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PRELIMINARY STUDIES ON THE PHYSICAL PARAMETERS OF ORODISPERSIBLE TABLETS USING SUPERDISINTEGRANTS

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ABSTRACT

There are various routes of drug administration available such as oral, sublingual, inhalation, and rectal. Among all, the oral route of drug administration is most widely used. Tablet is the most popular dosage form among all existing dosage forms. The most conventional tablets are immediate release but these tablets are only suitable for drugs with high solubility and high permeability. In this study, five different Orodispersible tablet formulations were prepared. Various Natural and Synthetic super disintegrants were used in all formulations including Plantago Ovata (F1), Sodium Alginate (F2), Fenugreek (F3), Croscarmellose Sodium (F4) & Crospovidone (F5). Various pre-formulation and post-formulation tests were performed for all five (05) formulations like Angle of repose, Bulk density, Tapped density and Compressibility index. Additionally, all of the prepared formulations were evaluated for weight variation, friability, hardness, drug content, and disintegration time and dissolution rate. Furthermore, stability testing of Risperidone Oro dispersible tablets was conducted. The results revealed that all the formulations F1, F2, F3, F4, and F5 complied with the official specification limits. Among all formulations, F1 showed the best results in terms of less disintegration and increased dissolution of drug as compared to other formulations, and the F1 formulation showed good stability results as well.

Keywords: Compression, Super disintegrants, Orodispersible Tablets, Risperidone

INTRODUCTION

United States Food and Drug Administration (FDA) defines orodispersible tablet as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". In order to mask the bitter taste of active ingredient, many substances are added in the orodispersible tablets and the active ingredient is swallowed by the oral route **[1, 2]**.

The Oral drug delivery remains the preferred route for administration of various drugs. The recent developments in technology have

prompted scientists to develop orally disintegrating tablets (ODTs) with improved patient compliance and convenience **[3]**. The primary action of Risperidone is to decrease dopaminergic and serotonergic pathway activity in the brain, therefore decreasing symptoms of schizophrenia and mood disorders **[4]**.

Risperidone has high affinity binding to serotonergic 5-HT2A receptors versus dopaminergic D2 receptors in the brain. Risperidone binds the D2 receptors with lower affinity than the traditional, first-generation antipsychotic drugs, which bind with very high affinity. A reduction in extrapyramidal symptoms in Risperidone use is attributed to its moderate affinity for dopaminergic D2 receptors **[5]**.

Risperidone is a solid dispersion, orally disintegrating tablet formulation and designed for non-destructive methods of evaluation **[6]**. Its acceptability is due to the disintegration rates of orally disintegrating Risperidone Tablets in patients with Schizophrenia or schizoaffective disorder **[7]**.

MATERIALS AND METHODS

Plantago Ovata, Sodium Alginate, Fenugreek Croscarmellose sodium & Crospovidone were purchased in powder form (China & India). Risperidone powder was a gifted sample from pharmaceutical industry. Microcrystalline cellulose (MCC), Magnesium Stearate, Talc & Aspartame were used in orodispersible tablets (Sigma, USA).

Standard Calibration curve of Risperidone

It was found that the estimation of Risperidone by UV spectrophotometric method at λ max 278nm and pH 6.8 in Phosphate buffer had good reproducibility. So, this method was used in the study.

Formulation Composition

Plantago ovata, Sodium Alginate, Fenugreek, Croscarmellose Sodium & Crospovidone in powder form and each one of them was used 25% in five formulations. Risperidone Powder 1%, Microcrystalline cellulose (MCC), Magnesium Stearate, Talc & Aspartame 74% were used in orodispersible tablet formulation (Table 1).

Table 1. Chemical composition of all five formulations of orodispersible tablets of Risperidone.

