FORMULATION AND EVALUATION OF RISPERIDONE FAST DISSOLVING TABLETS

*Rubesh Kumar * [1], Dr. V. Uma maheshwar rao, D. Pavani, D. Shashikumari, N. Suraj singh, Ch. Dilip kumar*
Teegala ram reddy college of pharmacy, Hyderabad-500059

ABSTRACT:*The main aim of present research investigation is to formulate the Risperidone Fast Dissolving tablets. Risperidone, an atypical antipsychotic, belongs to BCS Class-II and used for treating schizophrenia, bipolar mania and autism by blocking D_2 and 5-HT_{2A} receptors. The Fast Dissolving tablets of Risperidone were prepared employing different concentrations of Crospovidone and Croscarmellose sodium in different combinations as a Superdisintegrants by Direct Compression technique. The concentration of Crospovidone and Croscarmellose sodium was selected as independent variables, Totally four formulations were designed, preapred and are evaluated for hardness, friability, thickness, Assay, Wetting time, Disintegration time, In-vitro drug release.*

Keywords: *Risperidone, sodium starch glycolate, croscaramellose, direct compression technique, in vitro drug release studies.*

I.INTRODUCTION

Fast dissolving tablets are ideal for all types of people, including for people who have swallowing difficulties, pediatric, geriatric, and bedridden patients.[1,2] It is also for active patients who are busy, travelling and may not have access towater[3]. Fast dissolving tablets are also known a s orodispersible tablets,mouthdissolving tablets, orally disintegrating tablets, melt-in mouthtablets, rapimelts, porous tablets, quick dissolving etc. Many drugs have the potentials to be made into orodispersible tablets.[4] Risperidone, a benzisoxazole derivative, is an atypical antipsychotic drug with high affinity for 5-hydrotryptamine (5-HT) and dopamine D2 receptors.[5] It is used primarily in the management of schizophrenia, inappropriate behaviour in severe dementia and manic episodes associated with bipolar I disorder. Aim of this research work was to develop mouth dissolving tablet that disintegrates rapidly in mouth by using co-processed superdisintegrants and enhance the solubility of the drug facilitating for quick release.[6,7]

II. MATERIALS AND METHODS[8,9]

Risperidone was collected as a gift sample from Hetero labs, Hyderabad and various excipients like croscaramellose, sodium starch glycolate were purchased from AR chemicals, Hyderabed.

METHODOLOGY [10]

Formulation Development

(a) Preparation of fast dissolving tablets

Preparation of Risperidone by Direct Compression Method

Weigh all the ingredients in required quantity. Transfer all ingredients into a mortar, triturate for 10minutes until to get fine powder and sieve the material. (#60) then transfer the material into blender for proper distribution of drug in blend for 10minutes then addition of lubricant, mix well. Perform the micromeritic properties (Precompression studies) and Compression the tablets.

Table-1: Preparation of Risperidone fast dissolving tablets

S.NO.	INGREDIENTS	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
1	Risperidone	3	3	3	3
2	Croscaramellose sodium	10	15	-	-
3	Sodium starch glycolate	-	-	10	15
4	Microcrystalline cellulose	82	77	82	77

5	Magnesium stearate	3	3	3	3
6	Talc	2	2	2	2
7	Total wt	100	100	100	100

Evaluation of tablets[11,12]

Post compression parameters

i. Weight variation

The weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. The USP weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablets met the USP specification that not more than 2 tablets are outside the percentage limits and no tablet differs by more than 2 times the percentage limit.

ii. Hardness Test

Hardness indicates the ability of a tablet to withstand mechanical shocks while packaging, handling and transportation. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and analyzed for hardness. The mean values were calculated.

iii. Friability

A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.

