RESEARCH ARTICLE

Formulation and Characterization of Anti-fungal (Posaconazole) O/W Nanoemulsion

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Received: 24th March, 2021; Revised: 15th April, 2021; Accepted: 04th May, 2021; Available Online: 25th June, 2021

ABSTRACT

This research aims to prepare and evaluate posaconazole nanoemulsion to improve its solubility and release. Nanoemulsion was prepared by titration method and subjected to ultra-sonication to reach nano-size. Based on the solubility study, capmul mcm was selected as an oil phase, tween -80, and Cremophor EL as a surfactant, while methanol and transcutol –p represent the co-surfactant s-mixture. Stability study, light transmittance, particle size, polydispersibility, zeta potential, drug content were investigated. The optimum nanoemulsion formula (F11) consisting capmul mcm, cremophor EL, transcutol–p, and deionized water (DW), had 17.4 nm, 0.235, 45.73mv particle size, polydispersibility, and zeta potential, respectively. This formula shows 92.27% of drug release during 8hr which is considered a significant improvement compared to posaconazole suspension that gave only 18.19%.

Keywords: Posaconazole, nanoemulsion, pseudo-ternary diagrams.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.2.15

How to cite this article: Nasser S, Abdulrassol AA. Formulation and Characterization of Anti-fungal (Posaconazole) O/W Nanoemulsion. International Journal of Drug Delivery Technology. 2021;11(2):322-328.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

A nanoemulsion is a thermodynamically stable and translucent dispersion of two immiscible phases of material, such as an oil phase and a water phase. There is interfacial friction between the two liquids wherever they come in contact due to variations in enticing interactions between molecules of two liquid phases. To that this interfacial strain, amphiphilic surface-active molecules or surfactants are applied. Nanoemulsion droplet size typically falls in the range of 10–200 nm and shows a narrow distribution of the size.[1]

Advantages of Nanoemulsion [2]

- Large surface area, non-toxic, non-irritant are properties of nanoemulsion which make it suitable to delivering a drug through the skin and mucous membrane.
- Because of the tiny particle size of the interphase, nanoemulsion will uniformly spread on the site of application.
- Sufficient Brownian movement of nanoemulsion leads to a reduction in gravity force, so no sedimentation and creaming will occur during storage.
- Low interfacial tension of o/w nanoemulsion and low surface tension of the whole system cause improvement in wettability, penetration, and spreading properties of nanoemulsion.
- Surfactant concentration considers being reasonable if compared with the concentration used in microemulsion preparation. (note: surfactant used must be approved for human consumption)
- Nanoemulsion gives a soft aesthetic property because of its transparency and fluidity, and that thickening agent not used in its preparation.
- The style of drug release from nanoemulsion is controlled release, and also it helps target purposes.
- Nanoemulsion is suitable for human and veterinary therapeutic use because it does not cause damage to healthy human and animal cells.
- It is helpful in different rout of administration like intra-venous, topical, ocular, and intrapulmonary.
- Improve bioavailability and absorption of the drug.
- Enhance lipophilic drug solubility and consider as a good test mask approaches.
- Nanoemulsion can protect medication from oxidation and light degradation, so it increases their stability.

Nanoemulsion components:

Oils, aqueous phase surfactants, and co-surfactants (emulsifying agents) are the main components of nanoemulsion.

Oils: The oil layer is the second most effective carrier after water due to its properties to solubilize lipophilic drug molecules and increase the absorption by the lipid layer present in the body. Oil is beneficial for delivering lipophilic active ingredients because of its unique penetrating cell wall ability.[3]

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Aqueous Phase: The composition of the aqueous liquid, i.e., pH, ionic content of the aqueous fluid, and electrolytes, influences the droplet size and nanoemulsion consistency. Pure water, simulated gastric fluid (pH 1.2), Ringer's solution, simulated intestinal fluid (pH 6.8), and phosphate-buffered saline can be used as an aqueous phase to prepare nanoemulsion spontaneously. From the above aqueous phase properties, especially the pH of the aqueous phase, when a drug with pH-dependent solubility is loaded into the system, it dramatically influences the phase behavior of nanoemulsions. So that double DW consider the most appropriate one.[4]

