Research Article

FORMULATION AND EVALUATION OF TELMISARTAN LIQUISOLID COMPACT TABLETS

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ABSTRACT

The main objective of this study is to enhance the dissolution and there by availability of a poorly soluble antihypertensive drug by liquisolid compact technique. Liquisolid mixture comprising of MCC & silicon dioxide along with a non-volatile solvents like PG, PEG 200, PEG 300, PEG 400, Polysorbate 20 & 80, Span 80 and Glycerin formed a part of liquisolid system. The process was optimized in terms of nature of non-volatile solvent. The optimized liquisolid mixture was characterized by FTIR and DSC studies. The liquisolid mixtures were evaluated for their various pre compressional parameters, micromeritic properties and compressional properties. The liquisolid mixtures were then compressed into tablets and were evaluated for different parameters. Results indicated that micromeritic and compressional properties of the liquisolid mixtures were greatly influenced by nature and type of non-volatile solvent incorporated. The dissolution efficiency of the tablets prepared from liquisolid mixture showed remarkable increase compared to tablets prepared by conventional direct compression. Observations also revealed that by varying the type of non- volatile desired release rate can be obtained. Hence it can be concluded that Liquisolid technique opens a wide scope for pharmaceutical research due to its ability to alter various important physicochemical parameters of the drug substance along with improving the solubility.

Keywords: Liquisolid mixture, Liquisolid technique, Telmisartan, Compressibility, Micromeritics.

INTRODUCTION

Tablets and Capsules represent the unit oral solid dosage forms which have been in existence since the nineteenth century. They comprise of a mixture of ingredients presented in a single entity, usually containing an accurate dose of a drug. There are other types of solid oral dosage forms also which are given orally but they are intended for systemic delivery. Tablet is the major oral solid dosage form, having significant advantage over capsules because of its tamper proof nature. They also offer the greatest capabilities of all oral dosage forms for the greatest dose precision and least content variability. Other factors like low cost, compactness, easy packing and shipping, simple product identification, better patient compliance, achievement of desired release profile, better suitability to large scale production also adds to the potential popularity of the tablets among oral solid dosage forms. It is well known that most common methods for tablet manufacturing include dry granulation, wet granulation and direct compression. It has been reported that among all the tabletting techniques. Poorly soluble drugs that are administered orally will generally exhibit slow dissolution rates and incomplete bioavailability due to poor wettability. Over the years,[1] various techniques have been employed to enhance the dissolution profile and the absorption efficiency and bioavailability of water insoluble drugs and/or liquid lipophilic medications. These include.

a) Reducing particle size via micronisation or nanonisation of the drug to increase the specific surface area.
b) Solubilization in surfactant systems.
c) Formation of water-soluble complexes.
d) Drug derivatisation such as a strong electrolyte salt forms that usually have higher dissolution rate
e) Manipulation of solid state of drug substance to improve drug dissolution, i.e. by decreasing crystallinity of drug substance through formation of solid solutions.
f) Inclusion with cyclodextrins.
g) Solid dispersion.
h) Microencapsulation and inclusion of drug solutions or liquid drugs into soft gelatin capsules or specially sealed hard shell capsules. A new addition

to the above mentioned approaches is "liquisolid technology". This technique has been applied to convert water insoluble drug into rapid release solid dosage form.

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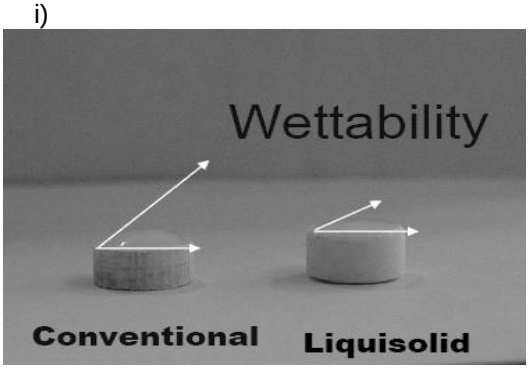

Fig. 1: Comparison of wettability between Conventional tablet and liquisolid compacts

LIQUISOLID TECHNIQUE

Liquisolid systems are acceptably flowing and compressible powdered forms of liquid medications. Liquisolid system refers to powdered forms of liquid medications formulated by converting liquid lipophilic drugs, or drug suspensions or solutions of water insoluble solid drugs in suitable non-volatile solvent systems into dry,[30] non-adherent, free-flowing and readily compressible powder admixtures by blending with selected carrier and coating materials.[31] Various grades of microcrystalline or amorphous cellulose may be used as carriers, whereas very fine particle size silica powders may be used as coating materials. The carrier and coating materials can retain only certain amounts of liquid and at the same time maintain acceptable flow and compression properties.

MATERIALS AND METHODS

Telmisartan, was received as gift samples from Zydus Cadila Ltd., Ahmedabad. Other reagents and organic solvents used were of analytical grade.

EXPERIMENTAL

Formulation of liquisolid mixture

The liquisolid compacts were prepared according to the method described by Spireas and Bolton. Telmisartan was dissolved in a suitable non-volatile liquid vehicle to prepare the drug solution. The mixture of carrier-coating materials (Avicel PH 102 as the carrier powder and Aerosil 200 as the coating material) was added to the drug solution and blended in a porcelain mortar avoiding excessive trituration and particle size reduction. The mixing was done in two stages: first, the system was mixed slowly to allow uniform distribution of carrier-coating material with drug solution; second, the mixture was spread as a uniform layer on the surface of the mortar and left to stand for a few minutes.

