CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.10019521

https://www.iajps.com/volumes/volume10-august-2023/40-issue-08-august-23

Available online at: http://www.iajps.com Research Article

RISPERIDONE LIQUISOLID COMPACTS–FORMULATION AND EVALUATION

Kulkarni Rupanjali [1], Devara Raj kumar [2]

[1,2] Mother Teresa College of Pharmacy, N.F.C Nagar, Ghatkesar, Medchal, Telangana.

Article Received: June 2023 Accepted: July 2023 Published: August 2023

Abstract:

Risperidone is an atypical antipsychotic agent used for serious brain illness like schizophrenia. However low aqueous solubility of this risperidone leads to its lower dissolution and thus lower bioavailability. Therefore, the development of risperidone liquisolid compacts was done with an aim to improve its dissolution rate via increasing the solubility of the drug. This results in improvement of its oral bioavailability. Aim of the present study was to augment the dissolution rate of Risperidone, thus increasing the oral bioavailability of poorly soluble drug. Preformulation studies like flow properties. The Fourier Transform Infrared spectroscopy (FTIR) results revealed that, there was no interaction among excipients (carrier, coating material, non-volatile solvent), and the drug risperidone. In-vitro drug dissolution studies showed improved in drug release of risperidone compared to pure drug. So, PEG 400, PG could be economic substitute as dissolution enhancing agent. It was determined that first order kinetics provided the greatest fit for the release data based on mathematical information obtained from models. The diffusion-controlled release mechanism is described by the Higuchi equation; the risperidone compacts' diffusion exponent indicating non-Fickian diffusion. Among PEG 400, PG, PEG 400 in 1:1 ratio with risperidone (F11, F12, F16, F17, F18) using carrier's spray dried lactose and syloid 244FP in ratio's of 10:1 and 20:1 with coating material aerosoil 200 was showing best results. F18 best among the successful formulations with highest drug release rate was compared with marketed preparation and results were better than marketed preparation.

Keywords: *Risperidone, liquisolid compacts, FTIR, Carriers, Preformulation ,In-vitro drug release.*

Corresponding author:

Devara Raj kumar,

Mother Teresa College of Pharmacy, N.F.C Nagar, Ghatkesar, Medchal, Telangana.

QR code

Please cite this article in press ***Kulkarni Rupanjali*** *et al,* ***Risperidone Liquisolid Compacts–Formulation And Evaluatio ,*** *Indo Am. J. P. Sci, 2023; 10 (08).*

INTRODUCTION:

The active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract [1]. The poor dissolution rate of water-insoluble drug is a substantial problem confronting the pharmaceutical industry. The absorption rate of a poorly water-soluble drug from solid oral dosage form is poor due to the low dissolution rate of the drug. Hence, dissolution rate is the rate determining step in drug absorption.

Various methods such as crystallization by solvent change, preparation of inclusion complexes with β-cyclodextrins, formation of water-soluble salts, micellar solubilisation, solid dispersion, lyophilisation, microencapsulation, liquisolid technique and the inclusion of drug solutions or liquid drugs into soft gelatin capsules are some of the techniques that have been reported to enhance the dissolution characteristics of water-insoluble drugs [2].

The technique of liquisolid compacts is one of the most promising techniques [3, 4]. Liquisolid concept is used to enhance the solubility of poorly water-soluble drugs at least for the first two hours (active absorption phase) and thereby increasing drug dissolution and absorption rate of drugs. The liquisolid technique as described by Spireas 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. Liquisolid powder is a free flowing and a compressible powder form of liquid medication [5]. The term liquid medication implies liquid drug and solution or suspension of water insoluble solid drug carried in suitable non-volatile liquid vehicles. Using formulation technique, a liquid medication can be converted into a dry-looking, non-adherent, free flowing, and readily compressible powder by blending with selected powder excipients referred to as the carrier and coating materials. Various grades of cellulose, starch, lactose silica powder may be used as the coating (or covering) material [6].

In liquisolid compact, the drug is in a tablet or encapsulated dosage form and it is held in a solubilised liquid state, which consequently contributes to increased drug wetting properties, thereby enhancing drug dissolution. In liquisolid formulation the drug is in either solubilised or molecularly dispersed state in the liquid vehicle, which is absorbed into or onto the carrier and coating material respectively. Hence, increased surface area of drug in powder form and enhanced dissolution of drug [7].

MATERIALS AND METHODS:

Materials:

Risperidone is a gift sample Finoso Pharm Pvt Ltd, Hyderabad. Avicel pH 102, Spray Dried Lactose, Syloid 244FP, Aerosil 200 are procured from S.D. Fine Chem. Limited, Mumbai and used in the study.

Methods:

Formulation of Liquisolid Compacts:

Non-volatile solvent selection:

The solvent in which the drug was having more solubility was selected as non-volatile liquid [8].

Carrier and coating materials selection:

In the present study based on the literature available, Spray Dried Lactose, Microcrystalline cellulose of grade avicel pH 102 and Syloid 244FP were selected as carrier and Aerosil was selected as coating material. Here carrier material is selected depending on its liquid holding capacity and it should require less compression force and should have flow improving character [9]. Selection of carriers is based on liquid loading factor.

Determination of liquid loading factor (Lf):

Lf was calculated for different carrier materials in PEG 400 and propylene glycol solvents by using formula

$$Lf = W/Q$$

W: Amount of liquid medication and Q: Amount of carrier material,

The amount of carrier and coating materials in each formulation was determined using the drug loading factors. From this equation amount of carrier required for the formulations are determined [10].

