



RESEARCH ARTICLE

Formulation and Evaluation of Ofloxacin Liquisolid Tablets

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ABSTRACT

The aim of our study was to improve the bioavailability of ofloxacin a practically insoluble anti-infective drug, as a model drug by using liquisolid technique. The effect of powder substrate composition on the flowability and compressibility of liquisolid compacts were evaluated. Specifically, several liquisolid formulations, containing 200-mg ofloxacin, which containing different carrier to coating ratios in their powder substrates and a fixed liquid medication, were prepared. The dissolution profiles of ofloxacin liquisolid tablets were determined according to USP method. The obtained dissolution profiles were compared to that of a commercial product. In the present study, the formulated liquisolid systems exhibited acceptable flowability and compressibility. In addition, liquisolid tablets displayed significant enhancement of the dissolution profiles compared to this of commercial one.

KEYWORDS

Liquisolid Tablets, Ofloxacin, Formulation and Evaluation

INTRODUCTION

Solubility is one of the important parameter to achieve the desired concentration of drug in systemic circulation for pharmacological response to be shown¹ two consecutive transport processes can be identified to describe the oral absorption of drugs from solid dosage forms.

- (1) Dissolution of the drug in vivo to produce a solution.
- (2) Transport of the dissolved drug across the G.I. membrane².

Poorly water soluble drugs are defined as those with high permeability but whose solubility in aqueous media is not sufficient for the whole dose to be dissolved in the gastrointestinal tract. For these substances dissolution is therefore the rate determining step to absorption.

The poor dissolution rates of poorly water soluble drugs is still a substantial problem confronting drug development, such as hindering the development of parenteral products and limiting the bioavailability of oral products³. Liquisolid Technology The concept of liquisolid compacts can be used to formulate liquid medication such as oily liquid drug and solutions or suspensions of water-insoluble solid drugs in non-volatile vehicles, into acceptably flowing and compressible powders.

Using this new formulation technique, a liquid medication may be converted into a dry-looking, non-adherent, free flowing and readily compressible powder by a simple blending with selected powder excipients referred to as carrier and coating materials. Various grades of cellulose, starch, lactose, etc, may be used as the carrier, whereas a very fine particle size silica powder may be used as the coating material⁴. Since drug dissolution is often the drug limiting step in gastrointestinal absorption,

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the significant increase in wetting properties and surface area of the drug particles available for dissolution from liquisolid compacts may be expected to display enhanced drug release characteristics and, consequently, improved oral bioavailability. Ofloxacin is an antibiotic that belongs to the class of medication called quinolone. It is used to treat certain infections caused by bacteria. It is most commonly used to treat infection by lung, urinary tract and skin; it can also use to treat certain prostate infections and sexually transmitted infections. The usually recommended adult dose is 200-400 mg twice daily, depending on the type of infection being treated. Due to insufficient aqueous solubility at gastrointestinal pH, thus making solubility the rate-determining step in the gastric absorption of ofloxacin. Therefore, ofloxacin establishes a good candidate for testing the potential of rapid-release liquisolid compacts. The aim of this study was to increase the dissolution rate of ofloxacin using liquisolid technique. The drug was formulated into 200 mg liquisolid tablets using PEG 400 as the water miscible non-volatile liquid vehicle and appropriate amount of excipients (carrier and coating materials) for each liquid vehicle to produce acceptable flowing compactable powders. The liquisolid powder system which showed the acceptable flowability was then compacted into tablets and the in-vitro drug dissolution rates of liquisolid formulations were compared to that of conventional, directly compacted tablets. There is no single non-volatile liquid vehicle which is suitable for a variety of hydrophobic drugs in preparing liquisolid tablets. Propylene glycol, Tween 80 and Polyethylene glycol (PEG 400) had been used as non-volatile liquid vehicles in the preparation of fast release liquisolid tablets with different drugs.

MATERIALS AND METHODS

Materials

The following materials were used as received ofloxacin powder from Ranbaxy laboratories ltd (Dewas), Microcrystalline cellulose (Avicel pH 101) Qualikems (Vadodara), Amorphous fumed silica cab-o-sil fisher scientific (Mumbai), Span

80, Tween 40, Tween 80, and PEG 400 from Ranbaxy (Dewas), Sodium Starch Glycolate Qualikems (Vadodara), Magnesium Stearate Himedia (Vadodara).

