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Development of Fluconazole Loaded Clove Oil Based Microemulsion for Topical Delivery

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Keywords: Fluconazole, Clove oil, Microemulsion, Microemulsion gel, Pseudo ternary phase diagram, antifungal effect

ABSTRACT

The goal of the current investigation is to formulate Fluconazole loaded microemulsion (ME) with clove oil for deeper skin penetration and to obtain the dual benefit of drug and oil combination to improve antifungal efficacy of a drug with a reduced dose. We developed a Pseudo ternary phase diagram to identify the microemulsion zone by using the oil (clove oil), surfactant (Tween 20 and Tween 80), and co-surfactant (Propylene glycol) by water titration method. We formulated six different formulations (ME1 – ME6) by changing the oil/surfactant and cosurfactant ratio. The developed microemulsion formulation was characterized for various parameters % Transmittance, viscosity, pH, drug content, surface morphology, zeta potential, and in-vitro drug release study. The optimized microemulsion emulsion formulation is further converted into Microemulgel by dispersing the ME into 2% w/v Carbapol gel (MEG) and further evaluated for various parameters. The antifungal efficacy was carried out for ME and Microemulgel by diffusion method against *Candida albicans* (MTCC no: 227) and compared with marketed gel which showed ME and MEG have a better antifungal effect than marketed product, proved that the synergistic effect could be achieved by both clove oil and fluconazole drug by microemulsion formulation with deeper skin penetration effect.

INTRODUCTION

Emulsions are pharmaceutical formulations made up of at least two immiscible liquids, most commonly oil and water. A microemulsion is a dispersion that includes oil, a surfactant, a co-surfactant, and an aqueous phase. It's a single optically isotropic and thermodynamically stable liquid solution with droplet diameters usually ranging from 10 to 100 nanometers. Microemulsions have a variety of advantages over traditional formulations, including improved drug solubility, good thermodynamic stability, ease of manufacture, and permeation enhancement capacity, all of which have been used in drug delivery systems.[1]

Microemulsions are macroscopically isotropic mixtures that include at least one hydrophilic, hydrophobic, and amphiphilic portion. Their thermodynamic stability and nanostructure are two key features that set them apart from conventional emulsions, which are thermodynamically unstable. Schulman and Winsor were the first to note microemulsions in the 1950s. Oil-in-water (o/w), water-in-oil (w/o), and bicontinuous phase microemulsions are the three types of traditional microemulsions.[2]

All microemulsions are fluids with low viscosity. Microemulsions are classified as water-in-oil (w/o), oil-in-water (o/w), or bicontinuous systems based on their composition, water, and oil phases have exceptionally low interfacial tension. Due to the presence of both lipophilic and hydrophilic domains, a wide range of lipophilic and hydrophilic drugs can be incorporated into these systems. Enzymatic hydrolysis and oxidation are prevented through these flexible delivery systems. The solubilization and bioavailability of lipophilic drugs are improved. These systems can be used for topical, intravenous, and oral delivery as well as for sustained and targeted delivery. Many poorly soluble drugs have their oral bioavailability improved.[3]

Microemulsions have been used in a variety of fields to deliver a drug in a continuous or managed manner for extended release, as opposed to a traditional dosage method for topical applications with limited systemic absorption. Depending on the phase behavior and properties of the constituents, a low energy emulsification method may be used to facilitate the formation of extremely small droplets using co-surfactants that involve self-emulsification. The phase conduct can be used to test and incorporate low-energy technologies for the treatment of warts, bacteria, corns, and other skin conditions. The proposed microemulsion drug would improve poorly soluble drugs' solubility, increase

bioavailability, protect unstable drugs from environmental conditions, and have a long shelf life.[4]

Essential oils are illustrious antibacterial, antifungal, antioxidant, antigiardial, and antidiabetic agents. Different essential oils and oil-based formulations are reported to be efficient antimicrobial agents that can be used to prevent food spoilage. The antibacterial activity may be due to the ability of oil components to damage the bacterial membranes and hence, resulting in lysis of the cell.[5]

Clove is loaded up with antibacterial and disinfectant properties. Clove oil contains a compound called eugenol that helps in treating skin break out. It battles the skin break-out microbes and helps in diminishing expansion and redness. Clove oil makes them astonish skin benefits. This oil helps in forestalling and getting out the current skin break out alongside decreasing redness, torment, imperfections, and imprints.

Fluconazole is a bis-triazodifluorophenyl-2-propanol antifungal agent that has efficacy against Candida albicans both in vitro and in vivo. Fluconazole is a safe and effective antifungal agent for treating Candida albicans on the skin. It has a long plasma half-life of approximately 25 to 30 hours in humans, with a primary renal excretion mode, and the drug is easily dispersed across the tissues.[6]

Hence, in the present investigation, we would like to study the antifungal effect of Fluconazole along with essential oil like Clove oil to be formulated as microemulsions and explore the benefit of better antifungal effect.

MATERIALS AND METHOD

MATERIALS

Fluconazole was acquired as a blessing gift samples from Karnataka antibiotic pharma. Ltd. Bangalore. Tween 20, Tween 80 and Propylene glycol (SD-Fine substance ltd, Mumbai), Clove oil (Sri Banashankari brokers, Bangalore, Karnataka).