Preparation of Risperidone liquisolid compacts:

In a 20-mL glass beaker, calculated doses of risperidone and PEG 400 were correctly weighed and well mixed. Calculated amounts of carrier and coating components then contained the produced drug. Three steps were taken in the mixing process. To properly spread the liquid medication in the powder in the first, the system was mixed for about a minute [11]. In the second, a mortar's surface was coated with a uniform layer of the liquid/powder mixture, which was then let to stand for around five minutes to allow the drug solution to permeate the powder particles. In the third, an aluminium spatula was used to scrape the powder off the mortar's surface. The coating material was then added to this mixture and combined in a mortar, continuing with Carrier. The formulations are then assessed for flow characteristics, drug content, and dissolution.

Propylene glycol was used as a non-volatile solvent to create a similar set of compositions.

Method of Preparation:

Different ratios of carrier coating material are prepared (5:1, 10:1 and 20:1) Drug and non-volatile solvent are taken in equal ratios and blended properly. The drug

gets solubilize in the solvent and the resultant mixture is in a liquid form. Then to this carrier coating mixture is added until a free flowing and dry looking powder is obtained [12]. Both absorption and adsorption take place in this step. Drug particles get absorbed on to the carrier surface and then excess solvent is adsorbed by the coating material. Finally, the resulted powder is further evaluated.

Table 1: FORMULATION CHART

Formulation Code	Non-Volatile Solvent used	Carrier Material	R
F1	Propylene Glycol	Avicel pH 102	5
F2	Propylene Glycol	Avicel pH 102	10
F3	Propylene Glycol	Avicel pH 102	20
F4	PEG 400	Avicel pH 102	5
F5	PEG 400	Avicel pH 102	10
F6	PEG 400	Avicel pH 102	20
F7	Propylene Glycol	SDL	5
F8	Propylene Glycol	SDL	10
F9	Propylene Glycol	SDL	20
F10	PEG 400	SDL	5
F11	PEG 400	SDL	10
F12	PEG 400	SDL	20
F13	Propylene Glycol	Syloid 244FP	5
F14	Propylene Glycol	Syloid 244FP	10
F15	Propylene Glycol	Syloid 244FP	20
F16	PEG 400	Syloid 244FP	5
F17	PEG 400	Syloid 244FP	10
F18	PEG 400	Syloid 244FP	20

Compatibility studies:

Fourier Transform Infrared Spectroscopy:

FTIR spectra of the formulations using a Shimadzu FT-IR 8400 S spectrophotometer determined whether the drug is compatible with the formulation. Potassium bromide crystals that were dry and powdered were fully mixed with the samples [13]. After being compressed onto a disc, the combination was then introduced to a spectrophotometer, where the spectrum was recorded. The formulation's FTIR spectra were contrasted with the spectra of the pure substance and polymers. The FTIR spectra of the medication in its pure form, the polymer, and in combination are recorded.

Preformulation studies:

Saturation solubility studies:

Solubility tests were carried out in order to choose the best non-volatile solvents; during this process, pure drugs were dissolved in several non-volatile solvents. The non-volatile solvents were mixed with an excessive amount of pure medication [14]. This saturated solution was continuously vibrated for 48 hours at 25°C on the rotary shaker. The saturated solution was subjected to a 48-hour period of filtering through filter paper, followed by UV spectrophotometer analysis. [15,38, 43, 53].

Micromeritic properties [15,16]

Angle of repose:

The pure drug's angle of repose was calculated using the fixed funnel method. A funnel contained precisely weighed pure medication. The funnel's height was adjusted such that its tip just brushes the top of the powder stack. The powder was allowed to drip onto the surface from the funnel.

$$\text{Tan}(\theta) = h/r$$

Bulk density:

Bulk density equipment was used to calculate the loose bulk density and the tapped density. Pouring the mixture into a graduated cylinder allowed us to calculate the apparent bulk density. The powder's bulk volume (Vb) and weight (M) were calculated.

$$D_b = M/V_b$$

Where Db is the bulk density

M is the mass of powder

V_b is bulk volume of powder

Tapped density:

The measuring cylinder was tapped at a constant speed until a constant volume was achieved after the powder is believed to have acquired the most stable arrangement. The tapped volume (Vt) of the powder was then used to compute the final bulk density (Dt), which was then calculated using the formula below.

$$D_t = M/V_t$$

Where D_t is the tapped density

M is the mass of powder and V_t is tapped volume of powder.

Carr's Index(CI)/ Compressibility Index (%):

Indirect measurements of bulk density, size, shape, surface area, moisture content, and cohesiveness of

material were proposed using the compressibility index. It is the most straightforward method of determining how well powder flows. Using the equation below, it is determined.

CI (%) = (Tapped density – Bulk density)/Tapped density x100

Hausner's Ratio:

Hausner's ratio is an indication of powder flow property. By using following formula Hausner's ratio can be calculated

Hausner's ratio = Tapped density (D_t)/Bulk density (D_b)

Evaluation of optimized Risperidone Liquisolid Compacts:

Assay

In each formulation, six liquisolid capsules are chosen at random. Emptying capsules into a china dish yields powder, which is filtered with filter paper after being dissolved in methanol for 30 minutes [17]. At a wavelength of 237 nm, a UV spectrophotometer was used to check the drug content. The average was derived by doing each measurement in triplicate.

$$\text{Drug Content (Assay)} = \frac{\text{Practical Drug content}}{\text{Theoretical Drug content}} \times 100$$

Dissolution Test of Risperidone Liquisolid Compacts

Dissolution test USP type I (basket) was used to determine drug release from risperidone capsules. At predetermined intervals (5, 10, 15, 30, 45, 60, and 90 minutes), 5ml aliquots of the dissolution medium were removed and replaced with new medium of a constant volume 18]. Samples were cleaned up and put through a UV spectrophotometer for analysis. The unknown concentrations were calculated using a standard calibration curve.