Equipment

Shaking water bath (Southern scientific lab instrument Noombal Chennai), Tablet punch Machine (National Scientifico), Dissolution Apparatus (Rolex Teknik), Disintegration Apparatus (Teknik), Ultraviolet Spectrophotometer (Sistonic), Monsanto hardness tester (Hicon, NASCD), Vernier calipers scale (Teknik), Oven (Dhruv oven).

Methods

Preformulation Studies

Almost all drugs are marketed as tablets, capsules or both. Prior to the development of these major dosage forms, it is essential that certain fundamental, physical and chemical properties of the drug molecule and other divided properties of the drug powder are determined. This information decides many of the subsequent events and approaches in formulation development. This first learning phase is known as Preformulation. Therefore, before starting the development of liquisolid tablet containing the selected drug ofloxacin, Preformulation studies of the drug were carried out. The drug was tested for identification, solubility in various solvent and requirements. The standard curve of drug was prepared in the 0.1N HCl

Identification of Drug

Melting Point Determination: A thin capillary was taken. One end of which was heated and sealed. Small amount of drug was filled in the capillary. Then capillary and thermometer were placed at the specific place in melting point apparatus. The temperature was increased and the temperature at which the drug started to melt in the capillary was noted down.

FTIR Spectroscopy

FTIR studies were performed to determine the chemical interaction between the drug and excipients used in the formulation. The presence

of drug peaks in the formulation and absence of extra peaks indicates there is no chemical interaction⁵. The IR spectra were recorded using Fourier Transform Infra-Red spectrophotometer with diffuse reflectance principle. Sample preparation involved mixing the sample (2 mg) with potassium bromide (KBr), triturating in glass mortar and finally placing in the sample holder. The spectrum was scanned over a frequency range 4000–400 cm⁻¹.

Determination of λ_{max}

The standard solution of ofloxacin (10 µg/ml) was scanned in the wavelength region of 200-400 nm and the λ_{max} was found to be 293 nm⁶.

Preparation of Standard Curve of Drug in 0.1 N HCl

The standard stock solution of ofloxacin was prepared by transferring accurately weighed 10 mg of drug to 10 ml volumetric flask and dissolving it with 0.1N HCl to get a concentration of 1000 µg/ml. The solution was diluted accordingly to get a concentration of 100 µg/ml and was kept as the stock solution. The prepared stock solution was diluted with 0.1N HCl solution to get working standard solutions of concentrations 0.2-20 µg/ml. Finally the calibration curve was plotted between concentration (x-axis) and absorbance (y-axis).

Solubility Determination

To select best non-volatile solvent for dissolving or suspending of ofloxacin in liquid medication, solubility studies was carried out in various different non-volatile solvents. In this study solubility of ofloxacin was determined in PEG 400, PEG 600, tween 40, tween 80, tween 20, span 80, glycerin, and distilled water. Drug solutions were prepared by adding a pinch of drug to the solvent, observed visually then more drugs was added until drug was stopped to dissolve.

Determination of Angle of Slide of Microcrystalline Cellulose (Carrier Material) and Silica (Coating Material)

Powder flowability is of critical importance in production of solid pharmaceutical dosage

forms in order to get a uniform feed as well as reproducible filling of tablet dies, otherwise, high dose variation will occur. In order to ensure the flow properties of the liquisolid systems to be compacted into tablet, the angle of slide for MCC (carrier material) and silica (coating material) were measured. Exactly weighted 5 g of the carrier or coating material was placed at one end of a metal plate with a polished surface. The plate was gradually raised until the plate made an angle (θ , angle of slide) with the horizontal plane at which the powder was about to slide over the polished surface. An angle of slide of 33° corresponded to optimum flow.