A combination of oil and water produces a rough temporary emulsion, which would be divided into two distinct phases due to the coalescence of the scattered globules while standing. Emulgents or emulsifying agents may grant these structures. *Surfactant:* To make the dispersion of all surfactant materials smoother, the interfacial stress, closest to zero, must be reduced. In preparation of W/O, nanoemulsion surfactants with hydrophilic-lipophilic balance (HLB) values 3-6 are useful, where O/W nanoemulsion surfactants with higher HLB values 8-18 are useful for preparation. Surfactants with an HLB value greater than 20 serve as co-surfactants to reduce surfactant concentrations to a reasonable level and develop emulsions. The following are surfactant types. [5]

Co-surfactant: The interfacial tension between oil and water is lower to a degree, allowing nanoemulsion produced spontaneously so that large concentrations of single-chain surfactants are required. Owing to fluidizing groups such as unsaturated bonds, cosurfactant enhances interface fluidity and demolishes liquid crystalline or gel structure. Further, it alters the HLB value in such a way that nanoemulsion is spontaneously produced.

In addition to its emulsifying properties, emulsifying agents (surfactant and co-surfactant) should be non-toxic and consistent with the substance for its flavor, odor, and chemical stability. Some of an emulsifying agent's essential properties are: [6]

- The surface tension will be decreased to below 10 dynes/cm when it is used.
- Forming a complete and cohesive film to avoid coalescence
- Appropriate zeta potential and viscosity in the system can be supported to ensure optimal stability.
- Effective at a relatively low concentration.

Applications of nanoemulsions in intranasal drug delivery, transdermal delivery drug, parenteral drug delivery, vaccine delivery, pulmonary drug delivery, drug targeting.[7]

Posaconazole (POZ), a broad-spectrum triazole antifungal agent, has been approved by US Food and Drug Administration (FDA), for the treatment of oropharyngeal candidiasis for patients at high risk of such infection developing due to extreme immune compromise, such as hematopoietic stem cell transplantation in patients at high risk of itraconazole and/or fluconazole refractories and/or as a prophylaxis of invasive aspergillus and candida infections. Furthermore, posaconazole as a therapeutic agent for infections by some filamentous fungi is promising. According to the biopharmaceutical classification system, posaconazole is a class II drug, i.e., low solubility and high permeability**.** The antifungal mechanism of POZ is highly similar to other antifungal azole agents, primarily inhibiting CYP-dependent 14-α demethylase in the ergosterol biosynthetic pathway, a key component of the fungal cell membrane. The accumulation of toxic 14-a methyl sterols and ergosterol depletion occurs due to enzyme inhibition, resulting in disruption of the function of the fungal cell membrane, cell growth, and division blockage. Half-life ($t_{0.5}$) of POZ is in the range of 20–66 hours (mean $t_{0.5}$ about 35 hours), and its total body clearance is 32 L/hr. The major elimination pathway is via feces (mainly parent drugs). At the same time, minor elimination occurring by renal clearance (about 13% of radiolabeled taken dose). This study aims to prepare POZ as a nanoemulsion to improve its solubility, study its release, and compare it with POZ suspension, the only available marketed product.[8]

MATERIALS

Posaconazole (POZ), capmul mcm, cremophor EL, tween 80, and transcutol p were purchased from Hyperchem, China. Methanol was purchased from Chemlab, Belgium. Dialysis membrane; MwCO: 8000-14000 D product of USA. Phosphate buffer pH 7.4 was obtained from HiMedia Laboratories, India.

METHODS

Determination of Posaconazole Melting Point and λmax

Posaconazole (POZ) melting point was determined by using a capillary tube method as mentioned in USP. Using a capillary glass tube that is one end sealed, the drug powder tapped on a solid surface to obtain a compact column of POZ powder. This capillary tube is then positioned in the electrical melting point apparatus. Increasing the temperature gradually and stopped till powder completely melted, the temperature reading was recorded as the melting point of the drug.[9]

For λmax detection, Stock solutions of POZ (100 µg/mL) in methanol and pH 7.4 phosphate buffer with 0.5% sodium lauryl sulfate were prepared and diluted suitably, then scanned by UV spectrophotometer (UV 6100 PC, EMC Lab, Germany) between 200–400 nm.[10]