Table 1: Formulation of various batches of Liquisolid compacts

Ingredients	LF0	LF1	LF2	LF3	LF4	LF5	LF6	LF7	LF8	LF9
Telmisartan (mg)	400	400	400	400	400	400	400	400	400	400
Propylene Glycol (mg)	266	-	-	-	-	-	-	-	-	-
PEG 200 (mg)	-	266	-	-	-	-	-	-	-	-
PEG 300 (mg)	-	-	266	-	-	-	-	-	-	-
PEG 400(mg)	-	-	-	266	-	-	-	-	-	-
Polysorbate 20 (mg)	-	-	-	-	266	-	-	-	-	-
Polysorbate 80 (mg)	-	-	-	-	-	266	-	-	266	266
Span 80 (mg)	-	-	-	-	-	-	266	-	-	-
Glycerin (mg)	-	-	-	-	-	-	-	266	-	-
Poloxamer 338 (mg)	-	-	-	-	-	46	-	-	-	-
Sodium Lauryl Sulfate (mg)	-	-	-	-	-	-	-	-	46	-
Microcrystalline cellulose (mg)	1333	1333	1333	1333	1333	1333	1333	1333	1333	1333
Aerosil 200 (mg)	293	293	293	293	293	293	293	293	293	293

Characterization of Telmisartan
The estimation of drug was carried out by UV spectroscopy.

Determination of λ_{max}
The solution of telmisartan in the concentration of 10 µg/ml was prepared using 0.1N HCl. It was scanned over the wavelength range of 200-400nm using double beam UV spectrophotometer using 0.1N HCl as blank.

Calibration curve of telmisartan
Telmisartan was accurately weighed (100mg) and was dissolved in 0.1N HCl to produce a primary stock solution of 1mg/ml. The primary stock solution was suitably diluted to produce working solutions in concentrations ranging from 2-10µg/ml. The absorbance of the solutions was recorded at 291.5nm using double beam spectrophotometer with 0.1N HCl as a blank. The plot of absorbance versus concentration (µg/ml) was plotted and the linear regression was analyzed using Microsoft Excel®. Experiments were done in triplicate.

PREFORMULATION STUDIES
Flow properties of drug
The Bulk density, Tapped density, Hausner's ratio, Carr's index, Angle of Repose of the pure drug was determined

Bulk density
The sample equivalent to 1.5 g was accurately weighed and filled in 10 ml graduated cylinder and the powder was leveled and the unsettled volume (V_0) was noted. The bulk density was calculated in g/cm^3 by the formula,

$$\text{Bulk density } (\rho_0) = \frac{M}{V_0}$$

Where,
M = mass of powder taken
V_0= apparent unstirred volume

Tapped density
The weight of sample equivalent to 1.5 g was filled in 10 ml graduated cylinder. The mechanical tapping of the cylinder was carried out using tapped density tester at a constant rate for 100 times. Volume was considered as tapped volume (V_f). The tapped density was calculated in g/cm^3 by the formula,

$$\text{Tapped density } (\rho_t) = \frac{M}{V_f}$$

Where,
M = weight of sample powder taken
V_f = tapped volume

Percentage compressibility or Carr's index
Based on the poured density and tapped density, the percentage compressibility of the agglomerates was computed using the Carr's compressibility index by the formula

$$\text{Carr's index (\%)} = \frac{\text{tapped density} - \text{poured density}}{\text{tapped density}} \times 100$$

Hausner's ratio
Hausner's ratio was calculated using the formula,

Hausner's ratio = tapped density/ poured density

Determination of angle of repose
Angle of repose of the agglomerates was determined by the fixed funnel method. A funnel was fixed to a desired height and agglomerates were filled in it. They were allowed to flow down on a graph paper fixed on a horizontal surface and angle of repose was calculated using the formula,

$$\theta = \tan^{-1} (h/r)$$

Where,
h = height of the pile.
r= radius of the pile

Evaluation of tablets containing liquisolid powders
The compressed tablets were evaluated for the following parameters.

Thickness
Six tablets were randomly selected and the thickness of each tablet was measured by digital Vernier caliper. Mean and standard deviation were computed and reported.

Hardness
The hardness of 10 tablets was measured using Monsanto hardness tester. The mean and standard deviation were computed and expressed in kg/cm^2.

Friability
The friability of the tablets was determined using Roche friabilator. Ten tablets were initially weighed and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 min. After 4 min the tablets were weighed again. The % friability was then

calculated using the formula,

$$\%F = (1-W/W0) \times 100$$

Where,

W0 = is the weight of the tablets before the test

W= is the weight of the tablets after the test

Limits for friability: % friability should not be more than 1%.

RESULTS AND DISCUSSION

Calibration curve of Telmisartan

The data for calibration curve of Telmisartan in 0.1N HCL solution is shown in table 16. The calibration curve was constructed over a concentration range of 2µg/ml to 10µg/ml and was found to be linear with r^2=0.9995 and the equation of the regression line was Y=0.061X.

Table 2: Calibration curve of Telmisartan

Concentration (µg/ml)	Average± S.D
2	0.134±0.006
4	0.255±0.003
6	0.378±0.003
8	0.498±0.003
10	0.621±0.006

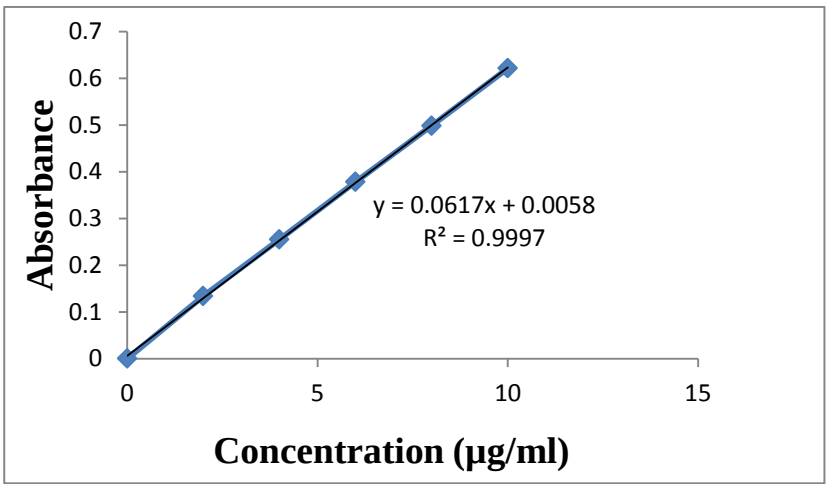

Fig. 2: Calibration curve of Telmisartan at 291.5 nm

Preformulation Studies

The results of preformulation studies are tabulated in table 2 and 3.

