# *Preparation and Characterization of Lipid-Based Formulation Lipsphere to Enhance the Oral Delivery of the Ferulic Acid*

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***Abstract***

*The investigation aimed to improve bioavailability of the phytoconstituent 'ferulic acid' through the oral route using the liposphere formulation. The 'ferulic acid' loaded liposphere was prepared using the melt dispersion technique. The ferulic acid liposphere was prepared and investigated under the presence of various parameters like types of lipids, varying amounts of lipids, varying amounts of surfactant, and surfactant. The liposphere formulation comprised of the stearic acid was a uniform, homogenous powder. The other two lipids cetyl alcohol and palmitic acid demonstrated the aggregation of particles. The % amount recovery of all prepared batches of liposphere formulations were ranging 43.111±0.412% to 97.349±0.389%. The % amount recovery of FLS7 and FLS8 formulations was greater, at 95.538±0.472% and 97.349±0.389%, respectively. The percentage encapsulation efficiencies for various batches of lipospheres generated ranged from 40.311±0.557% to 92.769±0.620%. Among all batches of the liposphere formulation loaded with ferulic acid FLS7 showed the highest percentage drug entrapment of ferulic acid (92.769±0.620%). Percentage drug loading of all prepared batches of ferulic acid loaded liposphere formulation ranging from 11.856±0.164% to 20.748±0.076%. The liposphere formulation containing ferulic acid ranges in particle size from 44.223±0.914 µm to 177.830±0.845 µm. In vitro drug release demonstrated that ferulic acid loaded liposphere formulation showed the rapid and sustained phase. In conclusion, it can be observed that liposphere formulation would be a viable option to augment the bioavailability of phytoconstituent drug administered through oral rout.*

***Keyword:*** *Ferulic Acid, Liposphere, Cetyl Alcohol, Palmitic Acid, Melt Dispersion, Surfactant.*

## 1. Introduction

Lipospheres are defined as a dispersion containing the particle comprise of the solid lipids and stabilized phospholipid monolayer with a size ranging from 0.01 to 100µm. [1] These particulate carriers were designed to deliver bioactive compounds topically and orally. [2] Lipids are known to promote mucosal adhesion in the GIT and to boost absorption of drugs in the GIT, because of their less size and longer GIT residence time. Moreover, lipid particles protect the drugs within from enzymatic and chemical breakdown and deliver the active pharmaceutical ingredients into the bloodstream gradually, leading to better therapeutic profiles than free drugs. Lipospheres can even improve patient compliance, through decreasing side effects, decreasing the frequency of therapeutic doses, and minimizing fluctuations in plasma drug levels. Since its debut in the early 1990s, liposphere use has been thoroughly demonstrated for the delivery of many drugs via various routes. [3-5] These lipid-based sphere particles have been employed for the parenteral, oral, nasal as well as ocular administration. Additionally, these have been used for Protein and peptide drug delivery and gene delivery as well. [6,7]

A variety of approaches employed to create carrier for oral delivery that improve the water-insoluble drug's absorption efficiency by improving its dissolving profile. The

liposphere is described spherical solid lipid particles ranging between 0.2 and 100µm in diameter comprising of core containing solid hydrophobic fat cores such as, stabilized and surface covered by monolayer of phospholipids. Lipospheres has been immerged as promising drug deliver carrier for augmenting the dissolution ability of drug with less water solubility such as Ferulic Acid. Ferulic acid, a hydroxycinnamic acid, refers to the large fennel (Ferula communis). Ferulic acid, categorized as a phenolic phytochemical, has a solid crystalline powder with an amber tint. [8] It has a solubility of 0.78 g/L in water [9]. Ferulic acid demonstrated hepatic, neuro, and photoprotective benefits, as well as antibacterial and anti-inflammatory properties, it offers a broad therapeutic effect that may be helpful in the treatment of 'cancer', 'diabetes', 'lung', and 'cardiovascular disorders. [10] However, its low solubility limits its uses. Ferulic acid possesses the strong 'antioxidant' and 'anti-inflammatory properties. The reported research demonstrated that the has ability to stop free radical chain reactions and decreases the risk of 'coronary heart disease'. FA has been utilized in traditional Chinese medicine to promote blood flow and reduce blood stasis. FA, when given orally as regular pills and granules, has low absorption in the gastrointestinal tract due to its low aqueous solubiltiy. This limited absorption increases the intake of the daily dose of ferulic acid by the patient. [11] Following oral dosing, FA exhibits less plasma half-life, low bioavailability, low GI stability, resulting in limited therapeutic use. Following oral delivery, the GI tract absorbs almost 70% of FA in less than 30 minutes and quickly eliminates it. Following absorption, approximately 6% of FA is converted to conjugated forms in plasma and bile, and more than 50% of FA is distributed and eliminated by the kidney.[12] The objective of this research is to increase retention time and getting sustained release of ferulic acid as well as enhance its loading.

## 2. Methodology

### Materials

For the preparation of liposphere, Ferulic acid was obtained from p.c chem India and stearic acid as a lipid and poloxamer 188 as a surfactant is used

**Table 1:** Chemicals List

| S. No. | Material | Source |
|---|---|---|
| 1. | Ferulic acid | P.C. Chem India |
| 2. | Soylecithin | Mitushi biopharma |
| 3. | Stearic acid | SRL |
| 4. | Mannitol | Loba chemie |
| 5. | Chloroform | Qualikems |
| 6. | Methanol | Finar |
| 7. | Disodium Hydrogen orthophosphate | Finar |
| 8. | Potassium dihydrogen orthophosphate | Finar |
| 9 | Sodium Hydroxide | Finar |

**Table 2:** Instruments List

| S. No. | Equipment | Manufacturer |
|---|---|---|
| 1. | Bath Sonicator | Raj Analytical Services, |

| | | |
|---|---|---|
| 2. | Electronic weighing balance | Sartorius |
| 3. | Magnetic stirrer | Remi Scientific Instruments, Mumbai |
| 4. | Cooling centrifuge | Electrolab, Mumbai, India |
| 5. | pH meter | Electrolab., Mumbai, India |
| 6. | UV spectrophotometer | Electrolab Mumbai, India |

**Method of Preparation**

The ferulic acid loaded lipid-based sphere particles were formulated by 'melt dispersion technique as shown in figure 1. [13,14]

Figure 1. Flowchart depicting preparation of Liposphere using Melt Dispersion Method

The weighed amount of the lipid was melted at 5°C above its melting point

↓

250mg ferulic acid was solubilized in the melted lipid and emulsified in the 50 ml of aqueous poloxamer surfactant solution under continuous stirring at 1000rpm and 70°C using the mechanical stirrer

↓

Solution was transferred to the ice cooled bath and rapidly cooled to 20°C under stirring to obtained uniform dispersion of liposphere

↓

The dispersion was filtered and obtained solid lipid based spherical particle was then washed with water

The composition of various ferulic acid containing liposphere formulation were shown in Table 3.

**Table 3:** Composition of various batches of ferulic acid loaded lipospheres

| S. No. | Formulation code | Amount of Ferulic acid | Amount (mg) | | | Poloxamer 188 (%w/v) |
|---|---|---|---|---|---|---|
| | | | Stearic acid | Palmitic acid | Cetyl alcohol | |
| 1 | FLS1 | 250 | 500 | - | - | 0.2 |
| 2 | FLS2 | 250 | - | 500 | - | 0.2 |
| 3 | FLS3 | 250 | - | - | 500 | 0.2 |
| 4 | FLS4 | 250 | 250 | - | - | 0.2 |
| 5 | FLS5 | 250 | 750 | - | - | 0.2 |
| 6 | FLS6 | 250 | 1000 | - | - | 0.2 |
| 7 | FLS7 | 250 | 750 | - | - | 0.4 |
| 8 | FLS8 | 250 | 750 | - | - | 0.6 |
| 9 | FLS9 | 250 | 750 | - | - | 0.8 |

## Evaluation of ferulic acid liposphere

### Pre-formulation studies

In the Pre-formulation studies organoleptic properties, melting point, UV Visible Spectra, partition coefficient and solubility studies were performed.