Preparation of Calibration curves in Different Media

Calibration curves POZ in the methanol and pH 7.4 with 0.5% sodium lauryl sulfate (SLS) the solutions were constructed from a stock solution of 100 µg/mL of the concentration by making serial dilutions different amounts. At the wavelength of maximum absorbance of POZ, spectrophotometric analysis of samples was performed. The calculated absorbances were reported and compared to the respective concentration. The equation of calibration curve and R^2 value was achieved.[11]

Determination of Saturated Solubility of POZ in Different Solutions

Measurement of saturated solubility was carried out by applying an excessive amount of POZ powder to 5 mL of each

solvent (oil), surfactant, co-surfactant, and for each dissolving medium collected in tightly closed small glass tubes. The substances were stirred with a vortex mixer and then shaken with a water bath shaker at 25 ± 1°C (oils, surfactants, and co-surfactants) and at 37 ± 1ºC (dissolution media) for 72 hours to reach equilibrium. The sample was centrifuged for about 20 minutes at (3000 rpm). The supernatants were removed and filtered through the membrane (0.45 µm Millipore filter). The filtrate was correctly diluted so that a spectrophotometric analysis could be carried out with a spectrophotometric calculation of the drug concentrations reflecting saturated solutions.[12]

Substances used as an oil phase in this study are castor oil, capmul mcm, grab seed oil, liquid paraffin, and oleic acid. Used surfactants were cremophor EL, labrasol, span 20, triacetin, and tween 80 and co-surfactants were ethanol, polyethylene glycol 200, polyethylene glycol 400, propylene glycol, and transcutol-p, while dissolution media used was (pH 7.4) phosphate buffer with 0.5% sodium lauryl sulfate at 37°C.[12]

Construction of Pseudo-ternary Phase Diagrams

Depending on results from solubility studies, the pseudo-ternary phase diagram was developed by the aqueous titration process. DW has been employed as an aqueous medium, mixed with different mixtures of surfactant (Tween 80 and cremophor) and co-surfactant (methanol and transcutol p) in 1:2, 1:1, and 2:1 ratios, based on rising surfactant levels, as well as rising co-surfactant concentration. Chosen oils Capmul mcm with S-mix were combined progressively at varying ratios for each phase diagram in different vials of glass in ratios of (9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, 1:9) (w / w). A precise and uniform mixture by a vortex blend for 5 minutes was applied to the volumes in each surfactant and co-surfactant mixture (Smix). Every mixture was then titrated under a gentle magnetic stirrer without heating with DW. The water concentration at the end of the titration was measured, in which apparent turbid changes occurred. These mixtures were then used to determine the limits on the nanoemulsion region that fit the value of the oils selected. In each diagram, the greater the spectrum of emulsion indicates higher hydration. According to the results, the optimal percentage w/ w of the emulsion composition for further studies is chosen. CHEMIX software was used to create the pseudo ternary phase diagrams.[13]

Preparation of Posaconazole Nanoemulsion

Different o/w NE formulations, as listed in Table 1 were prepared by water titration method according to pseudo-ternary phase diagrams using the Smix and oil concentrations. To prepare 10 gm of 1% POZ nanoemulsion, the primary emulsion was prepared by dissolving 100 mg of POZ in (Capmul MCM oil) using a vortex mixer for ten minutes by the addition of the selected S-mix in a fixed proportion until a clear solution was achieved. DW was then added into the clear solution with continuous stirring by magnetic stirrer at room temperature (~500 rpm) until clear emulsion was formed. The prepared emulsions were subjected to ultra-sonication using a 25 kHz sonicator for 1-minute to achieve tiny droplet sizes. Nanoemulsions were moved to the new vial and placed in the refrigerator at 4°C. The final formulas (F1-F12) obtained was subject to characterization (Table 1).[14]

Evaluation of Prepared POZ Nanoemulsion

Accelerated Physical Stability Study

Accelerated storage experiments using centrifugation and thermal stress tests, including freeze-thawing and heating-cooling cycles, have been done to determine the physical stability of nanoemulsions. Formulations that overcome these thermodynamic stress tests have been taken for further studies. *Centrifugation:* The centrifugation has been conducted for 30 minutes at 3500 rpm, and the cracking, creaming, phase separation, and precipitation have been inspected, and the heating-cooling cycle test was done for the selected stable formulas. *Heating-cooling cycle:* six cycles were performed between the refrigerator temperature 4°C and 45°C, with storage at each temperature not less than 48 hours, and the formulations were examined at these temperatures for stability. *Freeze-thaw cycle:* For all prepared nanoemulsion formulations, three freeze-thaw cycles between -21 and +25°C with storage at each temperature for at least 48hr were performed.[15]

