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DEVELOPMENT AND EVALUATION OF BACLOFEN BASED TOPICAL MICROEMULSION

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ABSTRACT

Spasticity is a condition in which there is an abnormal increase in muscle tone or stiffness of muscle, which might interfere with movement, speech, or be associated with discomfort or pain. Baclofen has significant pharmacokinetic drawbacks when taken orally because it has a short biological half-life of 3–4 hours and is absorbed in the upper small intestine making its duration of action limited. Patient failure to comply results from the requirement that it be taken often. Recent studies attempted to develop oral dosage forms of sustained release in response to all the prior restrictions of oral baclofen, but the efforts failed for a variety of reasons, including dose dumping. Baclofen is a great choice for transdermal drug delivery because of its excellent physical - chemical and biological data, which were obtained from the best sources.

Keywords: Baclofen, Microemulsion, D-Optimal Design and Ternary phase diagram.

INTRODUCTION

The formulation and development of novel drug delivery system with the nature of enhancing the effectiveness of existing of drug is an ongoing process in pharmaceutical research. Since there are many types of drug delivery systems that have been developed. The microemulsion concept was introduced in 1940s by Hoar and Schulman who generated a clear single-phase solution by triturating a milky emulsion with hexanol. They prepared the first microemulsion by dispersing oil in an aqueous surfactants solution and adding an alcohol as a co-surfactant, leading to transparent stable formulation[1].

Microemulsion is defined as microemulsion are clear, transparent, thermodynamically stable dispersions of oil and water, stabilized by an interfacial film of surfactant frequently in combination with a co-surfactant. Alternative names for these systems, such as swollen micelle, transparent emulsion, solubilized oil and micellar solution, are often used. Microemulsions are bicontinuous systems that are essentially composed of bulk phases of water and oil separated by a surfactant/cosurfactant rich interfacial region. These systems have advantages over conventional emulsions in that they are thermodynamically stable liquid systems and are spontaneously formed. Microemulsions are currently the subject of many investigations because of their wide range of potential and actual utilizations[2]. The high capacity of microemulsions for drugs makes them attractive formulations for pharmaceuticals. These systems also offer several benefits for oral administration, including increased absorption, improved clinical potency and decreased toxicity.

Skeletal muscle relaxants are used for a variety of conditions, including musculoskeletal conditions such as low back pain, and spastic conditions such as multiple sclerosis, spinal cord injuries, and cerebral palsy. Approximately 2 million people/year report using a skeletal muscle relaxant, primarily for back pain, with an estimated 300,000 of these patients being elderly. This staggeringly large number is a concern given the consistent warnings about use of these drugs in the geriatric patient population due to adverse effects such as sedation and weakness. The enormity of skeletal muscle relaxant use requires that we carefully evaluate the proper selection of muscle relaxants for appropriate patients and conditions[3].

Skeletal muscle relaxants consist of both antispasticity and antispasmodic agents, distinction prescribers often overlook. The antispasticity agents—baclofen, tizanidine, dantrolene, and diazepam—aid in improving muscle hypertonicity and involuntary jerks. Antispasmodic agents, such as cyclobenzaprine, are primarily used to treat musculoskeletal conditions. Much of the evidence from clinical trials regarding skeletal muscle relaxants is limited because of poor methodologic design, insensitive assessment methods, and small numbers of patients[4].

Spasticity is a stretch reflex disorder, manifested clinically as an increase in muscle tone that becomes more apparent with more rapid stretching movement. It is a common consequence of lesions that damage upper motor neurons causing upper motor neuron syndrome[5]. It can range from mild muscle stiffness to severe, painful, and uncontrollable muscle spasm. It is

associated with some common neurological disorders: Multiple sclerosis, stroke, cerebral palsy, spinal cord and brain injuries, and neurodegenerative diseases affecting the upper motor neuron, pyramidal and extrapyramidal pathways. Left untreated, it gives rise to many problems, such as pain, spasms, limb contracture, and deformity [6].

Baclofen is a chlorophenyl derivative of gamma aminobutyric acid (GABA), a naturally occurring inhibitory neurotransmitter in the brain and spinal cord. It is of proven therapeutic value in reducing the severity of flexor or extensor spasms resulting from spinal cord injury or disease[7].

Animal metabolic studies have shown baclofen to be rapidly and completely absorbed from the gastrointestinal tract, with the plasma half-life varying from one to four hours, depending on the species tested. In man, the half-life is three to four hours. As with most hydrophilic compounds, baclofen does not pass the blood-brain membrane readily, but in man and other animals tested, it reaches an effective con¬ centration in the brain and spinal cord at peak plasma levels. Excretion of baclofen in man is rapid and virtually complete, more than 80% being eliminated by the kidney within one day after oral administration[8].

Microemulsions: Microemulsions are transparent systems of two immiscible fluids, stabilized by an interfacial film of surfactant or a mixture of surfactants, frequently in combination with a cosurfactant. These systems could be classified as water-in-oil, bicontinuous or oil-in-water type depending on their microstructure which is influenced by their physicochemical properties and the extent of their ingredients[9].

Types of Microemulsion: Microemulsions are thermodynamically stable but are only found under carefully defined conditions[10].

According to Winsor, there are four types of microemulsion phases exists in equilibria, these phases are also referred as Winsor phases. They are,

Oil- in- water microemulsion or Winsor I, Water – in oil microemulsion or Winsor II, Bicontinuous microemulsion or Winsor III and Single phase homogeneous mixture or Winsor IV.

Oil- in- water microemulsion or Winsor I

In Oil-in-water type of microemulsions droplets of oil is surrounded by a surfactant (and may be cosurfactant) film that forms the internal phase distributed in water, which is the continuous phase. This type of microemulsion generally has a larger interaction volume than the w/o microemulsions.