**Physical appearance** Physical appearance parameters of ferulic acid loaded liposphere were visually observed to detect the presence of aggregation, drug particle, or phase separation.

## Percentage yield

Percentage yield of the all-prepared batches of ferulic acid loaded liposphere was determined using the below equation [13]:

$$\text{Percentage yield} = \frac{\text{Observed Amount of liposophere}}{\text{Theoritical amount of the drug and excipients}} \times 100$$

## Percentage Drug entrapment

The % drug entrapment of all manufactured batch of ferulic acid-loaded liposphere was ascertained by measuring the amount of free drug adsorbed on the liposphere's surface. The weighed 100mg of the all-prepared batches of ferulic acid loaded liposphere formulation was added in the volumetric flask containing 10ml of methanol under continuous shaking for 5min using the vortex shaker and centrifuged at 18000 and 4°C for 30min. The supernatant was appropriately diluted in methanol solvent before being placed in the UV cuvette and scanned using a UV spectrophotometer across a 200–400 nm range. The absorption of each solution was noted and determine the amount of ferulic acid using the standard calibration curve. [15] The percentage of drug entrapment of ferulic acid was determined employing the below equation:

$$\text{Percentage drug entrapment} = \frac{\text{Initial amount of drug} - \text{Amount of drug in supernatent}}{\text{Initial amount of drug}} \times 100$$

$$\text{Percentage drug loading} = \frac{\text{Amount of drug entrapped}}{\text{Weight of the lipospheres}} \times 100$$

### Particle size

The particle size of each prepared batch of liposphere loaded with ferulic acid was ascertained using the calibrated optical microscope.

## Scanning electron microscopy

The optimized lipospheres were investigated for shape and surface morphology using a scanning electron microscope. The liposphere sample was kept adhesive tape and smacked on an aluminum stub. After the prepared sample was evaporated, gold was applied to aluminum stubs to make them conductive in an argon environment. After that, liposphere photomicrographs were captured and examined. [13]

## FT-IR Analysis

FTIR spectra of the ferulic acid and the liposphere formulation loaded with ferulic acid were recorded using the FTIR spectrophotometer. KBR pellets were prepared for each sample. The sample was scanned between 400 and 4000 $cm^{-1}$ after the KBS pellets were placed in the FTIR spectrophotometer, and the sample spectra was captured. [13,15]

## *In- vitro* drug release

The release profile of the ferulic acid from the ferulic acid loaded liposphere formulation and pure drug suspension was determined using the dialysis membrane. Initially the 'dialysis membrane' was activated by soaking the dialysis membrane in 20%v/v aqueous ethanolic solution for overnight. Next day the membrane was washed 2-3 times with water. The liposphere formulation and pure drug suspension equivalent to the 250mg of ferulic acid was suspended in 10ml of the water. The suspension was transferred to the dialysis bad and titled both end of the dialysis bad. The dialysis bag was transferred to the beaker containing the drug release medium 0.1NHcl for initial 2hr and phosphate buffer pH 6.8. The beaker containing drug release medium was maintained at 37°C and 100rpm. At determined time intervals ('0hr, 0.25hr, 0.5hr, 1hr, 2hr, 4hr, 8hr, 12hr, and 24hr') accurately measured 5ml sample was withdrawn from and compensated by the fresh drug release medium. The withdrawn samples were centrifuged at 10000rpm for 10min. The withdrawn was transferred to a UV cuvette. The solution containing the UV cuvette was transferred in the UV spectrophotometer. Sample was scanned and note the absorbance of sample and determined the amount of the ferulic acid using the standard calibration curve [13].

## Drug release kinetics

Kinetic models that were used to study drug release were Zero-order kinetics, First order kinetics, Higuchi model and Korsmeyer peppas model [13,14].

## 3. Result and Discussion

## Pre-formulation study

**Organoleptic properties:** Ferulic acid appeared as a 'white' or off-white crystalline', 'odorless' powder.

**Melting point:** The observation confirmed the melting point of ferulic acid was ranging $169.147^0C \pm 1.023$-$171.910^0C \pm 0.938$ similar to the observations indicated in the literature. [16]

**Table 4:** Melting point of ferulic acid

| Drug | Specification | Observation |
|---|---|---|
| Ferulic acid | 168-172°C [16] | $169.147^0C \pm 1.023$-$171.910^0C \pm 0.938$ |

**Standard calibration curve of ferulic acid in methanol**

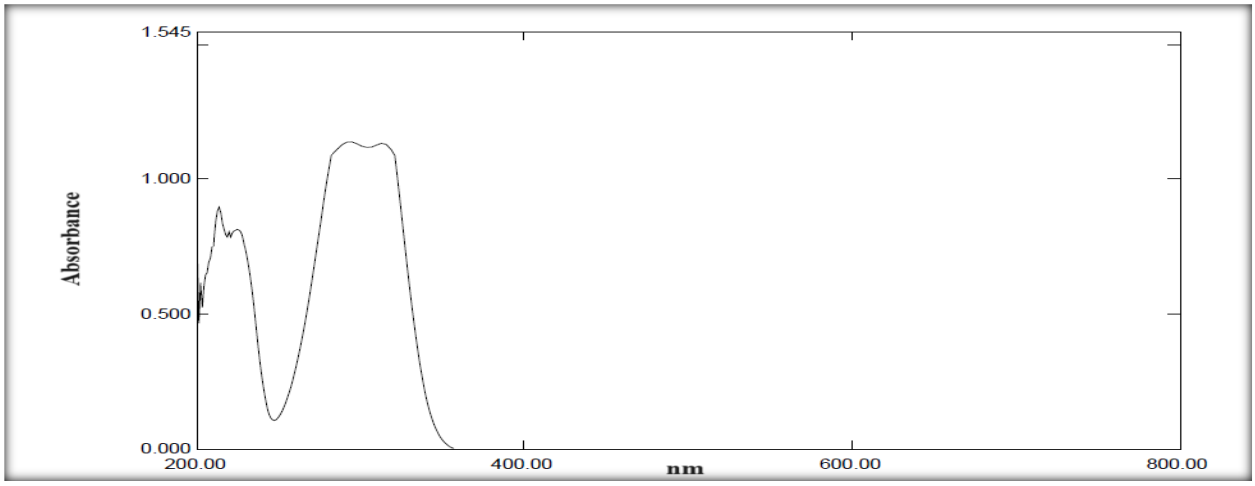


**Figure 2:** UV spectrum of ferulic acid in methanol solvent

**Table 5:** Absorption maxima of Ferulic acid

| S. No. | Observed Absorption maxima | Reference Absorption maxima | Reference |
|---|---|---|---|
| 1 | 321nm | 323nm | [16] |

**Table 6:** Standard linearity curve between absorbance and concentration of Ferulic acid in methanol

| S.No. | Concentration (µg/ml) | Absorbance | STD |
|---|---|---|---|
| 1 | 2 | 0.107 | 0.002 |
| 2 | 4 | 0.223 | 0.005 |
| 3 | 6 | 0.334 | 0.006 |
| 4 | 8 | 0.439 | 0.005 |
| 5 | 10 | 0.537 | 0.003 |
| 6 | 12 | 0.642 | 0.006 |
| 7 | 14 | 0.745 | 0.005 |
| 8 | 16 | 0.836 | 0.004 |
| 9 | 18 | 0.970 | 0.003 |

**Discussion:** The linearity curve of ferulic acid in methanol solvent was obtained in a range of concentration 2–18µg/ml at 321 nm [16] using a UV spectrophotometer. Based on the Lamber-Bear Law, the concentration range of 2–18 µg/ml was chosen. As seen in Figure 3, the calibration curve was produced by plotting the concentration at the X axis and the corresponding absorbance at the Y axis. The linear regression equation and regression coefficient were found to be y=0.0526x+0.0109 after the linear graph was plotted, and 0.999 suggested good linearity.

