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Design and Evaluation of Piroxicam Microemulsion

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ABSTRACT

The main objective of the present research work was to improve the oral bioavailability of BCS class II drugs which are known to have low solubility but have high permeability. In the present study, Piroxicam has been chosen as a model drug which is having low oral bioavailability and associated with many dose related side effects. If the bioavailability of this drug is increased reduction of the dose and the dose related side effects can be controlled and this would lead to more affordable therapy. An oral microemulsion formulation for enhancing the bioavailability of Piroxicam was developed and evaluated. A microemulsion is one of the novel pharmaceutical interests for drug delivery, and is normally composed of oil, water, surfactants and co-surfactants. Microemulsions were prepared by titrating different ratio of oil to surfactant mixtures (surfactant + co-surfactant) with water and microemulsion zone was recorded in the Pseudo-ternary phase diagram. Stable mocroemulsions were obtained with Sesame oil as oil phase, Tween80 as surfactant, Glycerin as co-surfactant and distilled water as aqueous phase. The ratio of components (oil, surfactant, co-surfactant and water) was found to affect the pH, Conductivity, Clarity, Dilution shock, *In vitro* release and Intestinal permeability, Zeta potential and Particle Size. The higher permeability achieved with the microemulsion systems compared to the marketed product (Pirox-20) was encouraging. The developed microemulsion system improved the permeability by increasing the lipophillicity due to the oil phase and also by destabilizing the epithelial membrane due to the surfactants, and may be used as a vehicle for enhanced delivery of BCS class II drugs.

KEYWORDS

Microemulsion, Bioavailability, BCS class II, Piroxicam, surfactant, co-surfactant.

INTRODUCTION

Colloidal dispersions consisting of microdomains of oil and/or water stabilized by an interfacial film of alternating surfactant and cosurfactant molecules. The various attractive advantages of Microemulsions such as nanosize (<200 nm), ease of scale-up and manufacturing, long shelf life, ability to improve dissolution rate and lymphatic transport of hydrophobic Drugs give them an edge over other novel delivery systems such as liposomes, dendrimers and polymeric nanoparticles. Thus, microemulsions can be considered as a vehicle of choice for oral drug delivery.[1]

Microemulsions emerged during the 1940s as a term to describe systems where oil and water could mix approximately in equal proportions promoted by surfactants and co-surfactants. These systems differed from emulsions by the absence of strong light scattering and it was inferred that the systems contained smaller aggregates. Later it was also realized that the

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systems were thermodynamically stable. On the basis of what was known for ordinary solubilization, it was natural to assume that the microemulsions contained either globular aggregates of surfactant and oil in water or the reverse with surfactant water aggregates in oil.[2]

Microemulsions seem to be ideal liquid vehicles for drug delivery because of their several advantages such as thermodynamic stability (long shelf-life), very small droplet size (5–100 nm), easy formulation (low interfacial tension and almost spontaneous formation), low viscosity (with Newtonian behaviour) and high surface area (high solubilisation capacity).[3]

Colloidal drug delivery vehicles have been studied for almost 30 years. An improved knowledge of the physiological constraints governing the distribution and fate of these carriers has allowed for more rational design and the development of 'second-generation' systems. The formulations already on the market are mainly concerned with reducing the side effects of the encapsulated drugs. With the arrival of 'Stealth™' liposomes and nanoparticles that avoid rapid phagocytosis, the range of sites that can be reached has been extended. Even without specific targeting technologies, it has already been shown that sites of inflammation and infection and solid tumors can be reached, as well as intravascular sites. If specificity for a particular cell type is required, ligands such as monoclonal antibodies, sugars, lectins, or growth factors can be coupled to these long-circulating systems. Colloidal drug carriers are particularly useful for formulating new drugs derived from biotechnology (peptides, proteins, genes and oligonucleotides) because they can provide protection from degradation in biological fluids and promote their penetration into cells. They also have applications with respect to small hydrophobic molecules, because they can provide an ultra dispersed form without the use of irritating solvents and allow rapid drug dissolution. Therefore, it is likely that colloidal systems able to improve the efficacy of both established drugs and new molecules will soon be available[4].

