SciMedCentral

Journal of Drug Design and Research

Research Article

Research Article: Design, Development and Evaluation of Microemulsion for Topical Drug Delivery System Using Model Drug

Akshata Bhonge*, and Bakade BV

Pataldhamal Wadhwani College of Pharmacy, Yavatmal

***Corresponding author**

Akshata Bhonge, Pataldhamal Wadhwani College of Pharmacy, Yavatmal

Submitted: 06 June 2024

Accepted: 28 June 2024

Published: 30 June 2024

ISSN: 2379-089X

Copyright

© 2024 Bhonge A, et al.

OPEN ACCESS

Keywords

- Microemulsion
- Thermodynamically stable
- Oil
- Surfactant
- Co-surfactant

Abstract

The objective of this research work was to design, characterize and evaluate microemulsion. The anti-fungal drug miconazole nitrate has a low solubility in water, leading to reduced therapeutic efficacy. In addition, the size of the droplets in such microemulsions remains constant and ranges from (0.02-0.20µm). Microemulsions dramatically enhance the therapeutic efficacy of drugs and reduce the volume of the drug delivery vehicle, thus minimizing toxic side effects. Miconazole-nitrate microemulsions were developed and assessed for topical skin delivery, prepared through spontaneous emulsification with isopropyl palmitate as an oil phase. The surfactant phase included span 80 and co-surfactant polyethylene glycol 400 (peg 400). As per the Placket Burman DoE F15 formulations were developed using independent variables concentration of oils, surfactant and co-surfactant. Microemulsions was characterized for various parameters like, viscosity, Density, pH, drug content, surface morphology, Particle size determination, Zeta potential, In-vitro drug diffusion study. The optimum formulation F4 and F15 showed 100% and 98.75% drug diffusion in 3 hrs and 5 hrs. Desired viscosity F4 showed 48.7 ± 43.2cps and F15 showed 56.8 cps, Density F4 showed 0.97g/cc and F15 showed 0.98g/cc, comfortable pH F4 showed 7.07 ± 0.1 and F15 showed 6.97 %, drug content F4 showed 86.45% and F15 showed 94.06%, F4 showed 0.02µm and F15 showed 0.14µm particle size and zeta potential of F15 showed -19 ± 8.24 mV of globule size, this outcome signified its potential suitability as a carrier for effectively administration of miconazole through topical delivery.

INTRODUCTION

Microemulsions comprise a special class of "dispersion" that may be transparent or translucent in appearance. They were first discovered by Hoar and Schulman (1943) in their experimental study of titration of long-chain fatty acids (soapy milky emulsions) with medium shortchain alcohols producing translucent or transparent system of emulsions. Microemulsions are one of the best candidates as novel drug delivery system because of their long shelf life, improved drug solubilization with ease of preparation and administration. Microemulsions are thermodynamically stable and optically isotropic liquid solutions of oil, water and amphiphile. They have emerged as novel vehicles for drug delivery which allow controlled or sustained release for ocular, percutaneous, topical, transdermal, and parenteral administration of medicaments.

Pharmacological Applications of Microemulsions have been studied extensively as potential drug delivery vehicles for poorly water-soluble drugs. They are extensively being used as drug carrier systems for topical, oral, and parenteral administration of drugs, offering a variety of advantages such as ease of preparation, spontaneous formation and scale-up, thermodynamic stability, enhanced drug solubilization, and bioavailability. Microemulsions dramatically enhance the therapeutic efficacy of drugs and reduce the volume of the drug delivery vehicle, thus minimizing toxic side effects. Besides, in case of lipophilic drug administration, the ability of cell membrane to solubilize lipophilic component tremendously aids its absorption [1].

Microemulsions are isotropic, thermodynamically stable, transparent (or translucent) systems of oil, water, and surfactant, frequently in combination with a co-surfactant with a droplet size usually in the range of 0.02-0.20µm. These homogeneous systems, which can be prepared over a wide range of surfactant concentration and oil to water ratio, are all fluids of low viscosity. Microemulsions or Micellar emulsion are dynamic system in which the interface is continuously and spontaneously fluctuating [2].

Structure of Microemulsion

Micro emulsions or Micellar emulsion are dynamic system in which the interface is continuously and spontaneously fluctuating. Structurally, they are divided in to oil in water (o/w), water in oil (w/o) and bi-continuous micro emulsions. In w/o micro

emulsions, water droplets are dispersed in the continuous oil phase while o/w micro emulsions are formed when oil droplets are dispersed in the continuous aqueous phase. In system where the amounts of water and oil are similar, the bi-continuous micro emulsions may result. The mixture oil water and surfactants are able to form a wide variety of structure and phase depending upon the proportions of component [3] [Figure 1].

Components of Microemulsion

Oils: Saturated fatty acid-lauric acid, myristic acid, capric acid linoleic acid, linolenic acid Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid. Example: (GlycerylMonoanddicaprateisopropylmyristate, sunflower oil, soyabean oil.

Surfactants: Polyoxyethylene/Polysorbate/Tween 20,40,60, 80; Sorbitan Monolaurate (Span), Soybean lecithin, egg lecithin, lyso lecithin, Sodium dodecyl sulphate (SDS), Sodium bis (2–ethylhexyl) sulphosuccinate (Aerosol OT), Dioctyl sodium sulphosuccinate.

