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SOLUBILITY ENHANCEMENT OF REPAGLINIDE BY LIQUISOLID TABLET TECHNIQUE

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Keywords:

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ABSTRACT

Liquisolid system is the one of the novel technique to enhance the dissolution rate of poor-water soluble drug such as Repaglinide. It is suggested here that liquisolid technique has the potential to enhance solubility and dissolution rate of BCS class II. This technique shows delivering of drugs, which is suitable mostly for lipophilic drugs. In this technique liquisolid system refers to formulation of formed by water insoluble drug mix with non-volatile solvent which is further converted into free flowing, non adherent powder form and which is directly compressed into tablets. In that the polyethylene glycol (PEG-400) is used as non-volatile solvent in which drug having high solubility, microcrystalline cellulose and aerosil (silica) acts as carrier and coating material in the ratio of 10:1, 15:1 and 20:1 respectively. Cross-povidone acts as superdisintegrant and magnesium stearate as glidants in liquisolid system. The aim of the present work is to improve the solubility and dissolution rate of poorly water-insoluble drug Repaglinide (REPA), by using this technique. REPA was dispersed in PEG-400 as a liquid vehicle. Then a binary mixture of carrier-coating materials (Microcrystalline cellulose-Aerosil) was added to the liquid medication under continuous mixing. Precompresion studies, such as flow properties were also carried out. The formed mixing was compressed to get tablets by using the tabletting machine. The prepared liquisolid tablets were evaluated by hardness, friability and disintegration test and in-vitro dissolution studies.

Fourier Transform Infrared spectroscopy (FTIR), X-Ray Diffraction (XRD) and Differential Scanning Calorimetry (DSC) study shows no interaction between the drug and excipients. The investigation suggest that liquisolid tablets of REPA with increasing the amount of carrier to coating ratio along with super disintegrating agent resulted in higher dissolution rate, which are directly proportional to the amount released. In conclusion, the results showed that the liquisolid technique could be a promising alternative technique to increase dissolution of water-insoluble drugs Repaglinide.

1. INTRODUCTION

During the last 3 decades the pharmaceutical industries devote the time and money in research of tablet compaction. The reason behind it the oral dosage forms are self administered by patient and more profitable to manufacture than parenteral dosage forms. Also their low cost of manufacture, package, shipment, increased stability and tamper resistance. There are many types of tablet formulation that provide for release of drug to the delayed or control the rate of drug availability. And some tablets are the fast disintegrating or fast dissolving tablets are present to give the quick effect of drug [1, 2].

For poorly soluble and highly permeable (Class II) drugs, the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract [3, 4]. Therefore, together with permeability, the solubility and dissolution behavior of a drug are key determinants of its oral bioavailability.

There have been numerous efforts to improve drug dissolution rate. These include.

1) Reduction particle size to increase surface area, thus increasing dissolution rate of drug.
2) Solubilization in surfactant systems.
3) Formation of water-soluble complexes.
4) Use of prodrug and drug derivatisation such as strong electrolyte salt forms that usually have higher dissolution rate.
5) Manipulation of solid state of drug substance to improve drug dissolution (i.e. by decreasing crystallinity of drug substances through formation of solid solutions) [5].

Diabetes is the metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipaemia, negative nitrogen balance and ketonemia. Type II diabetes (also known as non-insulin dependent diabetes mellitus (NIDDM) or adult-onset diabetes) is one of the most serious medical conditions affecting our nation today. The number of people who have it has been rising widely. For this the fast delivery of drug is required to the diabetic patient [6].

Repaglinide (REPA) is an amino-acid derivative that lowers blood glucose levels by stimulating insulin secretion from the pancreas. This action is dependent upon functioning beta-cells in the pancreatic islets. Repaglinide interacts with the ATP-sensitive potassium (K+ATP) channel on pancreatic beta-cells. The subsequent depolarization of the beta cell opens the calcium channel, producing calcium influx and insulin secretion. The extent of insulin release is glucose dependent and diminishes at low glucose levels. The tablets have to be taken before meal [7].

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 anti-diabetic drug Repaglinide by following liquisolid tablets. And to compare the in vitro drug release profile of formulated liquisolid tablets with marketed and conventional tablet.

A "liquisolid system" refers to formulations formed by conversion of liquid drugs, drug suspension or drug solution in non-volatile solvent into dry, non-adherent, free-flowing and compressible powder mixture by blending the suspension or solution with selected carrier and coating materials [8].

The term "liquid medication" implies oily liquid drugs and solution or suspensions of water insoluble solid drugs carried in suitable non-volatile system. Based on the type of liquid medication contained, liquisolid systems are classified into three categories:

a) Powdered drug solution (containing a drug solution)
b) Powdered drug suspension (containing a drug suspension)
c) Powdered liquid drug (containing a liquid drug)

Various grades of cellulose, starch and lactose are used as the carrier; whereas very fine particle size silica powder may be used as the coating material.

2. MECHANISM OF SOLUBILITY ENHANCEMENT:

The definite mechanism behind enhancement of solubility of drug in liquisolid tablets is the increased in surface area of drug available for release, an increase in aqueous solubility of drug, and improved wettability of drug particles present [9, 10].Due to notable increased in wetting property and surface area of drug available for dissolution [11]. The release is much greater than that of drug particles within directly compressed tablets. The drug dissolved in the liquid vehicle is incorporated into a carrier material which has porous surface. The liquid initially absorbed in the interior of the particles and it is captured by its internal structure, and after saturation of this process, adsorption of liquid onto the internal and external surfaces of porous carrier particles occur [12]. Liquid vehicle (Non-volatile solvent) present in liquisolid system can either acts as the surface active agent or has a low surface tension thus improves wetting of drug particles by decreasing interfacial tension between dissolution medium and tablet surface [13,14].