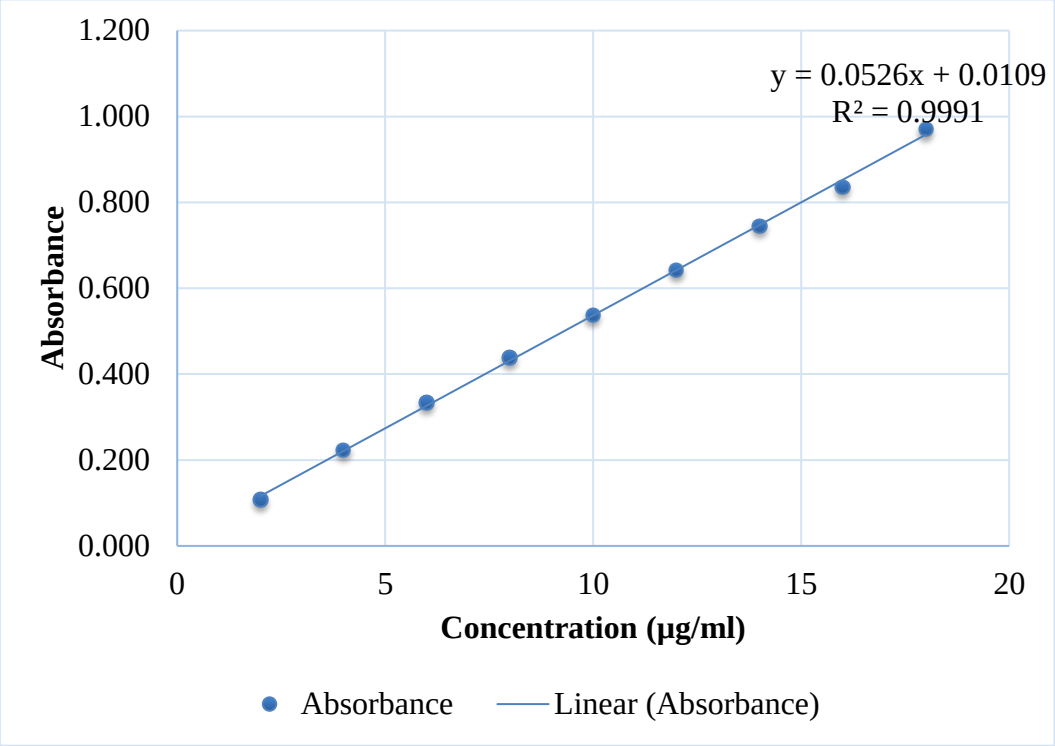


**Figure 3:** Standard Calibration curve of Ferulic acid

**Solubility studies of drug:** The observation related to the solubility of Ferulic acid in water, buffers water miscible solvent and organic solvent were shown in Table 7.

**Table 7:** Solubility (mg/ml) of Ferulic acid in different solvents.

| S.No. | Solvent | Solubility (mg/ml) | Outcome |
|---|---|---|---|
| **1** | Water | 0.858±0.007 | Very slightly soluble |
| **2** | Methanol | 10.699±0.086 | Sparingly soluble |
| **3** | Ethanol | 7.695±0.115 | Slightly soluble |
| **4** | Chloroform | 9.489±0.095 | Slightly soluble |
| **5** | Phosphate Buffer 6.8pH | 1.174±0.010 | Slightly soluble |

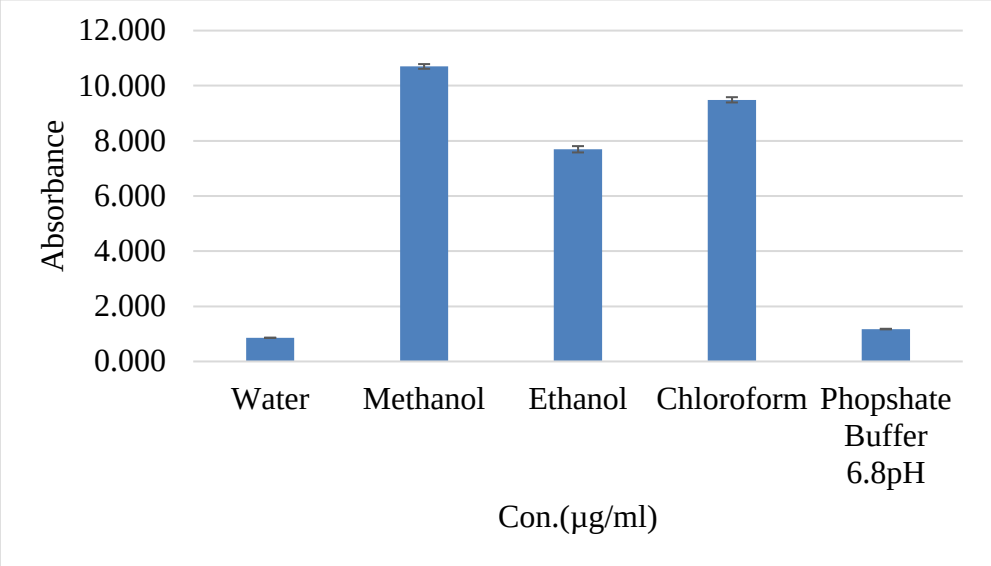


**Figure 4:** Solubility data of Ferulic acid in various solvent

**Discussion**: The observations associated with the solubility confirmed that Ferulic acid displayed was slightly soluble in ethanol, chloroform, and phosphate buffer, sparingly soluble in methanol, and very slightly soluble in water.

## Partition coefficient of drug

The partition coefficient was determined in a mixture of the n-octanol and water 1:1 ratio was determined. The observed value of the Partition coefficient of ferulic acid was observed to be 1.547 ± 0.009 closely similar to the literature value of 1.51 [17] indicating the lipophilic property of the ferulic acid.

## Preparation and ferulic acid loaded

Previous literature confirmed the melt dispersion technique is ideal for the encapsulation of low aqueous solvent soluble drugs in the liposphere formulation. [18] The current study investigates the effects of several lipid types (stearic acid, cetyl alcohol, and palmitic acid) and varying amount of selected lipid and surfactant over the physicochemical properties of the prepared batches of ferulic acid loaded liposphere. [19]

## Evaluation of ferulic acid liposphere

## Physical Appearance

**Table 8:** Physical appearance of ferulic acid loaded liposphere

| S.No. | Formulation code | Physical appearance |
|---|---|---|
| 1 | FLS1 | Uniform, Homogenous and Spherical Particles |
| 2 | FLS2 | Irregular shape with aggregation of particles |
| 3 | FLS3 | Irregular shape with aggregation of particles |
| 4 | FLS4 | Uniform, Homogenous and Spherical Particles |
| 5 | FLS5 | Uniform, Homogenous and Spherical Particles |
| 6 | FLS6 | Uniform, Homogenous and Spherical Particles |
| 7 | FLS7 | Uniform, Homogenous and Spherical Particles |

| | | |
|---|---|---|
| 8 | FLS8 | Uniform, Homogenous and Spherical Particles |
| 9 | FLS9 | Uniform, Homogenous and Spherical Particles |

**Discussion:** The prepared batches of the ferulic acid loaded liposphere formulation was observed for the physical appearance of the ferulic acid loaded liposphere shown in Table 8. The observation confirmed that the liposphere formulation were uniform, homogenous powder. The other two lipids cetyl alcohol and palmitic acid demonstrated the aggregation of particles.