Table 3: Results of flow properties of Telmisartan

PARAMETER	VALUE
Bulk Density (gm/cm^3)	0.248±0.02
Tapped Densit (gm/cm^3)	0.570±0.03
Hausner's ratio	1.96
Carr's Index	38.72%
Angle of repose	36.28º±0.12º

Table 4: Results of solubility studies of Telmisartan

Medium	Solubility(µg/ml)
Distilled Water	8.47±0.54
0.1N HCL	18.37±0.42
4.0 PH Buffer	3.83±0.35
7.4 PH Buffer	9.58±0.84

Calculation of loading factor:

Table 5: Data of loading factor with PEG 400

Carrier : Coating material (1.5g)	PEG 400	Loading Factor
2:1	450 mg	0.3
3:1	400 mg	0.266
4:1	350 mg	0.233
5:1	350 mg	0.233

CHARACTERIZATION OF LIQUISOLID MIXTURES

Fourier Transform Infra Red (FTIR) spectroscopy

The IR spectra of telmisartan and IR spectra of liquisolid mixtures containing different non-volatile solvents are shown in figures below:

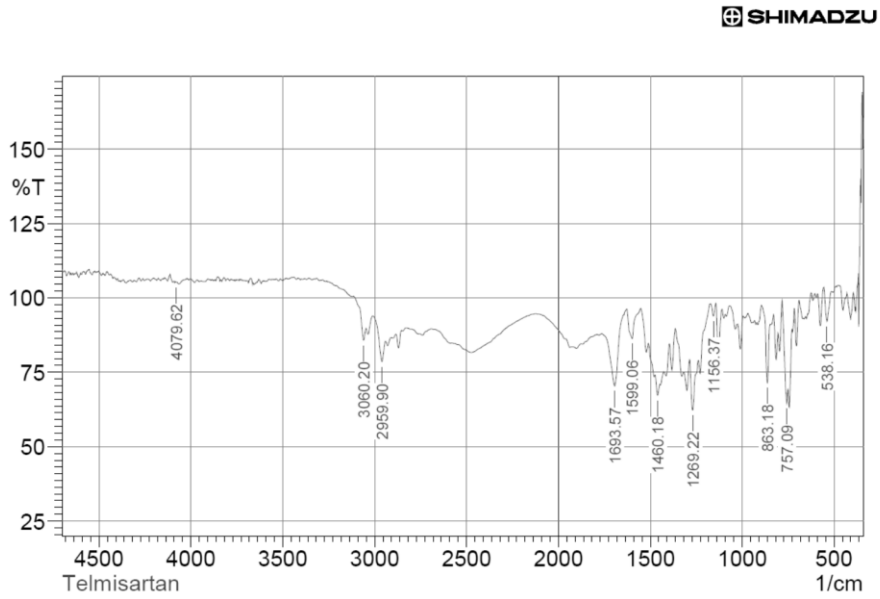

Fig. 3: IR spectrum of Telmisartan

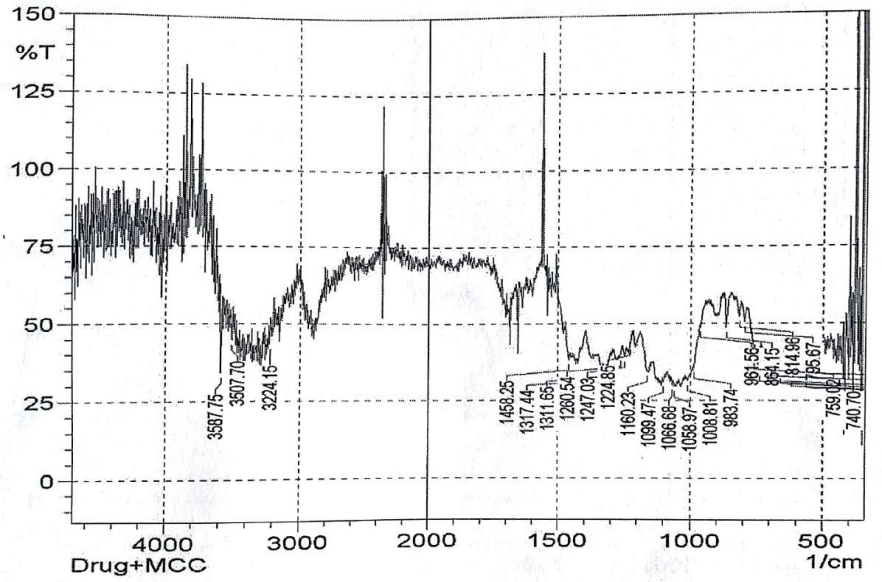

Fig. 4: IR spectra of liquisolid mixtures containing MCC

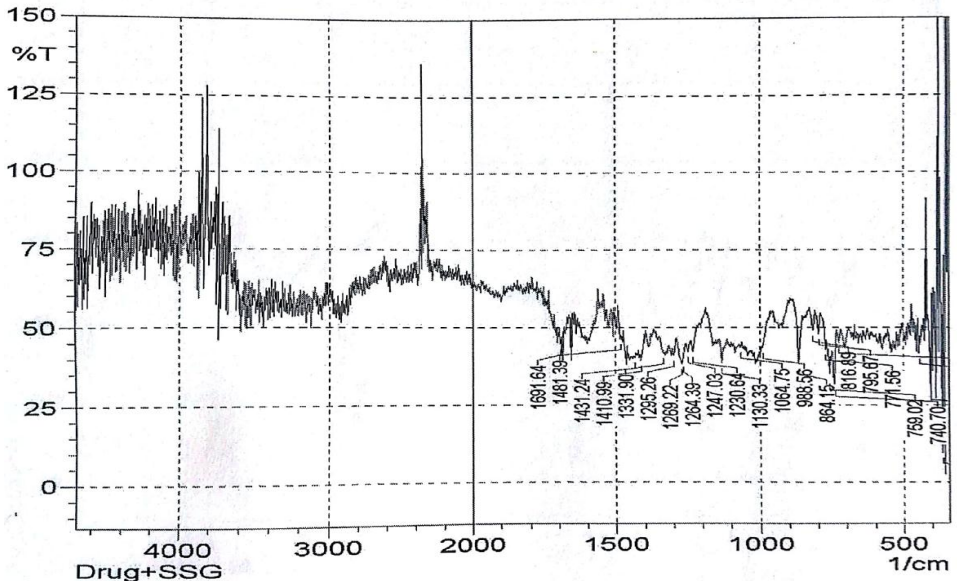

Fig. 5: IR spectra of liquisolid mixtures containing SSG

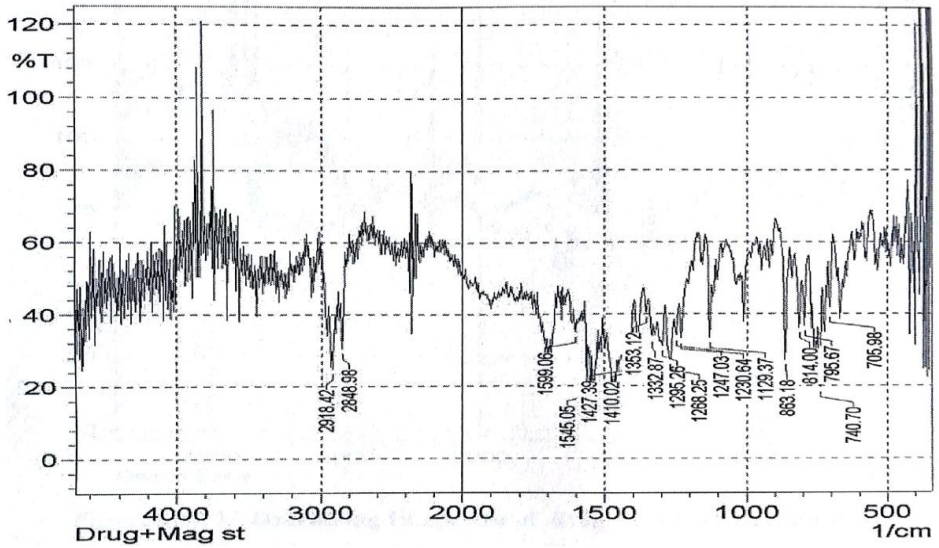

Fig. 6: IR spectra of liquisolid mixtures containing Magnesium Stearate

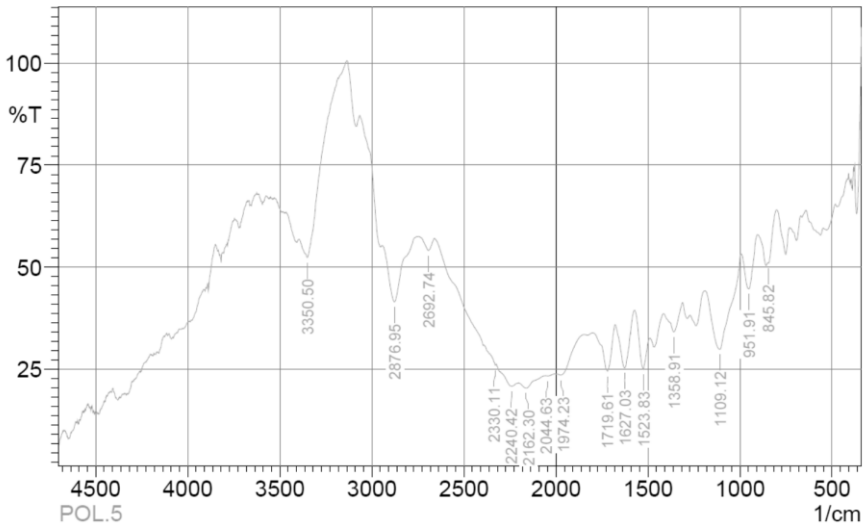

Fig. 7: IR spectra of liquisolid mixtures containing Polaxamer 338

DSC STUDIES

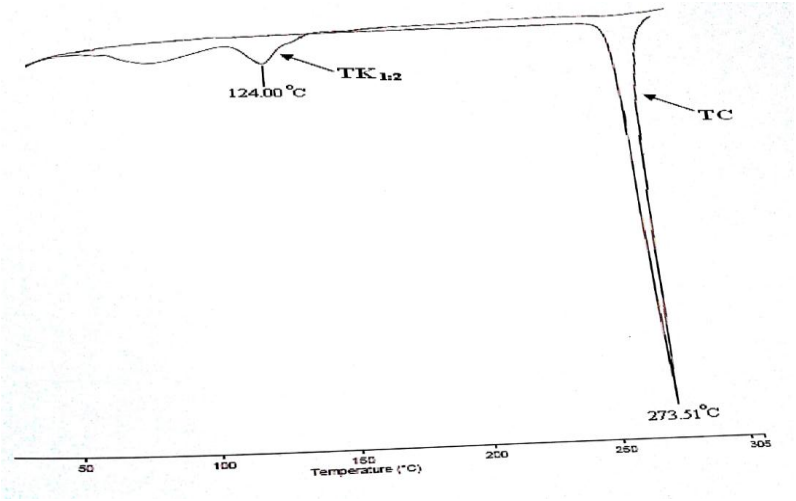

