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

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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 F3 were found to be satisfactory comparing to other formulations. F3 Formulation 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.

I.INTRODUCTION

The concept of "solid dispersions" is one of the most victorious, advanced and leading technique that have been broadly implemented for enhancement of solubility and dissolution rate or sustained release of drug [1]. 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[2].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[3]. Solid dispersion was introduced in the early 1970s, refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. There are different approaches which can be used for increasing the dissolution of poorly soluble drugs.[4] "a dispersion involving the formation of eutectic mixtures of drugs with water soluble carriers by melting of their physical mixtures"; they classified solid dispersions into the following representative types. Combinations of the previous five types.[5]This strategy includes complete removal of drug crystallinity, and molecular dispersion of the poorly soluble compound in a hydrophilic polymeric carrier. Solid dispersion is a promising approach to improve the dissolution and bioavailability of hydrophobic drugs. The preparation and storage conditions of solid dispersions are crucial since changes may alter the dissolution characteristics of the active ingredients.[6] The development of solid dispersions as a practically viable method to enhance bioavailability of poorly water-soluble drugs overcame the limitations of previous approaches such as salt formation, solubilization by co solvents, and particle size reduction.[7] When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. The resulting enhanced surface area produces a higher dissolution rate and bioavailability of poorly water-soluble drugs.[8]

II. MATERIALS AND METHOD

2.1 MATERIALS

Risperidone was collected as a gift sample from Hetero ltd, Hyd, polymers and other excipients were purchased from AR Chemicals, Hyd.

2.2 METHODODOLOGY

Compatibility studies:

The drug-polymer compatibility was ascertained by subjecting the drug and homogenates of drug and polymer to Infrared spectrophotometric study.

Fourier Transform Infrared Spectroscopy (FTIR)[9,10]

Assessment of possible incompatibilities between an active drug substance and different excipients forms an important part of the preformulation stage during the development of a dosage form. The use of FTIR technique allows pointing out the implication of the different functional groups of drug and excipients by analysing the significant changes in the shape and position of the absorbance bands. In this method individual samples as well as the mixture of drug and excipients were ground mixed thoroughly with potassium bromide (1:100) for 3-5 mins in a mortar and compressed into disc by applying pressure of 5 tons for 5 mins in hydraulic press. The pellet was kept in the sample holder and scanned from 4000 to 400 cm-1 in FTIR spectrophotometer. Then the characteristics peaks were obtained of all sample as well as mixtures.

Table-: 1 Formulation table of solid dispersion

S.No	Ingredient	F-1	F-2	F-3	F-4
1	Resperidone	100	100	100	100
2	PEG - 6000	100	200	-	-
3	PEG - 4000	-	-	100	200

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[11].

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[12].

Table-: 2 Formulation table of Oro-Disintegrating Tablets

S.No	**Ingredient**	**F-1**	**F-2**	**F-3**	**F-4**
1	Solid dispersion	100	100	100	100
2	Lactose	20	20	20	20

3	Magnesium stearate	3	3	3	3
4	Crosspovidone	5	5	5	5
5	Talc	2	2	2	2
6	MCC	70	70	70	70
7	Total	200	200	200	200

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. compressed the powder materials lubricated blend by using 8mm round punches by using Remetek mini press II MT tablet punching machine[13].

EVALUATION STUDIES

Bulk Density

Bulk density is defined as the mass of powder divided by bulk volume.

It is calculated using the following equation[14]:

Bulk density = weight of sample taken /volume noted.

Tap density

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and the volume (v_o) was measured[14].

Tapped density = weight of sample taken / tapped volume

Compressibility index

Based on the apparent bulk density and the tapped density, the percentage Compressibility of the bulk drug was determined by the following formula[14].

Carr's index = Tapped density - Bulk density / Tapped density X 100

Hausner's ratio

It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powder is called Hausner's ratio[15].

Hausner's ratio = Tapped density / Bulk density

Angle of repose

The flow characteristics are measured by 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[15].

$\tan\theta = h/r$

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

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 than two of the individual tablet weight deviates from the average weight by more than the percentage[16].

Thickness

Twenty tablets were randomly selected form each batch and there thickness was measured by using vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated[17].

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 were determined[17].

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. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed. Compressed tablets should not loose more than 1% of their weight[18].

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

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 Whattmann filter paper. The filtrate was analysed by U.V. spectrophotometer (LAB INDIA) at 282 nm[18].

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[19].

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° 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 analysed by U.V. spectrophotometer (Labindia) at 282 nm. The drug release was plotted against time to determine the release profile of various batches[20].

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The prepared disintegration tablets of Risperidone 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[20].

III.RESULTS AND DISCUSSION

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.

