FORMULATION DEVELOPMENT, CHARACTERIZATION AND EVALUATION OF LIQUISOLID TABLET CONTAINING ORLISTAT

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Abstract: **The aim of present study was to improve the solubility of Orlistat, a practically insoluble anti-obesity drug by using Liquisolid technique. Orlistat is class II molecule according to BCS (Biopharmaceutical Classification System), having low solubility and low permeability. The rate and extent of absorption of class II compounds is highly dependent on the performance of the formulated product. These drugs can be successfully formulated for oral administration, but care needs to be taken with formulation design to ensure consistent bioavailability. Solubility of Orlistat was evaluated in various non-aqueous carriers. Different Liquisolid tablets were prepared using a mathematical model to calculate the required quantities of powder and liquid ingredients to produce acceptably flowable and compressible admixture. Avicel PH 102, Aerosil 200 and Sodium starch glycolate were employed as carrier, coating material and disintegrant respectively. The drug release rates of Liquisolid tablets were distinctly higher as compared to directly compressed tablets, which show significant benefit of Liquisolid tablets in increasing wetting properties and surface area of drug available for dissolution. The optimized formulation showed the higher drug release during ex-vivo and in-vivo study against conventional and marketed tablet preparation. From this study it concludes that the Liquisolid technique is a promising alternative and best suitable method for enhancing solubility of Orlistat.**

Keywords: **Orlistat, Liquisolid Tablets , *ex-vivo* and *in-vivo* absorption, Avicel PH 102, Aerosil 200.**

I. INTRODUCTION

Dyslipidemia is a disorder of lipoprotein metabolism. Dyslipidemia is the elevation of plasma cholesterol, triglycerides, or both. It can also be manifested by the elevation of low-density lipoprotein (LDL), cholesterol and the decrease of high- density lipoprotein (HDL) cholesterol in the blood. Dyslipidemia is a primary risk factor that contributes to the development of atherosclerosis in the general population and in diabetic patients. Most people with high serum cholesterol also have elevated LDL because much of the serum cholesterol is transported in LDL. The concept therefore has emerged that LDL is the predominant atherogenic lipoprotein. The remarkable finding that LDL lowering therapy reduces the risk for subsequent coronary events even in patients with advanced atherosclerotic disease discloses a role for LDL in late stages of atherogenesis.(1) Orlistat, [(1S)-1-[(2S, 3S)-3-hexyl-4-oxo- oxetan -2-y1] methyl] dodecyl] (2S)-2-formamido-4-methyl–9pentonate also known as tetrahydrolipstatin, is designed to treat obesity. It reduces the LDL concentration in the blood by inhibiting gastric and pancreatic lipases (the enzymes that break down triglycerides in the intestine).The primary effect of Orlistat is local lipase inhibition within the GI tract after an oral dose. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids and are excreted undigested instead, thereby reducing caloric intake.(2,3) A single dose of Orlistat will prevent approximately 30% of dietary fat from being absorbed, which indicates its effectiveness in controlling dyslipidemia. It also exhibits anti proliferative and antitumor properties in prostate and breast tissues. In a study conducted in an obese population over four years, the incidence of type-2 diabetes was reduced with Orlistat (6.2%) when compared with placebo.(4,5) Hence, Orlistat is an important drug in prophylactic management of obesity and for the management of type-2 diabetes. Orlistat has a short half-life (<2 hr) and requires administration multiple times a day. The absorption window is restricted to the upper part of the gastrointestinal tract, which may lead to variability and non-uniform absorption and makes the bioavailability unpredictable.(6) Pharmaceutical compositions containing Orlistat have been formulated using various technological processes, such as extrusion and spheronization, micronization and other relatively time-consuming and demanding procedures. In contrast, formulations with Orlistat can also be produced by relatively simple and rapid methods such as blending and mixing with additives. It has been included in film delivery systems (Myers et al., 2009) and soluble fiber tablets. The problematic nature of Orlistat thus indicates the need for developing a novel drug delivery system that will be able to satisfy most of the formulation and pharmacodynamic requirements. (7) Liquisolid

technique is a new and promising method that can change the dissolution rate of drugs. It has been used to enhance dissolution rate of poorly water- soluble drugs. The novel 'liquisolid' technique may be applied to formulate liquid medications (i.e., oily liquid drugs and solutions, suspensions or emulsions of water- insoluble solid drugs carried in nonvolatile liquid vehicles) into powders suitable for tableting or encapsulation.(8) The term 'liquisolid systems' (LS) is a powdered form of liquid drug formulated by converting liquid lipophilic drug or drug suspension or solution of water-insoluble solid drug in suitable non-volatile solvent systems, into dry looking, non adherent, free-flowing and readily compressible powdered mixtures by blending with selected carrier and coating materials.(9)

II. Experimental Methods

2.1 Solubility Studies

Saturated solubility study of drug was carried out in three different non volatile solvents, i.e.PG, PEG 400, Cremophore EL and Tween 80 by preparing saturated solutions of the drug in these solvents and analyzing their drug content spectrophotometrically. Saturated solutions of Orlistat were prepared in vehicles and kept in orbital shaker for 48 hr at 25°C. After this period, the solutions were filtered, diluted and analysed by UV spectrophotometer at 208 nm. Three determinations were carried out for each sample to calculate the solubility of Orlistat. The results were extrapolated to determine the percent w/w of Orlistat in its saturated solution with the solvent under investigation.

