FORMULATION AND CRYSTALLIZATION OF LUMEFARATINE COCRYSTAL BY SOLVANT EVAPORATION METHOD

1Mr. Patil Nikhil Dinesh (Research student)
2Dr. Mrs. Samiksha Prashant Warke, 3Ms.R.V.Patil, 4Dr.P.R.Patil (2Associate Professor) (3Assistant Professor) (4Principal)

Department of Pharmaceutics
KYDSCT’s College of Pharmacy, Sakegaon (Bhusawal) Dist. Jalgaon, Maharashtra, India.

Abstract:
The main aim of this research is to formulation and characterization of Lumefantrine co-crystal with improved physicochemical and dissolution properties. The choice of correct solvent system is important for the synthesis of co-crystals which requires the knowledge of solution complexation. The present work to enhance solubility by modifying the crystal habit and enhance stability. Lumefantrine is a BCS class II drug. Standard solution of Lumefantrine in Methanol was prepared in 100μg/ml. Absorbance was measured at 234 nm. To characterize co-crystals for morphology and surface topography by Scanning Electron Microscopy, for crystal polymorphism study by Differential Scanning calorimetry (DSC) and for crystallinity by Powder X-ray diffraction. Preparation of co-crystals by solvent evaporation method. Saccharin, Croscarmellose sodium, Avicel 102, PVP K30, Magnesium stearate these excipients was used for formulation. Evaluation and optimization of co-crystals was done by different methods.

Keywords: - Lumefantrine, solvent evaporation, optimization, co-crystals.

1. Introduction

Almost more than 90% drugs are orally administered. Sufficient drug absorption and reproducible bioavailability, pharmacokinetic profile of orally administered drug substances is highly dependent on solubility of that compound in aqueous medium. The major problem faced during the oral administration of active agent is the bioavailability factor, which ultimately depends on the solubility of the agent. 40% of the drugs discovered are hydrophobic which produce side effects such as gastric irritation, peptic ulceration etc. whereas only 8% of new drug candidates have shown both high solubility and permeability. The solubility may be expressed as a concentration, molality, mole fraction, mole ratio, etc[1].

Biopharmaceutical Classification System:
(BCS) system allows restricting the prediction using the parameters solubility and intestinal permeability. The tenets of bio-pharmaceutics, solubility and permeability, are of pivotal importance in new drug discovery and lead optimization due to the dependence of drug absorption and pharmacokinetics on these two properties. The BCS is a scientific framework for classifying drug substances based on their aqueous solubility and intestinal permeability.

Class I (High Permeability, High Solubility)
e.g. Metoprolol, Diltiazem, Verapamil, Propranolol
Class I drugs exhibit a high absorption number and a high dissolution number. These compounds are generally very well absorbed. For those Class I compounds formulated as immediate release products, dissolution rate generally exceeds gastric emptying. Therefore, nearly 100% absorption can be expected if at least 85% of a product dissolves
within 30 min of in vitro dissolution testing across a range of pH values accordingly, in vivo bioequivalence data are not necessary to assure product comparability.

**Class II - (High Permeability, Low Solubility)**

e.g. Phenytoin, Danazol, Ketaconazole, Mefenamic acid, Nifedipine

Class II drugs have a high absorption number but a low dissolution number. *In vivo* drug dissolution is then a rate limiting step for absorption except at a very high dose number. The bioavailability of products containing these compounds is likely to be dissolution-rate limited. For this reason, a correlation between in vivo bioavailability and in vitro dissolution rate (an IVIVC) may be observed.

**3. Class III (Low Permeability, High Solubility)**

e.g. Cimetidine, Acyclovir, Neomycin B, Captopril For Class III drugs, permeability is rate limiting step for drug absorption. These drugs exhibit a high variation in the rate and extent of drug absorption. Absorption is permeability-rate limited but dissolution will most likely occur very rapidly.

**4. Class IV (Low Permeability, Low Solubility)**

e.g. taxol, hydrochlorothiazide, furosemide. Those compounds have a poor bioavailability. Usually they are not well absorbed over the intestinal mucosa and a high variability is expected with very poor oral bioavailability. These compounds are not only difficult to dissolve but once dissolved, often exhibit limited permeability across the GI mucosa. These drugs tend to be very difficult to formulate and can exhibit very large inter subject and intra subject variability. In the last years, crystal engineering of APIs through co-crystallization has gained an increased interest as means of optimizing the physical properties and/or stability of solid dosage forms[4].