3. MATERIALS ABD METHODS:

3.1. Materials –

Repaglinide was obtained from Aurobindo Pharma limited, Hyderabad- India as a gift sample. Polyethylene glycol-400 was purchased from Merck Specialties Pvt. Ltd, Mumbai,

India. Microcrystalline cellulose (Avicel pH 101) and Silicic Avid (Aerosil 200) LR was purchased from Research- Lab Fine Chem. Industry. Mumbai (MS), India. Crosspovidone, Sodium Starch Glycolate, Magnesium Stearate was purchased from Scottish chemical industry, Mumbai (MS), India. All the other chemicals and reagents were of analytical grade.

3.2. Components of Liquisolid system – [15, 16, 17]

The major formulation components of Liquisolid tablets are:

1. Non- volatile solvent:

The solvent selected should possess ability to dissolve adequate amount of the drug candidate. Inert, preferably water-miscible and not highly viscous organic solvent systems having high boiling point e.g. propylene glycol, liquid polyethylene glycols, polysorbate, glycerin, N, N-dimethyl-acetamide; fixed oils etc. are the suitable vehicles.

2. Carrier material:

The carrier material should possess porous surface and closely matted fibers in the interior. Carriers are involved in the sorption process of liquid medication which improves the effective surface area for dissolution. These also assist the compression. Carriers due to relatively large, preferably porous particles, possess a sufficient adsorption property and matted fibers in interior contribute in absorption of liquid medication. e.g. various grades of cellulose, starch, lactose, sorbitol etc.

3. Coating material:

Coating material forms a uniform film around the particles of carrier. Thus they prevent the aggregation of particles as well as reduce the inter-particulate friction. This phenomenon improves the flowability as well as gives the Liquisolid a dry-looking appearance by covering the wet carrier particles and by absorbing any excess liquid. Coat materials are usually very fine (10 nm to 5,000 nm in 149 diameter) and highly adsorptive coating particles e.g. colloidal silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.

4. Disintegrant:

The use of disintegrant, its type and concentration in the formulation will be mainly based on the objective of the investigation. For solubility enhancement studies, incorporation of super-disintegrant is encouraged. Most commonly used disintegrant is sodium starch glycolate (Explotab13, Pumogel etc.). While for matrix type of systems intended for sustained release, disintegration is not required.

4. METHOD OF PREPARATION OF LIQUISOLID SYSTEM:

4.1. Determination of Solubility of Repaglinide –

The solubility determination of Nateglinide was carried out in distilled water, 0.1 N HCl, propylene glycol, polyethylene glycol, glycerol, glycerin and tween-80. The excess drug was added gradually to 10 ml of each solvent contained in 100 ml beaker. The beaker was place on magnetic stirrer for 48 hr until solubility equilibrium was reached. The solutions were filtered through Whatmann filter paper. Aliquots of the filtrate were suitably diluted and the dilutions were analyzed spectrophotometrically at 242 nm.

4.2. Application of mathematical model for preparation of liquisolid tablets:

4.2.1. Determination of liquid load factor (L*f*) –

It is defined as the ratio of liquid medication (w) to weight of coating material (q). It is determined by dissolving or dispersing the drug in non volatile solvent and to this carrier-coating material admixture is added and blended. The amount of carrier-coating admixture is used to convert free flow powder and is determined by using the following formula.

$$Lf = \frac{W}{Q}$$

Where,

W = Weight of liquid medication,

Q = Weight of carrier material,

The Φ value is for calculating excipients quantities.

Equation is,

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

Where, Φ and Φ are values of carrier and coating material [17].

It is used to calculate amount of carrier and coating material in each formulation.

The excipients ratio R of powders is defined as the ratio of carrier and coating material present in the formulation. R is suitably selected for successful formulation.

$$R = Q/q$$

Where,

Q = weight of carrier, q = coating material [18, 19]

4.2.2. Determination of holding capacity of the excipients –

The capacity of each excipient to hold liquid and behave like dry powder (holding capacity) was determined using the following simple technique: Different weights of Polyethylene glycol were transferred to a mortar. The constant weight of powder excipients was added

gradually and the mixture was triturated after each addition to help distributing the liquid throughout the powder particles. The addition of powder and the trituration was continued until mortar contents start to look like dry powder [20].

5. FORMULATION OF REPAGLINIDE TABLETS BY LIQUISOLID TECHNIQUE:

5.1. Preparation liquisolid tablets –

Weigh accurately 50 mg Repaglinide in each batch and place in the mortar and add the polyethylene glycol as non-volatile solvent to form liquisolid powder mix well. Add the small amount of the binary mixture of carrier and coating material (Avicel pH 102 and Aerosil 200) in it and mix. Depending upon the type of carrier in formulation, different liquid loading factors were employed in liquisolid preparations. Finally, 5 % (w/w) of Crosspovidone as disintegrant and 1% magnesium stearate were mixed with mixture for 5-10 minutes. Final mixture was compressed on 8 mm punch and die. The batch design is reported in table-I [21].

Table-1: Formulation design of REPA Liquisolid tablets

Ingredients	**Formulation code**								
Quantity(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Repaglinide	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
PEG – 400	100	100	100	200	200	200	300	300	300
Avicel pH-102	200	300	400	200	300	400	200	300	400
Aerosil-200	20	20	20	20	20	20	20	20	20
R*-Value	10	15	20	10	15	20	10	15	20
L*f**-Value	0.250	0.166	0.125	0.250	0.166	0.125	0.250	0.166	0.125
Total Weight (mg.)	220.5	320.5	420.5	220.5	320.5	420.5	220.5	320.5	420.5

(# 5% Crosspovidone + 1% Mg-stearate are added)

6. PREPARATION OF LIQUISOLID BASED TABLETS:

Calculated quantities of Repaglinide and Polyethylene glycol were accurately weighed in a 25mL glass beaker and stirred with glass rod until drug dissolve. Then assimilated the calculated quantities of carrier (Q) and coating materials (q). Mixing process is carried out in three steps as described by Spireas.et.al. [22]. Firstly, the system was blended at an approximate mixing rate of one rotation per second for approximately 10-20 minutes, in order to evenly layer on the surface of a mortar and left standing for approximately 5-10 minutes to allow the drug solution to be absorbed inside powder particles. In the third step, the powder was then scraped off the mortar surface using an aluminum spatula and then super

disintegrating agents like Crosspovidone and Magnesium stearate as lubricant was added to this mixture and blended with mortar. This provides the liquisolid based tablet, which finally compressed into tablet by using an 8mm diameter single punch tablet compression machine. The formulation was shown in table-1.