Fig. 8: DSC of Telmisartan

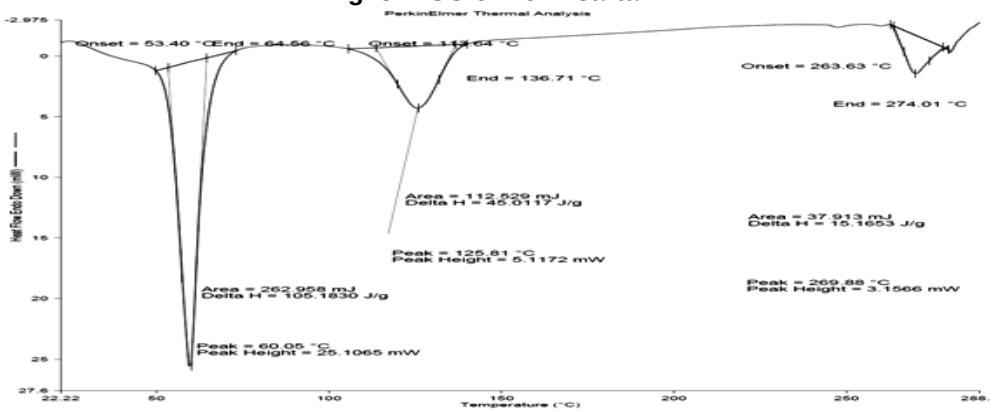

Fig. 9: DSC of liquisolid mixtures containing Polaxamer 338

Post compression parameters

The properties of the tablets like thickness, hardness and friability, for the formulations F_0 to F_9 were determined and the results are reported in table 7. The results of weight variation, *in vitro* disintegration time and drug content for the formulations F_0 to F_9 & F_C, were determined and the results were reported.

EVALUATION OF LIQUISOLID MIXTURE

Table 6: Flow properties of liquisolid mixtures

Formulations	Bulk density $(gm/cc)^3$	Tapped density $(gm/cc)^3$	Carr's index (%)	Hausner's ratio	Angle of repose
Pure Drug	0.238±0.02	0.370±0.03	35.72	1.66	36.38º±0.12º
F0	0.286±0.03	0.328±0.02	12.86	1.15	29.76º±0.15º
F1	0.385±0.02	0.465±0.04	17.31	1.21	32.47º±0.20º
F2	0.370±0.02	0.435±0.03	14.82	1.17	28.60º±0.18º
F3	0.417±0.03	0.488±0.05	14.58	1.17	25.34º±0.22º
F4	0.400±0.02	0.476±0.03	16.00	1.19	28.61º±0.13º
F5	0.385±0.03	0.435±0.05	11.54	1.13	26.57º±0.21º
F6	0.295±0.01	0.351±0.02	16.18	1.19	29.48º±0.24º
F7	0.278±0.03	0.322±0.03	13.88	1.16	28.60º±0.18º
F8	0.392±0.01	0.434±0.04	9.80	1.10	24.44º±0.13º
F9	0.400±0.03	0.440±0.03	8.00	1.08	23.49º±0.15º

Table 7: Results for Thickness, Hardness, Friability

Formulations	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)
F_0	3.35±0.02	3.66±0.16	0.416±0.02
