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FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLETS OF BROMOCRIPTINE MESYLATE BY DIRECT COMPRESSION METHOD

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ABSTRACT

Oral route of administration continues to be the most preferred route among the different routes of administration of drugs due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. Immediate release tablets have gained popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. The present work involves the formulation development, optimization and in-vitro evaluation of immediate release Bromocriptine Mesylate tablets. To minimize critical process parameters and since Bromocriptine Mesylate is moisture and heat sensitive potent crystalline drug, direct compression method was selected for the formulation of immediate release tablets. Tablets were prepared containing Bromocriptine Mesylate, pharmatose DCL 21, starch, aerosil-200, magnessium stearate, sodium starch glycolate and cross carmellose sodium, in different concentrations. During the course of study it was found that the formulation F5 containing cross carmellose sodium as super disintegrant exhibited acceptable disintegration time, percentage drug content per tablet and *In vitro* drug release. So at last it was concluded that immediate release Bromocriptine Mesylate tablets containing pharmatose DCL 21 as diluent and 5% cross carmellose sodium as super disintegrant can be prepared using direct compression which met the required specifications.

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INTRODUCTION

An immediate release dosage form allows a manufacturer to extend market exclusivity, while offering patients a convenient dosage form or dosage regimen. Immediate Release Tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques.[1,2] Immediate release and fast dispersing drug delivery system may offer a solution to these problems. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance. They are also a tool for expanding markets, extending product life cycles and generating opportunities.[3,4] Bromocriptine Mesylate is rapidly absorbed after oral administration, bioavailability of the drug is 28% of the oral dose absorbed and the plasma protein binding amounts to 96%. It is highly distributed in the liver, stomach and intestine. The drug is extensively metabolised in the liver. The fate of Bromocriptine Mesylate primarily involves with renal excretion of two major metabolites accounting for 6% of the total dose. The elimination of the parent drug from the plasma is biphasic with a terminal half life of 15 hours. Bromocriptine Mesylate stimulates dopamine type-II receptors and antagonises type-I receptors in the hypothalamus and neostratiumof the CNS. It falls under the therapeutic class of anti-parkinsonism drug. Parkinsons disease is a degenerative disorder of the CNS that often impairs the motor skills, speech and other function of the sufferer. It is characterised by muscle rigidity, tremor, slowing of the physical movement i.e Bradykinesia and in extreme cases loss of physical movement i.e akinesia.

As the drug in current research is very potent with a therapeutic dose of as low as 2.5 mg, crystalline in nature, moisture and heat sensitive therefore direct compression method was selected for the formulation of immediate release tablets as it is done generally for the crystalline drugs with good physical properties required for the formulation of good tablets which satisfied all the critical process parameters. The main advantage of this technique is that it saves time as well as it is an economical method as compared to the other methods of compression.

Superdisintegrants are first choice of excipients which are extensively used for the formulation development of the immediate release tablets as they effectively result into the immediate disintegration, release and absorption of the drug after administration into the body. Cross carmellose sodium which is commonly known as Ac-di-sol is cross linked carboxy methyl cellulose sodium and sodium starch glycolate is a carboxy methyl starch and both of which are stable through hygroscopic material.

MATERIALS AND METHODS

Materials

Bromocriptine Mesylate was obtained from Alkem Research Lab. Pharmatose DCL 21, Sodium starch glycolate, and Cross carmellose sodium from DMV International Fonterra. Aerosil-200, Starch, Microcrstalline cellulose and Magnessium stearate were obtained from Signet Chemicals.

Preparation of immediate release Bromocriptine Mesylate tablets [5,6,7]

All the ingredients were accurately weighed as per formula F1 to F5 which is shown in Table 1 and were dispensed in clean polythene covers. Bromocriptine Mesylate and disintegrants were sifted through sieve no-30. Pharmatose DCL 21 and Micro crystalline cellulose were passed through sieve no-20 while Magnesium stearate and Aerosil-200 were passed through sieve no-40. The drug was mixed with the excipients by geometric mixing technique so as to form the blend for compression. Finally the blend was directly compressed into tablets using concave face round tooling on a Rimek- rotary tablet machine.

Evaluation of immediate release Bromocriptine Mesylate tablets

1. **Uniformity of weight [8]**

The weights were determined to within ±1mg by using Mettler Tolledo balance (Model AB- 204 S). Weight control is based on a sample of 20 tablets. Determinations were made in triplicate.

2. **Tablet hardness [9]**

The hardness of the tablets was determined by diametral compression using tablet hardness tester (Model no 1101, Dr. Schleuniger). A tablet hardness of about 50-60 N is considered adequate for mechanical stability. Determinations were made in triplicate.

3. **Tablet friability [10,11]**

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W0) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was

calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$(W \text{ initial}) - (W \text{ final}) / (W \text{ initial}) \times 100$$

Where, W initial = Initial weight of tablets .
W final = Final weight of tablets.

4. In-vitro disintegration test [12, 13, 14]

The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with non palable mass remaining in the apparatus was measured in seconds.

5. Assay

The test for assay was carried out by dissolving 0.50 gm in 80 ml mixture of 10 volume of anhydrous acetic acid and 70 volume of acetic anhydride and was titrated with 0.1 M perchloric acid. End point was determined potentiometrically.

