INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH

FORMULATION AND EVALUATION OF LIQUISOLID COMPACTS OF RISPERIDONE

Joslin J[*], Bharani S Sogali[**]

Department of Pharmaceutics, Krupanidhi College of Pharmacy,#12/1,Chikkabellandur,Carmelaram Post,Varthur Hobli, Banglore-560035, KA.

ARTICLE INFO

Article history
Received 09/06/2018
Available online
30/09/2018

Keywords
Risperidone;
Liquisolid Technique;
Dissolution Property;
Flow Properties.

ABSTRACT

According to the liquisolid methodology, liquid medications in solutions or suspension form of water insoluble drugs in suitable nonvolatile liquid solvent can be converted into readily flowing and adequately compressible powders by a simple addition with certain powder substrates, referred to as the carrier and coating materials. Release rates are enhanced due to the increased wetting properties and surface area of drug available for dissolution. Liquisolid tablets of Risperidone containing MCC and Aerosil 200 as powder substrates of different excipient ratios from 5 to 35 were prepared using PG as non volatile solvent. Before compression, powdered mass were evaluated for flow properties such as bulk density, tapped density, angle of repose, Carr's compressibility index and Hausner's ratio and the formulated liquisolid tablets were evaluated for post compression parameters such as weight variation, hardness, friability, drug content uniformity, and disintegration time. The release rates of all products were assessed using the USP type II dissolution apparatus. It was observed that maximum drug dissolution rates exhibited by systems that have powder substrates with optimum carrier to coating ratios (20:1). FTIR spectra and DSC illustrated no significant interaction between drug and excipients used. From this study it was concluded that the liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs.

Corresponding author
Joslin J
Department of Pharmaceutics,
Krupanidhi College of Pharmacy,
#12/1, Chikkabellandur, Carmelaram Post, Varthur Hobli, Banglore-560035,KA
joslinjo91@gmail.com
7093254363

*Please cite this article in press as **Joslin J** et al. Formulation and Evaluation of Liquisolid Compacts of Risperidone. Indo American Journal of Pharmaceutical Research.2018:8(09).*

INTRODUCTION

The most convenient drug delivery is by oral administration because of its patient compliance, non invasiveness, convenience, low manufacturing cost, improved stability, accuracy in dose and ease of production. They can be made in exceedingly non-sterile surroundings and its instrumentality and technology is well acknowledged, quite a hundred years of development.

But oral administration of poor water soluble drug usually requires high doses and frequent administration so as to reach therapeutic plasma concentrations due to insufficient dissolution rate of the drug, which is the rate determining factor in the oral bioavailability and one of the most challenging aspects of drug development. There is an established theory that the dissolution of active ingredients in oral dosage forms is the important step before absorption can take place from the gastrointestinal tract to the blood circulation system. Dissolution rate is the rate limiting factor in the absorption of class II (low solubility and high permeability) and class IV (low solubility and low permeability) drugs as defined by Biopharmaceutics Classification System (BCS) [1,2]. According to BCS more than 40% of drugs are poorly water soluble. These drugs have slow absorption into the plasma, leading to low and inadequate bioavailability, but also raised toxicity to the gastrointestinal mucosa due to its accumulation in the GI tract.

Liquisolid system is a novel and most innovative outbreak proposed by Spireas *et al.*, that can enhance both rapid release and dissolution rate of poorly soluble drug by keeping the drug in molecularly dispersed system, where the drug is dissolved or dispersed in a non-volatile solvent and this liquid medication is converted to non adhesive, free flowing and readily compactable powder by utilizing carrier (cellulose, starch, lactose, sorbitol, Avicel PH 102 and 200, Eugragit RL and RS) and coating material (Cab-0-Sil M5,Aerosil 200,Syloid 244FP) to which suitable excipients will be added and compressed to tablets by simple direct compression. [3]

Enhancement of drug release from liquisolid compact is explained by an increased surface area, increased aqueous solubility and improved wetting properties by nonvolatile solvent. [4,5]

So in this present investigation liquisolid technique was adopted which would provide scope for improving solubility and dissolution of risperidone, which is a poorly water soluble drug by dissolving in non volatile solvent and incorporating coating and carrier material.

MATERIALS AND METHOD

Table 1: List of materials used with their source.

SL. No.	Materials used	Manufacturer
1	Risperidone	Mankind pharma Ltd
2	Propylene glycol(PG)	SD Fine chem Ltd
3	Micro crystalline cellulose(MCC)	SD Fine chem. Ltd
4	Aerosil 200	Central house Ltd
5	Sodium starch glycholate(SSG)	SD Fine chem. Ltd
6	Magnesium stearate	SD Fine chem.Ltd

All other chemicals, reagents and solutions used were of analytical grade.