Co-surfactants: Ethanol, propanol, Isopropanol, butanol, pentanol, hexanol, sorbitol, n– pentanoic acid, n– hexanoic acid, 2- aminopentane, 1,2-butanediol, Propylene glycol. Cremophor RH40 (polyoxyl 40 hydrogenated castrol oil), Plurololeique (polyglyceryl–6– dioleate) [3].

Placket - Burman

Design of Experiments (DoE): The Design of Experiments (DOE) is a tool for optimization of experiments and refinement, The design of experiments is a methodology in which the input factors are varied to understand the impact on output variables. The Plackett-Burman model, can also be used in because it allows searches with "n" experiments investigate "n-1" factors and uses factors "ghosts", which serve to make the estimate of experimental error. (+1, 0, -1) Applied the method of exploratory research, through a fractional factorial array Plackett-Burman, which served to direct the application to a research and further optimization of batches. The Plackett-Burman method was used for being a model suitable for economically detect main effects of each formulations to analyzed separately to select the best method of design of experiments to be applied in each case, shows in Table 2 [4].

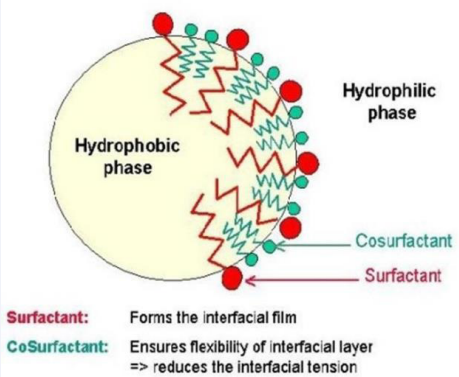

Figure 1 Structure of microemulsion

MATERIALS AND METHOD

Drug Miconazole Nitrate provided by Yarrow Chem Industry, Mumbai [Figure 2].

Miconazole is an azole anti-fungal that functions primarily through inhibition of a specific demethylase within the CYP450 complex, miconazole is typically applied topically and is minimally absorbed into the systemic circulation. It appears a white or almost white, crystalline, or micro-crystalline powder. Solubility in ethanol, methanol and chloroform melting point is 184-185 °C in range [5] [Table 1].

Table 1: Materials used to formulate in Miconazole Nitrate microemulsion

Materials	Manufacturer	Use
Isopropyl Palpitate	Loba Chemie Pvt.Ltd.	Oil
Span-80	Thermosil Fine Chem Industries, Pune	Surfactant
Polyethylene glycol-400	Loba Chemie Pvt.Ltd.	Co-surfactant
Methyl Cellulose	Acme Chemicals, Mumbai	Thickening agent
Methyl paraben	Thermosil Fine Chem Industries, Pune	Preservative

Table 2: Composition of Micro-emulsion formulation of Miconazole Nitrate

Sr. no	Batches	Miconazole Nitrate (ml)	Isopropyl Palmitate (ml)	Span 80(ml)	PEG 400(ml)	Methyl cellulose (mg)	Methyl paraben (mg)	Distilled water (ml)
1	F1	100	13(+1)	3.5(0)	0.7(0)	120	20	q.s
2	F2	100	10(0)	3.5(0)	0.7(0)	120	20	q.s
3	F3	100	7(-1)	3.5(0)	0.7(0)	120	20	q.s
4	F4	100	13(+1)	5(+1)	0.7(0)	120	20	q.s
5	F5	100	13(+1)	2.5(-1)	0.7(0)	120	20	q.s
6	F6	100	7(-1)	3.5(0)	0.9(+1)	120	20	q.s
7	F7	100	10(0)	3.5(0)	0.9(+1)	120	20	q.s
8	F8	100	13(+1)	5(+1)	0.5(-1)	120	20	q.s
9	F9	100	13(+1)	5(+1)	0.5(-1)	120	20	q.s
10	F10	100	7(-1)	2.5(-1)	0.5(-1)	120	20	q.s
11	F11	100	13(+1)	3.5(0)	0.5(-1)	120	20	q.s
12	F12	100	10(0)	3.5(0)	0.5(-1)	120	20	q.s
13	F13	100	7(-1)	2.5(-1)	0.9(+1)	120	20	q.s
14	F14	100	7(-1)	3.5(0)	0.5(-1)	120	20	q.s
15	F15	100	10(0)	2.5(-1)	0.5(-1)	120	20	q.s

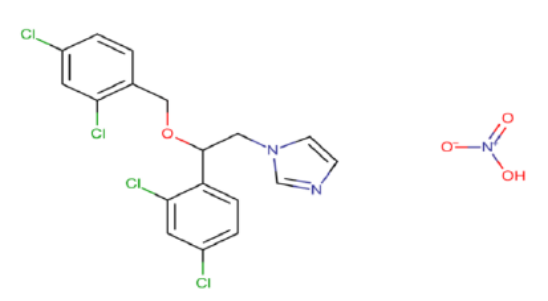

Figure 2 Structure of Miconazole Nitrate

Method

Miconazole Nitrate microemulsion were prepared by a high shear homogenization method. Aqueous phase solution contains co-surfactant and distilled water and oil phase solution contains oil, surfactant, drug and preservative.

Experimental Work

Preformulation may be described as a stage of development process during which the researches characterize the physical, chemical and mechanical properties of the drug substance to form effective, stable and safe dosage form.

