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**RESEARCH ARTICLE**

# Formulation and Evaluation Lumfantrine Nanoemulsion

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## ABSTRACT

The aim of the present study was to develop a self-nano emulsifying delivery system of lumefantrine (LF) to achieve rapid and complete dissolution independent of food-fat and surfactant in dissolution media. LF is a highly lipophilic fluorine derivative and a Biopharmaceutical Classification System CLASS II drug which is an important agent in the treatment of falciparum malaria. Poor oil solubility of LF has restricted the development of lipid-based system. In view of this inadequacy, the current study aims at improving the solubility of LF, especially to eliminate the co-administration of milk or any other fatty meal. Considering the basic nature of LF, we have planned to form LF-oleic acid ionic complex and to prepare self-emulsifying system of complex by addition of appropriate surfactant. Such a self-emulsifying hydrophobic complex enables rapid dissolution of LF, without the need of BKC in dissolution media, hence provide better correlation to *in vivo* condition.

**Keywords:** Dissolution rate, Dleic acid, Hydrophobic complex, Lipophilic, Lumefantrine, Nanoemulsion

## INTRODUCTION

Nanoemulsions can be defined as oil-in-water (O/W) emulsions with mean droplet diameters ranging from 50 to 1000 nm. Usually, the average droplet size is between 100 and 500 nm, terms sub-micron emulsion and mini-emulsion are used as synonyms. Since, the preparation of the first nanoemulsion in the 1940s, it can be of three types such as O/W, water-in-oil (W/O), and bi-continuous. The transformation between these three types can be achieved by varying the components of the emulsions. Due to their small droplet size, nanoemulsions possess stability against sedimentation or creaming with Ostwald ripening forming the main mechanism of Nanoemulsion breakdown. The main application of Nanoemulsions is the preparation of nanoparticles using a polymerizable monomer as the disperse phase (the so-called miniemulsion polymerization method) where Nanoemulsion droplets act as Nanoreactors.

## MATERIALS AND METHODS

### Material and instrument used for the study [Tables 1 and 2]

*In vitro* release studies were carried out using tablet USP XXIII dissolution test apparatus. The dissolution study, by using USP paddle Type Dissolution Apparatus was carried out at 37 ± 50C at 100 rpm frequency of the paddle and 900ml of 0.1N HCL as the dissolution media. The nanoemulsion was added in dissolution media and the sample of 1ml was removed from beaker at an interval of 30, 1, 2, 4, 6, and 8 hrs and diluted appropriately. The absorbance of each sample was noted at 243.0 nm.

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**Table 1:** List of drugs and excipients used

| Materials used | Grade/Company |
|---|---|
| Lumefantrine | Pharma Grade |
| Sodium Chloride | Sodium Chloride |
| Acetic acid | Acetic acid |
| Isopropanol | Isopropanol |
| Iso propyl Myrestate | Iso propyl Myrestate |
| Paraffin oil (Light) | Paraffin oil (Light) |
| Oleic Acid | Oleic Acid |
| Span 80 | Span 80 |
| Groundnut oil | Sunkem, India |

**Table 2:** List of instruments used

| Instrument | Manufacturer |
|---|---|
| Double beam UV Visible Spectrometer | Lab India 3000+ |
| FT-IR | Brukers Alpha |
| Dissolution Apparatus | Lab India DS-8000 |
| Electronic Balance | Wenser |
| Hot air oven | Labotech India |
| Melting point apparatus | Chemline |

FTIR: Fourier-transform infrared spectroscopy, UV: Ultraviolet

## Determination of $\lambda_{max}$ of lumefantrine (LF)

The $\lambda_{max}$ of LF was determined by running the spectrum of drug solution in double-beam ultraviolet spectrophotometer.

## Procedure

Accurately weighed 10 mg of drug was dissolved in 10 ml of 0.1 N Hcl buffer solution in 10 ml of volumetric flask. The resulted solution 1000 µg/ml and from this solution 1 ml pippet out and transfer into 10 ml volumetric flask and volume make up with 0.1 N Hcl buffer solution prepare suitable dilution to make it to a concentration range of 5–25 µg/ml. The spectrum of this solution was run in 200–400 nm range in the U.V. spectrophotometer (Labindia-3000+).
The spectrum peak point graph of absorbance of LF versus wavelength was shown in Figure 1.