Compatibility studies by FTIR

A Fourier transform infrared spectrum (FTIR) was used to identify if any interaction exist between Risperidone and excipients used.

Solubility studies of Risperidone

Solubility studies of Risperidone were carried out in propylene glycol, PEG 400, Tween 80. Saturated solutions prepared were rotated in an orbital shaker for 72 h at 25 °C. The solutions were filtered and their concentration was determined by UVspectrophotometry (Shimadzu Corporation Pvt. Ltd. Nishinokyo-Kuwabara-cho, Nakagyo-ku, Kyoto 6048511, Japan) at 272nm.

Determination of the optimal flowable liquid retention potential (φ–value) for MCC and Aerosil [6,7,8]

Angle of slide method has been used to determine the flowability of powder excipients used for liquisolid systems. Mathematical models were employed to calculate required amount of carrier and coating material for preparing the compacts. The φ–value of a powder is defined as the maximum amount of a given non-volatile liquid that can be retained inside its bulk per unit weight of powder whilst maintaining acceptable flowability. This φ–value is determined by estimating flow of powder/liquid admixture and this value is taken at an angle of slide corresponding to 33° (for optimal flow properties). The φ–value is calculated by using following equation,

$$\varphi = \text{weight of liquid/weight of solid} \quad \text{Eq. (1)}$$

The ψ value of powder is the maximum amount of liquid, the powder can retain inside its bulk per unit weight of powder whilst maintaining acceptable compactibility, to produce compacts having satisfactory hardness and friability, with no liquid squeezing out during compression. The ψ-number of powders can be determined using pactisity theory.

A maximum liquid load on the carrier material by maintaining acceptable flowability and compressibility of compacts is termed as a liquid load factor (Lf) and is defined as the weight ratio of the liquid medication (W) and carrier powder (Q) in the system, as given

$$Lf = W/Q \qquad \text{Eq. (2)}$$

For powder substrates containing a fixed amount of carrier and coat material, there should be a constant Lf to produce acceptably flowing liquisolid systems. Such Lf depends upon φ–value of both carrier and coat and upon excipients ratio (R). The R is a ratio of the weights of the carrier (Q) and coat (q) material present in the formulation and is given by equation.

$$R = Q/q \qquad \text{Eq. (3)}$$

The R and Lf of the formulations are related as follows,

$$\Phi Lf = \Phi + \varphi.(1/R) \qquad \text{Eq. (4)}$$

Lf value can be calculated from the linear relationship of Lf versus 1/R considering the values of φCA and φCO obtained from flow studies mentioned above. In current study, the flowable liquid retention potential was evaluated by measurement of angle of slide. Several homogeneous liquid vehicle/powder admixtures containing 10 g of the carrier (MCC)/coat material (Aerosil200) with increasing amount of the liquid vehicle (PG) were prepared and placed on the polished metal plate. Subsequently, the plate was tilted until the liquid/powder admixture just gradually slides over the plate. The angle formed between plate and horizontal surface was defined as the angle of the slide (θ). The φ–value of each liquid/powder admixture was then calculated by using equation (1)

Further, φ–values were plotted against the corresponding angles of slide θ. The angle of slide θ for optimal flow properties corresponding to 33° represents the flowable liquid-retention potential (φ–value) of the powder.

Preparation of liquisolid compacts

Liquisolid compacts were prepared as follows. The previously weighed solid drug and the liquid vehicle propylene glycol (PG) were mixed. The solution was then sonicated for 15 min until a homogeneous drug solution was obtained. Next, the calculated weight (W) of the resulting liquid medications (equivalent to 0.5 mg drug) were incorporated into the calculated quantities of the carrier material (MCC) (Q) and mixed thoroughly in a mortar for 2 minutes. The resulting wet mixture was then blended with the calculated amount of the coating material (Aerosil 200) (q) using a standard mixing process to form simple admixture which looks dry. Several factors were varied like carrier: coat ratios (different R values) ranging from 5 to 35 was employed. Different liquid load factors (Lf) ranging from 0.517 to 0.180 and finally 2.5% and 5 % w/w of sodium starch glycolate as the disintegrant were mixed in final powder blend. The prepared liquisolid powder systems were compressed into tablets by tablet punching machine.

Table 2: Ingredients used in the formulation.

