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Liquisolid Technique for Enhancement of Dissolution Rate of Ibuprofen

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ABSTRACT

Liquisolid system refers to formulations formed by conversion of liquid drugs, drug suspension or drug solution in non-volatile solvents in to non-adherant, free flowing and compressible powder mixtures by blending the solution or suspension with selected carriers and coating materials. The in vitro dissolution property of slightly water soluble Ibuprofen was improved by exploring the potential of Liquisolid system (LS). The *in vitro* release pattern of Liquisolid compacts and directly compressed tablets were studied using USP-II apparatus. Different Liquisolid compacts 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 101, Aerosil and Sodium starch glycolate were employed as carrier, coating material and disintegrant respectively for preparing Liquisolid compacts. The prepared Liquisolid compacts were evaluated for their flow properties such as bulk density, tapped density, angle of repose, Carr's compressibility index and Hausner's ratio. The interaction between drug and excipients in prepared Liquisolid compacts were studied by differential scanning calorimetry (DSC) and FT-IR. The drug release rates of Liquisolid compacts were distinctly higher as compared to directly compressed tablets, and marketed Tablet which show significant benefit of Liquisolid compact in increasing wetting properties and surface area of drug available for dissolution. The LS-16 of Liquisolid powder system showed acceptable flowability, Carr's compressibility index and Hausner's ratio. The DSC and FT-IR studies conforms the no significant interaction between the drug and excipients used in Liquisolid compacts. From this study it concludes that the Liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs.

KEYWORDS

Liquisolid System, Carrier material, Coating material, Non-volatile solvents, Ibuprofen

INTRODUCTION

Therapeutic effectiveness of a drug depends upon the bioavailability which is dependent on the solubility and dissolution rate of drug molecules. Solubility is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown. Poorly water soluble drugs will be inherently released at a slow rate owing to their limited solubility within the GI contents.

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The dissolution rate is often the rate determining step in the drug absorption. The challenge for poorly water soluble drugs is to enhance the rate of dissolution. This in turn subsequently improves absorption and bioavailability. Formulation methods targeted at dissolution enhancement of poorly soluble substances are continuously introduced[1].

As large proportions of new drug candidates have poor aqueous solubility, various formulation strategies were reported to overcome such a problem. Among these techniques is complexation with cyclodextrins,

micronization, solid dispersion, co-precipitation and recently, the technique of 'liquisolid compacts'. Several studies have shown that the liquisolid technique is a promising method for promoting dissolution rate of poorly water soluble drugs[2-8]. In liquisolid compact, a liquid medication is converted into acceptably flowing and compactable powder forms. The term 'liquid medication' implies liquid lipophilic (oily) drug and solution or suspension of poorly water soluble drugs carried in suitable water miscible non-volatile liquid systems termed the liquid vehicle. By simple blending with suitable excipients 'carrier and coating materials', the liquid medication may be converted into a drylooking, non-adherent, free flowing and readily compactable powder[9].

Since drug dissolution is often the rate limiting step in gastrointestinal absorption, the significant increase in wetting properties and surface area of drug particles available for dissolution from liquisolid compacts may be expected to display enhanced drug release characteristics and, consequently, improved oral bioavailability.

The technique of liquisolid compacts has been successfully employed to improve the *In Vitro* release of poorly water soluble drugs such as Carvidilol[10], Bromhexine Hydrochloride[11], furosemide[12], carbamazepine[13], Fenifibrate[14], Indomethacin[15], Aceclofenac[16], ketoprofen[17], theophylline[18], propranolol hydrochloride[19], Lansoprazole[20], Irbesartan[21], Lornoxicam[22], simvastatin[23], tramadol hydrochloride[24], and fenofibrate[25].

Ibuprofen, is one of the propionic acid class of non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic effects. The major problem associated with the formulation and effectiveness of the ibuprofen is its variable oral absorption due to insufficient aqueous solubility at gastrointestinal pH, thus making dissolution the rate-determining step in the gastric absorption of ibuprofen[26]. Therefore, Ibuprofen establishes a good candidate for testing the potential of rapid-release liquisolid compacts.

The main objective of this work is to develop and explore a new formulation to enhance the bioavailability of a highly permeable and a poorly soluble non steroidal anti-inflammatory drug ibuprofen by following liquisolid compacts. And to compare the invitro drug release profile of formulated liquisolid tablets with marketed conventional tablet.

MATERIALS AND METHODS

MATERIALS

Ibuprofen was purchased from ACS chemicals, Ahmadabad avicel pH 101 was procured from Chemdyes Corporation. Aerosil, Magnesium stearate, Sodium starch glycolate were procured from seva fine chemicals. Polyethylene glycol 400 was procured from delta.

METHOD

Drug-Excipient compatibility study

FT-IR spectroscopy[27]

Fourier-transform infrared (FT-IR) spectra were obtained using an FT-IR spectrometer (Shimadzu 8400S, Japan). The samples (Ibuprofen and Excipients) were previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample:KBr) ratio, respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 min in a hydraulic press. Forty scans were obtained at a resolution of 4 cm^{-1}, from 4000 to 400 cm^{-1}.

