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Formulation and Evaluation of Telmisartan Liquisolid Compact Tablets

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HUMAN

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ABSTRACT

Telmisartan is an Angiotensin Receptor Blocker and acts by blocking the effect of angiotensin II and used in the management of hypertension. Telmisartan is BCS class II drug having absolute bioavailability is 42-58%. The poor dissolution rate of water-insoluble drugs is still a major problem confronting the pharmaceutical industry. The liquid solid compact was found to be a promising technique for improving the dissolution rate of poorly soluble drug and to enhance the bioavailability of a poorly soluble, insoluble or lipophilic drug. The objective of the present investigation was to develop liquid solid compacts of Telmisartan to improve the dissolution enhance the dissolution rate, aqueous solubility & preparation of immediate release tablets of Telmisartan. Liquisoild compact was prepared using oleic acid as a nonvolatile solvent, microcrystalline cellulose, Neusilin US2, Fujicalinsg as a carrier material and Aerosil 200 as a coating material in different ratio. The interaction between drug and excipients was characterized by DSC and FT-IR studies, which showed that there is no interaction between drug and excipients. The powder characteristics were evaluated by different flow parameters to comply with pharmacopoeial limits. The prepared liquisolid powders were evaluated for the flow properties like tapped density, bulk density, the angle of repose, Carr's compressibility index and Hausner's ratio. The formulated liquisolid compacts were mixed with a super disintegrant (sodium starch glycolate), lubricant(magnesium stearate), the Glidant (talc) and compressed in to tablets (lsc1-lsc 6) and were evaluated for various post compression parameters such as hardness, friability, weight variation, content uniformity, disintegration time, wetting time. In addition, in vitro drug dissolution study was carried out. Stability studies were performed at 30^0C and 75%RH for one month. The formulation was found to comply with Indian pharmacopoeial limits for tablets.The dissolution studies of an optimized formulation(LSC 6) compared with plain drug and marketed preparation were carried out, and it was found that LSC 9 showed significant higher drug release rate than plain drug and marketed preparation. From this study, it was concluded that the liquisolid compact technique is an effective approach to enhance the dissolution rate of Telmisartan.

INTRODUCTION

Solubility is one of the most important physicochemical properties of any drug because low solubility can affect the bioavailability of orally administered dosage forms. Thus, it is very important to enhance the solubility of a poorly soluble drug. For absorption, a drug must be present in the form of an aqueous solution at the site of absorption. Solubility defines as the phenomenon of dissolution of the solute in the solvent to give a homogeneous system. Low aqueous solubility is the major problem with formulation development of new chemical entities. Poorly water-soluble drugs often require high doses in order to reach therapeutic plasma concentrations after oral administration.[1] The BCS is a scientific framework for classifying a drug substance based on aqueous solubility and intestinal permeability and dissolution criteria.[2]

Liquisolid drug delivery system has gained the attention of pharmaceutical researchers due to its contribution in the solubility enhancement as well as dissolution retarding approaches depending on the need and design of the formulation.

The liquisolid technique as described by Spires is a novel concept, where a liquid may be transformed into a free flowing, readily compressible and apparently dry powder by simple physical blending with selected carrier and coating material. The liquid portion, which can be a liquid drug, a drug suspension or a drug solution in suitable non-volatile liquid vehicles, is included in the porous carrier material.[3]

Telmisartan is angiotensin II receptor blocker (ARB), which is used in the prevention and treatment of hypertension. It belongs to class II drugs, these types of drugs according to biopharmaceutical classification system characterize by low aqueous solubility and high permeability and often solubility is the rate-limiting step for absorption [9]. Thus, one of the major problems with telmisartan is its low solubility in biological fluids, which results into poor bioavailability after oral administration (~42%) and late onset of action [4].

In this study, telmisartan was selected as a model drug, since it is a very slightly water-soluble drug, and thus, it establishes an ideal candidate for testing the potential of rapid-release liquisolid compacts. The flowability and compressibility of liquisolid compacts were addressed simultaneously in the ‘‘new formulation mathematical model of liquisolid systems”, which was used to calculate the appropriate quantities of the excipients (carrier and

coating materials) required to produce acceptably flowing and compressible powders based on new fundamental powder properties called the flowable liquid retention potential.

MATERIALS AND METHODS

Telmisartan was received as a gift sample from Cipla pharmaceutical (Patalganga, Mumbai), Neusilin US2, Fujicalin SG was received as a gift sample from Gangwal chemical industries(Mumbai).Sodium starch glycolate (SSG), Microcrystalline cellulose, Aerosil 200, Oleic acid was purchased from Research Lab (Mumbai), Magnesium Stearate, Talc were of analytical grade.

1. Preformulation study

1.1 Determination of Drug Solubility in Various Non Volatile Solvents[5]

The solubility study was assessed using shake flask method. The solubility of Telmisartan as the pure drug was determined in polyethylene glycol 6000, propylene glycol, polyethylene glycol-400, oleic acid, HCl pH1.2, phosphate buffer pH 6.8, tween 20, tween 80. Excess quantities of the pure drug were added in 25 mL of solvent in 250 mL conical flask and shaken for 72 hours at room temperature on rotary flask shaker. The entire samples were protected from light by wrapping the flask in aluminum foil. After the time, a sample was filtered and diluted. The absorbance of the resulting solution was measured by UV spectrophotometer at 295.30nm.solubility data are reported in Table 1 & 2, Figure 1 & 2.

1.2 Determination Flowable Liquid-Retention Potential (ø -value)[6]

Powder admixture containing 5 gm of either carrier or coating with increasing quantity of nonvolatile liquid vehicle (oleic acid) were mixed using a mortar and pestle. Each admixture angle of repose is measured.

In constant weight of carrier/coating material (NeusilinUS2, Fujicalin SG, MCC as the carrier and Aerosil 200 as coating material), increasing amount of solvent (oleic acid) was incorporated and on each addition, an angle of repose was determined. The flowable liquid retention potential (Ø -value) of each liquid/powder admixture was calculated using the following equation.

Ø value = weight of liquid/weight of solid

The Ø -values were plotted against the corresponding angle of repose (for optimal flow properties). Corresponding to 33^0 of a liquid/powder admixture represented the flowable liquid-retention potential. Liquid retention potential is given in Table 4.

1.3 Determination of Liquid Load Factors (Lf) & Carrier and Coating Ratio (R Value)[5,6]

Appropriate amounts of carrier and coating materials were used to produce an acceptable flowing and compactible powders, which were, be calculated using following equation.

$$\mathbf{Lf} = ØCA + ØCO\ (1/R)$$

Where,

Øca and Øco value of carrier and coating material.

The maximum amount of liquid loads on the carrier material, termed ‘‘load factor” (Lf). R is calculated by using following equation

$$\mathbf{R = Q/q}$$

R represents the ratio between the weights of the carrier (Q) and coating material (q) present in the formulation.

Where,

Q- Weight of carrier material

q -weight of coating material

The data are shown in Table 5.

2. Drug-Excipient Compatibility Studies [7]

Different types of excipients like Aerosil 200, Neusiline US2, Fujicalin SG, were kept for drug-compatibility study. This study was carried out for physical characterization and determination of related substances. It mainly included Fourier-transform infrared (FT-IR).The drug –excipient compatibility study is shown in figure 3.

3. Preparation of Telmisartan Liquisolid Compact [5, 7, 8]

1. The drug Telmisartan was initially dispersed in the nonvolatile solvent (oleic acid) termed as liquid vehicles with the different drug: vehicle ratio.

2. Then a mixture of carrier and coating materials were added to the above liquid by continuous mixing for a period of 10 to 20 minutes in a mortar. The amount of carrier and coating materials are enough to maintain acceptable flow and compression properties. Preparation of liquisolid blend is shown in Table 1.

Table 1: Preparation of telmisartan liquisolid compact

Formulation code	Ingredients								
	Drug (gm)	R	LF	Oleic acid (gm)	MCC (gm)	Neusilin US2 (gm)	Fujicalin SG (gm)	Aerosil 200 (gm)	Total weight (gm)
LSC 1	0.02	10	0.469	0.1	0.665	-	-	0.066	0.851
LSC 2	0.02	12	0.444	0.1	0.702	-	-	0.058	0.880
LSC 3	0.02	15	0.419	0.1	0.744	-	-	0.049	0.913
LSC 4	0.02	10	1.009	0.1	-	0.227	-	0.022	0.369
LSC 5	0.02	12	0.984	0.1	-	0.233	-	0.019	0.372
LSC 6	0.02	15	0.959	0.1	-	0.239	-	0.015	0.374
LSC 7	0.02	10	0.645	0.1	-	-	0.312	0.031	0.463
LSC 8	0.02	12	0.620	0.1	-	-	0.325	0.027	0.472
LSC 9	0.02	15	0.595	0.1	-	-	0.338	0.022	0.480

4. Evaluation of Blend of liquisolid Compact [9, 10]

The characterization of the mixed blend was done for determination of mass-volume relationship parameters. The evaluated parameters are the angle of repose, bulk density, tapped density, Hausner's ratio and compressibility index. Evaluation parameter is represented in table 6.