METHOD

Method of preparation

a) Development of pseudo ternary stage outline:

The pseudo ternary stage graph was utilized to discover the present scope of microemulsions, and stage outlines were built utilizing the water titration strategy at encompassing temperature (25 ºC). Given the accessible dissolvability profile of the drug. The Clove oil was chosen as an oil stage; Tween 20, Tween 80 were utilized as a surfactant, and Propylene glycol was utilized as a co-surfactant. The Smix (surfactant + Co-surfactant) proportions were chosen to be 1:1, 2:1, and 3:1 w/w and utilized. For each stage chart at explicit Smix focus and clove oil was added from a scope of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1 (%w/w) and add and mix with refined water by the consecutive option of 0.1ml of water. The water was added drop by drop while blending on an attractive stirrer at room temperature, and the samples were set apart as being optically clear or turbid. The microemulsion areas were recognized as straightforward and isotropic combinations. The level of three unique stages oil, water, and a combination of surfactant and co-surfactant were determined (Table 1). From the endpoint synthesis of titrated tests, the mass percent piece of the segments like oil, Smix, and water was determined and afterward plotted on a three-sided organize to build the pseudo ternary stage diagram.

Table No. 1: Formulation development of Clove oil-based Fluconazole microemulsion with selected percentages of Oil, Smix, and Water from the Pseudo ternary Phase.

Formulation code	Smix ratio	Surfactants	Oils	Percent w/w component in the formulation			
				Oil %	Smix %	Water %	Drug %
ME1	1:1	**Tween 80**	**Clove oil**	37	52	11	0.5
ME2	2:1			30	55	15	0.5
ME3	3:1			25	60	15	0.5
ME4	1:1	**Tween 20**	**Clove oil**	15	55	30	0.5
ME5	2:1			20	50	30	0.5
ME6	3:1			35	50	15	0.5

b) The Solubility of Fluconazole:

The Solubility was performed for the oil, surfactants, and co-surfactant for forming microemulsion. The solvency of the Fluconazole in oil is a fundamental advance for the microemulsion plan. So before building the stage outline one should need to choose the oil, surfactant, and co-surfactant in which the medication shows the most extreme solvency, to be in the ideal dissolvability range, which is fundamental for the detailing of a microemulsion drug conveyance framework. The powder medication of Fluconazole has included overabundance to every one of the oils, surfactants (S), cosurfactant (CoS), and afterward vortexed for blending. After vortexing, the examples were saved for 72 hours at the surrounding temperature for achieving harmony. The equilibrated tests were then centrifuged at 5000 rpm for 30 minutes to eliminate the undissolved medication. The supernatant was taken and weakened with methanol and saw by UV spectrophotometric strategy at 260 nm.[7]

c) Formulation Fluconazole microemulsion:

Microemulsion (ME1- ME6) was prepared by the high-energy emulsification method by the high-pressure homogenization technique. clove oil, Surfactant, and co-surfactant were mixed thoroughly by vortex mixture. To the uniform mixer required quantity of water, added and homogenized by high pressure homogenize for 10min at 6,000rpm. The prepared Microemulsion will be stored properly and the optimized formulation will be incorporated in a suitable gel base (Carbopol 2 % W/V). Both ME and MEG were evaluated for various parameters. [8]

EVALUATION OF FLUCONAZOLE MICROEMULSION [9-16]

The prepared microemulsion formulation was characterized for parameters like Drug content, Particle size analysis, Determination of viscosity, Surface morphology, FT-IR analysis, Zeta potential. *In-vitro* drug release and *In-vitro* antifungal activity. The optimized formula was incorporated into 2% carbapol gel and evaluated for spreadability, rheological property, pH and *In-vitro* drug release, and *In-vitro* antifungal activity.

***In-vitro* release studies**

An *in-vitro* drug release study was performed using diffusion cells. Egg membrane was placed between receptor and donor compartments. Microemulsion gel equivalent to 1 gm was

placed in the donor compartment and the receptor compartment was filled with phosphate buffer pH 7.4. The diffusion cells were maintained at 37 ± 0.5 ℃ with stirring at 100 rpm throughout the experiment. At a fixed time, interval, 5 ml of aliquots were withdrawn for every 1, 2, 3, 4, 5, and 6 hrs from the receiver compartment through the side tube and analysed by UV spectrophotometer at λ max 260 nm.

Antifungal activity against *Candida albicans*

Methodology

Sample preparation: The samples were prepared using 100% DFM.

The fungal strain used in this study was *Candida albicans* MTCC no: 227 The strain was used to determine the Antibacterial activity by well diffusion method.

Preparation of inoculums

The fungal strain was transferred from the stock solution to PDA agar and incubated for 48 hRS at 37°C. A single colony from the plate was transferred to the PD broth and incubated at 37°C, for 48 h, and used as inoculums. The turbidity of the suspension was adjusted spectrophotometrically (range of 0.5–1.0) to the McFarland 0.5 turbidity standard (1.5×10^8 CFU/mL).

Antifungal activity by well diffusion method

The antifungal activity of given samples was investigated using the well-diffusion method. Test plates (diameter 10 cm) were prepared with 20 mL of PD agar (PDA). After the media get solidified, 100 µl of 48 h fungal culture (1.5×10^8 CFU/mL) was added and uniformly spread over plates using L shaped loop. Then make well (about 6mm diameter) and add 20 µL of Clove oil, different concentrations of the given samples 5ug/ml drug, 80ug/ml gel, and 80 ul of formulations. The wells loaded with sterile media are considered Blank. 30ug/40ul of flucos (marketed gel) was used as a standard. After loading plates were kept in a sterile condition until complete absorption of the test compounds. Plates were incubated at 37°C in an appropriate gaseous condition for 48 hrs. Zones of inhibition of microbial growth around the well were measured and recorded after the incubation time. The inhibitory zone was considered the shortest distance (cm) from the outside margin of the samples to the initial point of the microbial growth.