7. EVALUATIONS:

7.1. Flow Properties –

Flow properties of liquisolid formulation were studied by angle of repose, Carr's index, and Hausner's ratio. Each analysis was carried out in triplicate. Bulk density measurements were carried by placing a fixed weight of powder in a graduated cylinder, and the volume occupied was measured and the initial bulk density was calculated. The cylinder was then tapped at a constant velocity until a constant volume was obtained. The tapped density was then calculated. The angle of repose was calculated by the fixed-height cone method. All studies were done in triplicate. Then after the Carr's index, and Hausner's ratio was calculated from bulk and tapped density [20].

7.2. FTIR Spectra Analysis –

In the preparation of liquisolid Tablets, REPA and excipients may interact as they are in close contact with each other, which could lead to the instability of drug to overcome this problem, FTIR Spectroscopy was employed to ascertain the compatibility between REPA and excipients.

7.3. Evaluation of Liquisolid Tablets –

7.3.1. Hardness –

The hardness of liquisolid tablets was determined using Monsanto hardness tester. The mean hardness of each was determined.

7.3.2. Thickness and Diameter –

The diameter and thickness of tablets were calculated by Vernier caliper.

7.3.3. Weight variation –

Weight variation was measured by weighing 20 tablets and average weight was found of the individual tablet should fall within specified limits.

7.3.4. Friability –

As weight of tablet was less than 650 mg so tablets corresponding to 6.5 gm were taken for the test. All tablets were de-dusted carefully and weighing accurately the required number of tablets were placed in the drum and rotated about 100 times at an rpm of 25 in friability test

apparatus. Tablets were removed from the drum and loose dust was removed from the tablets, weighed accurately. The percentage weight loss was calculated.

7.3.5. Disintegration Test –

The disintegration test is done using USP disintegration test apparatus.

7.3.6. Uniformity of contents –

Five tablets were powdered and blend equivalent to 10mg drug. It was dissolved in methanol and absorbance taken at λmax 240. The tablet preparation complies with the test, only if each individual's content lies between 85 to 115% of the average content [23].

7.3.7. FTIR Spectrum Analysis –

In the preparation of liquisolid Tablets, REPA and excipients may interact as they are in close contact with each other, which could lead to the instability of drug. FTIR Spectroscopy was employed to ascertain the compatibility between REPA and excipients.

7.3.8. X-Ray diffraction study –

PXRD analysis was done by irradiating the samples with mono-chromatized Cu Kα radiation (1.506 Å) and analyzed between 3° and 60° (2θ) employing a Bruker AXS D8 Advance Diffractometer with Lynx Eye Detector. The step was at rate of 0.020^0 with step time of 32.8 sec. The diffractogram was produced by using Diffract plus Software.

7.3.9. Differential Scanning Calorimetry –

The powdered sample (3 mg) was hermetically sealed in aluminum pans and heated at a constant rate of 10 °C/min, over a temperature range of 30–300 °C with nitrogen flow rate of 30 ml/min. Thermograms of the samples were obtained using differential scanning calorimetry (DSC-60, Shimadzu, Japan). Thermal analysis data were recorded with Shimadzu software programs. Indium standard was used to calibrate the DSC temperature and enthalpy scale.

7.3.10. In-Vitro Release Study –

The test is designed to determine compliance with the dissolution requirement for solid dosage forms administered orally.

Dissolution test was performed in dissolution apparatus Type I (IP)/ Type II (USP).

Apparatus: Paddle

RPM: 50

Temperature: $37^0C \pm 2^0C$

Method: Tablet was placed in jar containing 900ml of *0.1M hydrochloric acid* for two hours and samples at different time interval 5ml of aliquots were removed and filtered through whatmann filter paper no.52 at time interval specified (10- 120 min) and 1ml sample was further diluted to 10ml using 0.1N HCl and analyzed by UV-Visible spectroscopy at 242 nm using 0.1M hydrochloric acid as blank.

Same method is perform for marketed drug (EUREPA-0.5 Torrent pharma) and plane drug (Repaglinide).

4. RESULTS AND DISCUSSION:

The aim of present search is to prepare and evaluate the liquisolid tablet of Repaglinide; water insoluble drug which shows the biological half life of 1 hrs. Liquisolid tablet of Repaglinide were prepared by using non-volatile solvent as drug solubilizing agent and super-disintegrating agent were used in the formulation for enhance the dissolution rate.

Repaglinide was selected as the model drug for this study, since it is a water-insoluble candidate, an ideal candidate for the potential of rapid-release liquisolid tablets. A standard graph is plotted in 0.1 N HCl by measuring absorbance at 242nm. The concentration was in the range of 5-30µg/mL to obey beer's Lambert law. The Standard graph of Repaglinide in 0.1 N HCl solution has obtained regression coefficient (r^2) of 0.999. It indicates the linearity of the graph and passing through the origin.

4.1. Determination of solubility of Drug –

The (figure-2) gives experimentally determined solubility of used drug substances in distilled water, 0.1 N HCl, polyethylene glycol, propylene glycol, Tween-80, Glycerin. The drug show low solubility in distilled water, Tween-80, Glycerin and shows significant solubility in 0.1 N HCl, polyethylene glycol and propylene glycol. Hence polyethylene glycol was used in study.