Sl.No	Ingredients	Formulation code									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Risperidone	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
2	Propylene Glycol	77.5	77.5	77.5	77.5	77.5	77.5	77.5	77.5	77.5	77.5
	Ca:Co(R)	5	10	15	15	20	20	25	25	30	35
4	Lf	0.517	0.320	0.259	0.259	0.228	0.228	0.207	0.207	0.189	0.180
5	MCC(Q)	149.7	242.18	299.3	299.3	339.9	339.9	372.5	372.5	410	430
6	Aerosil(q)	29.9	24.21	19.9	19.9	16.9	16.9	14.9	14.9	13.6	12.3
7	SSG	5%	5%	2.5%	5%	2.5%	5%	2.5%	5%	5%	5%
8	Unit weight(mg)	270	361.07	406.6	416.6	445.1	456.0	476.7	488.1	526.15	545.7

Evaluation of Liquisolid compacts [9, 10, 11, 12]

Pre compression parameters

Angle of Repose

Angle of repose was determined by using equation given below,

$$\tan \theta = h/r;$$

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

Bulk Density
Bulk density is calculated by following formula,

Bulk density = Weight of powder / Bulk volume

Tapped density
A given quantity of powder is transferred to a measuring cylinder and is tapped mechanically till a constant volume is obtained.

Tapped density = Weight of powder / Tapped volume

Carr's Index
It is used to evaluate flowability of powder by using formula

$$\% \text{ compressibility} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}}$$

Hausner's Ratio
Hauser's ratio is used to determine the flow property of powder and can be calculated by the following formula

Hausner's Ratio= Tapped density/ Bulk density

Post compression parameters
Hardness
It is measured using hardness tester (Monsanto hardness tester). The mechanical strength of a tablet is associated with the resistance of a tablet to fracture or attrition.

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

Disintegration Time
The time taken to disintegrate 6 tablets of each tablet formulation was determined using disintegration tester.

Drug Content Uniformity
Three tablets from each formulation were powdered. The powder equivalent to 0.5mg of Risperidone was weighed and dissolved in 0.1N HCl 100ml in standard flasks. From this suitable dilution was prepared and the solution was analyzed at 272nm using UV spectrophotometer using 0.1N HCl as blank.

Friability Test
10 tablets were weighed accurately, and rotated up to 4 minutes at 25rpm in friabilator. After 4 minutes remove the tablets and weigh the friability from initial weight to final weight.

% Friability= weight of tablet before test(X1) - weight of tablet after test(X2)/ (X1)

In vitro Dissolution Studies
The USP dissolution apparatus II was used with 900 ml dissolution media as 0.1N HCl and the apparatus was run at 50 rpm on 37± 0.5°C. Aliquots were withdrawn at a specified time intervals and replenished by fresh dissolution medium. Aliquots were diluted and concentrations of aliquots analyzed spectrophotometrically at 272 nm using UV Spectrophotometer.

Differential Scanning Calorimetry (DSC)
The thermal behavior of Risperidone and the optimised formulation (F6) was studied using Differential Scanning Calorimetry. The samples were heated from 0 to 200ºC at a heating rate of 5ºC/min under a nitrogen flow, flowing at a rate of 40cc/min through the DSC cell.

Short-term stability studies
Stability studies was carried out at two different storage conditions at 25°C ±2°C/60% ± 5% RH and 40°C±2°C/75%±5% RH for 1 month. The physical appearance, % drug release and drug content uniformity was calculated after 30 days.

RESULTS AND DISCUSSION

Solubility studies

The solubility studies were conducted in different solvents like Propylene glycol (PG), PEG 400, Tween 80, PG-Tween 80 (0.5%), and PG-Tween 80 (1%). The results of the solubility studies were given Table 4. Highest solubility of risperidone was observed in Propylene glycol (7.7 mg/ml). As the solubility of the drug in non volatile solvent is important to make uniform molecular dispersion for improving the dissolution rate, PG was selected as solvent for developing formulations.

Table 3: Saturation solubility study of Risperidone.

SL. No.	Solvent	Solubility(mg/ml)
1	Tween 80	2.5
2	PG+ Tween 80(0.5%)	6.9
3	PG	7.7
4	PEG 400	4.01
5	PG+ Tween 80(1%)	2.9

Determination of the optimal flowable liquid retention potential (φ–value) for MCC and Aerosil

Figure 1 shows the relationship between the angle of slide and the corresponding φCA-value (MCC) and φCO-value (Aerosil). Results indicated that the flowable liquid-retention potential for carrier (φCA) and coating (φCO) was 0.12 and 1.9, respectively.

