



## Formulation and Evaluation of Olanzapine Liquisolid Tablets for Improving Dissolution

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### ABSTRACT

The oral route remains the most preferred method for drug administration due to its ease, cost-effectiveness, and patient compliance. However, drugs with poor aqueous solubility have challenges to oral bioavailability and therapeutic efficacy. Bioavailability is mostly affected by drug dissolution and its release from the dosage form, and it mainly depends on solubility of drug. For the development of new pharmaceutical products, the major issue any pharmaceutical industry faces are solubility, which ultimately results in low bioavailability. There are various methods to enhanced solubility such as micronization, nanonization, self-emulsification, solid dispersion, co-solvency, solid lipid nanoparticles, co-precipitation technique, particle size reduction and complexation all have been used in recent research to increase the solubility of the drug, but the liquisolid compact has demonstrated superior results for enhancing dissolution. Liquisolid technology is a novel and promising approach used to treat low dose with poorly soluble drugs. OLZ is a BCS Class-II drug prescribed for Schizophrenia, depression, and bipolar disorder. The present study aims to enhance the solubility and dissolution rate of Olanzapine using the Liquisolid Compact Technique. Four formulation batches of OLZ liquisolid tablets were prepared using Tween 80 as non-volatile solvent, Fujicalin as carrier material and Aerosil 200 as coating material and evaluated for general appearance, thickness, hardness, friability, Average weight, disintegration, content uniformity, *in-vitro* drug release. A drug having a low dose can be formulated by this method.

**Keywords:** Fujicalin, Tween 80, Liquisolid technology, solubility, *in-vitro* drug release.

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### INTRODUCTION:

Antipsychotics are a class of medications primarily used to manage psychotic disorders, including schizophrenia, bipolar disorder, and severe depression with psychotic features. These drugs help reduce or control symptoms such as delusions, hallucinations, thought disorder, and agitation. They work mainly by blocking dopamine receptors (particularly D2 receptors) in the brain, which is believed to be involved in the pathophysiology of psychosis. Olanzapine, an atypical Antipsychotic drug used in the treatment of schizophrenia and bipolar disorder, belongs to the Biopharmaceutics Classification System (BCS) Class II, characterized by low aqueous solubility and high permeability.<sup>[1]</sup>

Oral drug administration is the most common and preferred route due to its convenience, low cost, and patient

compliance, accounting for 60–70% of pharmaceutical formulations.<sup>[2]</sup> However, challenges like low solubility, enzymatic degradation, first-pass metabolism, and variable GI transit can limit drug bioavailability.<sup>[3]</sup> Factors such as drug properties and GI conditions affect absorption.<sup>[4]</sup> To overcome these barriers, advanced oral delivery systems like solid dispersions<sup>[5,6,7]</sup>, Solid Lipid Nanoparticles<sup>[7]</sup>, Co-Precipitation Technique<sup>[7]</sup>, self-emulsifying drug delivery systems (SEDDS)<sup>[7]</sup>, Nanonization<sup>[8]</sup>, Hydrotropy<sup>[8]</sup>, complexation<sup>[8]</sup>, micronization<sup>[8]</sup>, Co-solvency<sup>[9]</sup>, pH Adjustment<sup>[10]</sup>, have been developed to enhance solubility, control release, and improve absorption.

The latest and most advanced method for improving solubility is the Liquisolid Technique. This approach has proven to be highly effective in enhancing the bioavailability

of Biopharmaceutics Classification System (BCS) Class II drugs, which typically have poor water solubility.

The liquisolid technique is an innovative and effective method for transforming liquid drugs, drug solutions, or suspensions in non-volatile solvents into dry, free-flowing, and compressible powders. This is achieved by mixing them with specific excipients like carriers and coating materials.<sup>[11]</sup> These resulting powders can then be compressed into tablets or encapsulated, making it easier to orally deliver drugs that have poor water solubility.

The liquisolid system provides a straightforward and effective approach to improve the dissolution rate and oral bioavailability of poorly water-soluble drugs. In this method, the drug is either dissolved or dispersed in a non-volatile solvent to create a "liquid medication," which is subsequently transformed into a dry, free-flowing powder by incorporating excipients like microcrystalline cellulose as a carrier and colloidal silicon dioxide as a coating agent.<sup>[12]</sup>

#### Advantages:<sup>[13]</sup>

1. It can be used for formulation of partially, very little, or practically insoluble in water.
2. It is appropriate for the development of sustained release drugs.
3. It enhances medication photostability in solid dosage form.
4. The process is straight forward, like traditional solid dosage forms.
5. Suitable for large-scale manufacturing of tablets and capsules.
6. Improved bioavailability of a water-insoluble medication taken orally.
7. The cost of production is lower than that of soft gelatin capsules.
8. The drug is formulated in tablet and resulting in better wetting qualities and dissolving profiles.
9. The liquisolid system can be designed for immediate or sustained release dosage forms.
10. They avoid useful methods such as nanonization and micronization.