RESULT AND DISCUSSION

The pseudo ternary stage charts of different proportions of surfactants (Tween 20, Tween 80)/Co-surfactant (Propylene glycol) were utilized to develop. The Smix weight proportions [1:1, 2:1, 3:1] are addressed in Figure 1 to Figure 2 in the pseudo-ternary stage graph where microemulsion regions are noticed by using Ternary plot.com software. The optimized microemulsion ME3 was formulated into a gel by the use of Carbopol 934 gels containing 2% w/w gel was found to be suitable for gelling the microemulsion because of desirable consistency. And the optimized formulation was further evaluated for spreadability, viscosity, pH, and percentage assay as shown in Table 6.

Construction of Pseudo ternary phase diagrams

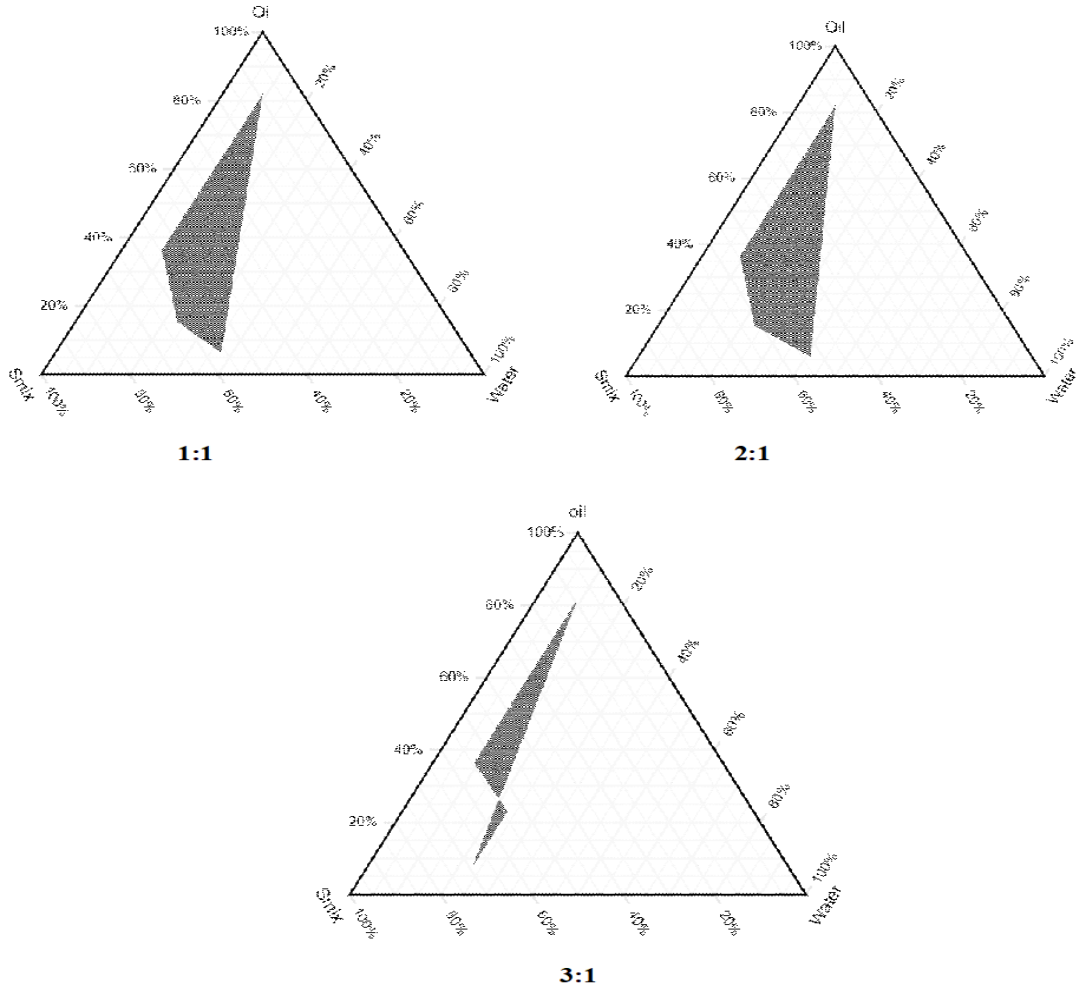

Figure No. 1: Pseudo ternary phase diagram using clove oil as oil, Tween 20 as surfactant, propylene glycol as co-surfactant, and water (Tween 20: Propylene glycol = 1:1, 2:1 and 3:1).

