Evaluation of solubility and dissolution of lamotrigine using lipid based microparticulate carriers: An in-vitro analysis

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Abstract: The present study was designed to develop novel lipid microparticles in order to improve solubility, dissolution and bioavailability of a lipophilic drug of BCS class II, lamotrigine. For that purpose, increase in solubility of the model drug was investigated using different lipids and the promising lipids were further used for the fabrication of microparticles. Solid lipid (GMS) and liquid lipid (olive oil) were used along with an emulsifier (Tween 80) and a stabilizer (Poloxamer 188) to prepare microparticles by melt emulsification method. Prepared formulations were characterized for physicochemical properties such as solubility, particle size, zeta potential, polydispersity index and entrapment efficiency. In vitro dissolution studies were carried out in 0.01 N HCl for 24 h. The findings provided that the solubility of lamotrigine was reasonably increased in GMS, olive oil, Tween 80 and poloxamer 180. The lamotrigine solubility was increased 4.92 fold with G4 microparticles formulation. Size analysis revealed that the microparticles were in range of 11.1 to 178.8 µm and the zeta potential values were from -13 to -20 mV. Microparticles prepared with solid and liquid lipids exhibited satisfactory entrapment efficiency ranging from 59 to 87%. Conclusively, the outcomes of the studies suggest the appropriateness of selected ingredients for improving solubility as well as loading of lamotrigine in microparticles for its sustained and effective delivery.

Keywords: Solid lipid, liquid lipid, lamotrigine, microparticles, solubility improvement.

INTRODUCTION

Oral bioavailability of drugs is mainly dependent on solubility as well as permeability in gastrointestinal tract (GIT). The poor solubility of drugs in GIT has been a major challenge in achieving the desired therapeutic outcomes from oral dosage forms especially of poorly soluble drugs. However, the pharmaceutical scientists are continuously putting vigorous efforts in developing such drug delivery systems that could provide reasonable bioavailability from oral route of administration in order to improve patient compliance (Carriere, 2016).

The efficiency of drugs is reduced due to their insufficient absorption to reach the desired site for therapeutic action. To overcome this problem, colloidal systems are developed for such drugs to provide site specific drug delivery with optimal drug release profile. Microparticles are colloidal systems of submicron size that can be prepared from a large variety of materials. Depending on the chemical composition of microparticles, these could carry a wide variety of drug molecules, making them efficient drug delivery vehicles (McClements, 2018). It is clearly evident from literature that various types of pharmaceutical excipients are used in microparticulate carriers in order to improve drugs bioavailability and hence effectiveness. For instance, solid lipid microparticles (SLM), nanostructure lipid carriers (NLCs) and self-micro-emulsifying preparations are generally considered most efficient drug delivery systems. Out of these, solid lipids microparticles could be used for various routes such as oral, rectal, nasal, inhalation, ocular and for topical application without any specific limitation (Trotta et al., 2018). Lipid microparticles are being prepared by using different techniques such as solvent evaporation, melt emulsification and diffusion emulsification etc. To make microparticles as effective dosage carrier, combination of hydrophilic and lipophilic polymers are also used to improve drug delivery and to reduce side effects (Wu et al., 2018). In the recent years, lipid polymers are extensively used to prepare nanoparticles and microparticles to improve oral bioavailability. The polymer-lipid hybrid microparticles have improved the desired effects with nominal side effects (Liu et al., 2018).

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BCS class II drugs are well known for their poor solubility. Lamotrigine is an anticonvulsant drug and belongs to Biopharmaceutics Classification System (BCS) class II drugs. It is used to treat different type of seizures and depression. It has solubility of 0.17 mg/ml in water. It inhibits the release of excitatory glutamate and amino acid by blocking the sodium channel receptors of neuronal membranes (Gieszinger et al., 2017).

The main objective of this study was to develop lipid microparticles that potentially could improve the solubility of lamotrigine, a hydrophobic model drug. To address this issue, lipids microparticles are designed by utilizing appropriate materials such as solid lipid (glyceryl monostearate, stearic acid), liquid lipid (olive oil), surfactant (tween 80) and stabilizer (poloxamer 188) in order to improve the solubility leading to escalate dissolution as well as bioavailability. The developed microparticulate could be incorporated in multiple dosage form like tablets and capsules in future.

