RESEARCH PAPER

Formulation and characterization of liquisolid system of benidipine as a solubility enhancement technology

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Abstract

Benidipine is a potent calcium channel blocker used in the management of hypertension and angina pectoris. However, its poor aqueous solubility presents a significant challenge in formulation development and may result in inadequate dissolution and variable oral bioavailability. The present study was therefore undertaken with the objective of developing and characterizing a liquisolid system of Benidipine as a solubility enhancement technology. The liquisolid technique was selected because it converts a liquid medication or drug solution/suspension into a dry, free-flowing and compressible powder by incorporating suitable carrier and coating materials. In the present formulation, Benidipine was dissolved or dispersed in a suitable non-volatile liquid vehicle and converted into liquisolid powder using appropriate carrier and coating materials. Different formulation batches were prepared by varying the concentrations and ratios of the formulation components and were evaluated for pre-compression and post-compression parameters. The prepared liquisolid formulations were characterized for flow properties, drug content, weight variation, hardness, friability, disintegration time and in-vitro drug dissolution. Drug–excipient compatibility was investigated using FTIR spectroscopy, while the improvement in dissolution behavior was compared with the pure drug or conventional formulation. The optimized formulation demonstrated satisfactory micromeritic and tablet properties with uniform drug content and acceptable mechanical strength. The liquisolid system showed a marked improvement in the dissolution rate of Benidipine compared with the pure drug, which may be attributed to enhanced wetting, increased effective surface area and improved molecular dispersion of the drug in the liquid vehicle. Thus, the developed Benidipine liquisolid system can serve as a promising solubility enhancement approach and may potentially improve the dissolution characteristics and oral performance of this poorly water-soluble drug.

Keywords: Benidipine, Liquisolid system, Solubility enhancement, Poorly water-soluble drug, Dissolution enhancement, Liquid vehicle, Carrier.

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1. Introduction

Oral drug delivery is the most widely preferred route for administering therapeutic agents because of its convenience, patient compliance, ease of administration, and cost-effectiveness. However, the development of oral dosage forms is often limited by the physicochemical properties of the drug, particularly poor aqueous solubility. For a drug to exert its therapeutic effect after oral administration, it generally needs to dissolve in gastrointestinal fluids before it can be absorbed. Therefore, inadequate aqueous solubility can lead to slow dissolution, incomplete absorption, variable bioavailability, and consequently reduced therapeutic effectiveness. Improving the dissolution and solubility of poorly water-soluble drugs has consequently become an important objective in pharmaceutical formulation development.[1]

Benidipine is a dihydropyridine calcium channel blocker used primarily in the treatment of hypertension and angina pectoris. It produces its pharmacological action by inhibiting calcium influx through L-type and T-type calcium channels, resulting in relaxation of vascular smooth muscle and reduction of vascular resistance. Although Benidipine possesses desirable pharmacological activity, its poor aqueous solubility creates a formulation challenge. Limited dissolution of the drug in gastrointestinal fluids can influence the rate and extent of drug absorption. Hence, an appropriate formulation strategy is required to improve the dissolution characteristics of Benidipine and potentially enhance its oral bioavailability.[2]

Several approaches have been investigated to improve the solubility and dissolution of poorly water-soluble drugs, including particle-size reduction, micronization, nanosizing, solid dispersion, complexation, use of surfactants, self-emulsifying systems, salt formation, and lipid-based formulations. Although these techniques can improve drug dissolution, some may involve complex

manufacturing procedures, high processing costs, physical instability, or limitations in large-scale production. Therefore, the development of simple, economical, and efficient formulation technologies remains important for improving the pharmaceutical performance of poorly soluble drugs.[3]