**Figure 5:** Image of ferulic acid loaded liposphere

## Percentage yield

**Table 9:** Percentage yield of the all ferulic acid loaded liposphere formulation

| S.No | Formulation code | Percentage yield (%) |
|---|---|---|
| 1 | FLS1 | 88.162±0.803 |
| 2 | FLS2 | 43.111±0.412 |
| 3 | FLS3 | 71.280±0.476 |
| 4 | FLS4 | 67.481±0.691 |
| 5 | FLS5 | 92.030±0.499 |
| 6 | FLS6 | 93.079±0.487 |
| 7 | FLS7 | 95.538±0.472 |
| 8 | FLS8 | 97.349±0.389 |
| 9 | FLS9 | 97.072±0.528 |

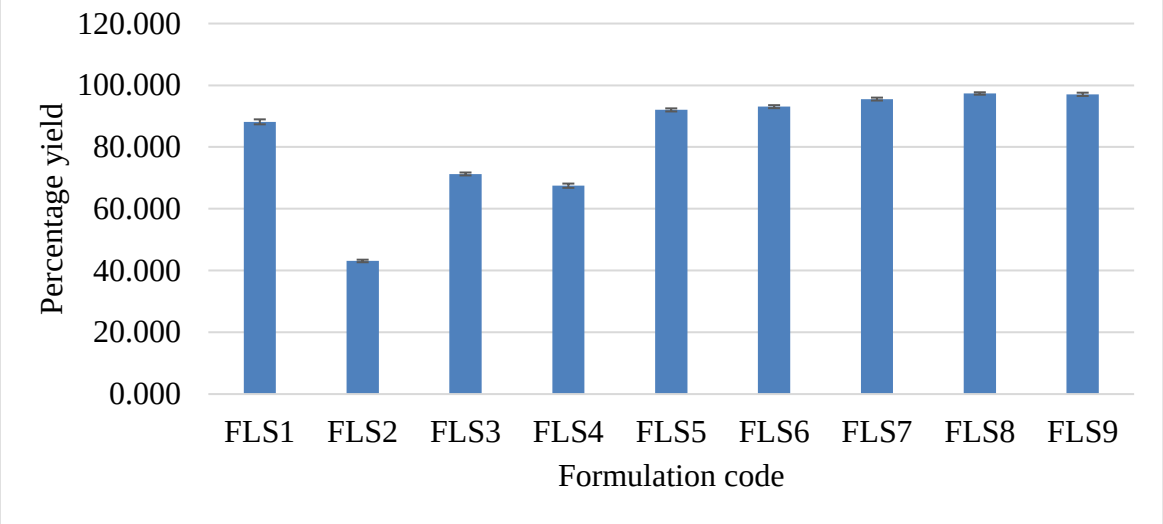


**Figure 6:** Percentage yield of the all ferulic acid loaded liposphere formulation

**Discussion:** The percentage yield of the prepared batches of liposphere formulations were found to be in range of 43.111±0.412% to 97.349±0.389. The liposphere comprise of stearic acid demonstrated higher percentage yield than the other two lipids palmitic acid and cetyl palmitate. Moreover, the on increasing the amount of stearic acid, the percentage yield also increased. [20]
As surfactant concentration is varying from 0.2%w/v to 0.6%w/v, the percentage yield rises accordingly. The percentage yield of FLS7 and FLS8 formulations was greater, at 95.538±0.472 and 97.349±0.389%, respectively.

## Percentage drug entrapment

**Table 10:** Percentage drug entrapment of all ferulic acid loaded liposphere formulation

| S.No. | Formulation code | Percentage drug entrapment (%) |
|---|---|---|
| 1 | FLS1 | 61.728±0.404 |
| 2 | FLS2 | 49.683±0.614 |
| 3 | FLS3 | 40.311±0.557 |
| 4 | FLS4 | 47.787±0.697 |
| 5 | FLS5 | 91.292±0.335 |
| 6 | FLS6 | 88.629±0.214 |
| 7 | FLS7 | 92.769±0.620 |
| 8 | FLS8 | 85.820±0.496 |
| 9 | FLS9 | 82.990±0.430 |

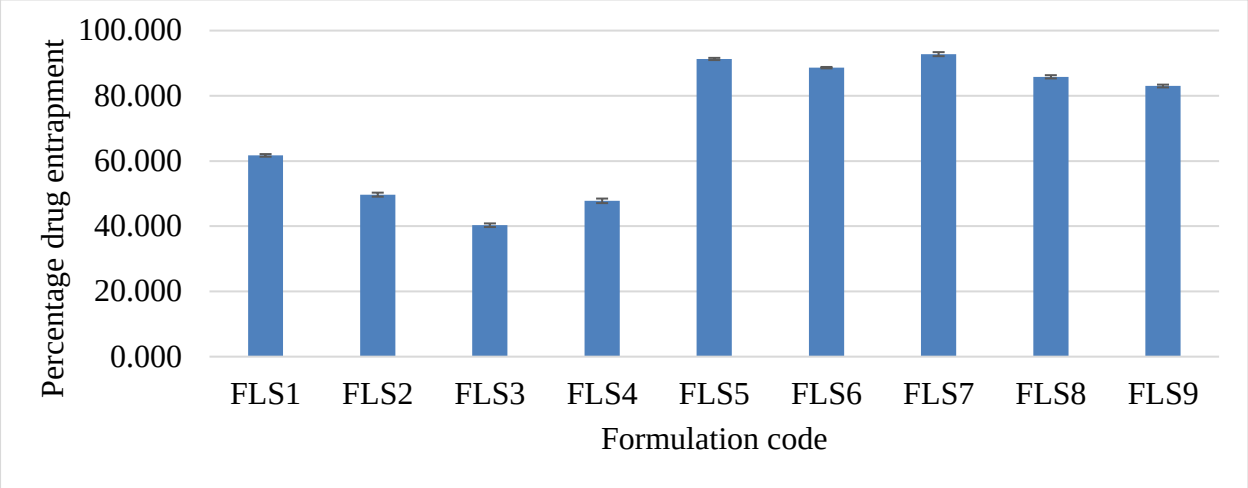


**Figure 7:** Percentage drug entrapment of ferulic acid loaded liposphere formulation

**Discussion:** The percentage encapsulation efficiencies for various batches of lipospheres generated ranged from 40.311±0.557 to 92.769±0.620%. The entrapment effectiveness of ferulic acid in lipid was enhanced with an increase in lipid content. Increased entrapment efficiency demonstrated the drug's better solubility inside the solid lipid core, which the melt technique made possible. [21]
An increment in amount of poloxamer 188 resulting in an equivalent rise in entrapment efficiency was observed for FLS5, FLS7, and FLS8; however, a further increment in amount of poloxamer 188 amount leads to decline in entrapment efficiency as observed for FLS8 and FLS9. Among all batches of the liposphere formulation loaded with ferulic acid FLS7 showed the highest percentage drug entrapment of ferulic acid (92.769±0.620%).