#### Disadvantages:<sup>[13]</sup>

1. It is unsuitable for high-dose, and water-insoluble medicines.
2. To prepare liquid-solid systems, the medication must be soluble in the liquid vehicle.
3. Adding extra carrier to produce free-flowing powder can increase tablet weight and make swallowing difficult.
4. Difficulty mixing small amounts of viscous liquid solutions on big carrier materials.

#### Mechanisms of Enhanced Drug Release from Liquisolid Systems

1. Increased surface area of drug available for release.<sup>[14]</sup>
2. Increased aqueous solubility of the drug.<sup>[15]</sup>
3. Improved wettability of the drug particles.<sup>[16]</sup>

#### Theory of Liquisolid Systems:<sup>[17]</sup>

To enhance solubility or sustain release, a mathematical approach is necessary. This method determines the appropriate carrier and coating materials for optimal powder flow and compressibility. Two important parameters must be computed for a given carrier and coating substance. These are the flowable ( $\Phi$ -value) and compressible ( $\Psi$ -value) liquid retention potentials. The former number represents the maximum amount of liquid (w/w) contained by a powder while maintaining an acceptable flow. The latter value represents the greatest amount of liquid (w/w) retained by a powder while maintaining adequate compressibility and displaying no liquid squeezing-out phenomenon. Common flowability tests include the angle of repose, Hausner's ratio, and Carr's index. Compressibility and compatibility can be verified through practice testing.

The excipient ratio (ER), which is the ratio between the weight of the carrier (Ca) and the coating material (Co) in the formulation (Equation 1):

$$ER = Ca / Co \dots\dots\dots (Equation 1)$$

Liquid load factor (Lf), which is the ratio between the weight of the liquid medication (W) to that of the carrier material (Ca) (Equation 2):

$$Lf = W / Ca \dots\dots\dots (Equation 2)$$

The liquid load factor that allows acceptable flow is calculated according to the following equation (Equation 3):

$$\Phi Lf = \Phi + \Phi (1 / ER) \dots\dots\dots (Equation 3)$$

Where  $\Phi$  and  $\emptyset$  are the flowable liquid retention potentials of the carrier and coating material, respectively.

Similarly, the liquid load factor, which allows acceptable compressibility, can be calculated according to the following equation (Equation 4):

$$\Psi Lf = \Psi + \Psi (1 / ER) \dots\dots\dots (Equation 4)$$

Where  $\Psi$  and  $\Psi$  are the compressible liquid retention potentials of the carrier and the coating material, respectively.

The optimal liquid load factor (Lo) based on which formulation will be developed is equal to either  $\Phi Lf$  or  $\Psi Lf$ , whichever has the smallest value.

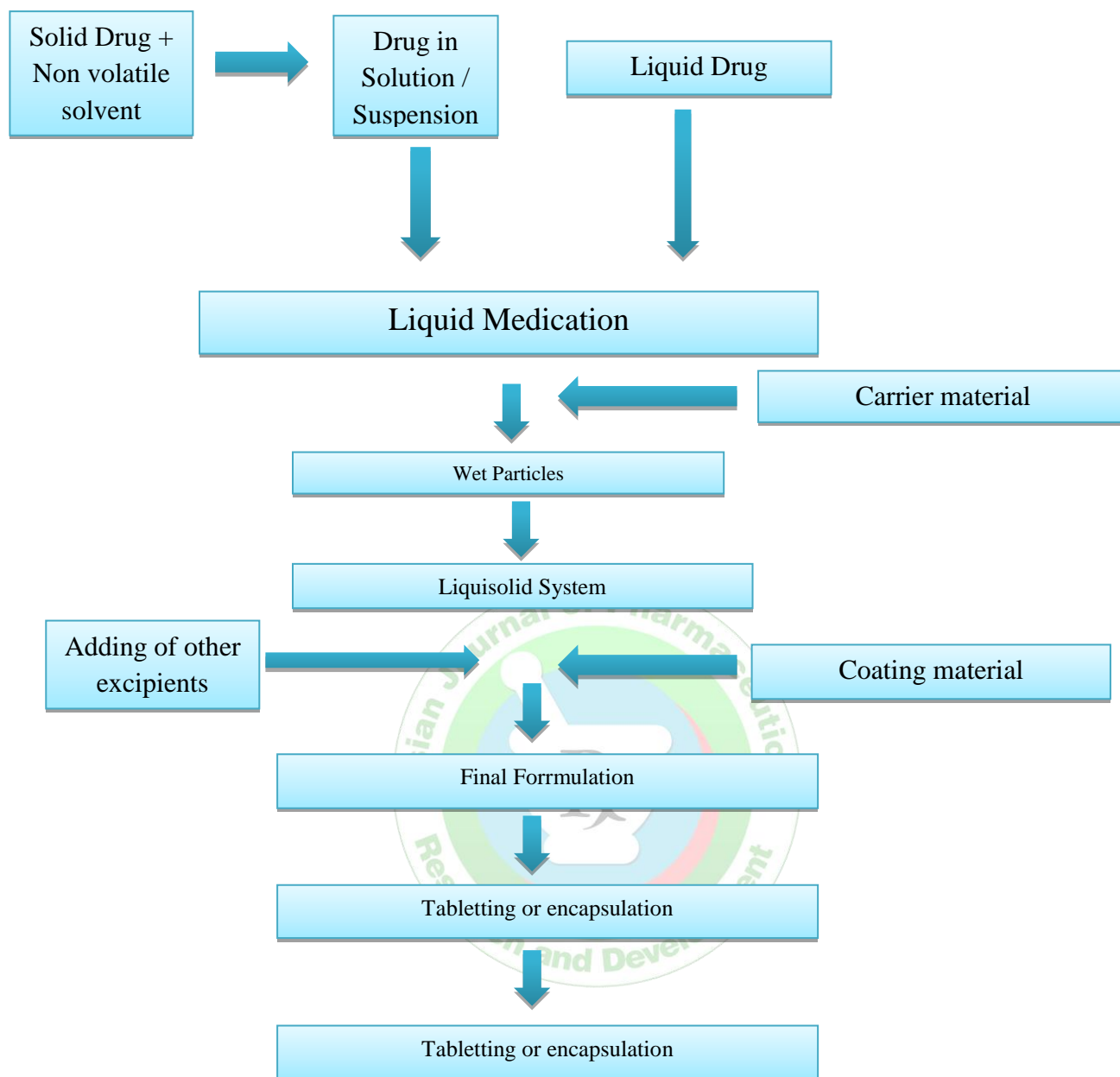
Accordingly, the carrier Ca, and coating material Co can be calculated:

$$Ca = W / Lo \dots\dots\dots (Equation 5)$$

$$Co = Ca / R \dots\dots\dots (Equation 6)$$

#### MATERIALS AND METHOD:

Olanzapine was obtained from K. C. Laboratory, Ankleshwar, Gujrat. Tween 80, Fujicalin, Aerosil 200, Starch, Magnesium Stearate were obtained from Ozone® international, Mumbai. All the chemicals used in this work were of analytical grade.

**Preparation and Formulation of Liquisolid:** <sup>[18]</sup>**Table 1:** Composition of various batches of liquisolid compact of Olanzapine

Ingredients	Ingredient role	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Olanzapine	Drug	10	10	10	10
Tween 80	Non-Volatile agent	10	10	10	10
Total weight of drug and non-volatile solvent (W)	-	20	20	20	20
ER=Ca/Co	-	20:1	30:1	40:1	50:1
$L_f = W/Ca$	-	0.22	0.21	0.21	0.20
Fujicalin	Carrier (Ca)	91.8	94.6	96.1	97.09
Aerosil 200	Coat (Co)	4.59	3.15	2.40	1.94
Starch	Disintegrant (10%)	11.63	11.78	11.8	11.9
Magnesium Stearate	Lubricant (1%)	1.16	1.18	1.18	1.19
Total weight each tablet	-	129.18	130.71	131.48	132.12

**Preformulation Studies**

**Solubility:<sup>[19]</sup>**

Solubility is defined as the amount of solute that dissolves in a particular solvent to form a saturated solution at a fixed temperature and pressure. This parameter is also used to select drug-solvent systems that may occur during drug delivery.

**Melting point:<sup>[19]</sup>**

A pure substance melts at one specific temperature. The melting Point of Olanzapine was determined by using a Digital Melting Point Apparatus.

**UV spectroscopy:**

The standard solution of pure drug was prepared in 7.4 Phosphate buffer. The prepared solution was scanned in the range of 200-400 nm to determine the wavelength of maximum absorbance.

**Preparation of Phosphate buffer (7.4 pH) as per IP:**

Dissolve 2.38 g of Disodium hydrogen phosphate, 0.19 g of Potassium dihydrogen phosphate and 8.0 g of Sodium chloride in sufficient water to produce 1000 ml. Adjust the pH if necessary.

**Preparation of stock solution:**

Accurately weighed 10mg of OLZ and dissolved in 10 ml of Methanol and dilute up to 100ml 7.4 Phosphate Buffer to give stock solutions (100µg/ml). From the standard stock solution, 2 ml was withdrawn and diluted up to 10 ml to get 20µg/ml. The solution was then scanned in the range of 200-400nm to determine the wavelength of maximum absorbance.

**Standard calibration of Olanzapine:**

From Standard stock solution pipette out 0.2,0.4,0.6,0.8,1.0 ml in 10 ml volumetric flask separately and make up the volume up to 10ml to get the solution of 2,4,6,8,10 µg/ml. The absorbances of these solutions were measured at 252nm using UV-spectrophotometer against the blank 7.4 PBS.

**Fourier transformed Infrared Spectroscopy:**

The IR spectrum of OLZ was recorded using Bruker Alpha II (410015) instrument. The interaction between the OLZ and excipients were determined by using the FT-IR spectroscopy

where infrared spectra of OLZ with Tween 80, Fujicalin and Aerosil 200 were determined. The scanning range was 4000 to 500 cm<sup>-1</sup>.