- Color, odor, taste, and appearance.
- Nature: A white or almost white, Crystalline, or micro-crystalline powder
- Melting point: 184-185 °C
- Solubility: Soluble in Ethanol, methanol, Chloroform

Calibration curve of Miconazole Nitrate in phosphate Buffer of pH 7.4: The drug solution (10, 20, 30, 40, 50, 60 µg/ml) in Phosphate buffer pH 7.4 was taken. From the stock solution 0.25 ml solution was pipetted out in 25 ml calibrated volumetric flask and final volume was made upto 25 ml with phosphate buffer 7.4 to obtain stock solution of 10 µg/ml concentration, from this solution 0.25 ml, 0.5 ml, 0.75 ml, 1 ml, 1.25 ml was pipetted out in different 25 ml volumetric flask respectively and final volume as made upto 25 ml with phosphate buffer pH 7.4 to obtain concentration 10µg/ml concentration, and its concentration is determined by UV-spectrophotometer at 232 nm phosphate buffer pH 7.4 as blank by UV Spectrophotometric method. A graph is plotted by using concentration at X-axis Vs absorbance at Y-axis.

Fourier Transform Infrared (FTIR): Drug Excipients Interaction Study was carried out to check the interaction between the drug and microemulsion by using FT-IR spectrophotometer. The Miconazole Nitrate Microemulsion and pure drug Miconazole Nitrate were placed separately on the sampling plate of FT-IR spectrophotometer. Then scanning of the sample was performed and IR spectra were obtained.

Formulation of Micro-Emulsions

Microemulsion was formulated by dissolving the drug in a mixture of solid, lipid, surfactant and co-surfactant. Microemulsion were prepared by a high shear homogenization method. Aqueous phase solution contains co-surfactant and distilled water and oil phase solution contains oil, surfactant, drug and preservative. Both the solutions were heated step by step until it soluble properly. The oil phase was poured drop by drop on to the aqueous phase and homogenization was carried out at 6000 rpm for 15 min using high shear homogenizer. Drug loaded in microemulsion were finally obtained by allowing to cool to room temperature. [Table 2].

Evaluation Parameters of Microemulsion

Organoleptic Characteristics

The Organoleptic properties, including physical appearance, color, texture, phase separation, homogeneity, and immediate skin feel of the selected topical formulations [6].Particle size analysis:

The size of dispersed particles in an microemulsion actually determines its appearance to the naked eye by optical microscope and Zeta sizer instrument.

pH Determination: The pH values of the formulation Miconazole Nitrate Microemulsion were measured by immersing the electrode directly into the dispersion using a calibrated pH meter.

Density: The specific gravity or density of microemulsion emulsion formulation is two crucial parameters. A decrease in the formulation's density is typically a sign that there is trapped air inside its composition. Density at certain temperatures can be determined with high-precision hydrometers.

Viscosity: The viscosity was determined using Brookfield Viscometer. Brookfield Viscometer consist of a cup, which is stationary and a spindle which is rotating. Different sized rotating spindles are used and immersed in test material. For liquids with low viscosity, large size spindles (large diameter and surface area) are used while for higher viscosity liquids small spindles (small diameter and surface area) are used. Rotate the spindle in the microemulsion till we get a constant dial reading on the display of the Viscometer.

Drug content analysis: 1 ml of Miconazole Nitrate Microemulsion was taken in 10 ml volumetric flask containing 1 ml ethanol and Volume was made up to 10 ml with phosphate buffer 7.4 pH. From the above solution, 1 ml was further diluted with 10 ml phosphate buffer to get 10 µg/ml. The resultant solution was filtered through Whatman filter paper and absorbance of the solution was measured at 232 nm using UV spectrophotometer.

Centrifugation: Those formulations that passed the heating cooling cycle then subjected to were centrifuged test, The microemulsion were centrifuged at 3500 rpm for 5 min. Those formulations that did not show any phase separation some formulation show phase separation test.

Freeze Thaw: Freeze-thaw cycle testing is a part of stability testing that allows to determine the microemulsion formulation will remain stable under various conditions. It consists of quick freezing and thawing were to kept in test tube for 24 hrs at freezing temperation and 24 hrs at room temperation and then measured the temperation by using thermometer heating upto 50°C to observed the formulation was stable at under conditions.

***In-Vitro* Diffusion study:** The in vitro diffusion study of the microemulsion was carried out in Franz Diffusion cell Figure 10

using Dialysis membrane. The membrane was previously soaked in phosphate buffer pH of 7.4 for 24 hours was clamped carefully to one end of the hollow glass tube of diffusion cell. Then ME was pour uniformly on the dialysis membrane in donar compartment. 50 ml of phosphate buffer was taken in a beaker, the donar compartment was kept in contact with receptor compartment. This whole assembly was kept on a magnetic stirrer and the solution on the receptor side was stirred continuously and temperature of the cell was maintained at 37°C. A similar blank set was run simultaneously as a control. Sample (3 ml) was withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. The Samples were analyzed spectrophotometrically at 232 nm and the cumulative percent drug release was calculated.

Stability Study: In order to exclude the possibility of meta-stable formulations, stress testing is required. Thermodynamic stability confers long shelf life to the micro-emulsion as compared to ordinary emulsions. Stability study was performed on F4 and F15 formulations which were filled in Borosilicate Glass bottle and kept in stability chamber at 40°C and 75 % RH for one month [7].