1. Angle of Repose

The angle of repose was determined by using fixed funnel method. The 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 interparticle 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. The angle of repose was determined by substituting the values of the base radius 'r' and height of the pile 'h' in the following equation.

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Here, h = Height of pile

r = Radius of pile

θ = Angle of repose

2. 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.

Bulk density(ρ) = (Weight of the powder /bulk volume)

3. Tapped Density

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

Tapped Density = (Weight of the powder / tapped volume)

4. Carr's Index

It is used to evaluate flowability of powder by comparing the bulk density and tapped density of a powder. The percentage compressibility of a powder is the direct measure of the

potential of powder arch or bridge strength is calculated according to the equation given below.

Compressibility Index (%) = [(Tapped density –Bulk Density) X 100] / Tapped density

5. Hausner's Ratio

Hauser's ratio is an important character to determine the flow property of powder and

Granules. This can be calculated by the following formula·

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

5. Formulation of Telmisartan Liquisolid Compact Tablets [7]

Direct Compression

Different tablet batch formulations (LSC1-LSC9) were prepared by direct compression method. To the above binary mixture (Liquisolid compact) disintegrant like sodium starch glycolate and another remaining additive like magnesium stearate as a lubricant and talc as glidant are added according to their application and mixed in the mortar. Then the final mixture was directly compressed into tablets to achieve tablet hardness or encapsulation. Tablet hardness was kept within the range of 3-5kg/cm^2. Formulation of the liquisolid compact is shown in Table 7.

6. Evaluation of Liquisolid Compact Tablets [11-15]

All the formulations were subjected to weight variation, thickness, hardness, friability, drug content, *in-vitro* disintegration time, *in-vitro* dissolution studies were carried out. All the formulations were passed the parameter, which was shown in Table 8.

1. Weight Variation

With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. In practice, 20 tablets were taken and weighed individually on a digital weighing balance. Average weight was calculated and the individual tablet weight was compared to the average. The tablet passes the test if no more than two

tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

% deviation=individual weight of tablet -Average weight/average weight ×100

2. Thickness

The thickness of tablet is important for uniformity of tablet size. Thickness was measured using Vernier calipers. It was determined by checking three tablets from each formulation. Thickness was reported in Table 8

3. Hardness

Hardness is defined as the "force required to break a tablet in the diametric compression test." Hardness is hence, also termed as the tablet crushing strength. The resistance of tablets to breakage under conditions of storage, transportation or handling before usage depends on its hardness. Tablet hardness was measured with Pfizer tester. The tablet was held between a fixed and moving jaw. The scale was adjusted to zero and load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of the hardness of the tablet. Hardness was expressed in kg/cm2. Hardness was reported in Table 8

4. Friability Test

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Friability generally reflects poor cohesion of tablet ingredients. The initial weight of 10 tablets is taken and these are placed in the friability, which is consist of a circular plastic chamber, divided into 2-3 compartments. The chamber rotating at 25 rpm for 4min and drops the tablets by a distance of 15cm and gives 100 revolutions. After that, the tablets are weighed once again. The difference in the weight is noted and expressed as the percentage. It should be preferably below 1.0%. Friability was reported in Table 8

%Friability = [(W1-W2)/W1] X 100)

Where,

W1= weight of tablets before test,

W2 = weight of tablets after test

5. Content Uniformity

Five tablets were powdered; and20mg equivalent weight of Telmisartan was accurately weighed and transferred to a 100ml volumetric flask. Initially, 10ml of methanol was added and shaken for 10min.Then; the volume was made up to 100ml with phosphate buffer pH 6.8. The solution in the volumetric flask was filtered, diluted suitably, and analyzed spectrophotometrically at 295.30 nm using UV-visible double-beam spectrophotometer (UV1800, Shimadzu, Japan).Content uniformity was reported in Table 8

6. Disintegration time

In vitro disintegration time was measured using USP disintegration test apparatus (Electrolab ED-2AL). Randomly six tablets were selected from each batch for disintegration test. Disintegration test was performed in 900ml distilled water at 37±0.5°C temperature and at the rate of 30±2 cycles/min. Disintegration time was reported in Table 8.

7. Wetting Time

Wetting time is the important step for disintegration process to take place a circular tissue paper of 10 cm diameter was placed in three Petri dish with a 10cm diameter, one in each after folding. 10 ml of simulated salivary solution (phosphate buffer pH 6.8) was poured into the tissue paper placed in the Petri dish. A tablet was placed carefully on the tissue paper surface. The time needed for the solution to arrive the upper surface of the tablet was recorded as the wetting time. The percentage deviation was calculated and results were tabulated. Wetting time was reported in Table 8

8. *In-Vitro* Dissolution Studies [16]

Details of Dissolution Test

- Apparatus: USP Type – II (Paddle)
- Volume of medium: 900 mL
- Temperature: 37± 0.5°C
- Speed: 50 rpm
- Dissolution medium used : 0.1N HCl (pH1.2) & PB(pH6.8)

- Aliquot took at each time interval: 10 ml
- Time : 5,10,15,20,25,30,35min
- Filter: Whatman filter paper

The *in vitro* dissolution study of liquisolid formulations was performed using USP-XXIV Type-II paddle Apparatus-II (Electrolab, Mumbai Model TDT- 08L, India).

900 ml phosphate buffer pH 6.8 and 900ml 0.1N HCl pH 1.2 maintained at 37±0.5°C was used as dissolution medium stirred at 50rpm. At appropriate intervals (5, 10, 15, 20, 25, 30, and 35min), 10 ml aliquots were periodically collected and replaced 10ml fresh prepared dissolution media to maintaining sink condition[7,8]. After filtration through 0.45 µm membrane filter, Telmisartan was estimated spectrophotometrically at 295.30 nm. Cumulative percentage drug release was calculated in both dissolution media using an equation obtained from a calibration curve. All drug release experiments were conducted in triplicate (n=3). The results of HCl pH 1.2 are shown in Table 9, and the result of phosphate buffer pH 6.8 are shown in Table 10**.** A plot of comparison is shown in Figure 6,7.

9. Evaluation of Optimized Formulation [17,18]

1 FTIR Spectroscopy

The FTIR spectra of LSC 6 formulation were recorded on Shimadzu, Japan. (Model FTIR-8400S) using KBr pellet from over the wave number 4000 to 600 cm^{-1}.range. The pellets were prepared by mixing 5mg of the sample with 100mg potassium bromide and compacted under vacuum at a pressure of about 12,000psi for 3 minutes. FITR spectra of liquisolid compact is showed in Figure 8

2 X-Ray Powder Diffraction (XRD)

The XRD patterns of optimized formulation LSC 6 were recorded at room temperature on Simens D5000 X-ray diffractometer using Ni-filtered Cu K radiation (wavelength 1.540 ˚A).The X-Ray diffraction patterns are shown in Figure 9

3 Differential Scanning Calorimetry (DSC)

DSC studies of optimized formulation LSC 6were performed using a Mettler Toledo (*SW920). the instrument was calibrated with an indium standard. Accurately weighed

samples (5–10mg) were placed in closed, pierced, flat bottom aluminum pans. DSC scans were recorded at a constant heating rate of 10^0C/min from 30 to 350^0C. Nitrogen gas was pumped at a flow rate of 80 mL/min. The thermogram of optimized formulation (LSC 6) was showed in Figure no. 10

10. Comparison of *In-vitro* Dissolution Profile of Plain Drug, Opti mixed Formulation and Marketed Preparation.[8,19]

In vitro dissolution studies for batch LSC 6, Plain drug and conventional marketed tablet in HCl pH 1.2 and phosphate buffer pH 6.8 were carried out using USP apparatus type II at 50 rpm.The results are shown in Table 11, 12. A plot of comparison is shown in Figure 11, 12

11. Accelerated Stability Study of Optimized Formulation [7,19]

Stability study was conducted by storing tablet at 30°C/75% RH for a period of one month. The content and dissolution behaviors from Telmisartan liquisolid compact tablets were tested monthly for one month, which is shown in Table 13 and Table 14**.**

Each tablet was individually weighed and wrapped in aluminum foil and packed in black PVC bottle and put at above-specified conditions in a heating humidity chamber for three months. After each month, tablet sample was analyzed for hardness, dissolution and drug content. The results are shown in the form of plots in Figure13 and Figure 14.