MATERIALS AND METHODS

Materials
Lamotrigine was donated by Standpharm Pharmaceuticals (Pvt Ltd) Lahore, Pakistan. Glyceryl monostearate (GMS) and Tween 80 were purchased from Sigma-Aldrich, Germany. Olive oil was kindly gifted by Revolon Chemical, Pakistan. Poloxamer 188 was donated by Gattefosse, France. Stearic acid was purchased from Morgan Chemicals, Pakistan. Dialysis membrane (molecular weight cut off value 12000-14000 Da) and membrane clumps were procured from Central Chemicals, Pakistan. All other chemicals and reagents purchased were of analytical grade.

Methods
Solubility determination of lamotrigine
Flask shaking method was used to determine the saturated solubility of lamotrigine in distilled water, 0.01N HCl, methanol and phosphate buffers (pH 5.5 and 7.4). The excess quantity of lamotrigine was placed in 10 ml of each solvent. These samples were placed in a rotating orbital shaker with a speed of 100 rpm at 37 °C for 36 h. Then supernatant samples were taken, filtered and analyzed spectrophotometrically. Pluger et al. (2018).

Preparation of calibration curve of lamotrigine
Calibration curve of lamotrigine was prepared by stock dilution method. Accurately weighed 50 mg lamotrigine was dissolved in 25 ml of 0.01N HCl, sonicated for 10 minutes and final volume was made up to 50ml with 0.01N HCL. This stock solution was further diluted with 0.01N HCl to make working dilutions of 5, 10, 15, 20, 25, 30 μg/ml, respectively. Filtration was performed at every dilution. Then these dilutions were scanned for maximum absorbance using UV-spectrophotometer and the calibration curve was plotted as shown in the fig. below:

![Calibration curve of lamotrigine in 0.01N HCl](image)

Preparation of lipid microparticles
Table I shows the detail description of prepared microparticles formulations. Accurately weighed amounts of GMS and lamotrigine were taken and melted in a 200 ml beaker on a hot plate magnetic stirrer. This mixture was poured into another beaker containing aqueous solution of tween 80 and poloxamer 188. The temperature of both phases was kept at 70°C. To assure the uniform mixing of the ingredients, high speed homogenizer with 17500 rpm was used for 10 minutes, followed by sonication for 3 minutes. After mixing both phases, beaker was placed in cold water to reduce the temperature of mixture and then centrifuged at 15000 rpm for 20 minutes to get moist mass of microparticles. Finally, the remaining mixture was filtered through Whastman filter paper of 0.45µm pore size to maximize yield. The residue was subjected to lyophilization to get dried mass, which was kept in a dry container for further use (Scalia et al., 2015).

Fourier transformation infrared spectroscopy (FTIR)
In order to find out presence of any interaction, the samples including individual drug, polymers and the prepared lipid microparticles were scanned in the range of 500 to 4000 cm⁻¹ by using Agilent Carry 360 FTIR (Évora et al., 2019).

Determination of entrapment efficiency (EE), loading capacity and % yield
The entrapment efficiency was checked by ultracentrifugation method. Sample microparticles were centrifuged at 14000-23000 rpm for 15 minutes,
supernatant was collected, filtered and analyzed UV-spectrophotometrically at 270 nm to calculate the amount of entrapped drug by using equation 1 (Severino et al., 2017). The loading capacity of drug captured in lipid microparticles was calculated by using equation 2 (Wu et al., 2016). The % yield was calculated by dividing total mass of the microparticles produced by the total solid constituents used for the preparation of microparticles (equation 3).

$$EE(\%) = \frac{\text{Total amount of free drug} - \text{Amount of free drug}}{\text{Total amount of drug}} \times 100$$  

Equation 1

$$L.C(\%) = \frac{\text{Total drug} - \text{Amount of free drug}}{\text{Microparticles weight}} \times 100$$  

Equation 2

$$%\text{Yield} = \frac{\text{Microparticles weight}}{\text{Total solid weight}} \times 100$$  

Equation 3

Particle size and zeta potential analysis
Size analysis of microparticles was performed using Malvern Zeta Sizer (Nano ZS, Malvern Instruments UK). The samples were run in triplicate and standard deviation was calculated. In addition, polydispersity index (PDI) of developed microparticles was determined (Ding et al., 2018). The charge on the surface of lamotrigine loaded lipid microparticles was determined by mixing microparticles in double distilled water and then poured in a cuvette for measurement of zeta potential using Malvern Zeta sizer (Nano ZS, UK) (Ding et al., 2018).