**Pre- compression Evaluation study****Bulk Density:<sup>[20]</sup>**

Bulk density is the weight of a powder or granule divided by its bulk volume, expressed in g/ml.

**Procedure:**

1. Clean and dry the measuring cylinder to prevent contamination.
2. Weigh 25 mg of the powder sample (W).
3. Transfer it to the dried graduated cylinder.
4. Record the volume occupied by the powder (V).
5. Calculate bulk density

$$\text{Bulk Density (g/ml)} = \frac{\text{Weight of the Powder}}{\text{Bulk Volume}}$$

**Tapped Density:<sup>[20]</sup>**

Tapped density is the weight of a powder divided by its volume after being compacted by tapping, expressed in g/ml.

**Procedure:**

1. Weigh 25 mg of powder (W).
2. Place in a clean, dry graduated cylinder and record initial volume (V<sub>1</sub>).
3. Place cylinder in tapped density apparatus.
4. Tap 50 times, then record final volume (V<sub>2</sub>).
5. Use a second cylinder to balance the apparatus if needed.
6. Calculate tapped density:

$$\text{Tapped Density (g/ml)} = \frac{\text{Weight of the Powder}}{\text{Tapped Volume}}$$

**Angle of Repose:<sup>[20]</sup>****Procedure:**

1. Fix a clean funnel (20–30 mm stem) on a stand, 2 cm above a graph paper on a flat surface.
2. Gently pour powder to form a cone that just touches the funnel tip.
3. Draw a circle around the base of the heap.
4. Measure the cone's height (h) and radius (r).
5. Calculate angle of repose:

$$\theta = \tan^{-1}(h / r)$$

**Compressibility Index (Carr's Index):<sup>[20]</sup>**

Carr's Index is used to assess the flowability and compressibility of a powder. It compares the difference between a powder's bulk density and tapped density. A low index (closer values) indicates good flow, while a high index suggests poor flow due to strong interparticle interactions.

**Formula:**

$$\% \text{ Compressibility} = \frac{(\text{Tapped Density} - \text{Bulk Density})}{\text{Tapped Density}} \times 100$$

This index is commonly used in pharmaceuticals to evaluate powder handling and processing behavior.

**Hausner's Ratio: <sup>[20]</sup>**

Indicates powder flowability based on the ratio of tapped to bulk density. Hausner's ratio below 1.25 shows good flow, above 1.5 shows poor flow, and 1.25–1.5 can be improved with a glidant.

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

**Bulk Density****Solubility Study of Lquisolid System:**



The absorbance was determined using a UV-Vis double beam spectrophotometer after the powder was dissolved in water until a supersaturated solution was created.

### Preparation of Olanzapine Liquisolid Tablets:

The Liquisolid powder blend containing Olanzapine was compressed by using Karnavati multi-station rotary press machine using the 6 mm punches.

### Post Compression Evaluation Study

#### General appearance:<sup>[19]</sup>

The general appearance of tablet and its identity is essential for consumer acceptance. The tablet examined visually for color, presence or absence of surface roughness.

#### Thickness:<sup>[20]</sup>

Thickness is measured in mm using a vernier caliper.

#### Hardness Test:<sup>[19]</sup>

Tablet hardness indicates its strength and resistance to handling. For uncoated tablets, 4 kg/cm<sup>2</sup> is considered satisfactory. Using a Monsanto tester, place the tablet between the jaws, rotate the screw until it breaks, and record the reading.

#### Friability Test:<sup>[19]</sup>

Friability measures the tablet's resistance to mechanical shock and abrasion. Ten tablets are weighed and placed in a Roche friabilator, run at 25 rpm for 4 minutes (100 rotations). Afterward, tablets are dedusted and reweighed. The percentage weight loss is calculated, and a loss of less than 0.5–1% is considered acceptable.

$$\text{Friability \%} = \frac{(\text{Initial Weight} - \text{Final Weight})}{\text{Initial Weight}} \times 100$$

#### Initial Weight

#### Weight Variation Test:<sup>[19]</sup>

Ten tablets are weighed to find the average weight. Each tablet's weight is compared to the average. No more than two tablets can deviate beyond the allowed percentage, and none should exceed twice that limit. The allowed weight variation

depends on the average tablet weight: for tablets weighing 80 mg or less, a maximum deviation of 10% is allowed; for those between 80 mg and 250 mg, up to 7.5% deviation is permitted; and for tablets over 250 mg, the maximum allowed deviation is 5%.

$$\text{Weight Variation (\%)} = \frac{(\text{Individual weight} - \text{Average weight})}{\text{Average Weight}} \times 100$$

#### Disintegration Test:<sup>[21]</sup>

Six tablets are placed in basket tubes immersed in pH 7.4 phosphate buffer at 37°C. The basket moves up and down at 29–32 cycles/min until tablets fully disintegrate. The test passes if all tablets disintegrate within the specified time.