The liquisolid technique is a promising formulation approach for enhancing the dissolution rate of poorly water-soluble drugs. In this technique, the drug is dissolved or dispersed in a suitable non-volatile liquid vehicle and subsequently converted into a dry, free-flowing and compressible powder by blending it with appropriate carrier and coating materials. Commonly used carrier materials provide the bulk required for the formulation, whereas fine coating materials improve flowability and powder characteristics. The liquid vehicle incorporated into the system can enhance drug wetting and maintain the drug in a solubilized or molecularly dispersed state, thereby facilitating its release when the dosage form comes into contact with dissolution medium.[4]

The enhancement in dissolution from a liquisolid system can be explained by several mechanisms. The presence of the liquid vehicle improves the wetting of drug particles and reduces the interfacial resistance between the drug and dissolution medium. Furthermore, the drug may be present in a molecularly dispersed state within the liquid vehicle, eliminating or reducing the need for dissolution of individual crystalline drug particles. The increased effective surface area available for dissolution and improved wetting characteristics can consequently produce faster drug release compared with the untreated drug.[5]

The selection of suitable formulation components is an important factor in the successful development of a liquisolid system. The type and concentration of liquid vehicle, carrier material, coating material, drug concentration, and liquid load factor can influence powder flow, compressibility, tablet properties, drug content, disintegration, and dissolution behavior. Therefore, systematic formulation and evaluation are necessary to obtain a liquisolid system with satisfactory physical characteristics and improved drug-release performance.

Characterization of the prepared liquisolid formulations provides important information regarding their pharmaceutical quality and suitability for oral administration. Pre-compression evaluation may include angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio to assess the flow and packing characteristics of the powders. Post-compression evaluation may include appearance, weight variation, hardness, friability, thickness, drug content, disintegration time, and in-vitro dissolution studies. Fourier-transform infrared spectroscopy (FTIR) can also be employed to investigate possible drug–excipient interactions and to confirm the compatibility of the formulation components.[6]

In view of the solubility limitations associated with Benidipine, the present study was designed to develop and characterize a liquisolid system of Benidipine as a solubility enhancement technology. The study focuses on converting Benidipine into a suitable liquisolid formulation using an appropriate liquid vehicle, carrier, and coating material, followed by evaluation of its physicochemical and pharmaceutical properties. The developed system is intended to improve the wetting, dissolution rate, and overall dissolution performance of Benidipine, thereby demonstrating the potential of the liquisolid technique.[7]

2. Methodology

Pre-formulation drug characterization

Solubility studies

Solubility studies of drug is carried out in Propylene glycol,Polyethylene glycol 400 (PEG 400), Tween 80 , PEG -600, and Tween -20 . Saturated solutions are prepared by adding excess drug to the vehicles and shaking on the shaker for 48 hours at 25 ± 0.5 ^{0}C under constant vibration. After this period the solutions are filtered, diluted and analysed by UV Spectrophotometer. Three determinations are carried out for each sample to calculate the solubility.[8,9]

Flowable liquid-retention potential of the excipients (avicel PH 101 and aerosil 300)

i. Determination of the angle of slide

The Angle of slide for carrier and coating material (10 gm of Avicel PH 101 and Aerosil 300) is measured as follows:The excipients are weighed accurately and placed at one end of a metal plate with a polished surface. This end is raised gradually until the plate made an angle with the horizontal at which as a measure for the flow characters of powders. An angle of slide θ corresponding to 33°corresponded to optimal flow properties .[10]

ii. Determination of flowable liquid-retention potential (φ-value)

To the 10 g of excipients, increasing amounts of liquid vehicle are added and mixed well. The excipients adsorbed liquid vehicle resulting in a change in its flow properties. At each concentration of liquid vehicle added, the angle of slide θ for excipients are re-determined as stated above. The corresponding Φ-value is calculated from the following equation: Φ-value = weight of liquid/weight of solid .The Φ-values are plotted graphically against the corresponding angles of slide. The Φ-value corresponding to an angle of slide of 33° represented the flowable liquid-retention potential of excipients. The Φ-value for Avicel PH and Aerosil