Water - in - oil microemulsion or Winsor II

In Water-in-oil type of microemulsions droplets of water surrounded by a continuous oil phase. These are recognized as “reverse micelles”, where the polar headgroups of the surfactant are facing into the droplets of water, with the fatty acid tails facing into the oil phase. A w/o microemulsion used orally or parenterally may be destabilized by the aqueous biological system.

Bicontinuous microemulsion or Winsor III

In bicontinuous microemulsion system the amount of water and oil present are similar, in this case, both water and oil exist as a continuous phase. An irregular channel of oil and water are combined and looks like a “sponge-phase.” Transitions from o/w to w/o microemulsions may pass through this bicontinuous state. Bicontinuous microemulsion, may show non-Newtonian flow and plasticity. These properties make them especially useful for topical delivery of drugs or for intravenous administration.

Single phase homogeneous mixture or Winsor IV

In single phase homogeneous mixture or Winsor IV, the oil, water and surfactants are homogenously mixed [11].

Composition of Microemulsion:

Oils, Surfactant, Co surfactant/Cosolvent, Aqueous phase

Surfactants: Surfactants are formed by two parts with different affinities for the solvents, water (polar solvents) and oil phase (non-polar solvents). The surfactants used in self-emulsifying formulations are known to increase the bioavailability by various mechanisms including increased intestinal epithelial permeability, improved dissolution increased tight junction permeability to GIT [12].

Co-surfactant/Co-solvents: It help to dissolve large amounts of hydrophilic surfactants or the hydrophobic drug in the lipid base.

Oils: Oils can solubilize the lipophilic medication in a specific amount. Increase in the sum of lipophilic drug transported via the

intestinal lymphatic system, subsequently increase in the absorption from the GI tract. Fatty acid esters such as ethyl or methyl esters of lauric, myristic and oleic acid have also been utilised as the oil phase. Lipophilic drugs are preferably solubilized in o/w microemulsions. The main principle for selecting the oil phase is that the drug should have high solubility in it.

Aqueous phase: Generally, the aqueous phase contains hydrophilic active ingredients and preservatives. Sometimes Buffer solutions are used as aqueous phase.

Ternary Phase Diagram Construction

A ternary graph, triangle plot is a barycentric plot on three variables which sum to a constant. It graphically depicts the ratios of the three variables as positions in an equilateral triangle. It is used in physical chemistry and other physical sciences to show the compositions of systems composed of three species[13]. Ternary phase diagrams used in microemulsion systems are called "pseudo ternary phase" diagrams. These are equilateral triangles, and the corners typically represent a binary mixture of two components, such as surfactant/ cosurfactant, water/drug, or oil/drug if the formulation components are more than three [14]. Phase diagrams were prepared with 1:1, 1:2 weight ratios of surfactant to cosurfactant. The oil phase and the surfactant mixture were then mixed at the weight ratios of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1. The oil and surfactant mixture were mixed homogeneously and were diluted dropwise with purified water under magnetic stirring (300 rpm) at room temperature until transparent microemulsion was obtained. The concentration of components was recorded in order to complete the pseudo ternary phase diagram.

Methods of Preparation: (Phase Titration Method and Phase Inversion Method)

Phase Titration Method (Spontaneous emulsification method)

Microemulsions are prepared by phase titration method and can be described through phase diagrams. Construction of phase diagram is a beneficial method to study the complex series of interfaces which can take place when the different constituents are mixed. As quaternary phase diagram is time consuming and tough to understand, the pseudo ternary phase diagram is frequently constructed to find the different zones comprising microemulsion zone, in which each corner of diagram represents 100% of the constituent [15].

Phase Inversion Method: Property of surfactant Phase inversion of microemulsion take place upon addition of excess of dispersed phase or in response to temperature. For non-ionic surfactants, this can be accomplished by altering the temperature of system, forcing a conversion from oil in water microemulsion at low temperature to a water in oil microemulsion at high temperature. During cooling, the system crosses a point of zero spontaneous curvature and negligible surface tension, supporting the development of finely dispersed oil droplets[16].

Baclofen: Baclofen has a biological half-life of 2.5-4 hours. Hence, the conventional tablets need to be administered 3-4 times a day (for several days) leading to poor patient compliance. Therefore, Baclofen is suitable candidate for the development of once-daily formulation. Adverse events associated with Baclofen can be minimised when administered as once-daily formulation. Absorption of the Baclofen is limited to stomach or upper part of the GI tract i.e. its absorption on arrival to colon (or even before) is low or non-existent and therefore its bioavailability is incomplete when administered as a normal sustained release formulation. The bioavailability of the drug can be increased by making the drug completely absorbed in the stomach by sustained release gastro-retentive drug delivery system considering the fact that Baclofen is stable under gastric condition.

MATERIALS

Baclofen purchased from Yarrow chem products, Mumbai. Flaxseed oil purchased from S-D Fine chem limited, Baroda, Gujarat

PEG600 purchased from Rolex chemical industries, Mumbai.All other chemicals were in analytical Grades.

METHODS

Preformulation studies:

Melting point determination: Melting point of the drug was determined by taking a small amount of the drug in a capillary tube closed at one end and was determined using by Thiele tube method and the temperature at which the drug melts was noted. Averages of triplicate readings were taken[17].

Screening of oils and surfactants by solubility studies of drug

Solubility of Baclofen in various oils, surfactant, co-surfactant was determined by adding 10mg of drug in screw capped vials containing 10 ml of vehicle. This mixture was mixed by vortex mixture to facilitate the solubilization. Mixtures are centrifuged 500 rpm for 15 minutes; the supernatant was taken and measured the absorbance at 200-400 nm using UV-visible spectrophotometer[18].