The percentage friability was determined by the formula:

$$\% \text{ Friability} = (W_1 - W_2) / W_1 \text{ X } 100$$

W_1 = Weight of tablets before test

W_2 = Weight of tablets after test

iv. Content uniformity

Ten tablets were selected randomly and crushed, from that average weight of one tablet was dissolved using20ml methanol and 20ml of 0.1N HCl until drugs get dissolved then added the dissolution media (0.1N HCl &6.8 pH Phosphate buffer) to make volume 100ml, 0.45µ membrane filter. Standard also performed with the same concentration then this would read at 276 nm by UV spectroscopy.

$$\text{Amount of drug} = \frac{\text{Sample absorbance}}{\text{Std.absorbance}} \times \frac{\text{Std.dilution}}{\text{Sample dilution}} \times \text{Conversion factor} \times 100$$

Conversion factor Provastatin = Molecular wt of Provastatin

$$\% \text{ Purity} = \frac{\text{Amount}}{\text{Label claim}} \text{x } 100$$

v. Wetting Time

Ten millilitres of the buffer solution of pH 6.80 as of saliva was taken in petri dish. A circular tissue paper having diameter 8 cm folded twice was placed in the petri dish. Single mouth disintegrating tablet was placed on tissue paper and time for complete wetting was noted.

vi. In-Vitro Dissolution Studies

The dissolution conditions used for studying the drug release from fast dissolving tablets:

vii. Stability Studies

Selected Formulation was subjected to stability studies as per ICH guidelines.

Following conditions were used for Stability Testing.

1. 25^0C/60% RH analyzed every month for period of one month.
2. 30^0C/75% RH analyzed every month for period of one month.
3. 40^0C/75% RH analyzed every month for period of one month.

III.RESULTS AND DISCUSSION

Fourier Transformation Infra-red (FTIR) analysis:

Infra-red spectroscopy analysis was performed by Fourier Transformation Infrared Spectrophotometer Alpha Brooker FTIR (Tokyo, Japan).The instrument was calibrated by using polystyrene film.

(a) (i) Fourier Transformation Infra-red (FTIR) analysis of Risperidone:

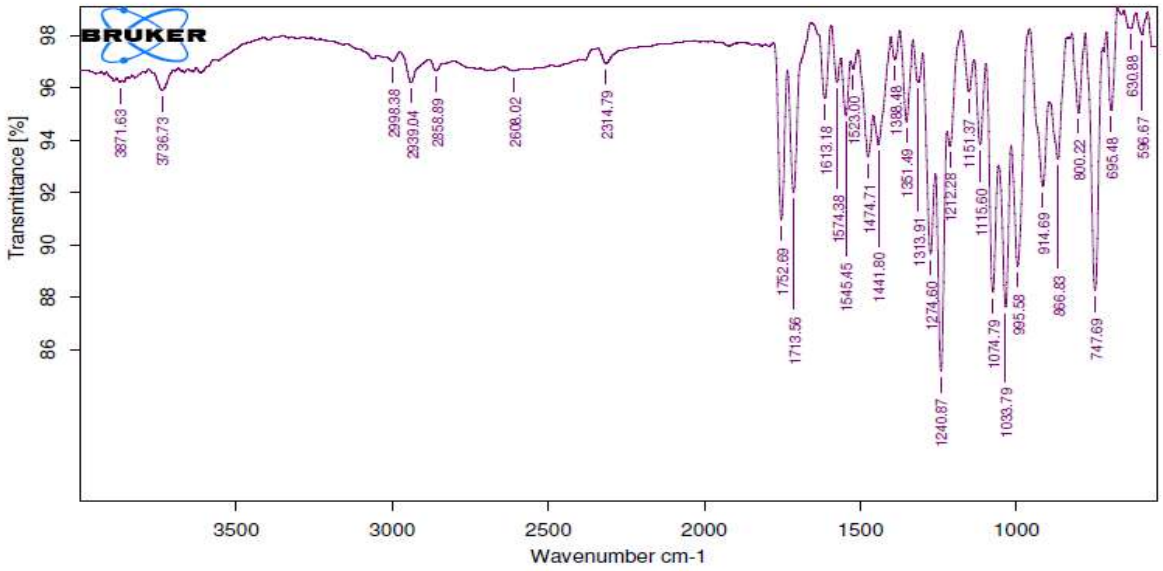

Fig-1: FT-IR graph for Risperidone Pure drug

(b) (i)FourierTransformation Infra-red (FTIR) analysis of Risperidone :