Colloidal System containing Particle size below 1 mm having[5] High specific surface area, discrete particles dispersed in a different medium, in pharmaceutical emulsions or suspensions, particle size ranges from Colloidal to visible or coarse.

Microemulsions are clear, isotropic liquid mixtures of oil, water and surfactant and cosurfactant. Compared to ordinary emulsions, microemulsion form up on simple mixing of the components and do not require high shear conditions.

Various theories concerning microemulsion formation, stability and phase behavior have been proposed over years. One explanation for their thermodynamic stability is that the oil/water dispersion is stabilized by the surfactant present and their formation involves the elastic properties of the surfactant film at the oil/ water interface, which involves as parameters, the curvature and the rigidity of the film.

These parameters may have an assumed or measured pressure and/or temperature dependence (and/or) the salinity of the aqueous phase, which may be used to infer the region of stability of the microemulsion, or to delineate the region where there coexisting phases occur.

Microemulsion systems are attractive drug carriers due to their ability to solubilize non hydrophilic compounds, to stabilize hydrolytically susceptible drugs, to target drug delivery and to provide controlled drug release.

Pharmaceutical applications of microemulsions include drug synthesis, purification and extraction, as well as drug delivery vehicles[6,7] and controlled drug release systems.

The biopharmaceutics classification system classifies drugs according to their solubility and permeability. Thus, according to BCS drugs exhibiting log P or log cP greater than or equal to values of metoprolol (1.75 & 1.35 respectively.), which is chosen as reference are

categorized as permeable drugs and those drugs which have dose number of ≤ 1 are classified as soluble. Based on this the drugs are classified as

studies. However, there continues to be a need to develop improved formulations for the oral delivery of Piroxicam.

Table: 1 Biopharmaceutics Classification System

	← SOLUBILITY	
↑ PERMEABILITY	**CLASS I** (HIGH SOLUBILITY & HIGH PERMEABILITY) EX:PROPRANOLOL,METOPROLOL,VERAPAMIL, DILTIAZEM, etc	**CLASS II** (LOW SOLUBILITY &HIGH PERMEABILITY) EX:-DANAZOL, KETOCONAZOLE, PIROXICAM, etc
	CLASS III (HIGH SOLUBILITY &LOW PERMEABILITY) EX:-NEOMYCIN , RANITIDINE, ACYCLOVIR, ATENOLOL, etc	**CLASS IV** (LOW SOLUBILITY & LOW PERMEABILITY) EX:-CYCLOSPORIN, ITRACONAZOLE, CEFUROXIME, etc.

The aim of BCS is to provide a regulatory tool for replacing certain bio-equivalence studies by accurate in vitro dissolution test, which will certainly reduce unnecessary drug exposure in healthy subjects. This mode of classification is only meant for oral products, which are absorbed via the GIT.

Piroxicam is a potent non-steroidal, anti-inflammatory agent belonging to BCS Class II, used in treatment of rheumatoid arthritis, osteoarthritis, traumatic contusions and different regional inflammatory disorders such as muscle pain. It is thought that the poor absorption of Piroxicam from the gastrointestinal tract is attributed to its poor water solubility[8].