Solubility of oils, surfactant, co surfactant in Drug Baclofen

The term 'solubility' is defined as maximum amount of solute that can dissolved in a given amount of solvent. Quantitatively it is defined as concentration of solute in a saturated solution at certain temperature. In qualitative terms, solubility defined as spontaneous interaction of two or more substances to form a homogenous molecular dispersion. Solvents for the study were selected based on the good solubilizing capacity for Baclofen. In present study the solubility of baclofen was investigated in different oils like isopropyl myristate, Flaxseed oil, Olive oil etc. and surfactants and co-surfactants like tween 80, tween 40, Ethanol Propylene glycol etc[19].

Drug – Excipient compatibility studies by FTIR

Excipients are integral components of almost all pharmaceutical dosage forms. To investigate any possible interaction between the drug and utilized excipient (Flaxseed oil , PEG600, Propylene glycol etc.) IR spectrum of pure drug (Baclofen) and its physical mixture were carried by using FTIR. Infra-red spectroscopy is one of most effective analytical techniques to identify functional groups of drugs, for analysis very, small quantitative of drug placed on lens of equipment directly with the help of spatula and pressure was applied through screwed up to specified mark. The spectrum was recorded between 4000-500 cm^{-1} [20].

Standard Calibration Curve

Preparation of pH 7.4 Phosphate Buffer

Dissolve 2.38 g of disodium hydrogen phosphate, 0.19 g of potassium dihydrogen phosphate and 8.0 g of sodium chloride in sufficient water to produce 1000 mL Adjust the pH if necessary [21].

Preparation of standard stock solution: For the determination of absorption maxima stock solution was prepared by dissolving 100mg of accurately weighed Baclofen in 100ml of phosphate buffer 7.4 pH to get 1mg/ml solution. Further 10ml of this solution was pipetted into 100ml of volumetric flask and diluted to 100ml with phosphate buffer 7.4 to get 100µg/ml solution. This stock solution was subjected for UV scanning in the range of 200-800 using Double beam UV-VIS spectrophotometer, the absorption maxima obtained at 260 nm with a characteristic peak.

From the above stock solution pipette out 2,4,6,8,10 into a series of 10ml volumetric flask and was made up to 10ml with phosphate buffer pH 7.4 to get 20,40,60,80,100µg/ml of Baclofen respectively. The absorbance of the different diluted solutions was measured in a UV spectrophotometer at 200 -400 nm.

Preparation of Baclofen microemulsion.

The microemulsion was prepared by using phase titration method. These pseudo ternary phase diagrams will be best suited for making different possible compositions of oil surfactant/co-surfactant and water. Different mixtures of surfactant (PEG 600) to co-surfactants (Propylene glycol) were prepared and the weight ratios were fixed to 2:1, 1:1. These mixtures (S/Cos) were mixed with oil phase (Flaxseed oil) to give weight ratio of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9, water was added drop by drop and stirred using magnetic stirrer until homogeneous dispersion or solution was obtained.

After each addition, the system was examined for appearance and flow property. The end point of the titration was the point in which the solution becomes cloudy or turbid. The quantity of aqueous phase required to make the mixture turbid was noted[21].

Construction of Pseudo - ternary phase diagram.

The advantage of using a ternary plot for depicting compositions is that three variables can be conveniently plotted in a two-dimensional graph. Ternary plots can also be used to create phase diagrams by outlining the composition regions on the plot where different phases exist. Every point on a ternary plot represents a different composition of the three components. There are three common methods used to determine the ratios of the three species in the composition[22] .

Constructing ternary phase diagrams is the most important and essential step in the preparation of microemulsion formulation. These diagrams are used to find the region of the microemulsion existence and study the effect of different surfactant/co-surfactant weight ratios on the extent of a stable microemulsion area. One of the simplest and preferred methods for the ternary phase diagram is to organize and plot the experimental data as oil/water/surfactant percentages. After this step, the optimum formulation is selected using the centroid of the largest microemulsion region [23].

Optimization: Optimization is an approach to search along process variable of input variables to satisfy a goal such as maximizing / minimizing / targeting a responsible variable. Amount of oil, Smix and % water was selected. The goal of DOE was to optimize the critical process parameters to achieve desired globule size, transmittance, drug release at 6 hours and 12 hours. D optimal quadratic design was selected to carry out with 12 experimental runs for the formulation of microemulsion. The analysis was performed actual v/s predicted and optimization were conducted in quadratic model[24].

Evaluation of Microemulsion

Physical appearance: For Physical appearance microemulsion can be inspect visually for homogeneity, fluidity, and optical clarity[25].

Globule size and zeta potential measurements: The globule size and zeta potential of the microemulsion can be determined by dynamic light scattering, using a Zeta sizer HSA 3000 [26] .

Assessment of the Rheological Properties (Viscosity measurement): It can be determined by Brookfield digital viscometer. Change in the rheological characteristics help in determining the microemulsion region and its separation from another region [27].

In-vitro diffusion drug release: The diffusion study can be carried out on a modified Franz diffusion cell, within volume of 250mL. The receptor compartment was filled with of buffer. The donor compartment was fixed with cellophane membrane, containing the microemulsion formulation and the plain drug solution, separately. At predetermined time intervals samples were withdrawn from the receptor compartment and analysed for drug content, using a UV spectrophotometer at specific wavelength[28].

Release kinetics: The results of in vitro release profiles obtained for formulations were fitted into models of data treatment as follows[29]

Cumulative percent drug released versus time (zero-order kinetic model), Log cumulative percent drug remaining versus time. (First-order kinetic model), Cumulative percent drug released versus square root of time (Higuchi's model) and Log cumulative percent drug released versus log time (Korsmeyer Peppa's equation).