Differential scanning calorimetry[28]

The DSC study was carried out using DSC-60 (Shimadzu, Tokyo, Japan). The instrument comprises of calorimeter, flow controller, thermal analyzer and operating software. The samples (drug and excipients) were heated in sealed aluminum pans under nitrogen flow (30 ml/min) at a scanning rate of 5°C/min from 25 to 250°C. Empty aluminum pan was used as a reference. The heat flow as a function of temperature was measured for the samples.

Solvent screening[29]

The solubility of ibuprofen in different solvent was determined by preparation of saturated

solution in 1 ml PEG 400, PEG 600, propylene Glycol and Glycerin.Excess Ibuprofen stirred in above solvent then sonicated for half hour and kept for 24 hour.Above four solution was filtered and diluted 10,000 times with methanol and absorbance was taken in U.V. spectrometer at 221.8 nm and matched with calibration curve.

Calculation of Flowable Liquid retention potential[29]

Carrier (Avicel) and coating (Aerosil) material was taken from 5:1 to 50:1 ratio and drug solution in PEG400 was added until good flow remain and liquid load factor calculated from below equation,

$$\text{Liquid load factor } Lf = W/Q$$

Where w = weight of liquid medication
And Q = weight of carrier material
From that different liquid load factor obtained for different carrier, coating material ratio (1/R) and graph of liquid load factor $\longrightarrow$ 1/R was plotted. Equation obtained was matched with below equation,

$$Lf = \Phi + \theta\,(1/R)$$

Where Φ and θ are the liquid retention potential of carrier and coating material respectively.

Preparation of conventional tablet and liquisolid Tablet[30]

Ibuprofen conventional tablets were produced by mixing the drug with microcrystalline cellulose–silica (with different ratios of microcrystalline cellulose to silica) and the additive for a period of 10 min in a cubic mixer .The mixture was mixed with sodium starch glycolate (5%, w/w, of the formulation) and magnesium stearate (1% w/w of the formulation) for 10 min. The mixture was compressed on a 10-mm punch and die using a manual tableting machine (Rimek). Sufficient compression load was applied in order to produce tablets with the hardness.

Several liquisolid compacts were prepared as follows. Ibuprofen was dispersed in PEG 400. Then a binary mixture of carrier-coating materials (microcrystalline cellulose as the carrier powder and silica as the coating material) in the ratio of 5:1(F-1 to F-5), 10:1 (F-6 to F-10), 20:1(F-11 to F-15) and 30:1(F-16 to F-20) was added to the obtained liquid medication under continuous mixing in a mortar. Depending upon the type of carrier in formulation, different liquid loading factors were employed in our liquisolid preparations. Finally, 5 %(w/w) of sodium starch glycolate as the disintegrant and 1 % magnesium sterate were mixed with the mixture for a period of 10 min. The final mixture was compressed using the manual tableting machine to achieve tablet hardness.

Evaluation of liquisolid granules

Angle of Repose[31]

This is the maximum angle possible between the surface of a pile of powder and the horizontal plane.10 gm of powder was allowed to flow by funnel from 4 cm of height from the base. The height of pile and diameter of base was measured and calculate the angle of repose by following formula

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

Where, θ = angle of repose,

h = Height of the heap,

r = Radius of the heap.

Bulk Density[31]

An accurately weighed quantity of powder, which was previously passed through sieve # 40 [USP] and carefully poured into graduated cylinder. Then after pouring the powder into the graduated 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;

Bulk density = Weight of powder / Bulk volume

Tapped Density[31]

After measuring the bulk volume the same measuring cylinder was set into tap density apparatus. The tap density apparatus was set to 300 taps drop per minute and operated for 500 taps. Volume was noted as (Va) and again

Table: 1 Formulation composition of liquisolid tablets

Formula	Ibuprofen (mg)	PEG 400(mg)	Avicel pH101(mg)	Aerosil (mg)	R	Lf	Total weight (mg)
F-1	200	200	579.7	115.9	5	0.69	1165.1
F-2	200	190	565.2	113	5	0.69	1138.1
F-3	200	180	550.7	110.1	5	0.69	1110.8
F-4	200	170	536.2	107.2	5	0.69	1079.1
F-5	200	160	521.7	104.3	5	0.69	1052.5
F-6	200	200	833.3	83.3	10	0.48	941.6
F-7	200	190	812.5	81.2	10	0.48	1358.7
F-8	200	180	791.6	79.1	10	0.48	1324.7
F-9	200	170	770.8	77.8	10	0.48	1291.8
F-10	200	160	750	75	10	0.48	1255.8
F-11	200	200	1000	50	20	0.40	1550
F-12	200	190	975	48.7	20	0.40	1497.9
F-13	200	180	950	47.5	20	0.40	1459
F-14	200	170	935	46.4	20	0.40	1421.1
F-15	200	160	900	46	20	0.40	1383
F-16	200	200	1176.4	39.21	30	0.34	1717.6
F-17	200	190	1147	38.23	30	0.34	1671.2
F-18	200	180	1117.6	37.25	30	0.34	1635.8
F-19	200	170	1088.2	36.27	30	0.34	1582.5
F-20	200	160	1058.8	35.29	30	0.34	1544.1
CT	200	-	579.7	115.9	5	-	941.6

