wjpmr, 2021,7(9), 216 – 221.

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

FORMULATION AND EVALUATION OF ORO DISINTIGRATING TABLET OF RISPERIDONE BY USING SOLID DISPERSION TECHNIQUE

[1]*G. Mary Ratna Anitha, [2]Kanukuntla Sushma, [2] Gade Divya, [2]Ranjith Kumar and [2]Relaker Preethi

[1]Associate Professor, Sree Dattha Institute of Pharmacy.

[2]Student, Sree Dattha Institute of Pharmacy, Ibrahimpatnam, Hyderabad, Telangana-501510.

***Corresponding Author: G. Mary Ratna Anitha**

Associate Professor, Sree Dattha Institute of Pharmacy.

Article Received on 11/06/2021 **Article Revised on 01/07/2021** **Article Accepted on 21/07/2021**

ABSTRACT

The purpose of the present study was to formulate solid dispersion incorporated fast dissolving tablet of Resperidone to improve the aqueous solubility, dissolution rate and to facilitate faster onset of action. Solid dispersion of Resperidone was prepared with various super disintegrants in different drug: carrier ratio using solvent dispersion technique.The objective of the study was to formulate and evaluate fast dissolving tablet of Lamotrigine. Direct compression method was used to formulate orally disintegrating tablet of Resperidone by employing solid dispersion, magnesium stearate (lubricant), Talc (glidant). These prepared formulations were then evaluated. In vitro Dissolution tests were performed using USP apparatus II and ultraviolet spectrophotometry, respectively. All formulations showed compliance with pharmacopeia standards. The effect of super disintegrant concentration and direct compression method on drug release profile was studied. Release profile of F3were found to be satisfactory comparing to other formulations. F3Formulation as processed excipient was found to be the best super disintegrants for the preparation of Resperidone fast dissolving tablets formulations. Due to it has exhibited faster disintegration time and best dissolution profile when compared to other formulations.

KEYWORDS: Resperidone, super disintegrants, FTIR studies, Solid dispersion, direct compression technique, in-vitro drug release studies.

INTRODUCTION

The term solid dispersion leads to a combination of solid products composed of minimum two dissimilar components, or usually an inert carrier or matrix which is hydrophilic that may exist in either crystalline or amorphous forms and a drug which is hydrophobic. The medicament can be able to be dispersed uniformly either in amorphous (clusters) or crystalline states. One of the basic ideologies of solid dispersion formulation is attainment of the amorphous form which is found to be having high solubility, effective as compared to the crystalline form.[1]

Preparation of Solid Dispersions

Solid dispersions can be prepared by various methods those are deals with the mixing of matrix and a drug, preferably on a molecular level, while the matrix and drug are generally poorly miscible. During the preparation of solid dispersion techniques, de-mixing and the formation of different phases are observed. Phase separations like crystallization or amorphous of drug clusters formation are sometimes difficult to control and therefore unwanted. So the phase separation can be minimized by the rapid cooling procedure. Generally phase separation can be prevented by maintaining a low molecular mobility of the matrix and drug during preparation. And also, maintain the driving force by keeping the mixture at an elevated temperature, there maintains miscibility for as long as possible.[2,3,4]

Solid Dispersion Methods[4,5,6]

1. Solvent evaporation method

Basic process of preparing solid dispersion consists of dissolving the drug and the polymeric carrier in a common solvent such as ethanol, chloroform, or a mixture of ethanol and dichloromethane.

2. Fusion method/Melting method

The fusion method is sometimes known as the melt method. The physical mixture of a drug and a water-soluble carrier was heated directly until it gets melted. The melted mixture was subsequently cooled and solidified rapidly in an ice bath under rigorous stirring. The final dense mass was crushed, pulverized, and sieved.

3. Hot melt extrusion method

Hot-melt extrusion (HME) technique represents a novel application of polymer processing technology to prepare pharmaceutical dosage forms. The process involves

embedding a drug in a polymer while shaping the composite material to form a pharmaceutical product. This technique is similar as the fusion method. The only difference is the case that in this method, intense mixing of the components is induced by the extruder.

4. Supercritical fluid technology (SCF)[7]
SCF techniques can be taken to the preparation of solvent free solid dispersion dosage forms to enhance the solubility of poorly soluble compounds. Super critical fluid is the one that where substances existing as a single fluid phase above their critical temperature and pressure.

5. Dropping method
This method is another procedure for producing round particles from melted solid dispersions. Methodology includes that the solid dispersion of melted drug–carrier mixture is dropped onto a cooling plate, where it gets solidifies into round particles.