1.Zero Order Kinetics: A zero-order releases would be predicted by the following equation.

$At = A0 – K0t$

Where: At = Drug release at time 't'

A0 = Initial drug concentration

K0 = Zero-order rate constant (hr)

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K0.

2.First Order Kinetics: A first-order release would be predicted by the following equation[30]

$Log\ C = Log\ C0 – 303.2Kt$

Where: C = Amount of drug remained at time 't'

C0= Initial amount of drug.

K = First-order rate constant (hr).

When the data are plotted as a log of percent cumulative drug release remaining versus time yields a straight line, indicating that the release follows First-order kinetics.

The constant 'K' can be obtained by multiplying 2.303 with slope values.

3.Higuchi's Model: Drug released from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation [31] .

$Q = A\ [D\ (2C - Cs)\ Cs\ t]\ 1/2$

Where, Q = Amount of drug released at time 't'

D = Diffusion coefficient of the drug in the matrix

A = Total amount of drug in unit volume of matrix

CS = The solubility of the drug in the diffusion medium

ε = Porosity of the matrix

τ = Tortuosity

t = Time (hrs) at which 'Q' amount of drug is released

simplified equation if one assumes that D, CS and A are constant. Then equation becomes:

$(32)Q = Kt^{½}$

4.Korsmeyer and Peppas Model: The release rates from controlled release polymeric matrices can be described by the equation [32]

n Q = K1t

Q is the percentage of drug released at time 't'

K is a kinetic constant incorporating structural and geometric characteristics

'n' is the diffusional exponent indicative of the release mechanism

Drug stability: The optimized microemulsion was kept under cold condition (4-8°C), room temperature and at elevated temperature (50 ± 2 °C). After every 2 months the microemulsion can be analysed for phase separation, % transmittance, globule size and % assay[33].

Determination of thermal stability: Twenty millilitres of drug-loaded microemulsions are stored in a 25 ml transparent borosil volumetric container at three different temperatures, i.e., 4°, 25° and 40°C, 1°C in BOD for a period of 1 month. Samples are removed periodically for visual inspection to observe any physical changes like loss of clarity, coalescence and turbidity, etc. Also, the samples can be observed for the determination of loss of aqueous phase that is an essential part of the microemulsion stability [34].

Specific gravity testing at 28°C: To determine the specific gravity, a capillary gravity bottle method is used. Washed and dried, the precaution was necessary during the drying of the gravity bottle as a little amount of moisture could increase the errors in the data of the specific gravity of the samples [35].

pH of the microemulsions: The microemulsion samples is taken into the sample tubes and a pH meter is used to determine the pH of the different samples as the pH of the formulation is not the only factor and that the stability of the microemulsions also imparts a role to alter the bioavailability of the drug through microemulsion at the site of permeation[36].

RESULTS AND DISCUSSION

Melting Point: The melting point of pure drug was found to be 179-181°C.

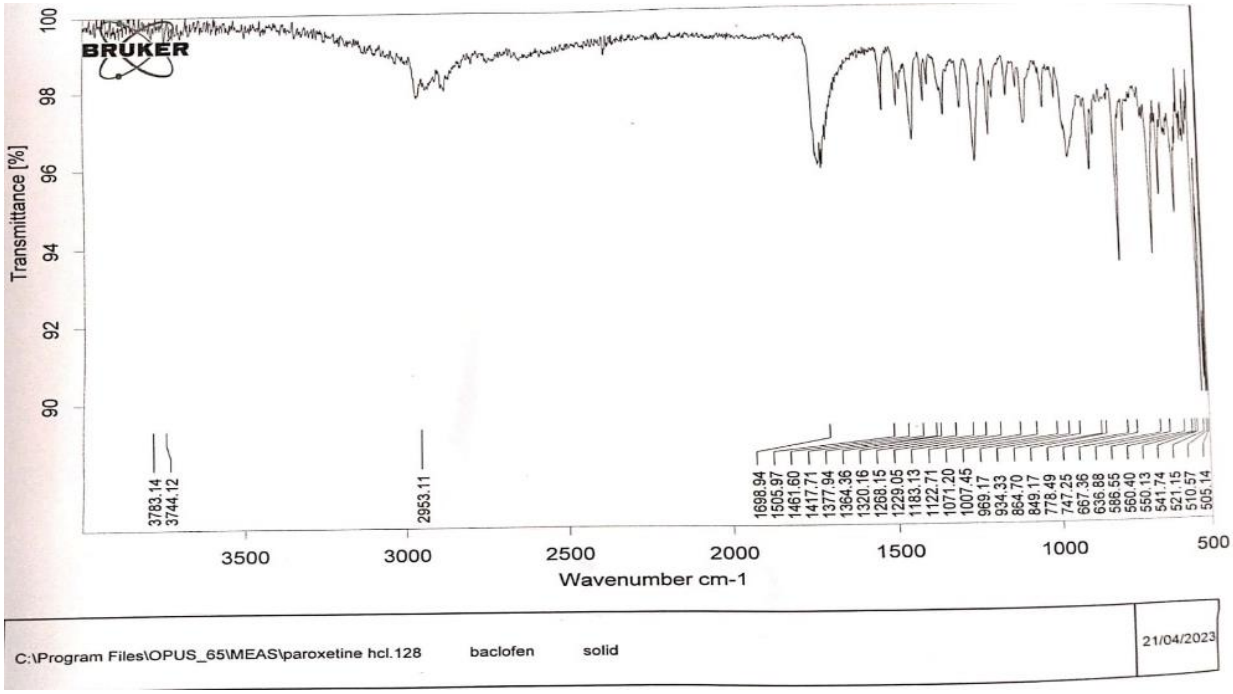
Solubility studies:

Formulation code	IPM (ml)	S-MIX (ml)	WATER (ml)
F1	5	31	63.29
F2	3	20	76.99
F3	5	15	80
F4	3	38.7	58.24
F5	5	43.45	51.54
F6	5	50	45
F7	5	23.23	71.76
F8	3	15	82
F9	4	32.5	63.5
F10	3	28.41	68.58
F11	3	50	47
F12	4	15	80.9

Table No:1 Composition formulation of Baclofen Microemulsion

Phase type	Excipient	Solubility	Percentage
Oil	Sesame oil	0.257	10.28%
	Almond oil	0.958	38.32%
	Flaxseed oil	2.408	96.0%
	Olive oil	1.803	72.01%
Surfactant	Tween20	0.639	25.5%
	PEG 600	1.118	44.72%
	Tween 80	0.256	10.24%
	Span 80	0.122	4.88%
Co surfactant	Methanol	0.170	6.8%
	Propylene glycol	2.426	97.04%
	Ethanol	1.783	71.2%

Table No:2 Formulation design by DOE of Baclofen Microemulsion



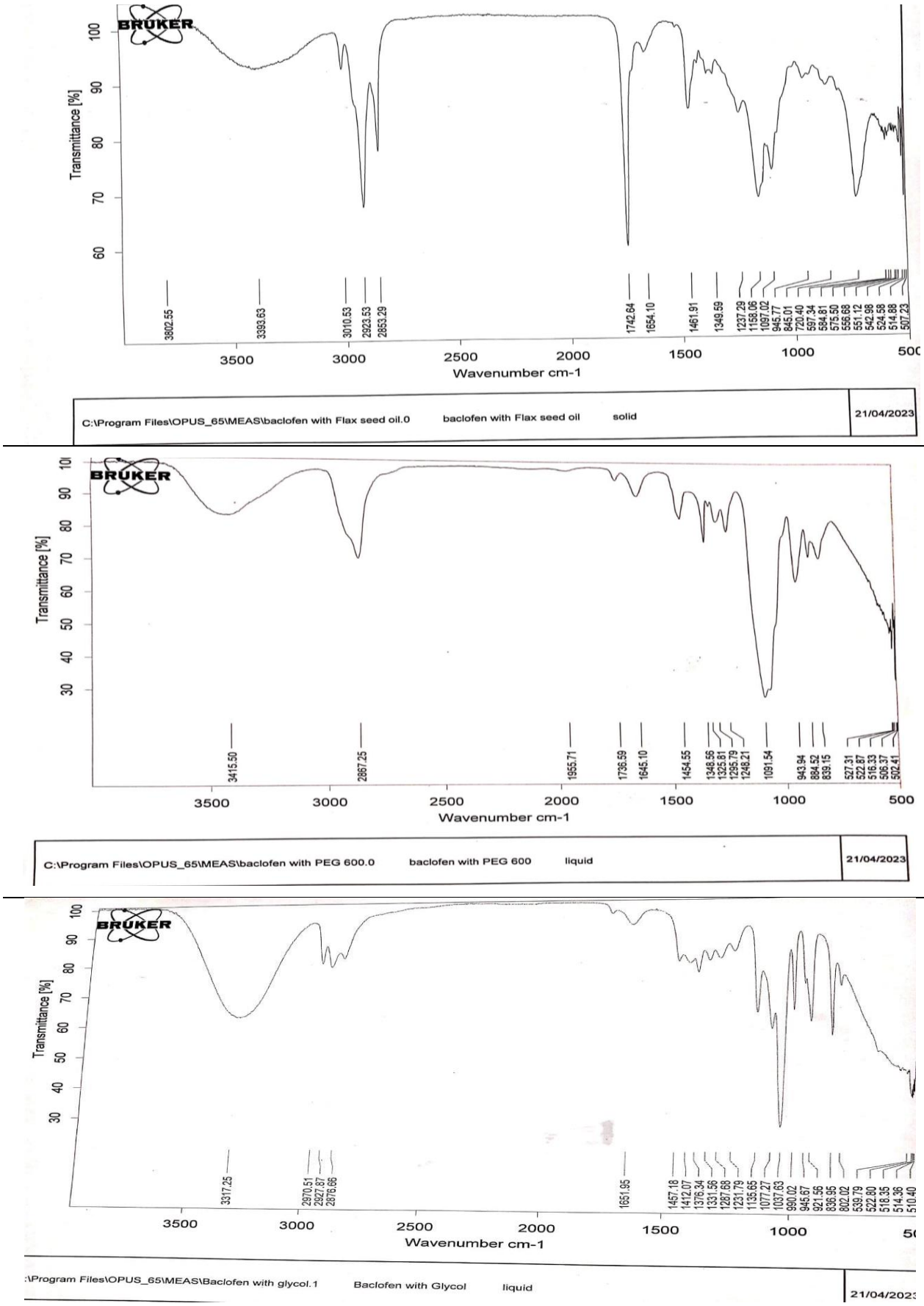


Figure: 1 FTIR Spectrum of pure drug Baclofen with combinations of Flaxseed oil, PEG600 and propylene glycol

Oil	S mix	Water (1:1)	Appearance	Water(2:1)	Appearance
9 mL	1 mL	3.6 mL	Turbid	1.7 mL	Turbid
8 mL	2 mL	1.7 mL	Turbid	1.5 mL	Turbid
7 mL	3 mL	3.9 mL	Turbid	2.8 mL	Turbid
6 mL	4 mL	3.8 mL	Turbid	3.1 mL	Turbid
5 mL	5 mL	4.8 mL	Turbid	3.6 mL	Turbid
4 mL	6 mL	4.5 mL	Turbid	4.2 mL	Turbid
3 mL	7 mL	3.2 mL	Turbid	4 mL	Turbid
2 mL	8 mL	3.8 mL	Turbid	3.4 mL	Turbid
1 mL	9 mL	4.3 mL	Clear	2.6 mL	Turbid