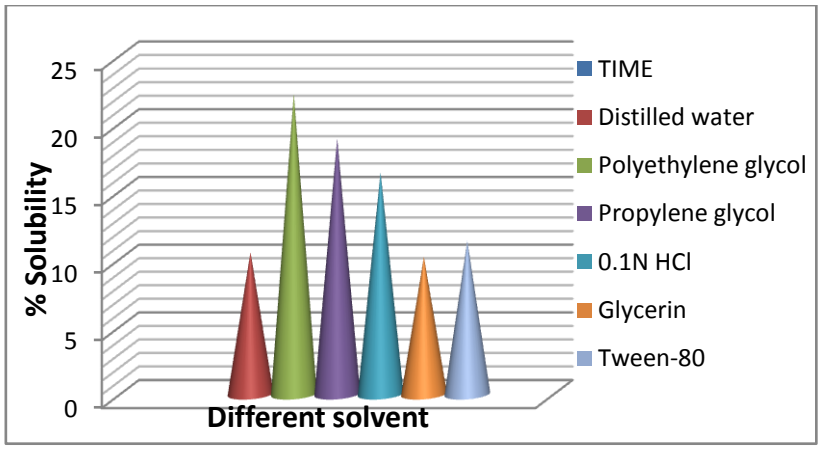
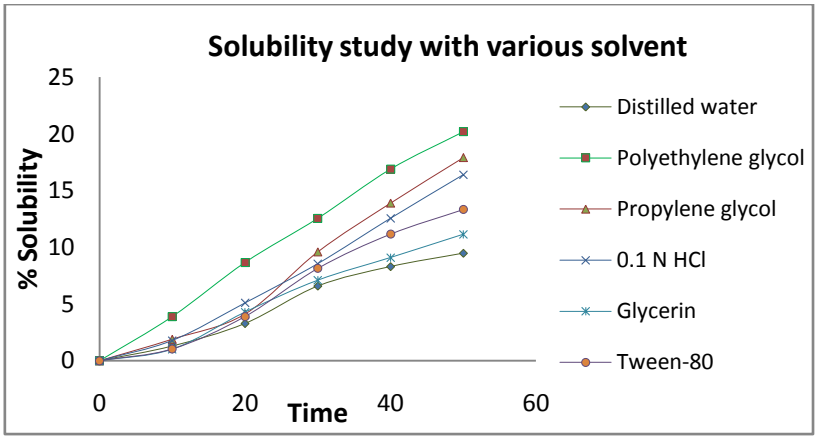


Figure-1: Drug Solubility profile of REPA



4.2. Flow Properties –

The flow properties of liquisolid powders were analyzed before compression to compact. By using bulk density, tap density, hausner's ratio, and Carr's index. The hausner's ratio below 1.15 shows good flowability for direct compressible tablet. The Carr's index is between 12 to 21 shows good to fair flowability. The angle of repose is between 27 to 31 shows good to fair flowability of powder. The Hausner's ratio of batch F7 shows normal value. The Carr's index of batch F7 shows more values. The angle of repose of the all batches shows acceptable results reported in table-2. The diameter and thickness of the tablets were varied with all batches because of the all bathes having variable in their weight. Uniformity of contents of tablets is between 85 to 115% which is acceptable for further study. Hardness of tablet was determined by Monsanto hardness tester hence average hardness was found to be between 2.0 to 3.0 kg/ cm^2, stated in table-3

Table- 2: Flow properties of Liquisolid powder system

Batch No.	Bulk density (gm/cm^3) ±S.D.	Tapped density (gm/cm^3) ±S.D.	Compressibility index (%) ±S.D.	Hausner's ratio ±S.D.	Angle of repose (ɵ) ±S.D.
F1	0.412 ± 0.012	0.481 ± 0.020	14.20 ± 0.059	1.166 ± 0.025	27.75 ± 1.340
F2	0.455 ± 0.021	0.528 ± 0.019	13.80 ± 0.058	1.160 ± 0.019	30.34 ± 1.224
F3	0.464 ± 0.010	0.537 ± 0.031	13.52 ± 0.058	1.156 ± 0.053	30.57 ± 1.234
F4	0.408 ± 0.011	0.485 ± 0.014	15.99 ± 0.045	1.190 ± 0.035	28.81 ±1.107
F5	0.462 ± 0.031	0.536 ± 0.022	13.80 ± 0.058	1.160 ± 0.026	29.05 ±1.134
F6	0.461 ± 0.021	0.535 ± 0.011	13.87 ± 0.056	1.161 ± 0.020	30.76 ±1.340
F7	0.416 ± 0.024	0.500 ± 0.016	16.68 ± 0.064	1.200 ± 0.040	28.51 ± 1.105
F8	0.468 ± 0.031	0.523 ± 0.021	10.34 ± 0.050	1.115 ± 0.012	30.76 ± 1.340
F9	0.459 ± 0.014	0.515 ± 0.031	10.81 ± 0.052	1.121 ± 0.015	30.01 ±1.230