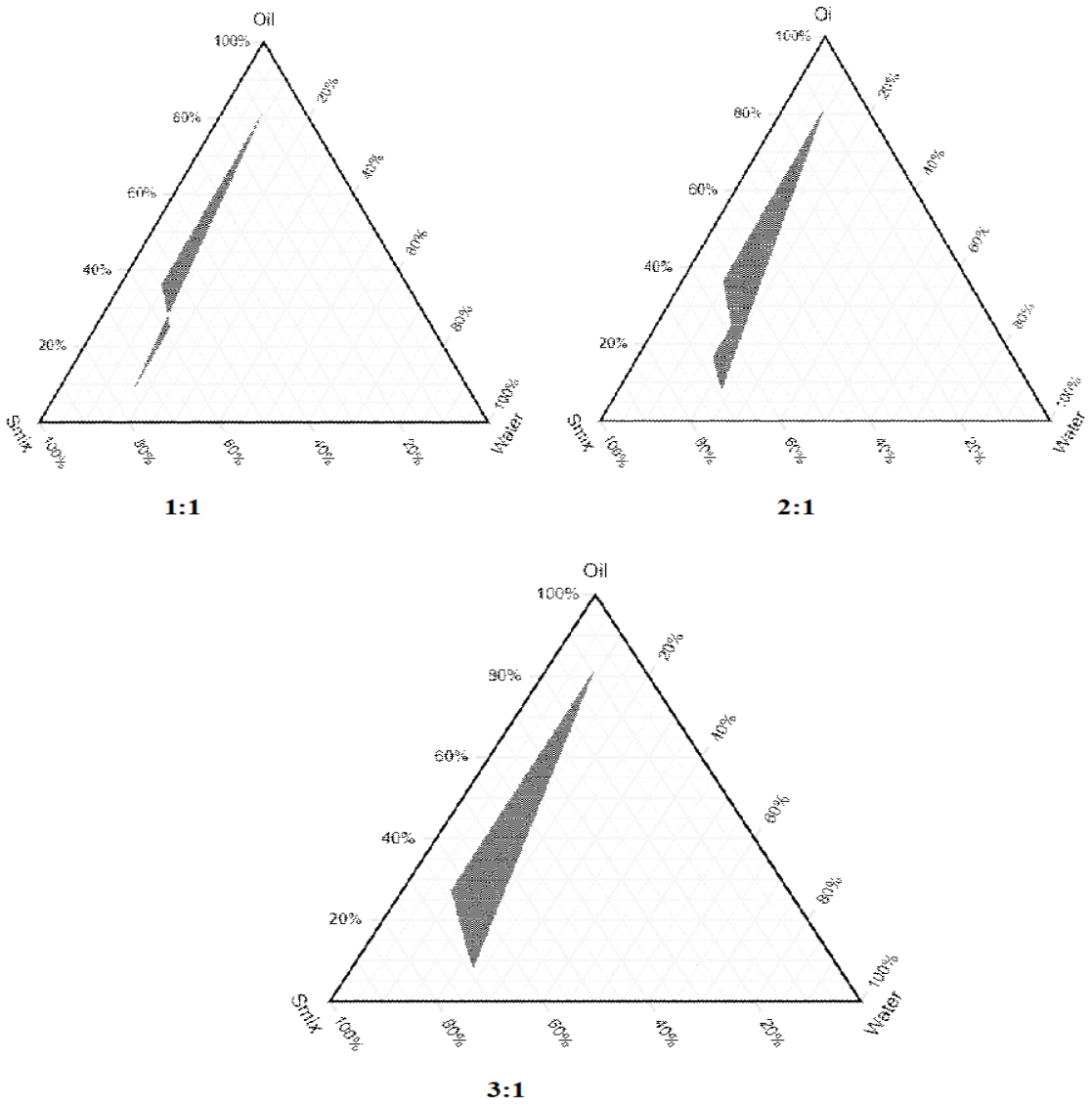

Figure No. 2: Pseudo ternary phase diagram using clove oil as oil, Tween 80 as surfactant, propylene glycol as co-surfactant, and water (Tween 80: Propylene glycol = 1:1, 2:1 and 3:1).

Greatest solvency of fluconazole in surfactants was found in Tween 80 (94 ± 0.279mg/ml), Tween 20 (60 ± 0.370mg/ml) and co-surfactant propylene glycol (90.23 ± 0.083mg/ml) and furthermore dissolvable in pH 7.4 phosphate cushion (50.98 ± 0.029mg/ml) as shown in Table 2.

Table No. 2: Solubility analysis of Fluconazole

Phase type	Excipient	Solubility mg/ml
Aqueous	water	4.63±0.726
Oil	Lemongrass Oil	90 ± 0.073
	Clove Oil	50 ± 0.273
Surfactant	Tween 20	60 ± 0.370
	Tween 60	46 ± 0.435
	Tween 80	94 ± 0.279
Co-Surfactant	Propylene glycol	90.23 ± 0.083
	PEG 400	71.53 ± 0.16
Phosphate Buffer	pH1.2	00.63 ± 0.517
	pH 4.4	56.00 ± 0.141
	pH 6.8	40.93 ± 0.191
	pH 7.4	50.98 ± 0.029

The drug content of all the formulations of fluconazole microemulsion is shown in Table 3. ME3 was exhibited 98.62±0.55% higher drug content than other formulations. The microemulsion drug content of all formulations was found to be within the range of 85-99% which was within the limits of USP specifications. The prepared Fluconazole microemulsion gel ME3-G was subjected to drug content uniformity. The microemulsion gel was in the permissible range of 93.45 % it indicated the drug uniformly dispersed throughout the formulation. (Table 6).

Table No. 3: Determination of % transmittance, viscosity and pH, and % drug content of the microemulsion formulation

Formulation code	%Transmittance	Viscosity in cps	pH	% drug content
ME1	94.55±0.25	13.23±0.62	6.2±0.10	92.34±0.24
ME2	93.9±0.2	14.64±0.11	6.13±0.11	90.76±0.11
ME3	99.25±0.15	12.40±0.63	6.26±0.15	98.62±0.05
ME4	97.55±0.35	14.99±0.53	5.93±0.05	89.36±0.36
ME5	95.85±0.25	19.35±0.48	6.23±0.05	91.85±0.47
ME6	97.87±0.35	20.80±0.16	6.36±0.110	95.29±0.06

All the prepared formulations were checked for their pH. All the formulations were showing pH in the range of 6.13 to 6.36 as shown in Table 3. This is well in the range for topical administered formulation and formulation. The pH value of optimized microemulsion formulation ME3 was 6.26±0.15 (Table 3) and is suitable for topical as well as a transdermal application because of the pH of the skin in the range of 5.5 to 7.0. The pH of microemulsion gel ME3-G gel was found to be 6.3 ± 0.36. (Table 6) and is suitable for topical as well as transdermal application.