Release kinetics [19,20]:

Kinetic Release models:

Table 2: Kinetic equations of different models

S. No.	Model	Equation
1	Zero order	$Q_t = Q_0 + K_0 t$
2	First order	$L_n Q = K t$
3	Hixson crowell	$Q_0^{1/3} - Q_t^{1/3} = K_{HC} t$
4	Higuchi	$Q = K_{HG} t^{½}$
5	Korsemeyer-peppas	$M_t / M_\alpha = K_{kp} t^n$

The cumulative amount of drug release from the formulations (F1-F18) at different time intervals were fitted to model dependent methods such as Zero order kinetics, first order kinetics, Higuchi model, Hixson-Crowell model and korsemeyer-peppas model to characterize the mechanism of drug release.

RESULTS AND DISCUSSION:

Compatibility studies:

It was anticipated that the hydroxyl groups found in Spray Dried Lactose, MCC, and the ketone (=o) group or hydroxyl (-OH) group of Risperidone might form an intermolecular hydrogen bondThe findings showed that following successful formulations, the distinctive absorption peaks attributable to pure risperidone were still visible in the liquisolid compacts without any appreciable change in their position, indicating no chemical reaction between risperidone and carrier materials.

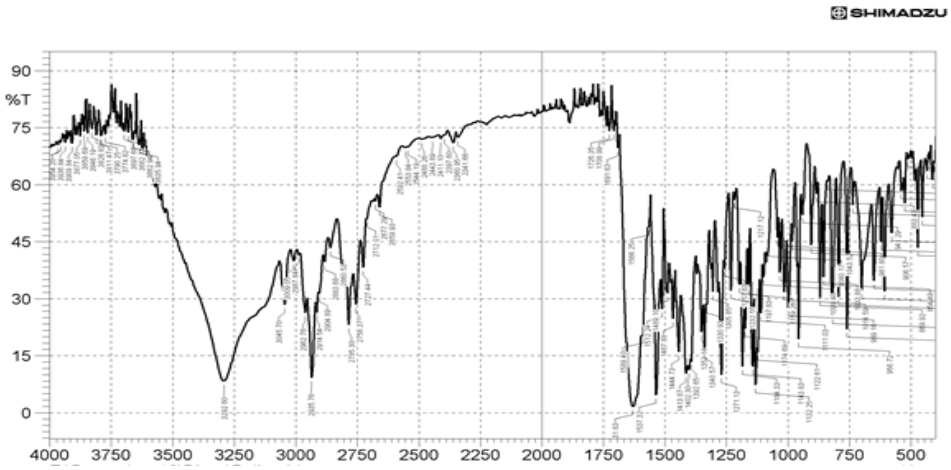

Figure 1: FTIR Graph for Risperidone

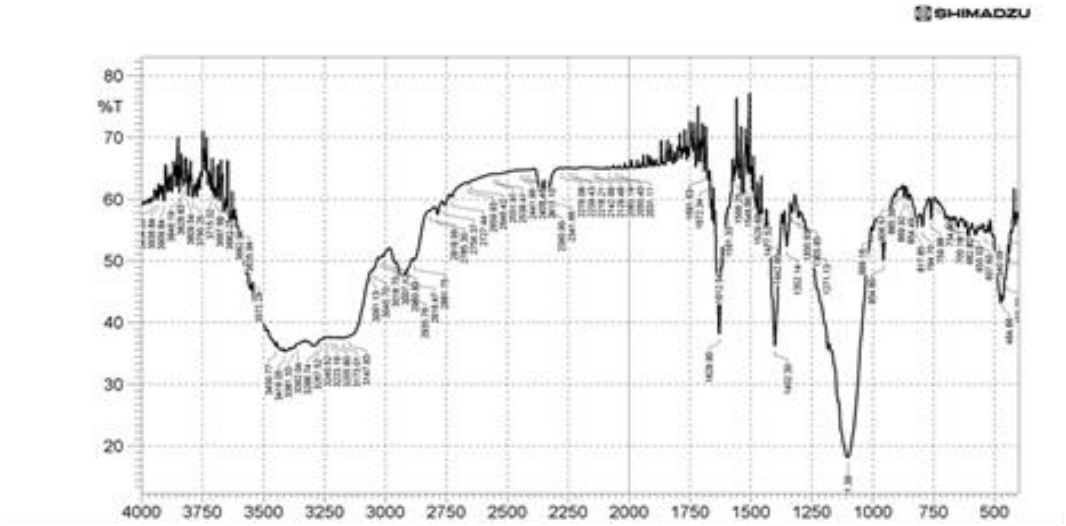

Figure 2: FTIR Graph for Optimized Formulation (F18)