**Co-crystal Design:**

Co-crystals are designed based on the principles of crystal engineering and supramolecular chemistry, where co-crystal components are selected based on favorable molecular recognition interactions. Co-crystals depend on non-covalent, nonionic interactions, which include hydrogen bonding, π-π, and van der Waals interactions. Analysis of co-crystal structures in the Cambridge Structural Database (CSD) indicates that hydrogen bonding is the most prevalent mode of interaction among co-crystals.

**Advantages of Co-crystal:**

- It offers stable crystalline form as compared to amorphous form.
- During co-crystallization there is no need to form covalent bond, so new compound with improved physicochemical properties are synthesised in short time.
  - All APIs is having ability to form co-crystal with numerous potential co-formers which provides counter molecules for hydrogen bonding
- There are numbers of co-former like food additives, preservatives, pharmaceutical excipients and other APIs.
- Co-crystal can be produced using solid state synthesis, green technology with high yield and no by-product[11].

**2. Experimental work :-**

**2.1 Drug authentication:**

Lumefantrine was procured from vital laboratories pvt lmd, Mumbai. Drug was authenticated by melting point, IR spectra DSC and SEM.

**2.1.1 Melting Point:**

The melting point is one of the key parameter to identify drug and its crystalline nature. Variation in melting point is due to impurity and gives clue about drug purity. The melting point of pure lumefantrine was determined using the open capillary tube method. Lumefantrine was placed in capillary tube that was attached with thermometer. The whole assembly was kept in liquid paraffin bath and progress in temperature was monitored. The point at which drug started melting was noted and experiment was performed for three times. The mean melting point was considered as melting point of drug .

**2.1.2 UV Spectra:**

Accurately weighed 10 mg of the drug was dissolved in some quantity of methanol and then volume was then adjusted to 100 ml with the same. The prepared standard solution has the concentration 100 μg/ml. The prepared stock solution was diluted to produce working solution of 2μg/ml, 4μg/ml up to 10μg/ml. The absorption maximum of the standard solution was scanned between 200-400 nm regions on Agilent carry60 spectrophotometer. The absorption maximum was found to be 234 nm in methanol. The spectrum obtain from 10μg/ml was compared with reference spectrum [57].
2.1.3 IR Spectra:
The IR spectrum of Lumefantrine in pure form and lumefantrine co-crystals with saccharin was recorded using the spectra were recorded over the wave number of 4000-650cm-1. The FTIR spectra of mixtures were compared with that of the pure drug and co-former to assess any change in the principal peaks of spectra of pure drug and co-former [58].

2.1.4 Differential Scanning Calorimetry:
Differential scanning calorimetric (DSC) studies of pure lumefantrine and co-crystals of drug lumefantrine was performed to assess what changes had actually occurred when co-crystals were formed and by what phenomenon this enhanced drug solubility. The sample was kept on DSC reference pan and DSC curves were obtained by differential scanning calorimeter (DSC 60; Shimadzu) at a heating rate of 10°C/min from 0 to 300°C in nitrogen atmosphere.

2.2 Analytical Method Development:

2.2.1 Analytical method 1:
Preparation of standard solution of Lumefantrine in Methanol:
Accurately weighed 10mg of lumefantrine was dissolved in little quantity of methanol. The solution is sonicated until drug particles solubilize in methanol. Then volume was adjusted to the same to 100ml in volumetric flask. The prepared standard solution has the concentration 100μg/ml [59].

Scanning of Lumefantrine in Methanol:
The absorption maximum of the standard solution was scanned between 200-400 nm regions on Agilent carry60 spectrophotometer. The absorption maximum was found to be 234.1nm.