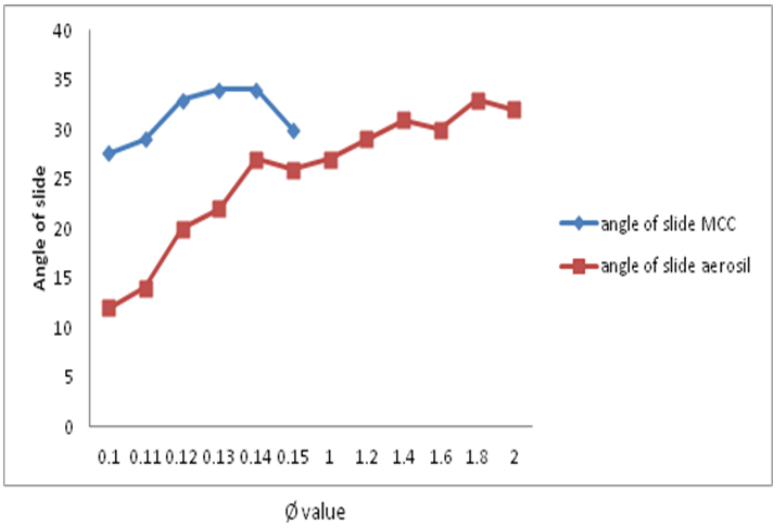

Fig 1: Determination of flowable liquid retention potential.

Drug excipient interaction (FTIR) study

From the spectra of Risperidone and formulation (F6), given in fig 2 and 3, it was observed that all characteristic peaks of Risperidone were present in the combination spectrum, thus indicating compatibility of Risperidone and excipients used.

The IR spectrum of Risperidone exhibits characteristic peaks at 1350 cm-1(C–F functional group), 1747cm-1 (C=O group stretching vibration), 1614cm-1 (N-H functional group), 1645cm-1(C=N). The peak at 3000 cm-1 indicates the presence of methyl group.

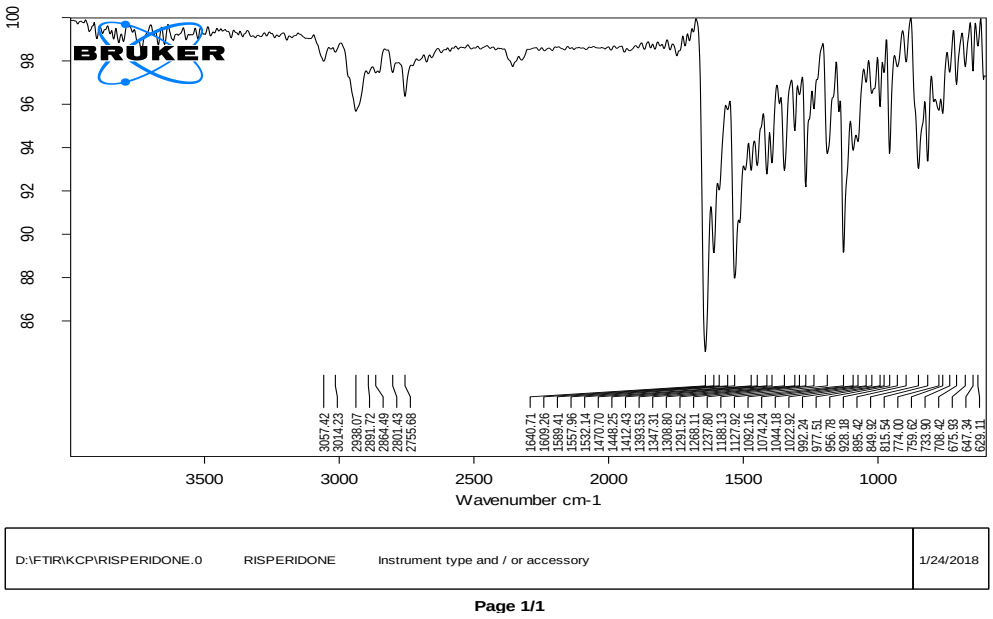

Fig 2: IR spectra of Risperidone.