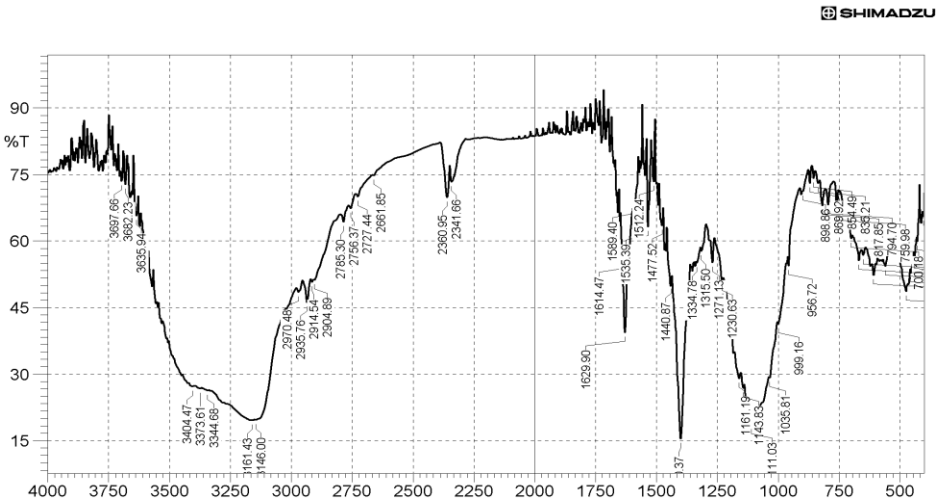

Figure 3: FTIR Graph for Optimized Formulation (F12)

Preformulation studies

Saturation solubility studies

Table 3: Results of risperidone solubility in various solvents

S. No	Solvent	Solubility(mg/ml)
1	Water	0.04±0.18
2	Phosphate buffer solution pH 6.8	0.40±0.08
3	Glycerine	0.3±0.18
4	Tween 80	0.06±0.15
5	Propylene glycol	0.6±0.22
6	PEG 400	0.59±0.08
7	0.5% SLS	0.33±0.24
8	1% SLS	0.39±0.30

Solubility of the risperidone was high in PEG 400 and propylene glycol compared with other non-volatile solvents tween 80 and glycerin and also in SLS. PEG400, with a large non polar part and several hydroxyl groups is responsible for the enhanced solubility. Propylene glycol with its hydroxyl groups may be enhancing the solubility. Therefore, PEG 400 and propylene glycol may be better choices for solvents among the non-volatile solvents.

Micromeritic properties of risperidone:

Table 4: Flow properties of risperidone

Angle of repose	48±0.1
Bulk density	0.62±0.03
Tapped density	0.95±0.03
Carr's Index	29±0.3
Hausner's ratio	1.29

Angle of repose of pure drug was about 48˚ which was greater than 47˚ (limits provided in IP 2007). Carr's index is the ratio between bulk density and tapped density which was found to be about 29 which was greater than 26 (as per limits provided in IP 2007). Hausner's ratio was about 1.29 which is greater than 1.25 (as per limits provided in IP 2007). Thus, it can be concluded that pure Risperidone has flow properties. Liquisolid technology thus is also used to improve flow properties of pure drug.

Formulation studies of risperidone liquisolid formulations:

Risperidone has high solubility in PEG 400 and propylene glycol compared to tween 80, glycerin and SLS. Thus PEG 400 which has high drug solubility of about 0.66mg/ml and propylene glycol having drug solubility of 0.58mg/ml were selected as non-volatile organic liquid vehicles for the risperidone liquisolid compacts.

Carrier and coating material selection:

In the present study, based on the literature available Spray dried lactose, Avicel PH 102, Syloid 244FP were selected as a carrier material and Aerosil 200 was selected as a coating material.

The carrier material is selected depending on its liquid holding capacity and it should require less compression force and should have flow improving character. It should be coarser granular form. Selection of carriers is based on liquid loading factor. SDL, MCC (Avicel pH 102) and also Syloid 244FP fulfill these requirements, thus are selected as carriers.

Coating material must possess high adsorptive capacity,

Liquid loading factor determination:

Table 5: Results of liquid loading factor for different carrier materials in PEG 400

Carrier material	Liquid loading factor (L_f)
Lactose	0.42
MCC (Avicel pH 102)	0.51
Syloid 244FP	0.59

From these values we can conclude that syloid 244FP is better carrier than compared to Avicel pH 102 and SDL. Thus, Syloid might impart good flow properties and higher dissolution rates to the Liquisolid formulations compared to Avicel pH102 and SDL.

Table 6: Results of liquid loading factor for different carrier materials in PG

Carrier material	Liquid loading factor (L_f)
Lactose	0.41
MCC (Avicel pH 102)	0.52
Syloid 244FP	0.57

By following the procedure given in experimental methodology results were tabulated and given in the Table 5 and they were found to be about 0.41 for Spray dried lactose, 0.52 for MCC (Avicel pH 102) and 0.57 for syloid 244 FP when the solvent used was Propylene Glycol. The values of Liquid load factor when compared in different solvents (PEG 400 and PG), values show that Syloid is better carrier and it gives higher liquid load factor with PEG 400 than with Propylene Glycol. This may be due to the effect of viscosity of the non-volatile solvents.

Pre compression evaluation studies for risperidone liquisolid formulations:

Table 7: Results of micromeritic properties

Evaluation parameter	F1	F2	F3	F4	F5	F6
Angle of repose	34.2±0.3	35.3±0.5	35.5±0.3	31.80±0.6	35.2±0.2	35.0±0.8
Bulk density(g/ml)	0.62±0.03	0.62±0.02	0.6±0.01	0.62±0.01	0.62±0.01	0.6±0.02
Tapped density(g/ml)	0.74±0.02	0.7±0.01	0.73±0.01	0.73±0.04	0.74±0.03	0.7±0.02
Carr's index (%)	15.6±0.2	15.3±0.3	15.8±0.41	15.12±0.2	16.2±0.22	16.1±0.3
Hausner's ratio	1.18	1.18	1.18	1.178	1.19	1.19

All formulations from F1-F6 showed good flow properties when compared to the angle of repose values of pure drug given in the table no 14. Formulations F1, F4 showed good flow. The corresponding angle of repose values are 34.2˚ and 31.80˚. Formulations F2, F3, F5 and F6 showed fair flow. The corresponding angle of repose values are 35.3˚, 35.5˚, 35.2˚ and 35.0˚ respectively.