300 is reported in the table below and hence there is no need to determine it practically These values are used for the preparation of liquisolid tablets. The flowable liquid-retention potential (Φ-value) is defined as the maximum amount of liquid medication that a powder can retain while still exhibiting acceptable flow properties. Materials with a higher Φ-value can hold a larger quantity of liquid medication without becoming sticky or losing their flowability. This enables the incorporation of higher amounts of dissolved or suspended drug into the liquisolid system. [11,12]

Table1: Φ–values for carrier material and coating material

Non-Volatile liquid Vehicles	Φ-value for carrier material (Avicel PH101)	Φ-value for coating material (Aerosil 300)
Propylene glycol	0.16	3.31
Polyethylene glycol400	0.006	3.22
Tween 80	0.004	3.26
Cremophor EL	0.11	0.81
Capryol 90	0.13	0.41

Procedure for preparation of liquisolid system:

Several liquisolid formulations are prepared in different drug concentration Each formulation contains Avicel PH101 as carrier and Aerosil 300 as coating material, at carrier/coat ratio(R value) of 15 ,20 and 25. The appropriate amounts of carrier and coating materials used for each formulation depend upon Lf of that formulation. The ΦCa and ΦC_0 values for particular liquid vehicle are used to calculate Lf of that respective liquid vehicle. Once the liquid load factor (Lf) and amount of liquid medication (W) are determined, amount of carrier (Q) and coating (q) can be calculated . The drug-vehicle liquid system is produced by mixing drug in non-volatile liquid vehicle using a mortar and pestle. To this liquid medication, the calculated amount of the carrier (Avicel PH101) is added by continuous mixing in the mortar. Then the coating material (Aerosil 300) is carefully added and mixed until mortar contents start to look like dry powder. In the last stage of the preparation, a 5% (w/w) sodium starch glycolate as a super disintegrant and 0.75% (w/w) of magnesium stearate as a lubricant are added and mixed. All liquisolid preparations are compacted into tablets using a single punch tablet machine having 10mm flat punch.[13,14]

Table 2: Composition of liquisolid tablet

F		Drug (mg)	Liquid vehicle(mg)	Lf	Avicel PH 101(Q) (mg)	Aerosil 300 q (mg)	Disintegrant (mg)	Mg stearate (mg)	Wt of tab. (mg)
F1		50	50	0.821	121.64	24.11	17.26	2.6	265.70
F2		50	50	0.492	203.65	20.20	16.14	2.4	342.52
F3		50	50	0.381	263.16	17.63	19.06	2.8	401.97
F4		50	50	0.3	307.	15.	21.09	3.1	446

				24	68	37			.57
F5		50	50	0.29	342.93	13.68	22.75	3.4	481.85
F6		50	50	0.27	370.36	12.35	24.11	3.6	510.05

Precompressional evaluation of powder blend

i. Angle of repose

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. In this method, a fixed funnel method procedure is performed in triplicate and average angle of repose calculated .[15]

ii.Bulk density

Bulk density is the ratio between given mass of powder and its bulk volume. Bulk density is carried out in triplicate. Bulk density measurements are carried by placing fixed weight of powder in graduated cylinder and volume occupied is measured and initial bulk density is calculated. It is expressed in gm/ml.[16]

iii. True density

True density is the ratio between given mass of powder and constant volume of powder after tapping. True density measurements are carried by cylinder is then tapped at a constant velocity till a constant volume is obtained. Then tapped density is calculated. [17]

iv. Carr's Index

Flowability is assessed from Carr's compressibility Index (CI %). The CI is calculated from the poured (bulk density) and tapped densities. Tapped density is measured by tapping fixed weight of the sample into 100 ml measuring cylinder several times using a tap density apparatus till a constant volume is obtained, where the powder is considered to reach to its most stable arrangement. Carr's compressibility index is then calculated . The smaller the value of the CI%, the superior the flow properties of the powder.[18]

v. Hausner's Ratio

Hausner's ratio is the ratio of tapped density to bulk density. Lower the value of Hausner's ratio better is the flow property. Values less than 1.25 indicate good flow (=20% carr), and greater than 1.25 indicates poor flow (=33% carr). Between 1.25 and 1.5, added glidant normally improves flow.[19]