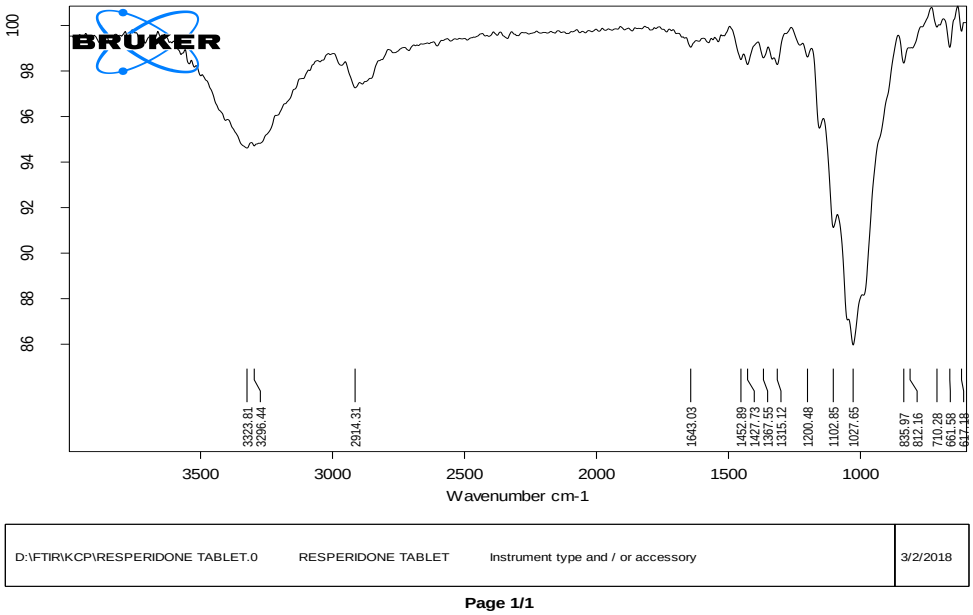

Fig 3: IR spectra of Formulation F6.

Evaluation of prepared liquisolid compacts

Pre compression parameters

The flow properties and compressibility of LS compacts were estimated using angle of repose, hausner ratio, Carr's index and compressibility index. Formulation F1 was not free flowing and formed an adhesive powder. Formulations F2 showed poor flow characters. F4 to F8 showed good flowability where as F3, F9, and F10 showed passable limits. The results of these parameters are given in Table 4.

From the above results, the LS systems with low Lf and high R values have better flow properties. This can be explained by the fact that, the LS systems with low Lf values and high R contain high amounts of carrier material (MCC) and low quantities of liquid.

Table 4: Characterization of powder of F2 – F10.

Sl no	Bulk density (g/ml)* ±S.D	Tapped density (g/ml)* ±S.D	Hausners ratio*±S.D	Carrs index* ±S.D	Angle of repose* ±S.D
F2	0.343±0.001	0.499±0.004	1.45±0.005	31.28±0.001	35.66±0.4
F3	0.395±0.001	0.48±0.004	1.23±0.008	17.7±0.004	34.58±0.4
F4	0.396±0.001	0.486±0.008	1.26±0.008	18.7±0.008	33.33±0.5
F5	0.396±0.001	0.486±0.008	1.26±0.008	18.7±±0.002	33.33±0.5
F6	0.455±0.005	0.573±0.001	1.29±0.001	20.06±0.008	31.66±0.5
F7	0.425±0.001	0.561±0.002	1.32±0.002	24.24±0.002	32.4±0.5
F8	0.427±0.001	0.551±0.002	1.29±0.002	22.58±0.002	33.54±0.5
F9	0.446±0.001	0.604±0.005	1.35±0.005	26.15±0.001	32.66±0.4
F10	0.466±0.005	0.682±0.001	1.34±0.001	25.67±0.001	30.21±0.8

*Note: Values are expressed as Mean ±SD, n=3

Post Compression parameters

Table 5: Characterization of tablets of F3 – F9.

Sl no	Hardness(kg/cm) ±S.D(n=6)	Friability(%) ±S.D(n=10)	%Weight variation(mg) ±S.D(n=20)	Thickness (mm) ±S.D(n=6)	Drug content ±S.D(n=3)	Disintegration time(sec) ±S.D(n=6)
F3	3±0.001	0.145±0.003	497±0.14	4.12±0.11	93.57±0.004	17±0.5
F4	4±0.001	0.154±0.001	505±0.16	4.10±0.21	93.64±0.003	14±0.5
F5	5.5±0.003	0.143±0.004	499±0.11	4.06±0.01	96.01±0.02	19±0.08
F6	5.5±0.004	0.125±0.002	503±0.11	4.02±0.01	99.44±0.02	14±0.5
F7	5±0.006	0.140±0.002	504±0.11	4.07±0.03	98.28±0.02	25±0.08
F8	6±0.003	0.133±0.002	498±0.25	4.14±0.11	96.49±0.004	21±0.5
F9	5.5±0.007	0.146±0.003	497±0.52	4.37±0.14	97.45±0.07	25±0.2

*Note: Values are expressed as Mean ±SD

The compressed tablets of ten different LS compacts were subjected to hardness, thickness, weight variation, friability and disintegration test. The drug content uniformityof the compressed tablets was also performed. The results are given in Table 5. Hardness from 3 to 6 kg/cm2 was obtained for prepared LS Tablets. Thickness of all formulations was found to be 4.02mm to 4.37mm. Drug content of all the prepared tablets was found to be 93.57%to 99.54% .F6 showed hardness (5.5 kg/cm2), thickness of 4.06mm, friability of 0.19 and disintegration time of 14 sec. Among different formulations, F6 showed good flowability and compressibility and showed sufficient hardness, and other parameters were within the limits as given in table (5).