CT= Conventional Tablet

tapped for 750 times and volume was noted as (Vb). If the difference between Va and Vb not greater than 2% then Vb is consider as final tapped volume. The tapped density is calculated by the following formula

Tapped density = Weight of powder / Tapped volume

Carr's Index [Compressibility Index] [32]

It is one of the most important parameter to characteristic the nature of powders and granules. It can be calculated from the following equation-

Carr's index = Tapped density - Bulk density / Tapped density X 100

Hausner's Ratio[32]

Hausner's ratio is an important character to determine the flow property of powder and granules. This can be calculated by the following formula-

Hausner's ratio = Tapped density / Bulk density

Evaluation of Tablets[32]

Weight variation

Weight variation was measured by weighing 20 Tablets and average weight was found and percentage weight variation of the individual tablet should fall within specified limits in terms of percentage deviation from the mean.

Thickness

Thickness of tablet was measured by vernier caliper.

Hardness

It is a measure of the mechanical strength of a tablet using hardness tester (Monsanto hardness tester). The mechanical strength of a tablet is

associated with the resistance of a tablet to fracture or attrition.

Friability

It was determined using Roche friabilator, the percentage loss in tablet weight before and after 100 revolutions of 3 tablets were calculated and taken as a measure for friability.

Disintegration time

The time necessary to disintegrate 3 tablets of each tablet formulation was determined using disintegration tester.

Drug content

Uniformity of Ibuprofen was determined by collecting a sample of 3 tablets from each batch followed by a determination of the drug concentration in each tablet spectrophotometrically at 221.8 nm. The average drug content is calculated and the percentage drug content of the individual tablet should fall within specified limits in terms of percentage deviation from the mean.

In vitro dissolution studies

The USP dissolution apparatus II was used with 900 ml, to ensure sink conditions, (Phosphate buffer solution pH 7.2) at 37±0.5°C; the apparatus was run at 100 rpm.Samples of the dissolution medium were withdrawn at a specified time intervals and compensated by fresh dissolution medium. Samples were properly diluted and Ibuprofen concentrations were analyzed spectrophotometrically at 221.8nm. The percentage drug released at time interval was calculated and plotted against time.

Stability Study of Optimized Batch[33]

Stability studies were performed according to ICH and WHO guidelines. Batch F-16 was packed in an airtight amber glass bottles. The bottles were kept at 25ºC ± 2ºC / 60% ± 5% RH and 40ºC ± 2ºC / 75% ± 5% RH tested at 1 month. The sample of Liquisolid Tablet was than evaluated for stability by determining drug content, disintegration time and physical appearance.

RESULTS AND DISCUSSION

Drug-Excipient compatibility study

FT-IR spectroscopy FT-IR spectra of Ibuprofen, Ibuprofen + avicel pH 101, Ibuprofen+ Aerosil and physical mixture were given below.