## Percentage drug loading

**Table 11:** Percentage drug loading

| S.No. | Formulation code | Percentage drug loading (%) |
|---|---|---|
| 1 | FLS1 | 18.155±0.119 |
| 2 | FLS2 | 14.613±0.181 |
| 3 | FLS3 | 11.856±0.164 |
| 4 | FLS4 | 19.912±0.290 |
| 5 | FLS5 | 20.748±0.076 |
| 6 | FLS6 | 16.413±0.040 |
| 7 | FLS7 | 19.323±0.129 |
| 8 | FLS8 | 16.504±0.096 |
| 9 | FLS9 | 14.820±0.077 |

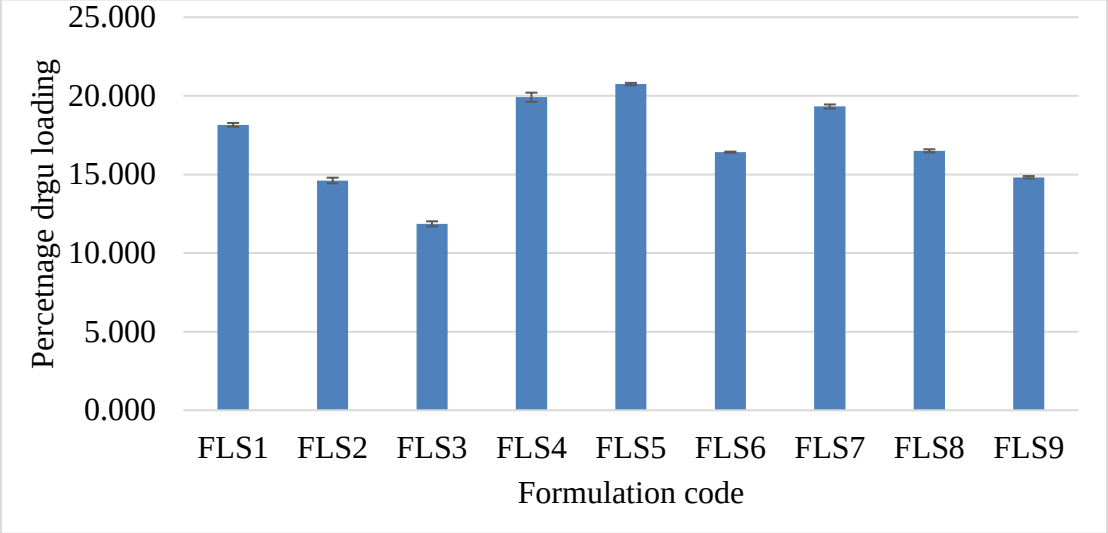


**Figure 8:** Percentage drug loading of the ferulic acid loaded liposphere formulation

**Discussion:** Percentage drug loading of ferulic acid loaded liposphere formulation ranging 11.856±0.164% to 20.748±0.076% as indicated in Table 8.

## Particle size

**Table 12**: Particle size

| S.No. | Formulation code | Particle size (µm) |
|---|---|---|
| 1 | FLS1 | 61.490±0.460 |
| 2 | FLS2 | 151.730±0.507 |
| 3 | FLS3 | 177.830±0.845 |
| 4 | FLS4 | 49.367±0.520 |
| 5 | FLS5 | 54.897±0.696 |
| 6 | FLS6 | 76.010±0.481 |
| 7 | FLS7 | 44.223±0.914 |
| 8 | FLS8 | 46.380±0.719 |
| 9 | FLS9 | 54.653±0.578 |

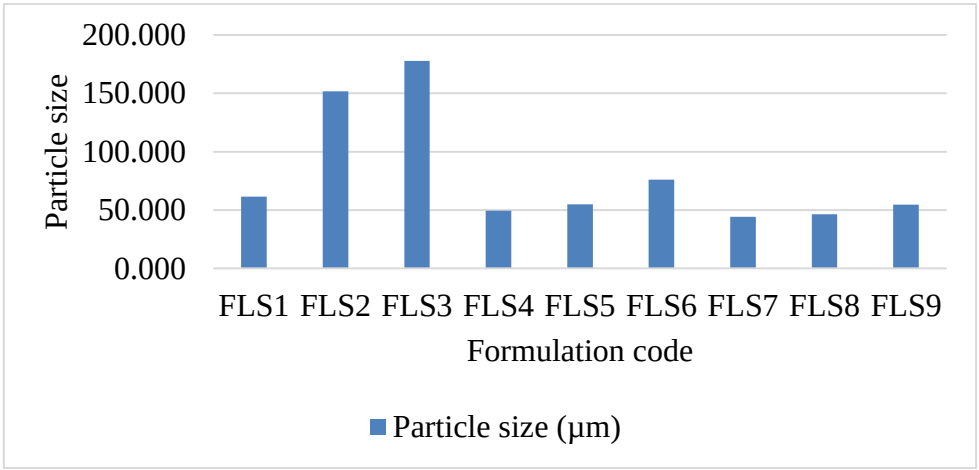

**Figure 9:** Particle size of the all ferulic acid loaded liposphere formulation

**Discussion:** The liposphere formulation containing ferulic acid ranges in particle size from 44.223±0.914 µm to 177.830±0.845 µm. Compared to the other two lipids, stearic acid produced ferulic acid-loaded lipospheres with a narrower dispersion and smaller particle sizes. Poloxamer 188 concentration also had a favorable influence on particle size up to a certain point. This implies that increasing poloxamer concentration twice reduced the size of the particles since poloxamer functions as a surfactant, which reduces surface area growth and particle size. [22]

On the basis of the above characterization parameters the formulation FLS7 was selected for further evaluation.

## Scanning electron microscopy

The surface morphology of the FLS7 formulation was determined using the 'scanning electron microscopy'. The SEM image indicates the smooth surface of the particles as shown in Figure 10.