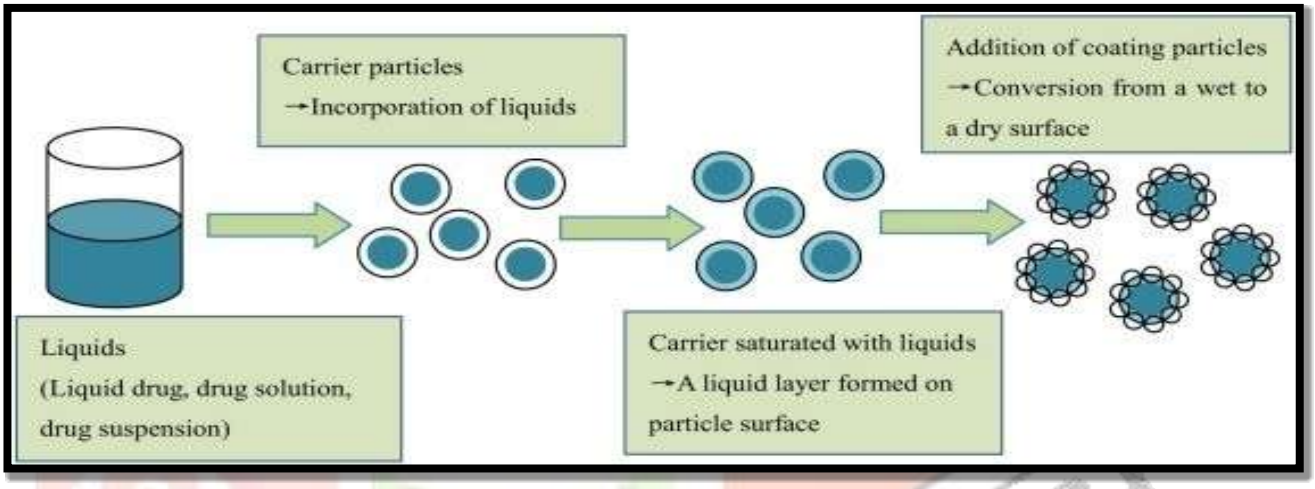

Figure 1. Application of the mathematical model for designing the liquisolid systems

In the following study, Cremophore EL was used as liquid vehicle; Avicel PH 102 and Aerosil 200 were used as the carrier and coating materials, respectively. In order to attain optimal Orlistat solubility in the liquisolid formulations, several factors were varied like the concentration of the liquid vehicle Cremophore EL, concentration of carrier and coating materials. The outline of the constituents of each of the formula prepared is demonstrated in **Table 1**. In order to address the flowability and compressibility of liquisolid compacts, simultaneously, the ''new formulation mathematical model of liquisolid systems" was employed as follows to calculate the appropriate quantities of excipients required to produce liquisolid systems of acceptable flowability and compressibility. This mathematical model was based on new fundamental powders properties (constants for each powder material with the liquid vehicle) called the flowable liquid retention potential (Φ-value) and compressible liquid retention potential ψ-number) of the constituent powders (carrier and coating materials). (9) According to the new theories, the carrier and coating powder materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties. Depending on the excipients ratio (R) or the carrier: coating ratio of the powder system used.

Where;

$$R = Q/q \quad ... (1)$$

As R represents the ratio between the weights of carrier (Q) and coating (q) materials present in the formulation. An acceptably flowing and compressible liquisolid system can be prepared only if a maximum liquid on the carrier material is not exceeded; such a characteristic amount of liquid is termed the liquid load factor (Lf) and defined as the ratio of the weight of liquid medication (W) over the weight of the carrier powder (Q) in the system, which should be possessed by an acceptably flowing and compressible liquisolid system. i.e;

$$Lf = W/Q \quad ... (2)$$

Flowable liquid retention potentials (Φ -values) of powder excipients used to calculate the required ingredient quantities, hence, the powder excipients ratios R and liquid load factors Lf of the formulations are related as follows [10]

$$Lf = \Phi + \Phi (1/R) \quad ... (3)$$

Where, Φ and Φ are flowable liquid retention potential of carrier and coating material respectively. So in order to calculate the required weights of the excipients used, first, from Eq.(3), Φ and Φ are constants, therefore, according to the ratio of the carrier/ coat materials (R), Lf was calculated from the linear relationship of Lf versus 1/R. next, according to the used liquid vehicle concentration, different weights of the liquid drug solution (W) will be used. So, by knowing both Lf and W, the appropriate quantities of carrier (Q_o) and coating (q_o) powder materials required to convert a given amount of liquid medication (W) into an acceptably flowing and compressible liquisolid system could be calculated from equation (1) and (2).