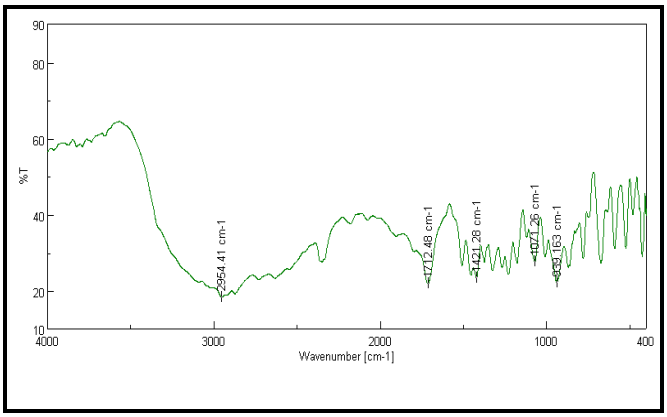

Figure: 1 FT-IR spectra of Ibuprofen

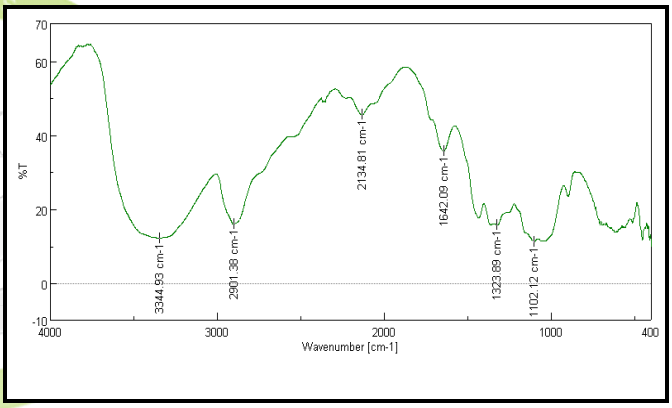

Figure: 2 FT-IR spectra of Ibuprofen + Avicel pH101

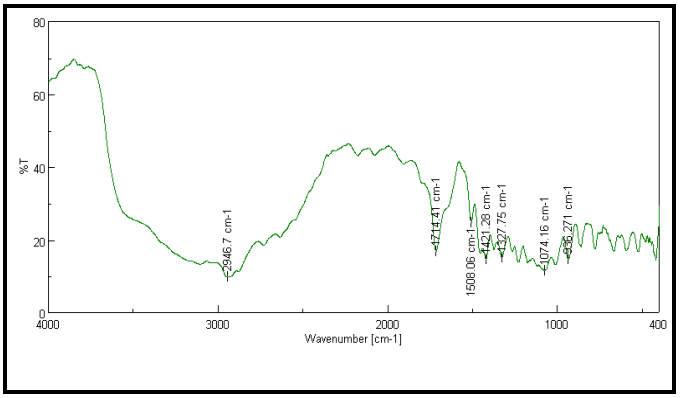

Figure: 3 FT-IR spectra of Ibuprofen + Aerosil

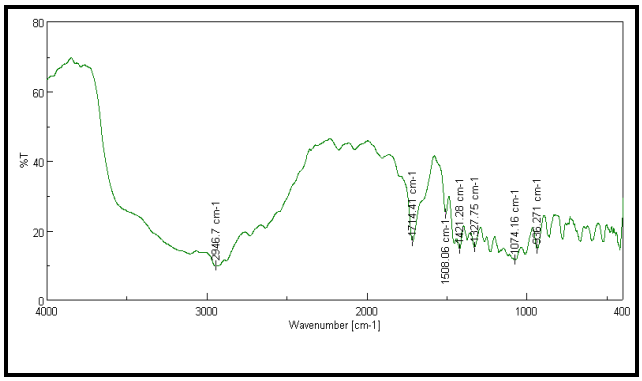

Figure: 4 FT-IR spectra of Physical mixture

The peaks obtained in the spectra of each formulation correlates with the characteristic peaks(C-H, O=C, C=C, and C-O) of drug spectrum. It does not show any well-defined interaction between Ibuprofen and excipients. This indicates that the drug is compatible with the formulation components.

Differential scanning calorimetry DSC spectra of Ibuprofen and Ibuprofen + physical mixture were given below.

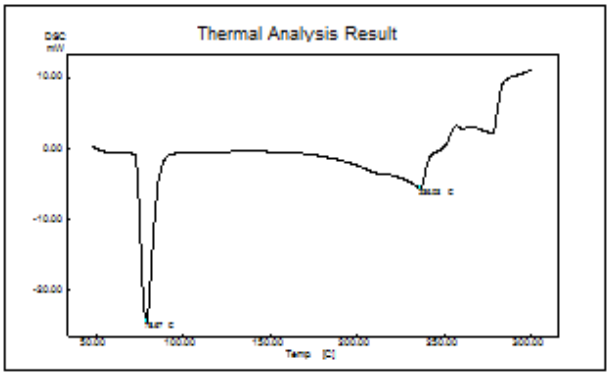

Figure: 5 DSC spectra of Ibuprofen

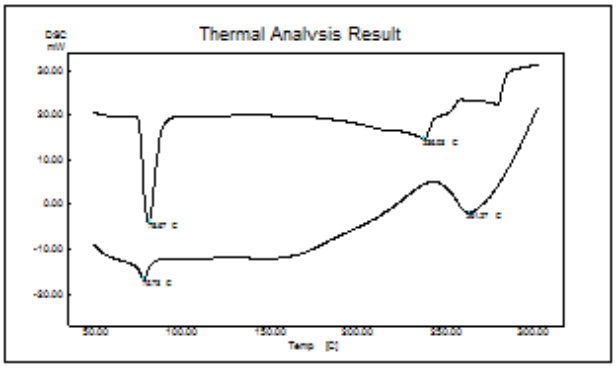

Figure: 6 Overlay DSC spectra of Ibuprofen and physical mixture

The thermal behavior of Ibuprofen and Excipients mixture was investigated by heating the respective samples at 20°C/min. For the physical mixture an endothermic peak was observed at 75.7°C. The pure Ibuprofen had endothermic peaks at 78.6°C. This clearly showed that there was no interaction between the drug and other excipients used in the study.

Solvent Screening

The solubility of Ibuprofen in different Non-volatile solvent was found by UV method is given in below table. Solubility of Ibuprofen in PEG 400, PEG 600, Propylene glycol and Glyrine is 121.9, 116.7, 58.1, and 84.2 gm/ml. Maximum solubility of Ibuprofen in PEG 400 so it was selected as solvent in this investigation.