RESULT AND DISCUSSION

1. Preformulation study

1.1 Solubility studies

Telmisartan was selected as a model drug for these studies since it is water insoluble drug and thus ideal candidates for testing the potential of rapid release of liquisolid compact solubility studies in different media at different pH were conducted to find a suitable dissolution medium that provides sink condition. Solubility data of drug Telmisartan in various liquid vehicles are shown in Table 2 & Table 3 Telmisartan appears to be more soluble in oleic acid than other vehicles. The solubility is an important factor in liquisolid systems, as the higher solubility of the drug in the liquid vehicle can lead to higher dissolution rates since the drug will be more molecularly dispersed and more surface of a drug will be exposed to the dissolution medium. The solubility of Telmisartan in oleic acid was found to be 22µg/ml as

were represented in Table 2. Therefore, oleic acid was the appropriate solvent in the preparation of Telmisartan liquisolid compact. Solubility is graphically represented in Figure 1 & 2.

Table 2: Solubility data of telmisartan in various nonvolatile solvents

Non Volatile Solvent	Solubility (µg/ml)
Polythene glycol	11.30
Polypropylene glycol 6000	4.14
Polypropylene glycol 400	2.56
Tween 20	1.10
Tween 80	1.47
Oleic acid	22.00

Table 3: Solubility data of telmisartan in various dissolution media

Dissolution Media	Solubility (µg/ml)
Phosphate buffer pH 6.8	0.41
HCl pH 1.2	2.69

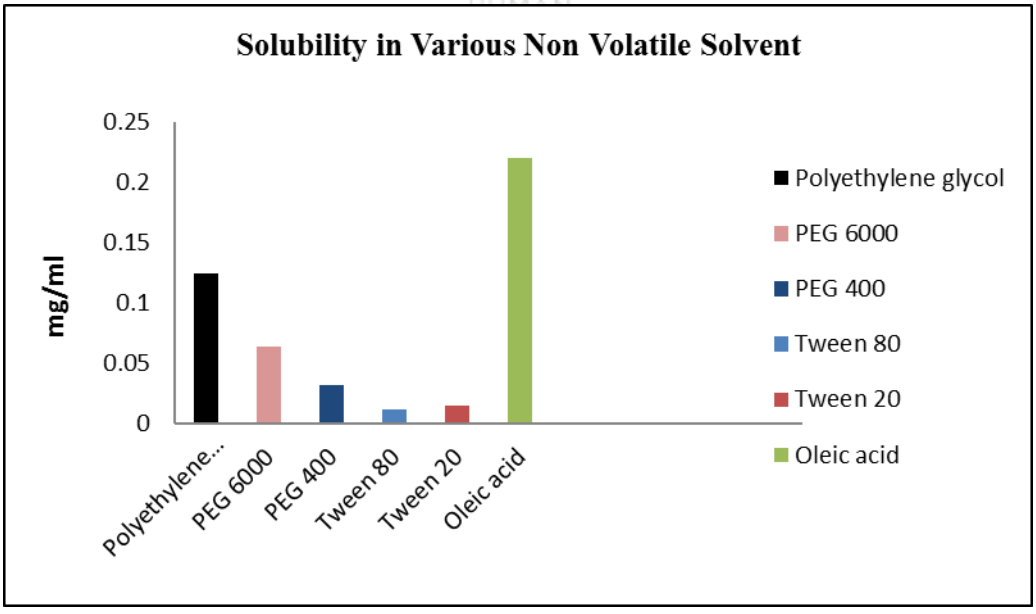


Figure 1: Solubility data of Telmisartan in various nonvolatile solvents

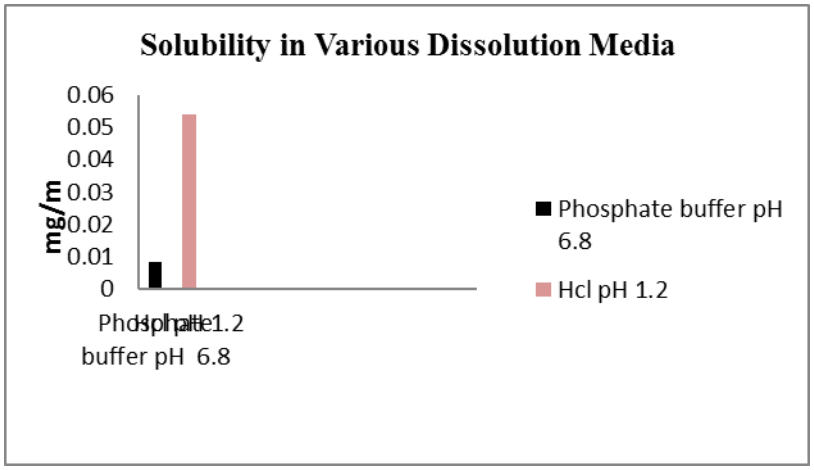


Figure 2: Solubility data of telmisartan in various dissolution media

1.2 Determination of Flowable Liquid Retention Potential of Carrier and Coating Material in Oleic Acid

Table 4: Flowable liquid retention potential

MCC		Neusilin US2		Fujicalin SG		Aerosil 200	
Angle of repose (Θ)	Liquid retention potential Φ-value	Angle of repose (Θ)	Liquid retention potential Φ-value	Angle of repose (Θ)	Liquid retention potential Φ-value	Angle of repose (Θ)	Liquid retention potential Φ-value
33±0.16	0.190	35±0.12	0.780	33±0.17	0.496	35±0.18	0.783
37±0.14	0.166	33±0.15	0.860	35±0.13	0..470	33±0.14	1.490
34±0.19	0.175	37±0.13	0.833	34±0.16	0.512	34±0.16	1.28

From above result, Neusilin US2 and fujicalin SG showed greater Liquid retention potential i.e 0.860 & 0.496 respectively than microcrystalline cellulose (0.190) due to the high specific surface area of Neusilin US2 and Fujicalin SG. The Φ values obtained for 3 different ratios are given in **Table 4.**

1.3 Determination of R & Liquid Load Factor

The loading factor was found out by taking the selected solvent in a mortar and then adding the selected powder excipients in small increments with constant mixing, till a free flowing powder was produced. The weight of the excipients required to produce the free flowing powder was found out. The corresponding loading factor was then calculated using the formula LF= W/Q. The coating material (Aerosil 200) was also added where required to get the required powder flow property.

Table 5: Carrier: coating ratio & LF

Carrier: Coating ratio (R)	LF		
	MCC	Neusilin US2	Fujicalin SG
10	0.469	1.009	0.645
12	0.444	0.984	0.620
15	0.419	0.959	0.595

Where, R= Ratio of carrier to coating ratio;

Lf= Liquid load factor.

A formulation containing R = 15 showed good flowability than the formulation containing R = 10. This could be probably due to the presence of higher amount of silica in R=15. The aerosol is known to be hydrophobic in nature in nature, which retards the flow properties. At higher R-values the greater amount of carrier may overcome to some extent the flow properties of the powder. From above result, it can be concluded that the liquid load factor increase (LF) with decrease carrier to coating ratio (R).The ratio R=15 is selected for the formulation of Telmisartan liquisolid compacts. Further, the compressible liquid retention potential for R=15 is determined and obtained as 0.866 (NeusilinUS2:Aerosil200), 0.496(fujicalinSG: Aerosil200) and 0.190 (Microcrystalline cellulose: Aerosil 200) admixtures. From the values of loading factor, it is evident that Neusilin has the best carrying capacity than Fujicalin and Microcrystalline cellulose. The data is reported in Table 5.