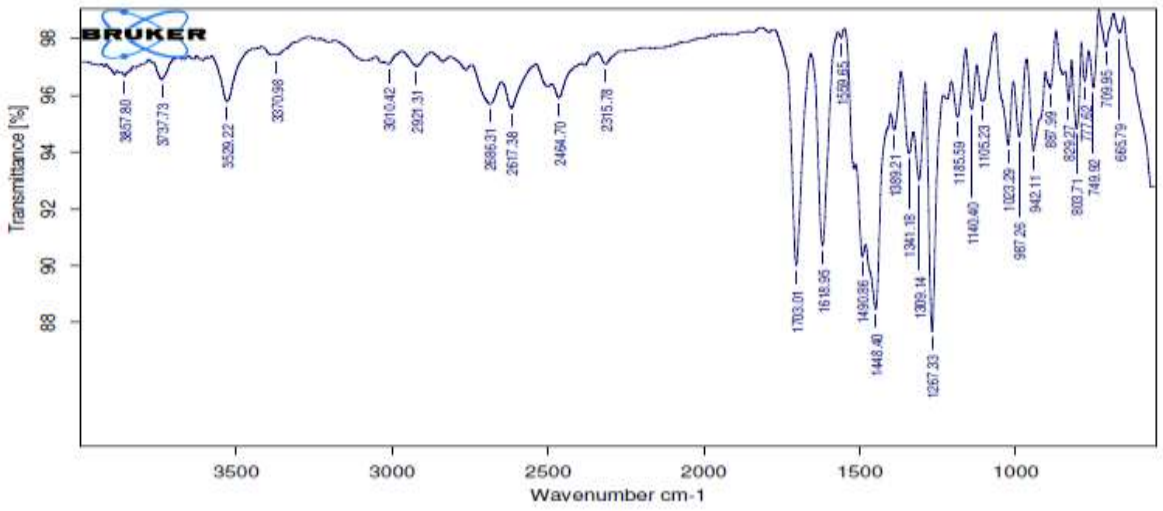

Fig- 2: FT-IR graph for Optimized formulation

In the present study, it has been observed that there is no chemical interaction between Risperidone and the polymers used. From the figure it was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers. This further confirms the integrity of pure drug and compatibility of them with excipients.

Evaluation of the prepared tablets for physical parameters

Table-2: Evaluation Parameters for Optimized formulation

Parameter	F1	F2	F3	F4
Weight variation	99	100	98	100

Thickness (mm)	2.1	2.5	2.4	2.5
Hardness (kg/cm^2)	4.41	4.42	4.3	4.3
Friability (%)	0.67	0.62	0.61	0.62
Wetting time	64	83	75	76
Disintegration time	35	36	38	34
Drug content	88	93	91	88

Uniformity of weight:
All the prepared fast dissolving tablets of Risperidone were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ± 5%.
Hardness and friability:
The hardness of the tablet formulations was found to be in the range of 4.3 to 4.42 kg/cm^2. The friability values were found to be in the range of 0.61to 0.67 %.
Uniformity of drug content:
The low values of standard deviation indicates uniform drug content within the tablets The percent drug content of all the tablets was found to be in the range of 98 to 96 percent (which was within the acceptable limits of ±5%.).
Discussion: All Formulations tested for Physical parameters like Hardness, thickness, Weight Variation, Friability and found to be within the Pharmacopoeial limits. The results of the tests were tabulated. The drug content of the formulation was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.
In vitro Dissolution studies: The dissolution conditions used for studying the drug release from fast dissolving tablet:

Table-3: In-vitro dissolution Profiles for tablets

Time (Hrs)	F1	F2	F 3	F4
0	0	0	0	0
1	17.65	18.63	17.91	15.56
5	39.93	34.92	26.92	23.67
10	64.69	47.93	51.25	56.95
15	78.98	89.76	73.94	72.18
20	84.52	92.92	79.56	81.26
25	89.56	95.42	82.16	84.58
30	92.42	98.56	91.26	93.65