The clarity of the microemulsion formulation was checked by % transmittance. All formulations of transmittance values are above 90% as shown in Table 3, which indicates that the microemulsions were transparent which is considered as the primary property of a microemulsion. The ME3 formulation showed 99.25± 0.15% compare to other formulations.

The viscosity of microemulsion formulation was determined as shown in Table 3, all samples exhibited Newtonian flow behavior and formulation ME3 showed 12.40±0.63 cps shows less viscous compared to other microemulsion formulations. And the optimized gel ME3-G viscosity was found to be 6898.72 ± 64.13 cps.

The surface morphology was studied by SEM for the optimized formulations which were confirmed that the particles are globular with globule size in the nanometre scale with a smooth surface as shown in Figure 3, for ME3. This can have the ability to form a microemulsion.

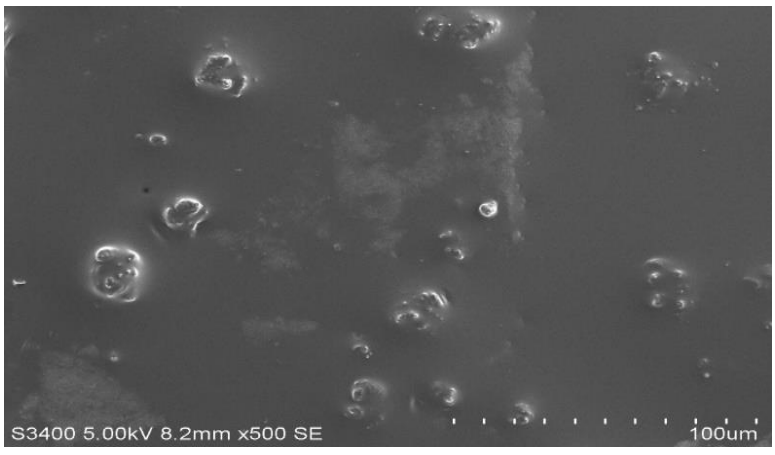

Figure No. 3: SEM image of ME3

The particle size and zeta potential were measured by a Marwin zeta analyzer and it was Found that 50.3nm for ME3. Confirmed that ME are within the required size ranges

confirmed formation ME. The Zeta potential of microemulsion ME3 was found to be 27.38 Mv (Fig 4) which shows that they are adequate to be stable.

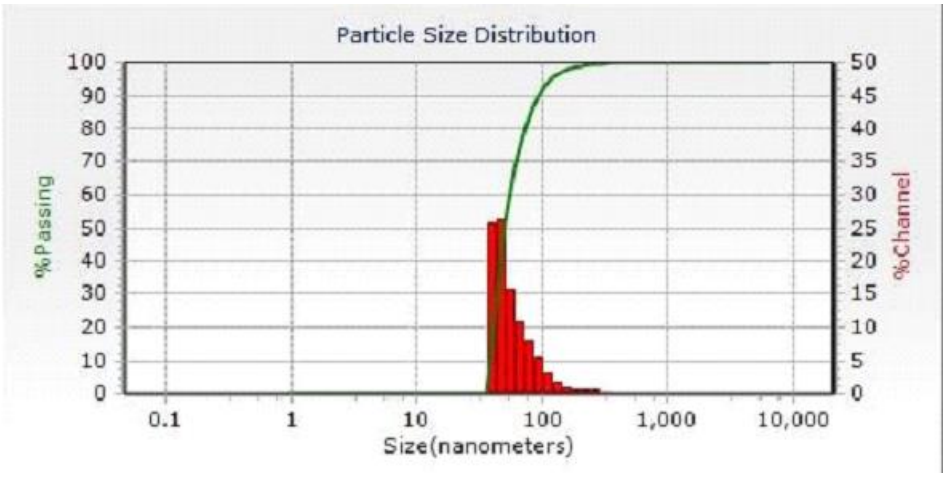

Figure No. 4: Result of particle size of the formulation ME3.

FTIR Spectrum of Fluconazole was obtained by scanning the drug in the range of 4000 to 400. Major peaks observed were as 3676.45, & 3350.46 cm-1 (-OH Stretch), 1417.73, & 1635.69 (C-F),1620.26 & 1635.69 cm-1 (C=C), 1676.20 1670.41 cm-1 (C=C), 1676.20, & 167041cm-1 (C=N Stretch) and 2800.73, & 2879.82 cm-1 (C-H Stretch), and, 3018.03 & 3311.89 cm-1 (C-H Aromatic Stretch) whose presence resembled the structure of Fluconazole. Observed FTIR spectra and standard values were as depicted in Figure 5.1,5.2 and Table 4. The observed value was within the range or very close to the characteristic peaks of standard value confirming the drug as Fluconazole. And there is no interaction between drugs and other components.