Post compression evaluation of liquisolid tablets

a) Thickness

Three tablets are randomly selected from each formulations and thickness is measured individually by vernier caliper. It is expressed in millimeter (mm) and average is calculated .[20]

b) Hardness

Tablet requires a certain amount of hardness and resistance to friability to withstand mechanical shakes of handling in manufacture, packing and shipping. The hardness of the tablets is determined using Monsanto hardness tester. It is expressed in Kg/cm2. Three tablets are randomly selected from each formulation and hardness of the tablets is determined. The results are expressed in average value .

c) Weight variation

Twenty tablets are randomly selected from each formulation and average is determined. Then individual tablet are weighed and individual is compared with average weight. The tablet pass the USP test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.[21]

d) Friability test

The friability of tablets is determined using Roche friabilator. Twenty tablets are randomly selected from each formulation and initial weight of 20 tablets are calculated and then transferred into friabilator. The friabilator is operated at 25 rpm for 4 minutes (100 revolutions). The tablets are dedusted and weighed again (final weight). Compress tablet that lose less than 0.1 to 0.8% of the tablet weight are considered acceptable .[22]

f) Disintegration test

Disintegration is defined as that state in which no residue of the tablet or capsule remains on the screen of the apparatus. The disintegration time of the liquisolid tablets is determined using disintegration test apparatus. Introduce one tablet into each tube and floating of the tablets can be prevented by placing a perforated plastic disc to each tube. Suspend the basket rack in the beaker containing the 900 ml of distilled water and move the basket containing the tablets up and down through a distance of 5-6 cm at a

frequency of 28-32 cycles per minutes and the disintegration time for each formulations is noted.
Disintegration time: Uncoated tablets: 5- 30 minutes and Coated tablets: 1-2 hours.

In vitro release studies

In vitro release studies is performed by using USP type II Paddle dissolution apparatus in 900 ml of distilled water maintained at 37° C ± 0.5° C and rotation speed of 50 rpm. Samples (5 ml) are withdrawn at suitable time intervals (5, 10, 15, 20, 25, 30, 45, 60 minutes) and filtered through whatman filter paper. Sink conditions are maintained throughout the study. The withdrawn samples are analyzed by UV- visible spectrophotometer (Shimadzu UV-1700 pharma spec, Japan) .

Assessment and comparison of drug dissolution rates

The dissolution rate of drug is the amount of drug (in µg) dissolved per minute by each tablet formulation during first 10 min is calculated.[23]

3. Result

Solubility studies

The solubility of drug was determined in various non-volatile liquid vehicles such as Propylene glycol (PG), Polyethylene glycol (PEG 400), Tween 80. From the results, it was observed that the solubility of drug in Propylene glycol was higher when compared with other liquid vehicles.

Table 3: Solubility study of benidipine in non volatile solvents

Sr.No	Surfactant	Solubility (%)
1	PEG-200	23.98
2	PEG-400	31.67
3	PEG-600	19.94
4	Tween 80	15.9
5	Tween 60	19.65
6	Tween 20	12.44
7	Propylene glycol	82.20

Flowable liquid-retention potential (φ-value) for excipients

Angle of slide was used to determine the Φ-value for the excipients (which are needed for calculation of the L_f). The Φ_{CA}-value (carrier) and Φ_{CO}-value (coating material) decided the appropriate quantities of carrier and coating materials required to convert a given amount of liquid medication into a dry-looking, free flowing and readily compressible liquisolid formulation. Flowable liquid-retention potential values for excipients were taken from literature .The flowable liquid-retention potential (Φ-value) for Avicel PH101 (carrier) in propylene glycol was approximately 0.16. The flowable liquid-retention potential (Φ-value) for Aerosil 300 (coating material) in propylene glycol was approximately 3.31.