F_1	3.31±0.01	3.33±0.17	0.559±0.01
F_2	3.34±0.05	4.00±025	0.345±0.01
F_3	3.29±0.01	3.50±0.16	0.432±0.05
F_4	3.25±0.03	3.00±0.00	0.562±0.06
F_5	3.27±0.05	3.50±0.16	0.496±0.07
F_6	3.32±0.06	3.00±0.25	0.501±0.12
F_7	3.34±0.02	3.66±0.16	0.459=0.08
F_8	3.31±0.08	3.83±0.17	0.411±0.09
F_9	3.28±0.03	4.00±0.20	0.376±0.02
Fc	3.272±0.06	4.6±0.22	0.423±0.09

Table 8: Results for weight variation, *In vitro* disintegration time, drug content

Formulation	Weight variation (%)	*In vitro* disintegration time (seconds)	Drug content (%)
F_0	0.32	786	98.33
F_1	0.45	312	101.35
F_2	0.48	235	100.32
F_3	0.38	197	100.33
F_4	0.44	220	100.85
F_5	0.28	700	100.82
F_6	0.39	066	100.85
F_7	0.60	682	100.32
F_8	0.29	659	99.35
F_9	0.49	580	98.34
Fc	0.29	897	100.66

***In - vitro* Dissolution Studies**

Table 9: Percentage cumulative release of tablets containing liquisolid compact for formulations F0 to F9

TIME (min.)	PERCENTAGE CUMULATIVE RELEASE									
	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
10	14.55	22.49	28.80	34.35	47.83	48.71	62.01	5.16	53.54	56,19
20	17.78	35.81	41.44	46.12	59.86	61.36	74.20	10.89	73.14	77.42
30	18.90	43.01	44.71	56.20	60.85	74.26	47.99	13.63	75.39	79.70
40	19.07	51.49	53.91	68.91	61.99	76.46	77.22	18.16	78.73	83.43
50	20.99	59.46	66.04	74.77	64.48	90.07	78.01	20.38	84.97	87.18
60	22.99	65.46	76.04	82.77	74.48	98.55	88.23	25.72	90.97	93.88