Many different approaches for improving Piroxicam bioavailability have been reported; such as salt formation[9], complexation with cyclodextrins[10], solid dispersion[11] and self emulsifying drug delivery systems[12]. Some of these alternative formulations showed enhanced oral bioavailability in animal and/or human

The apparent water solubility of the lipophilic drugs is enhanced by incorporating them in the emulsions, furthermore, nanosize create a larger surface area and therefore favor increased absorption. Moreover, the intestine has special mechanism(s) to absorb particles, and there may be a size exclusion phenomenon in the gastrointestinal absorption of particles, with 100 nm particles showing a significantly higher uptake (10 to 250 folds) than larger particles (500nm to 10μm).[13]

Piroxicam is given in small doses, which makes it an excellent candidate to be incorporated in microemulsion. It has been hypothesized that the absorption of Piroxicam can be improved by entrapping it into emulsions and would be advantageous with regard to rapid onset of action, especially in various painful conditions where an acute analgesic effect is desired. Furthermore, a consequent reduction in the contact time of Piroxicam with the gastric and duodenal mucosa might reduce the local toxicity

of Piroxicam associated with localized high concentration in gastrointestinal tract.

MATERIALS AND METHODS

MATERIALS

Piroxicam Gifted by Zydus Cadila Ltd., India. Caster oil, Seasum oil, Peanut oil, Cotton seed oil gifted by Sigma-aldrich, USA. Olive Oil gifted by Bretolli, Italy. Tween 20, Tween 40 gifted by Sigma-Aldrich, USA. Tween 60, Tween 80 gifted by Merck, India. Span 20 Fluka, USA. Absolute Ethanol, Glycerine gifted by Merck, India. Water used was semi-quartz distilled (Qualigens). All other chemicals and reagents used were of A.R. grade, procured commercially and used as received.

METHODS

Solubility Studies

Solubility is of prime importance for developing solution that can be injected either intravenously or intramuscularly. In general, solubility is the function of chemical structure. The solubility measurement was carried out for piroxicam in different oils (water immiscible solvents), surfactant, co surfactant (water miscible solvents) and water.

Procedure

In 1 ml of the solvent, sufficient amount of drug was dissolved until no further drug could be solubilised. The system was centrifuge and filtered, washed with 2-3 times with water and then undissolved drug taken for its solubilization and recrystalization in absolute ethanol. Amount of undissolved drug substracted from the initial taken amount, for getting the amount dissolved in each formulation.

Selection of Surfactant and Co-surfactant

We had selected different formulations, in which Km ratio (surfactant to cosurfactant) was fixed. A series of surfactants with different HLB values have been screened such as Tween20, Tween40, Tween60, Tween80, glycerin, Soya lecithin and we found that combination of Tween80 with equal proportion in combination with co surfactant glycerin was best for formulating a microemulsion.

Construction of Phase Diagram[14, 15]

Pseudo ternary phase diagram was constructed to examine the formation of microemulsion using four components, oil surfactant, cosurfactant and aqueous phase system. The four component system consisted of oil as sesame oil, surfactants as Tween80 (Polysorbate 80), and a cosurfactant glycerin and double distilled water as aqueous phase. These components have been taken on weight basis.

Pseudo ternary phase diagram was constructed keeping the ratio of Tween80 and glycerin constant and varying the remaining two components. For convenience, the phase diagram was constructed by drawing “water dilution lines” representing increasing water content and decreasing surfactant and cosurfactant levels. The water was titrated along dilution lines drawn from the surfactant, cosurfactant apex (100% surfactant – cosurfactant) to the opposite oil side of triangle. The line was orbitarily denoted as the value of the line intersection with the oil scale. If turbidity appeared fallowed by phase separation were considered to be biphasic. If clear and transparent mixtures were visualized after stirring, the samples were considered monophasic. The samples were marked as points in the phase diagram. The area covered by these points was considered to be the microemulsion region of existence. The final diagrams were generated using Origin 6.0 software (Microcal, USA). The Km ratio of 4:1 was found to give the maximum microemulsion zone in the pseudo ternary phase diagram.

Formulation Stage

After the development of phase diagram,13 different formulations has been selected by keeping the total quantity of the formulation constant as 100% and varying all components of the system. Each formulation has been loaded with piroxicam of 1 mg/ml. All 13 formulations as been evaluated for different parameters such as pH, conductivity, clarity, dilution shock, in

vitro release, and in vitro intestinal permeability study.