6. Electrostatic spinning method[8]
This technology is used in the polymer industry were in it combines solid solution/dispersion technology with nanotechnology. In this process, a potential between 5 and 30 kV is implemented in the liquid stream of a drug/polymer solution.

7. Co-precipitation method
In this method, while during constant stirring, a non-solvent is added drop wise to the drug and carrier solution and the drug and carrier is co-precipitated to get micro particles, and then this micro particle suspension is filtered and dried.

Mechanism of action of disintegrant[9]
Various mechanisms proposed in this concern include water wicking, swelling, deformation recovery, repulsion and heat of wetting.

1. Water wicking
The ability of disintegrant to draw water into the porous network of tablet is essential for effective disintegration. On keeping the tablet into suitable aqueous medium, the medium enters into tablet and replaces the air adsorbed on the particles which weakens the intermolecular bonds and breaks the tablet into fine particles.

2. Swelling
Although water penetration is a necessary first step for disintegration, swelling is probably the most widely accepted mechanism of action for tablet disintegrants. For swelling to be effective as a mechanism of disintegration, there must be a superstructure against which disintegrant swells.

3. Heat of wetting
When disintegrants with exothermic properties get wetted, localized stress is created due to capillary air expansion, which aids in disintegration of tablet.

4. Particle repulsive forces
This is another mechanism of disintegration that attempts to explain the swelling of tablet made with non-swell able disintegrants.

5. Deformation recovery
Deformation recovery theory implies that the shape of disintegrant particles is distorted during compression and the particles return to their precompression shape upon wetting, thereby causing the tablet to break apart.

Technologies used for manufacturing of orally disintegrating tablets[10,11]
Various processes employed in formulating FDTS including conventional technologies and patented technologies.

1. Freeze drying or lyophilization
2. Direct compression
3. Molding
4. Mass extrusion
5. Melt granulation
6. Phase transition process
7. Sublimation

MATERIALS AND METHODS

Material
Drug/Excipients: Risperidone, PEG 4000 Croscaramellose, PEG 6000, Lactose Magnesium stearate, Crosspovidone, talc, Micro crystalline cellulose.

Equipments: UV/VIS Double beam Spectrophotometer, Tap Density Tester, Tablet dissolution tester USP, Weighing balance, Hardness tester, Friability tester.

Method
Determination of solubility
The solubility of the Resperidone was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined by taking supernatant and analyzing it on Lab India, double beam spectrophotometer.

Standard curve
Preparation of 6.8 phosphate buffer
28.80 gm of disodium hydrogen phosphate and 11.45gm of potassium dihydrogen phosphate dissolve in 1000 ml of water.

Preparation of standard solution of Resperidone
Stock solution – I
Accurately weighed 10 mg of Risperidone was placed in a 10 ml volumetric flask. The volume was made up to 10 ml using 6.8 phosphate buffers to give 1000 mcg/ml solution.

Stock solution -II
From stock solution I 1ml a liquote was taken and placed in a 10 ml volumetric flask and diluted with 6.8 phosphate buffer to 10ml to get 100mcg/ml.

Stock solution-III
From stock solution -II, a 1ml of aliquote was made up to 10ml to get 10mcg/ml Similar dilutions were prepared from stock solution -I in different media like pH 6.8 buffer solutions.

Determination of absorption maxima (λ_{max}) for Resperidone
A 10mcg/ml standard solution of Resperidone was scanned on a double beam spectrophotometer against respective media blanks. An absorption maximum (λ_{max}) of 282 nm was obtained for all solutions and was selected to prepare standard curve.

Preparation of standard curve for Resperidone
Standard curves for Resperidone were obtained in 6.8 pH buffers and water. Aliquotes of 10, 20, 30, 40 and 50 ml of Resperidone standard solution of 100mcg/ml (stock solution-II) was taken and diluted to obtain concentrations from 10 to 50mcg/ml with appropriate media. The absorbance of solutions were determined at 282 nm against respective media as blank. The experiment was repeated five times for each buffer and a calibration curve was determined from the mean value.

Preparation of Solid Dispersions by Solvent evaporation method
The solid dispersions of Resperidone and super disintegrants in various drug-to-carrier weight ratios were prepared by solvent evaporation method. Required amount of super disintegrants was dissolved in q.s. of acetone in a beaker and Resperidone was added and mixed to dissolve. Then the solvent was allowed to evaporate. Solid Dispersions prepared were crushed, pulverized and sifted through sieve number #40 and stored in desiccators.