Pre compressional evaluation of powder blend

Powder flow is a critical character that might affect uniformity of the tablet weight. Therefore, the flow properties of the powder blend of all liquisolid formulations were determined.

Table 4: Precompressional evaluation of powder blend

Formulation code	Angle of repose θ ± SD	Bulk density (g/ml) ± SD	Tapped density (g/ml) ± SD	Carr's index (%) ± SD	Hausner's ratio ± SD
F1	28.95± 0.73	0.205± 0.02	0.251± 0.01	17.58± 2.13	1.21±0 .04
F2	27.93± 0.78	0.325± 0.03	0.368± 0.01	11.83± 0.62	1.14±0 .02
F3	28.17± 1.04	0.645± 0.07	0.783± 0.05	17.64± 0.04	1.20±0 .04
F4	29.35± 0.81	0.496± 0.02	0.602± 0.04	18.04± 1.17	1.21±0 .05
F5	28.92± 0.69	0.514± 0.02	0.641± 0.07	19.53± 0.76	1.22±0 .09
F6	25.01± 0.26	0.824± 0.07	0.915± 0.02	9.95±1 .43	1.12±0 .04

All the above pre compressional evaluations were done for directly compressed tablets and they were within the limit .

Post compressional evaluation of liquisolid tablets

Tablets of different formulations were evaluated for the post compressional parameters such as weight variation, hardness, thickness, friability, disintegration time and drug content for tablets.

Table 5: post compressional evaluation of liquisolidtablets

Formulation	Hardness (kg/cm2)	Thickness (mm	Weight variation(mg)	Friability	Disintegration Time(sec)

code		m)		(%)	
F1	4	2.53	265.1.±.1.87	0.48	5 min 23 sec
F2	4	3.24	342.19±2.44	0.39	7 min 15 sec
F3	5	3.45	401.7±1.81	0.29	6 min 41 sec
F4	5	2.47	446.21±2.96	0.27	4 min 32 sec
F5	5	2.52	481.58±2.28	0.43	3 min 11 sec
F6	5	4.96	510.42±3.22	0.19	2 min 10 sec

In vitro release studies:

In vitro dissolution studies were carried out by USP type II method by using distilled water as a medium. The studies were performed in all the formulations for 1 hour. Two formulation parameters such as effect of drug concentration in the liquid medication) and effect of carrier/coating ratio (R- value) that would affect the drug dissolution rate in immediate release liquisolid tablets were investigated.

Table 6: In vitro release study of formulations

Time (min.)	CUMULATIVE PERCENTAGE DRUG RELEASE ± SD*					
	F1	F2	F3	F4	F5	F6
5	30.97±0.63	31.70±1.26	33.08±0.36	32.49±0.36	37.93±0.63	27.91±0.63
10	41.77±0.63	41.14±0.63	45.67±0.63	43.56±0.36	47.99±0.96	49.76±0.36
15	48.97±0.63	49.28±0.36	50.98±0.63	49.49±0.36	55.42±0.63	55.94±0.96
20	62.01±0.63	61.15±0.96	61.91±0.63	61.57±0.36	65.85±0.63	68.37±0.97
25	69.15±0.97	68.23±0.37	68.80±0.36	68.49±0.63	73.59±0.97	77.34±1.27
30	78.54±0.64	76.19±0.37	77.20±1.68	76.42±0.36	80.53±0.64	84.03±0.65

45	85.83±0.64	84.87±0.64	85.97±1.33	87.51±0.97	89.99±1.28	91.93±1.28
60	90.45±0.65	91.56±0.64	92.87±0.35	93.24±0.62	94.64±0.35	99.67±0.99

Conventional Tablet (min)	7.76±0.3 (5min)	12.97±0.6 (10min)	16.41±0.3 (15 min)	19.61±0 6 (20 min)	25.50±0.6 6 (25 min)	29.94±0.9 (30min)	34.34±0.6 6 (45 min)	39.20±0 6 (60 min)

Assessment and comparison of drug dissolution rates

The concentration of propylene glycol is one of the main factors for the formulation of a liquisolid tablets and has considerable effect on the 10 min dissolution rate. Dissolution rate increased with an increase in the concentration of propylene glycol. F6 formulation showed maximum dissolution rate so it will be the optimized formulation.