Table- 3: Post- compression evaluation of liquisolid tablet

Batch Name	Parameters						
	Thickness (mm) ± S.D.	Hardness (kg/Cm^2) ± S.D.	Friability (%) ± S.D.	Uniformity of Content (%) ± S.D.	Uniformity of Weight (mg)		Disintegration time (Min) ± S.D.
					Avg Wt ± S.D.	% Variation ± S.D.	
F1	4.26 ± 0.001	2.53 ± 0.22	0.516 ± 0.03	98.05 ± 2.2	219.2 ± 1.12	0.440 ± 0.32	7.48 ± 0.25
F2	5.34 ± 0.002	2.56 ± 0.24	0.443 ± 0.02	98.26 ± 1.7	320.2 ± 2.10	0.327 ± 0.24	7.37 ± 0.18
F3	5.79 ± 0.007	2.90 ± 0.31	0.413 ± 0.01	99.39 ± 1.9	420.2 ± 3.12	0.321 ± 0.17	7.45 ± 0.20
F4	4.35 ± 0.001	2.56 ± 0.22	0.520 ± 0.04	98.40 ± 1.1	220.7 ± 1.15	0.449 ± 0.33	8.04 ± 0.08
F5	5.36 ± 0.003	2.60 ± 0.26	0.406 ± 0.02	98.62 ± 1.9	320.4 ± 3.10	0.306 ± 0.27	7.23 ± 0.22
F6	5.75 ± 0.005	2.89 ± 0.29	0.390 ± 0.01	98.47 ± 2.6	419.5 ± 3.10	0.319 ± 0.36	7.50 ± 0.14
F7	4.32 ± 0.002	2.40 ± 0.18	0.393 ± 0.01	99.50 ± 1.2	219.7 ± 1.10	0.482 ± 0.34	8.53 ± 0.21
F8	5.17 ± 0.01	2.35 ± 0.12	0.440 ± 0.02	98.56 ± 2.6	319.2 ± 2.08	0.332 ± 0.24	8.12 ± 0.18
F9	5.74 ± 0.003	2.50 ± 0.21	0.436 ± 0.01	99.17 ± 2.1	420.4 ± 3.05	0.391 ± 0.21	8.19 ± 0.05

The disintegration time revealed that the all formulations disintegrated in 10-15 min. All the Repaglinide liquisolid tablets had acceptable friability which had no exceed than the 1%, no tablet was crack or broken in all batches. Since all the prepared batches shows acceptable durability and withstand abrasion in handling, packaging.

4.3. FTIR Interference Study –

The FTIR spectrum of pure Repaglinide showed an absorption band at 3306.76 cm^{-1} (RCO-OH and C=C-CO-OH, stretching), 2840.60 cm^{-1} (-CH2 and RCH2CH3), 1585.67cm^{-1} (C-C in ring), 1635.52 cm^{-1} (RCONHR' 6-ring), 1496.66 cm^{-1} (C-C in ring and N-O nitro comp.), 1384.79 cm^{-1} (-CN3), 608.13 cm^{-1} (RC-CH). The FTIR spectrum of physical mixture and pure and pure Repaglinide show all the peaks for drug and excipients, hence no interaction was observed between them. The results were shown in figure-2 and figure-3.