Scanning electron microscopy (SEM)
Particles shape was determined by using a scanning electron microscope. (SEM Analyzer S3400 Hitachi, Japan). Scanning electron microscope produced images by scanning the surface of sample using electron beam. By this method, high resolution images were obtained of samples. Multiple scans were performed to get better statistical accuracy. Morphological information about shape, surface texture and roughness was obtained.

In vitro drug release studies
USP type II dissolution apparatus was used to study drug release from microparticles using 50 rpm rotation speed at 37±0.5°C. Microparticles containing lamotrigine equivalent to 10mg were placed inside dialysis bags having molecular weight cut off value 12000-14000 Da. The dialysis bags were attached to the rotating paddles and dissolution vessels were filled with 900ml of 0.01N HCl (pH 1.2). In one vessel, 10mg lamotrigine was placed to study the release profile of pure drug. Samples were drawn at pre-determined time intervals and diluted appropriately, filtered and analyzed on an UV-spectrophotometer. Analysis were performed in triplicate (Gaur et al., 2014).

Process parameters
Moreover, the effect of process parameters such as mixing speed, influence of temperature, addition rate of phases, homogenization time and sonication time were evaluated to obtain optimized formulation of microparticles.

STATISTICAL ANALYSIS
Release data of lamotrigine from microparticles was assessed by the model-dependent methods (zero-order, first-order, Higuchi, Korsmeyer Peppas and Hixson-Crowell Model) using DD Solver. SPSS software (version 21) was used to perform analysis of variance (One-way ANOVA) for the estimation of release data at the significance level of p ≤ 0.05.

RESULTS

Solubility determination of lamotrigine
The solubility of lamotrigine was determined in different media including distilled water, methanol, 0.1N NaOH, 0.01N HCl, phosphate buffer 5.5 and 6.8. The wavelength was scanned for every respective media. It was 245 nm for distilled water, 270 nm for acidic buffer 0.01N HCl (pH 1.2) and 307 nm for phosphate buffers (PBS; pH 5.5 and pH 6.8). The solubility of lamotrigine in different media is shown in (table 2).

The preliminary data helped in selecting appropriate medium for further study of lipid microparticles. 0.01N HCL was used for performing dissolution studies. The
solubility of lamotrigine was very low in distilled water and 6.8 phosphate buffer. The saturated solubility of lamotrigine in different type of solid lipids and lipid lipids is given in table 3.

The solubility of lamotrigine was increased many folds in GMS, stearic acid, olive oil as well as in surfactant solutions of tween 80 and poloxamer 188. Therefore, these excipients were selected for development of microparticulate formulations.

**Fourier transformation infrared spectroscopy (FTIR)**

The FTIR spectra of drug, lipids, surfactants and formulations did not reveal any incompatibility among them (fig. 2).

**Particle size analysis, polydispersity and zeta potential of microparticles**

Table 4 depicted that the particle size of the prepared microparticles was in range from 11.1 ± 3.1 to 178.8 ± 2.5 μm. The large size microparticles 121.2, 134.8 and 178.8 μm were obtained from formulations S2, S3 and S4 respectively. The larger particles size may be attributed to the higher concentration of stearic acid in these formulations. Prepared microparticles has shown homogeneous distribution with micron size range. Table 4 is demonstrated PDI values in range of 0.09 to 0.373. Zeta potential values of the prepared microparticles formulations were found from range -12.95 to -20.17 mV (table 4).

**Morphological analysis**

SEM of the compacted samples was performed under vacuum using Hitachi SEM S3400 instrument. SEM results clearly revealed that the microparticles were spherical smooth and uniform shape without any noticeable aggregation (fig. 3).

**Entrapment efficiency and percentage yield**

The performance of manufacturing method and quality of lipid microparticles could be evaluated by entrapment efficiency. Formulations (G1-G4) containing glyceryl monostearate have shown 59 to 78% entrapment efficiencies whereas formulations with stearic acid (S1-S4) have provided entrapment efficiencies in range of 66 to 87%. It could be clearly observed that EE has improved as function of concentration of lipids in the formulations. In addition, low percentage yield was seen in formulations having low solid lipid contents (table 5).