Table 7: Dissolution rate of conventional tablet and formulation in 10 min

S. NO	**Formulation code**	**Dissolution rateafin 10 min**
1	F1	90.12
2	F2	
3	F3	
4	F4	
5	F5	
6	F6	
7	**Conventional tablet**	26.51

Conclusion

The present study was successfully undertaken to formulate and characterize a liquisolid system of

Benidipine with the objective of enhancing its solubility and dissolution behavior. The liquisolid technique provided an effective approach for incorporating Benidipine into a suitable liquid vehicle followed by conversion into a dry, free-flowing and compressible formulation using appropriate carrier and coating materials. The developed formulations were evaluated for their pre-compression and post-compression characteristics to determine their suitability for oral drug delivery.

Among all the prepared formulations, F6 was identified as the best and optimized formulation based on its overall physicochemical and pharmaceutical characteristics. F6 demonstrated satisfactory flow properties, uniform drug content, acceptable tablet characteristics, adequate hardness, low friability, and suitable disintegration behavior. These results indicated that the selected proportions of liquid vehicle, carrier, and coating material in F6 produced a physically acceptable and stable liquisolid formulation.

FTIR characterization of the optimized F6 formulation indicated compatibility between Benidipine and the selected excipients, without major changes suggestive of significant chemical interaction. The satisfactory physicochemical properties and enhanced dissolution behavior of F6 confirmed that the optimized formulation was superior to the other investigated batches.

Thus, F6 was considered the optimized liquisolid formulation of Benidipine, providing an effective improvement in drug dissolution through the liquisolid technique. The findings establish that liquisolid technology is a simple and promising solubility enhancement approach for poorly water-soluble drugs such as Benidipine. Further stability and in-vivo studies may be undertaken to confirm the long-term stability and potential improvement in oral bioavailability of the optimized F6 formulation.

References

1. Abdul Hasan Sathali A., Gopinath M., 2013. Formulation and evaluation of paliperidone nanocrystals, *BioMedRx*, 1(5), 422-438.
2. Brahmankar D.M., Sunil B. Jaiswal., 1995. Biopharmaceutics and Pharmacokinetics- A Treatise, 2(2), 401-409.
3. Doney Alex Baby., Soumya Saroj., Sabitha.M, 2012. Mechanism of solubility of liquisolid formulation in non volatile solvent: A review, *Int. J. Pharm. Pharm. Sci.* Vol 4(3), 710-715.
4. Hitendra S. Mahajan., Manoj R. Dhamme., Surendra G. Gattani., Ashwini D. Rasal., Hannan T. Shaikh., 2011. Enhanced dissolution rate of Glipizide by a liquisolid technique, *Int. J. Pharm. Sci. Nanotech*, 3(4), 1205-1213.
5. Kapure V.J., Pande V.V., Deshmukh P.K., 2013. Dissolution enhancement of Rosuvastatin calcium by liquisolid compact technique. *J. pharma*. 1-9.
6. Karmakar A.B., Gonjari I.D., Hosmani A.H., Dhabale P.N., Bhise S.B., 2009. Dissolution rate enhancement of fenofibrate using liquisolid tablet technique, *Lat. Am. J. Pharm.* 28(2), 219-225.
7. Karmarkar A .B., Gonjari I. D., Hosmani A .V., 2009. Liquisolid Tablets: A novel approach for drug delivery, *Int. J. Health Res.* 2(1), 93-98.
8. Marc Vermeir., Ineke Naessens., Bart Remmerie., Geert Mannens., Jan Hendrickx., Patrick Sterkens., Krishna Talluri., Sandra Boom., Marielle Eerdekens., Nancy van Osselaer., Adriaan Cleton., 2008. Absorption, metabolism, and excretion of paliperidone, a new monoaminergic antagonist, in humans, Drug metabolism and Disposition, 36, 769-779.
9. Pathan A.B., Doijad R.C., Gaikwad S.S., Baraskar S.S Pawar N.B., Maske V.D., 2012. Liquisolid: A novel technique for dissolution enhancement of poorly soluble drugs, *CPR,* 3(1), 735-749.
10. Prasanth Sai R.V., Pujitha I., Srinivas Thota., Nagu A., 2011. Formulatioon and development of Entecavir Tablets, *Int. J. Res. Pharma. and Biomed. Sci.* 2(3), 1239-1247.
11. Rajesh K., Rajalakshmi R., Uma Maheswari J., Ashok Kumar C.K., 2011. Liquisolid technique: A novel approach to enhance solubility and bioavailability, *Int. J. Biopharm.* 2(1), 8-13.
12. Rambabu C., Umamahesswar K., Ramu G., 2013. A reverse phase HPLC method development and validation for the determination of paliperidone in pure and dosage forms, Chem. Sci. Trans, 2(1), 41-46.
13. Raymond C Rowe., Paul J Sheskey and Sian C Owen., 2006. The handbook ofPharmaceutical excipients, Pharmaceutical Press, London, 5th edition, 132-135, 188-191, 430-433, 545-550, 580-584, 572-579, 624-626, 701-704, 767-769.
14. Sambasiva Rao A., Naga Aparna T., 2011. Liquisolid technology: An overview, *Int. J. Res. Pharm. & Bio. Sci.* Vol 2(2), 401-409.
15. Sean C Sweetman., 2009. Martindale, The complete drug Reference, Pharmaceutical Press, London, 36th edition, 1015.
16. Shasidher Burra., Madhusudhanrao Yamsani., Venkateswarlu Vobalaboina., 2011. The