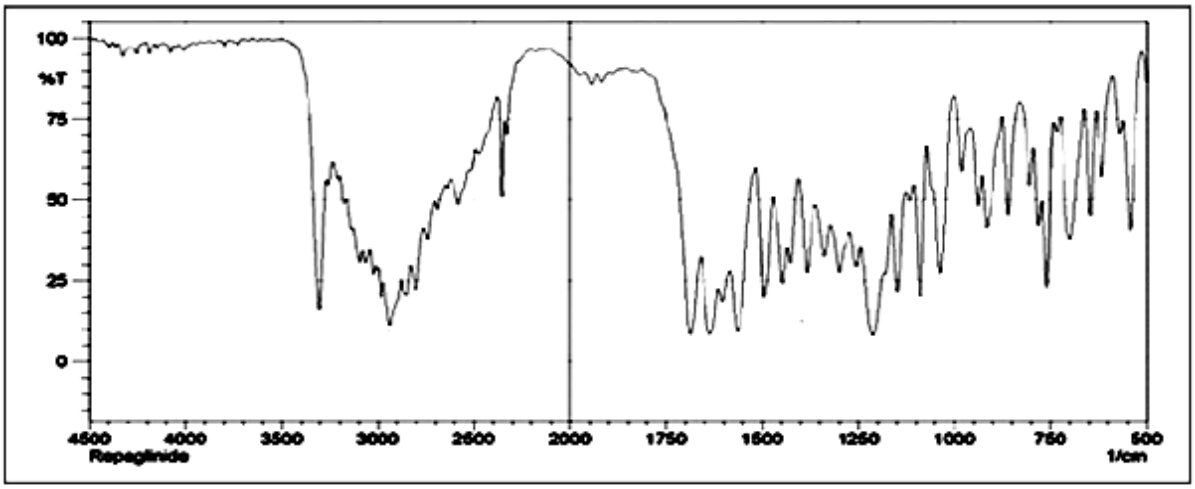


Figure-2 IR Spectra of plain Repaglinide

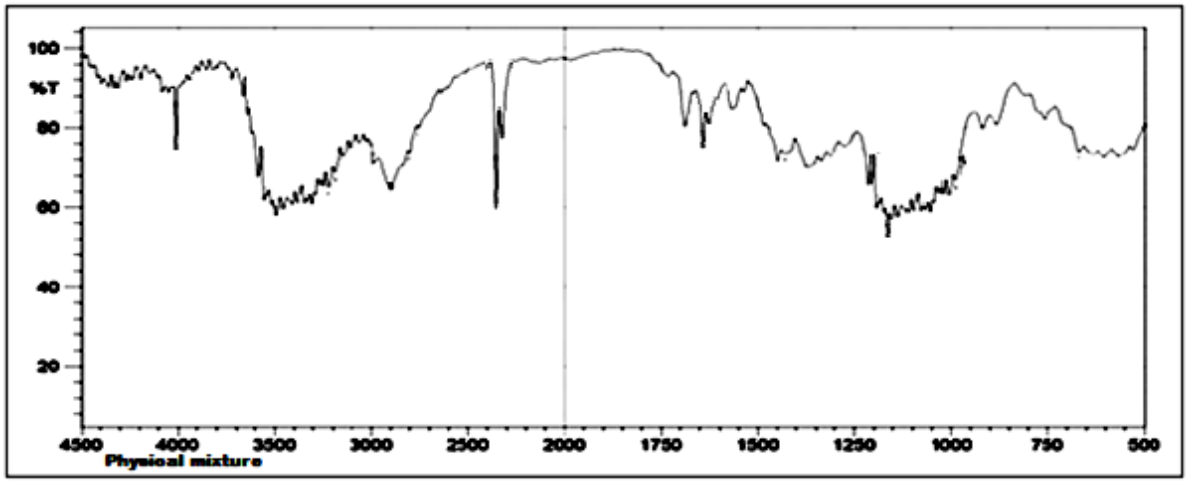


Figure-3 IR Spectra of Physical mixture

4.4. X-Ray Diffraction study –

X-ray diffraction patterns in (Figure-4) revealed that pure Repaglinide was clearly in crystalline state as it showed sharp distinct peaks notably at 2θ diffraction angles of 10.66 θ, 11.23 θ, 11.61 θ. In the (Figure-5) clearly show that the disappearance of 2θ angles in the liquisolid compact formulation is evident that crystalline pure drug is converted into amorphous state due to its molecular solubilization of the drug in the non-volatile solvent, which proves the enhancement of solubility by this technique.

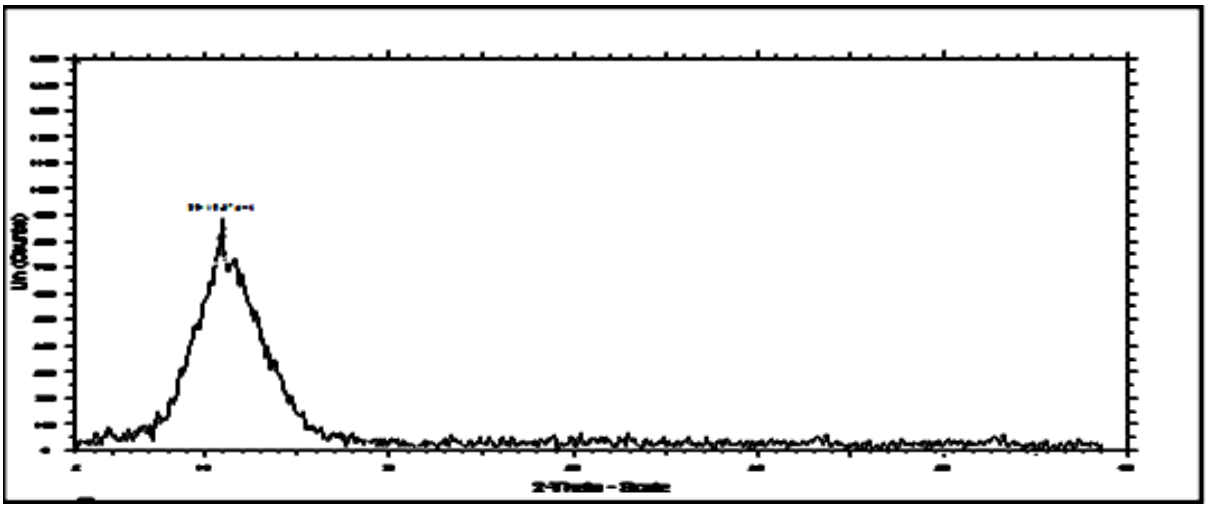


Figure-4: X-Ray Diffraction pattern of pure Repaglinide drug

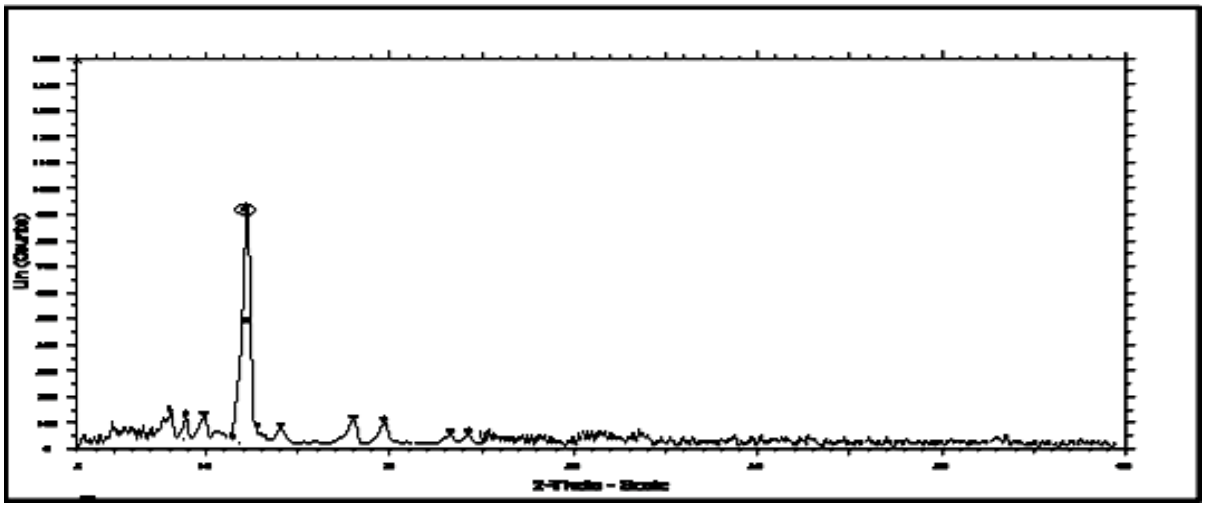


Figure-4: X-Ray Diffraction pattern of Physical mixture

4.5. Diffraction Scanning Calorimetry –

DSC thermograph of Repaglinide is shown in (figure-5) which shows melting endothermic at 138.99^{0}c (130^{0}c-140^{0}c) i.e. melting point and crystalline state of drug. DSC thermograph of Repaglinide liquisolid tablet is shown in (figure-6) which shows melting endothermic at 142.00^{0}c i.e. melting point and crystalline state of drug.