**In vitro release from lipid microparticles**

Microparticles formulations containing GMS exhibited different release pattern in comparison to the formulations containing stearic acid. Slow release of drug from G4, S3 and S4 could be linked to the presence of high concentration of solid lipid content (fig. 4). Lamotrigine was released 15.5% in one hour from G4 microparticles while 14.3% lamotrigine was released in one hour from S4 microparticles. After 12 hour, 77 and 71.5% drug was released from G4 and S4 microparticles respectively.

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**Table 1: Description of microparticles formulations of lamotrigine**

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Solid Lipid</th>
<th>Liquid Lipid</th>
<th>Surfactant</th>
<th>Co-surfactant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GMS (mg)</td>
<td>Stearic acid (mg)</td>
<td>Olive oil (ml)</td>
<td>Tween 80 (mg)</td>
</tr>
<tr>
<td>G1</td>
<td>250</td>
<td>0</td>
<td>0.25</td>
<td>3.75</td>
</tr>
<tr>
<td>G2</td>
<td>500</td>
<td>0</td>
<td>0.50</td>
<td>7.51</td>
</tr>
<tr>
<td>G3</td>
<td>750</td>
<td>0</td>
<td>0.75</td>
<td>11.26</td>
</tr>
<tr>
<td>G4</td>
<td>1000</td>
<td>0</td>
<td>1.00</td>
<td>15.01</td>
</tr>
<tr>
<td>S1</td>
<td>0</td>
<td>250</td>
<td>0.25</td>
<td>3.75</td>
</tr>
<tr>
<td>S2</td>
<td>0</td>
<td>500</td>
<td>0.50</td>
<td>7.51</td>
</tr>
<tr>
<td>S3</td>
<td>0</td>
<td>750</td>
<td>0.75</td>
<td>11.26</td>
</tr>
<tr>
<td>S4</td>
<td>0</td>
<td>1000</td>
<td>1.00</td>
<td>15.01</td>
</tr>
</tbody>
</table>

**Table 2: Solubility of lamotrigine in different media at 37 ± 0.5 °C**

<table>
<thead>
<tr>
<th>Solubility (μg/ml) after 36 h</th>
<th>Media maintained at 37 ± 0.5°C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Distilled Water</td>
</tr>
<tr>
<td></td>
<td>293</td>
</tr>
</tbody>
</table>

**Table 3: Solubility of lamotrigine in different excipients**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Solubility, mg/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMS</td>
<td>64</td>
</tr>
<tr>
<td>Stearic Acid</td>
<td>103</td>
</tr>
<tr>
<td>Olive oil</td>
<td>42</td>
</tr>
<tr>
<td>Tween 80</td>
<td>46</td>
</tr>
<tr>
<td>Poloxamer 188</td>
<td>38</td>
</tr>
<tr>
<td>Myristic acid</td>
<td>26</td>
</tr>
<tr>
<td>Carnauba wax</td>
<td>12</td>
</tr>
<tr>
<td>Geleol glyceride</td>
<td>32</td>
</tr>
</tbody>
</table>

**In vitro release from lipid microparticles**

Microparticles formulations containing GMS exhibited different release pattern in comparison to the formulations containing stearic acid. Slow release of drug from G4, S3 and S4 could be linked to the presence of high concentration of solid lipid content (fig. 4). Lamotrigine was released 15.5% in one hour from G4 microparticles while 14.3% lamotrigine was released in one hour from S4 microparticles. After 12 hour, 77 and 71.5% drug was released from G4 and S4 microparticles respectively.
DISCUSSION

Solubility of pharmaceutical active moieties is considered very imperative for bioavailability enhancement (Shilpi D et al., 2017). The aqueous solubility of lamotrigine is cited about 170µg/ml in literature. The saturated solubility obtained in our study was 293µg/ml after 36h. The lamotrigine showed high solubility in acidic media with respect to basic media. Solubility was decreased with increase of pH of dissolution medium. The solubility of lamotrigine was found higher in 0.01N HCl compared to phosphate media (table 2). This could be explained that drug being weak base did not dissociate properly above its pKa value (5.7). The lamotrigine exhibited commendable solubility increase in lipid polymers such as stearic acid and glyceryl monostearate, olive oil, tween 80 and poloxamer 188 with respect to myristic acid, carnauba wax, castor and almond oil. Thus lipid polymers with higher drug solubility were selected for microparticulate development (GMS, stearic acid, olive acid, Tween 80 and poloxamer 188) and 0.01N HCl media was selected for solubility and dissolution determination.