Preparation of solid dispersions by kneading method
Solid dispersions were prepared in the ratios of 1:1 and 1:2(Drug: carrier) ratios with Gelucire, PEG - 4000.Initially weighed amount of drug and carriers were placed in a mortar and were ground with pestle for few minutes. Then 5ml of alcohol: water (1:1) was added and then triturated until alcohol: water gets evaporated. Then the obtained dry dispersions were preserved in a desiccator for overnight. The dry dispersion was then passed through the 100# mesh sieve and is stored in moisture free area till further use.

Preparation technique
Direct compression method
Drug and polymers pass through 40 # mesh separately and then transfer it to polyethylene bag and mix it for 3 minutes.Add diluents and other excipients to the above mixture. Finally add the Glidant (Talc) and Lubricant (Magnesium Stearate) to the above blend mix it for 2min.Compresse the powder materials lubricated blend by using 8mm round punches by using Remetek minipress II MT tablet punching machine.

Evaluation of tablet
Weight variation
Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more then two of the individual tablet weight deviate from the average weight by more than the percentage.

Thickness
Twenty tablets were randomly selected form each batch and there thickness was measured by using vernier calliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness
Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

Friability
Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose.

Drug Content
The drug content was determined by triturating tablets in a mortar and pestle. The 100 mg of sample powder was dissolved in 6.8 phosphate buffer. The solution was filtered through Whatman filter paper. The filtrate was analyzed by U.V. spectrophotometer (LAB INDIA) at 282 nm.

In Vitro Disintegration Test
The disintegration time of tablets was determined by using Disintegration test apparatus (scientific). Tablets were placed in disintegration test assembly and disc was placed on tablets in each glass tube of assembly. The assembly was dipped in a vessel containing 900 ml distilled water at 37°C. The time for disappearance of tablet residue above mesh was noted as disintegration time.

In- Vitro Release study
In-Vitro drug release studies were carried out using Tablet dissolution test apparatus USP II at 50 rpm. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for remaining period of time. Temperature maintained at 37 ± 1^{o} C. The sample of 5ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. The solution was filtered through Whattmann filter paper. The filtrate was analyzed by U.V. spectrophotometer (Labindia) at 282 nm. The drug release was plotted against time to determine the release profile of various batches.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The prepared disintegration tablets of Resperidone were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2°c and refrigerator 2-8°c for a period of 30 days.

RESULTS AND DISCUSSION

Preparation of standard curve of Resperidone

Standard curve of Resperidone was determined by plotting absorbance V/s concentration at 282 nm. Using solution prepared in pH 6.8 at 282 nm. And it follows the Beer's law. The R^2 value is 0.9982.

Table 1: Data for standard graph of Resperidone in Phosphate buffer pH 6.8.

S. no	Concentration (µg/ml)	Absorbance
1	0	0
2	1	0.112
3	2	0.234
4	3	0.319
5	4	0.426
6	5	0.545

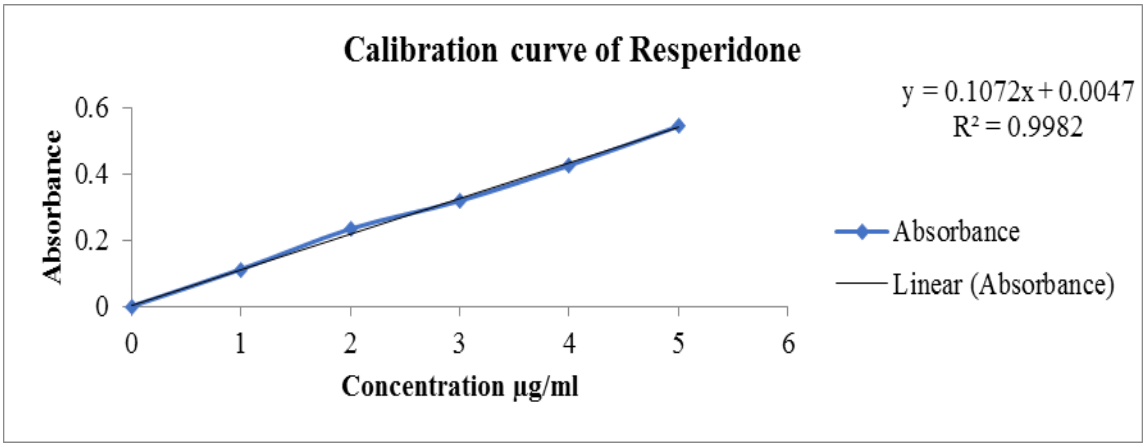

Fig 1: Standard graph of Resperidone in pH 6.8 buffer

FT-IR Spectrum of Resperidone

FT-IR Spectra of Resperidone and excipients were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Resperidone and super disintegrant. It also confirmed that the stability of drug during microencapsulation process.