Procedure:
From the standard solution, aliquots of 0.2, 0.4, 0.6, 0.8, and 1ml were transferred to the series of 10ml volumetric flasks and final volume was made upto 10ml with methanol. Absorbance of these solutions were measured against methanol solution as blank at 234.1nm using Agilent carry60 spectrophotometer

2.2.2 Analytical Method 2:
Preparation of 2% BKC in 0.1N HCl:
20ml of benzylkomium chloride was taken and dissolved in little quantity of distilled water. To prepare 0.1N HCl 8.3ml of conc. Hydrochloride acid was taken and dissolved in little amount of distilled water. Both the solutions were transferred into 1000ml volumetric flask and volume was made upto 100ml by distilled water [60].

Preparation of standard solution of Lumefantrine in 2% BKC in 0.1N HCl:
Accurately weighed 10mg of drug was dissolved in little quantity of 2% BKC in 0.1N HCl and volume was then adjusted to 100ml with the same. The prepared standard solution has the concentration 100 μg/ml.

Scanning of Lumefantrine in 2% BKC in 0.1N HCl:
The absorption maximum of the standard solution was scanned between 200-400 nm regions on Agilent carry60 spectrophotometer. The absorption maximum was found to be 341nm.

Procedure:
From the standard solution, aliquots of 0.2, 0.4, 0.6, 0.8 and 1ml were transferred to 2% BKC in 0.1N HCl the series of 10ml volumetric flasks and final volume was made upto 10ml with. Absorbance of these solutions were measured against 2% BKC in 0.1N HCl solution as blank at 341nm using Agilent carry60 spectrophotometer.

2.3 Preparation of Co-crystals:
The co-crystals of Lumefantrine were prepared by solvent evaporation method with saccharin as crystal forming agent. Co-crystals were prepared in different equimolar ratio of drug and crystal forming agent as 1:1, 1:2 and 2:1. Drug and co-former were accurately weighed by stoichiometric ratio. Ethyl acetate is used as solvent. The drug and co-former were added in solvent and allowed to evaporate slowly by keeping on water bath. As the solvent evaporated the porcelain dishes were put in oven for drying and after drying crystals were collected [61].

2.4 Formulation of tablet:

2.4.1 Direct compression:
All the ingredients were accurately weighed as per formula F1 to F9 (table no.8.1) and were dispensed in clean polythene covers.
Lumefantrine and Croscarmellose sodium were sifted through sieve no. 30
Microcrystalline Cellulose pH-102 were passed through sieve no-20.
Magnesium stearate, PVP K30 and talc passed through sieve no-40.
Lumefantrine, Microcrystalline Cellulose pH-102, and croscarmellose sodium were mixed in polythene cover (PC1)
Magnesium stearate, PVP K30 and talc were mixed in polythene cover (PC2)
Both (PC1, PC2) mix thoroughly for 30 min
2.4.2 Procedure for Scale up of Lumefantrine Tablets:-

Table: 1 Content of Lumefantrine Tablet.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity in batch (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>Co-crystals</td>
<td>230</td>
</tr>
<tr>
<td>Avicel 102</td>
<td>28</td>
</tr>
<tr>
<td>Cross Carmellose Sodium</td>
<td>8</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>12</td>
</tr>
<tr>
<td>PVP K30</td>
<td>4</td>
</tr>
</tbody>
</table>

Scale up was done by following the same procedure as given for direct compression. Mixing was carried out in a Double cone blender for 15 min. This blend is then subjected to direct compression on a Double Rotary Compression Machine (12 stations). Tablet compressed using 8 mm punch.

2.5.1 Fourier Transformation Infrared Spectroscopy: (FTIR) [62]

FTIR spectra were obtained using a Shimadzu FTIR spectrometer (shimadzu 8400s, japan) spectrometer. The scanning range was kept from 4000 to 650 cm$^{-1}$

2.5.2 Differential Scanning Calorimetry: (DSC) [63]

Differential scanning calorimetric (DSC) studies of Lumefantrine co-crystals with sachharin Lumefantrine was performed to assess what changes had actually occurred when co-crystals were formed and by what phenomenon this enhanced drug solubility. The sample was kept on DSC reference pan and DSC curves were obtained by differential scanning calorimeter (DSC 60; Shimadzu) at a heating rate of 10°C/min from 0 to 300°C in nitrogen atmosphere.