The hot melt emulsification method for preparation of microparticles with GMS polymer was found suitable. The solubility of lamotrigine was increased significantly with all microparticles formulations. The highest solubility (837µg/ml) was obtained from G-4 microparticles. The concentration of GMS have effect on release of lamotrigine from microparticles. With the increase amount of GMS, the release of lamotrigine was decreased. The release of drug from stearic acid microparticles was 54-74% in 8 hour and complete drug was release in 24 hour. The drug release from GMS 54 to 70% in 8 hour and almost complete lamotrigine was release in 24 hour. The zero order kinetic release model gave R² value 0.751 whereas first order release model

Fig. 3: SEM micrographs of (A) Lamotrigine, (B) GMS, (C) formulation G2 and (D) formulation S4.
gave \( R^2 \) value 0.990. Thus it means lamotrigine was released by concentration dependent release pattern. The value of \( n \) in korsmeyer-peppas model was obtained to be 0.60 that was higher than 0.45 depicting non-fickian drug release pattern from microparticles. The initial burst release was caused by presence of drug on the outer surface of microparticles. Drug release may be affected by concentrations of surfactants, lipids, type of lipids, presence of liquid lipid and melting point of lipids in the microparticles formulation.

The small size microparticles (11.1 to 28.70 µm) were obtained with GMS. The size of microparticles obtained from stearic acid was large (74.6 to 178.8 µm). The incorporation of surfactants and co-surfactants in microparticles formulation have influence on size of microparticles directly or indirectly. The properties of surfactant could influence size as well as shape of microparticles. A possible explanation of large microparticle size might be due to low or insufficient quantity of surfactant in the formulations with respect to lipids. Formulations of microparticles containing GMS (G1-G4) have produced small size particles due to good emulsifying characteristics of surfactant with GMS. (Xue J et al., 2018). Thus appropriate selection of lipids and surfactants is important for desirable size and shape. Furthermore, particle size of lipid microparticles are found very close to each other which may be due the presence of liquid lipid leading to more imperfections in crystal. The presence of liquid lipid (olive oil) promote molecular mobility of lipid matrix resulting in formation of small size particles. Outer phase with less viscosity may result into smaller size particles. Less viscous lipids produce stable small size microparticles. The obtained PDI values of developed microparticles were ranges from 0 to 0.37. Microparticles with less than 0.25 PDI values provide homogenous distribution of particles with no noticeable aggregation.

The shape of the obtained microparticles was spherical and no agglomeration was depicted by SEM micrographs (fig. 3). To behave as a good carrier, the shape of prepared microparticles plays a vital role, which is particularly depend on concentration of lipid polymer, surfactant and viscosity of outer phase (Kalaycioglu and Aydogan, 2016). The spherical shape of microparticles could be acquired by appropriate homogenization in the presence of adequate surfactant. Otherwise irregular shape, large size particle with high PDI values are produced. Microparticles with non-spherical shape could collapse as a function of time showing broader distribution of particles (Zhao et al., 2017). The G2 microparticles are composed of appropriate combination of GMS, olive oil, tween-80 and poloxamer-188. The obtained zeta potential values were in the range of -13 to -20 mV. The results of zeta potential are good indicative of stable microparticles. Usually, zeta potential values above -30 mV are considered ideal for stable colloidal system. Higher zeta potential values mean greater repulsive forces between the particles and lesser chance of agglomeration. The potential charge on microparticles depend upon the nature of selected polymers and surfactants. The types of attraction and repulsion forces among particles determine the positive or negative charge on microparticles. No flocculation of microparticles was detected in our microparticles at these zeta potential results. (Alam et al., 2015). The major peaks from FTIR of individual ingredients, physical mixture and prepared microparticles