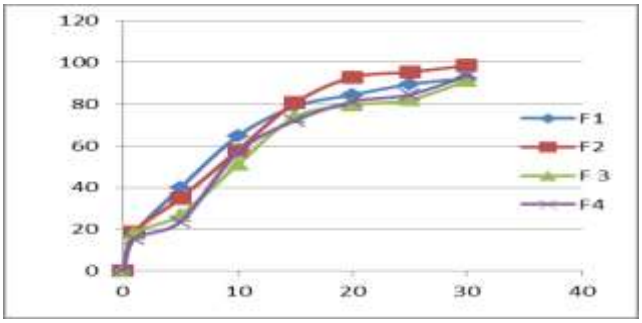

Fig-3: In-vitro dissolution Profiles for tablets

Among all formulations, F2 shows better drug release when compared with all other formulations. So formulation F2 selected as optimized formula.

Stability studies

Table-4: Stability Studies of Optimized Formulation

S.NO	Time in days	Physical changes	Mean % drug content ± SD		
			Fast dissolving tablet		
			25^0C/60%	30^0C/75%	40^0C/75%
1.	01	No Change	98.56	98.56	98.56
2.	30	No Change	97.86	97.99	97.59

There was no significant change in physical and chemical properties of the tablets of formulation F2 after one month, parameters like % drug release and assay values at various conditions(at 40^0C/ 75% RH) as per ICH guidelines quantified at various time intervals were shown in Table and dissolution profile.

IV. CONCLUSION

The aim of the present study was to develop an optimized formula for fast dissolving tablet containing Risperidone for the management of schizophrenia. After pre-formulation studies it was decided to prepare tablets prepared by direct compression method. In the formulation of immediate release sodium starch glycolate and croscaramellose 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 bilayer tablets were also evaluated for weight variation, hardness, friability, drug content, disintegration time and in vitro drug release. In the above studies F2 formulation showed promising results. It was further supported by FTIR analysis which showed that F had no interaction with excipients. The stability studies were carried out for the optimized batch F2 for one month and it showed acceptable results. So F2 formulation was considered as the optimized formulation.

REFERENCES

1. Litchenckert, S.; Lurdgren, C. and Ferno, O.; "Chewable smoking substitute composition", US Patent, 1975, 3901248.
2. Lowenthal, W.; "Journal of Pharmaceutical Sciences", 61, 1972, pp 1695
3. Siegel, S.; "Journal of Pharmaceutical Science", 51, 1962, pp 1069. Allen, L.V., Wang, B. and Davis, J.D.," Rapidly Dissolving Tablet", **US patent No.,** US5807576, 1998. , Bhaskaran, S. and Narmada, G.V., Fast Dissolving drug delivery systems: A brief overview, **Indian Pharmacist,** 2002, 1 (2), 9-12.
4. Devrajan, P.V, Gore, S.P., Fast Dissolving Tablets: The Future Compaction, Express Pharma Pulse, 2000: 23, 7(1), 16.
5. Kuchekar, B.S., Badhan, A.C., Mahajan, H.S., Fast Dissolving drug delivery systems: A brief overview, Pharma Times, 2003, 35, 7-9.
6. Reddy, L. H., Ghose, B. and Rajneesh, Fast Dissolving drug delivery systems: A brief overview, Indian J. Pharm. Sci.**, 2002**, 64(4): 331- 336, Parakh, S.R. and Gothoskar, A.V., Fast Dissolving drug delivery systems: A brief overview, **Pharma. Tech.,** 2003, 92- 100.
7. Lalla, J.K. and Sharma, A H., **Indian Drugs,** 1994, 31(11), 503-508.
8. www. ElanNanoCrystal_Technology.htm.
9. Indian Pharmacopoeia, Ministry of Health and Family Welfare, Govt. of India, Vol 1, 342.
10. Gray, B.N.; Jones, C.; "Journal of controlled release"; 8, 1989, pp 251- 257.
11. http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=7c25b695-bbed-4ad1-aa47-de47091bc808
12. http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=f5eb861f-0ebd-4d37-a62a-5fecde4c65bd