Table No. 4: FTIR comparison of the characteristic peak of pure drug and formulation

Functional group	**Wavenumber (cm^{-1}) of pure drug**	**Wavenumber (cm^{-1}) of ME3formulation**
-OH (Stretch)	3676.45	3350.46
C-F	1417.73	1357.93
C=C	1620.26	1635.69
C=N(Stretch)	1676.20	1670.41
C-H (Stretch)	2800.73	2879.82
C-H (Aromatic Stretch)	3018.03	3311.89

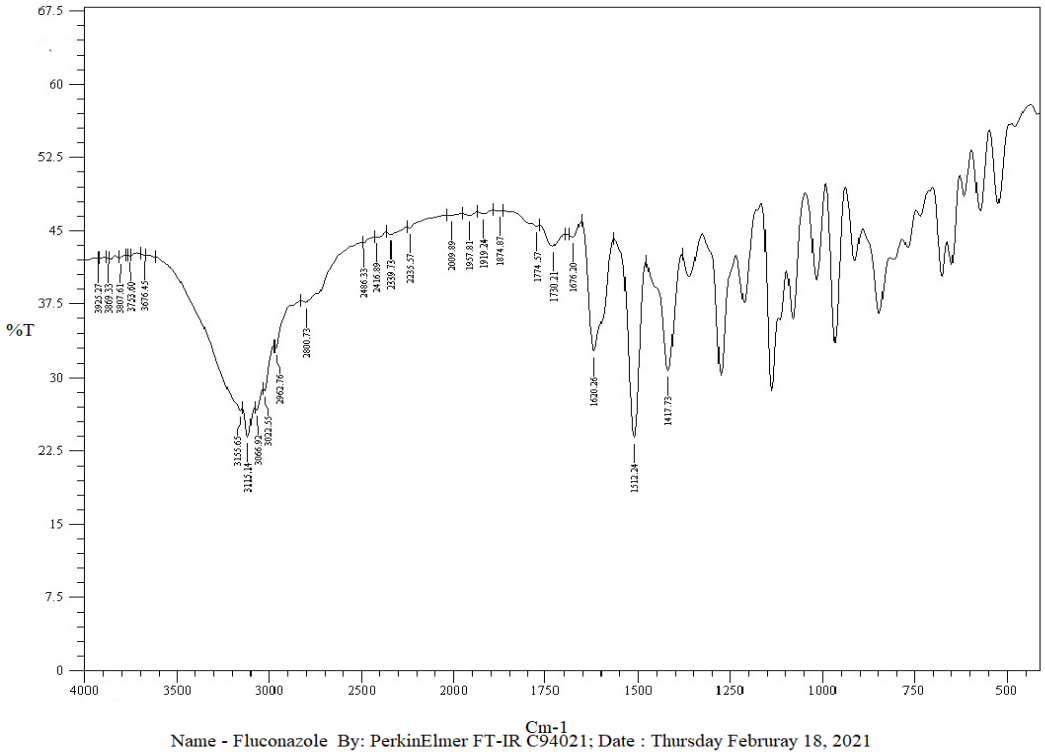

Figure No. 5.1: FTIR spectra of Fluconazole

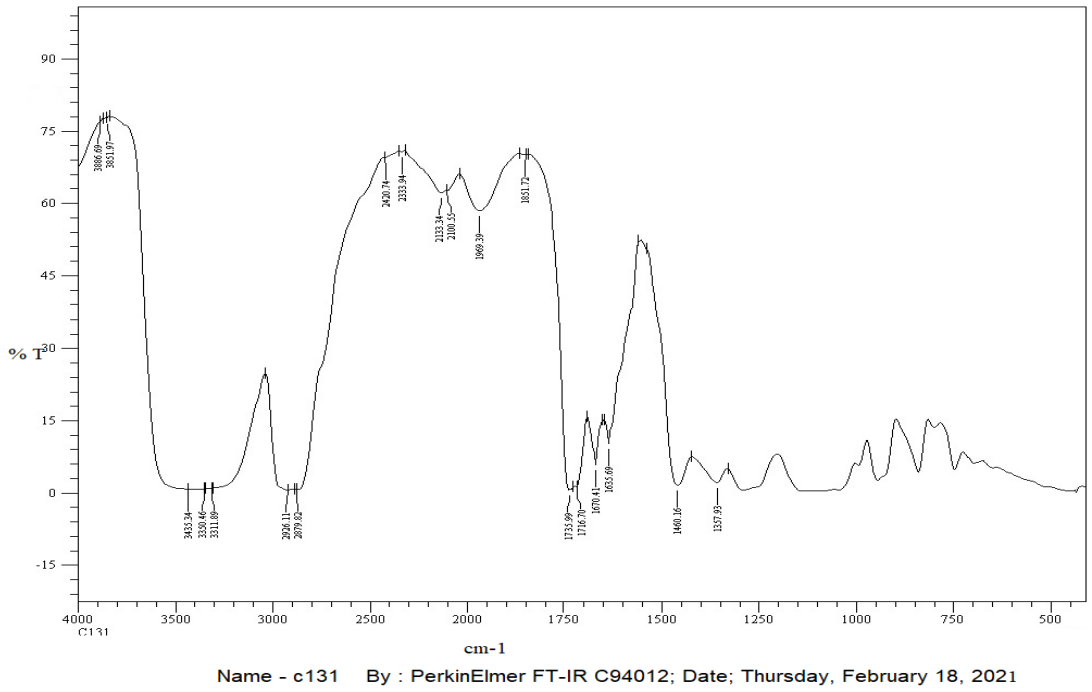

Figure No. 5.2: FTIR spectra of ME3 formulation

From the *in-vitro* release studies, we observed that 0 - 20% of the drug was delivered in 1hrs and over half the drug released in 3 hrs, and more than 80% of the drug released in 6 hrs. The

formulation of ME3 showed 93.08% (Figure 6). And it has shown a higher % of medication discharge when compared with other formulations. (Table 5) The result of the in-vitro release of fluconazole from the gel formulation. However, the results clearly show that the gels can retain the drug for prolonged periods. The % CDR of microemulsion gel formulation ME3-G was found to be 89.08 %, respectively as shown in Figures 7.