Table 1: Composition of posaconazole nanoemulsions

F. No.	*Oil 10%*	*SAA*	*CO-SAA*	*S-mix ratio*	*S- mix %*	*DDW%*	*Drug %*
F1	Capmul-mcm	Tween-80	Methanol	1:1	39	50	1
F2	Capmul-mcm	Tween-80	Methanol	2:1	39	50	1
F3	Capmul-mcm	Tween-80	Methanol	1:2	39	50	1
F4	Capmul-mcm	Tween-80	Trans-p	1:1	39	50	1
F5	Capmul-mcm	Tween-80	Trans-p	2:1	39	50	1
F6	Capmul-mcm	Tween-80	Trans-p	1:2	39	50	1
F7	Capmul-mcm	Cremophor	Methanol	1:1	39	50	1
F8	Capmul-mcm	Cremophor	Methanol	2:1	39	50	1
F9	Capmul-mcm	Cremophor	Methanol	1:2	39	50	1
F10	Capmul-mcm	Cremophor	Trans-p	1:1	39	50	1
F11	Capmul-mcm	Cremophor	Trans-p	2:1	39	50	1
F12	Capmul-mcm	Cremophor	Trans-p	1:2	39	50	1

Light Transmittance Measurement (%T)

This test was done to measure nanoemulsion transparency. The percent of light transmittance was measured for all prepared nanoemulsions. The measurement was made using a UV-visible spectrophotometer at 650 nm, keeping distilled water blank.

Droplet size, polydispersity index (PDI) determination, and Zeta potential measurement

The particle size determination was carried out using the Nano Brook 90 Plus particle size analyzer (Brookhaven instruments. the USA). This particle size analyzer offers different options. The essential is determining an average diameter and calculating the polydispersity required for many applications until measurement nanoemulsion was diluted with 100-fold distilled water and stirred gently to improve homogeneity.

The potential of Zeta for all formulas Using the 'Nano Brook 90Plus-zeta seizer' (Brookhaven Instruments USA) nanoemulsion was measured. The diluted sample of each formula was put in the electrophoretic cell, measured at 25 ± 1°C, and the average values were determined.

Estimation of Drug Content

UV spectroscopic approach has measured the amount of POZ in prepared nanoemulsions. The drug content was represented to the theoretical quantity added as a percentage of drugs inside the system. An estimated 1 mL of nanoemulsion was dissolved in methanol, and the resulting solution was analyzed at 288 nm in the UV-Visible Spectrophotometer.[16]

Selection of Different Formulas for in vitro Release Study

Depending on (particle size, PDI, and zeta potential) values, four formulas (F2, F5, F8, and F11) were selected to study their release profile compared with 4% POZ suspension. In dissolution apparatus, USP type II (Campbell electronics, India) 300 mL of (pH 7.4) phosphate buffer with 0.5% sodium lauryl sulfate used as a dissolution media at 37 °C, dialysis bags (8000-14000D) used as a donor part this dialysis membrane was soaked in phosphate buffer overnight before the experiment and filed with 1 gm of prepared POZ nanoemulsion (10 mg of posaconazole). The release study was done at 50 rpm, and five mL of dissolution medium was withdrawn at each time interval (0.5, 1, 1.5, 2, 2.5, 3.5, 4, 5,6,7, and 8 hours) and replaced with 5 mL of a freshly prepared buffer. The measurements were performed in triplicate, and values were the mean ± SD. Spectrophotometrically, the samples obtained were analyzed at λ max 288 nm.