Table No:3 Formulation of Microemulsion for S Mix Ratio (1:1) with Observed Appearance

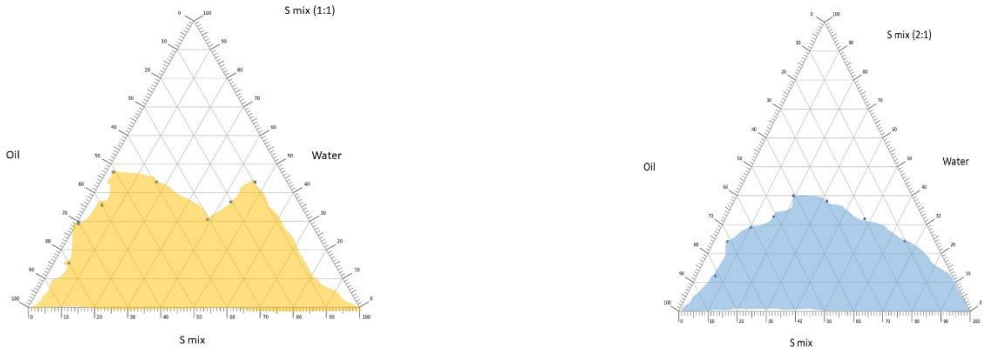


Figure: 2 Pseudo Ternary Phase of S Mix (1: 1) and (2:1)

Figure: 3 Microemulsion Preparation of Smix ratio (1:1) and (2:1)

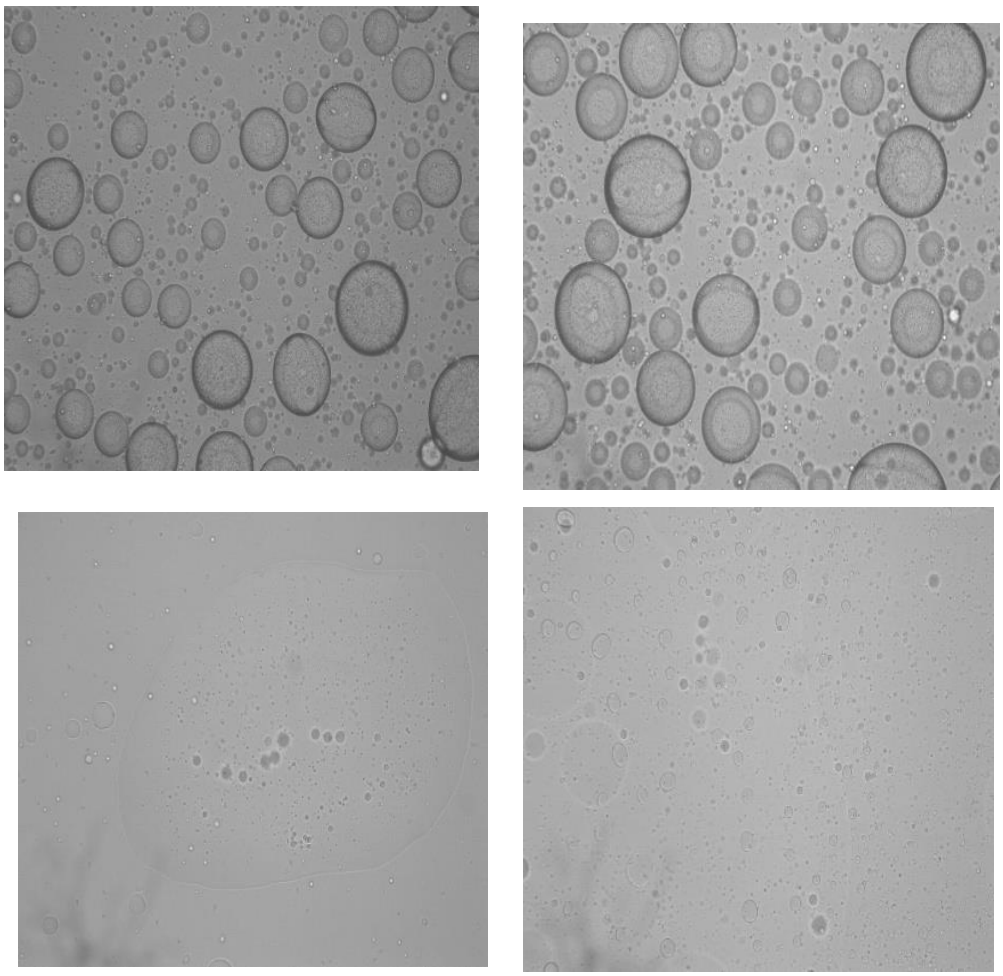


Figure: 4 Optical Microscopic Images of Prepared Microemulsion

Response	Source	Sum of Squares	df	Mean Square	F-value	p-value	
Globule size	**Model**	659.67	6	109.94	56.85	0.0002	significant
% Transmittance	**Model**	9.92	6	1.65	7.12	0.0240	significant
Drug release at 6 hours	**Model**	42.03	6	7.01	7.68	0.0204	significant

Table No:4 Optimization of Flaxseed Oil, PEG 600, Propelyene Glycol Based Baclofen Microemulsion.