It was found that there is a relationship between Lf value and the hardness of the tablets. The Lf value was inversely proportional to the hardness of the tablets i.e., when the Lf value increases, the hardness of the tablet will decrease. This can be explained by that, increasing Lf value increases the amount of solvent used and decrease the amount of highly porous material and the amount of coating material and this subsequently leads to decreased hardness of the tablets.

All the liquisolid tablets had acceptable friability as none of the tested tablet was cracked, split or broken in any formula. Hence they are expected to show acceptable durability and withstand abrasion in handling, packaging and shipment.

Fast disintegration of tablet can be explained by the disintegrating property of microcrystalline cellulose. In addition use of SSG accelerates the disintegration of tablets by its unique ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration.

DSC studies

Thermogram of pure drug Risperidone revealed that the pure drug has a sharp endotherm at 174ºC(fig15) whereas Risperidone in F6 formulation has broad peaks shifted to higher range of 375ºC (fig 16). Formulation F6 doesn't show any melting endothermic peak of the drug, which shows complete change of crystalline drug to amorphous state which implies that the drug was completely molecularly solubilzed within non volatile solvent propylene glycol. DSC studies show that there was no significant interaction between drug and the excipients used as given in fig 4 and 5.

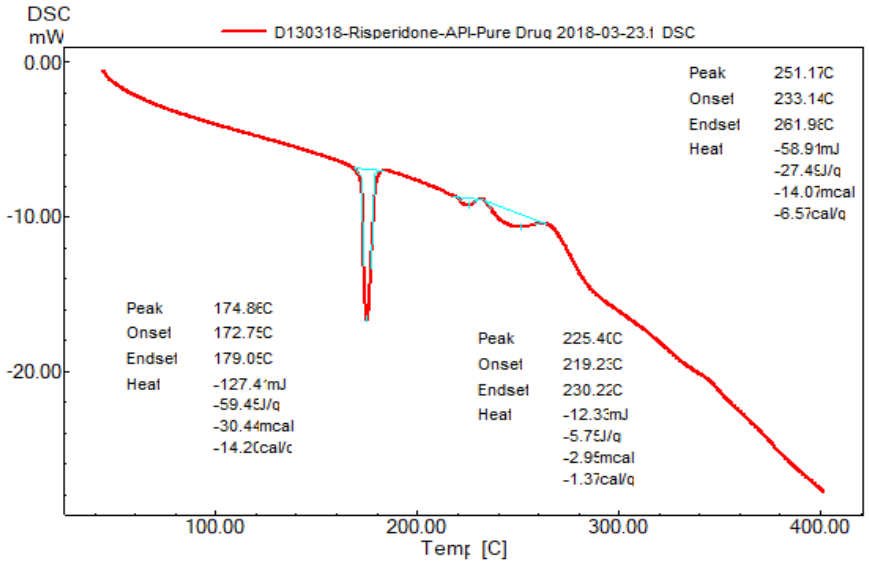

Fig 4: DSC of Risperidone pure drug.

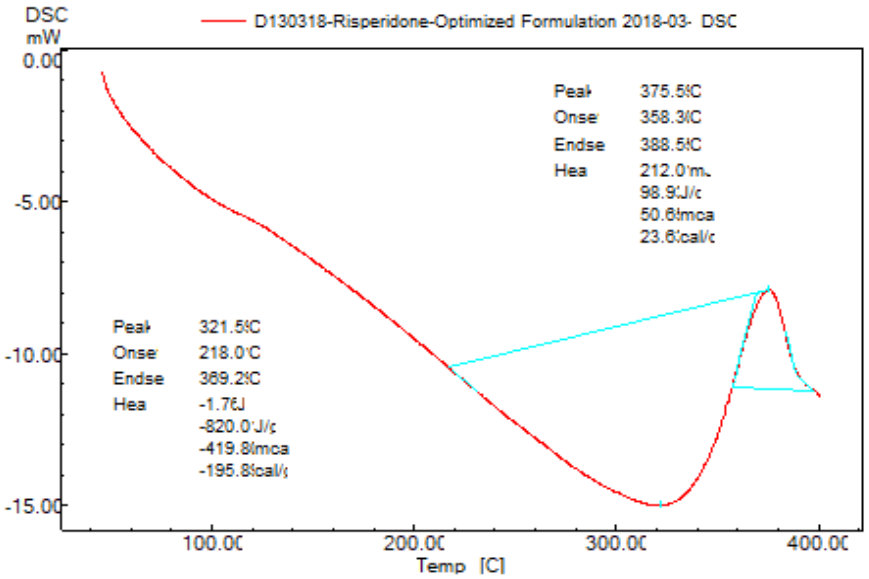

Fig 5: DSC of formulation F6.