2.2 Preparation of Directly compressible tablet (DCT) and Liquisolid compact

Directly compressible tablets (DCT) of were prepared by direct compression using multiple tablet punch machine, each containing drug with Avicel PH 102, Aerosil 200 and sodium starch glycolate. Various Liquisolid compacts (F1 to F9) containing Orlistat were prepared by dispersing in non-volatile vehicles such as Cremophore EL. Then a binary mixture of carrier microcrystalline cellulose (Avicel PH 102) and coating material (Aerosil-200) was prepared. This binary mixture was added to the admixture of drug and vehicle. Depending upon the type of vehicle in the formulation, different liquid load factors were employed in Liquisolid preparations. Therefore, different concentrations of Avicel and silica were used to prepare different Liquisolid formulations. Finally sodium starch glycolate as disintegrant was added in above powder blend and mixed. The final powder blend was subjected to compression.

Formula	Drug Conc. in Cremophore EL	R	Lf	Avicel (Q=W/Lf)mg	Aerosil (q=Q/R)mg	SSG 5%	Unit Dose Weight
F1	1:0.5	30	0.50	395	13.16	26.65	533
F2		35	0.48	411	11.74	27.45	549
F3		40	0.43	438	10.95	28.85	577
F4	1:1	30	0.33	592	19.73	37.35	747
F5		35	0.31	640	18.2	39.35	795
F6		40	0.30	658	16.45	40.7	814
F7	1:1.5	30	0.27	710	23.6	43.75	875
F8		35	0.25	820	23.42	49.55	991
F9		40	0.23	850	21.25	49.9	998

Table1. Important formulation characteristics of Liquisolid compacts

Where;

R= Q/q, R represents the ratio between the weights of carrier (Q) and coating (q) materials present in the formulation.

Lf = Liquid load factor. Where, Lf = W/Q.

Q = Weight of carrier material **(Q=W/Lf) mg** i.e. Avicel PH 102.

W= Weight of liquid medication i.e Orlistat and Cremophore EL.

2.3 Flow properties of Liquisolid system

The flowability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as reproducible filling of tablet dies otherwise high dose variations will occur. Flow properties of the Liquisolid were estimated by tap density, bulk density, Angle of repose, Carr's compressibility index and Hausner's ratio. Angle of repose was measured according to the fixed funnel method. The tap density was determined using bulk density apparatus and calculated the Carr's compressibility index and Hausner's ratio.

III. Angle of Repose

Angle of repose was determined by using fixed funnel method. Powder is poured from a funnel onto a horizontal surface, it will form a cone. The angle between the sides of the cone and the horizontal is referred to as the angle of repose. The angle is a measure of the cohesiveness of the powder, as it represents the point at which the inter-particle attraction exceeds the gravitational pull on a particle. A free-flowing powder will form a cone with shallow sides, and hence a low angle of repose, while a cohesive powder will form a cone with steeper sides. Angle of repose was determined by substituting the values of the base radius 'r' and height of the pile 'h' in the given equation given below[(11)]

Angle of repose, θ = $\tan^{-1}(h/r)$

Where;

θ =Angle of repose;

h = height of pile;

r = radius of pile

IV. Bulk Density

An accurately weighed quantity of powder, which was previously passed through sieve # 22 and carefully poured into measuring cylinder. Then after pouring the powder into the measuring cylinder the powder bed was made uniform without disturbing. Then the volume was measured directly from the graduation marks on the cylinder as ml. The volume measured was called as the bulk volume and the bulk density is calculated by following formula.[(12)]

Bulk density = Weight of powder / Bulk volume Tapped Density

A given quantity of powder (2gm) is transferred to a measuring cylinder (10ml) and is tapped mechanically till a constant volume is obtained. This volume is the bulk volume and it includes true volume of powder and void space among the powder particles. The tapped density is calculated by the following formula. [(12)]

Tapped density = Weight of powder / Tapped volume

V. Friability Test

Take 10 tablets and weigh accurately, keep the friabilator on and rotate up to 4 minutes at 25 rpm. After 4 minutes remove the tablets and weigh the friability from initial weight to final weight.