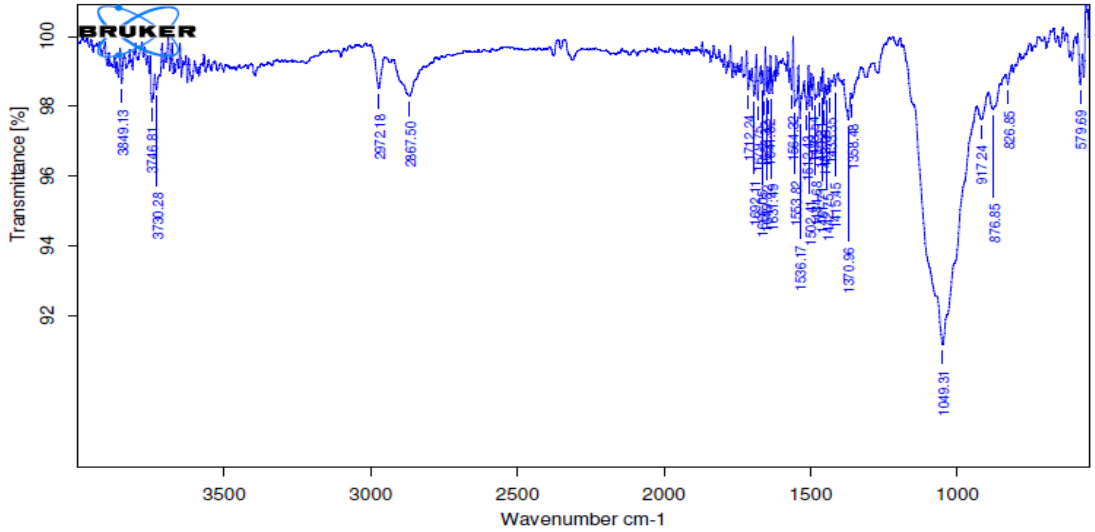

Fig.1. FTIR Studies of Resperidone

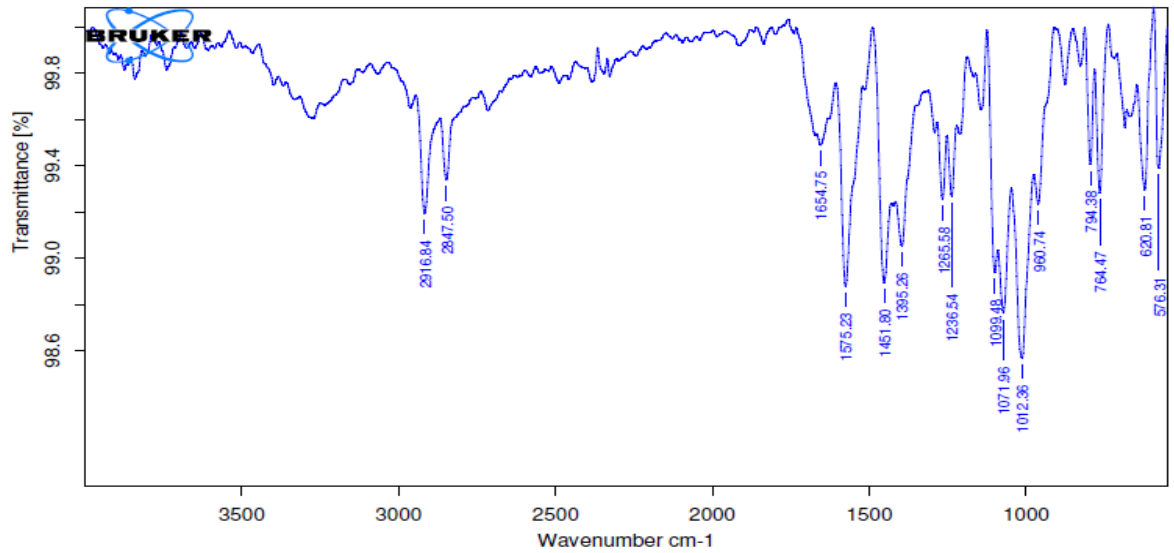

Fig.2. FTIR Studies of Physical mixture of drug and excipients

Evaluation studies

Pre compression parameters

a) Bulk Density: The bulk density for the formulated blend was carried out for all formulation and found in the range of 0.435-0.462.

b) Tapped density: The tapped density for the formulated blend was carried out for all formulation and found in the range of 0.526-0.570.

c) Angle of repose: The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 28 to30^0

d) Compressibility index: Compressibility index was carried out, it found between 17.30% to 19.17 % indicating the powder blend have the required flow property for compression.

Characterization of Formulation

Table-: 3 Pre compression parameters of Resperidone fast dissolving tablets

S.no	Bulk density	Tapped density	Compressibility index	Hausner ratio	ANGLE OF REPOSE
F1	0.435	0.526	17.30	1.20	28^0c
F2	0.441	0.539	18.18	1.22	30^0c
F3	0.445	0.547	18.64	1.22	29^0c
F4	0.438	0.529	17.20	1.20	28^0c

Post compression parameters

Weight variation:

All the formulated (F1 to F4) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low

standard deviation values.