Determination of Flowable Liquid Retention Potential for MCC (Φ CA-value) and Silica (Φ CO-value)

An increasing amount of the non-volatile liquid vehicles (PEG 400) were added to 5 g of MCC or silica powder and mixed using pestle and a mortar to give powder admixtures. The carrier and coating materials adsorbed the liquid vehicle resulting in a change in material flow properties compared to pure powder of MCC or silica powder previously measured. At each concentration of the non-volatile liquid vehicle, the angle of slide was determined as stated previously. The corresponding flowable liquid retention potentials were calculated using the following equation:

$$\Phi - \text{Value} = \frac{\text{Weight of liquid}}{\text{Weight of solid}}$$

Then, the obtained Φ -values were plotted against the corresponding angle of slides. The Φ -value which corresponded to an angle of slide of 33° represented the flowable liquid retention potentials of powder admixture. In cases where the Φ -value did not correspond to 33°, the highest Φ -value reached was chosen as the flowable liquid retention potential.

Determination of Liquid Load Factor

With the help of following formulas the liquid load factor and the quantity of carrier and coating material were calculated.

$$L_f = \Phi_{\text{carrier}} + \Phi_{\text{coating}} (1 / R) \dots\dots\dots (1)$$

$$L_f = \frac{W}{Q} \dots\dots\dots (2)$$

$$R = \frac{Q}{q} \dots\dots\dots (3)$$

L_f=liquid load factor

R=carrier and coating material ratio

W=weight of liquid medication (drug + liquid vehicle)

Q= weight of carrier material

q= weight of coating material

Precompression Study (IP)

Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder. The bulk density of powder depends primarily on particle size distribution, particle shape and the tendency of particle to adhere to one another. It is expressed in gm/cc and is given by-

$$DB = \frac{M}{V_0} \dots\dots\dots (4)$$

M = Mass of powder

V₀= Bulk volume of powder

Method: It was measured by pouring the weighted powder in to a measuring cylinder and the initial volume was noted. This initial volume is called bulk volume. From this, the bulk density was calculated according to the formula mentioned above.

Tapped Density

It is the ratio of total mass of powder to the tapped volume of powder. It is expressed in gm/cc and is given by-

$$DT = \frac{M}{V_0} \dots\dots\dots (5)$$

Method: This volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and then tapped volume was

noted (the difference between these two volume should be less than 2)

Angle of Repose

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose.

$$\tan \theta = \frac{H}{R}$$

Where, θ is the angle of repose

H is the height of the pile

R is the radius of the base of pile

Different ranges of flow ability in terms of angle of repose are given in table.

Table 1: Relationship between Angle of reposes and flow properties

Angle of repose θ	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Method: A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on the graph sheet was taken to measure the area of pile, thereby evaluating the flowability of granules. Height of the pile was also measured.

Compressibility Index

The flowability of powder can be evaluated by comparing the bulk density and tapped density of powder and the rate at which it packed down. Compressibility index is calculated by-

$$\text{Compressibility index (\%)} = \frac{DT - DB}{DB} \times 100$$

Where,

DT = Tapped density

DB = Bulk density

Table 2: Grading of the powder for their flow properties according to Carr's index

Percent Compressibility	Type of flow
5-15	Excellent
12-16	Good
18-21	Fare passable
23-25	Poor
33-38	Very poor
>40	Extremely poor

Hausner's Ratio

It is the ratio of tapped density to bulk density. It is given by-

$$\text{Hausner's Ratio} = \frac{DT}{DB}$$

Where

DT = Tapped density

DB = Bulk density

Preparation and Mixing of Powders for Conventional and Liquisolid Tablets

Tablet containing ofloxacin was prepared by mixing 200 mg of drug with microcrystalline cellulose (Avicel 102) sodium starch glycolate 10% w/w was used as a Disintegrants and mixed for 10 min. Glidant and lubricant were added and compressed by tablet punching machine.

In the case of liquisolid formulations, from the obtained results of optimum Φ_{CA} -and Φ_{CO} values (optimum flowable liquid retention values for the carrier and coating materials, respectively) with each liquid vehicle, the optimum liquid load factors (Lf) were calculated using Equation (1) with varying carrier: coat ratio (R) of (10, 15 and 20. Then, the amount of carrier (Q) and coating (q) materials were calculated using Equations 2 and 3 at drug: vehicle ratios of 2:1. Several liquisolid systems of ofloxacin (F-1 to F-6) were prepared. The

calculated amounts of the carrier (Q) and coating (q) materials at each liquid medication (W) are presented in.