Table No. 5: *In-vitro* diffusion study of Clove oil microemulsion

Time in hrs	% Cumulative drug release					
	ME1	ME2	ME3	ME4	ME5	ME6
0	0	0	0	0	0	0
1	12.164	13.814	15.567	13.814	16.185	12.783
2	29.606	39.931	33.763	25.498	29.955	39.921
3	52.169	52.288	54.100	50.082	52.2123	67.742
4	70.952	70.573	70.564	70.408	67.427	70.707
5	76.210	84.724	81.596	78.229	80.464	78.652
6	91.636	89.164	93.084	87.969	91.872	90.257

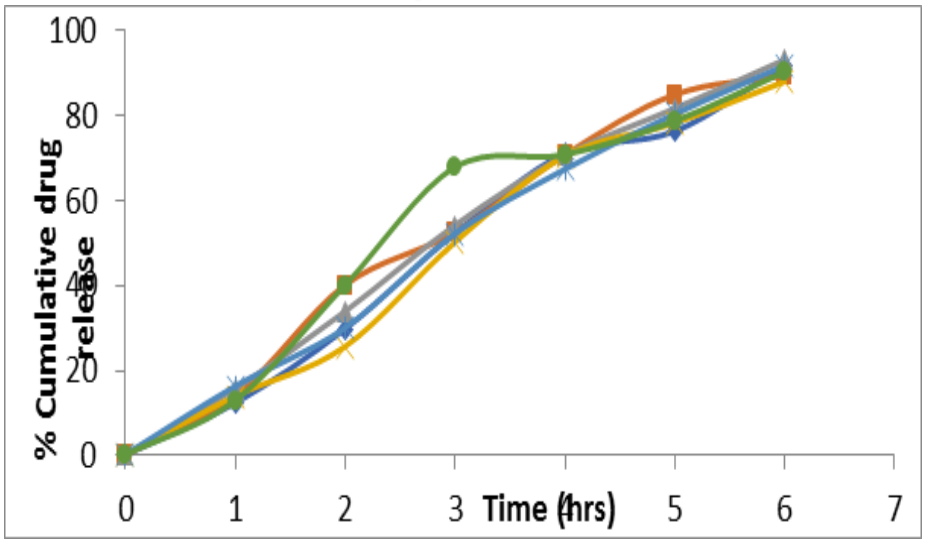

Figure No. 6: % cumulative drug release of ME1-ME6

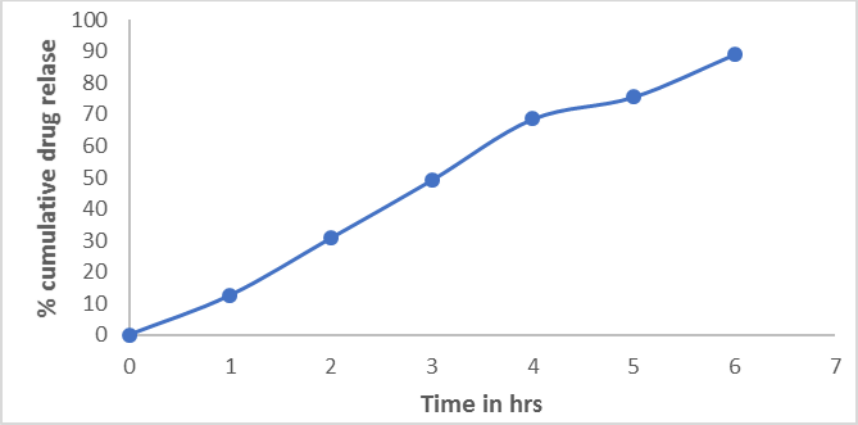

Figure No. 7: % cumulative drug release of ME3-G

The spreadability is an important property of topical formulation from a patient compliance point of view. The increase in the diameter due to the spreading of the formulation ME3-G was 7.1 ± 002. (Table 6). The viscosity of the gels of microemulsion formulations ME3-G was determined and 7214.67 ± 71.15 cps. (Table 6).

Table No. 6: Viscosity, pH, and % drug content of microemulsion gel

Formulation code	%Spreadability	Viscosity in cps	pH	% drug content
ME3-G	7.3 ± 0.03	6898.72 ± 64.13	6.4 ± 0.23	91.68 ± 0.16

In-vitro antifungal effect to evaluate the efficacy of optimized formulations, oils, and drugs against antifungal evaluation was carried out using fungal strain *Candida albicans MTCC no: 227.* The antifungal activity by the well-diffusion method was performed at a concentration of 80 µg/ml gels and sterile media as blank, Flucos (marketed product) as standard placed in well and measured zone of inhibition. *Candida albicans* were used as a standard fungus that has shown in Figure 8. The zone of inhibition was to be for drug 2.8 cm (5µg/ml), standard 1.5 cm (40 µl) clove oil 2.8 cm (20 µl), Microemulsion ME3 3.3cm (80 µl), Microemulsion gel ME3 2.7cm (80 µl) and ME3-G 2.7 cm (80 µl), shown in Table 7. The ME3 and ME3-G show a greater antifungal effect compare to the marketed product.