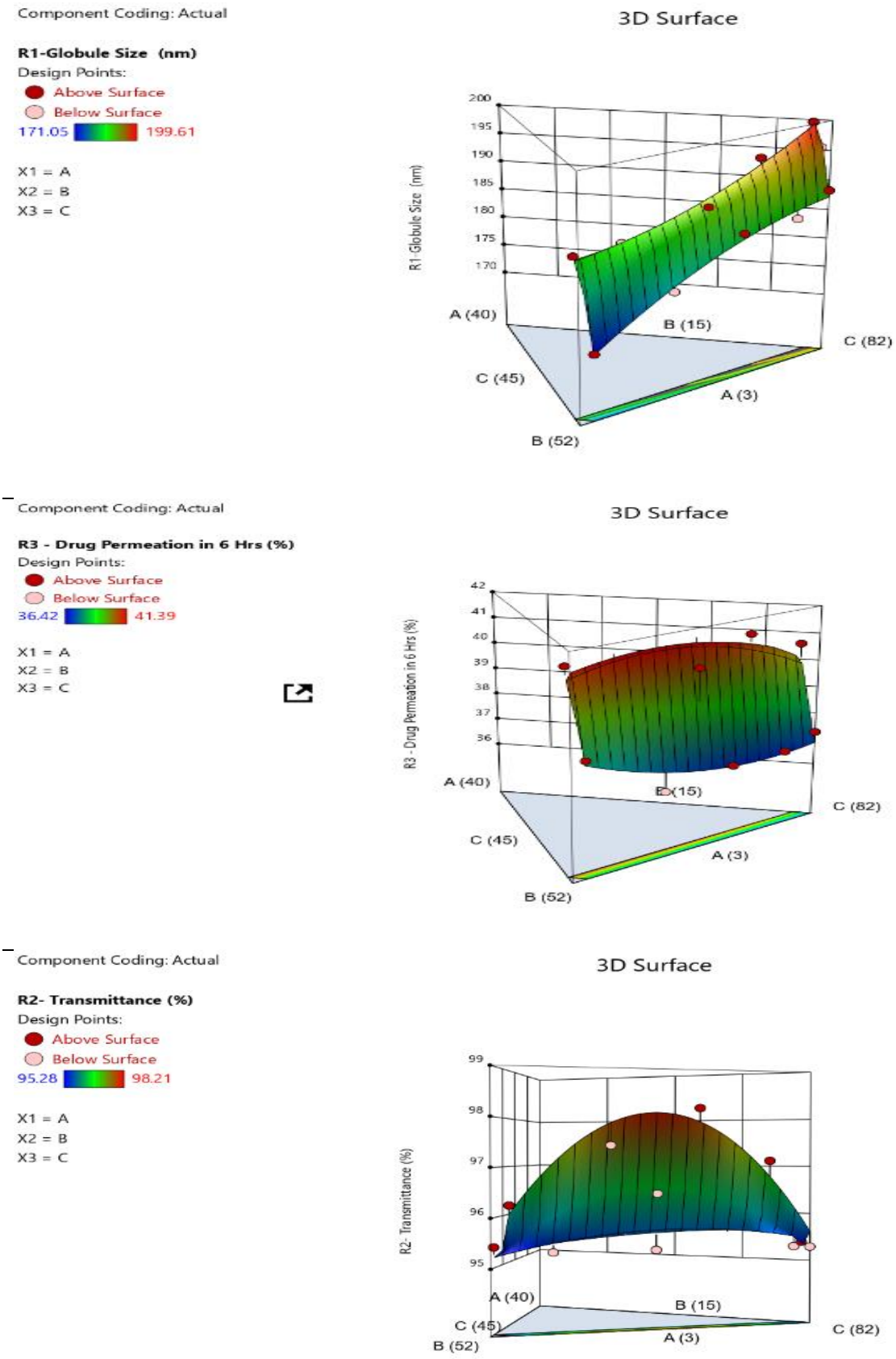


Figure: 5 3D Design Real contour graph for globule size, drug permeation in 6 hours and % Transmittance of Baclofen microemulsion

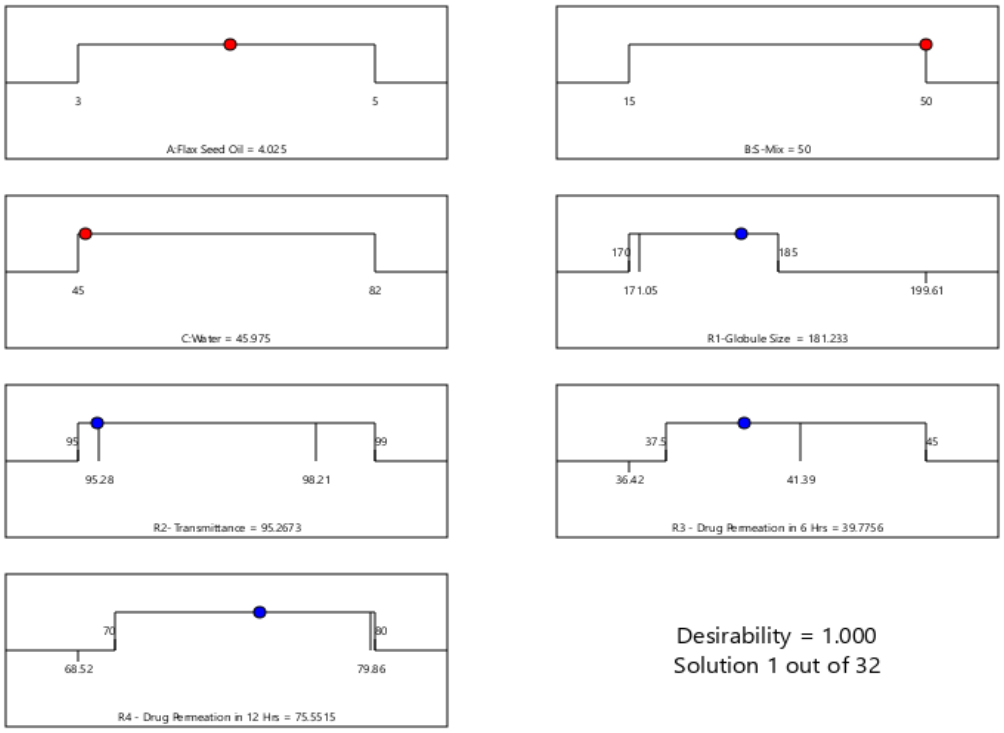


Figure: 6 Numerical optimized RAMP profile graph of Baclofen Microemulsion

INGREDIANTS	AMOUNT
Oil	4.112 mL
S-MIX	47.809 mL
WATER	48.079 mL

Table No:5 Optimized Formulation of F13 Baclofen Microemulsion.