2.5.3. Scanning Electron Microscopy [64]

Co-crystals that showed the best results in the solubility and dissolution studies were subjected to scanning electron microscopy (SEM) studies to confirm the changes mounting made during the formation of co-crystals. Samples were prepared by powder onto a brass stub using graphite glue and coated with gold under vacuum before use. Images were recorded at the required magnification at an acceleration voltage of 30 KV using a scanning electron microscope

2.6 Drug Content and Saturation Solubility:

2.6.1 Determination of Drug Content [65]:

Drug content was determined by dissolving samples of co-crystals equivalent to 10 mg of Lumefantrine in 100 mL of Methanol. The solution was filtered through Whatman filter paper no. 41, suitably diluted and absorbance was measured at 234 nm using double beam UV spectrophotometer (Agilent carry60)

2.6.2 Saturation Solubility Studies [66]:

Saturation solubility studies were performed in distilled water in triplicate according to the method reported by Higuchi and Connors. Excess of pure drug and co-crystals were added to 10 mL of distilled water taken in glass vial and shaken for 24 hrs in rotary flask shaker at a room temperature to achieve the equilibrium. Appropriate aliquots were then withdrawn and filtered through Whatman filter paper no. 41 and analyzed spectrophotometrically 268 nm. The results obtained from saturation solubility studies were statistically validated.

2.7 Evaluation of Flow Property (Flowability):

2.7.1 Bulk Density:

Bulk density of co-crystals was determined by pouring gently 25gm of sample through a glass funnel into a 100 ml graduated cylinder. The volume occupied by the sample was recorded. Bulk density was calculated as

\[
\text{Bulk Density} = \frac{\text{Mass (gm)}}{\text{Bulk Volume (mL)}}
\]

2.7.2 Tapped Density:

The tapped density was determined by pouring 25gm sample (co-crystal) through a glass funnel into a 100 ml graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping was recorded and tapped density was calculated.

\[
\text{Tapped Density} = \frac{\text{Mass (gm)}}{\text{Tapped Volume (mL)}}
\]

2.7.3 Carr’s Index (%):

It is also one of the methods to evaluate flow property of a powder by comparing the bulk density and tapped density.

\[
CI (%) = \left( \frac{(\text{Tapped density} – \text{Bulk density})}{\text{Tapped density}} \right) \times 100
\]
3. Result And Discussion

3.1 Pre-formulation studies:

3.1.1 Organoleptic Properties Of Drug (Lumefantrine):
* Color – yellow
* Odor – odorless

3.1.2 Melting Point Determination:
The melting point was found to be in the range of 129°C-131°C. The reported melting point range for lumefantrine is 128°C-132°C. Hence, experimental values are in good agreement with official value.

3.2 Spectroscopic Studies:

3.2.1 UV-Spectroscopic Analysis

A. Determination of λ max Lumefantrine in Methanol
The UV spectrum of Lumefantrine in 100ml methanol was scanned and λ max was found to be 234nm.

![UV spectra of lumefantrine in methanol](image)

Table no: 2 Calibration curve of lumefantrine in methanol

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Concentration (μg/ml)</th>
<th>Absorbance at 234 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>0.2099</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>0.4483</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.6271</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>0.8648</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0.9972</td>
</tr>
</tbody>
</table>

Fig: 2 Linearity of Lumefantrine in Methanol

Y = m x + c
Where, Y = absorbance, m = slope, x = concentration, c = constant(y-intercept).
B. Determination of \( \lambda_{\text{max}} \) Lumefantrine in 2% BKC in 0.1 N HCl

Two solutions were prepared in small amount of distilled water 2% BKC and 0.1N HCl. Both solutions were mixed and made up to 1000ml. lumefantrine was dissolved in 100ml of above solution and scanned. \( \lambda_{\text{max}} \) of lumefantrine from above solution was found to be 341nm.

\[
y = 0.0996x + 0.0321
\]

**Table no: 2. Calibration curve of Lumefantrine in 2% BKC in 0.1N HCl**

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Concentration (( \mu g/ml ))</th>
<th>Absorbance at 341 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>0.0599</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>0.1329</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>0.2134</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>0.2655</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0.3469</td>
</tr>
</tbody>
</table>

