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Journal of Chemical and Pharmaceutical Research

ISSN No: 0975-7384
CODEN(USA): JCPRC5

J. Chem. Pharm. Res., 2010, 2(5):307-312

Design, development and characterization of orally disintegrating tablet of prochlorperazine maleate

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ABSTRACT

In Present work, orally disintegrating tablets of Prochlorperazine maleate were design with a view to enhance Patient compliance by direct compression method. In this method sodium starch glycolate, crospovidone and croscarmellose sodium use as superdisintegrant (2-8% w/w) along with microcrystalline cellulose (pH 102), directly compressible lactose (DCL-11) and sodium Saccharin to enhance mouth feel. The prepared batches of tablet were evaluated for hardness, friability, content uniformity, wetting time, water absorption ratio and in vitro dispersion time. Based on in vitro dispersion time (Approximately 21 to 30 s), two promising formulation were tested for in vitro drug release pattern in pH 6.8 phosphate buffer. Among the two promising formulation, the formulation containing 8% sodium starch glycolate and 8% crospovidone emerged as the overall best formulation ($t_{50\%}$ 8-10 min) based on drug release characteristic in pH 6.8 phosphate buffer compared to commercial conventional tablet formulation ($t_{50\%}$ 22-25 min). Short-term stability studies on the promising formulations indicate that there are no significant changes in drug content and in vitro dispersion time.

Key words: orally disintegrating tablets, Prochlorperazine maleate, sodium starch glycolate, crospovidone, croscarmellose sodium.

INTRODUCTION

The oral route remains the preferred mode of administration for many type of medication due to its simplicity, versatility, convenience and patient acceptability. But, the most evident drawback of the commonly used oral dosage forms like tablet and capsule are as follow:

- It is not beneficial for drug that under go first pass effect.
- It is not suitable for drug that shows gastric degradation.
- The drug whose half life is short is not suitable for the oral dosage form.
- Many patients find difficult to swallow tablets and result in non-compliance.

To overcome these limitations, recent advance in novel drug delivery system aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is orally disintegrating tablets (ODT). ODTs are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Orally disintegrating tablet disintegrate in mouth within seconds and rapidly come to the contact with its dissolution medium which rapidly dissolve and shows faster action. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing. Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action. It provides good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients. It is easy to administer for pediatric, geriatric, and institutionalized patients (especially for mentally retarded and psychiatric patients). [1-3]

Prochlorperazine maleate (PCZM) is a phenothiazine antipsychotic and widely use in prevention and treatment of nausea, vomiting including that associated with migraine or drug induced emesis. The concept of formulating orally disintegrating tablets of prochlorperazine maleate offer a suitable and practical approach in serving desired objective of faster disintegration and dissolution characteristic with increase bioavailability. Therefore, in order to get better patient compliance in the treatment, it is necessary to design a new drug delivery system of the drug PCZM i.e. orally disintegrating tablets. The focus of the present investigation is to minimize disintegration time and improved drug release with faster onset of action. [4-6]

EXPERIMENTAL SECTION

Prochlorperazine maleate was a gift sample from kiwi Labs. LTD. Por GIDC, Vadodara. sodium starch glycolate (SSG), crospovidone (CP), croscarmellose (CM), microcrystalline cellulose (pH 102), and other excipients obtained from Kap Tab Pharmaceutical Pvt. Ltd. Vadodara.

Preparation of Orally Disintegrating Tablet of PCZM

Orally disintegrating tablets were prepared by direct compression method according to formula given in table 1. All the ingredients were passing through 40# mesh size except Mg. Stearate. Mg Stearate was passing through 60# mesh size. Drug MCC and lactose were mix by taking small portion of each and blending it to get a uniform mixture and kept a side. Then the other ingredients were weighed and mixed in geometrical order and tablets were compressed using 7 mm round flat punches to get tablets of 100 mg weight on 12 station rotator machine. A batch of 100 tablets was prepared for all the designed formulation. [9]