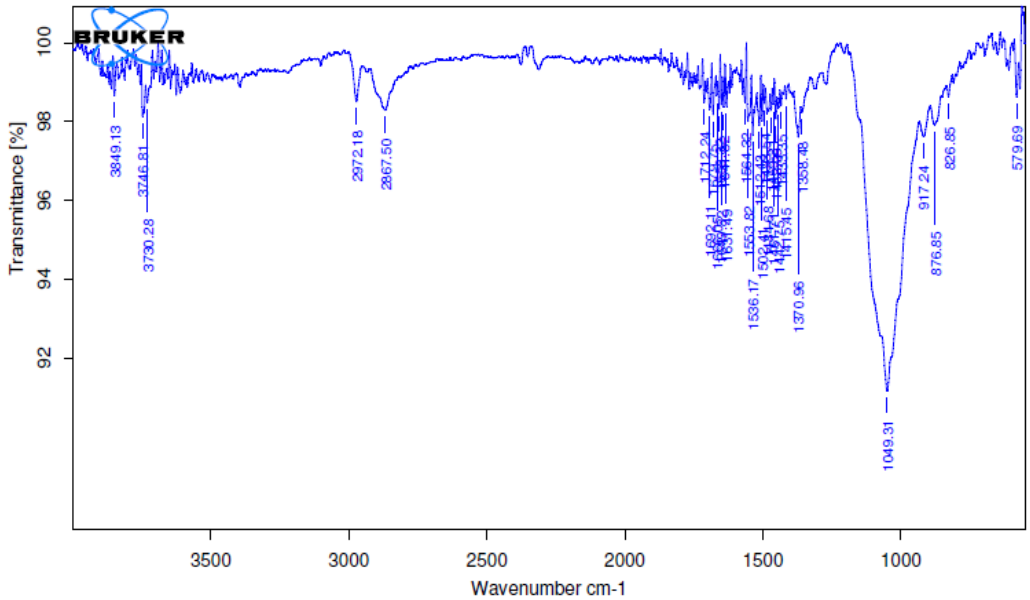

Fig. 2: FTIR Studies of Resperidone.

Table 2: Characteristic Peaks for Resperidone.

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3500-3000	2972.18
2	OH Bending	1000-1500	1049.31
3	C-H stretching	3000-2500	2867.50
4	C=O stretching	2000-1500	1692.11

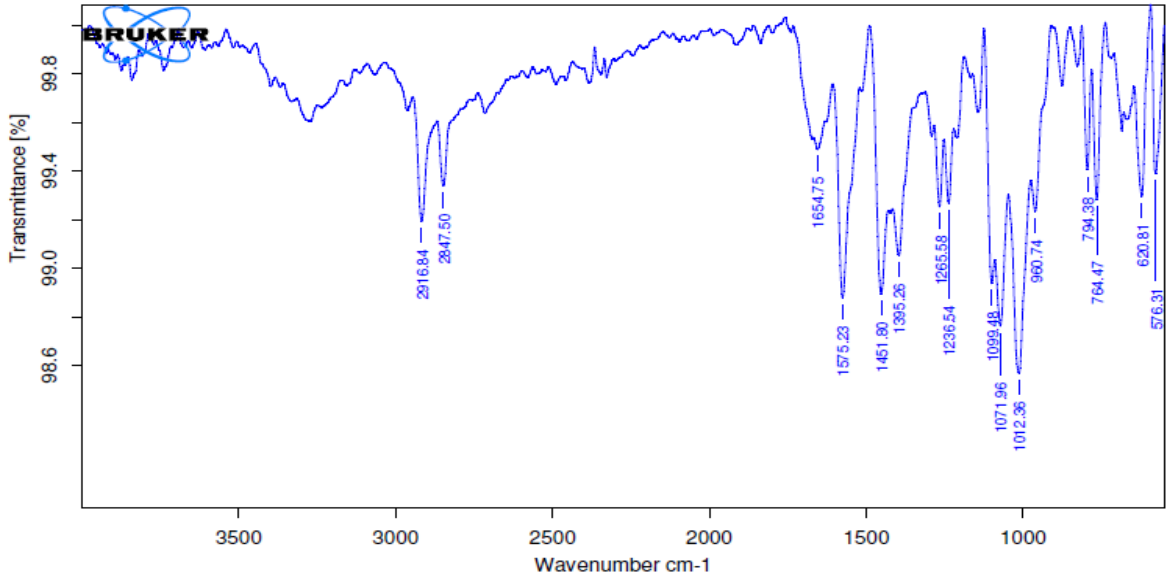

Fig. 3: FTIR Studies of Physical mixture of drug and excipients.