Table: 2 Solubility of Ibuprofen in different Non-volatile solvent

Solvent	Solubility (mg/ml)
PEG 400	121.9
PEG 600	116.7
Propylene Glycol	58.1
Glycerine	84.2

Calculation of liquid retention potential

At different ratio of 1/R different Lf was obtained and graph of Lf 1/R was given below.

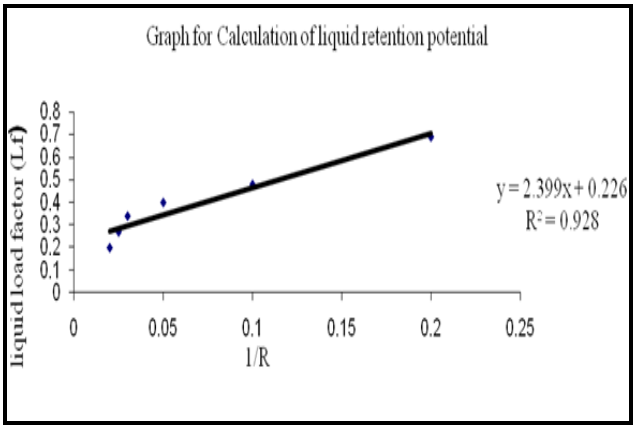

Figure: 7 Graph for Calculation of liquid retention potential

From the graph Equation Y= 0.2267+2.3999x and it was compare to Lf = Φ + θ (1/R) where Φ, θ are the liquid retention potential of carrier and coating material respectively, so Φ = 0.2267 and θ = 2.3999 Flawable liquid retention potential of carrier and coating material was found to be 0.2267 and 2.3999 respectively.

Evaluation of Liquisolid Granules

Angle of repose, density, Hauner ratio and carr's index of F-1 to F-20 and CT were given in above table. Angle of repose > 30,Hausner ratio > 1.25 and carr's index > 15 % in F-1 to F-10 formula so flow is passable and in formula F-11 to F-20 and CT Angle of repose < 30, Hausner ratio <1.25 and carr's index < 15 % indicate good flow.

Table: 3 Evaluation of Liquisolid Granules and conventional tablet

Formula	Angle of repose	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner ratio	Carr's index %
F-1	33.2	0.35	0.45	1.27	21.52
F-2	33.1	0.38	0.47	1.23	19.12
F-3	32.5	0.35	0.46	1.36	23.50
F-4	34.1	0.31	0.40	1.29	23.09
F-5	33.5	0.31	0.41	1.34	25.48
F-6	31.4	0.32	0.41	1.28	21.52
F-7	31.2	0.33	0.41	1.24	19.27
F-8	33.5	0.37	0.47	1.28	21.80
F-9	33.2	0.31	0.40	1.29	22.42
F-10	30.1	0.34	0.44	1.31	23.60
F-11	30.2	0.39	0.44	1.12	11.7
F-12	31.1	0.38	0.46	1.28	17.3
F-13	30.5	0.38	0.45	1.18	15.5
F-14	32.1	0.35	0.41	1.17	14.6
F-15	31.5	0.35	0.40	1.14	12.5
F-16	29.4	0.36	0.40	1.08	10.0
F-17	29.2	0.37	0.40	1.08	7.5
F-18	31.5	0.39	0.46	1.17	15.2
F-19	31.5	0.36	0.41	1.13	12.1
F-20	28.1	0.38	0.43	1.13	11.6
CT	27.48	0.39	0.42	1.07	7.1

Evaluation of Tablets

The results of weight variation, Thickness, Hardness, Friability, drug content and Disintegration time are given in above table. From result it was concluded that none of the investigated tablets weight differ from the mean by more than 10% so it met the requirement of BP. Hardness of Tablet ranges from 4.o to 5.7 (kg/cm^2).

Friability studies of liquisolid tablets are in the ranges of 0.42 to 0.73 %. This indicates that acceptable resistance is shown by liquisolid tablets to withstand handling. It was observable that formula F-1 to F-20 and CT complied with the standard of Ibuprofen content uniformity according to the IP by having drug content 97 to 99 %.