Particle Size and Zeta Potential Determination[16]

The particle size, zeta potential and zeta deviation of microemulsion was determined by dynamic light scattering (Nano ZS 3600, Malvern Instruments, Malvern, UK). All measurements were carried out at 25 °C using Disposable sizing cuvette, after appropriate dilution with distilled water.

Drug Loading Efficiency[17]

We had taken 1 gm of each microemulsion formulation and checked for drug content to study their drug loading efficiency. Further excess quantity of drug mixed with blank microemulsion and when the drug remained undissolved, filtered the formulations and the amount of drug which were remained undissolved was estimated by recrystallization of drug. From that, amount of drug, which was actually dissolved, was calculated.

***In vitro* Drug Release Study**[18]

Drug release study was carried using dialysis bag (HIMEDIA DM70, INDIA) having a pore diameter of 2.4 nm with molecular cut-off of 12-14 kDa. 2.5 mg Piroxicam equivalent formulation was added in dialysis sac. It was immersed in 90 ml of phosphate buffer pH 7.4 containing 0.2% sodium lauryl sulphate (SLS) maintained at 37°C on magnetic stirrer (100 rpm). At predetermined time points, 5 mL of the sample was withdrawn for up to 24 hr. At each time, equal volume of fresh release medium was replaced to maintain the sink. Each sample was analyzed spectrophotometrically at 333 nm for determination of drug content.

Also the same procedure was followed for the marketed product Pirox-20 (batch no. DJ 8174, Cipla Ltd.) and *in vitro* release was compared with the 13 formulations developed for the study.

***In vitro* Intestinal Permeability Study**[18]

Everted small intestinal sac technique was used to determine the drug absorption through intestinal mucosa. The male wistar rats had been allowed food and water ad libitum. They were fasten overnight prior to the study. The study protocol was approved by the Institutional Animal Ethics Committee of Krupanidhi College of Pharmacy, Bangalore. Briefly, 10 cm of small intestinal tissue (ileum) was cut off from anaesthetized rat and carefully everted. It was washed with tyrode solution and one side was tied off with surgical suture. 0.5 mg piroxicam equivalent formulation was injected in it and the other side was tied off properly. This sac was placed in 50ml of tyrode solution containing 0.2% SLS in a beaker, and stirred with magnetic stirrer (25rpm). Proper aeration (95% oxygen and 5% carbon dioxide) and temperature (37 ± 0.5°C) was maintained throughout study. 5ml of aliquot was withdrawn from release medium at predetermined time interval and replaced by fresh release medium. Drug content was estimated spectrophotometrically at 333nm from each aliquot. Studies were carried out in duplicate and the average and SD values were calculated.

Also the same procedure was followed for the marketed product Pirox-20 (batch no. DJ 8174, Cipla Ltd.) And observed the *in vitro* permeability of Pirox-20 and compared with the 13 formulations developed for the study.

RESULT AND DISCUSSION

Selection of Surfactant and Cosurfactant

To screen various surfactants and co-surfactants, they were added in various proportions with oil and water, the amount of water required to just induce turbidity in the system. A series of surfactants with different HLB values have been screened such as Span 20, Span 80, Tween 80, Tween 60, Tween 20, Plurol oleque, soya lecithin. The surfactants were taken alone and checked the best combination in terms of clarity of the clear single phase microemulsion and also observed for the maximum microemulsion zone

in the pseudoternary phase diagrm. Other then Tween80 all the surfactant in combination with various oils and co-surfactants failed to give clear microemulsion and also they failed to give maximum area in Phase diagram. But it was found that Tween80 in combination with a cosurfactant glycerin was best for formulating a microemulsion. The various Km ratios were tried, such as 4:1, 3:1, 2:1, 1:1, 1:2. Among these, km 4:1 was found to be the best combination, where microemulsion formed was less viscous, spontaneous in formation, had good drug loading capacity and best clarity was observed as compared to all other formulation with different Km ratios.