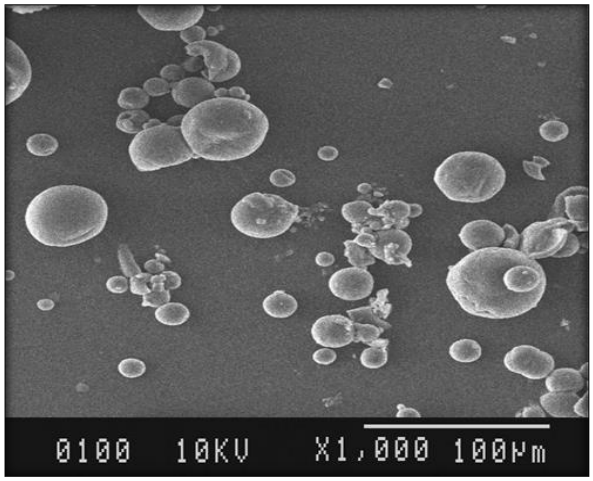


**Figure 10:** SEM micrograph of formulation FLS7

## FTIR spectroscopy

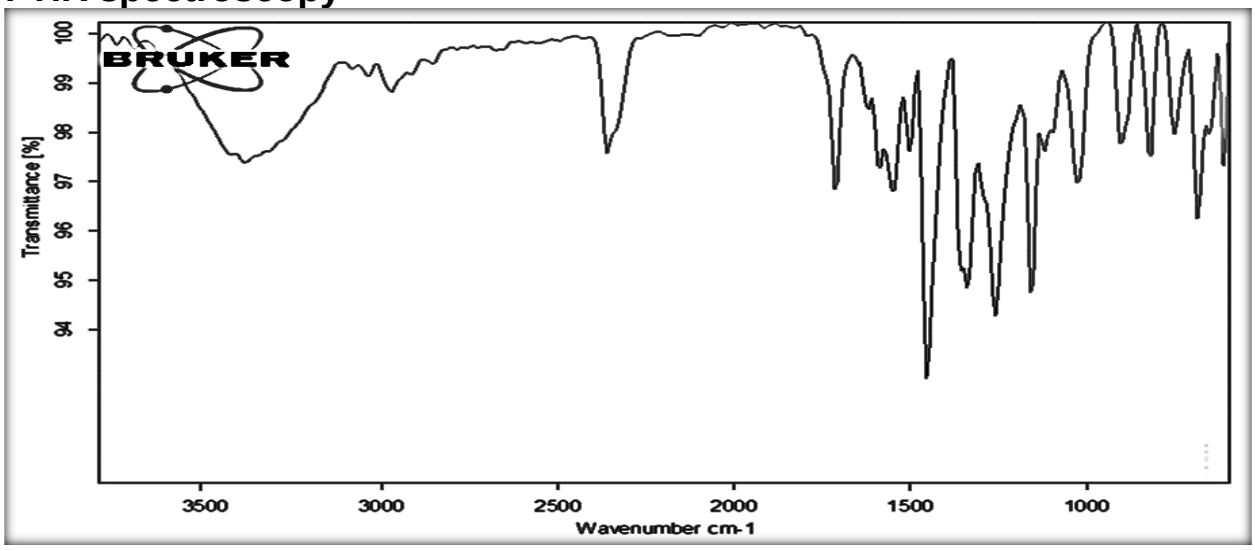


**Figure 11:** FTIR spectrum of Ferulic acid

**Table 13:** Reported and observed peak of ferulic acid

| S. No. | Reported Peaks | Observed Peaks | Functional group |
|---|---|---|---|
| 1 | 3496 $cm^{-1}$ | 3436 cm-1 | OH stretching |
| 2 | 3020 $cm^{-1}$ | 3016 $cm^{-1}$ | C–H stretching |
| 3 | 1519 $cm^{-1}$ | 1517 $cm^{-1}$ | C=C aromatic ring) |

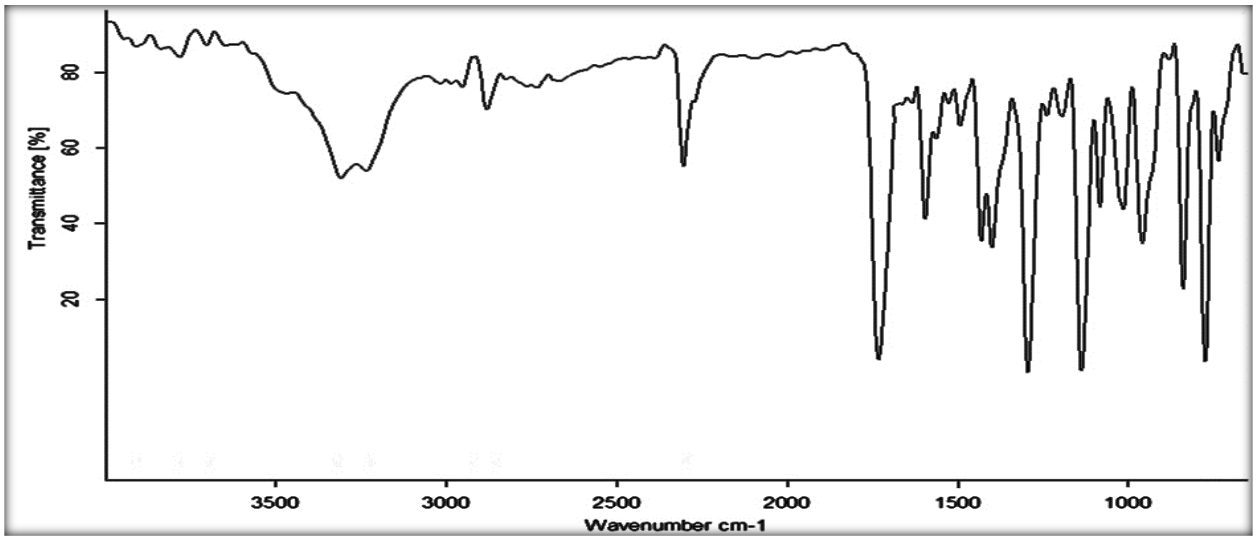


**Figure 12:** FTIR spectrum of physical mixture

**Table 14:** Reported and observed peak of ferulic acid in physical mixture

| S. No. | Reported Peaks | Observed Peaks | Functional group |
|---|---|---|---|
| 1 | 3496 $cm^{-1}$ | 3486 cm-1 | OH stretching |
| 2 | 3020 $cm^{-1}$ | 2996 $cm^{-1}$ | C–H stretching |
| 3 | 1519 $cm^{-1}$ | 1510 $cm^{-1}$ | C=C aromatic ring) |

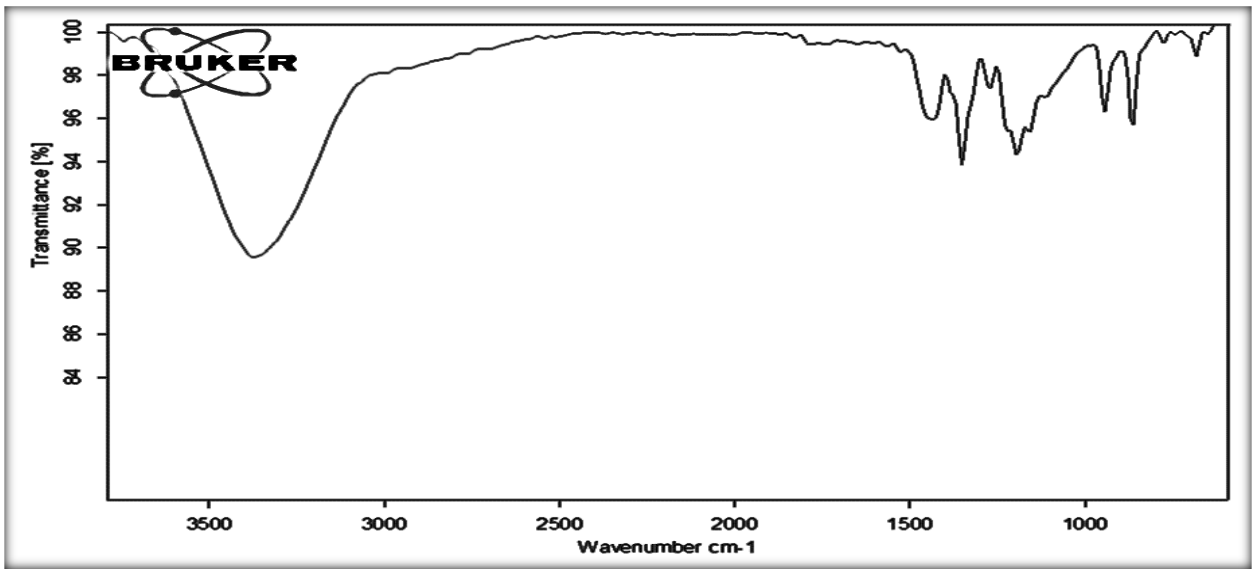


**Figure 13:** FT-IR Spectra of optimized formulation

**Table 15:** Reported and observed peak of ferulic acid in formulation

| S. No. | Reported Peaks | Observed Peaks | Functional group |
|---|---|---|---|

| | | | |
|---|---|---|---|
| 1 | 3496 $cm^{-1}$ | 3486 cm-1 | OH stretching |
| 2 | 3020 $cm^{-1}$ | - | C–H stretching |
| 3 | 1519 $cm^{-1}$ | - | C=C aromatic ring) |

**Discussion:** Ferulic acid FTIR spectra revealed peaks similar indicated in the literature. [23] The FTIR spectra of the physical mixture did not indicate the interaction between drug and excipients. The FITR spectra of the optimized formulation indicating the absence of the distinctive peaks of ferulic acid and the appearance of peaks with incredibly low intensities showed the ferulic acid's encapsulation within the liposphere lipid matrix.