Ingredients	F1	F2	F3	F4	F5
***Plantago Ovata* (mg)**	25	---	---	---	---
Sodium Alginate (mg)	---	25	---	---	---
Fenugreek (mg)	---	----	25	----	---
Croscarmellose Sodium (mg)	---	--	---	25	--
Crospovidone (mg)	--	----	---	--	25
Mg Stearate (mg)	3	3	3	3	3
Talc (mg)	2	2	2	2	2
Mannitol (mg)	68.9	68.9	68.9	68.9	68.9
Aspartame (mg)	0.1	0.1	0.1	0.1	0.1
Risperidone (mg)	1	1	1	1	1
Total weight (mg)	100	100	100	100	100

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Table 2. Pre-formulation studies of all five formulations of Risperidone orodispersible tablets

Formulation code.	Angle of Repose. ±SD	Bulk Density (gm/cm3) ±SD	Tapped Density (gm/cm3) ±SD	Compressibility Index.(%) ±SD	Hausner Ratio ±SD
F1	26±0.3	0.23±0.05	0.38±0.22	22.06±1.5	1.28±1.02
F2	33±1.2	0.21±0.33	0.41±0.35	38.78±0.2	1.45.±0.05
F3	42±0.5	0.36±0.25	0.49±0.02	26.53±0.22	1.36±0.81
F4	40±0.5	0.33±0.12	0.52±1.2	36.53±0.02	1.57±0.55
F5	45±1.4	0.30±0.30	0.49±0.11	38.77±0.31	1.63±1.22

Direct Compression Method

As its name implies, Direct Compression consists of compression of tablets directly from powdered material without modifying the physical nature of the material itself. Formerly, direct compression as the method of tablet manufacturing was reserved for small group of crystalline chemicals having all the physical characteristics required for the formation of a good tablet.

Pre-formulation studies orodispersible tablet

Pre-formulation studies are related to pharmaceutical formulation development of the drug substance.

Following Pre-formulation studies (Table 2) yield basic knowledge necessary to develop suitable formulation **[8, 9].**

1. Bulk Density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It is expressed in g/ml and is given by **Db = M / Vb** Where, M is the mass of powder **Vb** is the bulk volume of the powder.

2. Tapped Density (Dt)

It is the ratio of total mass of the powder to the tapped volume of the powder. It is expressed in g/ml and is given by, **Dt = M/Vt** Where, M is the mass of powder Vt is the tapped volume of the powder.

3. Angle of Repose

The friction forces in a loose powder can be measured by the angle of repose. It is an indicative of the flow property of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane $\theta = \tan^{-1}(h / r)$

Where, **ɵ** is the angle of repose.

h is the height in cm & **r** is the radius in cm.

4. Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is given as

$$I = \frac{Dt - Db}{Dt} * 100$$

Where, **Dt** is the tapped density of the powder and **Db** is the bulk density of the powder

5. Hausner's ratio

Relationship between % compressibility and flowability is given by Hausners ratio. It is an indirect index of ease of powder flow and calculated by the formula,

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Hausner ratio = Dt/Db

Where, Dt is the tapped density and Db is the bulk density. Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Post–Compression Evaluation of Orodispersible tablets

The post compression study after the compression of tablet to evaluate the tablet by different parameters and data help to enhance the quality of the product **[10, 11]**.

1. Weight variation

Standard procedures are followed as described in the official books. 20 tablets are selected randomly to check for weight variation. Weight variation specification as per I.P.is shown in Table 3.

Table 3. Weight variation specification as per I.P.

S. No.	Average weight of tablet ± SD
1	80 mg or less ± 10
2	More than 80mg but less than 250mg ±7.5
3	250mg or more ±5

2. Friability

Friability is a measure of mechanical strength of the tablet. If a tablet has more friability, it may not remain intact during packaging, transport or handling. Roche friabilator is used to determine the friability by following procedure. Pre weighed tablets are placed in the friabilator.

% Friability = 1- (loss in weight / initial weight) X 100

3. Hardness (Crushing strength)

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. It is expressed in kg/cm^2.

4. Wetting Time

Wetting time is carried out using a piece of tissue paper folded twice in a small culture dish (internal diameter, 6.5 cm) containing 6ml of water. A tablet is placed on the paper and the time for complete wetting is measured and the water absorption ratio was calculated **[12].**

R=(Wb-Wa)/ Wa

Where, Wa and Wb are the weight before and after water absorption respectively.