Table: 4 Evaluation parameter of LS Tablet from F-1 to F-20 and CT

Formula	Weight variation(mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability %	Drug content (%w/w)	Disintegration time (Min.)
F-1	1161.1 ± 0.34	3.8 ± 0.02	4.0±0.2	0.73	98.6 ± 0.5	2.4±0.04
F-2	1132.2 ± 0.53	3.8 ± 0.02	4.1±0.3	0.72	99.1 ± 0.6	2.4±0.05
F-3	1110.4 ± 0.30	3.9 ± 0.03	4.1±0.2	0.75	97.8 ± 0.3	2.3±0.03
F-4	1072.5 ± 0.60	3.9 ± 0.02	4.1±0.3	0.72	97.1± 0.4	2.2±0.01
F-5	1050.7 ± 0.17	3.9 ± 0.02	4.0±0.5	0.73	98.6± 0.3	2.3±0.02
F-6	1382.5 ± 0.51	4.0 ± 0.03	4.3±0.7	059	99.2± 0.4	2.1±0.02
F-7	1354.4 ± 0.31	4.1± 0.02	4.3±0.6	0.54	98.8± 0.5	2.2 ±0.04
F-8	1321.7 ± 0.22	4.1 ± 0.03	4.2±0.5	0.56	99.4± 0.2	2.1±0.01
F-9	1290.2 ± 0.12	4 ± 0.02	4.5±0.6	0.59	97.3± 0.3	2.1±0.02
F-10	1251.7 ± 0.32	4.1 ± 0.02	4.4±0.7	0.59	97.6± 0.4	2.3±0.04
F-11	1542.8 ± 0.46	4.2 ± 0.02	4.9±0.8	0.49	97.4± 0.3	1.9±0.02
F-12	1492.7 ± 0.34	4.1 ± 0.03	4.8±0.5	0.47	97.6± 0.5	1.8±0.03
F-13	1462.7 ± 0.21	4.1 ± 0.02	5.1±0.3	0.42	98.2± 0.7	1.9±0.02
F-14	1419.8 ± 0.09	4.2 ± 0.02	5.2±0.2	0.45	98.8± 0.7	1.7±0.04
F-15	1382.1 ± 0.06	4.1 ± 0.03	5.1±0.3	0.46	97.8± 0.6	1.9±0.04
F-16	1721.2 ± 0.2	4.2 ± 0.05	5.7±0.2	0.42	99 ± 0.5	1.5±0.01
F-17	1650.1 ± 1.26	4.2 ± 0.03	5.5±0.4	0.41	97.4 ± 0.3	1.6±0.03
F-18	1630.5 ± 0.35	4.1 ± 0.02	5.4±0.4	0.42	97.9 ± 0.2	1.5±0.02
F-19	1581.2 ± 0.08	4.2± 0.03	5.6±0.7	0.41	98.6 ± 0.5	1.7±0.01
F-20	1542 ± 0.12	4.2 ±.0.02	5.3±0.4	0.45	98.9 ± 0.4	1.6±0.03
CT	937.2 ± 0.46	4.2 ±.0.01	5.5±0.3	0.43	97.5 ± 0.2	1.8 ± 0.04

(Mean ± SD, n=3, n=20 for weight variation)

In-Vitro drug release

Table: 5 Dissolution data of F-1 to F-10 Batches

Time (Min.)	% Drug Release									
	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9	F-10
0	0	0	0	0	0	0	0	0	0	0
5	44.5 ± 2.1	42.9 ±2.4	41.3 ±2.6	39.8 ±1.4	36.2±1 .3	45.3±2 .1	43.9±1. 3	42.3±2. 2	40.8±2. 2	37.2± 1.9
10	67.2 ± 2.3	65.8 ±2.5	63.6± 2.1	59.2±2 .3	57.4±1 .2	68.3±2 .1	66.8±1. 5	64.6±2. 4	60.2±2. 5	58.4± 2.1
15	78.3 ± 1.4	76.1 ±1.7	74.8± 1.5	71.3±2 .6	68.9±1 .4	79.3±2 .5	77.1±2. 1	75.8±1. 5	72.3±2. 6	69.9± 2.3
30	89.6 ± 1.6	88.2 ±1.3	86.5± 1.3	85.4±1 .6	85.1±1 .4	90.6±1 .6	89.2±2. 4	86.9±1. 4	86.4±2. 1	86.1± 2.55
45	91.4 ± 1.4	90.3 ±1.4	89.8± 2.3	88.5±1 .4	87.8±2 .3	92.4±2 .5	91.3±1. 6	90.8±1. 7	89.5±1. 4	88.8±1. 2
60	92.4 ± 2.3	91.9±2. 4	91.4± 1.5	90.7±1 .5	90.3±1 .3	93.5±1 .5	92.4±1. 2	92.1±1. 1	91.7±1. 2	91.3±1. 2

Table: 6 Dissolution data of F-11 to F-20 Batches

Time (Min.)	% Drug Release									
	F-11	F-12	F-13	F-14	F-15	F-16	F-17	F-18	F-19	F-20
0	0	0	0	0	0	0	0	0	0	0
5	47.3±1.8	43.9±2.7	42.3±1.8	41.8±2.3	39.2±2.4	49.3±2.5	46.9±2.6	49.3±2.5	42.8±2.6	40.2±2.8
10	69.9±2.1	66.8±2.6	65.6±1.5	58.2±2.8	57.4±2.1	70.9±2.2	68.8±2.1	66.6±2.1	59.2±3.1	58.4±2.6
15	81.3±2.1	77.1±2.7	76.8±2.4	71.3±2.7	70.9±1.6	82.3±2.8	78.1±2.5	77.8±2.8	74.3±2.8	71.9±2.1
30	91.6±1.6	89.2±2.4	87.9±1.5	85.4±2.5	84.1±1.8	92.6±1.5	90.2±2.4	88.9±1.2	88.4±2.5	85.1±1.5
45	93.4±1.8	91.3±1.5	91.8±3.1	87.5±2.6	86.8±1.9	94.4±2.4	92.3±1.8	92.1±2.1	89.5±2.1	87.8±2.5
60	94.4±1.5	92.4±1.2	93.1±1.3	92.7±1.5	92.3±1.3	95.4±1.5	93.4±1.5	93.2±1.1	93.1±1.6	92.5±1.3