VI. Evaluation of Tablet

Drug release of Orlistat Liquisolid tablets

Apparatus type used was USP XXII type II (paddle), dissolution medium was 900 ml of 3% Sodium Lauryl Sulphate (SLS) and 0.5% sodium chloride w/v in distilled water at 37°C±0.5°C, Speed of rotation of paddle was 75 rpm, volume of sample withdrawn was 10 ml, sampling interval was 30 min for 3hr over entire duration of study. The tablets were placed into a dissolution medium and the dissolution test was carried out. Aliquots were withdrawn at predetermined time intervals and equal volume of fresh dissolution medium was added. After each withdrawal sample was filtered through Whatman filter paper (No. 41) and analyzed spectrophotometrically[15] for cumulative percentage drug release. Marketed formulation of the drug was also studied for drug release.

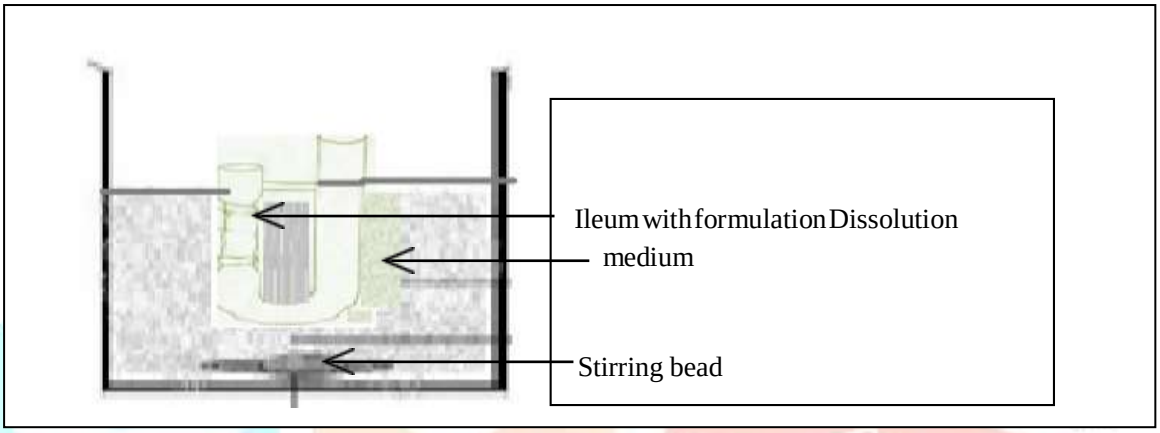

Figure 2. Apparatus for the Ex -vivo study using Ratileum

Drug release study was performed on rat ileum in dissolution apparatus equilibrated at 37°C±0.5°C. One end of rat ileum was tied and tablet granules were inserted into it followed by tying up of the other end., the ileum was dipped into the dissolution media (combination of 3% SLS and 0.5% Sodium chloride (w/v) solution in distilled water) in the dissolution vessel and the dissolution study was performed at 50 rpm and 37°C±0.5°C (Figure 2). Samples were withdrawn at predetermined intervals which were further analyzed for studies at the maximum wavelength of 208 nm on UV- spectrophotometer. The above procedure was performed for the pure drug and the marketed formulation. [16]

VII. Infrared Spectroscopy (FTIR)

Orlistat and liquisolid granules were mixed separately with IR grade KBr in the ratio of 1:1 and corresponding pellets were prepared by applying 10 metric ton of pressure in hydraulic press. The pellets were then scanned over a wave range of 4000-400cm $^{-1}$ in FTIR instrument (1800 Shimadzu).

VIII. Results and Discussion

Orlistat was selected as the model drug for present study, since it is water insoluble drug and thus, it is an ideal candidate for testing the potential of rapid- release Liquisolid compact. In addition, it can be easily assayed and quantities in solution using spectrophotometric method as it obeys Beer-Lambert's. The results of solubility study of Orlistat are given in **Table 2**, which shows higher solubility in Cremophore EL as compared to others non-volatile solvent which may be due to highest hydrophilicity and polarity(Amal Ali Alkordy 2012).In order to calculate the required ingredient quantities, the flowable liquid retention potentials (Φ-values) of powder excipients were utilized. [17]

Sr.No.	Solvent	Solubility(mg/ml)
1	PG	21.01
2	Tween 80	30.29
3	Cremophore EL	41.12
4	PEG 400	13.63

Table 2: Solubility of Orlistat in various solvents

8.1 Evaluation of Liquisolid Granules

The determination of angle of repose, Carr's index, Hausner's ratio is important before formulation because it influence compressibility, tablet porosity and dissolution. As a general guide angle of repose greater than 50^0 have unsatisfactory flow properties, minimum angle close to 25^0 correspond to very good flow property. Powders showing Carr's index up to 21 are considered of acceptable flow property. **(Table 3)** [18, 19]