RESULT AND DISCUSSION

Preformulation study: [Table 3].

Calibration curve of Miconazole Nitrate in phosphate buffer of 7.4

The absorbance of the drug solution was measured at 232 nm, using UV spectrophotometer. A graph of absorbance versus concentration in µg/ml was plotted which indicate in compliance to Beers-Lambert's law in concentration range as shown in Figure 3 and Table 4.

FTIR of Miconazole Nitrate: FTIR Spectra of Miconazole Nitrate and FTIR Interpretation of Miconazole Nitrate as Shown in the Figure 4 and Table 5.

FTIR of Miconazole Nitrate Microemulsion: FTIR Spectra of Optimized Miconazole Nitrate Microemulsion and FTIR Interpretation of Mixture of Miconazole Nitrate as shown in the Figure 5 and Table 6.

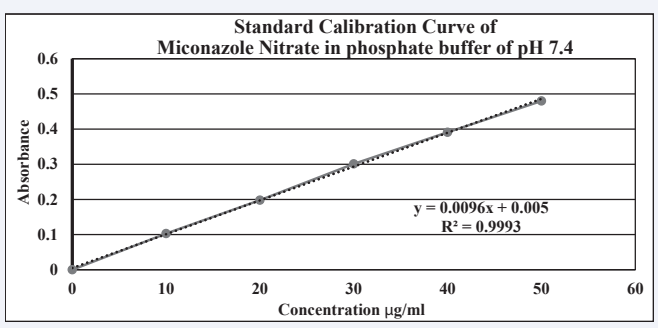

Figure 3 Standard curve for Miconazole Nitrate in phosphate buffer of pH 7.4

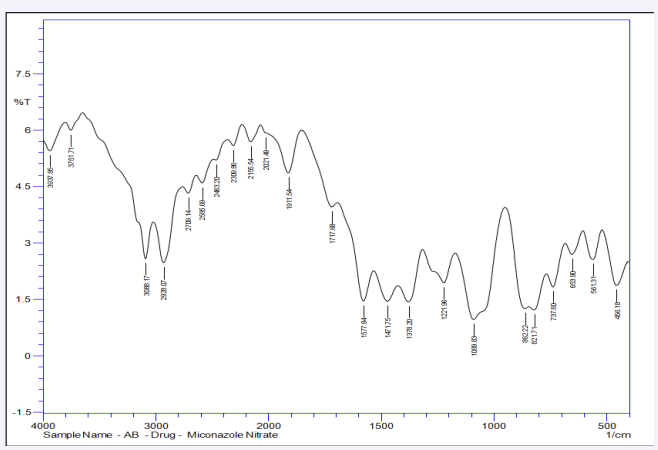

Figure 4 FTIR Spectra of Miconazole Nitrate

Table 3: Organoleptic characterization of drug

Identification Test	Observed Result
Appearance	Fine Powder
Colour	White or almost white crystalline powder
Odour	odourless
Melting point	184-185 °C
Solubility	ethanol, methanol, chloroform, Phosphate buffer of pH 7.4

Table 4: Standard curve of Miconazole Nitrate in phosphate buffer of pH 7.4

Concentration (µg/ml)	Absorbance λ_{max}(232 nm)
10	0.103
20	0.198
30	0.301
40	0.391
50	0.480

Table 5: FTIR Interpretation of Miconazole Nitrate

Functional groups present in Miconazole Nitrate	IR Peaks of Miconazole Nitrate (cm^{-1})
C-H	2709.1
N-H	3088.1
C=C	1577.8
C=O	1577.8
C-N	1378.2
C-O	862.2

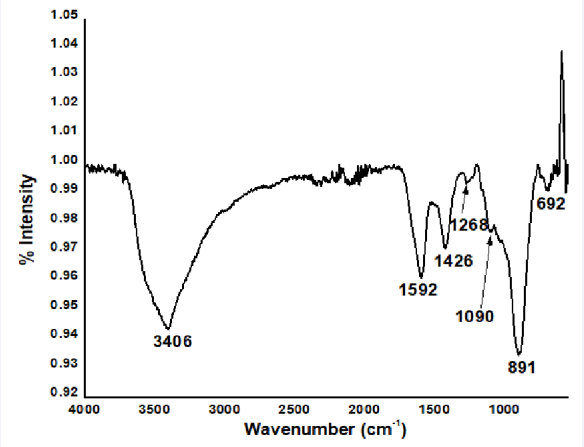

Figure 5 FTIR Spectra of Optimized Miconazole Nitrate Microemulsion

Table 6: FTIR Interpretation of Mixture of Miconazole Nitrate

Functional groups	IR Peaks of Miconazole Nitrate Microemulsion (cm^{-1})
C-H	2708.6
N-H	3087.8
C=C	1576.9
C=O	1576.9
C-N	1376.9
C-O	861.6

FTIR Interpretation: It has been observed that Miconazole Nitrate has functional groups like C-H, N-H, C=C, C=O, C-N and C-O whose peaks are observed that all these peaks of Miconazole Nitrate were found to be present in IR Spectrum of microemulsion. It is concluded from this observation that there is no interaction between Miconazole Nitrate and excipients used in microemulsion.