## *In-vitro* percentage drug release study

**Table 16:** *In-vitro* release of pure drug and liposphere formulation FLS7

| S. No. | Time (hr.) | % Drug release of Pure drug suspension | % Drug release of formulation FLS7 |
|---|---|---|---|
| 1 | 0 | 0±0 | 0±0 |
| 2 | 0.25 | 5.174±0.048 | 7.501±0.048 |
| 3 | 0.5 | 7.775±0.145 | 14.722±0.097 |
| 4 | 1 | 15.132±0.290 | 22.148±0.145 |
| 5 | 2 | 24.783±0.098 | 44.973±0.194 |
| 6 | 4 | 28.410±0.387 | 66.395±0.290 |
| 7 | 8 | 35.083±0.242 | 75.011±0.484 |
| 8 | 10 | 40.969±0.145 | 86.989±0.968 |
| 9 | 12 | 45.041±0.194 | 95.202±1.936 |
| 10 | 24 | 45.178±0.097 | 96.228±0.1452 |

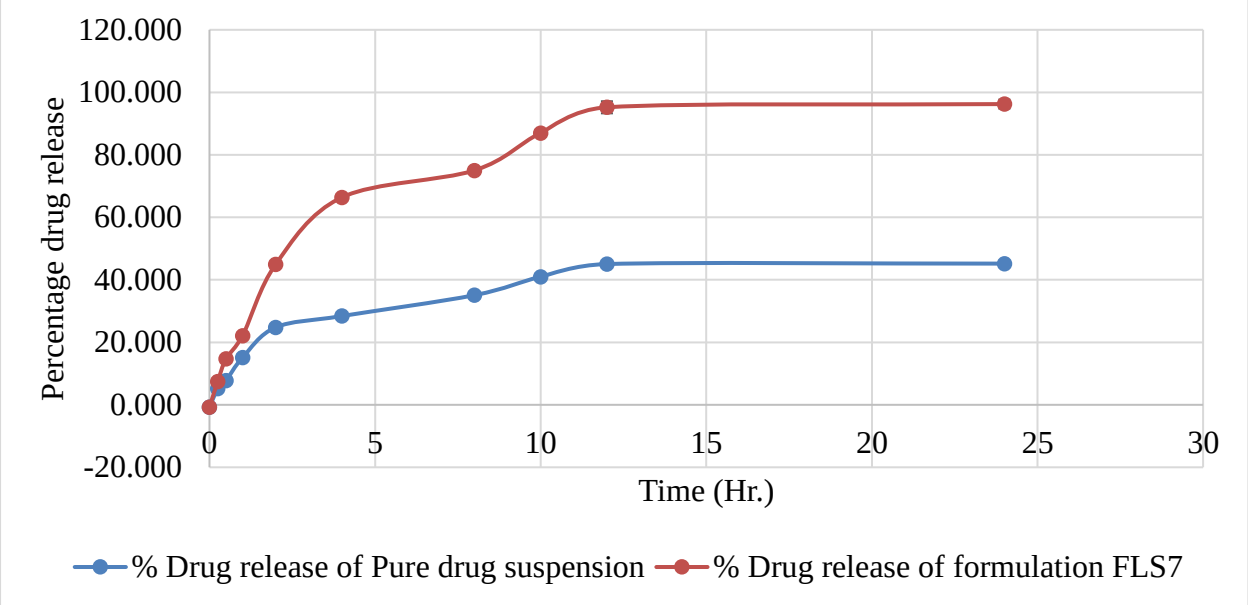


**Figure 14**: *In-vitro* drug release of drug suspension and optimized liposphere formulation FLS7

**Discussion:** The release profile of the ferulic acid from ferulic acid loaded liposphere was determined using drug release medium 0.1NHcl for 2hrs and Phosphate buffer pH 6.8 for up to 24 hours. The in vitro release studies of ferulic acid loaded liposphere FLS7 were investigated and found that the initially, very less burst effect was observed due to the rapid release drug associated at the surface of the liposphere. This burst release occurred at 1 hour and was characterized by a quick release (<22%). The drug release rate reached approximately 95% during the 12-hour time interval. [24]

## In-vitro drug release kinetic Study

The drug release profile of ferulic acid loaded optimized liposphere formulation FLS7 was subjected to various kinetic models like 'zero', 'first', 'Higuchi' and 'Korsmeyer peppas' model.