Phase Diagram

For developing a suitable formulation of microemulsion, the classical pseudo ternary phase diagram technique was followed. Briefly, oil was mixed with surfactants and cosurfactant and titrated with water till a turbid emulsion is reached. This was further verified by back titrating the turbid mixture of oil, surfactant and cosurfactant with water till a clear endpoint was reached. Phase diagram was subsequently constructed from the data generated by plotting % (weight) of oil (sesame oil), water and total surfactant and cosurfactant (Tween80 and glycerin) mixture at different ratios as three vertices of a triangle.

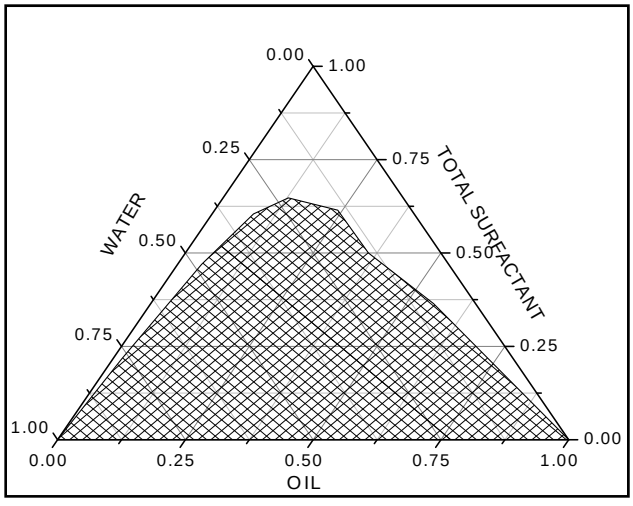

Figure: 1 Phase diagram of sesame oil: glycerin system (4:1)

(Hatched Portion indicates microemulsion zone)

Optimization of formulation

Certain points from the phase diagram of Sesame oil/ Tween 80 & glycerin/ water (Km 4:1) was selected from the microemulsion zone. The individual formulations were evaluated for pH, conductivity, clarity, dilution shock, in vitro release and in vitro intestinal permeability studies. The results are discussed below for the each parameter studied.

pH[19]**:** The pH of the designed formulations varied from 6.24-7.28.This was ideal and near blood pH(7.4). On dilution to 1:10 & 1:25 there was slight increase in acidity, may be due to dissolved CO_2 in the distilled water used.

Conductivity[20]**:** Each Microemulsions loaded with drug was tested for conductivity. The double distilled water which has been used for preparation of formulation showed conductivity of less than 4.50µS which has been taken has a reference. The formulation was having conductivity between 43-382 µS. Based on the conductivity measurements we can say that our formulation consisting of o/w type of microemulsion. Conductivity decreased relative to the undiluted MEs. However, the conductivity of both undiluted and diluted MEs were well above the conductivity of diluted water (≈4 µS) used in the formulations. This indicates existence of percolation phenomena, more pronounced in the undiluted MEs, progressively decreasing with increasing dilution.

Clarity[21]**:** All formulations had clear transparent yellowish to pale yellow color. The clarity has been represented in terms of % transmission, where absorbance and % transmission were noted at 650nm & 400nm. The best results have been reported for all the formulations at 650nm compared to 400nm. The % transmission was more than 90% for all the formulations. Visually all the formulations showed no change in the clarity and there was spontaneous formation of clear microemulsion, this is due to the adjustment time required for the surfactant and cosurfactant molecules orienting at the interface and for attaining the required curvature for the thermodynamic stability was less.

Dilution Shock[19]**:** All formulations were diluted to 1:10 & 1:25 with distilled water and their absorbance and % transmission was noted at 650nm and 400nm. The formulations have maintained a best clarity even after dilution to 10 times 25 times with water. In case of remaining all formulations the % transmission was more than 90% at 650 nm upon dilution.

