrier of Meloxicam.

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