## Calibration curve of LF at $\lambda_{max}$ 243 nm [Table 3 and Figure 2]

***Observation table***

The linear regression analysis was done on absorbance data points. The results are as follow for standard curve.

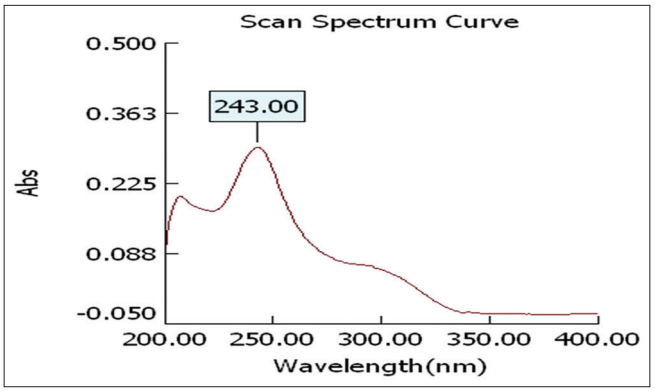


**Figure 1:** Standard calibration curve of lumefantrine

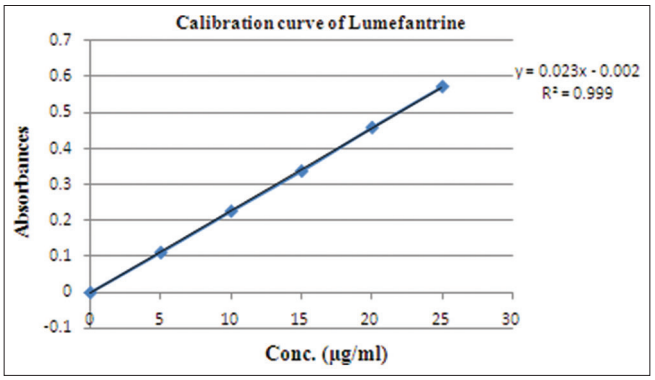


**Figure 2:** The linear regression analysis for standard curve

Slope = 0.023
The intercept = 0.002
The correlation coefficient ($r^2$) = 0.999.

## Preparation and characterization

Solubility determination in the various oils, surfactants, and cosurfactants for formulating nanoemulsion drug delivery system the solubility of the drug in different oils is an essential step for the nanoemulsion formulation. Hence, before starting the phase diagram one must have to select the oil, surfactant, and co-surfactant in which the drug shows maximum solubility, to be in the desired solubility range, which is essential for the formulation of nanoemulsion drug delivery system [Table 4].
On the basis of the above study, it was concluded that the solubility in the combination of surfactant and co-surfactant was found to be favorable for the nanoemulsion preparation of LF. The maximum solubility was obtained in a mixture of Ethanol and Tween 20, and Oleic acid was selected as oil phase

for further formulations developments.

Construction of pseudo-ternary phase diagrams surfactant and cosurfactant (Smix) in each group were mixed in different volume ratios (1:0, 1:1, 1:2, 1:3, 2:1, 3:1, and 4:1) and the stock of 100 mL of each groups was prepared. These smix ratios were chosen in increasing concentration of cosurfactant with respect to surfactant and increasing concentration of surfactant with respect to cosurfactant for detailed study of the phase diagrams for the nanoemulsions formation.

**Table 3:** Calibration curve of LF

| Conc. (µg/ml ) | Absorbance (λ max at 243 nm) | | | |
|---|---|---|---|---|
| | I | II | III | Average |
| 5 | 0.111 | 0.112 | 0.111 | 0.111 |
| 10 | 0.224 | 0.224 | 0.225 | 0.224 |
| 15 | 0.335 | 0.336 | 0.337 | 0.336 |
| 20 | 0.446 | 0.447 | 0.448 | 0.447 |
| 25 | 0.562 | 0.563 | 0.563 | 0.563 |