#### Uniformity of Content:<sup>[21]</sup>

Ten tablets are crushed into powder. 10 mg powder is dissolved in methanol and phosphate buffer, shaken for 30 minutes, diluted, and filtered. A diluted sample's absorbance is measured at 252 nm using a UV spectrophotometer to determine drug content.

#### In-vitro Dissolution Test: [22]

Using a paddle apparatus, 900 ml of pH 7.4 phosphate buffer is maintained at 37°C and stirred at 100 rpm. Samples (2 ml) are withdrawn at 10, 20, 30, 40, 50, and 60 minutes, replaced with fresh buffer, diluted to 10 ml, and absorbance is measured at 252 nm to assess drug release.

### RESULTS AND DISCUSSION:

#### Preformulation Studies:

##### Solubility:

The Olanzapine is soluble in Methanol and HCL, sparingly soluble in Tween 80 and Phosphate buffer and practically insoluble in water.

##### Melting Point:

The melting point of Olanzapine was found to be 196°C - 198°C which compiled with the standard range i.e. 195°C - 197°C.

##### UV-Visible Spectroscopy:

The  $\lambda_{\text{max}}$  of Olanzapine was found to be at 252nm. The UV Spectrum of Olanzapine is shown in Fig. No. 1

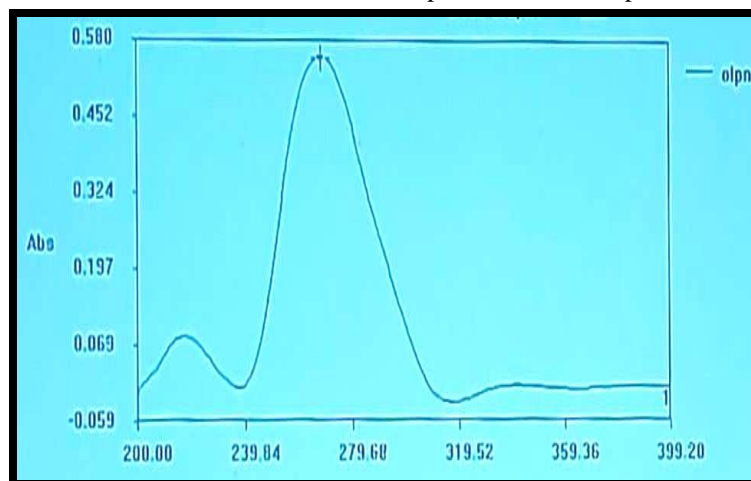


Figure 1: UV Spectra of Olanzapine

### Standard Calibration Curve in 7.4 Phosphate Buffer:

Graph of absorbance vs concentration was plotted, it was found to be linear over the range of 2, 4, 6, 8, 10 µg/ml

indicating its compliance with beer's and lambert's law. The correlation coefficient ( $R^2$ ) obtained was 0.9976 and equation was  $y = 0.0915x + 0.064$  as shown in Fig. No. 2