Accordingly, the liquisolid formulations were prepared as follows: the drug was suspended in the liquid vehicle in a mortar using pestle, then the calculated amount of the carrier material (Avicel® PH 101) was added with continuous mixing till homogenous wet mix was obtained. The coating material (fumed silica) was then added to the mix with gentle mixing (the powder admixture re-establish the dry powder consistency). Finally, each liquisolid formulation was blended with 5%w/w of a disintegrating agent (sodium starch glycolate).

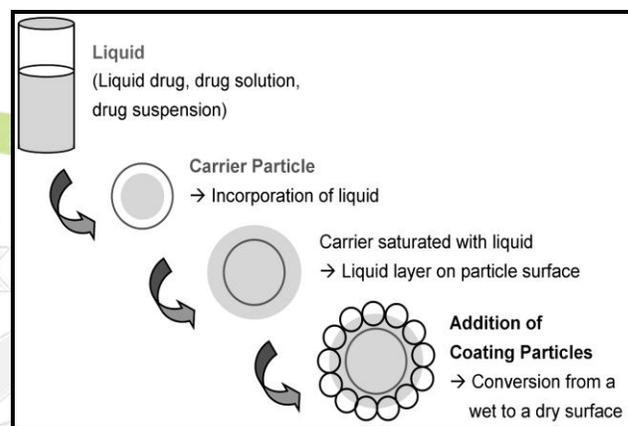


Figure 1: Schematic representation of liquisolid systems

Post-compression Parameters (IP)

Shape and Color

Uncoated tablet was examined under the lens for the shape of the tablet and color was observed by keeping the tablets in lights⁷.

Uniformity of Thickness

The crown thickness of individual tablet may be measured with a Vernier caliper which permit accurate measurements and provide information on the variation of tablets. Other technique employed in production involves placing 5 or 10 tablets in a holding tray, where there total crown thickness may be measured with a sliding caliper scale. Thickness should not deviate by $\pm 5\%$ from the standard thickness. It depends mainly upon die filling, physical property of

material being compressed force and compression force.

Hardness

Tablet requires a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shock of handling in manufacture, packaging and shipping. The hardness of tablet was determined using Monsanto hardness tester. The tablet was placed between both the punches of hardness tester and force was applied. The force at which the tablet was about to crush was noted. It was expressed in kg/cm². Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

Friability Test

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or irritation. The friability of tablet was determined by using Roaches Friabilator. It is expressed in percentage (%). Ten tablets were initially weighted (W_{initial}) and transferred into Friabilator. Weighted tablet sample is placed in the chamber and the Friabilator was operated at 25 rpm for 4 min. or run up to 100 revolutions and drop the tablet from a height of 15 cm with each revolution. The tablets were weighted again (W_{final}). The percentage friability was then calculated by-

$$\% \text{ Friability} = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{final}}} \times 100$$

% friability of the tablet less than 1% is considered acceptable

Weight Variation Test

The tablet were selected randomly from each formulation and weighted individually to check for weight variation. According to the official test, 20 tablets were generally weighted individually and collectively. Average weight per tablet was calculated from the collective weight. Then the weight of individual tablet is compared with the average weight to determine weight variation. The U.S. pharmacopoeia

allows a little variation in the weight of the tablet.

The percentage deviation in the weight variation is shown in table-3.

Table 3: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
130 mg or less	10
More than 130 mg and less than 324 mg	7.5
324 mg or more	5

Drug Content Uniformity

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch.

The amount of active ingredient(s) is determined by the method described in assay and the amount of active ingredient is calculated. Since active ingredient of present investigation is not official in any pharmacopoeia. The following method was used for determination of drug content.

Twenty tablets were weighted and powdered. The blend equal to 200 mg of ofloxacin was weighted and dissolved in sufficient quantity of 0.1 N HCl. The solution was filtered through watt man filter paper (No.41), suitably diluted with 0.1 N HCl and assayed at 294nm using a UV visible double beam spectrophotometer.