In vitro dissolution studies

Dissolution studies of LS compacts, was performed in 0.1 N HCl. Drug equivalent to 0.5 mg of risperidone was taken for the study. Among different formulations, tablets with F6 LS compacts had shown 100% drug release within 2mins of dissolution study as given in fig 6. LS compacts contain drug in a liquid state by dissolving in PG, which reduces interfacial tension between the particle and when such compacts with suitable coating material is exposed to dissolution medium, molecular dispersions would be forming which enhances the solubility and dissolution rate. Addition of super disintegrant aided in the immediate disintegration into fine particles.

The excipient ratio (R) value is an important parameter which is the ratio between the weights of the carrier and the coating material has an influence on drug release. An increase in the R value (F5-F10) resulted in an enhanced release rate. LS compacts with high R values contain high amounts of MCC, low quantities of CSD and low liquid to powder ratios. This is associated with enhanced wicking, disintegration and thus, enhanced drug release. In contrast, if high amounts of colloidal silica are used, which means that the R value is low (F1-F4), the LS compact is overloaded with liquid formulation due to a high Lf. In such cases, even though drug diffusion out of the primary particles may be rapid, oversaturation might occur resulting in local precipitation or recrystallization of the drug and thus decreased release rates.

The enhanced dissolution rates of liquisolid compacts may be attributed to the fact that, the drug is already in solution in PG. Thus, its release is accelerated due to its markedly increased wettability and surface area availability to the dissolution medium. PG facilitates wetting of drug particles by reducing interfacial tension between dissolution medium and tablet surface.

This study confirmed that the R value is an important parameter for LS systems and must be minimum 20 to obtain enhanced drug release.

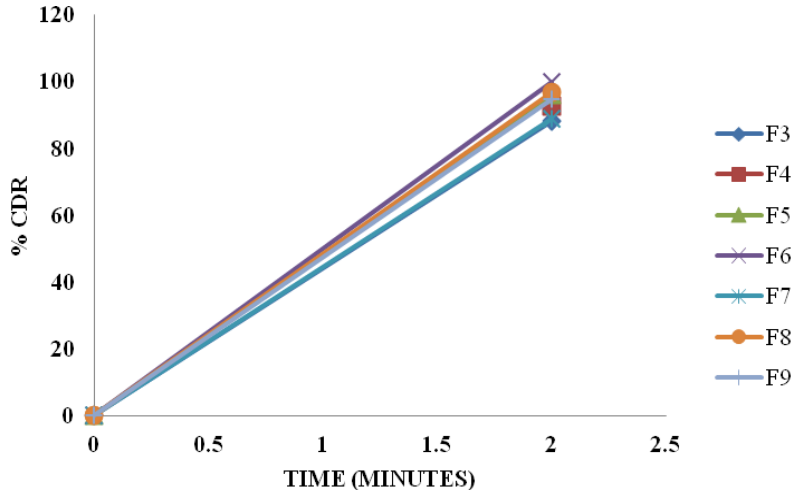

Fig 6: *In vitro* dissolution studies of Formulations F3-F9.

Short term stability studies

Table 6: Physical appearance and drug content uniformity of F6.

Physical appearance		Drug content Uniformity ± SD (n=3)	
25°C ±SD (n=3)	40°C±SD (n=3)	25°C ±SD (n=3)	40°C±SD (n=3)
White coloured tablet	White coloured tablet	98±0.32	97±0.03

Table 7: *In vitro* dissolution of F6 in 0.1N HCl after 30 days storage.

% CDR at at 25°C±2°C ±SD (n=3)	%CDR at 40°C±2°C ±SD (n=3)
99±0.41 in 2 min	97±0.54 in 2 min

CONCLUSION

The Liquisolid technique is innovative alternative for improvement of dissolution property of water-insoluble drugs. The enhanced release rate of Risperidone from liquisolid tablets is due to an increase in wetting properties and effective surface area of drug particles which is in solubilsed state in tablet available for dissolution. Even though the drug is in a solid dosage form, it is held within the powder substrate in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties.