6. In-vitro dissolution study [15, 16, 17,18]

The release rate of Bromocriptine from immediate release tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus I (basket method). The dissolution test was performed using 500 ml of 0.1 N Hcl, at 37± 0.50C and 120 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus 5, 15, 30, 45, and 60 minutes. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.45 µ membrane filter. Absorbance of these solutions was measured at 305 nm using a Shimadzu UV-1601 UV-Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

RESULTS AND DISCUSSION

In the present study, various formulations of immediate release Bromocriptine Mesylate tablets were prepared by direct compression. The use of super disintegrants for preparation of immediate release tablets is highly effective and commercially feasible. These super disintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Flow properties of the powder, resistance to particle movement can be judged from the angle of repose. Based on angle of repose it was observed that formulation batch F5 showed excellent flow properties than the rest of formulations. Carr's index of the optimized blends falls in the range of 10.54 to 18.08 % and Hausner's ratio values were in the range of 1.11 to 1.22. Based on the results obtained we can conclude that formulation batch F5 showed excellent flow.
Hardness and friability: The hardness of the tablet formulations was found to be in the range of 60 to 165 N (Tables-2). The friability values were found to be in the range of 0.113 to 0.326 %.(Tables-2).

Disintegration time: The disintegration time of formulation batch F5 was 1.50 minutes which is the best result obtained than the rest of the formulation.

Uniformity of weight: All the prepared tablets of Bromocriptine 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%.

Assay: The assay was performed on two formulation batches F4 & F5, the results of which are shown in Table-2.

In vitro dissolution study: In vitro dissolution studies were performed in 0.1N HCL on the above promising formulation. The results are shown in Table-3.

Table 1: Comparative data of various prototype formulations

F. No.	Drug(BM) mg/tab	Pharmatose DCL 21 mg/tab	Starch mg/tab	SSG mg/tab	CCS mg/tab	Aerosil-200 mg/tab	Mag. Stearate mg/tab	Total wt. in mg
F 1	2.87	195.13	-	-	-	1	1	200
F 2	2.87	185.13	10	-	-	1	1	200
F 3	2.87	175.13	20	-	-	1	1	200
F 4	2.87	185.13	-	10	-	1	1	200
F 5	2.87	185.13	-	-	10	1	1	200

Table 2: Evaluation of tablets

F. No.	Hardness (N)	Thickness (mm)	% Friability	Weight variation (mg)	Disintegration time (mins)	% Assay
F 1	165	2.48	0.113	196-204	12.00	-
F 2	160	2.50	0.119	196-204	8.40	-
F 3	140	2.54	0.147	196-204	6.36	-
F 4	75	2.88	0.276	196-204	3.20	101.20
F 5	60	2.96	0.326	196-204	1.50	100.37

Table 3: Dissolution profiles of tablets

F. No.	5 mins	15 mins	30 mins	45 mins	60 mins
F 1	41.7 %	61.1 %	70.2 %	77.6 %	87.8 %
F 2	41.8 %	62.3 %	70.7 %	79.7 %	89.2 %
F 3	43.2 %	62.7 %	71.4 %	80.9 %	95.2 %
F 4	45.6 %	64.0 %	73.2 %	83.7 %	97.6 %
F 5	50.7 %	64.2 %	76.5 %	85.5 %	99.8 %

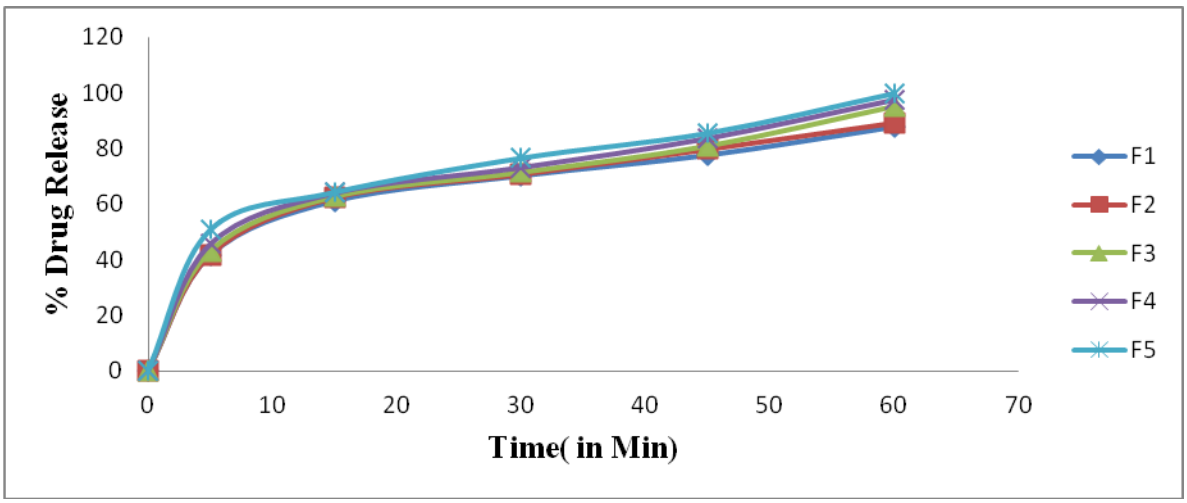

Figure 1: Percentage of drug release

CONCLUSION

In the present study, the formulation and evaluation of Bromocriptine Mesylate tablets have been developed. Bromocriptine immediate release tablets were successfully prepared (Formulation, F5) with pharmatose DCL 21 as diluent for direct compression and cross carmellose sodium as effective super disintegrant by direct compression method, which produced immediate release with good physical characteristics, predictable and reproducible drug release profile. Results of the present study confirmed the better drug release profile which by meeting all the specifications.

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