Thickness:

Tablets mean thickness were uniform in F1 to F4 formulations and were found to be in the range of 2.0 mm to 2.5 mm.

Hardness:

The measured hardness of tablets of each batch ranged between 3.15to 3.35kg/cm^2. This ensures good handling characteristics of all batches.

Friability:

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Content Uniformity:

The percentage of drug content for F1 to F4 was found to be between 89.69 % to 95.50% of Resperidone , it complies with official specifications.

Disintegration Time:

In the presented studies, three different types of in vitro methods of tablet disintegration were used: those where the only factor leading to the disintegration was water wicking into the matrix of the tablet, the tests with water agitation or stirring, and the methods where direct destructive forces were put on the tested tablet, such as grinding or pressing with additional weight. Therefore, disintegration tests showed great variability in the data measured with different methods. The shortest registered disintegration time was 49s, while the longest greatly exceeded 59sec.

Wetting Time:

The weight of the tablet before keeping in Petri dish was noted (W_b) using Shimadzu digital balance. The wetted tablet from the Petri dish was taken and re weighed (W_a) using the same. The shortest registered wetting time was 140sec, while the longest greatly exceeded 151 sec.

Table-: 4 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

Dissolution studies

All the four formulations of Resperidone fast dissolving tablets were subjected to in vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period of time.

Table-: 5 Drug release studies of all formulations

Time	F1	F2	F3	F4
0	0	0	0	0
5	20.15	19.61	21.54	23.78

10	35.63	32.74	46.52	32.42
15	45.89	44.17	54.63	43.63
30	65.43	61.23	73.75	63.87
45	78.18	72.31	85.29	75.73
60	94.25	93.48	98.32	91.93

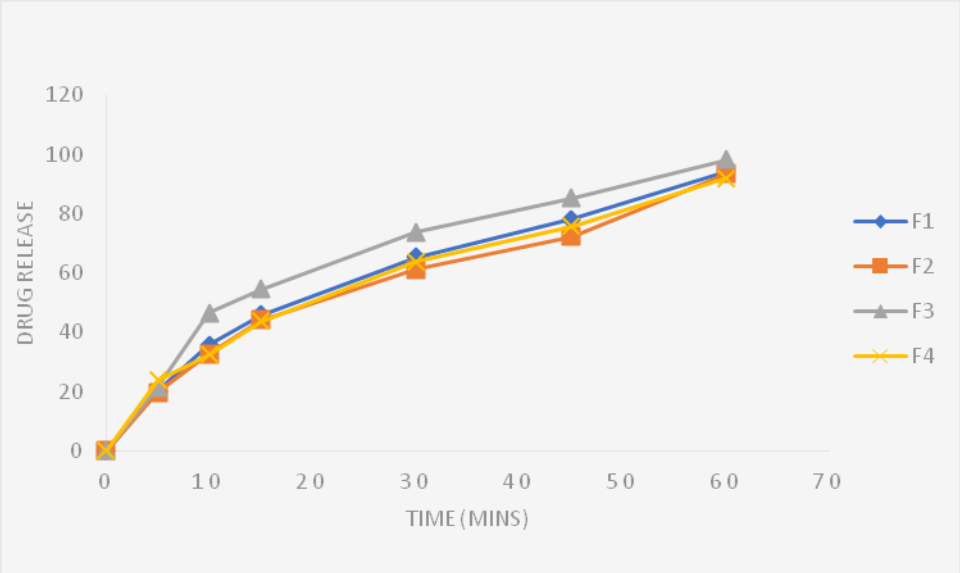

Fig.4. Invitro drug release of all formulations

Stability Study

There was no significant change in physical and chemical properties of the fast-dissolving tablets of formulation F-3 after 90 days. Parameters quantified at various time intervals were shown.

Table-: 6 Stability studies of optimized formulations

	Parameters	**Initial**	**1st Month**	**2nd Month**	**3rd Month**	**Limits as per Specifications**
F-3	**25^0C/60%RH % Release**	98.32	98.15	98.15	98.15	**Not less than 85 %**
F-3	**30^0C/75% RH % Release**	98.32	98.12	98.10	98.13	**Not less than 85 %**
F-3	**40^0C/75% RH % Release**	98.32	98.09	98.08	98.06	**Not less than 85 %**

IV. 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 Crosspovidone were 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, in vitro drug release and stability studies. In the above studies F3 formulation showed promising results. It was further supported by FTIR analysis which showed that F3 had no interaction with excipients. The stability studies were carried out for the optimized batch F3 for 90days and it showed acceptable results. So F3 formulation 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 Crosspovidone, PEG 4000 and PEG 6000 systems could be considered for formulations 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 the Solid dispersion technique can be used to enhance the solubility, Dissolution rate and oral bioavailability of water insoluble drugs.

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