3.3 Differential Scanning Calorimetry:

The melting point of a compound is a fundamental physical property determined for the purpose of characterization or purity identification of a compound. The DSC measurements were performed on a Differential Scanning Calorimeter with thermal analyzer DSC-61000 (Metller Toledo USA). The DSC measurements were performed on drug and optimized formulation. All accurately weighed samples (about 2 mg of samples) were placed in a sealed aluminum pan, and the samples were heated under nitrogen flow (10 mL/min) at a scanning rate of 10 °C per min from 25 to 300°C. An empty aluminum pan was used as reference.
3.4 IR Spectra:
3.4.1 IR Spectra of pure Lumefantrine

<table>
<thead>
<tr>
<th>Peak no</th>
<th>X(cm-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2932.58 C-H stretching alkane</td>
</tr>
<tr>
<td>2</td>
<td>1485.76 C-H bending alkane</td>
</tr>
<tr>
<td>3</td>
<td>1252.54 C-N stretching amine</td>
</tr>
<tr>
<td>4</td>
<td>872.76 C-Cl halo compound</td>
</tr>
</tbody>
</table>

Table no: 3. The IR frequencies for Lumefantrine
3.4.2 IR spectra of Lumefantrine Co-crystals:

![Fig: 6. IR spectra of Lumefantrine co-crystal](image)

Table: 4. IR frequencies of Lumefantrine co-crystal

<table>
<thead>
<tr>
<th>Peak no</th>
<th>X(cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3221.87 O-H stretching alcohol</td>
</tr>
<tr>
<td>2</td>
<td>2957.63 N-H stretching amine salt</td>
</tr>
<tr>
<td>3</td>
<td>1723.51 C=O stretching aldehyde</td>
</tr>
<tr>
<td>4</td>
<td>1624.70 C=C stretching cyclic alkene</td>
</tr>
<tr>
<td>5</td>
<td>1335.45 S=O stretching sulfonamide</td>
</tr>
<tr>
<td>6</td>
<td>1146.51 C-O stretching secondary alcohol</td>
</tr>
</tbody>
</table>

3.4.3 SEM photograph for evaluation of Surface Morphology:

The surface morphological properties of the co-crystals are shown below. It is evident from the microphotographs that the co-crystals of lumefantrine exhibit a stone shaped crystal arrangement.

![Fig: 7. SEM image of Lumefantrine co-crystals](image)
Effect of variable (PVP K-30): The graph shows that as PVP K30 concentration increases, % drug release was found to be decreased at some level and then there is increase in % drug release as concentration of PVP K30 increases.

3.4.4 Contour plot: Figure shows the counter plot of croscarmellose sodium and PVP K-30 is actual factor. It shows as croscarmellose sodium concentration increases the percentage release decreases at some level and then there is increase in % drug release as concentration of croscarmellose sodium increases. PVP K-30 concentration increases, % drug release was found to be decreased at some level and then there is increase in % drug release as concentration of PVP K-30 increases.

3.4.5 Diagnostic Case Statistics Of Experimental Matrix: The actual values were obtained from experiments, and the predicated ones were obtained from the models (software). As shown in fig the value prove that the predicted data, which were obtained from the empirical model for drug release, and are in good agreement with the experimental results due to their differences. Linear correlation was not observed between actual and predicted value shown in figure. 10
Fig: 10. Predicted Vs. actual value of % drug content

Three Dimensional Graphical Presentations 3D surface: The graph shows that as the concentration of croscarmellose sodium is increased there is increase in % drug content and as the concentration of PVP K30 increased there is increase in % drug content at some level and then there is decrease in % drug content.

Fig: 9 3D Surface Plot of % Drug Content of lumefantrine with Respect to croscarmellose sodium and PVP K-30