LF: Lumefantrine

**Table 4:** Solubility of LF in different oil, surfactants, and co-surfactants

| Component | Solubility |
|---|---|
| Span 20 | Slightly Soluble |
| Span80 | Freely Soluble |
| Tween 20 | Soluble |
| Tween 80 | Soluble |
| Pluronic F127 | Freely soluble |
| Castor Oil | Soluble |
| Sunflower Oil | Slightly soluble |
| Oleic acid | Soluble |
| PEG 400 | Soluble |
| Pluronic F127 | Soluble |
| Ethanol | Soluble |

LF: Lumefantrine

**Table 5:** Different volumes of surfactant and cosurfactant taken to make a stock Smix ratio

| Vol. of Surfactant (ml) | Vol. of Cosurfactant (ml) | Ratio of Smix (ml) |
|---|---|---|
| 100 | 0 | 1:0 |
| 50 | 50 | 1:1 |
| 33.3 | 66.7 | 1:2 |
| 25 | 75 | 1:3 |
| 75 | 25 | 3:1 |
| 80 | 20 | 4:1 |

**Different volumes of surfactant and cosurfactant taken to make a stock Smix ratio [Table 5]**

Procedure For each phase diagram, oil and specific Smix ratio was mixed thoroughly in different volume ratios from 1:9 in different small glass test tubes. Eight different combinations of oil and each Smix, 1:9, 1:8, 1:7, 1:6, 1:5, 5:1, 4:1, 3:1, were made so that maximum ratios were covered for the study to delineate the boundaries of phases precisely formed in the phase diagrams.[1-11]

## Formulation

After the development of phase diagram, Six different formulations has been selected by keeping the total quantity of the formulation constant as 100% and varying all components of the system. Each formulation has been loaded with LF of 10 mg/ml. All eight formulations have been evaluated for different parameters such as pH, *In-vitro* release, solubility and stability study.[12-21]

## Evaluation of formulations

***1 pH determination***

The pH of each formulation was found before and after dilution by using pH meter [Table 6].

## Centrifugation

This parameter characterized to check the physical stability of formulation. The nanoemulsion system was centrifuged at 5000 rpm for 10 min to determine whether the system shows signs of

**Table 6:** Results of pH of LF loaded nanoemusion

| Formulation code | pH* |
|---|---|
| F1 | 6.81±0.02 |
| F2 | 6.92± 0.01 |
| F3 | 7.11±0.02 |
| F4 | 7.04±0.01 |
| F5 | 6.84±0.02 |
| F6 | 6.95±0.03 |

LF: Lumefantrine

creaming or phase separation. The system was observed visually for appearance.

### Determination of % drug content in nanoemulsion

The mixture (Nanoemulsion) was centrifuged at 10000 rpm for 15 min, 0.2 ml of supernatant was taken and diluted with 0.1 N Hcl. Absorbance was measured at 243 nm by UV Spectrophotometer [Table 7]. Concentration of LF was determined using standard curve equation and % drug content was calculated. Results of Centrifugation and % Drug Content in nanoemulsion.

**Table 7:** Results of centrifugation and % drug content in nanoemulsion

| Formulation Code | Centrifugation | % Drug Content in nanoemulsion* |
|---|---|---|
| F1 | Transparent | 78.23±0.23 |
| F2 | Transparent | 75.58±0.15 |
| F3 | Transparent | 89.98±0.25 |
| F4 | Transparent | 82.25±0.25 |
| F5 | Precipitated | 70.15±0.65 |
| F6 | Precipitated | 65.56±032 |