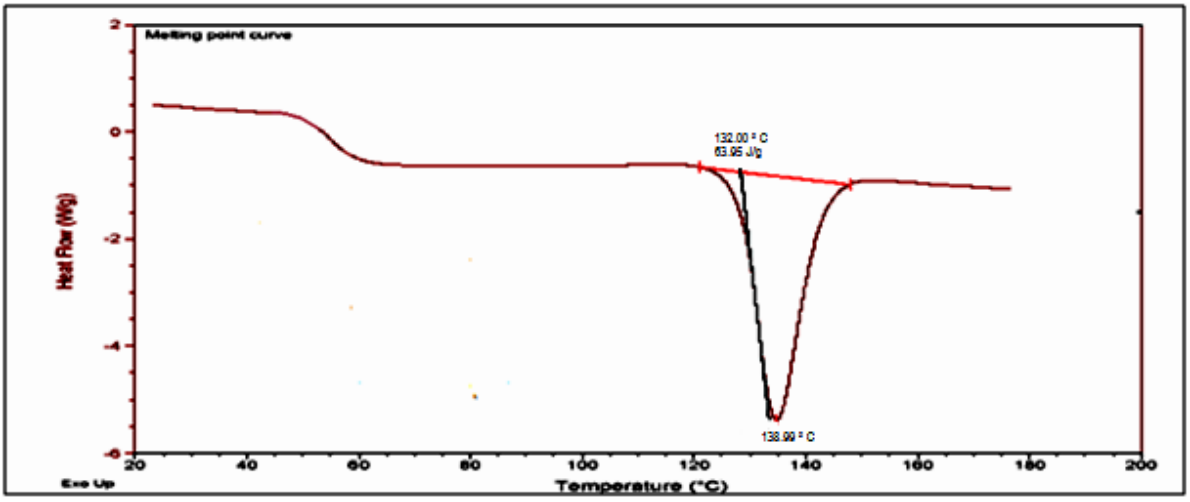


Figure -5: DSC Thermograph of REPAGLINIDE

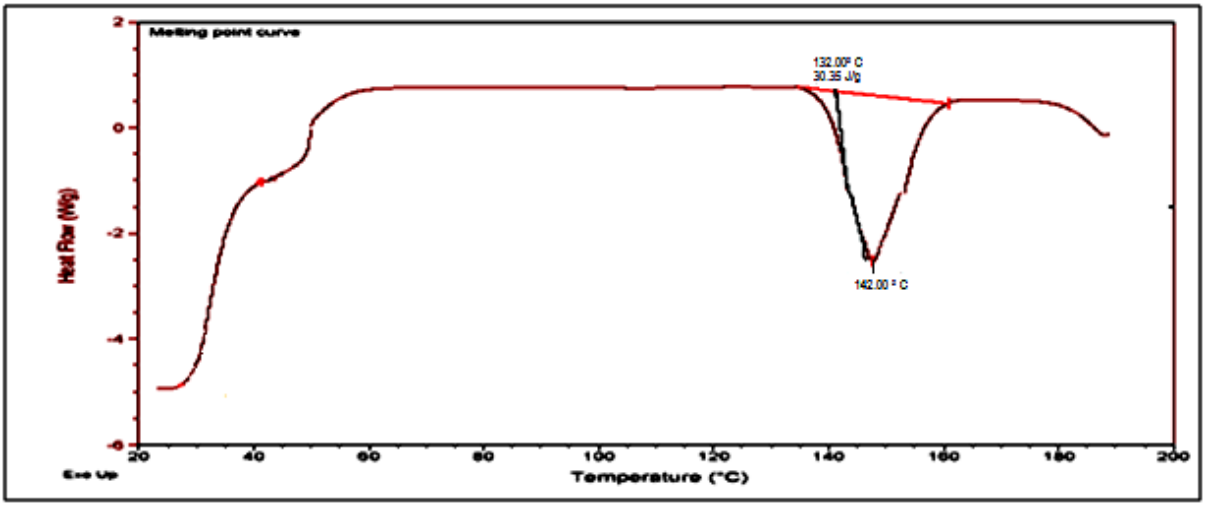


Figure -6: DSC Thermograph of REPAGLINIDE LIQUISOLID TABLET

4.6. In-Vitro Release Study –

In the dissolution study of Repaglinide liquisolid tablet the order of improving rate is F7 > F8 > F9 > F4 > F5 > F6 > F1 > F2> F3 shown in (figure-7). The batch F7 having 3:2 ratios showed more increase in solubility and dissolution having 73.60% cumulative drug release. Plain drug show 42.60% and marketed tablet (Torrent pharma, EUREPA-0.5) show 55.51 % release. Hence the batch (F7) was considered as optimized batch. It was also observed that the liquisolid tablet show the better drug release than plain drug and marketed tablet. Result were shown in (figure-7) and (figure-8).