In vitro Disintegration Time

The process of breakdown of tablet into smaller particles is called disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration apparatus as per IP specification.

Method: For a drug to be absorbed from a solid dosage form after oral administration, it must

first be in solution, and the first important step towards this condition is usually the break-up of the tablet; a process known as disintegration.

One tablet in each of the six tubes of the basket was placed and the apparatus subjected to run. The assembly be raised and lowered between 50 cycles per minute. The time in minute taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

Disintegration was measured in 900 ml purified water according to IP method without using disc at room temp. ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$).

In-Vitro Dissolution Studies

In-vitro studies were carried out using tablet USP-II dissolution test apparatus. Two objectives in the development of *in-vitro* dissolution test was to show that,

- i) Release of the drug from tablet is as close as possible up to 100% and
- ii) Rate of drug release is uniform from batch and is the same as the release rate from those proven to be bioavailable and clinically effective.

Table 4: Summary of general dissolution condition

S.No.	Parameter	Specification
1	Dissolution medium	900 ml 0.1 N HCl
2	Temperature	$37^{\circ}\text{C} \pm 5^{\circ}\text{C}$
3	Rotation Speed	50 rpm
4	Volume Withdrawn	5 ml
5	λ_{max}	294 nm
6	Tablet Taken	1 tablet

Method: The *in-vitro* release profiles of liquisolid compacts and directly compressed tablets were obtained using a dissolution test apparatus USP-II (Electro Lab). The dissolution study was carried out in 900 ml of 0.1 N HCl and distilled water as the dissolution medium at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and 50 rpm. The tablet was placed in this dissolution medium and allowed to rotate for a definite time period and at the constant speed every time. Then samples were collected for a time period at fixed intervals. The dissolution medium was replaced with fresh dissolution fluid to maintain sink conditions in the same amount of withdrawn dissolution medium. The withdrawn samples were filtered and analyzed spectrophotometrically. The mean of three determinations were used to calculate the drug release from each of the formulations.

RESULT

Preformulation Studies

Ofloxacin was selected as the model drug for this study, since it is a poor water-soluble substance and, thus, an ideal candidate for testing the potential of rapid-release liquisolid compacts. In addition, it can be easily assayed and quantities in solution using spectrophotometric principles and procedures. From the standard calibration curve of ofloxacin in 0.1 N HCl it was observe that the ofloxacin obeys Beer-Lambert's law in conc. range of 2-20 $\mu\text{g}/\text{ml}$.

Identification of Drug

Melting Point: The melting point was found to be in the range of 258°C which is in good agreement with the reported values.

Standard Curve of Drug in 0.1 N HCl

The standard curve of ofloxacin was prepared in 0.1 N HCl. On scanning the solution in the range of 200-400 nm, an absorption maximum was observed at 294 nm. The correlation coefficient obtained greater than 0.9 and which is an indication of significant linear relationship between absorbance and concentration in this concentration range.

Table 5: Standard calibration curve for ofloxacin in 0.1 N HCl

S.No.	Concentration $\mu\text{g/ml}$	Absorbance
1	2	0.102
2	4	0.2
3	6	0.323
4	8	0.412
5	10	0.533
6	12	0.655
7	14	0.755
8	16	0.89
9	18	0.98
10	20	1.2

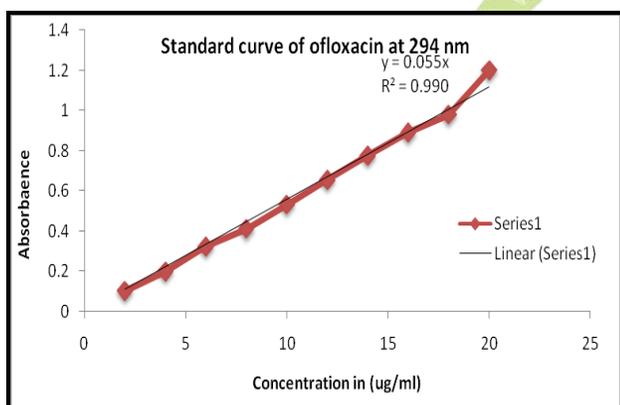


Figure 2: Standard curve of ofloxacin

Solubility of Drug in Different Solvents

The solubility of ofloxacin is determined in different solvents and the results of solubility are given in Table. The table shows that the solubility of ofloxacin in PEG 400 is higher in comparison with other solvents. For this reason PEG 400 was selected to be the suitable solvent for preparing ofloxacin liquisolid compact in this study. In fact, the higher fraction of drug in PEG 400 is in the molecular state in comparison with others solvents and this would help to increase dissolution rate of the drug because some percentages of drug is already dissolved.