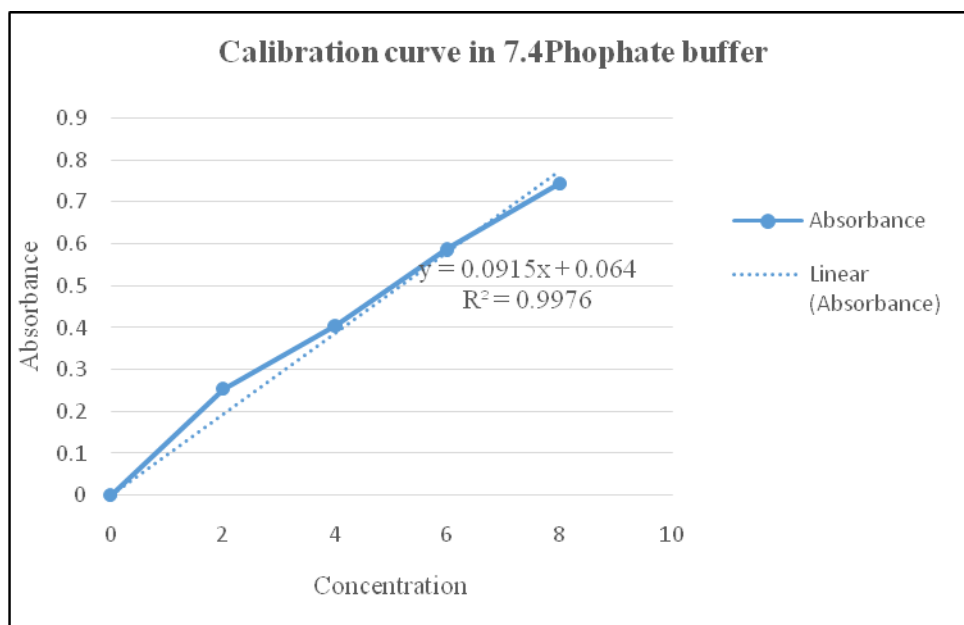


Figure 2: Calibration Curve of OLZ in 7.4 Phosphate Buffer

### FTIR Studies:

- Olanzapine

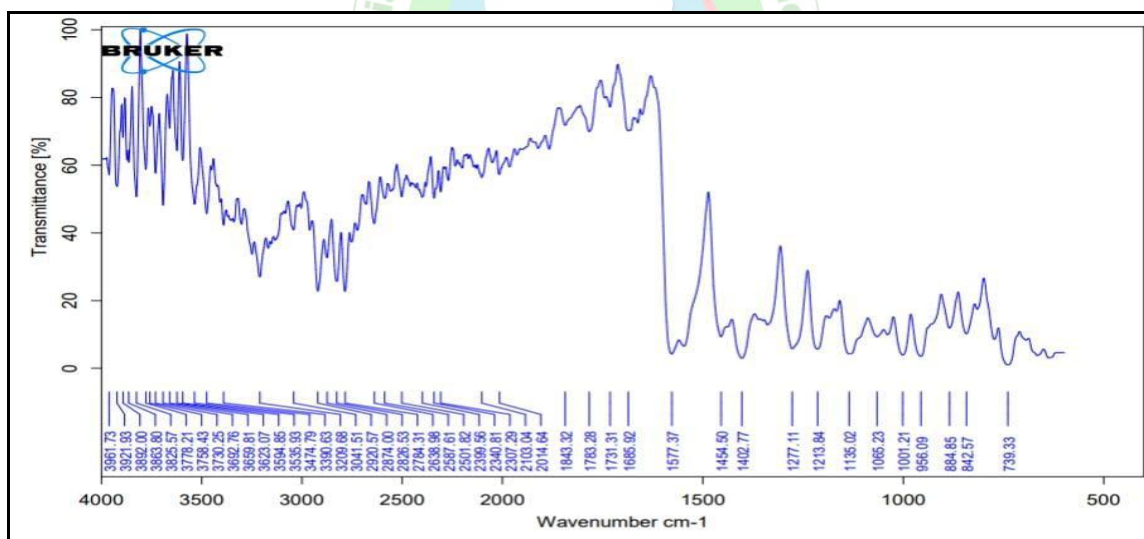


Figure 3: FTIR Spectra of OLZ

Table 2: Interpretation of IR spectra of Olanzapine

Sample	Wave number	Functional Group
Olanzapine	3390.63, 1577.37, 1454.50, 739.33	N-H, C=C, C-C, C-H

### Drug Excipients Compatibility:

Drug was found to be compatible with Tween 80, Fujicalin, Aerosil 200. IR data revealed that none of these excipients

interfered with any peaks. It indicated that excipient is compatible with drug.

## ❖ Olanzapine + Tween 80

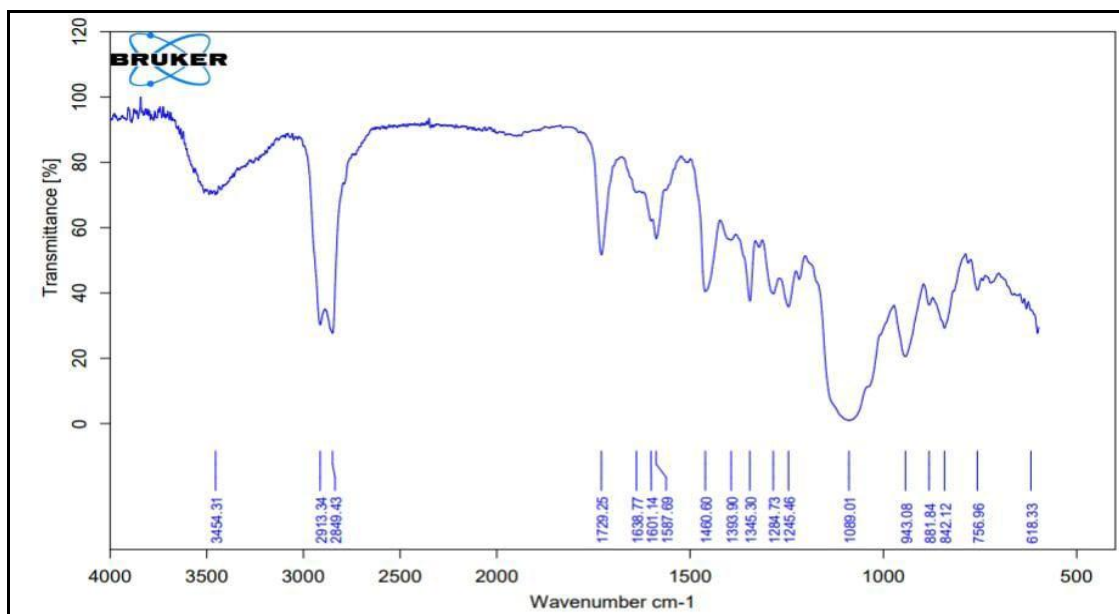


Figure 4: FTIR Spectra of Tween 80 with OLZ

Table 3: Interpretation of IR spectra of Interpretation of OLZ + Tween 80

Sample	Wave number	Functional Group
OLZ with Tween 80	2849.43, 1729.25, 1460.60, 1089.01.	C-H, C=O, C-H, C-O