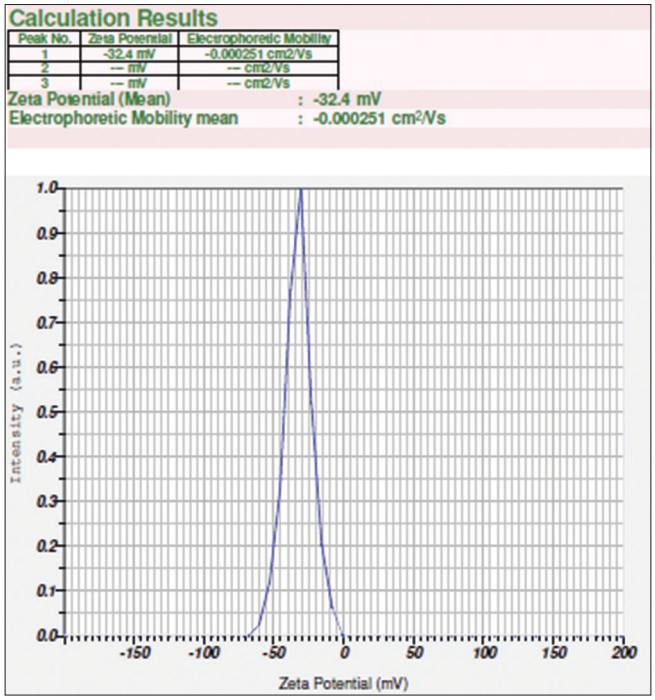


**Figure 3:** Result of Zeta Potential of Optimized Batch F3 = 32.4 mV

### Zeta potential and vesicle size measurement of optimized batch F3

Zeta Potential of samples was measured by Zetasizer. Samples were placed in clear disposable zeta cells and results were recorded [Figure 3].

### Result of vesicle size of optimized batch F3 [Figure 4]

*In vitro* ***drug release study***

*In vitro* release studies were carried out using tablet USP XXIII dissolution test apparatus. The dissolution study, by using USP paddle Type Dissolution Apparatus was carried out at 37 ± 50C at 100 rpm frequency of the paddle and 900 ml of 0.1 N HCL as the dissolution media. The nanoemulsion was added in dissolution media and the sample of 1 ml was removed from beaker at an interval of 30, 1, 2, 4, 6, and 8 h and diluted appropriately. The absorbance of each sample was noted at 243.0 nm.

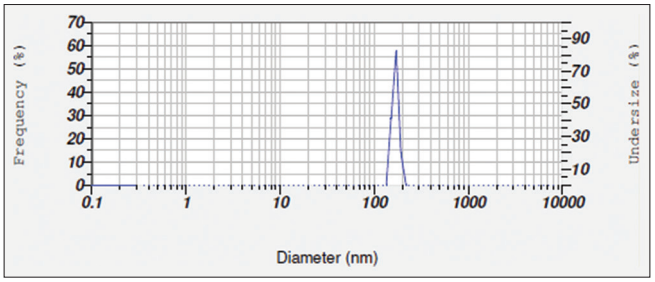


**Figure 4Z:** Result of Vesicle size of Optimized Batch

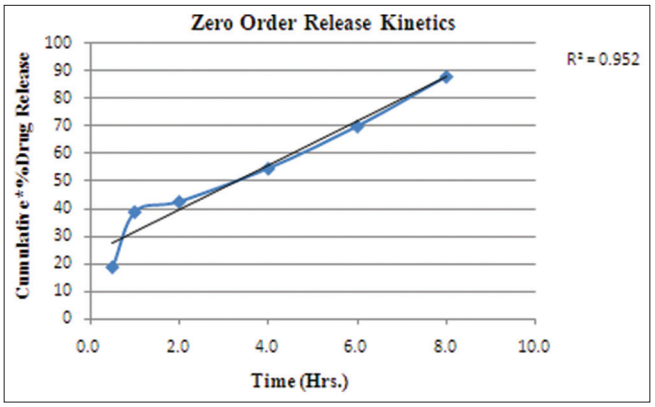


**Figure 5:** Cumulative % drug released versus Time

**Table 8:** *In-vitro* drug release data for formulation F1

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | -0.301 | 13.560 | 1.132 | 86.440 | 1.937 |
| 1 | 1.000 | 0.000 | 32.560 | 1.513 | 67.440 | 1.829 |
| 2 | 1.414 | 0.301 | 65.560 | 1.817 | 34.440 | 1.537 |
| 4 | 2.000 | 0.602 | 75.580 | 1.878 | 24.420 | 1.388 |
| 6 | 2.449 | 0.778 | 76.200 | 1.882 | 23.800 | 1.377 |
| 8 | 2.828 | 0.903 | 76.210 | 1.882 | 23.790 | 1.376 |

