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Original Article

DESIGN AND IN VITRO EVALUATION OF ORALLY DISINTEGRATINGTABLETS OF SELEGILINE

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ABSTRACT

Objective: The purpose of presenting research work to formulate oral disintegrating tablets of Selegiline to enhance therapeutic efficacy.

Methods: An attempt has been made to develop and evaluate Orally Disintegrating or Mouth Dissolving tablets of Selegiline for quick effect, better patient compliance and effective therapy. Fast dissolving tablets of Selegiline were prepared by direct compression technique using selected super disintegrants.

Results: The FTIR spectra revealed that, there was no interaction of drug with formulation ingredients. The prepared tablets were evaluated for drug content, friability, hardness, In vitro disintegration and In vitro release studies. All the tablets with different super disintegrants showed better results. However, required disintegration and dissolution behavior of Selegiline was achieved for tablets with Crospovidone (20%) as super disintegrant.

Conclusion: From experimental studies it is concluded that fast dissolving drug delivery systems can be a suitable approach to improve onset of action for getting instantaneous therapeutic response.

Keywords: Mouth dissolving tablets, Selegiline, Crospovidone, Direct compression, Orally disintegrating tablets.

INTRODUCTION

The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is well absorbed as the food stuffs that are ingested daily. In fact, the development of a pharmaceutical product for oral delivery, irrespective of its physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology [1]. Recently pharmaceutical industry has become increasingly aware of the need that pediatric and geriatric be considered as a separate and unique Medicare population. Though geriatric and pediatric patients constitute a minor proportion of the population, its growth rate is high and hence will have the significant impact on development of drug delivery systems. Thus, fast dissolving drug delivery systems are gaining more demand and popularity from a last few years [2].

The concept of Orally Disintegrating or Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphasia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Other categories that experience problems using conventional oral dosage forms includes mentally ill, uncooperative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attack or coughing. Sometimes it may be difficult to swallow conventional products due to unavailability of water. These problems led to the development of novel type of solid oral dosage form called "Mouth Dissolving Tablets". This tablet disintegrates instantaneously when placed on the tongue, releasing the drug that dissolves or disperses in the saliva [3].

Although the mechanisms for selegiline's beneficial action in the treatment of Parkinson's disease are not fully understood, the selective, irreversible inhibition of monoamine oxidase type B (MAO-B) is thought to be of primary importance. MAO-B is involved in the oxidative deamination of dopamine in the brain. Selegiline binds to MAO-B within the nigrostriatal pathways in the central nervous system, thus blocking microsomal metabolism of dopamine and enhancing the dopaminergic activity in the substantial nigra. Selegiline may also increase dopaminergic activity through mechanisms other than inhibition of MAO-B. At higher doses, selegiline can also inhibit monoamine oxidase type A (MAO-A), allowing it to be used for the treatment of depression [4]. Pursuing these objectives, this work was aimed at developing a fast release Selegiline tablets to enhance therapeutic efficacy.

MATERIALS AND METHODS

Materials

Selegiline was purchased from Dr. Reddy's Laboratories (Hyderabad, India). Sodium starch glycolate, Croscarmellose sodium, Crospovidone, Aspartame, Mannitol, Microcrystaline cellulose, Magnesium stearate were received as gift samples from FDC Limited, Mumbai. All other reagents and chemicals used were of analytical reagent grade.

Preparation of Metoclopramide containing Mouth dissolving tablets

Tablets, each containing 10 mg selegiline, were prepared by direct compression method as per composition given in table 1. The drug and excipients were passed through the sieve (#120) to ensure the better mixing. Mannitol was used as a direct compressible vehicle. Superdisintigrant like Crospovidone was used in different ratios. The powder was compressed using Rimek compression machine equipped with 8 mm round punch by direct compression technique.

A minimum of 20 tablets was prepared for each batch [5, 6].