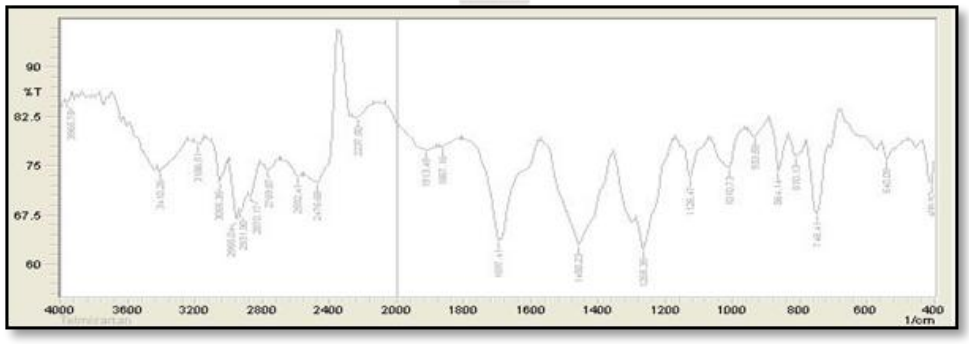
2. Drug Excipient compatibility study

1. Fourier Transform Infrared Spectroscopy (FTIR)

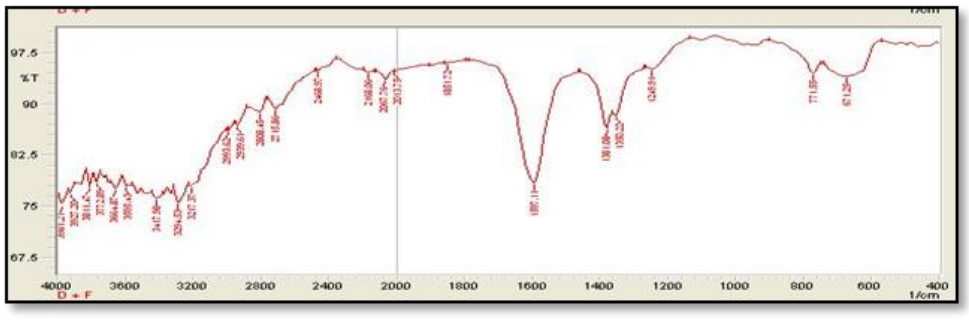
The Fourier transform infrared spectroscopy (FTIR) spectrum of Telmisartan was studied. IR spectra of Telmisartan presented in following Figures 3.These peaks can be considered as characteristic peaks of Telmisartan. Telmisartan shows N –H stretch at 3410.26 $^{cm-1}$, C-H Stretch(Aromatic) at 3055.35 $^{cm-1}$, OH at 3185.51 $^{cm-1}$, C-H Stretch Aliphatic at 2955.04 $^{cm-1}$, Carbonyl group at 1697.41 $^{cm-1}$, C=C Aromatic bend & stretch at 1458 $^{cm-1}$, C=O at 1867.16 $^{cm-1}$.

The IR spectra did not show any significant difference from those obtained for their physical mixture. These obtained results indicate that there was no positive evidence for the interaction between Telmisartan and Neusilin US2, Fujicalin SG and Aerosil 200. These results clearly indicate that the above excipient can be used without any interaction for the preparation of Telmisartan liquisolid compact tablets.

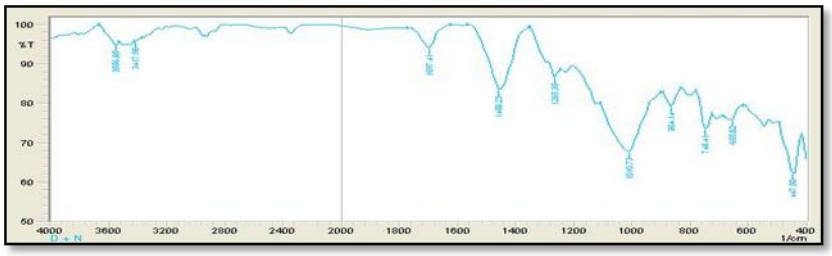
A.Telmisartan Pure Drug



B. Neusilin US2



C. Fujicalin SG



D. Aerosil 200

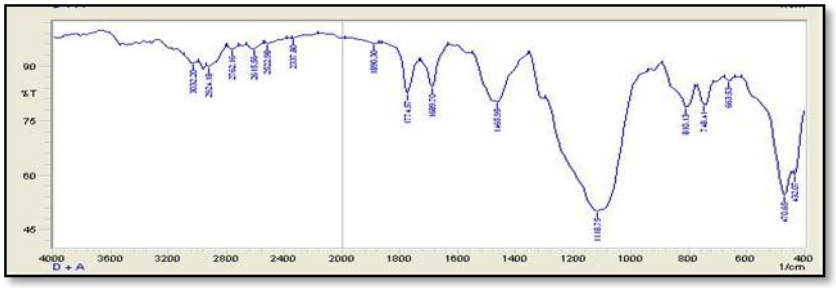


Figure 3: A: FTIR Spectra of Telmisartan pure drug. B: Neusilin US2**.** C: Fujicalin SG**.** D: Aerosil 200

2 X-Ray Powder Diffraction (XRD):

The API was subjected to powder X-Ray diffraction. The X ray diffractogram of Telmisartan exhibited several sharp peaks at the different angle (2θ) suggested that the drug existed as crystalline nature. The diffraction patterns of the pure drug were shown in Figure 4.

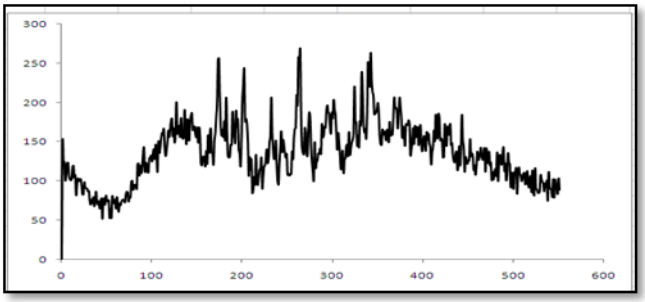


Figure 4: X-Ray diffraction pattern of telmisartan

3. Differential Scanning Calorimetry:

DSC of pure Telmisartan showed a characteristic, sharp endothermic peak at 272.86°C which is associated with the melting point of the drug and indicated the crystalline nature of Telmisartan Thus indicates the purity and confirmation of Telmisartan. The DSC thermogram of the pure drug was shown in Figure 5.

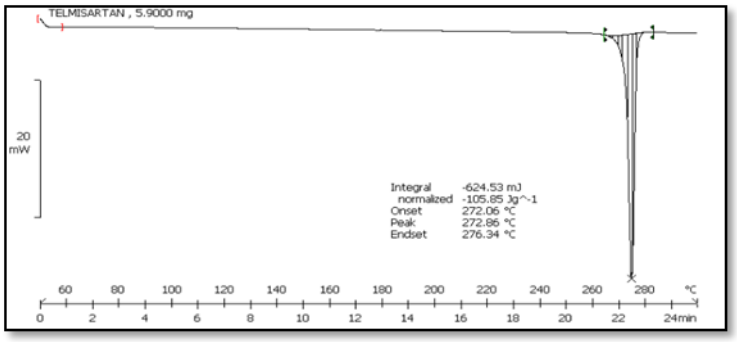


Figure 5: DSC thermogram of telmisartan

3. Preparation of liquisolid Blend

Liquisolid blend is prepared by using three carriers to coating ratio (R).i.e R 10(MCC: Aero sil200), R12 (Neusilin US2: Aerosil200), R15 (Fujicalin SG: Aerosil 200). Liquisolid blend was formulated as represented in above Table 1**.**

4. Evaluation of liquisolid Blend

The characterization of the blend was done for determination of mass-volume relationship parameters. The evaluated parameters are the angle of repose, bulk density, tapped density, Hausner's ratio and compressibility index was reported in Table 6.