(Mean ± SD, n=3)

Table: 7 Dissolution data of F-16, CT and Marketed Tablet

Time (Min.)	% Drug Release		
	F-16	CT	Marketed Tablet
0	0	0	0
5	49.3±2.5	28.5±1.2	22.8±0.9
10	70.9±2.2	49.7±1.3	36.5±1.2
15	82.3±2.8	64.4±1.2	49.9±2.1
30	92.6±1.5	82.1±2.1	58.2±1.3
45	94.4±2.4	86.4±2.2	71.4±1.3
60	95.4±1.5	88.3±2.1	78.6±1.1

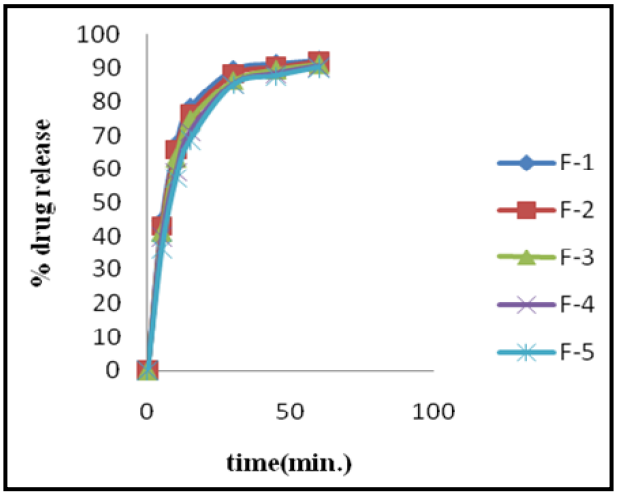

Figure: 8 Dissolution Profile of F- 1 to F-5

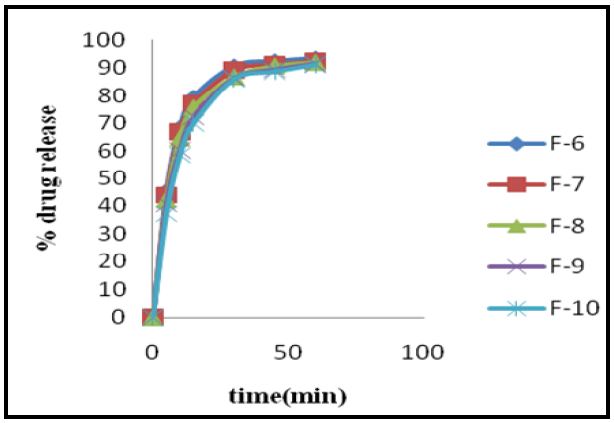

Figure: 9 Dissolution Profile of F-6 to F-10

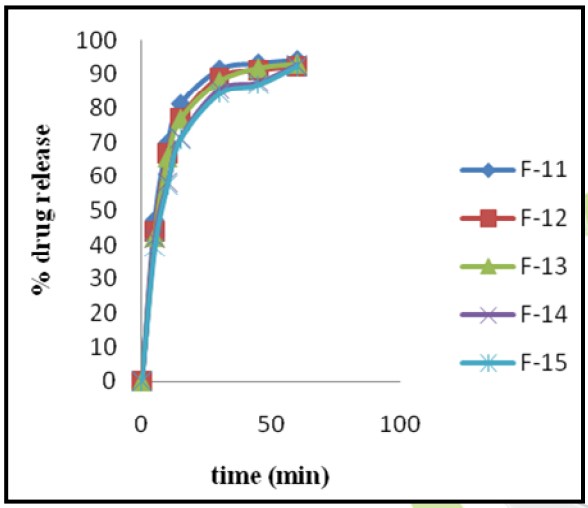

Figure: 10 Dissolution Profile of F- 11 to F-15

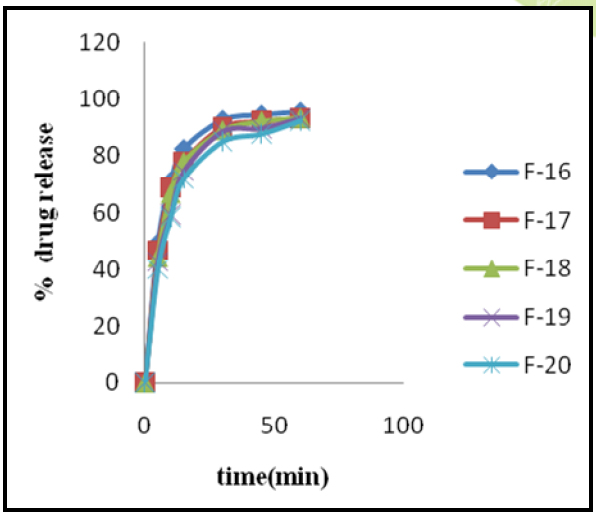

Figure: 11 Dissolution Profile of F-16 to F-20

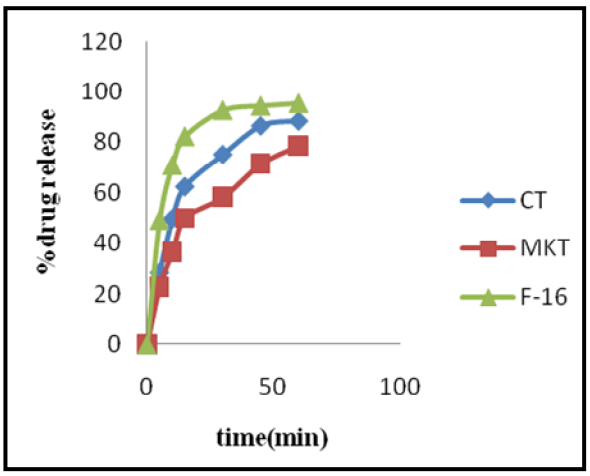

Figure: 12 Dissolution rate comparison (F-16, CT, MKT)

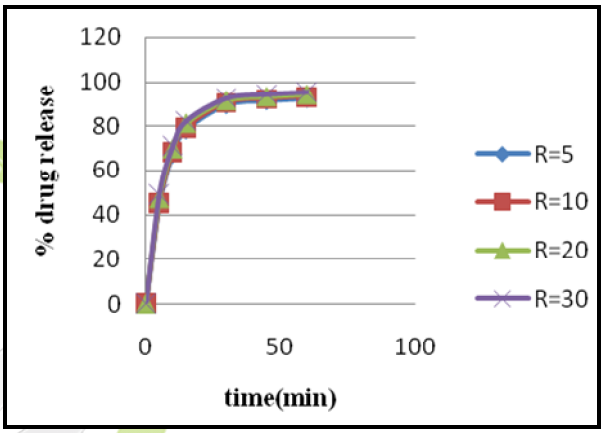

Figure: 13 Dissolution Profile at different R

Dissolution profile of F-1 to F-5, F-6 to F-10, and F-11 to F-15 and F-16 to F-20 were given Fig 6.12, 6.13, 6.14 and 6.15 respectively. All batches show more than 40 % drug release in 5 min, more than 60 % in 15 min, more than 75 % in 45 min and 90 or more than 90 % in 1 hour. There is slightly decrease in dissolution rate from F-1 to F-5,F-6 to F-10,F-11 to F-15 and F-16 to F-20 this is due to decrease in the concentration of PEG 400.From this it is concluded that as the concentration of solvent decrease dissolution rate of drug decrease. In this investigation some drug undissolved means drug medication in suspension form taken as the undissolved part of drug in solvent increase dissolution rate decrease. Dissolution profile at different carrier to coating material ratio was given in Fig 6.16.It shows that slightly increase dissolution rate as the ratio increase it is due to as the ratio increase Avicel concentration

increase so fast disintegration so fast dissolution.

From 20 batches F-16 batch show more dissolution rate than other batch also it's hardness more, friability less and disintegration time also less so it is better than other so it is selected as optimized batch. F-16 batch was compared to marketed tablets of Ibuprofen 200 mg (Ibugesic Coated Tablet, Cipla) and conventional directly compressed tablet.