Table 3: Evaluation parameters of Resperidone fast dissolving tablets.

F. No.	Weight variation(mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content(%)	Disintegration time(sec)	Wetting time(sec)
F1	200	2.5	3.24	0.42	90.15	51	147
F2	201	2.0	3.21	0.58	89.69	49	149
F3	198	2.2	3.28	0.45	95.50	59	151
F4	200	2.4	3.22	0.50	93.28	51	145

CONCLUSION

Resperidone was successfully formulated in fast dissolving tablets with desired characteristics. Solvent evaporation into aqueous solution thus may be a useful approach to produce tablets of poorly soluble drugs. The aim of the present study was to develop an optimized formula for fast disintegrating tablet containing Resperidone. This medication is used alone or with other medications to prevent depression.

Pre-formulation studies it was decided to prepare fast dissolving tablets prepared by direct compression method. In the formulation of Crossovidinewere used as super disintegrants.

Prior to compression the granules were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. The compressed tablets were also evaluated for weight variation, hardness, friability, drug content, disintegration time, wetting time, invitro drug release and stability studies.

In the above studies F3formulation showed promising results. It was further supported by FTIR analysis which showed that F3had no interaction with excipients. The stability studies were carried out for the optimized batch F3for 90days and it showed acceptable results. So F3formulation was considered as the optimized formulation. Among all the prepared solid dispersions F3 was found to be optimized. The study shows that the dissolution rate of Resperidone can be enhanced to a great extent by solid dispersion technique using solvent evaporation method. Hence, Resperidone crosspovidine, PEG 4000 and PEG 6000 systems could be considered for formulation of fast dissolving tablets of Resperidone. The fast dissolving tablets of Resperidone (F3) was shown higher drug release when compared toother formulations. From above results it can be concluded that solid dispersion technique can be used to enhance the solubility, dissolution rate, and oral bioavailability of water insoluble drugs.

ACKNOWLEDGEMENT

We are thankful first and foremost the Lord for his never ending grace. We would like to express our deepest gratitude and heartfelt thanks to both our supervisor and Co-supervisor to finish this project with ease.

REFERENCES

1. Ford, J. L.; "enhancement of dissolution rate of ibuprofen" ActaHelv, 1986; 61: 69 -88.
2. Ansel C. Howard, Allen V. Loyd, Popovich A. Nicholas, Pharmacetical dosage forms and drug delivery systems, 7 th edition, 2000; 248-252.
3. Modi A. and PralhadT., Enhancement of dissolution profile by solid dispersion (kneading) technique, AAPS, Pharm Sci Tech,2006;129-132.
4. Khadilkar M., Avari J and GudsookarV. R: Solid dispersions of Ketoprofen; the Eastern pharmacist, 1997, 40, 129-131.
5. Kuchekar B.S. and Yadav A.V: Studies on solid dispersion of Paracetamol; The Eastern Pharmacist, 1995, 38, 149.
6. D. M. Patel, R. R. Shah: Studies on release profile of Piroxicam solid dispersion; Indian Journal of Pharmaceutical Sciences, 2003, 65, 264-266.
7. Broman E., Taylor L.S., Khoo C.A. Comparison of alternative polymer excipients and processing methods for making solid dispersions of poorly water. Int. J. Pharm. 222(3): 139–151; 2001.
8. Serajuddin Abu T.M. Solid dispersion of poorly water-soluble drugs: Early promises, subsequent problems, and recent breakthroughs. J. Pharm. Sci., 1999; 88; 1058–1066.
9. Hand book of pharmaceutical excipients Edited by: Raymond C Rowe, Paul J Sheskey and Siân C Owen.
10. Lachmman L,Liberman HA,Konig Jl.The theory & practice of industrial pharmacy,3rd Edn,Vargheese publishing house, Bombay, 1991; 297-300.
11. Subrahmanyam cvs and thimmasetty j.Laboratory manual of physical pharmaceutics,1 st Edn, vallabh prakasham Delhi, 2002; 24-25.