Table 6: Evaluation liquisolid blend

Formulation code	Parameter				
	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of repose (Ɵ)	Compressibility Index (%)	Hausner's Ratio(H_R)
LSC 1	0.277 ±0.0097	0.381±0.006	37.82±0.49	27.22±0.117	1.37±0.0160
LSC 2	0.270 ±0.0092	0.352±0.012	38.79±0.61	23.24±0.159	1.30±0.011
LSC 3	0.297± 0.017	0.401±0.015	39.30±0.92	25.59±0.115	1.34±0.016
LSC 4	0.243± 0.014	0.289±0.017	27.85±0.25	15.60±0.160	1.18±0.014
LSC 5	0.248 ±0.016	0.290±0.008	28.86±0.92	14.42±0.105	1.16±0.010
LSC 6	0.227 ±0.018	0.263±0.013	27.11±0.49	13.63±0.150	1.15±0.012
LSC 7	0.326 ±0.014	0.400±0.015	29.79±0.61	18.63±0.013	1.23±0.016
LSC 8	0.294 ±0.015	0.352±0.015	28.82±0.41	16.47±0.145	1.19±0.017
LSC 9	0.277 ±0.011	0.328±0.018	30.30±0.60	16.93±0.140	1.20±0.012

All the studies were done in triplicate

5. Formulation of Telmisartan Liquisolid Compact Tablets

Different tablet batch formulations (LSC1-LSC9) were prepared by direct compression method. Liquisolid compact tablets were formulated as represented following table

Table 7: Formulation of telmisartan liquisolid compact tablets

Formulations	LS1	LSC2	LSC3	LSC4	LSC5	LSC6	LSC7	LSC8	LS9
Ingredients	**Unit formula(mg per tablet)**								
Telmisartan in oleic acid	100	100	100	100	100	100	100	100	100
Carrier:coating ratio(R)	10	12	15	10	12	15	10	12	15
Load factor	0.469	0.444	0.419	1.009	0.984	0.959	0.645	0.620	0.595
MCC	665	702	744	-	-	-	-	-	-
Neusilin US2	-	-	-	227	233	239	-	-	-
Fujicalin SG	-	-	-	-	-	-	312	325	338
Aerosil 200	66	58	49	22	19	15	31	27	22
SSG	50	50	50	50	50	50	50	50	50
Magnesium stearate	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10
Total	**901**	**930**	**963**	**419**	**422**	**424**	**513**	**522**	**530**

6. Evaluation of Telmisartan Liquisolid Compact Tablets

Table 8: Evaluation of telmisartan liquisolid compact tablets

Formulation code	Parameter						
	Thickness	Hardness test (Kg/cm^2)	Friability Test (%W/W)	Weight variation (%)	Drug content	Disintegration time (min)	Wetting time (sec)
LSC 1	4.3± 0.08	4.5± 0.4	0.83± 0.07	900±0.12	78.44±2.94	7.15±0.13	60±0.14
LSC 2	4.1 ± 0.12	4.7± 0.3	0.80± 0.05	931±0.32	81.37±2.31	7.23±0.09	65±0.095
LSC 3	4.5 ± 0.06	4.4± 0.5	0.82± 0.06	962±0.52	84.33±2.51	7.30±0.16	56±0.019
LSC 4	3.4 ± 0.08	4.6± 0.3	0.67± 0.03	420±0.46	86.30±2.48	2.01±0.0152	50±0.068
LSC 5	3.1 ± 0.11	4.4±0.4	0.68± 0.04	423±0.24	97.71±3.76	1.18±0.020	48±0.11
LSC 6	3.3± 0.09	4.1± 0.2	0.65± 0.02	425±0.65	99.82±3.60	1.15±0.015	45±0.054
LSC 7	3.6 ± 0.13	3.5± 0.3	0.71± 0.09	512±0.85	90.21±2.99	4.10±0.025	51±0.047
LSC 8	3.4 ± 0.04	3.7± 0.5	0.75± 0.12	521±0.68	91.30±2.78	3.45±0.010	63±0.032
LSC 9	3.5 ± 0.15	3.0± 0.4	0.72± 0.07	531±0.24	93.88±2.71	3.27±0.12	54±0.059

All the nine formulations passed weight variation test as the % variation was within the pharmacopoeial limit of ± 5%. It was found to be from 420±0.46 to 962±0.52mg. Thickness was found in the range from 3.1±0.011 mm to 4.2±0.15mm. Liquisolid compact formulation with Neusilin US2 and Fujicalin SG as a carrier showed less thickness as compared to the Microcrystalline cellulose. This is due to higher SSA of carrier that enables to load higher amount of liquid. Hardness was found to be within 4.1±0.2kg/cm2 to 4.7 ±0.3 kg/cm2. Friability was found well within the approved range of 0. 65± 0.02 to 0.83±0.07 % i.e. less than 1 %.Results revealed that the prepared tablets; resistance to loss of weight indicate the tablet's ability to withstand abrasion in handling, packaging, and shipment and good mechanical strength. The drug content of the tablets was found between drugs. All the formulations show disintegration time 1.15±0.015 to7.30±0.16. All the prepared liquisolid tablets had a disintegration time less than 8 min for liquisolid preparation intended for immediate drug release characteristics. The wetting time in all the formulation was very fast. This may be due to the ability of swelling and the capacity of absorption of water. All the formulations show wetting time 45±0.054 to 65±0.095 (sec).

All the nine formulations were subjected for the *in vitro* dissolution studies using tablet dissolution apparatus (USP) TDT-08L, Electrolab. Percentage drug release was calculated based on the mean amount of Telmisartan present in the respective tablet. The percentage of drug release in HCl pH1.2 at 35 min was 99.20% for LSC-6. The percentage of drug release in phosphate buffer pH 6.8 at 35 min was 99.82%.

The results obtained in the *In vitro* drug release for the all formulations LSC1 to LSC9 are tabulated in Table 9 & Table 10.The concentration of drug in liquid medication is an important aspect as it affects drug release.

The powder excipient ratio (R) also plays an important role in drug release rate ,it can be concluded from obtained data that there was a direct relationship between the power excipient ratio (R) and the release of drug from liquisolid tablets, when R value increases, the release rate will also increase i.e: liquisolid tablets of R=15 had higher drug release than liquisolid tablets of R=12, which had more release than that tablet of R= 10.so it can conclude from given data that LSC 9 was the best liquisolid formulation having optimized release profile among all other preparation.

These increases in dissolution rate of liquisolid tablets are because these formulations contain a solution of drug in non the volatile vehicle used for a preparation of the liquiusolid compact; the drug surface area available for dissolution is significantly increased.

Table 9: *In-vitro* dissolution profile of all liquisolid formulation in HCl pH 1.2

Time (min)	Cumulative % drug release								
	LSC 1	**LSC 2**	**LSC 3**	**LSC 4**	**LSC 5**	**LSC 6**	**LSC 7**	**LSC 8**	**LSC 9**
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	7.05±0.89	11.02±2.21	13.16±1.56	25.28±3.48	30.25±2.31	33.02±2.16	16.49±3.14	20.05±1.47	23.20±1.91
10	15.23±2.31	19.54±3.19	20.15±3.04	36.25±4.70	41.76±3.25	47.54±2.46	20.55±1.40	25.35±2.90	29.64±3.67
15	28.98±2.48	31.25±2.47	35.14±3.42	42.56±2.69	59.42±1.24	63.99±2.63	35.71±3.86	36.34±3.34	41.74±4.48
20	40.65±1.82	48.38±2.50	50.58±2.05	57.87±2.39	68.71±3.58	72.95±3.86	42.02±5.48	47.75±3.21	50.63±5.58
25	51.45±3.36	61.14±2.27	68.89±2.28	71.43±1.96	76.89±1.48	81.41±2.49	62.84±2.60	66.86±1.68	70.71±3.03
30	60.21±2.10	68.30±2.53	78.69±4.20	58.51±2.40	89.84±2.59	91.73±2.53	71.05±5.40	76.10±3.94	81.14±3.32
35	75.39±3.64	80.43±2.65	82.54±2.60	94.84±3.27	97.31±2.48	99.20±2.87	85.21±3.20	87.71±1.25	90.02±1.90

Results are mean of three determinations

Table 10: *In-vitro* dissolution profile of all liquisolid formulation in phosphate buffer pH 6.8

Time (min.)	Cumulative % drug release								
	LSC 1	LSC 2	LSC 3	LSC 4	LSC 5	LSC 6	LSC 7	LSC 8	LSC 9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	7.34± 1.51	11.39±4. 48	14.77± 4.13	27.51± 3.53	31.32±1. 55	34.89±3. 04	17.69±0. 87	20.15± 2.50	24.95±2. 99
10	16.20 ±3.13	20.45±3. 70	23.8 ±2.74	39.24± 4.87	42.84±2. 33	46.30±4. 06	24.98±3. 24	26.85± 2.98	35.72±2. 78
15	29.03 ±4.39	32.84±2. 67	38.23± 2.69	45.49± 3.70	60.71±2. 31	67.20±3. 18	38.53±2. 35	38.93± 2.71	40.95±4. 47
20	42.65 ±2.05	49.48±4. 46	52.34± 3.44	60.10± 3.55	71.33±1. 25	73.26±2. 52	44.12±1. 56	56.85± 3.21	58.63±2. 59
25	55.85 ±3.48	63.58±2. 34	70.49± 2.63	75.43± 2.49	78.44±3. 45	82.32±1. 89	67.43±2. 54	75.45± 3.60	77.85±2. 53
30	63.38 ±3.03	68.09±2. 28	79.32± 3.51	82.41± 3.39	90.21±3. 51	93.31±3. 23	84.70±2. 83	86.69± 3.22	87.79±3. 80
35	78.44 ±2.94	81.37±2. 31	84.33± 2.51	86.30± 2.48	97.71±3. 76	99.82±3. 60	90.21±2. 99	91.30± 2.78	93.88±2. 71