Table 6: Solubility status of ofloxacin in different solvent

Solvent	Solubility
Distilled water	-
Tween 40	-
Tween 80	+
Tween 60	++
Span 40	-
PEG 400	++++
PEG 600	++
Span 60	-

++++ = Very high soluble

++ = Sparingly soluble

+ = Poor solubility

- = Insoluble

Angle of Slide

Table 7: Characteristics of carrier and coating material

Material	Angle of slide	Liquid retention potential
Avicel	32	0.7
Aerosil	31	1.6

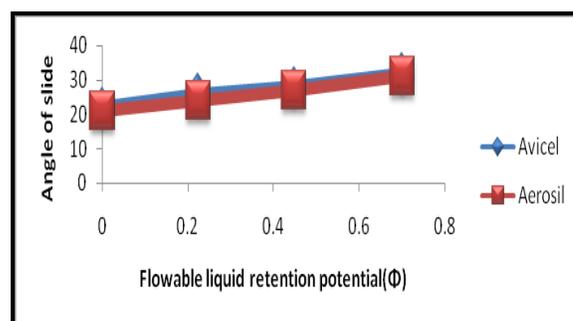


Figure 3: Flowable liquid retention potential (Φ)

Liquid Load Factor

In order to calculate the required ingredient quantities, the flowable liquid-retention potentials (Φ values) of powder excipients were utilized. According to procedure in PEG 400,

the Φ value was 0.7 for MCC and 1.6 for Silica. Liquid load factor was calculated from the flowable liquid-retention potential according to equation [$L_f = \Phi_{\text{carrier}} + \Phi_{\text{coating}}(1/R)$] using R value. The appropriate quantities of carrier (Q) and coating material (q) were obtained from equation [$L_f = W/Q$] and [$q = Q/R$] respectively.

Precompression Study

Evaluation of Flowability and Compressibility of Liquisolid Powder

Powder flow is a complicated matter and is influenced by so many interrelated factors; the factor's list is long and includes physical, mechanical as well as environmental factors.⁸ The powder has a good flowability; when the Hausner's ratio is lower than 1.2, while if the

ratio is more than 1.2 this indicates the flowability is bad⁹. It was showed that powders with interparticle friction, such as coarse spheres, had ratios of approximately 1.2, whereas more cohesive, less free-flowing powders such as flakes have Hausner's ratios greater than 1.6. Compressibility is indirectly related to the relative flow rate, cohesiveness, and particle size of a powder. A compressible material will be less flowable, and powders with compressibility values greater than 20-21 % have been found to exhibit poor flow properties¹⁰. As a general guide, powders with angles of repose greater than 50° have unsatisfactory flow properties, whereas minimum angles close to 25° correspond to very

Table 8: Ingredient of the formula from F-1 to F-6

Formula	Ofloxacin(mg)	PEG400(mg)	Avicel Ph 101(mg)	Aerosil(mg)	R	Lf	Total weight (mg)
F-1	200	100	306	16.2	5	0.98	622.2
F-2	200	100	348.8	34.8	10	0.86	683.6
F-3	200	100	375	25	15	0.80	700
F-4	200	100	384.6	19.4	20	0.77	704
F-5	200	100	398.4	13.2	30	0.753	711.6
F-6	200	100	392.6	15.7	25	0.764	708.3