Evaluations

Tablet dimensions (Tablet thickness and diameter)

Five tablets of each batch were picked randomly and its thickness and diameter were measured individually using calibrated varnier calipers. Tablet thickness should be controlled within±5% variation of a standard value [6, 7].

Hardness

The hardness of tablet of each formulation was measured by Monsanto hardness tester. The hardness was measured in terms of kg/cm ^{2}. Five tablets were randomly picked from each batch and the hardness of the tablets was determined. The mean and standard deviation values were ca;'lculated for each batch [7].

Friability

Roche friabilator was used for testing the friability using the following procedure. Ten tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution.

After 4 min, the tablets were weighed and the percentage loss in tablet weight was determined [7, 8].

% Loss = Initial wt. of tablets–final wt. of tablets × 100/Initial wt. of tablets

Weight variation

Weighed 10 tablets selected at random and calculated the average weight. Not more than the percentage as gave in IP and none deviates by more than twice that percentage [7].

In vitro dissolution studies

In vitro dissolution studies for all the fabricated tablets was carried out by using USP Type II apparatus (USP XXIII Dissolution Test Apparatus) at 50 rmp in 900 ml of phosphate buffer pH 6.8, maintained at 37±0.5 °C. 5 ml aliquot was withdrawn at the specified time intervals, filtered through whatmann filter paper and assayed spectrophotometrically at 270 nm using Shimadzu 1700 spectrophotometer.

An equal volume of fresh medium, which was pre warmed at 37 °C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate [7, 8].

Table 1: Composition of different batches of mouth dissolving tablets of Metoclopramide

S. No.	Ingredients	Formulation Code								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	selegiline	10	10	10	10	10	10	10	10	10
2	Sodium starch glycolate	10	15	20	-------	------	------	-------	------	-----
3	Croscarmellose sodium	-----	-----	-----	10	15	20	-----	------	------
4	Crospovidone	-----	-----	----	-----	-----	-----	10	15	20
5	Talc	4	4	4	4	4	4	4	4	4
6	Mannitol	36	36	36	36	36	36	36	36	36
7	Micro crystalline cellulose	36	31	26	36	31	26	36	31	26
8	Magnesium Stearate	2	2	2	2	2	2	2	2	2
9	Aspartame	2	2	2	2	2	2	2	2	2
	Total	100	100	100	100	100	100	100	100	100

*All quantities are in milligrams

Content uniformity

Ten tablets were weighed and triturated to get the fine powder. Weight equivalent to 10 mg of selegiline was dissolved in 10 ml of phosphate buffer pH 6.8 and sonicated for 10 min, the volume was adjusted to 100 ml using phosphate buffer pH 6.8 with continuous sonication for 5 min.

1 ml of this solution (withdrawn form supernatant aqueous part) was diluted to 100 mL with phosphate buffer pH 6.8. 3 ml of above solution was diluted with phosphate buffer pH 6.8 up to 100 ml, filtered through 0.45 µm whatman filter paper, and analyzed at 270 nm using UV spectrophotometer (Shimadzu, Japan) [7, 8]. The experiments were performed in triplicate.

RESULTS AND DISCUSSION

Formulated tablets were found to be satisfactory when evaluated for thickness (3.15±0.76 mm); Hardness (2.96±0.65 kg/cm^2), Friability less than 1% (as shown in table 2). The percent drug content of all formulations were found to be between 95.2±1.09% to 98.2±1.09% (table 2) which is within acceptable limits indicating dose uniformity in each batch. FITR analytical studies were revealed that all ingredients were compatible with active ingredient (showed in fig 1 and 2). All formulations showed good disintegration behaviour. Formulations showed good wetting properties due to the presence of superdisintegrats.

Results of wetting time are shown in table 2. In the present study, all formulations had different superdisintegrants with different quantities and remaining ingredients are in same concentrations. The wetting time was highest for tablets of formulation F1 (50±3 sec) and least F9 (35±7 sec). The plot of cumulative drug release Vs time plotted for all formulations are depicted in fig. 3. The release of drug from Crospovidone based tablets was rapid and more than Sodium starch glycolate, Croscarmellose sodium based tablets. Microcrystalline cellulose as diluent enhanced drug release from mouth dissolving tablets.