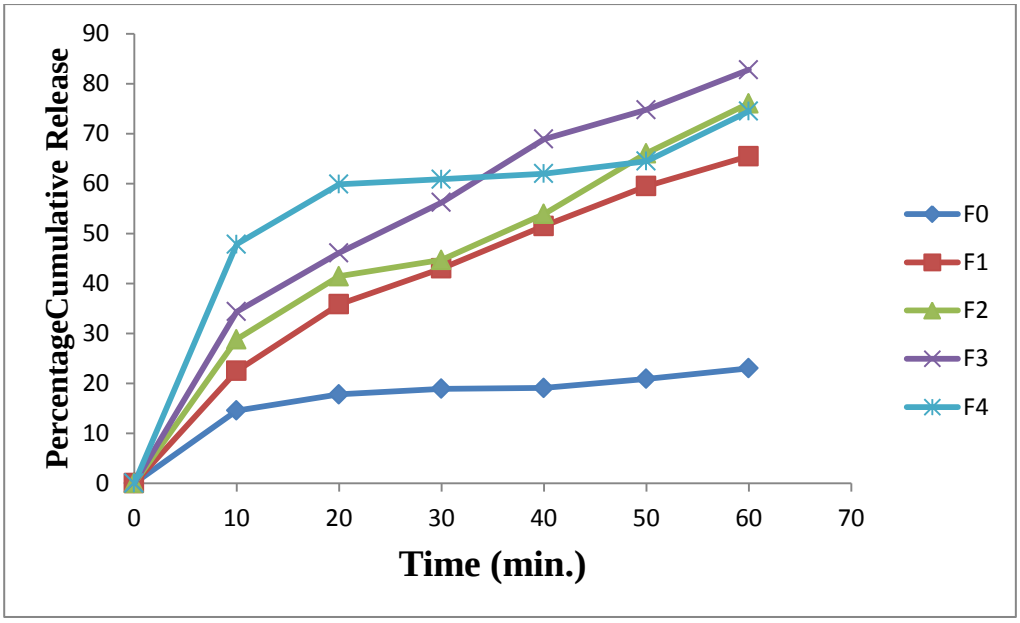

Fig. 14: Dissolution profile of Telmisartan from tablet containing liquisolid mixtures in batches F_0, F_1, F_2, F_3, and F_4

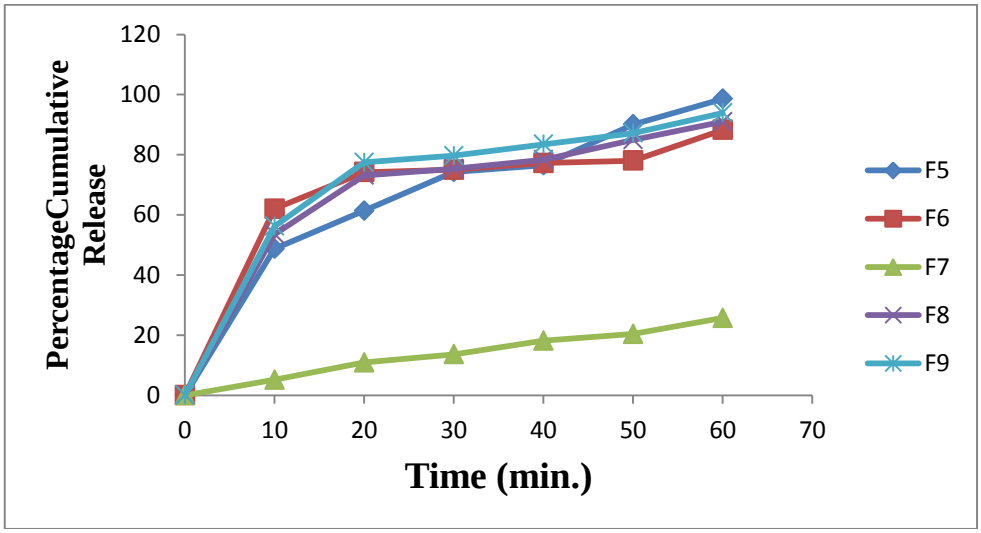

Fig. 15: Dissolution data of tablets containing liquisolid mixtures of batch F_5, F_6, F_7, and F8 & F9 Comparison between optimized formulation F5 & conventional Telmisartan table F_C

Table 11: Dissolution data of F_5 compared with Conventional tablet Fc

TIME (MINUTES)	PERCENTAGE CUMULATIVE RELEASE	
	F5	F_C
0	0	0
10	48.71±2.02	3.59±0.21
20	71.36±1.32	5.61±0.14
30	74.26±1.84	8.49±0.87
40	76.46±2.18	12.38±1.31
50	80.07±2.88	16.93±1.75