RESULTS AND DISCUSSION

Determination of Posaconazole Melting Point and λmax: The melting point for posaconazole was between 169-172°C. It was observed that the POZ powder had begun to melt at 167°C and had been fully converted to liquid at 171°C. The result was similar to that stated in the references. The small melting range demonstrated the purity of the POZ powder. The POZ UV scan in methanol showed a maximum peak of 288 nm as stated in the references, suggesting no change in the absorption maxima. While in pH7.4 artificial tear fluid with 0.5% sodium lauryl sulfate, there was a slight change in the λ_{max} value at 289 nm. As shown in Figure 1.[17]

Construction of Calibration Curves in Different Media: In both methanolic and pH 7.4 with 0.5% sodium lauryl sulfate solutions, calibration curves of POZ can be seen in Figure 2. Straight lines are derived from the absorption vs. concentration plot. The coefficient of square correlation (R^2) in the methanol was (0,999) and (0,996) for pH 7.4, both of which demonstrated strong linearity. The POZ calibration curves then agree with the Beer-Lamberts low within the spectrum of concentrations used.[18]

Determination of saturated solubility of POZ in different solutions: The development of NE depends on the pharmaceutical ingredient's solubility in these components (oil, surfactant, and cosurfactant) collection. The choice of oils was based on the solubility of the drug in the oil phase,

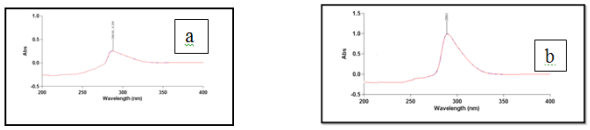

Figure 1: UV-scan of posaconazole in (a) methanol and (b) pH 7.4 with 0.5% sodium lauryl sulfate

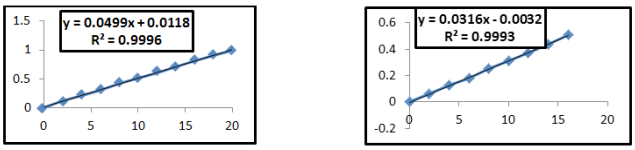

Figure 2: Calibration curve of posaconazole in methanol and Ph 7.4 with 0.5% SLS.

Table 2: Saturated solubility study results of POZ in different oils, surfactants, and co-surfactants

Oils	*Solubility of POZ mg/mL*
Castor oil	11.2 ± 0.19
Capmul MCM	121.18 ± 2.09
Grab seed oil	26.24 ± 1.06
Liquid paraffin	213.07 ± 3.27
Oleic acid	7.84 ± 0.12
Surfactant	*Solubility of POZ mg/mL*
Cremophor EL	15.27 ± 0.71
labrasol	12.39 ± 1.04
span 20	9.14 ± 0.84
triacetin	11.52 ± 0.92
tween 80	19.12 ± 1.02
Co-surfactant	*Solubilityof POZ mg/mL*
Methanol	8.77 ± 0.54
PEG 200	2.19 ± 0.04
PEG 400	3.51 ± 0.11
PG	2.4 ± 0.08
Transcutol -P	11.39 ± 1.25

as the increased solubility of the drug in the oil would help to retain the drug in a solubilized form in the o/w NE, so that precipitation would not occur and would also help to achieve the optimal loading of the drug, decrease the dose and reduce the side effect. The highest solubilizer potential for POZ, as seen in Table 2, was presented in the capmul MCM when screened with other different oils. Depending on saturated solubility study cremophor EL and tween-80 were chosen as surfactants and methanol and transcutol –p as co-surfactants to prepare nanoemulsions as these show the highest solubility for POZ. Fluid interfacial film and brief negative interfacial stress are seldom achieved by co-surfactant with surfactants, which reduces the interface bending stress and gives the interfacial film more consistency over a wide range of compositions to take up the various curvatures needed to shape a nanoemulsion. Solubility of POZ in water and pH 7.4 with 0.5 %SLS were 0.0039 ± 0.0011mg /mL and 0.109 ± 0.34 mg/mL respectively.[19]