Table 2: Physicochemical properties of selegiline Mouth dissolving tablets

Formulation code	Avg Weight (gm) mean±SD	Hardness(kg/cm2) mean±SD	Thickness(mm) mean±SD	Friabiliy (%)	In vitro disintegration time (secs) mean±SD	Wetting time(secs) mean±SD	% Drug content mean±SD
F1	101±0.12	2.87±0.9	3.13±0.16	0.3633	117±3	50±3	95.2±1.09%
F2	100.5±1.3	2.76±0.76	3.17±1.01	0.2103	150±5	49±5	95.4±2.56%
F3	100.5±1.5	2.70±0.93	3.18±0.21	0.1356	98±6	47±2	96.7±1.56%
F4	99.6±2.01	2.76±0.23	2.97±0.12	0.3496	150±4	42±5	95.5±0.56%
F5	100±1.5	2.24±1.6	3.13±1.3	0.3035	74±8	39±2	96.5±8.56%
F6	100.1±1.87	2.66±1.9	3.15±0.76	0.2130	40±3	38±7	97.1±2.65%
F7	100.1±1.34	2.24±1.45	2.90±0.45	0.4739	32±9	40±9	97.2±2.56%
F8	98.6±1.92	2.96±0.65	2.97±0.26	0.4500	22±7	38±5	97.6±3.6%
F9	99.4±1.05	2.90±0.98	2.98±0.41	0.4187	21±5	35±7	98.2±1.09%

±SD-Standard deviation for (n=5)

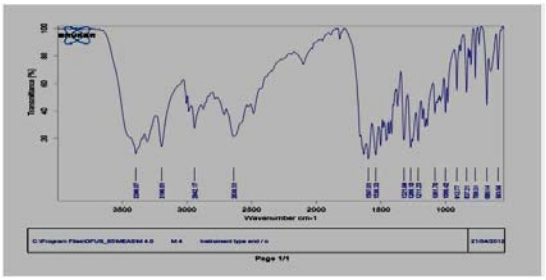

Fig. 1: **FTIR Spectra of pure drug**

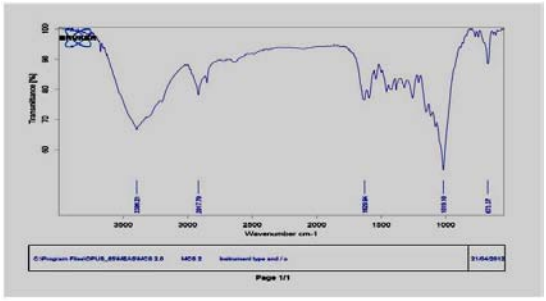

Fig. 2: **FTIR Spectra of Drug with formulation ingredients**

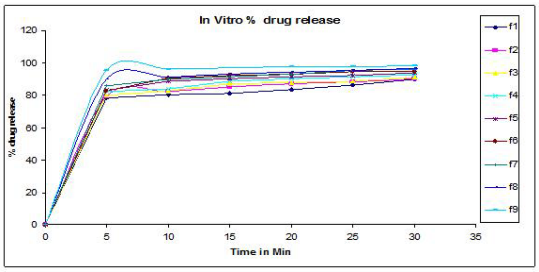

Fig. 3: **In vitro drug release of Selegiline mouth dissolving tablets**

CONCLUSION

Results of disintegration tests indicated that superdisintegrants increases the disintegration properties of tablets. From the results Cros povidone formulations showed better release properties. Sodium starch glycolate formulations showed more wetting time. In vitro release results indicated that the drug release was rapid and more for Crospovidone containing formulations. From above studies it is concluded that fast dissolving drug delivery systems can be a suitable approach to improve an onset of action for getting instantaneous therapeutic response.

CONFLICT OF INTERESTS

Declared None

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