*Average of three readings

**Table 9:** *In-vitro* drug release data for formulation F1

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | –0.301 | 20.250 | 1.306 | 79.750 | 1.902 |
| 1 | 1.000 | 0.000 | 45.580 | 1.659 | 54.420 | 1.736 |
| 2 | 1.414 | 0.301 | 68.890 | 1.838 | 31.110 | 1.493 |
| 4 | 2.000 | 0.602 | 73.250 | 1.865 | 26.750 | 1.427 |
| 6 | 2.449 | 0.778 | 73.560 | 1.867 | 26.440 | 1.422 |
| 8 | 2.828 | 0.903 | 74.150 | 1.870 | 25.850 | 1.412 |

*Average of three readings

**Table 10:** *In-vitro* drug release data for formulation F2

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | –0.301 | 18.890 | 1.276 | 81.110 | 1.909 |
| 1 | 1.000 | 0.000 | 38.890 | 1.590 | 61.110 | 1.786 |
| 2 | 1.414 | 0.301 | 42.560 | 1.629 | 57.440 | 1.759 |
| 4 | 2.000 | 0.602 | 54.650 | 1.738 | 45.350 | 1.657 |
| 6 | 2.449 | 0.778 | 69.980 | 1.845 | 30.020 | 1.477 |
| 8 | 2.828 | 0.903 | 87.980 | 1.944 | 12.020 | 1.080 |

*Average of three readings

**Table 11:** *In-vitro* drug release data for formulation F3

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | –0.301 | 20.250 | 1.306 | 79.750 | 1.902 |
| 1 | 1.000 | 0.000 | 38.980 | 1.591 | 61.020 | 1.785 |
| 2 | 1.414 | 0.301 | 56.650 | 1.753 | 43.350 | 1.637 |
| 4 | 2.000 | 0.602 | 75.580 | 1.878 | 24.420 | 1.388 |
| 6 | 2.449 | 0.778 | 81.150 | 1.909 | 18.850 | 1.275 |
| 8 | 2.828 | 0.903 | 81.560 | 1.911 | 18.440 | 1.266 |

*Average of three readings

***In-vitro drug release data [Tables 8-13]***

*In vitro* release studies were carried out using tablet USP XXIII dissolution test apparatus. The dissolution study, by using USP paddle Type Dissolution Apparatus was carried out at 37 ± 50 C at 100 rpm frequency of the paddle and 900 ml of 0.1N HCL as the dissolution media. The nanoemulsion was added in dissolution media and the sample of 1ml was removed from beaker at an interval of 30, 1, 2, 4, 6, and 8 hrs and diluted appropriately. The absorbance of each sample was noted at 243.0 nm.

**Table 12:** *In-vitro* drug release data for formulation F4

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | –0.301 | 45.580 | 1.659 | 54.420 | 1.736 |
| 1 | 1.000 | 0.000 | 68.890 | 1.838 | 31.110 | 1.493 |
| 2 | 1.414 | 0.301 | 70.120 | 1.846 | 29.880 | 1.475 |
| 4 | 2.000 | 0.602 | 71.560 | 1.855 | 28.440 | 1.454 |
| 6 | 2.449 | 0.778 | 72.250 | 1.859 | 27.750 | 1.443 |
| 8 | 2.828 | 0.903 | 70.250 | 1.847 | 29.750 | 1.473 |

*Average of three readings

**Table 13:** *In-vitro* drug release data for formulation F5

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | –0.301 | 45.690 | 1.660 | 54.310 | 1.735 |
| 1 | 1.000 | 0.000 | 60.250 | 1.780 | 39.750 | 1.599 |
| 2 | 1.414 | 0.301 | 64.560 | 1.810 | 35.440 | 1.549 |
| 4 | 2.000 | 0.602 | 65.250 | 1.815 | 34.750 | 1.541 |
| 6 | 2.449 | 0.778 | 65.250 | 1.815 | 34.750 | 1.541 |
| 8 | 2.828 | 0.903 | 65.320 | 1.815 | 34.680 | 1.540 |

*Average of three readings

**Table 15:** Regression analysis data of optimized formulation

| Batch | Zero Order | First Order |
|---|---|---|
| | $R^2$ | $R^2$ |
| F3 | 0.936 | 0.936 |