Formula	Angle of repose	Bulk density	Tapped density	Carr's index	Hausner's ratio
F1	33.3±0.03	0.36 ± 0.01	0.45 ± 0.02	18.19	1.22
F2	33.0±0.64	0.37 ± 0.04	0.46 ± 0.02	19.14	1.22
F3	32.3±0.78	0.34± 0.01	0.45± 0.01	21.77	1.26
F4	34.4 ±1.05	0.34 ± 0.05	0.44 ± 0.03	21.93	1.32
F5	34.3±1.2	0.31 ± 0.04	0.41 ± 0.02	22.55	1.27
F6	30.1 ±1.6	0.35 ± 0.04	0.40 ± 0.05	19.73	1.12
F7	29.4 ±0.66	0.35 ± 0.02	0.41 ± 0.01	21.56	1.18
F8	31.0 ±0.13	0.33 ± 0.02	0.43 ± 0.03	16.86	1.21
F9	32.50±0.69	0.32 ± 0.08	0.41 ± 0.03	1652	1.11

Table 3: Results of Pre-formulation Study

8.2 Evaluation of Liquisolid Tablet Hardness

Hardness was found to be in the range of 3.4 ± 0.02 kg/cm^2 to 3.9 ± 0.04 kg/cm^2. It is seen that as the amount of Avicel goes on increasing, hardness also increases. With decrease in R values, hardness was decreased. This low hardness could be attributed to the less amount of added Avicel and poor compressibility of Aerosil. The hydrogen bonds between hydrogen groups on adjacent cellulose molecules in Avicel PH 102 may account almost exclusively for the strength and cohesiveness of compacts. [18] The high compressibility and compactness of Avicel PH 102 can be explained by the nature of the microcrystalline cellulose particles themselves which are held together by hydrogen bonds, when compressed, such particles are deformed plastically and a strong compact is formed due to the extremely large number of surfaces brought in contact during the plastic deformation and the strength of the hydrogen bonds formed. Tablets with low hardness were not considered because they were not able to withstand abrasion in handling.

8.3 Weight Variation Test

Weight variation test results were shown in **Table 4**. All the formulations pass the weight variation test.

8.4 Disintegration Time

The disintegration time test revealed that the Liquisolid tablet formulae disintegrated within 5 min which is as per specifications given for the uncoated tablets in the IP. Microcrystalline cellulose has disintegration property, which could facilitate disintegration of tablets and dissolution of drug. Because of the presence of a nonvolatile solvent acting as a binding agent in the Liquisolid formulation, delayed disintegration time is expected. However, in the Liquisolid tablets containing microcrystalline cellulose, a fast disintegration of tablet occurred which can be explained by the disintegrating property of microcrystalline cellulose. In addition use of SSG accelerates the disintegration of tablets by virtue of its ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. [20]

8.5 Drug Content

A fundamental quality attribute for all pharmaceutical preparations is the requirement for a constant dose of drug between individual tablets. Uniform drug content was observed for all the formulations (96.9 ±9.10 % to 99.1 ±7.66%).

Formula	Weight variation	Hardness (kg/cm^2)	Disintegration Time (min)	Drug Content (%w/w)	Friability %
F1	545±2.9	3.6 ± 0.02	2.4 ± 0.52	97.0±2.31	0.69
F2	550±1.32	3.7 ± 0.04	2.3 ± 1.02	97.0±1.33	0.72
F3	575±2.01	3.4± 0.01	2.9± 0.71	98.3±2.78	0.71
F4	740±1.05	3.5 ± 0.05	2.3 ± 1.7	97.5±2.05	0.72
F5	785±12.8	3.6 ± 0.04	2.6 ± 0.88	97.7±1.8	0.75
F6	825 ±4.48	3.7 ± 0.02	2.3 ± 1.22	98.4 ±3.78	0.72
F7	875 ±7.66	3.8± 0.01	2.9 ± 1.2	99.1±7.66	0.73
F8	925 ±8.14	3.6 ± 0.02	3.3 ± 0.3	97.4 ±7.19	0.66
F9	960±2.10	3.2 ± 0.05	3.4 ± 0.93	96.9±9.10	0.61

Table 4: Evaluation of Liquisolid Tablets

8.6 Friability

All the Liquisolid compacts had acceptable friability as none of the tested formulae had percentage loss in tablet's weights that exceed 1%. Friability below 1% is an indication of good, mechanical resistance of the tablets. This ensures that tablets could withstand to the pressure, shocks during handling, transportation and manufacturing processes. The acceptable friability value is 0.5 to 1%.

From the above observations formulation 7 was selected for further studies as it showed passable pre-formulation studies and highest drug content.

IX. In-vitro drug release studies

The in-vitro studies were performed to compare the enhancement of solubility of Orlistat with respect to marketed and pure drug. The formulation F7 was released almost the 90% drug within 180 min as compared to marketed formulation and pure drug and hence it possessed maximum solubalisation efficiency and maximum release than marketed formulation and pure drug (figure 3and table 5). The release is accelerated due to its markedly increased wettability and surface availability to the dissolution medium. The wettability of the compacts by the dissolution media is one of the proposed mechanisms for explaining the enhanced dissolution rate from the Liquisolid compacts. Cremophore EL facilitates wetting of drug particles by decreasing interfacial tension between dissolution medium and tablet surface.