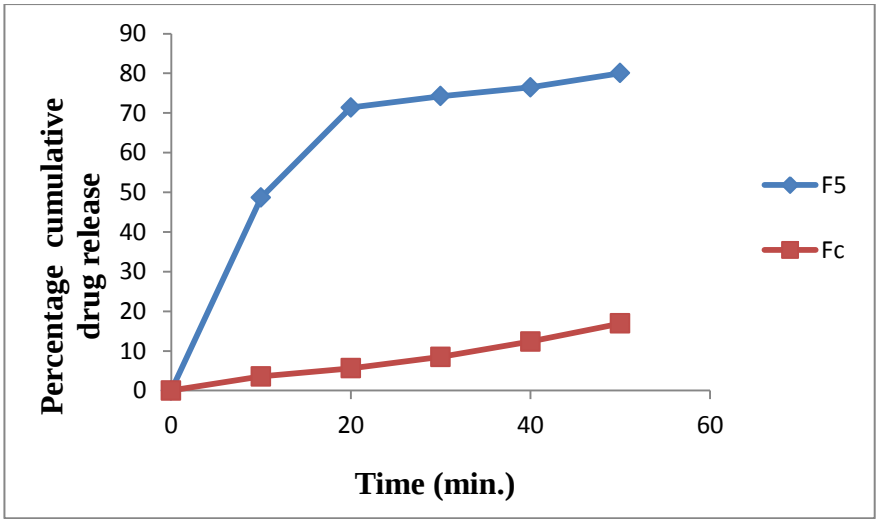

Fig. 16: Comparison of dissolution profiles of F_5 and F_C

DISCUSSION

Telmisartan is a poorly water soluble antihypertensive drug, resulting in reduced dissolution and absorption. Formulation of such drugs required employment of solubilization technique to improve solubility.

The present study attempts to improve the solubility and dissolution of the drug using liquisolid technique. The drug was estimated by UV spectroscopy. Telmisartan exhibited λ_{max} of 291.5 nm and its calibration curve in 0.1N HCL was found to be linear over a concentration range of 2-10 µg/ml with r^2=0.9995.

Preformulation studies indicated that the drug has poor flow property, Necessitating the use of conventional wet granulation technique to improve flow property. The aqueous solubility of the drug was found to be 8.5µg/ml, indicating that the drug has poor water solubility. Liquisolid technique is the new one promising method which has been used to enhance the dissolution rate of a poorly water soluble drug. The method involved converting of the drug solution or suspension in a non-volatile solvent into a dry, non adherent, free flowing and compatible powder mixture by blending the suspension or solution with a selected carrier and coating material. This technique has advantage of simplicity, low cost and capability of industrial production. In this technique, a definite quantity of drug solution or suspension is incorporated into a specific quantity of carrier & coating material which should be preferably of a porous mixture with sufficient absorption properties. Microcrystalline Cellulose was selected as the carrier material because of its porous nature and absorbing properties. The coating material should possess fine and highly adsorptive properties and silicon dioxide is reported to be most suitable. Loading factor was determined to evaluate the amount of the liquid which can be retained by the carrier coating material. The liquid load factor was calculated for various ratios of carrier coating material. Based on this result, it was observed that the carrier coating ratio of 2:1 have the capacity to hold more liquid, maintaining acceptable flow properties. However, tablets compressed using compacts of this ratio was found to be have less hardness. Thus, the carrier coating ratio of 5:1 was selected in further formulations. Various formulations with different non-volatile solvents were prepared using 5:1 carrier coating material ratio.

Formulations F_0 to F_7 were prepared using non- volatile solvents like Propylene Glycol, PEG 200, PEG 300, PEG 400, Polysorbate 20 & 80, Span 80 and Glycerin respectively. volatile solvents like Propylene Glycol, PEG 200, PEG 300, PEG 400, Polysorbate 20 & 80, Span 80 and Glycerin respectively. In formulations F_0, F_2, F_3, F_5, and F_7, the flow properties of the liquisolid mixtures were found to be good as indicated by Carr's index (11-15 %), Hausner's ratio (1.12-1.18) and angle of repose (20°-30°). The post compressional parameters were satisfactory and the percentage cumulative release after 50 minutes was found to be in the range of 20.38-80.07%. In formulations F_1, F_4 and F_6, the flow properties of the liquisolid mixtures were found to be passable. Formulations F_0 to F_7 were prepared by using 4 % sodium starch glycolate as disintegrant where as formulation F_8 and F_9 were prepared by using polysorbate 80 as non-volatile vehicle contains sodium starch glycolate (4%) and sodium lauryl

sulphate (2%) or poloxamer 338 (2%) respectively. In formulations F_8 and F_9, the flow properties of the liquisolid mixtures were found to be excellent as indicated by Carr's index (≤10 %), Hausner's ratio (1.0-1.11) and angle of repose (<20). The post compressional parameters were satisfactory and the percentage cumulative release after 50 minutes was found to be in the range of 84-87%. Among Span 80, polysorbate 80 and PEG 400 used, formulations were found to be satisfactory in both flow properties and percentage cumulative release. Since drug release from formulation F_5 (Polysorbate 80) was the maximum among formulations prepared, it was considered as the optimized formulation.

Thus liquisolid mixture containing polysorbate 80 was found to be better compared to conventional formulation resulting in better flow properties and drug release. Figure 16 indicates that drug release from formulation F_5 was better compared to F_C suggesting that liquisolid technique was beneficial in improving the solubility of drug. Further addition of disintegrant contributed in improving the solubility of drug to a certain extent.

CONCLUSION

From the present study, it can be concluded that the Liquisolid technique is a highly efficient technique to produce directly compressible mixture of Telmisartan. The liquisolid mixture drastically improved Micromeritic properties of the drugs and possessed higher solubility profiles which in turn, improved the dissolution rate of the drug. The prepared liquisolid mixture was directly compressible owing to their altered flow property and compaction behavior. Thus, the process of liquisolid technique is likely to have a strong impact on formulation development and can be a useful tool to ensure greater precision for solid dosage forms of poorly compressible drugs.