5. Disintegration time

According to the European pharmacopoeia the fast disintegrating or Orodispersible tablets should disintegrate within 3 minutes without leaving any residue on the screen. However, it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus, the disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth.

6. *In-Vitro* dissolution

The release of drug from the orodispersible tablet is determined by using USP dissolution testing apparatus. It is performed using 900 ml, of artificial saliva at 37 ± 0.5 $^{\circ}$C at 50 rpm.

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The samples are withdrawn at frequent intervals and analyzed by measuring the absorbance of the diluted sample. Other Medias such as Phosphate buffer pH 6.8 are also used **[13]**.

RESULTS AND DISCUSSION

Standard Calibration curve of Risperidone

It was found that the estimation of Risperidone by UV spectrophotometric method at λ max 278nm in Phosphate buffer at pH 6.8 had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2- 10µg/ml. The regression equation generated was y = 0.193x and R^2= 0.997. The calibration curve of Risperidone (Fig. 1) in Phosphate Buffer pH 6.8 showed good correlation with regression value of 0.997.

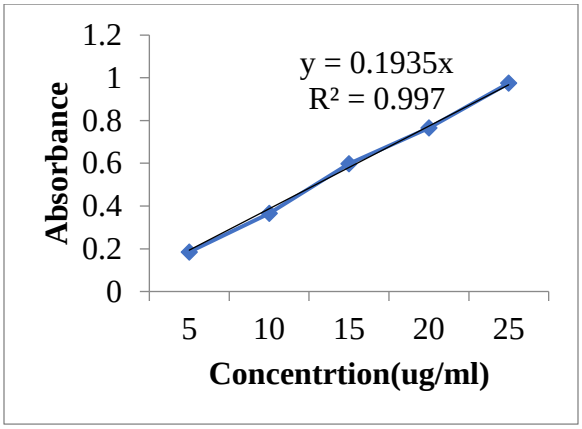

Figure 1. Standard Calibration Curve of Risperidone

Pre-compression parameters finding

From the results of all formulations, it is clear that the angle of repose of all formulations was within limits (Table 4) but the formulation F1 showed minimum value of angle of repose which was considered as excellent formulation among all formulations.

Table 4. Angle of Repose, Type of Flow.

1	**< 20 Excellent**
2	20-30 Good
3	30-40 Passable
4	>34 Very Poor

The bulk density of all formulations lies within the range of 0.21 to 0.36 but the formulation F1 showed maximum bulk density. The results of tapped density of all formulations showed the values were within official limits of 0.41 to 0.52.

The results of compressibility index of all formulations showed that the values were within official limit of 22.06 to 38.78 and has good flow rate. But the formulation F1 showed compressibility index of 22.06 which was the best formulation among all (Table 5).

Table 5. % Compressibility, Flow ability.

1	**5-12 Excellent**
2	12-16 Good
3	18-21 Fair passable
4	23-35 Poor
5	33-38 Very Poor
6	≥ 40 Very, Very Poor

The results of all the formulations showed that the values of Hausner ratio lay in between 1.28 to 1.63 while F1 formulation value showed good result according to reference values.

Post-Compression Finding

The post-compression results of formulations were shown in Table 6. The Wetting time (sec) lies in between 25 to 60 and the wetting time of F1 was very less as compared to other formulations. The other parameter was the hardness of all the formulation which was in

Table 6. Post-Compresssion studies of five formulations of Risperidone Orodispersible tablets.

Formulation.	Weight Variation. (mg)±SD	Hardness (Kg/cm²) ±SD	Friability (%Age) ±SD	Disintegration Time (Sec.)±SD	Assay. (%Age)	Wetting time. (Sec.) ±SD
F1	101±0.2	2.7±2.1	0.24±0.2	23±1.30	98.08	25±0.13
F2	98.5±1.5	2.4±1.4	0.31±0.5	30±1.33	94.76	36±0.02
F3	105±0.4	2.6±1.2	0.42±0.1	40±3.10	96.92	44±1.02
F4	104±0.2	2.7±1.5	0.34±0.3	35±2.66	93.06	37±1.15
F5	101±0.2	2.5±1.1	0.34±0.2	55±2.13	94.65	60±0.25

the range of 2.4-2.7 as per official range and dissolution time was in the official limits of orodispersible tablet. But maximum absorbance was shown at wavelength of 278 nm.