Construction of Pseudo-ternary Phase Diagrams: The goal was to define the current range of nanoemulsions regions, as is apparent in Figure 3. The region of translucent nanoemulsion is seen in phase diagrams. The remainder of the area on the phase diagram is based on visual observations of turbid and traditional emulsions. Pseudo ternary phase diagrams for capmul CMC, and each surfactant and co-surfactant at surfactant to-cosurfactant ratio have been constructed separately to define O/W nanoemulsion areas and optimize nanoemulsion formulations.[20] The pseudo ternary phase diagram was prepared depending on results obtained from solubility and compatibility studies. The capmul-MCM used as an oil phase, tween-80 and cremophor as surfactants, and finally methanol and trascutol-p represent the co-surfactants in surfactants: cosurfactants mixture (S-Mix) ratio. The selected S-Mix ratio was (1:1, 1:2, and 2:1) which helps to study the effect of these ratios on particle's nano-size and polydispersibility index. Nanoemulsion area increased with an increase in S-Mix ratio because of the increase in HLB value, leading to the formation of o/w nanoemulsion. The results showed that combining two non-ionic surfactants with significant differences in HLB values could yield stable preparations between them. This may be due to the dissolving in the oil process of low HLB surfactants and the dissolution of a high HLB in the water, allowing them to work together well enough to affect the surfactant co-surfactant mixture with closer HLB values substantially. But in the case of the S-mix is tween- 80: methanol in 1:2 ratio, which means the co-surfactant ratio is double the surfactant ratio. The nanoemulsion area is larger than with 2:1 ratio. This may be because the lowest interfacial tension on the surface of oil droplets and optimum curvature was achieved.[21]

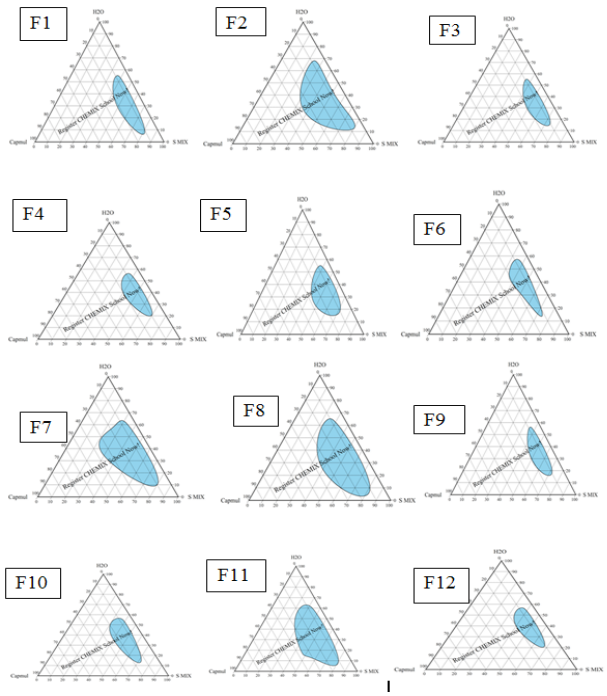

Figure 3: pseudo – ternary phase diagrams of) F1-F12)

Preparation of POZ Nanoemulsion: Low water solubility of POZ needs an adequate amount of oil to solubilize a 10 mg POZ dose in 1 mL nanoemulsion formulations. This is important for the consistency of the formulation and the high permeability of the medication since only the groups of drugs present in the formulation in the dissolved form can penetrate.[22] POZ saturated solubility studies in capmul MCM is approximately 121.18 ± 1.12 mg/mL. A 10% capmul MCM concentration represents 1 mL in 10 mL formulation, so POZ can be solubilized.

Characterization of Nanoemulsion

Accelerated Physical Stability Study: The assessment of long-term stability of prepared nanoemulsions shelf life under environmental storage conditions that could be very tedious and time-consuming, considered uneconomical. Upon completing the centrifugation procedure, heating-cooling, and freezing-thaw cycles, all the prepared nanoemulsions show no signs of instability like phase separation, creaming, and cracking.

Light Transmittance Measurement (%T): Percentage transmittance values close to 100 percent showed that all formulations were clear, transparent, and easy to transmit light. The highest transmittance percentage value (99.89 ± 0.491%) was found to be formulation (F 2), and (F34) was found to have the lowest transmittance percentage value (97.341 ± 0.5519 %). Their transparency is due to their small size, which is less than 25% of the light's wavelength. There is no major difference between all NE formulations in transmittance. Transmittance percentage values are shown in Table 3.[23]

Droplet size, Polydispersity Index (PDI) Determination, and Zeta Potential Measurement: From Table 3, we can see that there were five formulas out of twelve less than 100 nm in size. These five nanoemulsion formulas were prepared using a 2:1 mix ratio, which causes an improvement in the cosurfactant molecules that penetrated the surfactant film. This would reduce the fluidity and surface viscosity of the interface film, reduce the droplets' curvature radius, and create transparent systems. It was also observed that the droplet size of all the