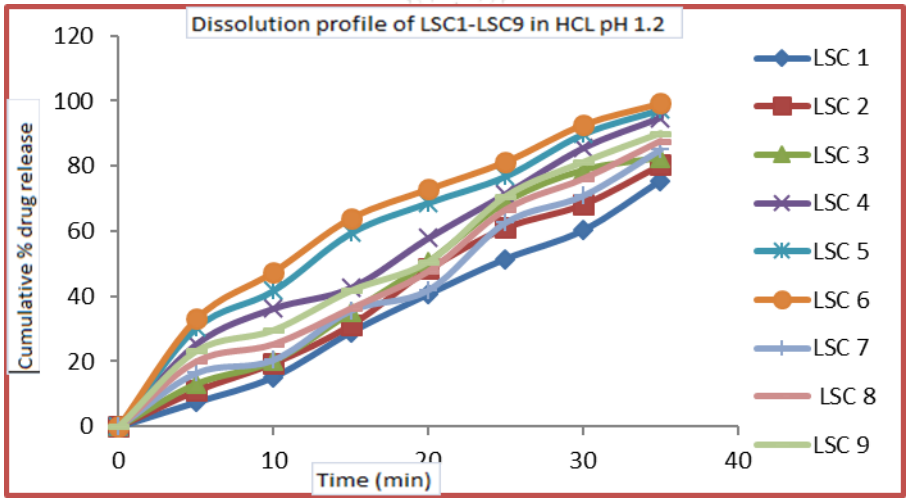


Figure 6: *In-vitro* Dissolution Profile of all liquisolid formulation in hydrochloric acid pH 1.2.

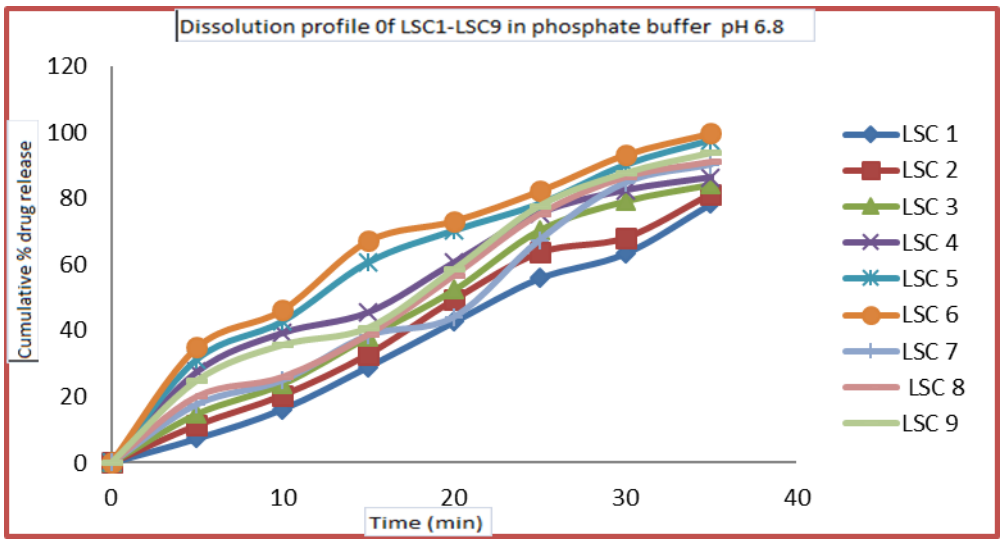


Figure 7: *In-vitro* dissolution profile of all liquisolid formulation in phosphate buffer pH 6.8.

From above evaluation parameter like hardness, friability, disintegration time & *in-vitro* dissolution study, we conclude that the formulation of LSC 6 was selected as optimized formulation.

9 Evaluation of Optimized Formulation

1. FITR of liquisolid Compact (LSC 6)

FITR spectra of the liquisolid compact are shown in Figure 8**.** The appearance of all these peaks and absence of any new peaks in the liquisolid formulation indicate no chemical interaction between the drug and excipients. In that major functional group of the Telmisartan shows no change or slight change from the standard value. From this study concluded that the above-given drug and excipient was compatible with each other. Drug excipients interaction studies revealed that there is no interaction between drug and excipients.

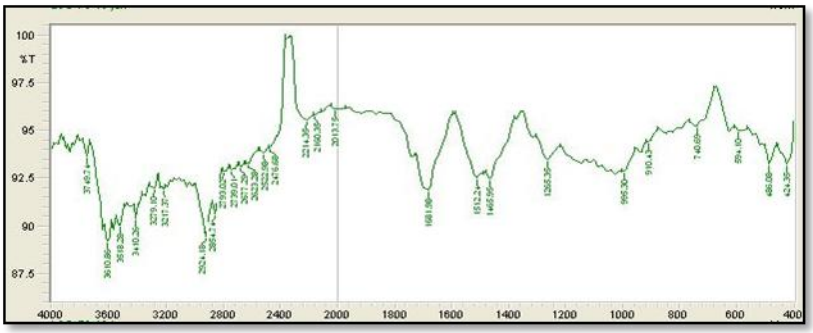


Figure 8: FTIR spectra of liquisolid compact (LSC 6).

2 X-Ray Diffraction

The optimized formulations were subjected to powder X-Ray diffraction. In the pure drug (Telmisartan) the diffraction patterns of the pure drug were present (though with reduced intensity). But in the liquisolid systems, all the peaks of the Telmisartan was lost. So it can be inferred that in the liquisolid system the crystal lattice of the drug was absent suggesting that the drug was present in the molecularly dispersed form in the liquisolid systems. The X-Ray diffraction patterns are shown in Figure 9

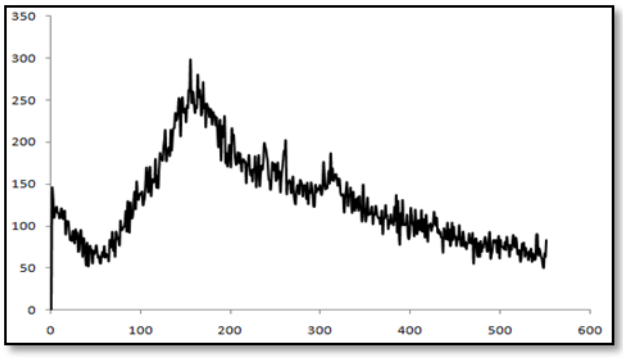


Figure 9: X-Ray diffraction pattern of liquisolid compact (LSC 6)

3 DSC Thermogram of Optimized Formulation (LSC 6):

The thermogram of the optimized batch (LSC 6) showed complete loss of the Telmisartan peak which is due to the fact that the drug has lost its crystalline structure and is present in its molecularly dispersed form. Hence it can be inferred that Telmisartan has been completely solubilized in Oleic acid. The thermogram of optimized formulation (LSC 6) was showed in Figure10

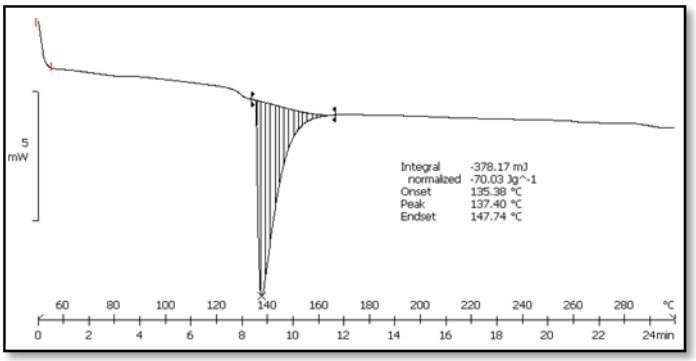


Figure 10: DSC thermogram of optimized formulation(LSC 6).

10. Comparison of *Invitro* Dissolution Profile:

A liquisolid formulation having optimized release profile among all other preparation. From Figures 11,12, it can be seen that the release rate of liquisolid compacts was higher than that of marketed tablet and plain drug. The percentage of drug release in HCl pH1.2 at 35 min was 99.20% and 50.45% and 67.40 for LSC-6, marketed tablet and, plain drug respectively are shown in table 10.and figure 10.The percentage of drug release in phosphate buffer pH 6.8 at 35 min was 99.82% and 62.19% and 70.22 for LSC-6, marketed tablet and plain drug respectively.