The results of %age friability of all the formulations showed a range of 0.24-0.42, which were in the official limits of not more than 1%. But F1 friability value was most suitable among all the formulations. From the results of %age assay of all formulations it was indicated that all the formulations were within official limits, in the range of 93.06 to 98.08.

The results of disintegration test of all 5 formulations of Risperidone were within limits but the formulation F1 indicated least disintegration time of 23 sec. (Fig. 2). The dissolution test of all 5 formulations of Risperidone orodispersible tablets showed absorbance within specified limits (Table 7, Fig. 3).

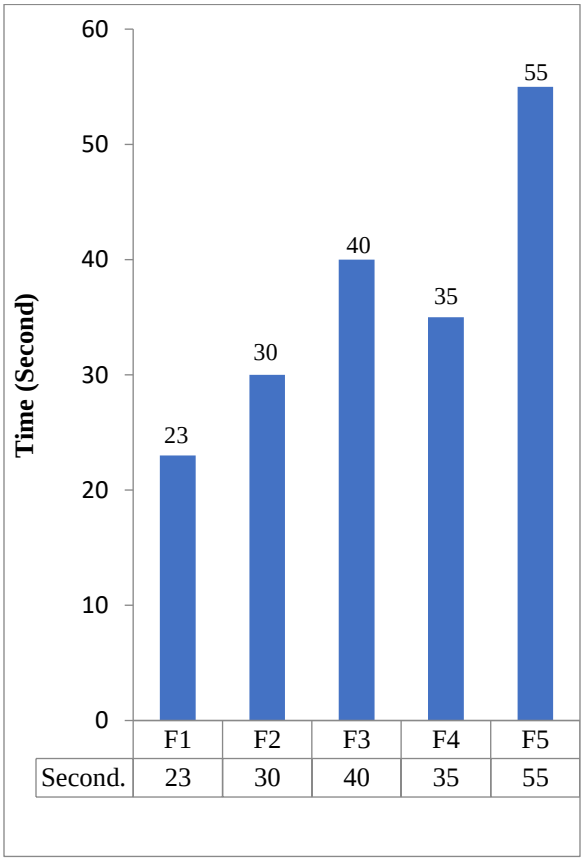

Figure 2. Disintegration Study of Risperidone orodispersible tablets

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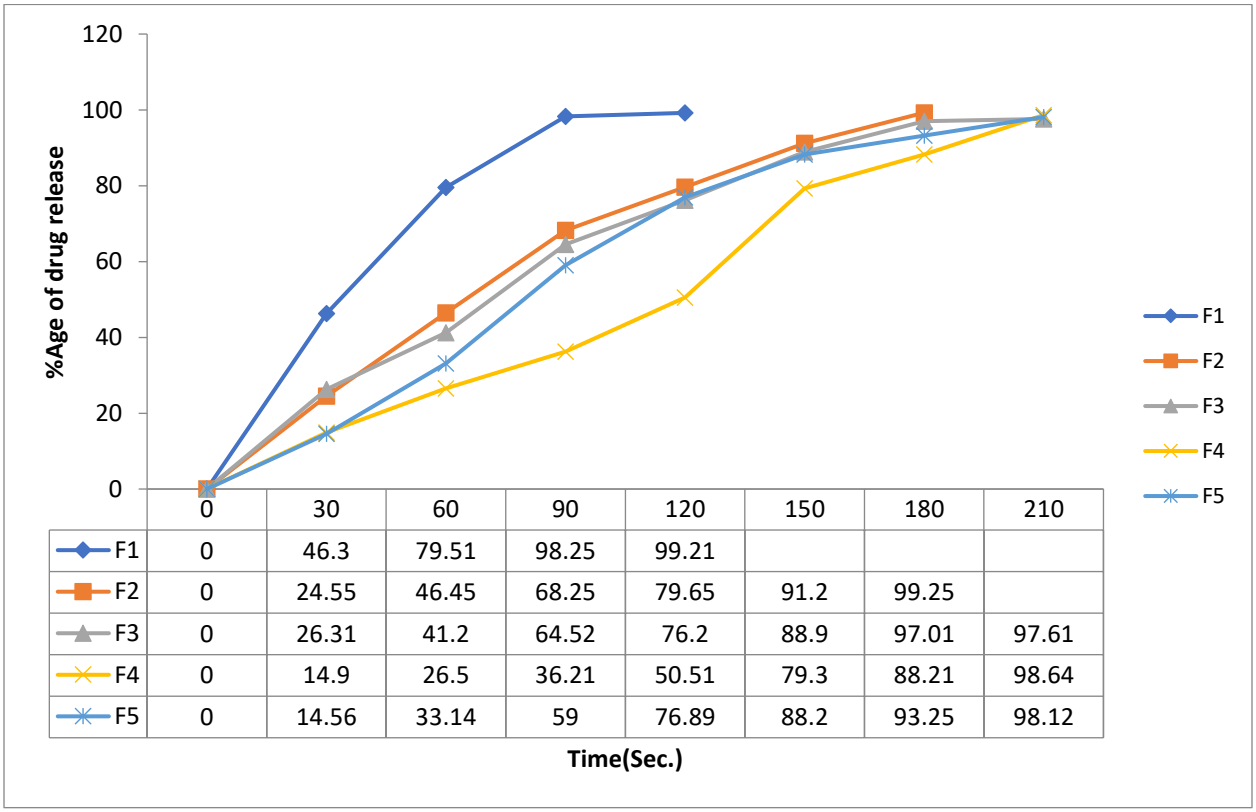
Table 7. In-vitro Dissolution studies of Risperidone orodispersible tablets.

Formulation	%DTR After 30Sec±SD	%DTR After 60Sec±SD	%DTR After 90Sec±SD	%DTR After 120Sec±SD	%DTR After 150Sec±SD	%DTR After 180Sec±SD	%DTR After 210Sec±SD
F1	46.30±0.02	79.51±0.02	98.25±0.03	99.21±0.01			
F2	24.55±0.02	46.45±0.04	68.25±0.03	79.65±0.1	91.2±0.02	99.25±0.04	
F3	26.31±0.01	41.20±0.02	64.52±0.02	76.20±0.01	88.90±0.03	97.01±0.01	97.61±0.05
F4	14.90±0.02	26.50±0.05	36.21±0.06	50.51±0.03	79.30±0.01	88.21±0.02	98.64±0.04
F5	14.56±0.02	33.14±0.05	59.00±0.06	76.89±0.05	88.20±0.02	93.25±0.01	98.12±0.01



	0	30	60	90	120	150	180	210