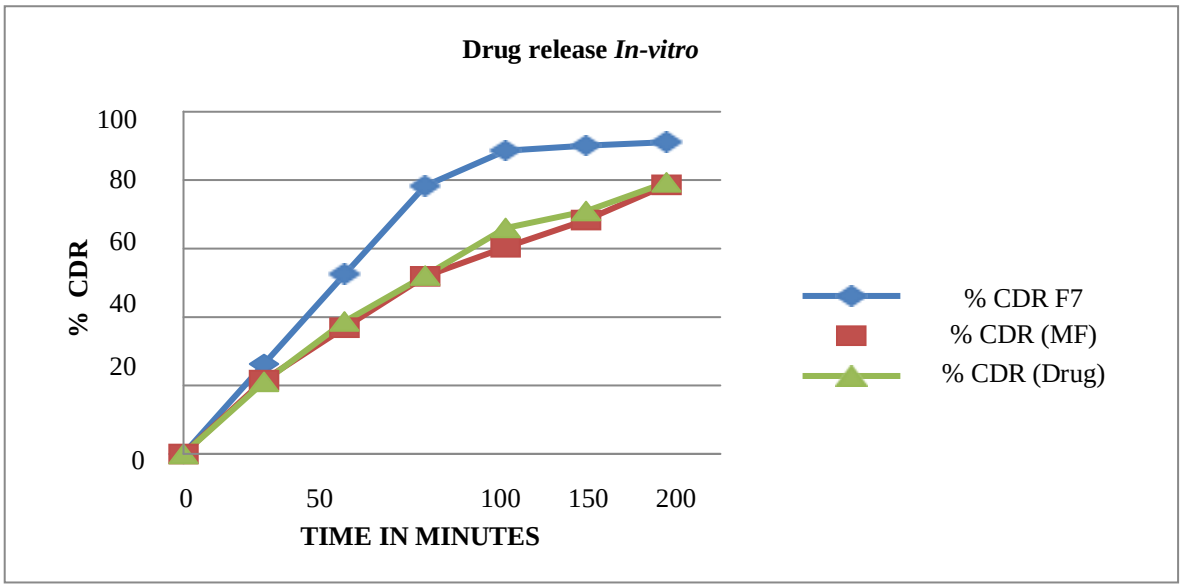

Figure 3: Cumulative drug release (CDR) of F7, marketed formulation (MF) and pure drug

Sr. No.	Time (min)	% CDR (F7)	% CDR (MF)	% CDR (Drug)
1	0	0	0	0
2	30	26.28±0.63	21.56±0.98	21.04±0.99
3	60	52.45±0.93	36.87±0.56	38.68±0.66
4	90	78.31±0.49	51.86±0.87	52.09±0.45
5	120	88.57±0.86	60.34±0.51	65.99±0.61
6	150	90.07±0.14	68.31±0.77	70.93±0.13
7	180	91.05±0.42	78.57±0.65	79.34±0.76

Table 5: Cumulative drug release of F7, marketed formulation (MF) and pure drug

X. *Ex-vivo* drug release studies

In *ex-vivo* drug release study of F7, marketed formulation (MF) and pure drug in dissolution medium of 3% SLS and 0.5% w/v. Sodium chloride solution in distilled water, the drug diffused at a faster rate from the Liquisolid system (F7) as compared to the plain drug and marketed formulation (figure 4 and table 6) due to enhanced solubility of drug. Such enhanced drug dissolution rates may be mainly attributed to the fact that this practically water insoluble drug is already in solution, while at the same time it is carried by the powder particles of the Liquisolid.