## ❖ Olanzapine + Fujicalin

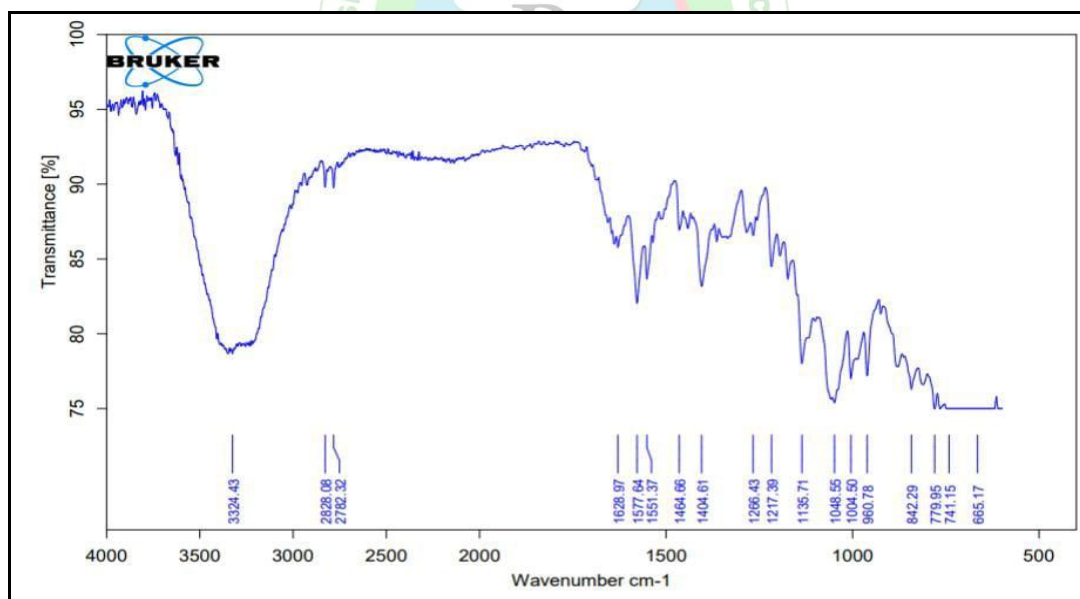


Figure 5: FTIR Spectra of Fujicalin with OLZ

Table 4: Interpretation of IR spectra of Interpretation of OLZ + Fujicalin

Sample	Wave number	Functional Group
OLZ with Fujicalin	3324.43, 2828.08, 1577.64, 1404.61	O-H, C-H, C=C, CH <sub>2</sub>

## ❖ Olanzapine + Aerosil 200

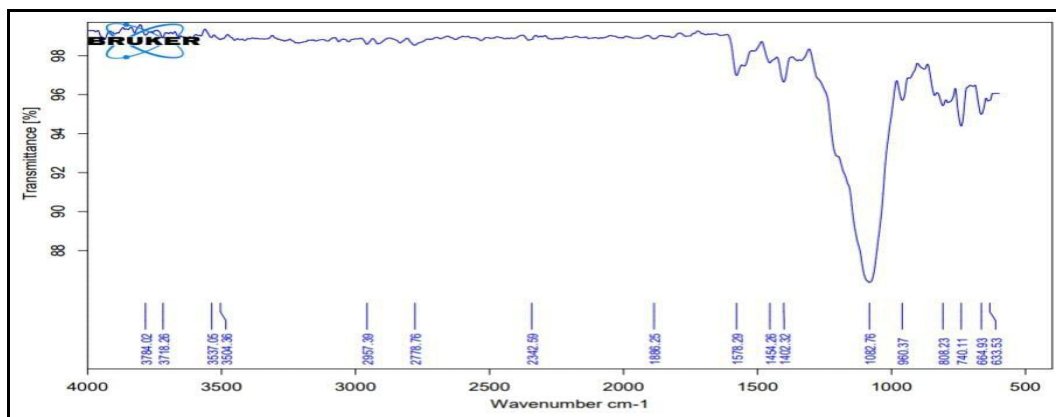


Figure 6: FTIR Spectra of Aerosil 200 with OLZ

Table 5: Interpretation of IR spectra of Interpretation of OLZ + Aerosil 200

Sample	Wave number	Functional Group
OLZ with Aerosil	3504.36, 2957.39, 1578.29	O-H, C-H, C=C

## Pre compression evaluation of Liquisolid system:

All formulations were evaluated for pre compression parameter such as Bulk density, tapped density, Angle of repose, Compressibility index, Hausner's ratio and Solubility. The result obtained is shown in the Table No. 2

Table No. 6: Pre compression evaluation of Liquisolid system

Formulation Batches	Pre compression Evaluation Parameter					
	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose (°)	Carr's Index (%)	Hausner's Ratio	Parts of solvent per part of solute
F1	0.357±0.1	0.455±0.01	27.40±0.02	21.53±0.13	1.27±0.02	1099.5
F2	0.385±0.03	0.476±0.06	22.42±0.06	19.11±0.09	1.23±0.06	967.62
F3	0.300±0.3	0.36±0.1	20.42±0.09	16.66±0.02	1.20±0.02	826.02
F4	0.350±0.02	0.392±0.02	17.12±0.03	10.71±0.05	1.12±0.02	605.00

All the value represents mean ± Standard deviation (n=3)

**Note:** Solubility of the drug is determined by parts of solvent required per part of solute and that is 10,617. The solubility of the drug is increased in these 4 formulations and that is noted in the above table.