*Average of three readings

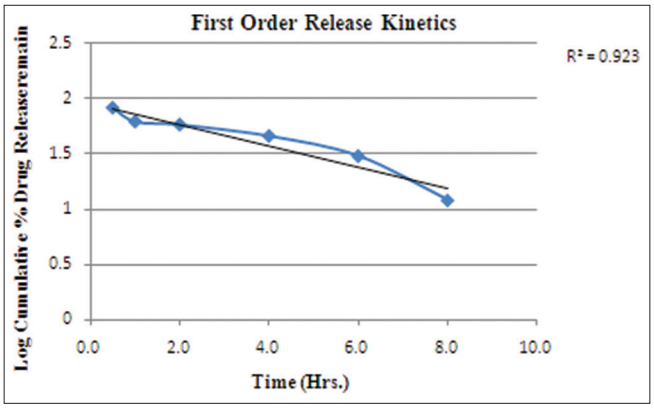


**Figure 6:** Log cumulative % drug remaining versus Time

## Release kinetics of optimized formulation F3 [Tables 15, Figures 5 and 6]

### *Stability studies*

LF loaded nanoemulsion was prepared and stored for 2 months first at refrigerating condition (2°C–8°C), room temperature and at elevated temperature (50°C ± 2°C) and shelf life of the stored nanoemulsion system was evaluated by visual inspection (phase separation) and % drug content. Samples were obtained on the 2nd month and evaluated.[22-27]

## CONCLUSION

Poor oil solubility of LF has restricted development of lipid based system. In view of this inadequacy, the current study worked to improving the solubility of LF, especially to eliminate the co administration of milk or any other fatty meal. Considering the basic nature of LF, we have planned to form LF-oleic acid ionic complex and to prepare self-emulsifying system of complex by addition of appropriate surfactant. The present work concluded that LF nanoemulsion formulation for solubility enhancement. Now a day, nanoemulsion as carrier systems are more acceptable in drug delivery system. Hence it is concluded the prepared nanoemulsion for LF can be further studied for topical application in the treatment of disease and work need to be performed towards the area of drug administration.