Table 9: Precompression parameters

Formulation Code	Parameters				
	Bulk Density (gm/cc ³)	Tapped Density (gm/cc ³)	Carr's Index	Hausner's Index	Angle of Repose
F-1	0.385	0.477	19.6	1.12	31.42
F-2	0.379	0.445	13.91	1.161	29.83
F-3	0.387	0.457	15.55	1.183	27.51
F-4	0.47	0.582	22.61	1.20	31.96
F-5	0.398	0.495	20.87	1.18	35.42
F-6	0.423	0.539	21.19	1.268	36.15

good flow properties¹¹. Table revealed that all the tested liquisolid systems had a satisfactory flow according to the obtained results of measuring the angle of repose for each liquisolid system. The range was from 27.51 for F-3 to 36.15 for F-6. The prepared ofloxacin liquisolid systems can be arranged in ascending order, regarding the angle of repose measurements as follows: F-3 < F-2 < F-1 < F-4 < F-5 < F-6.

Hausner's ratio and Carr's index were calculated from the density values. These results revealed all formulations that F-1 and F-5 had Hausner's ratio 1.12 and 1.18 respectively less than 1.2 this indicates good flowability. Carr's index all formulations were found to be less than 21% and this indicates that these formulae had a good flowability.

According to the result obtained of the angle of repose the F-2 (29.83) formulation showed excellent flow, F-3 (27.51), showed good flow of powder while other formulations F-1 (31.42), F-4 (31.96), F-5 (35.42), F-6 (36.15), were just passable.

Like angle of repose all the formulation showed acceptable flow properties in respect of compressibility index. According to the results obtained of the Carr's index formulation F-2 (13.91) showed excellent flow, F-3 (15.55) showed good flow and rest all the formulation showed fare flow properties.

Post-Compression Parameters

Shape and Color

The tablet is round shape and it is white in color.

Friability

All the ofloxacin liquisolid tablets had acceptable friability as none of the tested formulae had percentage loss in tablets weights that exceed 1% also, no tablet was cracked, split or broken in either formula. Since all the prepared formulae met the standard friability criteria, they are expected to show acceptable durability and withstand abrasion in handling, packaging and shipment. Ofloxacin liquisolid

tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing.

Table 10: Post-compression parameters

Formu. Code	Parameter		
	Thickness (mm)	Weight variation (mg)	Friability (%)
F-1	4.28	622.2	0.035
F-2	4.22	683.6	0.112
F-3	4.35	700	0.095
F-4	4.26	704	0.102
F-5	4.31	711.6	0.106
F-6	4.27	708.3	0.092

Weight Variation

The tablet weight of all the liquisolid formulation was greater than 324 mg and the acceptable percent weight variation for this category is 5%. All formulation from F-1 to F-6 did not show the weight variation greater than 5% thus all the formulations are acceptable.

Table 11: Some other post compression parameters

Formulation Code	Parameter		
	Hardness (kg/cm ²)	Disintegration Time (min)	Drug Content
F-1	4.38	17.04	97.55
F-2	4.2	16.3	97.68
F-3	4.12	13.92	98.51
F-4	4.28	12.7	98.75
F-5	4.33	12.02	99.42
F-6	4.25	9.7	100.65

Hardness

All the liquisolid formulations showed acceptable hardness. The optimized hardness for each liquisolid formulations was such that the

tablet would be sufficiently (4-5 kg hardness) hard to resist breaking during normal handling and yet soft enough to disintegrate after swallowing.

Drug Content

All these liquisolid formulations complied with the test of ofloxacin content uniformity according to standards. None of this formulation falls outside 97 to 100%.

Disintegration

The disintegration time for the prepared ofloxacin liquisolid tablets was shown in Table. It was found that, the mean of the disintegration times for all investigated tablets were less than 30 minutes, which met the Pharmacopoeial requirements. F-6 was found to be the fastest formula to be disintegrated (9.7 minutes), followed by F-5, F-4, and F-3, with disintegration time 12.02, 12.7, and 13.92, respectively. While, the slowest disintegrated formula was F-2, which took 16.3 minutes to disintegrate.