liquisolid technique: an overview, *Brazilian J. Pharm. Sci.* 47, 475-482.

17. Srinivas Vaskula., Sateesh Kumar Vemula., Vijay Kumar Bontha., Prasad Garrepally., 2012. Liquisolid compact: An approach to enhance the dissolution rate of Nimesulide, *J. Applied Pharm. Sci.* 02 (05), 115-121.

18. Vekariya Dhavalkumar., Zalavadia Dikesh., Doshi Sumit., 2012. Enhancement of bioavailability of poorly water soluble drugs by liquisolid technique: A Review, *Int. J. Pharm. and chem. Sci.* 1(2), 850-858.

19. Vikrant Arya., Narender Thakur., Sukhbir Lal Khokra., Dhamesh Sharma., Naseeb Singh Thakur., Rahul Purohit., 2011. A review on pharmaceutical applications of liquisolid technique, *American J. PharmTech Res*. 1(3), 1-18.

20. Vinay Kumar V., Kumara Swamy S., Thirveen Ch., Agariah Goud B., 2012. Enhancement of solubility and physicochemical characterization of paliperidone solid dispersions, *JAPS,*Vol 2(2), 278-288.

21. R. K. Yellela. Pharmaceutical technologies for enhancing oral bioavailability of poorly soluble drugs. Journal of Bioequivalence & Bioavailability 2010; 2 (2): 28–36.

22. G. L. Amidon, H. Lennernäs, V. P. Shah, J. R. Crison. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm. Res 1995;12: 413–20.

23. Kim C,Park J. Solubility enhancement for oral drug delivery: can chemical structure modification be avoided. Am.J.Drug Deliv 2004;2:113-30. 5. D. Sharma, M. Soni, S. Kumar, G. D. Gupta. Solubility enhancement— eminent role in poorly soluble drugs. Research Journal of Pharmacy and Technology 2009;2(2):220–224.

24. A. Kumar, S. K. Sahoo, K. Padhee, P. S. Kochar, A. Sathapathy, N. Pathak. Review on solubility enhancement techniques for hydrophobic drugs. Pharmacie Globale 2011;3(3):1-7.