This was an advantage of this system since when it reaches stomach it has greater ability to uptake of water and can resist its haziness; therefore, it may keep the particle size in microemulsion range. Therefore its solubility and bioavailability will be increased by higher surface area of the droplets, which is in nano range.

Table: 2 pH and Conductivity Determination

Sr No.	Formulation Code	Before Dilution		After Dilution 1:10		After Dilution 1:25	
		Cond.* µS	pH	Cond.* µS	pH	Cond.* µS	pH
1	F1	311.00	6.95	110.00	6.15	97.90	6.05
2	F2	143.00	6.98	157.00	6.24	47.80	6.10
3	F3	191.00	6.24	128.00	5.70	80.10	5.55
4	F4	223.00	7.04	117.00	6.20	85.70	5.95
5	F5	382.10	7.01	104.00	5.95	89.80	5.70
6	F6	78.00	7.14	110.10	6.42	60.70	6.22
7	F7	233.00	7.28	106.00	6.57	62.40	6.50
8	F8	100.00	6.55	103.90	5.65	50.60	5.35
9	F9	312.10	6.86	201.10	5.25	67.40	5.09
10	F10	43.10	7.05	101.00	6.35	84.90	6.02
11	F11	187.00	7.24	97.10	6.48	92.10	6.40
12	F12	210.10	6.64	128.90	5.84	106.10	5.20
13	F13	183.00	6.91	323.20	6.85	72.80	6.72

* Conductivity

Table: 3 Clarity Test And Dilution Shock Study

Formulation Code	% Transmitance					
	Clarity Test		Dilution 1:10		Dilution 1:25	
	AT 650nm	AT 400nm	AT 650nm	AT 400nm	AT 650nm	AT 400nm
F1	98.5%T	24.9%T	97.4%T	26.0%T	99.1%T	63.1%T
F2	99.0%T	52.1%T	98.4%T	26.1%T	99.2%T	62.5%T
F3	86.8%T	25.7%T	98.3%T	30.2%T	99.6%T	69.8%T
F4	91.5%T	22.0%T	98.0%T	32.1%T	99.4%T	69.5%T
F5	96.3%T	45.3%T	99.0%T	38.9%T	99.6%T	74.0%T
F6	99.8%T	29.1%T	98.2%T	28.7%T	99.4%T	55.9%T
F7	100.0%T	38.6%T	98.3%T	31.1%T	99.8%T	64.2%T
F8	70.4%T	31.9%T	81.4%T	10.5%T	92.5%T	42.9%T
F9	92.2%T	38.1%T	95.0%T	21.6%T	98.2%T	58.7%T
F10	80.1%T	23.8%T	83.0%T	15.0%T	85.6%T	43.6%T
F11	96.7%T	44.2%T	95.3%T	33.8%T	98.5%T	68.5%T
F12	91.3%T	49.5%T	90.2%T	38.8%T	96.5%T	69.7%T
F13	78.8%T	16.4%T	79.5%T	10.0%T	82.0%T	38.8%T

***In vitro* Drug Release Study:** The drug release after 8 hr for the formulations varied from 38% to 52% as compared to 49% for marketed product (Pirox-20). Results indicate in vitro drug release from micro emulsion where as marketed product gave the same in vitro release profile.