REFERENCES

1. Amrit BK, Indrajeet DG, Avinash HH, Pandurang ND, Satish BB. Dissolution Rate Enhancement of Fenofibrate using Liquisolid Tablet Technique. Latin American Journal of Pharmacy, 2009; 28(2):219-225.
2. Amrit BK, Indrajeet DG, Avinash HH, Pandurang ND, Satish BB. Dissolution Rate Enhancement of Fenofibrate Using Liquisolid Tablet Technique. Part II: Evaluation of In Vitro Dissolution Profile Comparison Methods. Latin American Journal of Pharmacy, 2009; 28(4):538-543.
3. Ajit SK, Nagesh HA. Liquisolid Systems: A Review. International Journal of Pharmaceutical Sciences and Nanotechnology, 2010; 3: 795-802.
4. Babatunde A, Amal AE, Ebtessam AE, Sahar E. Liquisolid Systems to Improve the Dissolution of Furosemide. Scientia Pharmaceutica, 2010; 1(20):325-347
5. Chandel P, Kapoor A. Liquisolid Technique: An approach for Enhancement of Solubility. Journal of Drug Delivery & Therapeutics, 2013; 3(4): 131-137.
6. Dongkai W, Pingtian D, Mei L. Liquisolid Technique and its Applications in Pharmaceutics. Asian Journal of Pharmaceutical Sciences, 2017; 4, 479-493.
7. Elkordy AA, Javaheri H. Wet Granulation to Overcome Liquisolid Technique Issues of Poor Flowability and Compactibility: A Study to Enhance Glibenclamide Dissolution. Journal of Pharmaceutics & Drug Development (2014);2(3) :2348-9782
8. Hitendra SM, Jadhav KR. Liquisolid compact: A new Technique for Enhancement of Drug Dissolution. International Journal of Research in Pharmacy & Chemistry, 2011; 1(3):705-713.
9. Javadzadeh Y, Shariati H, Movahhed DE. Effects of Different Grades of Microcrystalline Cellulose on Flowability, Compressibility and Dissolution of Liquisolid Systems. Drug Dev Ind Pharm, 2009; 35(2):243-251.
10. Jadhav R, Sahil M. Liquisolid compact: a New Technique for Enhancement of Drug Dissolution. International Journal of Research in Pharmacy and Chemistry, 2011; 1(3):2231-2781.
11. Lohithasu D, Ramana JV. A latest Review on Liquisolid Technique as a Novel Approach. World Journal of Pharmaceutical Research, 2014; 4(3): 479-493.
12. More SK. Solubility Enhancement of a Drug by Liquisolid Technique. International Journal of Pharmaceutical, Chemical and

Biological Sciences, 2014; 4(2):339-344.
13. Ngiik T, Amal AE. Effects of Liquisolid Formulations on Dissolution of Naproxen. European Journal of Pharmaceutics and Biopharmaceutics, 2009; 73:373-384.
14. Pawar JD, Jagtap RS. Liquisolid compacts: A Promising Approach for Solubility Enhancement. Journal of Drug Delivery & Therapeutics, 2017; 7(4):6-11.
15. Patel DS, Patel NM. Dissolution Enhancement of Glipizide using Liquisolid Tablet Technology. Indian Drugs, 2008; 45(4): 318-323.
16. Rania HF, Mohammed AK. Enhancement of Famotidine Dissolution rate through Liquisolid Tablets Formulation: *in-vitro* and *in-vivo* Evaluation. European Journal of Pharmaceutics and Biopharmaceutics, 2008; 69: 993-1003.
17. Ramya DP, Gowree M. Emerging liquisolid Compact Technology for Solubility Enhancement of BCS Class-II Drugs. Journal Pharmceutical Sciences & Research. 2011; 3(12): 1604-1611.
18. Spiro S, Srinivas S. Enhancement of Prednisolone Dissolution Properties Using Liquisolid Compacts. International Journal of Pharmaceutics, 1998; 166:177-188.
19. Spiro S, Srinivas S, Rakesh G. In vitro Release Evaluation of Hydrocortisone Liquisolid Tablets. Journal of Pharmaceutical Sciences, 1998; 87:867-872.
20. Spireas S, Wang T, Grover R. Effect of Powder Substrate on Dissolution Properties of Methylclothiazide Liquisolid Compacts. Drug Dev. India Pharmaceutical Research, 1999; 25:163-68.
21. Sanjeev RG, Ravindra J. Formulation and Characterisation of Atorvastatin Calcium Liquisolid Compacts. Asian Journal of Pharmaceutics, 2010; 5(2):50-60.
22. Shailendra SS, Pritesh P. Formulation and Evaluation of Curcumin Liquisolid Tablets. Current Research in Pharmaceutical Sciences, 2012; 4: 210-214.
23. Srinivas V, Sateesh KV. Liquisolid Compacts: An Approach to Enhance the Dissolution Rate of Nimesulide. Journal of Applied Pharmaceutical Science, 2012; 2 (5): 115-121,
24. Vijaykumar N, Ramarao T, Jayaveera KN. Formulation Development and Evaluation of Liquisolid Systems to Improve the Dissolution rate of Ketoprofen. International Journal Biomedical Research, 2011; 2(10):530-541.
25. Yousef J, Mohammad RS, Solmaz A, Ali Nokhodchi. Liquisolid Technique as a tool for Enhancement of Poorly Water-Soluble Drugs and Evaluation of their Physicochemical Properties. Acta Pharm, 2007; 57: 99-109.
26. Yadav VB, Yadav AV. Improvement of Solubility and Dissolution of Indomethacin by Liquisolid and Compaction Granulation Technique. Journal of Pharmaceutical Sciences and Research, 2009; 1(2):44-51.
27. Yousef J, Baharak JN, Ali Nokhodchi. Liquisolid Technique for Dissolution Rate Enhancement of a High Dose Water-Insoluble Drug (Carbamazepine). International Journal of Pharmaceutics, 2007; 341:26-34.