The solubility studies were conducted in different solvents like Propylene glycol (PG), PEG 400, Tween 80, PG-Tween 80 (0.5%), and PG-Tween 80 (1%). Highest solubility of risperidone was observed in Propylene glycol (7.7 mg/ml) and hence was selected as solvent for developing formulations. F4 to F8 showed good flowability where as F3, F9, and F10 showed passable limits. Hardness from 3 to 6 kg/cm^2 was obtained for prepared LS Tablets. Drug content of all the prepared tablets was found to be 93.57%to 99.54% .F6 showed hardness (5.5 kg/cm2), thickness of 4.06mm, friability of 0.19 and disintegration time of 14 sec. Among different formulations, F6 showed good flowability and compressibility and showed sufficient hardness, and other parameters were within the limits.

The FTIR spectra showed that there was no interaction between drug and excipients.From the results of release profile of drug from LSC, tablets with excipients ratio (R) of 20:1 and 5% SSG (F6) was found to be the better one with drug release of 100%±0.01 in 2 minutes. The stability study showed that the drug contents and dissolution profiles are not affected by stability conditions suggesting the chemical stability on exposure of accelerated conditions. Thus, liquisolid approach has potential application for formulation research in improvement of dissolution rate of Risperidone and can be further studied in animal models to establish improved dissolution characteristics.

ACKNOWLEDGEMENT

The authors are grateful to Dr. Amit Das, Principal, Prof. Suresh Nagpal, Chairman Krupanidhi College of Pharmacy, for providing infrastructure, essentials facilities, conferring full liberty to stay in the research labs and to extract the better out of the best. And I place on record a deep sense of gratitude and heartfelt thanks to my research guide Dr. Bharani S Sogali, for her help, support and constant encouragement throughout the progress of this work. At last but not least, I express my eternal heartfelt gratitude to my Family members and Teachers for their encouragement, inspirations, and support without which it would have been impossible to accomplish this task successfully.

CONFLICT OF INTEREST

The authors report that there is no conflict of interest.

REFERENCE

1. Vajir S, Sahu V, Ghuge N, Bakde BV. Liquisolid compact: A new technique for enhancement of drug dissolution. Int J Pharma Res Dev. 2012;4(3):302-06
2. Sowmya C, Reddy CS, Anilkumar D, Amrutha V, Anusha AL. Liquisolid technique: A novel approach to enhance solubility and bioavailability of BCS II drugs. Int Res J Pharm. 2012; 3(7):108-115.
3. Kiran J, Srawan JY, Santhosh P. Liquisolid compacts, an effective approach towards enhancement of dissolution rate of poorly soluble drugs. Int J Pharma Cli Res. 2015; 1(1):38-45.
4. Sanjay PD, Deepak M, Bhanudas SR. Liquisolid technology: Technique for formulation with enhanced bioavailability. World J Pharm and Pharm Sci. 2013; 3(1):368-87.
5. Vranikova B, Pavlokova S, Gajdziok J. Experimental design for determination of effect of superdisintegrant combination on liquisolid system properties. J Pharm. Sci. 2016; 13(1)1-9.
6. Gavhane KS, Sayyed F. Liquisolid compact a review. Int J Pharm Bio Res. 2013; 4(2):26-31.
7. Rajesh K, Rajalakshmi R, Umamaheshwari J, Ashok kumar CK. Liquisolid technique a novel approach to enhance solubility and bioavailability. Int J Biopharm. 2011; 2(1):8-13.
8. Pezzini BR, Beringhs AO, Ferraz HG, Silva MAS, Stulzer HK, Sonaglio D. Liquisolid technology applied to pellets: Evaluation of the feasibility and dissolution performance using Felodipine as a model drug. 2016; 110(1):62-9.
9. Vranikova B, Pavlokova S, Gajdziok J. Experimental design for determination of effect of superdisintegrant combination on liquisolid system properties. J Pharm. Sci. 2016; 13(1)1-9.
10. Baby JN, Manjila SB, Bijen EN, Constantine I, Pramod K, Valsalakumari J. Design and technology of liquisolid compacts. J App Pharm Sci. 2013;3(8):111-19
11. Swati M. Solubility enhancement of a drug by liquisolid technique. Int J Pharm Chem and Bio Sci. 2014; 4(2):339-44.
12. Sahir V, Ghuge N, Bakde BV. Liquisolid compact: A new technique for enhancement of drug dissolution. Int J Pharm Res & Dev. 2012; 4(3):302-06.