Evaluation Parameters of Miconazole Nitrate Microemulsion: Evaluation study of Miconazole Nitrate Microemulsion refer Table 7

In-Vitro Drug Diffusion Study

In-vitro drug diffusion study of batches F1 to F15 ie. Batch F4 and F15 shown in table respectively and %cumulative drug diffusion data for its recorded in Table 8. The obtained result indicates that the rate and extent of drug diffuse the concentration of excipients increased in the formulation [Table 8 and Figure 6-9].

From above graph the Drug Diffusion study of batches F11 and F15 showed the maximum percent release at 3-5 hrs, and given batches taken same concentration of oil, surfactant and co-surfactant using Placket Burman Design of Experiment (DoE).

Particle Size Analysis

Results – [Table 9 and Figure 10]

Particle size of optimized microemulsion were found to be 144.0 (r.nm) which is 0.14 µm respectively within the range of 0.01-0.20 µm.

Zeta Potential of optimized batch F15:

Results – [Table 10].

Result Quality – Good [Figure 11].

Zeta potential of optimized microemulsion were found to be -19.0 ± 8.24 mV respectively within the range of −8.11 ± 0.77 mV. It had been observed that as zeta potential is in between ± 30 mV, it is concluded that microemulsion is stable in nature.

Optimization of Batch

From the all formulation of 15 batches. F4 and F15 called as the Optimization of batch, because the F4, F15 had no phase separation and it had good stability as compared to the all batches. It was found that optimize batch F4 shows the better %

Table 7: Evaluation study of Miconazole Nitrate Microemulsion

Batches	Particle size (µm)	pH	Density (g/cc)	Viscosity (cps)	Drug content (%)	Centrifugation study (3500 rpm)	Freeze thaw study
F1	0.02	6.97	0.94	43.0	66.97	Stable	Stable
F2	0.02	6.97	0.96	34.4	31.14	Phase separation	Phase separation
F3	0.02	6.97	0.85	29.8	32.81	Stable	Stable
F4	0.02	7.07	0.97	48.7	86.45	Stable	Stable
F5	0.02	7.01	0.95	5.04	45.83	Phase separation	Phase separation
F6	0.02	7.02	0.98	17.6	23.02	Stable	Stable
F7	0.03	7.02	0.96	26.6	24.68	Phase separation	Phase separation
F8	0.02	7.03	0.96	46.4	44.27	Stable	Stable
F9	0.02	7.04	0.97	29.0	46.45	Stable	Stable
F10	0.02	7.02	0.98	43.3	36.45	Stable	Stable
F11	0.02	7.09	0.96	56.8	65.62	Stable	Stable
F12	0.02	7.08	0.96	41.5	81.04	Stable	Stable
F13	0.02	7.08	0.98	22.9	79.79	Stable	Stable
F14	0.02	7.07	0.98	16.7	71.04	Stable	Stable
F15	0.14	6.97	0.98	58.5	94.06	Stable	Stable

Table 8: In-Vitro Cumulative Drug Diffusion study of formulation F1-F15

Time(hr)	0	1	2	3	4	5
F1	0	62.5	75	121.67		
F2	0	56.25	66.25	67.5	80	
F3	0	50	56	75	68.75	
F4	0	66.25	98.75	100		
F5	0	37.5	55	67.5	75	
F6	0	62.5	67.5	77.5	96.25	
F7	0	41.25	55	60	86.25	
F8	0	47.5	60	71.25		
F9	0	95	98.75	122.5		
F10	0	68.75	95	120		
F11	0	40	72.54	111.25		
F12	0	45	62.5	97.5		
F13	0	52.5	67.5	62.5	75	
F14	0	36.25	57.5	88.75		
F15	0	12.5	33.75	38.75	51.25	98.75