This increases in dissolution rate of liquisolid tablets are because these formulations contain a solution of drug in non-volatile vehicle used for the preparation of the liquiusolid compact; the drug surface area available for dissolution is significantly increased. Therefore, in the case of liquisolid compact, the surface area of drug available for dissolution is much greater than of the marketed tablet. The data are represented in table 11,12.

Table 11: Comparison of *In vitro* dissolution profile of plain drug, optimized batch & marketed preparation in HCl pH 1.2

Time in (min)	Cumulative % drug release		
	Plain drug	Optimized batch(LSC 6)	Marketed preparation
0	0.00	0.00	0.00
5	20.59±1.52	33.02±2.16	5.89±2.37
10	31.52±2.06	47.54±2.46	10.68±2.49
15	39.43±1.16	63.99±2.63	17.87±1.34
20	48.25±1.15	72.95±3.86	28.09±1.02
25	52.48±1.01	81.41±2.49	33.71±2.57
30	64.75±0.92	91.73±2.53	41.74±4.35
35	67.40±0.99	99.20±2.87	50.45±3.91

Results are mean of three determinations

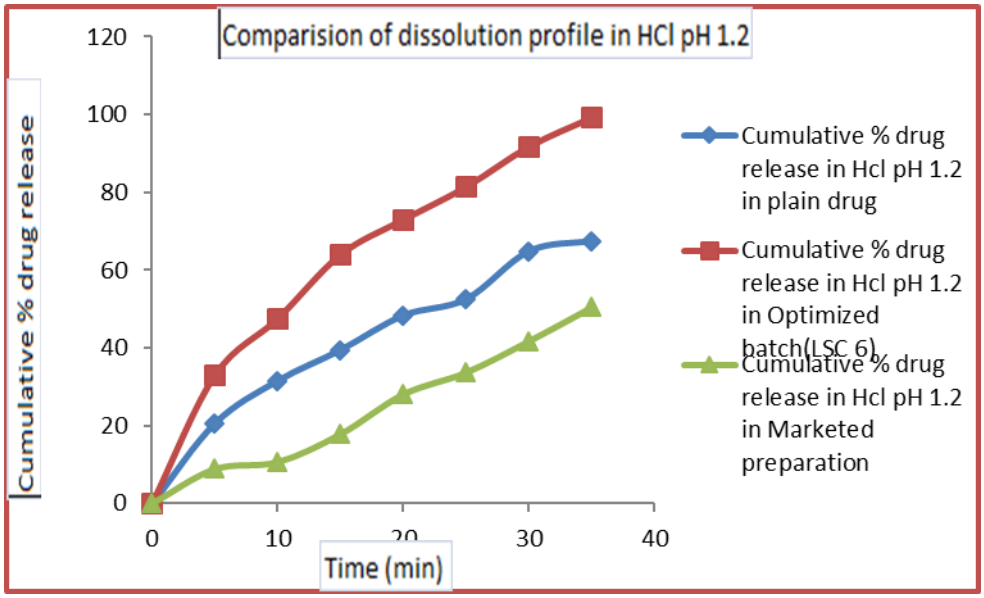


Figure 11: Comparison of *In-vitro* dissolution profile of plain drug, optimized batch and marketed preparation

Table 12: Comparison of *In vitro* dissolution profile of plain drug, optimized batch & marketed preparation in phosphate buffer pH 6.8

Time in (min)	Cumulative % drug release		
	Plain drug	Optimized batch LSC 6	Marketed preparation
0	0.00	0.00	0.00
5	25.34±0.94	34.89±3.04	8.26±1.42
10	34.67±1.47	46.30±4.06	13.86±2.05
15	48.55±2.48	67.20±3.18	21.36±1.23
20	52.85±2.10	73.26±2.52	32.62±6.23
25	58.6±2.15	82.32±1.89	47.67±5.03
30	67.41±1.52	93.31±3.23	58.29±2.3
35	70.22±2.39	99.82±3.60	62.19±0.12

Results are mean of three determinations

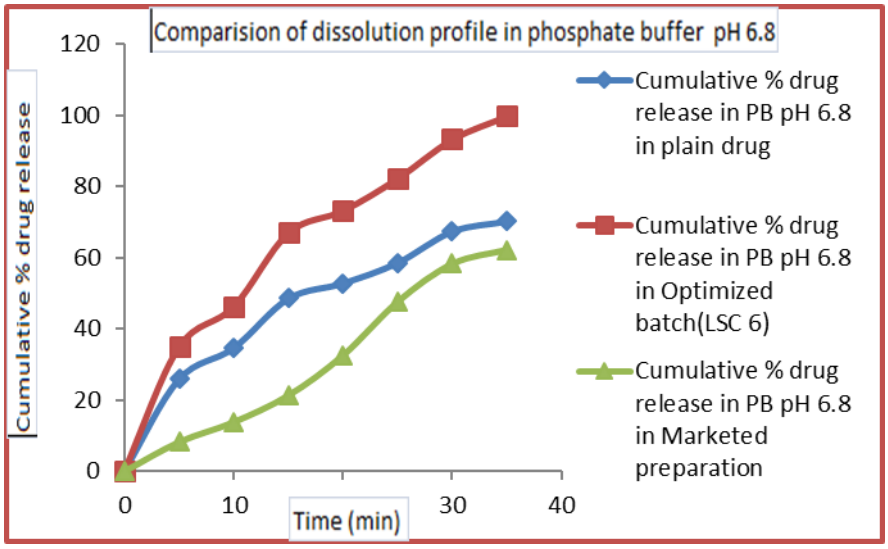


Figure 12: Comparison of *Invitro* dissolution profile of the plain drug, optimized batch and marketed preparation.

11. Accelerated Stability Study of Optimized Formulation

Selected Formulation was subjected to stability studies as per ICH guidelines. Following conditions were used for Stability Testing. The formulations LSC 9 was selected for stability studies based on their high cumulative percentage drug release and result of *in vitro* disintegration time studies. The stability studies were carried out at 30^0C/75 percentage relative humidity for the selected formulation up to one month. For every 1-month time interval, the tablets were analyzed for drug hardness, disintegration time, percentage drug release up to 1months. These formulations show not much variation in any parameter. The results obtained are tabulated in Table13,14 and represented in Figure 13,14.

Table 13: Stability data for optimized formulation at 30^0C/75%RH

Formulation	Parameter Evaluated	Initial	After 1 month
LSC 9	Hardness(kg/cm^2)	4.1±0.2	4.91±0.16
	Disintegration time (min)	1.15±0.66	1.17±0.43
	Content uniformity (%)	99.82±0.21	99.81±0.14

Table 14: Dissolution profile of optimized formulation lsc 6 after one-month stability study.

Time (Min)	Initial		1st Month	
	HCl pH 1.2	Phosphate buffer pH 6.8	HCl pH 1.2	Phosphate buffer pH 6.8
0	0.00	0.00	0.00	0.00
5	33.02±2.16	34.89±3.04	33.00±2.30	34.85±9.34
10	47.54±2.46	46.30±4.06	47.40±2.06	45.24±3.48
15	63.99±2.63	67.20±3.18	62.15±3.58	65.46±6.25
20	72.95±3.86	73.26±2.52	70.95±2.35	72.31±4.36
25	81.41±2.49	82.32±1.89	80.24±2.96	80.12±5.23
30	91.73±2.53	93.31±3.23	90.46±3.24	92.36±1.25
35	99.20±2.87	99.82±3.60	98.62±1.50	98.54±0.96

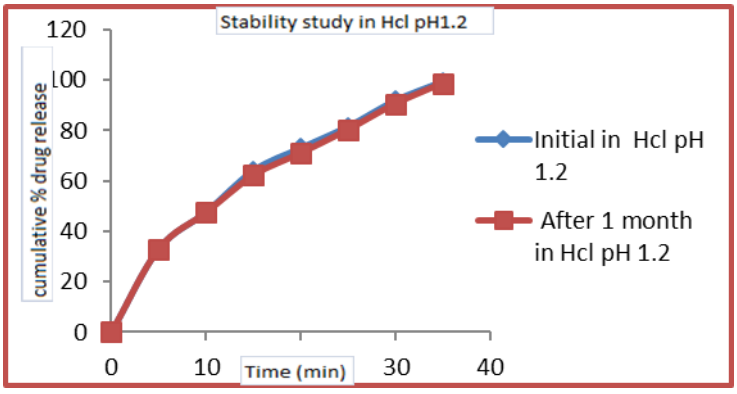


Figure 13: Dissolution profile of LSC 6 after one-month stability study in HCl pH 1.2.