### Table 4: Particle size, polydispersity index and zeta potential of formulations (n=3)

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Particle Size (µm), ±S.D.</th>
<th>Polydispersity Index, ± S.D.</th>
<th>Zeta Potential (mV), ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>11.10±3.10</td>
<td>0.09±0.02</td>
<td>-17.20±0.03</td>
</tr>
<tr>
<td>G2</td>
<td>12.80±13.20</td>
<td>0.24±0.07</td>
<td>-13.01±1.14</td>
</tr>
<tr>
<td>G3</td>
<td>14.00±10.50</td>
<td>0.02±0.02</td>
<td>-16.38±0.42</td>
</tr>
<tr>
<td>G4</td>
<td>28.70±19.10</td>
<td>0.37±0.03</td>
<td>-13.12±0.40</td>
</tr>
<tr>
<td>S1</td>
<td>74.60±0.70</td>
<td>0.14±0.08</td>
<td>-18.55±0.39</td>
</tr>
<tr>
<td>S2</td>
<td>121.20±1.90</td>
<td>0.11±0.02</td>
<td>-12.95±0.38</td>
</tr>
<tr>
<td>S3</td>
<td>134.80±10.60</td>
<td>0.30±0.03</td>
<td>-17.95±0.18</td>
</tr>
<tr>
<td>S4</td>
<td>178.80±2.50</td>
<td>0.21±0.01</td>
<td>-20.17±0.19</td>
</tr>
</tbody>
</table>

### Table 5: Entrapment efficiency and percentage yield of prepared microparticles

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Entrapment Efficiency, %</th>
<th>Percentage Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>59.00</td>
<td>69.00</td>
</tr>
<tr>
<td>G2</td>
<td>63.00</td>
<td>76.10</td>
</tr>
<tr>
<td>G3</td>
<td>64.00</td>
<td>88.00</td>
</tr>
<tr>
<td>G4</td>
<td>78.00</td>
<td>90.52</td>
</tr>
<tr>
<td>S1</td>
<td>66.00</td>
<td>71.40</td>
</tr>
<tr>
<td>S2</td>
<td>74.30</td>
<td>79.70</td>
</tr>
<tr>
<td>S3</td>
<td>82.20</td>
<td>89.30</td>
</tr>
<tr>
<td>S4</td>
<td>87.00</td>
<td>92.50</td>
</tr>
</tbody>
</table>

were matched reasonably with each other. No new band and peak was observed in spectra of microparticles with reference to individual drug, lipids and surfactants spectra regarding as standards.

In addition, the maximum entrapment efficiency of formulations (G4), (S4) were found 78% and 87% respectively. The structure of lipid and high hydrophobicity directly affect the entrapment efficiency of lipid. In order to achieve sustain release of drug from microparticle structure; immobilization of drug in lipid matrix is vital that can be facilitated by using higher concentration of lipids. It is reported that higher concentration of lipid could encapsulate higher drug loading but it might create problem of aggregation and stabilization. Additionally, the higher concentration of surfactants has revealed inverse effect on entrapment efficiency of microparticles. Increasing amount of surfactant lead to significant decrease in entrapment efficiency which might be due to partitioning of drug from inner phase to outer phase. The liquid lipids has helped in loading high amount of drugs in lipid matrix. Higher concentrations of liquid lipid produce more imperfection in ordered solid lipid crystals. Amorphous lipids have better capability to incorporate drugs compared to crystalline lipids because intact crystalline structure could expel drugs (Alam et al., 2015). Higher entrapment efficiency of the prepared lipid formulations might be linked with combine effect of liquid lipid, surfactant and stabilizer (Chella and Tadikonda, 2015).

The value of p obtained by One-way ANOVA on in-vitro drug release data was less than 0.05. The value of p illustrate that results of drug release are statistically significant.

CONCLUSION

Lamotrigine, a lipid soluble drug, was successfully encapsulated into lipid microparticles using melt emulsification method. The prepared microparticles has provided us promising tool to increase solubility and bioavailability of lipophilic drugs. Moreover, the effect of formulation variables such as concentration of lipids, their types, surfactants, stabilizers as well as process parameters such as homogenization speed, temperature, mixing and sonication time were evaluated to obtain the optimized formulation. Conclusively, a promising drug delivery system was found from the prepared lipid microparticles for enhancing therapeutic effectiveness of lamotrigine.

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