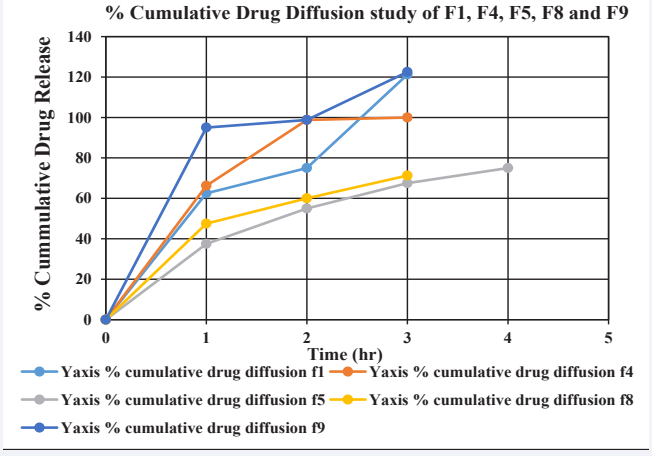

Figure 6 Diffusion profile of microemulsion formulation F1, F4, F5, F8, F9

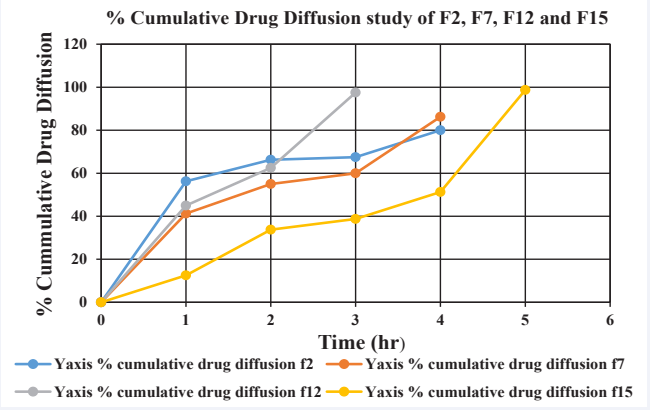

Figure 7 Diffusion profile of microemulsion formulation F2, F7, F12, F15

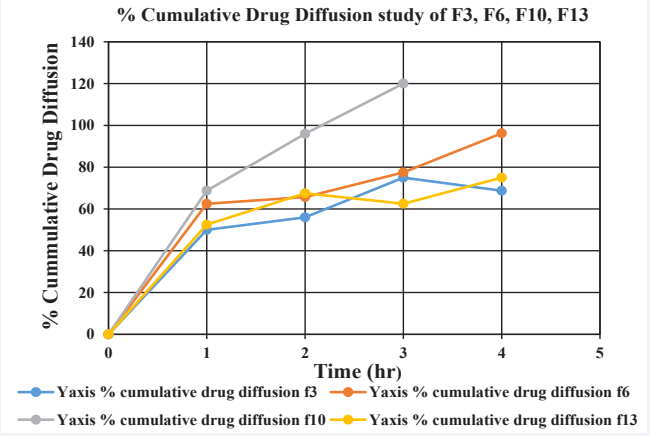

Figure 8 Diffusion profile of microemulsion formulation F3, F6, F10, F13

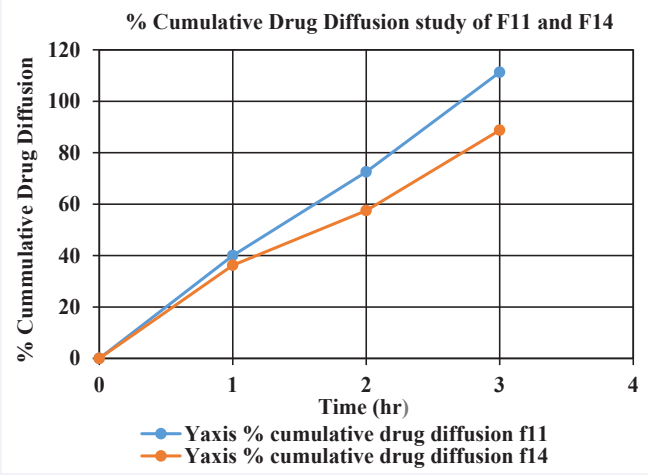

Figure 9 Diffusion profile of microemulsion formulation F11 and F14

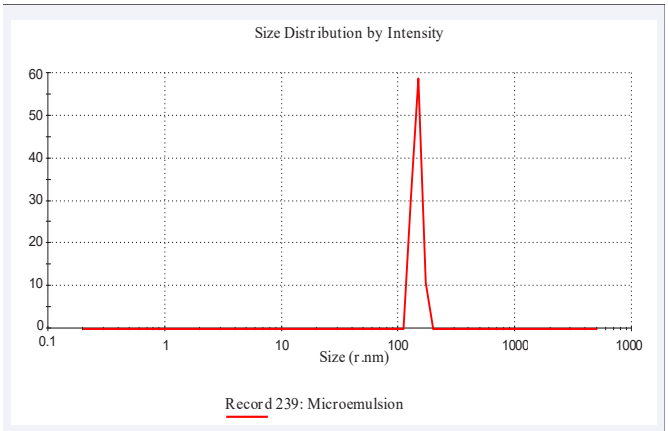

Figure 10 Particle size distribution graph

Table 9: Physical properties of microspheres

			Size (r.nm):	% Intensity	Width (r.n)
Z-Average (r.nm):	1128	Peak 1:	144.0	100.0	13.03
PdI:	1.000	Peak 2:	0.000	0.0	0.000
Intercept:	0.920	Peak 3:	0.000	0.0	0.000

Table 10: Zeta potential study

			Mean (mV)	Area (%)	Width (mV)
Zeta Potential (mV):	-19.0	Peak 1:	-19.0	100.0	8.24
Zeta Deviation (mV):	8.24	Peak 2:	0.00	0.0	0.00
Conductivity (mS/cm):	0.0932	Peak 3:	0.00	0.0	0.00

drug release. It showed 100 % cumulative drug diffusion study after 3 hour. It showed 0.97g/cc density, 48.7 cps viscosity, 7.07 pH, 0.02 µm Particle size and good stability. It was found that optimized batch F15 showed the better % drug release. It showed 98.75 % cumulative drug diffusion study after 5 hour. It showed 0.98g/cc density, 56.8 cps viscosity, 6.97 pH, 0.14 µm Particle size, Zeta potential -19.0 ± 8.24 mV and good stability.