Table 3: Evaluation tests results of nanoemulsion

F. No.	*Light Transmittances (%T):*	*P.S (nm)*	*PDI*	*Z.P(mv)*	*Drug content %*
F1	98.22 ± 0.02	220.9	0.315	-51.44	99.44 ± 0.27
F2	99.41 ± 0.11	27.4	0.205	-70.96	97.44 ± 0.25
F3	99.44 ± 0.05	284.2	0.112	-17.29	98.48 ± 0.28
F4	99.15 ± 0.08	95.9	0.303	-52.47	99.11 ± 0.30
F5	99.07 ± 0.14	14.8	0.197	-92.64	99.12 ± 0.18
F6	97.42 ± 0.51	236.1	0.327	-21.19	99.38 ± 0.16
F7	99.08 ± 0.04	147.1	0.33	29.41	98.83 ± 0.17
F8	99.58 ± 0.02	20.2	0.173	56.19	99.65 ± 0.09
F9	98.35 ± 0.04	283.5	0.423	25.03	99.03 ± 0.15
F10	98.38 ± 0.12	111.01	0.235	42.71	97.05 ± 0.14
F11	99.09 ± 0.02	17.4	0.235	45.73	99.65 ± 0.31
F12	99.38 ± 0.03	236.3	0.273	22.96	66.36 ± 0.20

PS= Particle Size, PDI= Polydispersity Index, ZP=Zeta Potential

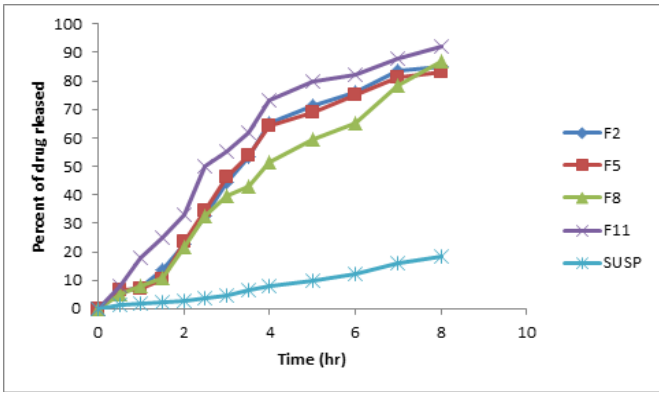

Figure 4: POZ nanoemulsion release profile from selected formulations.

formulations was in the nano range. The low polydispersibility values observed for all the formulations indicated uniformity of droplet size within each formulation. According to the classical electrical double layer theory, a zeta potential value above ± 30 mV demonstrates moderate repulsion between similarly charged particles, thereby decreasing flocculation or aggregation and potentially stabilizes the dispersion. The observed zeta potential values of F1-F12 were (-17.29–-70.96). [24]

Estimation of drug content: The drug content of prepared POZ nanoemulsions was in the range of (97.05 ± 0.14%–99.65 ± 0.31 w/v) as shown in Table 3. This high drug content which falls within the range listed by BP and USP indicates the stability of drugs during the preparation or nano-emulsification process, which is a critical need for good nanoemulsion without any precipitation.[25]

In-vitro Dissolution Studies of POZ. According to the results obtained in Figure 4, the percent of drug released from formulas F2, F5, F8, and F11 were 85.26 %, 83.31%, 87.08 %, and 92.27%, respectively, in comparison with suspension, which gave only 18.19%. It was concluded that the formula named F11 released the drug at a faster and higher rate when compared with other prepared nanoemulsions and higher than POZ suspension in terms of percent of drug released. That is why it was selected as the best formula. The higher release of drug from nanoemulsion is possibly due to nano-size, leading to increased surface area, which allowed higher solubility. Furthermore, it was noticed that the most affected factor in the drug release is the concentration of surfactant to the co-surfactant (S-mix ratio).[26]

CONCLUSION

The conclusion from this analysis was that a substantial dosage type for water-insoluble drugs was presented by nanoemulsion. Prepared with Capmul MCM, Cremophor and Transcutol-p, a nanoemulsion formula was a promising method to increase dissolution rate and posaconazole solubility. This research can be used as a model approach for the creation of other nanoemulsion drug systems.

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