Table: 4 *In Vitro* Drug Release For Formulations

Formulation Code	%CDR At different time interval (Hr)								
	0.5 hr	**1 hr**	**2 hr**	**3 hr**	**4 hr**	**5 hr**	**6 hr**	**7 hr**	**8 hr**
F1	11.79	15.51	20.08	25.58	31.10	34.83	40.39	45.06	50.65
F2	9.09	13.69	15.55	18.32	22.00	26.60	31.22	37.66	47.74
F3	7.27	16.37	21.85	23.75	31.06	35.70	40.35	45.93	51.53
F4	6.36	10.93	14.59	19.16	24.65	30.17	34.80	39.54	45.03
F5	11.79	15.51	20.08	25.58	31.10	34.83	40.39	45.06	50.65
F6	6.34	9.10	11.85	15.51	20.99	26.49	33.81	35.75	42.21
F7	7.23	10.91	12.75	16.42	19.19	28.29	34.73	35.77	38.62
F8	9.99	13.68	15.54	19.21	24.71	29.32	35.76	41.31	45.09
F9	9.89	14.59	17.36	20.13	23.82	30.24	34.87	40.42	46.90
F10	12.70	22.74	26.44	29.26	35.65	37.64	41.40	45.17	48.96
F11	13.57	20.92	26.42	31.04	33.87	38.51	44.08	48.77	49.86
F12	10.84	17.26	26.35	28.27	31.99	34.82	36.77	40.52	47.00
F13	8.16	17.27	22.96	29.17	30.19	33.01	35.85	36.90	38.85
PIROX-20	3.80	15.77	22.33	26.76	28.49	35.64	42.82	47.33	49.14

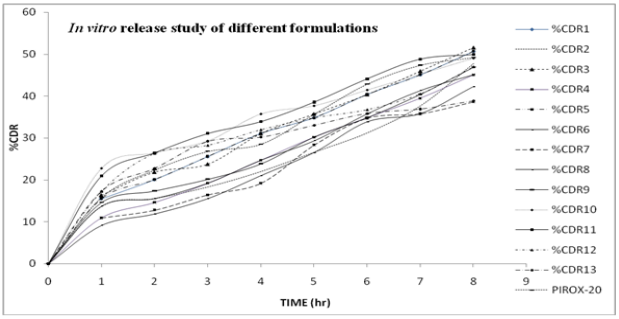

Figure: 2 *In vitro* drug releases for Formulations

***In vitro* permeation study:** The main objective of the work being bioavailability enhancement, permeation study was the major parameter of study. After 1 hour of permeation study, most of the formulations showed enhanced permeation compare to marketed product (Pirox-20). For surfactant rich system the permeation was high; however, for all microemulsion formulation it reached 16% to 29% in comparison of marketed product (Pirox-20) having very low permeability like 15% .

Table: 5 *In Vitro* Intestinal Permeability Study

Formulation Code	% Drug Permeation Through Rat Ilium At Different Time Interval (Min)					
	5 min	10 min	15 min	30 min	45 min	60 min
F1	5.41	8.14	9.53	12.28	16.39	23.22
F2	10.83	13.58	16.34	19.12	24.61	28.77
F3	1.35	5.42	8.15	12.24	17.71	23.20
F4	2.70	5.42	9.51	14.96	17.73	25.93
F5	4.06	8.14	13.59	17.70	20.48	21.92
F6	2.70	8.13	12.23	17.69	19.12	25.96
F7	0	4.06	12.20	14.96	17.73	24.57
F8	1.35	8.13	10.87	16.33	19.10	23.24
F9	4.06	5.43	9.51	13.61	20.44	28.65
F10	1.35	4.06	6.79	12.23	14.99	17.76
F11	2.70	4.07	9.50	13.60	15.01	19.13
F12	4.06	12.20	13.60	19.07	23.21	16.01
F13	9.47	12.22	13.62	19.10	21.88	24.68
Pirox-20	1.35	4.06	6.79	10.88	12.28	15.03