Drug Diffusion Release Kinetic Study

Table 11: Drug Diffusion Kinetic study of formulation batch F1-F15

Batch No.	zero order	First order	Matrix	Peppas	Hixon-crowell
F1	0.9813	0.8101	0.9680	0.9487	0.8027
F2	0.8802	0.7028	0.9922	0.9980	0.7390
F3	0.9511	0.7104	0.9927	0.9597	0.7663
F4	0.9959	0.9234	0.9434	0.9854	0.7673
F5	0.9805	0.9183	0.9928	1.0000	0.7973
F6	0.9011	0.9641	0.9930	0.9803	0.7356
F7	0.9430	0.8373	0.9997	0.9986	0.7650
F8	0.9524	0.9170	0.9993	0.9974	0.7679
F9	0.9123	0.8653	0.9950	0.9472	0.7405
F10	0.9778	0.9624	0.9936	0.9979	0.7878
F11	0.9986	0.8830	0.9464	0.9983	0.8619
F12	0.9922	0.9163	0.9659	0.9804	0.8198
F13	0.8794	0.8102	0.9676	0.9624	0.7320
F14	0.9973	0.9064	0.9573	0.9929	0.8384
F15	0.9871	0.9264	0.9431	0.9764	0.9598

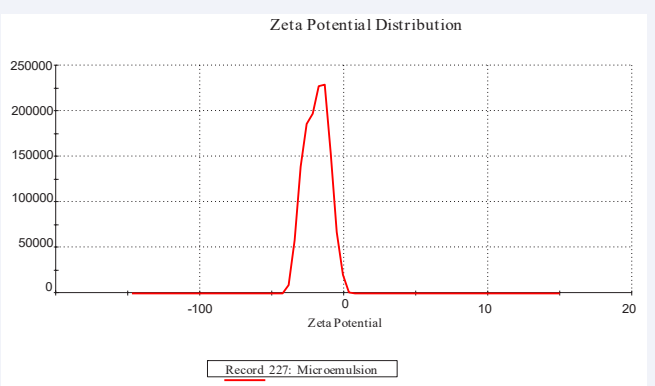

Figure 11 Zeta potential distribution graph

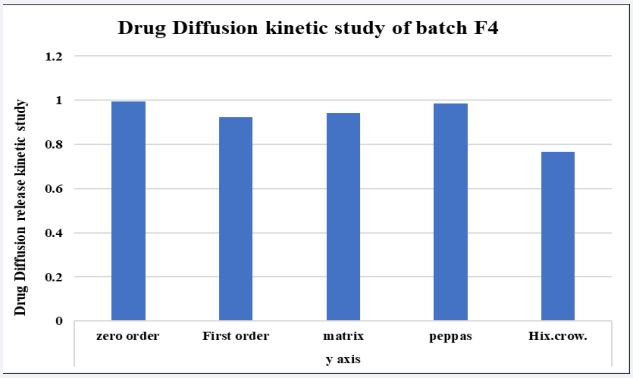

Figure 12 Drug Diffusion kinetic release study of optimized batch F4

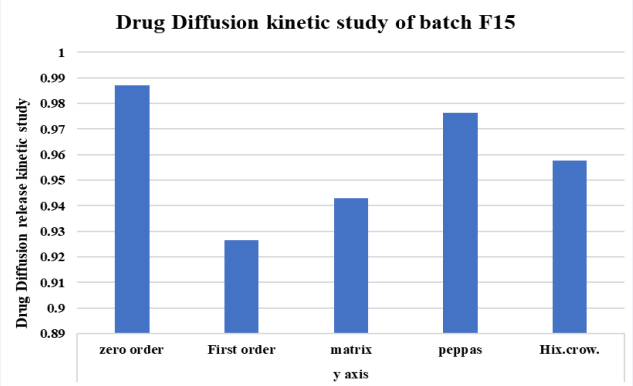

Figure 13 Drug Diffusion kinetic release study of optimized batch F15

Table 12: Evaluation parameters of optimized formulation (F4 and F15) before and after stability study

Sr no.	Parameters	Observation (Batch F4) Before	Observation (Batch F15) Before	Observation (Batch F4) After	Observation (Batch F15) After
1	pH	7.07	6.97	7.07	6,97
2	Density (g/cc)	0.97	0.98	0.91	0.86
3	Viscosity (cps)	48.7	58.5	46.5	59.1
4	Drug Content %	86.45	94.06	85.31	93.68
5	Centrifugation study (3500 rpm)	Stable	Stable	Stable	Stable
6	Freeze thaw	Stable	Stable	Stable	Stable
7	Particle size	0.2	0.14	0.3	0.12

The kinetic models and fixed equations used to explain the release kinetics of the Miconazole Nitrate microemulsion varied for all formulations. The tables below display the regression. coefficients (R) calculated for the different kinetic models. The R values were considered for both first-order and zero-order models. All the formulation were followed the zero order kinetic study. It was observed that the R values for the zero-order models were higher for formulation F4 0.9959 and F15 0.9871 as compared to the first-order models. Consequently, it showed that the drug release from the optimized batch F4 and F15 formulation followed zero-order kinetics in Figure10 and Table 11,12.

Stability Study

From all the formulations were evaluated for pH, particle size, Centrifugation, Freeze thaw, Viscosity, Density and Drug content and diffusion profile of microemulsion it was observed that there was no significant difference in the evaluation parameters and diffusion profile after 30 days stability studies. All the test results were found to be in range. Hence the formulations were stable under stated storage condition [Figure 14,15 and Table 12,13].