Formulations F1-F6 showed good flow properties when compared to the carr's index values of pure drug given in table no 11. Formulations F1 to F4 showed good flow. The corresponding values of carr's index are 15.6, 15.3, 15.8 and 15.12 respectively. Formulations F5 and F6 have fair flow and the corresponding carr's index values are 16.2 and 16.1.

Formulations F1-F6 showed good flow properties when compared to the Hausner's ratio values of pure drug given in table no 11. Formulations F1 to F4 showed good flow. The corresponding values of Hausner's ratio are 1.18, 1.18, 1.18 and 1.178 respectively. Formulations F5 and F6 showed fair flow and the corresponding values are 1.19 and 1.19 respectively.

Table 8: Results of micromeritic properties of risperidone liquisolid formulations prepared with SDL.

Evaluation parameter	F7	F8	F9	F10	F11	F12
Angle of repose	36±0.8	37.2±0.5	38.4±0.4	36.7±0.7	36.9±0.3	39.2±0.3
Bulk density(g/ml)	0.57±0.1	0.5±0.1	0.57±0.2	0.59±0.4	0.58±0.8	0.57±0.9
Tapped density(g/ml)	0.7±0.01	0.7±0.1	0.70±0.5	0.7±0.01	0.87±0.02	0.6±0.05
Carr's index(%)	18.4±0.8	18±0.3	18.3±0.3	15.7±0.01	17±0.43	18±0.61
Hausner's ratio	1.2	1.223	1.224	1.19	1.21	1.23

All formulations from F7-F12 showed good flow properties when compared to the angle of repose values of pure drug given in the table no 14. Formulations F7 to F12 showed fair flow. The corresponding angle of repose values are 36˚, 37.2˚, 38.4˚, 36.7˚, 36.9˚, and 39.2˚ respectively.

Formulations F7 to F12 showed good flow properties when compared to the carr's index values of pure drug given in table no 13. Formulations F7, F8, F9, F11 and F12 showed fair flow. The corresponding values of carr's index are 18.4, 18, 18.3, 17 and 18 respectively. Formulation F10 showed good flow and the corresponding carr's index value is 15.7.

Formulations F7 to F12 showed good flow properties when compared to the Hausner's ratio values of pure drug given in table no 13. Formulations F7 to F12 showed good flow. The corresponding values of Hausner's ratio are 1.2, 1.223, 1.224, 1.19, 1.21 and 1.23 respectively.

Table 9: Results of micromeritic properties of risperidone liquisolid formulations prepared with Syloid 244FP

Evaluation parameter	F13	F14	F15	F16	F17	F18
Angle of repose	31.2±0.2	32.3±0.3	33.4±0.2	31.3±0.4	31.8±0.3	32.2±0.1
Bulk density(g/ml)	0.61±0.1	0.62±0.6	0.62±0.3	0.61±0.2	0.65±0.8	0.66±0.4
Tapped density(g/ml)	0.74±0.1	0.74±0.0	0.7±0.01	0.73±0.1	0.76±0.3	0.76±0.2
Carr's Index (%)	13.1±0.2	16.6±0.3	15.1±0.4	16±0.32	14.5±0.3	13.2±0.6
Hausner's ratio	1.2	1.18	1.6	1.18	1.18	1.15

All formulations from F13 to F18 showed good flow properties when compared to the angle of repose values of pure drug given in the table no 14. Formulations F13 to F18 showed good flow. The corresponding angle of repose values are 31.2˚, 32.3˚, 33.4˚, 31.3˚, 31.8˚, and 32.2˚ respectively.

Formulations F13 to F18 showed good flow properties when compared to the carr's index values of pure drug given in table no 13. Formulations F13, F15, F17, and F18 showed good flow. The corresponding values of carr's index are 13.1, 15.1, 14.5, and 13.2 respectively. Formulation F14 and F16 showed fair flow and the corresponding carr's index values are is 16.6 and 16 respectively.

Formulations F13 to F18 showed good flow properties when compared to the Hausner's ratio values of pure drug given in table no 13. Formulations F14 to F18 showed good flow. The corresponding values of Hausner's ratio are 1.18, 1.6, 1.18, 1.18, and 1.15 respectively. Formulation F13 showed fair flow and the corresponding value was 1.2.

Drug content:

Table 10: Results of drug content of risperidone formulations (F1-F18)

Formulation	Drug content (%)	Formulation	Drug content (%)
F1	98.4±0.5	F10	99.8±0.3
F2	97.5±0.2	F11	97.6±0.4
F3	98.8±0.1	F12	99.2±0.3
F4	97.2±0.3	F13	97.2±0.3
F5	98.5±0.2	F14	97.6±0.4
F6	98.2±0.4	F15	98.2±0.4
F7	96.8±0.2	F16	98.4±0.5
F8	99.6±0.6	F17	97.2±0.3
F9	99.2±0.5	F18	99.8±0.3

Drug content results of all formulations from F1 to F18 of risperidone liquisolid compacts were within limits.

In vitro release studies:

In vitro release data of risperidone liquisolid formulations prepared with microcrystalline cellulose as carrier material (F1-F6) showed an increase in dissolution rate of risperidone liquisolid compacts when compared to that of pure drug whose values are given in

table no 21. The drug dissolution rate was increasing as the time of dissolution study increased from 10 minutes to 90 minutes.