## REFERENCES


1. Thomas VH, Bhattachar S, Hitchingham L, Zocharski P, Naath M, Surendran N. The road map to oral bioavailability: An industrial perspective. Expert Opin Drug Metab Toxicol 2006;2:591-608.
2. Stegemann S, Leveiller F, Franchi D, de Jong H, Lindén H. When poor solubility becomes an issue: From early stage to proof of concept. Eur J Pharma Sci 2007;31:249-61.
3. Patel AR, Vavia PR. Preparation and *in viv*o evaluation of SMEDDS (self-microemulsifying drug delivery system) containing fenofibrate. AAPS J 2007;9:E344-5.
4. Singh SP, Raju KSR, Nafis A, Puri SK, Jain GK. Intravenous pharmacokinetics, oral bioavailability, dose proportionality and in situ permeability of anti-malarial lumefantrine in rats. Malar J 2011;10:293.
5. Ezzet F, Mull R, Karbwang J. The population pharmacokinetics of CGP 56697 and its effects on the therapeutic response in malaria patients. Br J Clin Pharmacol 1998;46:553-61.
6. Ashley EA, Annerberg A, Kham A, Brockman A, Singhasivanon P, White NJ. How much fat is necessary to optimize lumefantrine oral bioavailability? Trop Med Int Health 2007;12:195-200.
7. Gahoi S, Jain GK, Tripathi R, Pandey SK, Anwar M, Warsi MH. Enhanced antimalarialactivity of lumefantrine nanopowder prepared by wet-milling DYNO MILL technique. Colloids Surf B Biointerf 2012;95:16-22.
8. Date AA, Nagarsenker MS. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for cefpodoxime proxetil. Int J Pharm 2007;329:166-72.
9. Pawar SK, Vavia PR. Rice germ oil as multifunctional excipient in preparation of self-microemulsifying drug delivery system (SMEDDS) of tacrolimus. AAPS PharmSciTech 2012;13:254-61.
10. Patel KD, Padhye SG, Nagarsenker MS. Duloxetine HCl lipid nanoparticles: Preparation, characterization, and dosage form design. AAPS Pharm Sci Tech 2012;13:125-33.
11. Babalola CP, Adegoke AO, Ogunjinmi MA, Osimosu MO. Determination of physicochemical properties of halofantrine. Afr J Med Med Sci 2003;32:357-9.
12. Cuiné JF, McEvoy CL, Charman WN, Pouton CW, Edwards GA, Benameur H, *et al*. Evaluation of the impact of surfactant digestion on the bioavailability of danazol after oral administration of lipidic self-emulsifying formulations to dogs. J Pharm Sci 2008;97:995-1012.
13. Lopez-Montilla JC, Herrera-Morales PE, Pandey S, Shah D. Spontaneous emulsification: Mechanisms, physicochemical aspects, modeling and applications. J Dispersion Sci Technol 2002;23:219-68.
14. Biradar SV, Dhumal RS, Paradkar AR. Rheological investigation of self-emulsification process: Effect of co-surfactant. J Pharm Pharm Sci 2009;12:164-74.
15. Bindschedler M, Degen P, Lu ZL, Jiao XQ, Liu GY, Fan F. Comparative Biovailability of Benflumetol after Administration of Single Oral Doses of Co-artemether under Fed and Fasted Conditions to Healthy Subjects (Abstract P-01-96). Proceedings of the Xivth International Congress for Tropical Medicine and Malaria, Nagasaki, Japan; 1996. p. 17-22.
16. Müller RH, Jacobs C, Kayser O. Nanosuspensions as particulate drug formulations in therapy. Rationale for development and what we can expect for the future. Adv Drug Deliv Rev 2001;23:3-19.
17. Umapathi P, Ayyappan J, Quine SD. Development and validation of a dissolution test method for artemether and lumefantrine in tablets. Trop J Pharm Res 2011;10:643-53.
18. Sanghai B, Aggarwal G, Harikumar S. Solid self microemulsifying drug delivery system: A review. J Drug Deliv Ther 2013;3:168-74.
19. Gupta E, Barends DM, Yamashita E, Lentz KA, Harmsze AM, Shah VP, *et al*. Review of global regulations concerning biowaivers for immediate release solid oral dosage forms. Eur J Pharm Sci 2006;29:315-24.
20. Yeung P, Hubbard J, Korchinski E, Midha, K. Pharmacokinetics of chlorpromazine and key metabolites. Eur J Clin Pharmacol 1993;45:563-9.
21. Kassem A, Mohsen M, Ahmed S, Essam M. Selfnanoemulsifying drug delivery system (SNEDDS) with enhanced solubilization of nystatin for treatment of oral candidiasis: Design, optimization, *in vitro* and *in vivo* evaluation. J Mol Liq 2016;218:219-32.
22. Hou J, Sun E, Zhang Z, Wang J, Yang L, Cui L, *et al*. Improved oral absorption and anti-lung cancer activity of paclitaxelloaded mixed micelles. Drug Deliv 2017;24:261-9.
23. Zhang B, Xue A, Zhang C, Yu J, Chen W, Sun D. Bile salt liposomes for enhanced lymphatic transport and oral bioavailability of paclitaxel. Pharmazie 2016;71:320-6.
24. Zhang T, Luo J, Fu Y, Li H, Ding R, Gong T, *et al*. Novel oral administrated paclitaxel micelles with enhanced bioavailability and antitumor efficacy for resistant breast cancer. Colloid Surf B Biointerfaces 2016;150:89-97.
25. Pooja D, Kulhari H, Kuncha M, Rachamalla SS, Adams DJ, Bansal V, *et al*. Improving efficacy, oral bioavailability, and delivery of Paclitaxel using protein-grafted solid lipid nanoparticles. Mol Pharm 2016;13:3903-12.
26. Ding D, Sun B, Cui W, Chen Q, Zhang X, Zhang H, *et al*. Integration of phospholipid-drug complex into selfnanoemulsifying drug delivery system to facilitate oral delivery of Paclitaxel Asian J Pharm Sci 2019;14:552-8.
27. Baloch J, Sohail MF, Sarwar HS, Kiani MH, Khan GM, Jahan S, *et al*. Self-nanoemulsifying drug delivery system (SNEDDS) for improved oral bioavailability of chlorpromazine: *In vitro* and *in vivo* evaluation. Medicina 2019;55:210.