8.9. *In vitro* Drug Release

Improvement in dissolution rate compared to pure drug. The comparative dissolution profile is studied by mean percentage release from 5, 10, 15, 20, 30, 40, 50, 60, 75 and 90 min parameters. The percentage drug release of different samples is shown in table 3.
<table>
<thead>
<tr>
<th>Time (min)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>1.87</td>
<td>2.87</td>
<td>4.28</td>
<td>2.03</td>
<td>2.23</td>
<td>3.52</td>
<td>1.92</td>
<td>1.39</td>
<td>3.03</td>
</tr>
<tr>
<td>10</td>
<td>3.86</td>
<td>3.49</td>
<td>8.58</td>
<td>5.52</td>
<td>3.34</td>
<td>7.68</td>
<td>4.20</td>
<td>3.44</td>
<td>6.49</td>
</tr>
<tr>
<td>15</td>
<td>6.02</td>
<td>6.02</td>
<td>11.09</td>
<td>8.66</td>
<td>5.27</td>
<td>9.07</td>
<td>9.85</td>
<td>9.87</td>
<td>8.64</td>
</tr>
<tr>
<td>30</td>
<td>12.28</td>
<td>7.90</td>
<td>18.74</td>
<td>14.61</td>
<td>7.45</td>
<td>14.34</td>
<td>24.04</td>
<td>15.11</td>
<td>11.66</td>
</tr>
<tr>
<td>45</td>
<td>20.50</td>
<td>23.61</td>
<td>33.07</td>
<td>25.61</td>
<td>22.63</td>
<td>28.45</td>
<td>37.72</td>
<td>28.0</td>
<td>22.91</td>
</tr>
<tr>
<td>60</td>
<td>28.64</td>
<td>44.09</td>
<td>47.51</td>
<td>37.82</td>
<td>46.17</td>
<td>40.41</td>
<td>42.64</td>
<td>40.71</td>
<td>37.80</td>
</tr>
<tr>
<td>90</td>
<td>34.96</td>
<td>58.23</td>
<td>55.13</td>
<td>43.00</td>
<td>58.11</td>
<td>53.40</td>
<td>53.40</td>
<td>54.02</td>
<td>52.540</td>
</tr>
<tr>
<td>120</td>
<td>65.87</td>
<td>63.56</td>
<td>68.48</td>
<td>64.56</td>
<td>61.36</td>
<td>65.2</td>
<td>67.23</td>
<td>64.78</td>
<td>66.55</td>
</tr>
</tbody>
</table>

Table no: 3. *In vitro* dissolution of co-crystal tablet for F1-F9 batches

**Fig: 10.** Graphical presentation of comparative drug release profile for F1 to F9 formulations
Table no: 4. Formulation of F1 to F9 batches

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Co-crystals</th>
<th>Croscarmellose sodium</th>
<th>PVP K-30</th>
<th>Avicel 102</th>
<th>Mg – stearate</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>230</td>
<td>8</td>
<td>4</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F2</td>
<td>230</td>
<td>14</td>
<td>4</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F3</td>
<td>230</td>
<td>20</td>
<td>4</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F4</td>
<td>230</td>
<td>8</td>
<td>8</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F5</td>
<td>230</td>
<td>14</td>
<td>8</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F6</td>
<td>230</td>
<td>20</td>
<td>8</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F7</td>
<td>230</td>
<td>8</td>
<td>12</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F8</td>
<td>230</td>
<td>14</td>
<td>12</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>F9</td>
<td>230</td>
<td>20</td>
<td>12</td>
<td>28</td>
<td>12</td>
</tr>
</tbody>
</table>

4. Conclusion:

Through crystal engineering technique we have developed the co-crystals of lumefantrine with pharmaceutical acceptable co-former, saccharin using solvent evaporation method which results in improvement of the physicochemical and micromeritic properties of the drug. Development of co-crystals of API’s result in the formation of new crystals forms with altered physical and chemical properties of drug which can be confirmed from FTIR, DSC analysis. The prepared co-crystals of lumefantrine show the altered melting point, size and shape of the crystals indicating modified crystal habit which could be responsible for dramatic improvement in flowability, solubility and dissolution properties of lumefantrine from the co-crystals. The choice of correct solvent system is important for the synthesis of co-crystals which requires the knowledge of solution complexation. On the basis of these results, it could be concluded that, pharmaceutical crystal engineering technique to lumefantrine with saccharin could be possible and served as an alternative and effective approach for manipulation of physicochemical properties of lumefantrine and the principle of crystal engineering can be applied for improvement of physicochemical and micromeritic properties of API’s while simultaneously retaining its activity.

Immediate release tablet of prepared co-crystals was formulated using croscarmellose sodium as suerdisintegrant shows 149 secs of disintegration time.
5. References:


35. Savjani, J.K., *Co-crystallization: An approach to improve the performance characteristics of active pharmaceutical ingredients*. Asian Journal of