F1 to F3 represent data of the formulations composed of Avicel as carrier and PG as non-volatile solvent. There is gradual increase in the dissolution rate as the carrier to coating material ratio increases from 5:1 to 20:1. The dissolution rate increases from 54.50% of F1 to 64.56% of F3 at 90min. This may be due to the combined effect of non-volatile solvent and carrier material on the dissolution of the drug in the formulation.

F4 to F6 represent data of the formulations composed of Avicel as carrier and PEG 400 as non-volatile solvent. There is gradual increase in the dissolution rate as the carrier to coating material ratio increases from 5:1 to 20:1. The dissolution rate increases from 58.55% of F4 to 95.44% of F6 at 90min. This may be due to the combined effect of non-volatile solvent and carrier material on the dissolution of the drug in the formulation.

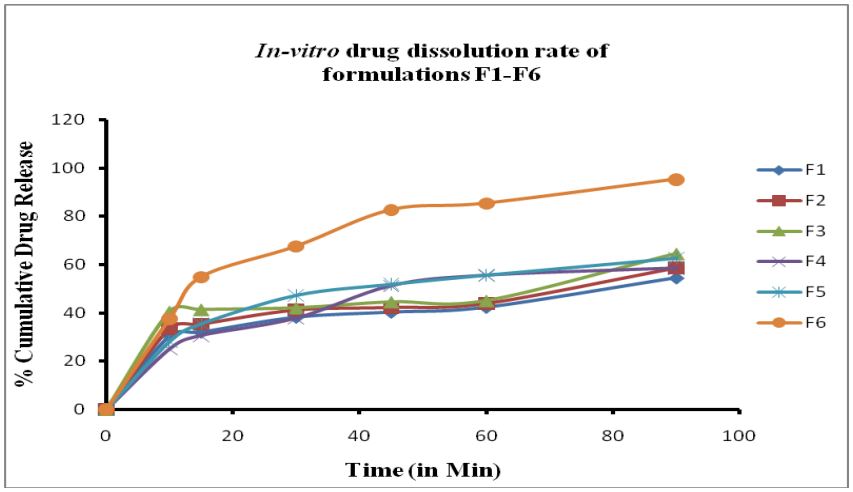

Figure 4: Dissolution profiles of risperidone liquisolid formulations prepared using Avicel pH 102

It was observed that F3 and F6 formulation has shown high dissolution rate 64.56% and 95.66% respectively within 90 min compared with other formulations. This might be due to the presence of high amount of carrier (20:1). Among both the formulations, F6 composed of PEG 400 and Avicel pH102 shows high dissolution rate of 95.66% at 90min.

F7 to F9 represent data of the formulations composed of SDL as carrier and PG as non-volatile solvent. The dissolution rate increases from 51.13% of F7 to 62.08% of F9 at 90min.

F10 to F12 represent data of the formulations composed of SDL as carrier and PEG 400 as non-volatile solvent. The dissolution rate increases from 95.67% of F10 to 101.16% of F12 at 90min. This may be due to the combined effect of non-volatile solvent and carrier material on the solubility of drug in formulation which in turn affects the dissolution of the formulation.

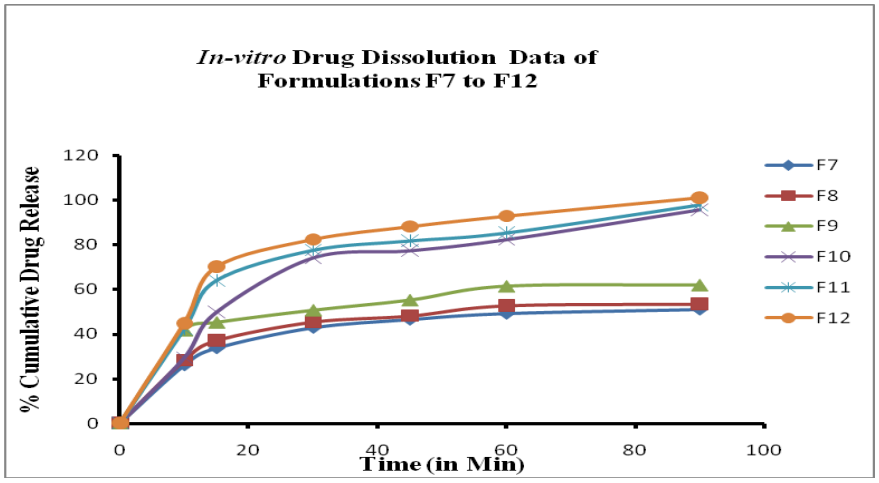

Figure 5: Dissolution profiles of risperidone liquisolid formulations prepared with Spray dried lactose.

Dissolution studies were conducted for the formulations (F7 to F12). F12 formulation was showing high dissolution rate (101.10% at 90min) compared with other formulations. This may be due to the presence of high amount of carrier material. Here the increased dissolution may be due to combined effect of carrier and non-volatile solvent used for the preparation of formulation.

It was observed that F9 and F12 formulation has shown high dissolution rate 62.08% and 101.16% respectively within 90 min compared with other formulations. This might be due to the presence of high amount of carrier (20:1). Among both the formulations, F12 composed of PEG 400 SDL shows high dissolution rate of 101.16% at 90min.