F1	0	46.3	79.51	98.25	99.21			
F2	0	24.55	46.45	68.25	79.65	91.2	99.25	
F3	0	26.31	41.2	64.52	76.2	88.9	97.01	97.61
F4	0	14.9	26.5	36.21	50.51	79.3	88.21	98.64
F5	0	14.56	33.14	59	76.89	88.2	93.25	98.12

Figure 3. Dissolution Study of Risperidone orodispersible tablets

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CONCLUSION

The orodispersible tablets of Risperidone were successfully formulated with super disintegrants with same ratios in different formulations by direct compression technique and optimized formulations were achieved. The basic tests were passed by the formulations.

No significant change was indicated by both pre formulation and post formulation parameters in all formulations but the critical analysis depicted that in all the formulations, F1-formualtion containing 25mg of *Plantago ovata*, showed better dissolution at 278nm and less disintegration time of 23 sec as compared to other formulations. So, this formulation was best fit for orodispersible tablets.

FUTURE PROSPECT OF THE RESEARCH

With the advancement in pharmaceuticals, ODT dosage forms is gaining popularity due to increased bioavailability and improve patient compliance.

Further investigations can be made by more super disintegrants. Study on human volunteers can also be performed to evaluate the taste of drug and in vivo drug release.

Similar studies can be performed as well by comparing it with the available brands of drug.

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