## Zero order

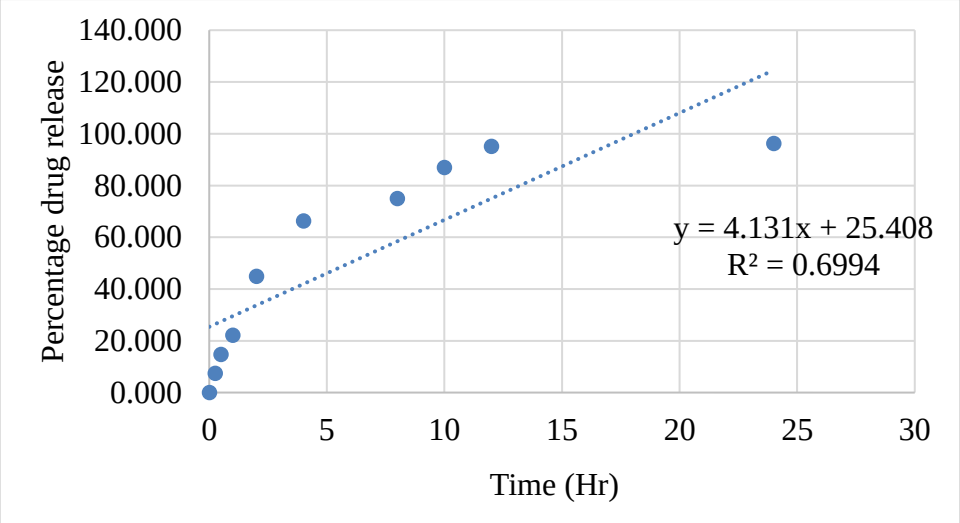


**Figure 15:** Zero order kinetics of FLS7

## First order

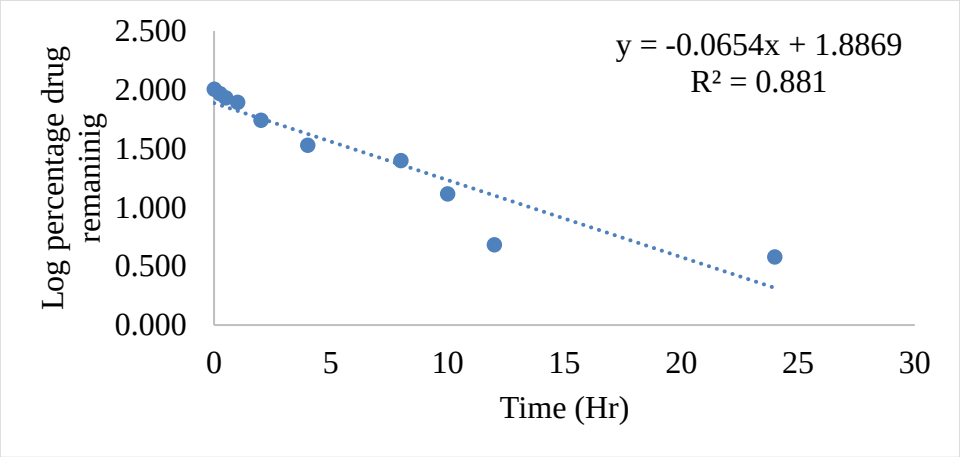


Figure 16: **First order kinetic of FLS7**

## Higuchi Model

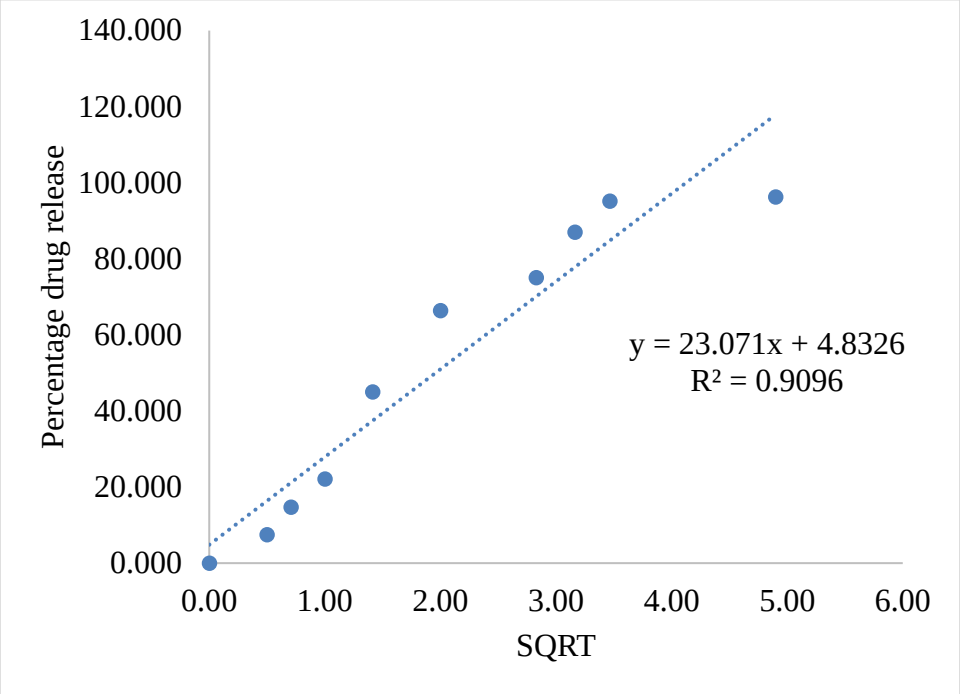


**Figure 17**: Higuchi model kinetic of FLS7

## Korsmeyer –Peppas model

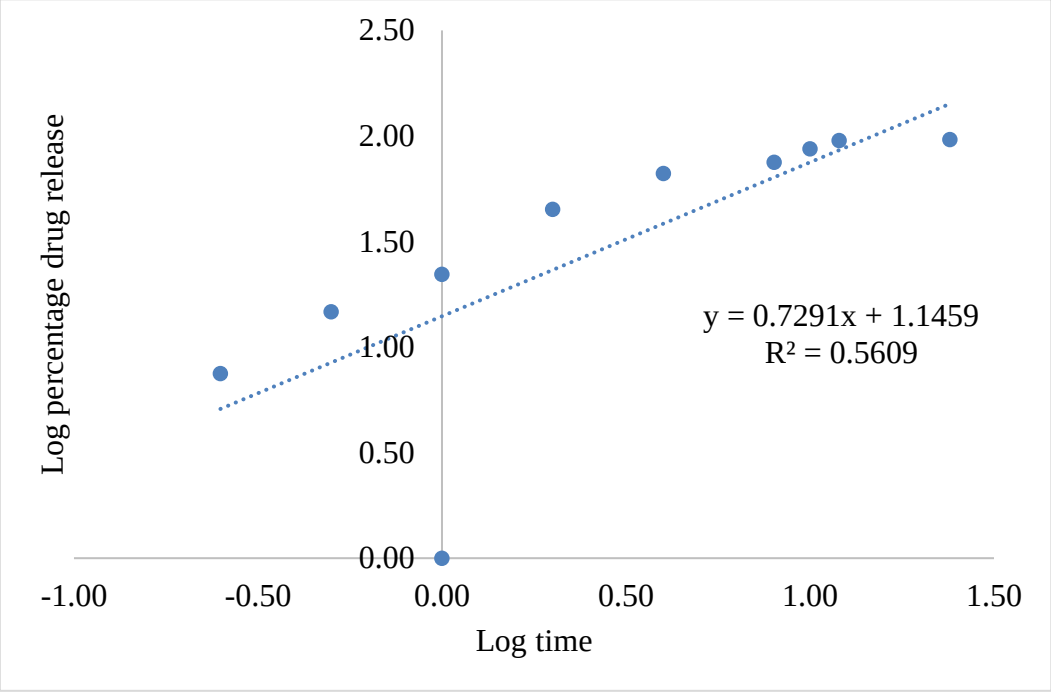


**Figure 18:** Korsmeyer–Peppas model kinetic of FLS7

**Table 17:** Regression coefficient of models

| S.No. | Models | Regression coefficient value |
|---|---|---|
| 1 | Zero order | 0.6982 |
| 2 | First order | 0.881 |
| 3 | Higuchi | 0.9096 |

| | | |
|---|---|---|
| 4 | Korsmeyer–Peppas | 0.5609 |

The drug release profile of liposphere formulation FLS7 was subjected to various drug release kinetic models and computed the $R^2$ of each kinetic model. The value of regression coefficient 0.9096 was observed higher for the Higuchi release model.

## 4. DISCUSSION AND CONCLUSION

Ferulic acid exhibits short plasma half-life, low bioavailability, low GI stability, and limited therapeutic use. The current investigation involves the development of the ferulic acid loaded liposphere to augment the bioavailability of the ferulic acid through the oral rout of administration. In preformulation study, Ferulic acid melting point was $169.147^0C\pm1.023$-$171.910^0C\pm0.938$. The standard linearity curve of ferulic acid was obtained over a concentration range of 2–18µg/ml at 321 nm in methanol using a UV spectrophotometer. The linear regression equation and regression coefficient were found to be y=0.0526x+0.0109 after the linear graph was plotted, and 0.999 suggested good linearity. The observations associated with the solubility confirmed that Ferulic acid displayed was slightly soluble in ethanol, chloroform, and phosphate buffer, sparingly soluble in methanol, and very slightly soluble in water. The observed value of the Partition coefficient of ferulic acid was observed to be 1.547 ± 0.009 indicating the lipophilic property of the ferulic acid.

The current study involves the ferulic acid loaded liposphere using the melt dispersion technique. The current study investigates the effects of several lipid types (stearic acid, cetyl alcohol, and palmitic acid) and varying amount of selected lipid and surfactant over the physicochemical properties of the prepared batches of ferulic acid loaded liposphere. In vitro characterization parameter, the observation of physical appearance confirmed that the liposphere formulation comprised of the stearic acid were uniform, homogenous powder. The other two lipids cetyl alcohol and palmitic acid demonstrated the aggregation of particles. The percentage yield of the prepared batches of liposphere formulations were found to be in range of 43.111±0.412% to 97.349±0.389. The percentage yield of FLS7 and FLS8 formulations was greater, at 95.538±0.472 and 97.349±0.389%, respectively. The percentage encapsulation efficiencies for various batches of lipospheres generated ranged from 40.311±0.557 to 92.769±0.620%. Among all batches of the liposphere formulation loaded with ferulic acid FLS7 showed the highest percentage drug entrapment of ferulic acid (92.769±0.620%). Percentage drug loading of all prepared batches of ferulic acid loaded liposphere formulation ranging 11.856±0.164% to 20.748±0.076%. The liposphere formulation containing ferulic acid ranges in particle size from 44.223±0.914 µm to 177.830±0.845 µm. Compared to the other two lipids, stearic acid produced ferulic acid-loaded lipospheres with a narrower dispersion and smaller particle sizes. On the basis of the above characterization parameters the formulation FLS7 was selected for further evaluation. The drug release profile of the ferulic acid from ferulic acid loaded liposphere was determined using drug release medium 0.1NHcl for two hours and Phosphate buffer pH 6.8 for up to 24 hours. The drug release rate reached approximately 95% during the 12-hour time interval. The drug release profile of liposphere formulation FLS7 was subjected to various drug release kinetic models and computed the $R^2$ of each kinetic model. The value of regression coefficient 0.9096 was observed higher for the Higuchi release model.

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