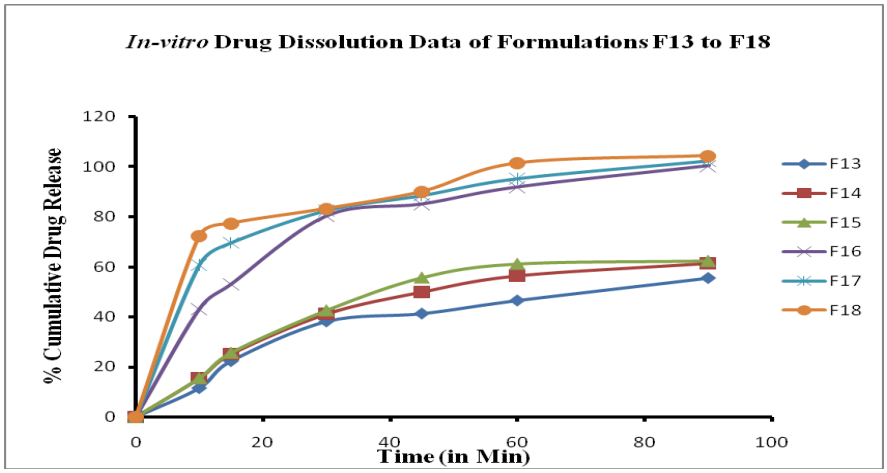

Figure 6: Dissolution profiles of risperidone liquisolid formulations prepared with syloid 244FP

Dissolution studies were conducted for the formulations (F13 to F18). F18 formulation was showing highest dissolution rate (101.41%) within 60min and 104.34% within 90min compared with other formulations. This is due to the presence of high amount of carrier material and also carrier material Syloid which has high liquid load factor with PEG 400.

Among both the formulations F15 and F18, F18 composed of PEG 400 and Syloid 244FP shows high dissolution rate of 104.34% at 90min.

Formulations F11,F12,F16,F17,F18 shows high dissolution rate among all formulations showing that both high amount of carrier and non-volatile solvent PEG 400 contributes in enhancing the dissolution rate of poorly soluble risperidone.

Among all F18 shows highest dissolution rate in less time. This is because syloid 244FP has high specific surface area. The optimized formulation showing dissolution rate of 101.41% within 60min and 104.34% drug release within 90min.

Comparison of optimized formulation with pure drug and marketed product

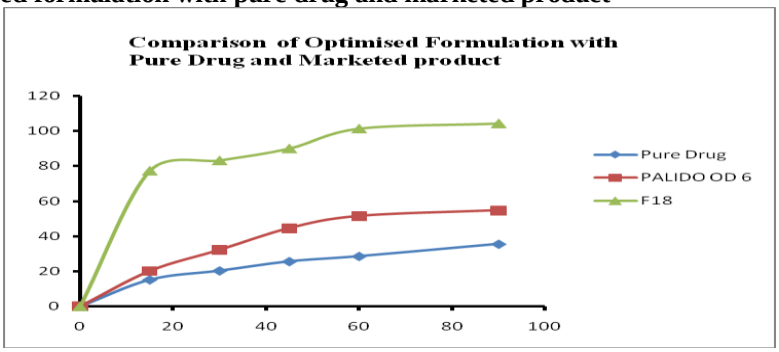

Figure 7: Comparison of Optimized formulation with pure drug and marketed product.

From the figure 7, optimized formulation F18 was showing highest dissolution rate (101.41%) within 60 min and 104.34% within 90min when compared with marketed product, it was showing less dissolution rate (51.51%) within 60 min and 54.80% within 90min.

The order of drug dissolution rate was F18 > PALIDO OD 6 (Marketed Preparation) > Pure Drug.

Pure Drug has poor flow characters and also poor solubility in water or gastrointestinal fluids when compared to formulation thus the dissolution rate which is affected by solubility of material is less in case of pure drug when compared to formulation.

Release kinetics:

A perusal to table seeing the correlation coefficient (R^2) values obtained showed that all the formulations (F1 to F18) had highest R^2 values for Zero order plots indicating that the dissolution data fits into Zero order equation when compared to First order equation. Therefore, all the formulations F1 to F18 found to follow Zero order release kinetics.

Table 11: Different Kinetic Models

Formulation	Zero order R^2	First order R^2	Higuchi Plot R^2	Peppas Plot	
				R^2	n
F1	0.838	-0.6782	0.822	0.768	0.15
F2	0.822	-0.7871	0940	0.932	0.21
F3	0.779	-0.8251	0.969	0.964	0.24
F4	0.892	-0.9718	0.973	0.985	0.4
F5	0.867	-0.9354	0.980	0.987	0.35
F6	0.877	-0.9821	0.968	0.971	0.4
F7	0.810	-0.8784	0.976	0.989	0.19
F8	0.798	-0.9072	0936	0.958	0.28
F9	0.757	-0.9104	0942	0964	0.3
F10	0.884	-0.9622	0.946	0.943	0.49
F11	0.834	-0.9296	0.940	0.939	0.33
F12	0.817	-0.9746	0.922	0.924	0.32
F13	0.909	-0.9929	0.953	0.964	0.64
F14	0.926	-0.9890	0.973	0.972	0.62
F15	0.930	-0.964	0.970	0.955	0.66
F16	0.865	-0.9569	0.960	0.991	0.39
F17	0.794	-0.9863	0.985	0.995	0.23
F18	0.748	-0.9885	0.982	0.975	0.17

Table 12: Kinetics data

Formulation	Zero order R^2	First order R^2	Higuchi Plot R^2	Peppas Plot	
				R^2	n
F11	0.8345	0.0752	0.9409	0.9346	0.33
F12	0.8170	-0.5531	0.9229	0.9271	0.32
F16	0.8658	-0.4870	0.9601	0.9401	0.39
F17	0.7944	-0.5937	0.9858	0.9126	0.23
F18	0.7480	-0.7063	0.9824	0.8984	0.17

R^2 values for the formulations were found to be maximum for the Higuchi model. This showed that the drug release from all the formulations followed diffusion-controlled release mechanism.