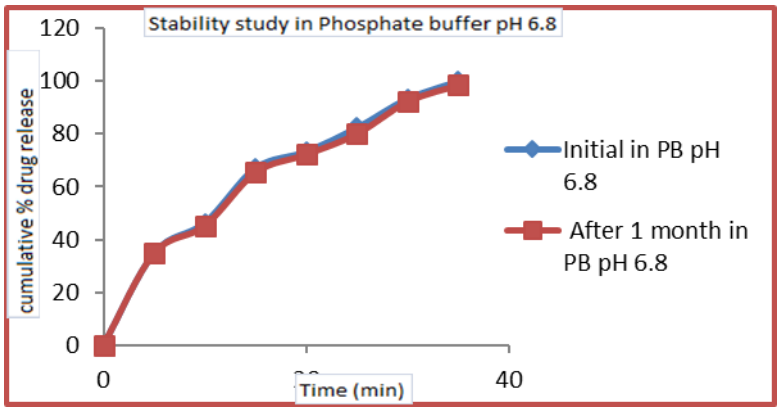


Figure 14: Stability dissolution profile of LSC 6 after one-month Stability Study in phosphate buffer pH 6.8.

There were no significant changes in physical and chemical properties of formulation LSC 6 after 1months. Parameters quantified at various time intervals. From results showed in Table 13,14 and Figure 13,14 it was concluded that LSC 9 is physically stable and retained their original properties when stored at 30±2ºC for one month and there was no significant difference in dissolution for optimized formulation.

CONCLUSION

Telmisartan is an Angiotensin Receptor Blocker and act by blocking the effect of angiotensin II and reduces blood pressure. Telmisartan is BCS class II drug having absolute bioavailability is 42-58%. Liquisolid compact was found to be a promising technique for improving the dissolution rate of poorly soluble drug and it may enhance the bioavailability of a poorly soluble, into the soluble or lipophilic drug.

- The present study was to enhance the rate of dissolution, aqueous solubility & preparation of immediate release tablets of practically insoluble drugs. The pre-formulation studies like Melting point, UV analysis, Fourier transform Infrared Spectroscopy, X ray diffraction & Differential Scanning Calorimetry were done.

- The result of the preformulation study shows that received sample of Telmisartan was pure and complies with standard and suitable for liquid solid compact technique. Drug excipient compatibility study was done. The FTIR spectra revealed that there was no interaction between polymer and drug. XRD &DSC studies indicated the reduction in crystallinity, a factor contributing to dissolution rate improvement of the drug. Polymers used were compatible with Telmisartan.

- Liquisolid compacts of Telmisartan can be prepared using the novel carriers like NeusilinUS2, Fujicalin SG, Microcrystalline cellulose and coating material like Aerosil 200and oleic acids none volatile solvent at three different carriers: coating ratio(R).Fujicalin SG and NeusilinUS2 showed greater potential to load the non-volatile solvent while maintaining good flow properties and helped to reduce the total tablet weight. Among the ratio of LSC blend 6 was found to be the best blend as compared to other prepared liquisolid compact blend. Due to the presence of carrier material having increasing liquid loading capacity with decreasing R value. From the evaluation parameter like Flow properties, Hardness, Wetting time, Friability, Disintegration time containing LSC 6 was selected as the best formulation. Due rapid disintegration time and superior *in vitro* dissolution study and

acceptable tablet properties. Post compression parameters revealed that the tablets were of good quality. From this study it can also be concluded, the release rate of the prepared liquisolid compacts is inversely proportional to drug concentration in the non-volatile vehicle and it is directly proportional to excipients ratio (*R*).

- In vitro dissolution studies showed dissolution improvement from Liquisolid tablets when compared to plain drug and marketed tablet. The liquisolid formulations containing novel carriers showed improved dissolution than the marketed tablet of Telmisartan and plain drug. To conclude that the novel porous carriers were found to be superior to microcrystalline cellulose. LSC 6 was showing best release as compared to other formulation from *in vitro* dissolution study.

- Optimized formulation showed better dissolution profile as compared with marketed preparation & plain drug. The optimized formulation showed pH independent release profile with significant improvement in dissolution compared to plain drug and conventional marketed formulation. Stability studies showed that there were no significant changes in physical and chemical properties of formulation LSC 6 after 1 month. So the liquisolid technique was proved to be an effective method for solubility enhancement and improving dissolution profile of the poorly soluble drug.

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REFERENCES

1. Amruta B, Varandal D, Magar A, Saudagar D. Different Approaches toward The Enhancement of Drug Solubility: A Review. Journal of Advanced Pharmacy Education & Research. 2013; 3(4): 415-426.
2. Chowdary K, Pavan A, Kumar S. Recent Research on Formulation Development of BCS Class II Drugs – A Review. International Research Journal of Pharmaceutical and Applied Sciences.2013; 3(1): 173-181.
3. Dalvi P, Ingale R. Liquisolid Technique: An Approach for Enhancement of Solubility .world Journal of Pharmacy and Pharmaceutical Sciences. 2014; 3(12): 434-446.
4. Sabbah z, Mansoor A, Kaul U. Angiotensin Receptor Blockers - Advantages of The New Sartans. Journal of the association of physicians of India. 2013; 6(1): 464-470.
5. Debnath M, Kumar A, Gopavarapu L. Formulation, Development and *In-Vitro* Release Kinetics of Telmisartan Tablet Prepared By Liquisolid Technique. Journal of Pharmaceutical Sciences. 2015; 4(3):36-50.

6. Ashokbhai M. Formulation, Optimization and Evaluation of Liquisolid Tablets Containing Tadalafil. International Journal of Pharma Sciences and Research. 2015; 6(6): 991-1001.
7. Prajapati S, Bulchandani H, Patel D, Dumaniya S, Patel C. formulation and evaluation of liquisolid compacts for olmesartan medoxomil journal of drug delivery.2013;1-9
8. Gunnam S, Saini S. Formulation and Evaluation of Liquisolid Compacts of Telmisartan. World Journal Of Pharmacy And Pharmaceutical Sciences.2015; 4(3): 782-798
9. Kankudte A, Jadhav A, Sarje G, Sakhare R, Bharkhad V. Formulation And Evaluation Of Aceclofenac Liquisolid Tablets International Journal For Pharmaceutical Research Scholars. 2013; 2(3): 27-399.
10. Chuahan P, Patel H, Patel B, Patel K, Patel P. Liquisolid Technique for Enhancement of Dissolution Rate of Ibuprofen. International Journal for Pharmaceutical Research Scholars. 2012; 1(2): 268-280.
11. Prajila A, Vipin V, Chandran C, Premaletha K, Augusthy A. Formulation and evaluation of Deflazacort liquisolid tablets. International Journal of Research in Pharmacy and Science. 2016; 6(1): 19 – 25.
12. Suthar M, Raval A, Patel R, Dr, Patel L. Formulation and Evaluation of Immediate Release Tablet of Rosuvastatin Calcium by Liquisolid Compact Technique. Journal of Biological Science .2016; 2(5): 18-35.
13. Yala P, Mahalingan S, Alladi S, Zalaki S. solubility enhancement of a model etoricoxib drug using liquisolid compacts. International Journal of Biological & Pharmaceutical Research. 2012; 3(4): 577-585.
14. Ramesh J, Kumar K, Reddy N. Formulation and Evaluation of Nicardipine Liquisolid Compact Tablets International Journal of Pharma and Bio Sciences. 2016; 7(2): 186 – 193.
15. Pokhariya P, Ganarajan G, Kothiyal P. Formulation and Evaluation of Mouth Dissolving Tablet of Telmisartan Using Natural Superdisintegrants. Indo American Journal of Pharmaceutical Sciences. 2016; 3(7): 713-727.
16. Sarraf M, Hussein A, Abdul A, Jabbar S. Dissolution Enhancement of Telmisartan by Liquisolid Compacts. International Journal of Pharmacy and Pharmaceutical Sciences. 2014; 6(2):743-749.
17. Kaparthi S, Babu P. Risperidone liquisolid compacts–Formulation and evaluation. Pelagia Research Library Der Pharmacia Sinica. 2015; 6(6): 9-15.
18. Bhairav B, Jadhav J, Saudagar R. Formulation and Evaluation of Liquisolid Tablet of Felodipine. World Journal of Pharmacy and Pharmaceutical Sciences. 2016; 5(7): 1670-1685
19. Chella N, Narra N, and Ramaro T. Preparation and Characterization of Liquisolid Compacts for Improved Dissolution of Telmisartan. Journal of Drug Delivery. 2014; 1-9.