## Evaluation of Liquisolid tablet:

All tablets formulation (F1 to F4) were evaluated for different parameters such as General Appearance, thickness, hardness,

friability, weight variation, disintegration test, drug content and *in-vitro* dissolution. The results are shown in below table.

It was observed that all the tablet formulations are yellow in colour with a smooth surface, exhibiting no signs of surface roughness.

Table 7: Evaluation parameters of tablets

Formulation Batches	Pre compression Evaluation Parameter					
	Thickness (mm)	Hardness (Kg/cm <sup>2</sup> )	% friability (%)	Average Weight of tablet (mg)	Disintegration (min)	Content uniformity (%)
F1	3.50 ±0.01	3.7±0.05	0.6±0.06	129.27±0.05	1.36±0.06	92.30±0.05
F2	3.52 ±0.01	3.5±0.08	0.5±0.02	130.66±0.04	1.33±0.04	93.20±0.1
F3	3.55 ±0.02	3.2±0.05	0.5±0.05	131.15±0.05	1.29±0.05	96.56±0.05
F4	3.57 ±0.05	3.1±0.02	0.3±0.04	132.06±0.05	1.24±0.02	98.85±0.02

All the value represents mean ± Standard deviation (n=3)

## In- vitro drug release studies:

The *In-vitro* drug release characteristics were studied in 7.4 PBS for 60 min using IP type II dissolution apparatus.



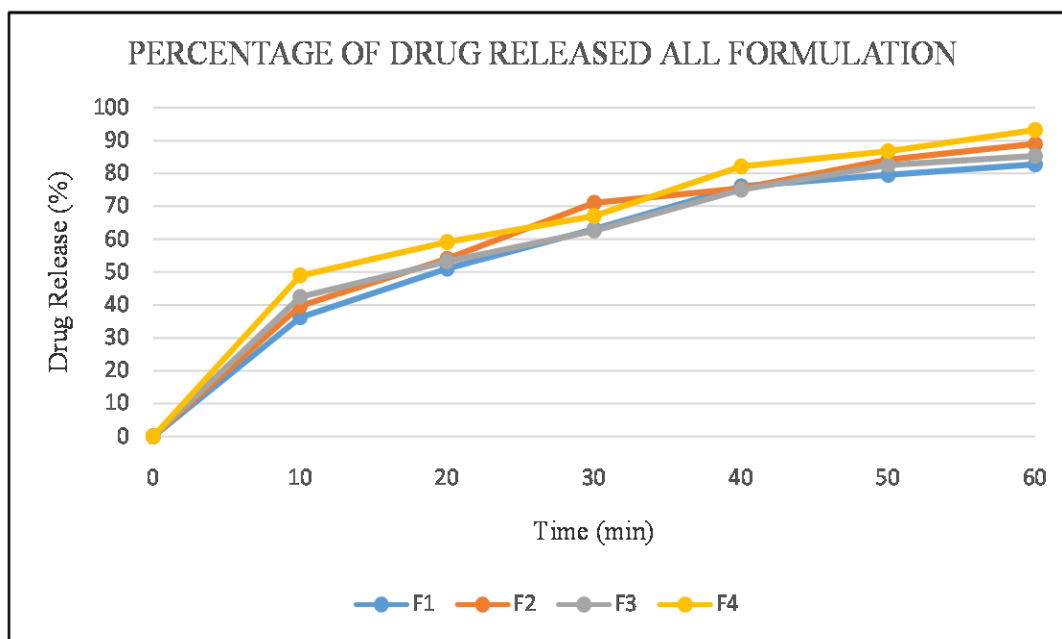


Figure 7: Percentage of drug released all formulation

## CONCLUSION:

The Liquisolid tablets of Olanzapine was prepared using Fujicalin as a carrier and Aerosil 200 as a coating material. The main goal of the liquisolid system is to make Olanzapine drug more soluble which ultimately enhances the dissolution. Olanzapine is water insoluble drug to enhance its solubility and dissolution rate liquisolid technique is used. The

Aqueous solubility of Olanzapine Liquisolid system was increased i.e. from practically insoluble to slightly soluble. All the Liquisolid formulations exhibited desirable flowability for processing into a tablet dosage form. The *in-vitro* dissolution was performed and drug release of F4 was found to be 93.23% after 60 mins. From the study, it was concluded that the solubility as well as dissolution rate of the Olanzapine was enhanced.

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