According to Korsmeyer-Peppas model, slope (n) value less than 0.45 indicates the Fickian diffusion. From the results obtained all the formulations except F13, F14 and F15 shows Fickian Diffusion. Formulations F13, F14 and F15 have 'n' value greater than 0.45 showing that they follow non-fickian diffusion.

CONCLUSION:

The observations showed that there was a poor drug release in case of conventional formulation. Improvement of aqueous solubility in such case is valuable goal to improve therapeutic efficiency. Thus, liquisolid compacts of Risperidone were formulated by using liquisolid technique showed better enhancement in drug release rate and solubility of drug. *In-vitro* drug dissolution studies showed improved in drug release of risperidone compared to pure drug. So, PEG 400, PG could be economic substitute as dissolution enhancing agent. It was determined that first order kinetics provided the greatest fit for the release data based on mathematical information obtained from models. The diffusion-controlled release mechanism is described by the Higuchi equation; the risperidone compacts' diffusion exponent indicating non-Fickian diffusion. F18 best among the successful formulations with highest drug release rate was compared with marketed preparation and results were better than marketed preparation.

REFERENCES:

1. Alonzo D.E., Zhang G.G., Zhou D., Gao Y., Taylor L.S. Understanding the behavior of amorphous pharmaceutical systems during dissolution. Pharm. Res. 2010; 27:608–618.
2. Avachat A.M., Parpani S.S. Formulation and development of bicontinuous nanostructured liquid crystalline particles of efavirenz. Colloids Surf., B. 2015;126:87–97.
3. Burra S., Yamsani M., Vobalaboina V. The liquisolid technique: an overview. Brazil. J. Pharm. Sci. 2011; 47:475–482.
4. Chella N., Narra N., Rama Rao T. Preparation and characterization of liquisolid compacts for improved dissolution of telmisartan. J. Drug Delivery. 2014; 2014:1–10.
5. Chella N., Shastri N., Tadikonda R.R. Use of the liquisolid compact technique for improvement of the dissolution rate of valsartan. Acta Pharm. Sin. B. 2012; 2:502–508.
6. Chiappetta D.A., Hocht C., Taira C., Sosnik A. Efavirenz-loaded polymeric micelles for pediatric anti-HIV pharmacotherapy with significantly higher oral bioavailability. Nanodrug. 2010; 5:11–23.
7. Elkordy A.A., Tan X.N., Essa E.A. Spironolactone release from liquisolid formulations prepared with Capryol™ 90, Solutol® HS-15 and Kollicoat® SR 30 D as non-volatile liquid vehicles. Eur. J. Pharm. Biopharm. 2013; 83:203–223.
8. Hentzschel C., Alnaief M., Smirnova I., Sakmann A., Leopold C. Enhancement of griseofulvin release from liquisolid compacts. Eur. J. Pharm. Biopharm. 2012; 80:130–135.
9. Javadzadeh Y., Jafari-Navimipour B., Nokhodchi A. Liquisolid technique for dissolution rate enhancement of a high dose water-insoluble drug (carbamazepine) Int. J. Pharm. 2007;341:26–34.
10. Patel G.V., Patel V.B., Pathak A., Rajput S.J. Nanosuspension of efavirenz for improved oral bioavailability: formulation optimization, in vitro, in situ and in vivo evaluation. Drug Dev. Ind. Pharm. 2014; 40:80–91.
11. Sathigari S.K., Radhakrishnan V.K., Davis V.A., Parsons D.L., Babu R.J. Amorphous-state characterization of efavirenz—polymer hot-melt extrusion systems for dissolution enhancement. J. Pharm. Sci. 2012; 101:3456–3464.
12. Siepmann J., Siepmann F. Mathematical modeling of drug dissolution. Int. J. Pharm. 2013; 453:12–24.
13. Wu L., Zhang J., Watanabe W. Physical and chemical stability of drug nanoparticles. Adv. Drug Deliv. Rev. 2011; 63:456–469.

14. Seth NS, "Formulation and evaluation of solid dispersion of olanzepine," Int. J. Pharm. Sci. Res.2011, v.2 (2): p.691-697.
15. Ramadevi Korni, Susheela Voodikala, C S R Gonugunta and Vijayaratna Jayanti. Liquisolid technique: An approach to enhance the dissolution rate of olanzapine. Indian J Pharm Sci., 2018; 80(6): 1003-1010.
16. 16.Vinod Kumar Yata Ananda Kumar Chettupalli , Ramkoteswar Rao Amara , Padmanabha Rao Amarachinta , Ram Mohan Manda , Baba Shankar Rao GarigeFormulation and Evaluation of Poly Herbal Liqui-Solid Compact for its Anti-Inflammatory Effect,2022,Biointerface Research in Applied Chemistry12(3),3883-3899.
17. Monali Kalbhor, Ashok Bhosale, Ravindra Patil, Sujit Kakade. Formulation and evaluation of telmisartan liquisolid compact tablet. Int J Pharmacy and Pharma Res., 2017; 9(4): 152-182
18. Anand D. Savkare, Malavi R. Bhavsar, Vishal D. Gholap and Pooja M. Kukkar liquisolid technique: a review. Int J Pharma Sci and Res., 2017; 8(7): 2768-2775.
19. Amol S. Deshmukh, Vinod G. Mahale, Vijay R Mahajan. Liquisolid compact techniques: A Rev. Res J of Pharm Dosage Forms and Tech, 2014; 6(3): 161-166.
20. Sahir V, Ghuge N, Bakde B V. Liquisolid compact: a new technique for enhancement of drug dissolution. Int J Pharm Res Dev., 2012; 3(1): 1-5.