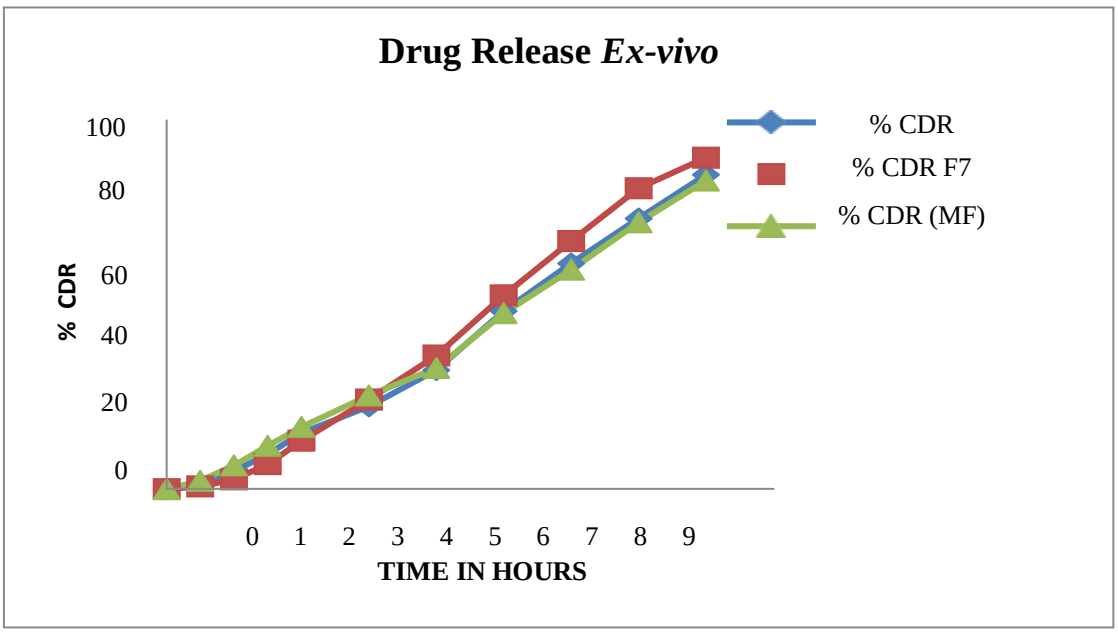

Figure 4: Cumulative drug release (*ex-vivo)* of F7, marketed formulation (MF) and pure drug

Sr. No.	Time in hrs	% CDR (Pure drug)	% CDR (F7)	% CDR (MF)
1	0	0	0	0
2	0.5	1.39±0.77	0.74±0.34	2.29±0.62
3	1	4.89±0.76	2.68±0.50	6.48±0.89
4	1.5	9.45±1.23	6.79±0.59	11.78±0.42
5	2	15.22±2.43	13.17±0.61	16.91±0.67
6	3	22.45±4.45	24.33±0.78	25.45±0.86
7	4	32.32±0.21	36.27±1.05	32.89±0.42
8	5	48.32±0.79	52.61±0.82	47.75±0.56
9	6	61.25±0.62	67.34±0.78	59.56±0.84
10	7	73.44±0.74	81.66±0.33	72.41±0.77
11	8	85.31±0.76	89.97±1.02	83.76±0.43

Table 6: Cumulative drug release (*ex-vivo)* of F7, marketed formulation (MF) and pure drug

XI. Infrared spectroscopy

It's important to check any kind of compatibility between drug candidate and inactive ingredient tin formulation. The inactive ingredient which is to be incorporated into formulation should be compatible with the drug. This compatibility study or interaction study was done using Fourier transformed infrared spectroscopy.

Pure Orlistat shows major peak at 1708, 2920, 887.7 and 1521.79 $(cm)^{-1}$ **(figure - 5)** and IR spectra of liquid solid (F7) revealed no considerable change in major peaks when compared to IR of pure drug which proved that there was no interaction between drug and excipients **(figure-6 and table 7).**