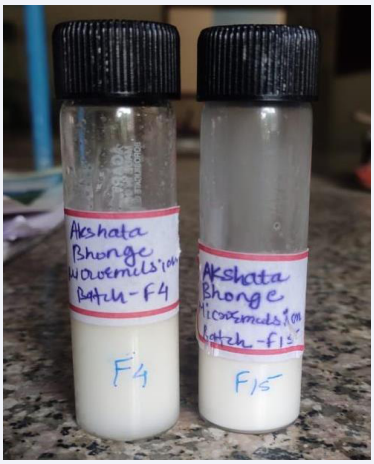

Figure 14 Photo of Optimized Microemulsion formulation after stability study

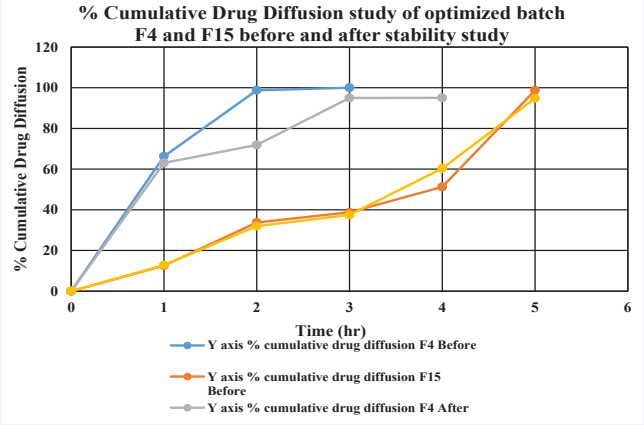

Figure 15 Diffusion profile of microemulsion formulation F4 and F15 after stability study

Table 13: In-Vitro Diffusion study data of optimized formulation F4 and F15 before and after stability study

Time (Hr)	0 Day (Batch F4)	0 Day (Batch F15)	30 Day (Batch F4)	30 Day (Batch F15)
1	66.25	12.5	63.05	12.8
2	98.75	33.75	71.89	31.97
3	100	38.75	95.01	37.48
4		51.25	95.07	60.33
5		98.75		94.81

CONCLUSION

The microemulsion containing Miconazole Nitrate was studied for topical delivery. Various type of components such as Isopropyl Palmitate, Polyethylene glycol 400, Span 80, Methyl cellulose, Methyl paraben and distill water used to preparation of microemulsion. All the components were selected for different concentration of oil, surfactant and co-surfactant by using Placket Burman Design of Experiment (DoE). Microemulsion were prepared by using high shear homogenization method. The microemulsion containing drug miconazole nitrate, Isopropyl palmitate, span 80, methyl paraben and methyl cellulose as an oil phase, co-surfactant polyethylene glycol 400 and distilled water as an aqueous phase. Formulated F1-F15 batches of Miconazole Nitrate microemulsion and selected the optimum batches of F4 and F15 for the optimization of further evaluation parameters and value of all the parameters such as batch F4 showed the 0.97g/cc density, 48.7 cps viscosity, 7.07 pH, 0.02 µm Particle size and good stability, It showed 100 % cumulative drug diffusion study after 3 hour. Batch F15 showed 0.98g/cc density, 56.8 cps viscosity, 6.97 pH, 0.14 µm Particle size, Zeta potential -19.0 ± 8.24 mV and good stability, it showed 98.75 % cumulative drug diffusion study after 5 hour. Finally, the Microemulsion formulation F4 and F15 was found to be better result, Therefore, it was selected as the best formulation. The drug diffusion release kinetic study for batch F4 and F15 followed to Zero-Order matrix model. After the stability study of microemulsion it was observed that there was no significant difference in the evaluation parameters and diffusion profile after 30 days stability studies. All the test results were found to be in range. Hence the formulations were stable under stated storage condition.

ACKNOWLEDGMENT

The author would like to acknowledge to Principal, Prof. (Dr.) A. V. Chandewar, P. Wadhwani College of Pharmacy, Yavatmal, Maharashtra for providing the necessary facilities to carry out current this research work and provided the Materials from Yarrow Chem Industries ltd, Mumbai. Also Acknowledge to my Prof. (Dr.) B. V. Bakade Mam for who provided knowledge and generous guided to me for my research work.

REFERENCES

1. Suhail N, Alzahrani AK, Basha1 WJ, Kizilbash N, Zaidi A, Ambreen J, et al. Microemulsions: Unique Properties, Pharmacological Applications, and Targeted Drug Delivery. Front Nanotechnol. 2021; 3: 1-6.
2. Gowda SP, Parthiban S, Senthilkumar GP. Microemulsion as advanced topical drug delivery: A Review. EJPMR. 2019; 6: 185-190.
3. Sonawane AN. A Review, on Microemulsion. IJPRA. 2023; 8: 836-846.
4. Henio F, Moura LE. Plackett - Burman Saturated planning for analysis of Opportunities and improvements in Supermarkets Retailers. RC Multi Core. 2018; 2: 111-126.
5. National Center for Biotechnology Information. Miconazole (CID 4189). PubChem. 2024; 1-19.
6. Khan J, Asmani F, Wei JC, Akram J, Samer AD, Kaleemillah M, et al. Formulation of Clindamycin Nano-emulsion. Int J Pharm Sci Res. 2015; 6: 1845-1854.
7. Bhavani, Jeeva, Karthick, Raghul, Pravin Kumar, Vijay. A Review on formulation and evaluation of microemulsion. IJPRA Journal. 2022; 7: 1644-1654.