Table No. 7: Antifungal effect of microemulsion formulation and oils against *C. albican*

Components	Quantity	Zone of inhibition in cm
Drug (Fluconazole)	5µg/ml	2.8
Standard (Flucos -marketed product)	40 µl	1.5
Clove oil	20 µl	2.8
Microemulsion ME3	80 µl/ml	3.3
Microemulsion gel ME3-G	80 µg/ml	2.7

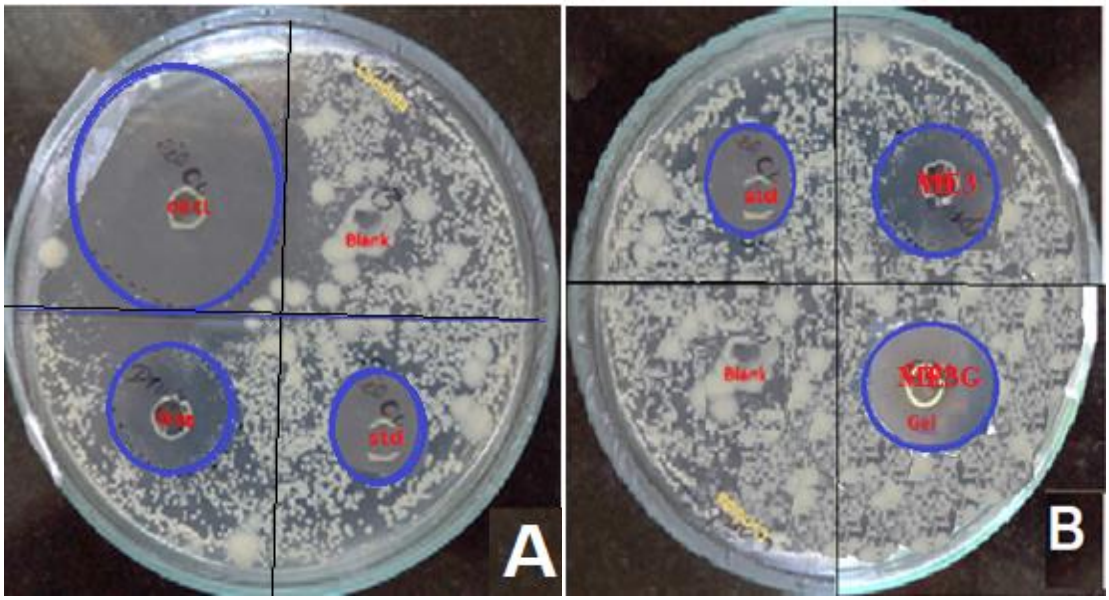

Figure No. 8: The Antifungal activity of (A) Clove oil with drug (B) Microemulsion ME3 and gel ME3-G against ***Candida albicans*** **using well-diffusion method.**

CONCLUSION

In this work, the optimized formulation of ME3 microemulsion and Microemulsion gel ME3-G showed a good antifungal effect of Fluconazole along with essential oil like Clove oil to be formulated as microemulsions, compared with other microemulsion formulation and marketed gel, ME and ME-G have a better antifungal effect than marketed product, this

proved that the synergistic effect could be achieved by both clove oil and fluconazole drug by microemulsion formulation with deeper skin penetration effect.

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REFERENCES

1. Anjali CH, Dash M, Chandrasekaran N, Mukherjee A. Antibacterial activity of sunflower oil microemulsion. Int J Pharm Pharm Sci. 2010;2(1):123–8.
2. Manognya JH. Design and characterization of microemulsion systems for etodolac. World J Pharm Pharm Sci. 2017;3(1):631–46.
3. Shahzadi I, Irfan Masood M, Chowdhary F, Ahmad Anjum A, Awais Nawaz M, Maqsood I, et al. Microemulsion formulation for topical delivery of miconazole nitrate. Int J Pharm Sci Rev Res. 2014;24(2):30–6.
4. Kreuter J. Colloidal Drug Delivery Systems. New York: M.Dekker CRC Press; 2014.
5. Ghosh V, Mukherjee A, Chandrasekaran N. Mustard oil microemulsion formulation and evaluation of bactericidal activity. Int J Pharm Pharm Sci. 2012; 4(4):497-500.
6. Schreiber W, Olbrisch A, Vorwerk CK, König W, Behrens-Baumann W. Combined topical fluconazole and corticosteroid treatment for experimental Candida albicans keratomycosis. Investigative ophthalmology & visual science. 2003;44(6):2634-43.
7. Madikattu K, Naidu SV, Srisailam K. Microemulsion based transdermal gels of Isradipine to enhance bioavailability: In vitro and in vivo evaluation. Asian J Pharm., 2016; 9(5): 23-30.
8. Samrudhi P and Padmini R. Honey based Clotrimazole microemulsion for topical delivery. Indo American J Pharm Res., 2016; 6(11): 6908-25.
9. Shah RR, Magdum CS, Patil SS, Niakwade NS. Preparation and evaluation of aceclofenac topical microemulsion. Iranian j pharm res: IJPR. 2010;9(1):5.
10. Muzaffar FA, Singh UK, Chauhan L. Review on microemulsion as futuristic drug delivery. Int J Pharm Pharm Sci. 2013;5(3):39-53.
11. Peira E, Carlotti ME, Trotta C, Cavalli R, Trotta M. Positively charged microemulsions for topical application. Int j pharm. 200;346(1-2):119-23.
12. Okur NU, Yavasoglu A, Karasulu HY. Preparation and evaluation of microemulsion formulations of Naproxen for dermal delivery. Chem Pharm Bull., 2014; 62(2): 135-43.
13. Hu L, Wu H, Niu F, Yan C, Yang X, Jia Y. Design of fenofibrate microemulsion for improved bioavailability. Int j pharm. 2011;420(2):251-5
14. Dev A, Dwivedi J, Momin M. Formulation and characterization of acyclovir based topical microemulsions by QBD approach. J. drug deliv. ther. 2019;9(1):237-43.
15. Tandel H, Patel P, Jani P. Preparation and study of Efavirenz microemulsion drug delivery system for enhancement of bioavailability. European J Pharm Med Res., 2015; 2(5): 1156-74.
16. PATEL TB, Patel TR, Suhagia BN. Preparation, characterization, and optimization of microemulsion for topical delivery of itraconazole. J. drug deliv. ther. 2018;8(2):136-45.

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