From Fig 13 Dissolution Profile F-16 (optimized batch) was compared with dissolution profile of conventional tablet and marketed tablet. Dissolution Rate of liquisolid tablet was faster than Marketed Tablet and Conventional Tablet. Liquisolid Tablet show 90 % drug release in 30 min. and 95 % in 1 hour while conventional tablet 75 % drug release in 30 min. and 88% in 1 hour finally Marketed preparation only 58 % drug release in 30 min. and 78 % in 1 hour. Reason for increase in dissolution rate is" Diffusion layer model", dissolution rate is directly proportional to concentration gradient in stagnant diffusion layer. Not only the concentration gradient, drug dissolution is directly proportional to surface area available for dissolution. As liquisolid tablets contain a drug dissolved, suspended or emulsified , so the drug surface available for dissolution is highly increased. In short, drug is present in the form of molecular dispersion, after its disintegration in the dissolution media. Hence, molecularly dispersed drug in liquisolid tablets may be responsible for greater dissolution rates compared to marketed formulations. This will also reflect enhanced oral bioavailability.

CONCLUSION

Ibuprofen release from Liquisolid tablet is faster than conventional and marketed tablet. Morover,with liquisolid Tablets containing the drug suspended in PEG 400,the release rate increase with rising fraction of dissolved drug in the liquid portion so for highest dissolution rate with liquisolid system containing a drug solution as liquid portion. Therefore, if the drug dose high or solubility of drug is low in liquid solvent, a high amount of solvent needed finally required high amount of carrier and coating materials. This results in an increase in tablet weight usually leading to unacceptably high tablet size.

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