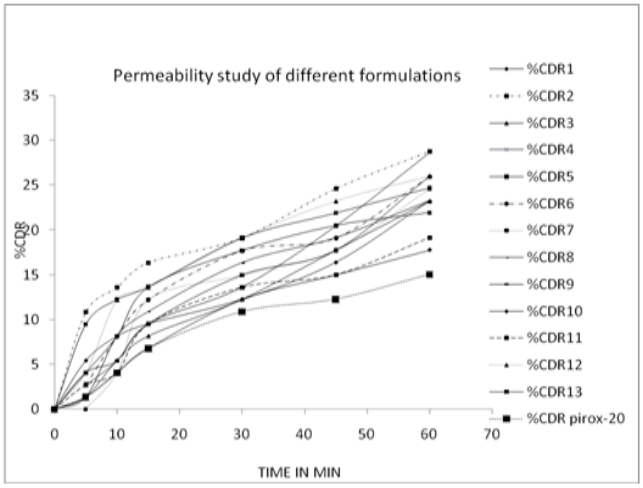

Figure: 3 *In vitro* permeation studies for Formulations through Rat ileum.

Particle size analysis: The size of microemulsion was determined by dynamic light scattering (Nano ZS 3600, Malvern Instruments, Malvern, UK), taking the average of 3 measurements, with varying duration greater than 60s. It gives the particle size in between the 50% to 99% intensity, in that they gave good result in 10 to 250 nm size range. However, the results need to be interpreted in terms of the procedure of measurement, where the formulations were dispersed in water prior to measurement. This will disrupt the initial structure of the MEs, leading to increase in droplet size. However, the conductivity of the formulations remained well above water conductivity (4 µS) at about 100 µS indicating

about 1:10 dilution and hence the size quoted are actually that of the 1:10 diluted MEs.

Zeta potential measurement: The surface charge of microemulsion, characterized by the zeta potential, was determined by measuring electrophoretic mobility of particles using zetasizer (Nano ZS3600, Malvern Instruments, UK), the zeta potential was measured for all the formulations ranges from -3.50mV to -7.50 mV. This indicates negatively charged droplets in line with fatty acids present in the oil phase and the polar groups in tween 80.

As a whole, from the results discussed, it appears that the improvement of bioavailability/absorption may be due to increased permeability due to the structural uniqueness of MEs compared to a drug suspension. Since, the in vitro release rates for the MEs were similar to that of the marketed product, while permeability was at best 10% higher at the same period, it is evident that the increase in permeability in the major reason for enhancement of absorption rate.

Therefore, our objective of enhancing the bioavailability of a BCS Class II drug has been successful with use of a colloidal dispersed system in the form of a ME.

CONCLUSION

Through this work, an attempt was made to improve the oral bioavailability of Piroxicam by formulating it in a microemulsion system. A microemulsion system consisting of a Sesame Oil (oil), Tween 80 (surfactants), Glycerin (cosurfactant) and double distilled water as aqueous phase with a drug load of 1mg/ml was formulated and evaluated for various parameters such as conductivity, pH, clarity, dilution shock, in vitro drug release and epithelial permeability profile, using isolated rat ileum segments and also particle size analysis and zeta potential studies has been carried out. Therefore, the objective of improving oral bioavailability of Piroxicam, a model BCS Class-II drug has been amply fulfilled. The work might be extended to whole animal and / or human studies in the future. Enhanced intestinal absorption by incorporation of Piroxicam within microemulsion as a promising carrier for oral delivery of poorly water soluble BCS Class-II drugs.

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Table: 6 Particle Size Analysis and Zeta Potential

Formulation No.	Size distribution			Zeta potential		
	Z-Avg (d.nm)	PDI*	% intensity	Zeta potential (mV)	Zeta deviation (mV)	% area
F1	12.88	0.297	89.8	-4.96	2.73	100
F2	17.03	0.360	84.5	-6.70	5.29	100
F3	23.94	0.277	80.9	-4.87	3.03	100
F4	192.4	0.300	51.5	-3.63	3.48	100
F5	22.67	0.474	82.5	-5.10	4.05	100
F7	741.5	0.807	46.4	-7.94	6.72	100
F9	41.27	0.551	50.1	-4.05	3.61	100
F11	128.9	0.208	98.3	-4.25	3.20	90.4

***Poly dispersity Index

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