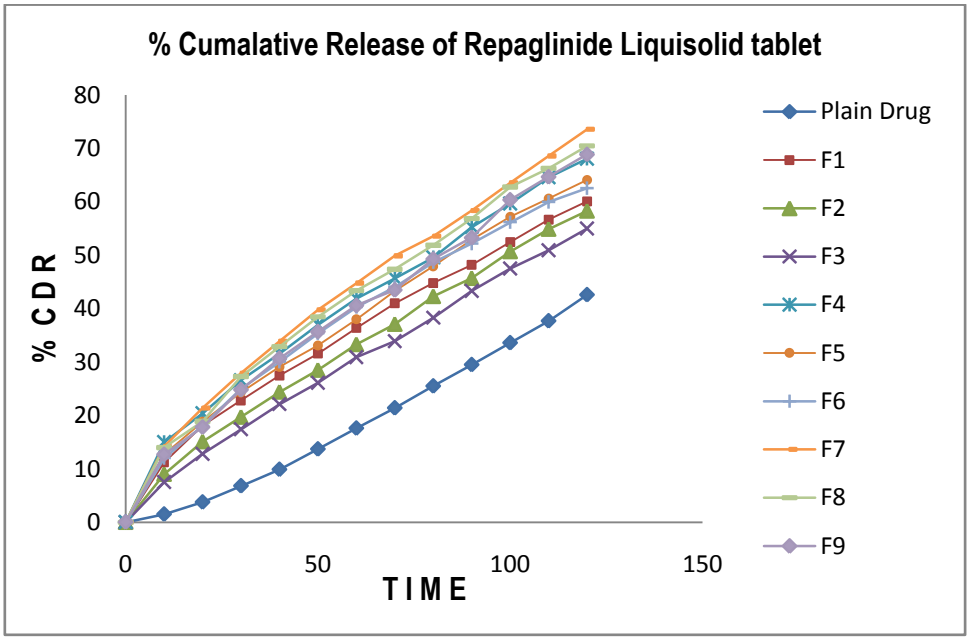


Figure-7: In-vitro profile of liquisolid batches

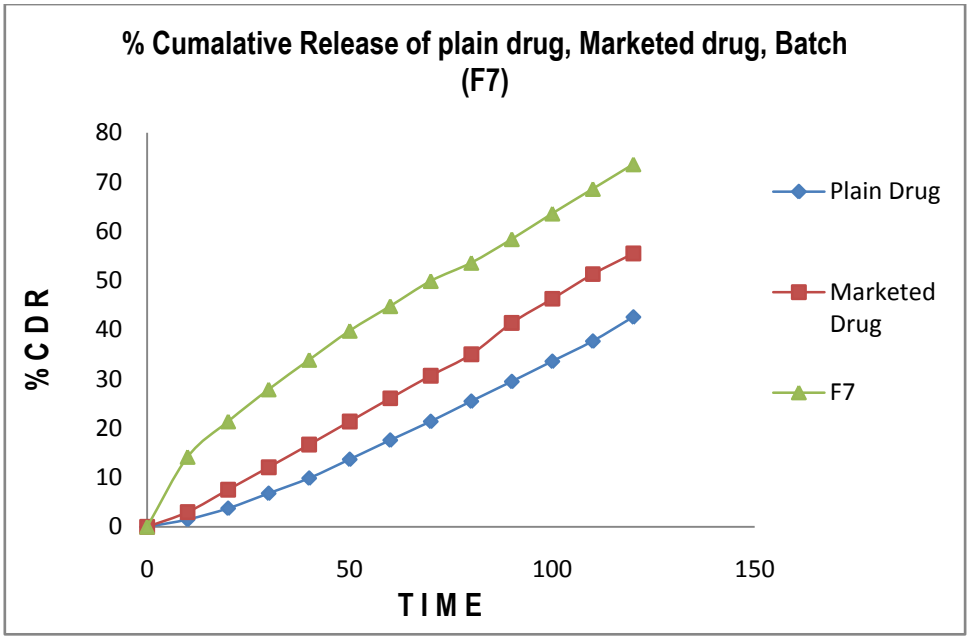


Figure-8: In-vitro profile of batch F-7 with Plain drug and Marketed tablet

4.7. Stability Study –

Results of stability studies showed that there was no significant change in organoleptic properties, hardness, disintegration, In-vitro study of Repaglinide liquisolid tablets. Thus the result showed that the formulations have good stability.

5.0. Discussion –

Liquisolid tablet is the technique in which the drug is mixed with non-volatile solvent and which is again mixed with carrier and coating material which have specified ratio and finally added super disintegrants and Glidants. Repaglinide tablet where prepared by liquisolid system. In literature the liquisolid tablet of Repaglinide no work on this technique for solubility enhancement hence the study is selected. Other techniques for solubility enhancement are given on this drug such as solid dispersion, nanoparticles, SEDDS. In this technique authentic mechanism of increasing in solubility is the wetting of drug particle and increase in surface area of the drug due to that the solubility of drug get increased. The research show that the solubility of Repaglinide is very less in water and hence the various non-volatile solvents having more solubility than the water hence among polyethylene glycol, propylene glycol, tween-80, glycerin shows more solubility of Repaglinide. Hence polyethylene glycol is selected for the preparation of liquisolid tablets. The microcrystalline cellulose (Avicel pH-102) and aerosil-200 was selected as carrier and coating material. Then Crosspovidone and MG-stearate was added as the disintegrant and Glidant in the formulation. The FT-IR, DSC and X-Ray diffraction studies show no interaction between drug and

excipients. The finally compressed into the tablets using tabletting machine by alternatively checking hardness of the tablets. The evaluation of the liquisolid tablets was done by two parts such as pre-compression study and post-compression study. In pre-compression study the all parameters like flow properties- bulk density, tap density, angle of repose, Hausner's ratio and Carr's index was performed and shows the significant results. In post compression evaluation the diameter, thickness, hardness, weight variation, disintegration time, friability was done. The in-vitro evaluation of the Repaglinide liquisolid tablets compared with all bathes the batch having more non-volatile solvent shows fast release of the drug from the tablets such as batch F7 shows fast release of drug than other bathes. The batch F7 which is compared with Plain drug and marketed tablets (MT) the liquisolid tablets shows significant release than that plain drug and marketed tablet. Hence the liquisolid tablet is the promising tool for enhancement of solubility of water insoluble drug.

CONCLUSION

The liquisolid tablets technique can be a auspicious standby for the formulations of water-insoluble drugs, such as Repaglinide (REPA) into fast release tablets. The higher dissolution rates of Formulation (F7) displayed by liquisolid tables may also implicit enhanced oral bioavailability due to the increased wetting properties and the surface of drug available for dissolution. It can also be concluded that from this study, the investigated liquisolid compacts of REPAGLINIDE with increasing the amount of carrier to coating ratio along with super disintegrating agent also resulted in higher dissolution rate, which are directly proportional to the amount of drug released.

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