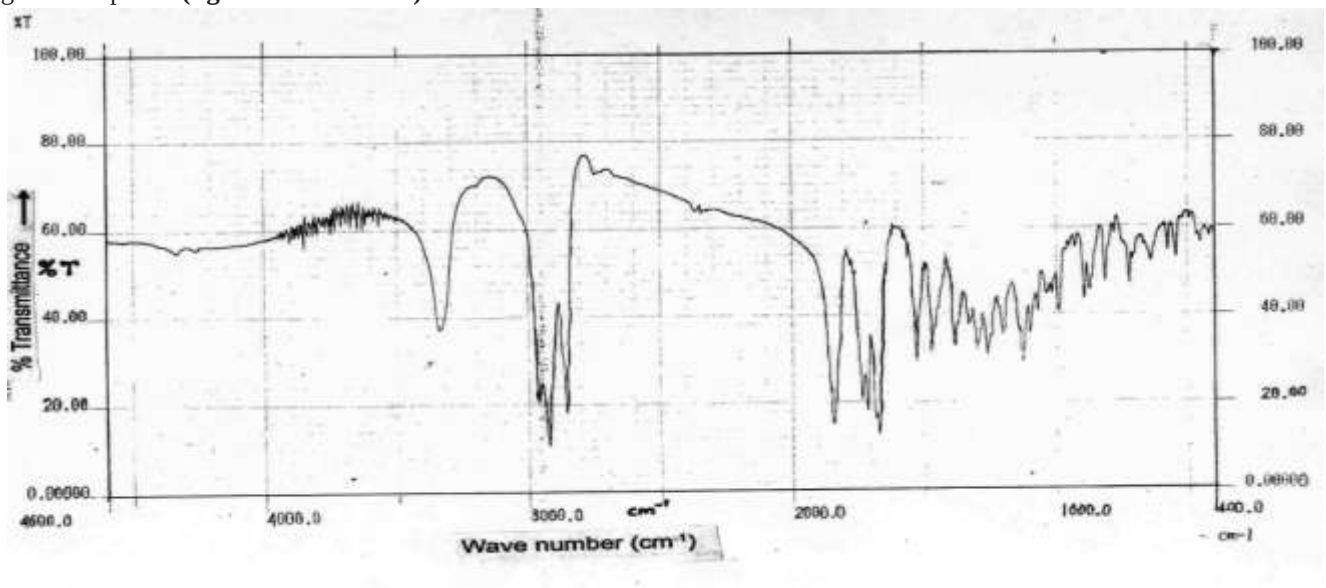

Figure 5: Infrared spectrum of Orlistat

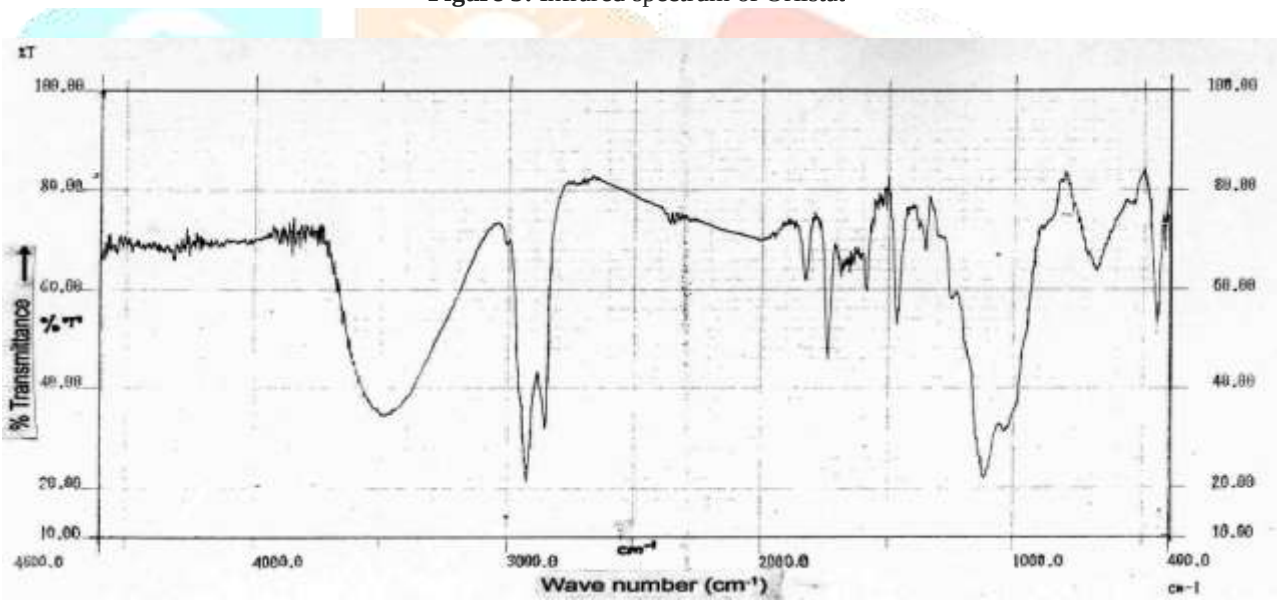

Figure 6: Infrared spectrum of liquid solid of Orlistat (F7)

Sr. No.	Wave number $(cm)^{-1}$	Group	Stretching / Deformation
1	1708	C=O	Stretching
2	2920	C-H	Stretching in CH_3
3	887.7	C-H	Deforming
4	1521.7	C=C	Aromatic stretching

Table 7: Interpretation of IR spectrum of liquid solid of Orlistat (F7)

XII. Conclusion

Liquisolid tablets contain a solution of the drug in suitable solvent (Orlistat in Cremophore EL), the drug surface available for dissolution is tremendously increased. In essence, after tablet disintegration, the Liquisolid primary particles suspended in the dissolving medium contain the drug in a state of molecular dispersion, whereas the directly compressed tablets are merely exposing micronized drug particles. In other words, in the case of Liquisolid tablets, the surface of drug available for dissolution is related to its specific molecular surface which by any means, is much greater than that of the Orlistat particles delivered by the plain, directly compressed tablets. Significantly increased surface of the molecularly dispersed Orlistat in the Liquisolid tablets may be chiefly responsible for their observed higher and consistent drug dissolution rates. Orlistat Liquisolid tablets F7 displayed significantly improved dissolution properties compared to Orlistat directly compressible tablet and MF.The drug release from Pure drug was less as compared to Liquisolid compacts. From above figures, it was apparent that formulations LS-7 have the highest drug release rate. Since the drug is molecularly dispersed within its water-miscible liquid vehicle, its release is accelerated due to its markedly increased wettability and surface availability to the dissolving medium. Such higher drug dissolution rates displayed by Liquisolid compact may also imply enhanced oral bioavailability From the above results it is clear that as there was increase in amount of liquid vehicle, there was increase in the dissolution rate.

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