Dissolution

The dissolution study was carried out for about 120 min. Results of dissolution show that the

release of the drug increased as the disintegration time of the drug decreased. Thus the release of the drug from the formulation is inversely proportional to the disintegration time. On the other hand it was displayed that there is a relationship between the powder excipients ratio and the *in vitro* Release of ofloxacin from liquisolid tablets. The powder excipients ratio was directly proportional to the *in vitro* release i.e., when the powder excipients ratio increased the release will increase. This may be attributed to the high microcrystalline cellulose content where Avicel PH 101 functions as a swellable disintegrant. In addition, the highly hydrophilic characteristic of microcrystalline cellulose could increase the wetting of ofloxacin and enhance its dissolution¹².

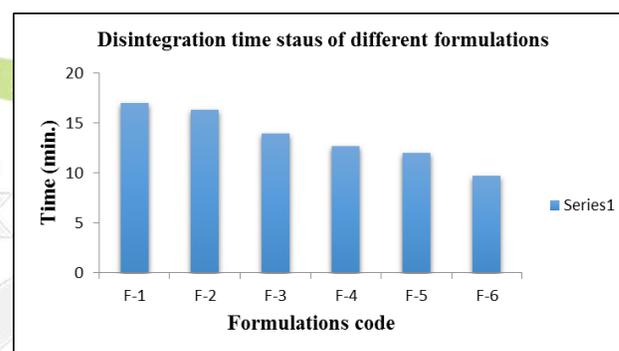


Figure 4: Disintegration time of different formulations

Table 12: Dissolution profile of formulations from F-1 to F-6

Time (min.)	F-1	F-2	F-3	F-4	F-5	F-6	C.T.
0	0	0	0	0	0	0	0
5	10.21	12.14	14.41	15.41	19.53	23.8	8.23
10	23.26	26.25	28.74	31.17	34.91	38.03	15.6
20	37.68	41.21	44.21	47.85	50.21	54.99	24.9
40	53.89	58.23	63.03	67.87	72.7	77.22	35.4
60	62.15	66.72	73.88	77.85	81.42	84.59	51.4
80	71.3	75.18	78.96	80.65	85.1	88.87	59.6
100	73.1	77	79.89	82.71	89.12	92.94	61.4
120	78.12	80.42	82.03	85.81	91.3	94.3	65.8

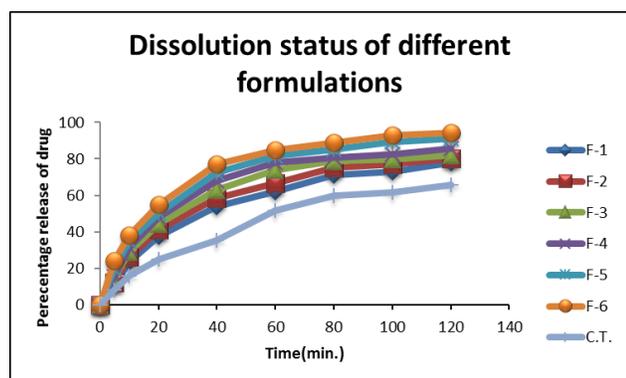


Figure 5: Dissolution status of different formulations

CONCLUSION

The present work showed that the liquisolid compact technique could be effectively used to prepare rapid release tablets of water insoluble drugs. Absorption of ofloxacin after its oral administration is limited by its low dissolution rate due to its very low aqueous solubility. Hence liquisolid technique was chosen to enhance the dissolution property of ofloxacin.

The ofloxacin liquisolid compacts were prepared using MCC and silica as carrier and coating material and PEG 400 was used as a liquid vehicle. In this technique drug is dissolved in a non volatile solvent and by this liquid medicament is converted to non adherent, dry looking and free flowing by using suitable carrier and coating material.

The flow properties of ofloxacin liquisolid compacts showed an acceptable flowability. The hardness, friability, weight variation and disintegration tests were within acceptable limit. The *in vitro* dissolution study confirmed enhanced drug release from liquisolid compacts. The higher dissolution rate showed by Liquisolid compacts may imply enhanced oral bioavailability due to the increased wetting properties and surface of drug available for dissolution.

The results showed that the liquisolid technique could be a promising alternative technique to increase the dissolution of water insoluble drugs. The solubility-dissolution behavior is the rate-limiting step to absorption from the

gastrointestinal tract of poorly water soluble drugs and needs to be enhanced.

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