Formulation code	Globule size	Transmittance	Drug release at 6hr	Drug release at 12 hr
ME13	182.726nm	95.499	39.894%	75.558%

Table No:6 Physicochemical evaluation of optimized formulation F13 of Baclofen microemulsion

Optimized formula	Globule size	Transmittance	Drug release at 6 hr	Drug release at 12 hr
Predicted	182.726nm	95.499	39.894%	75.558%
Experimental	183.62nm	96.48	38.256 %	74.369%

Table No:7 Comparison between the Experimental (E) and Predicted (P) Values for the Optimized Formulation F13 Baclofen microemulsion.

Baclofen shows good solubility with Flaxseed oil (oil), PEG600 (Surfactant), Propylene glycol (Co surfactant). Incompatibility studies FTIR: FTIR Spectra of pure drug, polymer and their physical mixtures were recorded. The drug, polymer and physical mixtures of drug and polymers were scanned for absorbance.

Globule size:

The globule size from F1 TO F12 ranged from 171.05 to 199.61 nm. The results are shown as F3 shows maximum range of 199.61 and F11 shows the minimum range of 171.05nm. The optimized formulation F13 Shows the globule size of 182.72 nm

Invitro drug diffusion study:

Finally, the microemulsions were evaluated for in vitro diffusion studies in phosphate buffer pH 7.4. Formulations F1 releases 78.29% at 12 hours, F2 at 69.56%, F3 at 77.55%, F4 at 71.45 %**,** F5 at 79.14 %, F6 at 79.86%, F7 at 77.79%, F8 at 68.52%, F9 at 74.15 %, F10 70.42 %, F11 at 71.48%, F12 at 73.88 %

Optimized formulation F13 releases 39.894% at 6 hours and 75.558% at 12 hours.

The comparison between the experimental and predicted values for Optimized formulation F13 shows the predicted value 39.894% at 6hours is reasonable adjusted to the experimental 38.256% at 6 hours. The predicted value 75.558% at 12 hours is reasonable adjusted to the experimental 74.369% at 12 hours.

Percentage transmittance:

The clarity of microemulsions was checked by transparency, measured in terms of transmittance (% T). Formulation F10 has transmittance values greater than 98%. These results indicate high clarity of microemulsion, Due to higher particle size, oil globules may reduce the transparency of microemulsion and there by values of % transmittance. The optimized formulation F13 shows 95.49 % of transmittance.

Thermal stability:

Microemulsions are thermodynamically stable systems and are formed at a particular concentration of oil, surfactant, co surfactant, with no separation, creaming or cracking. It is thermos stability which differentiates microemulsion from emulsion that have kinetic stability and will eventually phase separate. Thus, the prepared formulations were subjected to different thermodynamic stress like heating cooling cycle, Centrifugation and freeze thaw stress test. It was found that all the formulations F1-F13 Formulations were stable in Heating /cooling cycle, centrifugation and freeze thaw test due to phase separation selected for characterization and evaluations

Stability studies:

Stability studies of the microemulsion were carried out by subjecting temperature stability and centrifugation. The formulations labelled F1 to F12 are chosen along the line of dilutions, the results of physico chemical analysis attained before and after submitting samples, before samples were submitted to centrifugation and majority of samples were clear and no phase separations was observed after visual inspection. A formulation shows no sign of phase separation; thus, it was concluded that microemulsion formulation was stable thermally as well as stressful conditions.

CONCLUSION

The currently approved oral tablet dosage forms of baclofen are indicated for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. It may also be of value in patients with spinal cord injuries and other spinal cord diseases. Baclofen treatment can aid in restoring residual function to those patients who have reversible spasticity

Preformulation study for estimation of Baclofen was developed and drug polymer compatibility studies were carried out using solubility and FTIR to rule out any possible interactions between the drug and polymers, thus confirming the compatibility between the selected range of the drug and polymers. Various Microemulsion formulations were developed for selected drug Baclofen.

Microemulsions were prepared based on solubility of different excipients (oils, surfactant, water) in different ratios of Smix (1:1, 2:1) experimental, optimized formulation is compared with predicted microemulsion formulation and various evaluation and characterization was performed.

The Optimization is carried out for preparation of baclofen microemulsion with pseudo ternary phase is plotted, obtained 1:9 as clear microemulsion. Optimized formulation F13 were prepared on the amount of Flaxseed oil 4.11 ml,

S-MIX 47.80 ml, Water 48.07 ml. Physicochemical evaluations were performed globule size was about 182.72 nm, % transmittance 95.49% and drug release at 6 hour is 39.894%, Drug release at 12 hours 75.558%.

It is concluded that Baclofen microemulsion is the safe acceptable treatment option for severe resistant spasticity resulting in muscle relaxation and reduction of muscle spasms. Also, there is significant improvement in the relief of pain associated with involuntary muscle spasms. Further in vivo studies can be performed.

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