Table: 1 Formula of different batches of orally disintegrating tablet

Formulation	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9
Prochlorperazine maleate	5	5	5	5	5	5	5	5	5	5
Directly compressible Lactose	62	60	56	54	60	56	54	60	56	54
MCC (pH 102)	30	30	30	30	30	30	30	30	30	30
Sodium starch glycolate	-	2	4	8	-	-	-	-	-	-
Croscarmellose	-	-	-	-	2	4	8	-	-	-
Crospovidone	-	-	-	-	-	-	-	2	4	8
Sod. Saccharine	2	2	2	2	2	2	2	2	2	2
Mg. Stearate	1	1	1	1	1	1	1	1	1	1
Total	100	100	100	100	100	100	100	100	100	100

Evaluation of tablet

All the tablets were evaluated for the following parameters**:**

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight of these selected tablets was calculated.

Hardness

Tablet crushing strength, which is the force required to break the tablet, was measured with a Pfizer tablet hardness tester. The hardness (crushing strength) of three tablets per batch was determined and mean taken.

Friability

Tablet friability8 was measured using a ROCHE friabilator (USP) at 25 rpm for 4 min. The weight of twenty tablets before and after completion of the test was recorded and friability was calculated by the following

Formula:

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} X\ 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ (1)$$

Disintegration time

For measurement of disintegration time, a Petridis (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of Petridis and the time for the tablet to completely disintegrate into fine particles was noted.

Table: 2 Evaluation of Orally Disintegrating Tablet

Evaluation Parameter	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9
Appearance	100 mg, white colored, 6 mm, Flat Faced.									
Weight variation* %	Weight variation was found within IP specification below ± 7.5%									
Hardness* (Kg/Cm^2)	4.29± 0.05	4.33± 0.05	4.25± 0.05	4.33± 0.05	4.33± 0.05	4.31± 0.05	4.33± 0.05	4.33± 0.05	4.33± 0.05	4.31± 0.05
Thickness* (mm)	2.23± 0.05	2.25± 0.05	2.28± 0.03	2.23± 0.08	2.23± 0.06	2.34± 0.03	2.25± 0.05	2.27± 0.05	2.23± 0.07	2.25± 0.04
Friability (%)	0.34	0.33	0.43	0.32	0.35	0.38	0.40	0.22	0.30	0.24
Drug* content (%)	96.22	98.56±	99.43	99.76	96.42	98.11	100.10	99.55	98.58	100.13
Wetting* time (s)	217± 2	44± 2	30± 1	18± 2	58± 1	50± 3	35± 1	50± 2	31 ± 2	24± 2
Water absorption* ratio (%)	55.12± 1.33	62.24± 1.18	77.58± 0.89	83.00± 1.32	64.34± 0.75	69.42± 1.73	75.55± 1.08	60.12± 1.50	74.29± 0.84	81.41± 0.97
In vitro DT* (s)	212± 3	41± 2	26± 1	15± 2	52± 2	45± 1	32± 1	47± 2	28 ± 2	18± 1

**- Average of three determination. F3 and F9 were selected as promising and used in further studies*

Percentage drug content

The drug content was determined using a standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

Wetting time and Water Absorption Ratio

A piece of tissue paper fold twice was placed in a small petridis containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. The water absorption ratio 'R' was calculated using the following equation.

$$R = 100\ X \frac{(Wa - Wb)}{Wa} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ (1)$$

Where,

Wa = Weight of tablet after water absorption.
Wb = weight of tablet before water absorption.

In Vitro Dissolution

Medium: pH 6.8 Phosphate Buffer, $37^{o} \pm 0.5$, 900 ml.
Apparatus: USP Type II
RPM: 50 rpm.
Time interval: 0, 5, 10, 15, 30, 45, 60 min.

Procedure: Three tablets were use in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specified interval of time and analyze for drug content by measuring the absorbance at 254 nm. The volume withdrawal at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of PCZM release was calculated and plotted against time and plotted against time.

RESULT AND DISCUSSION

Orally disintegrating tablets of PCZM were prepared by direct compression method using Sodium starch glycolate, Croscarmellose and Crospovidone as superdisintegrant in different ratio along with microcrystalline cellulose and directly compressible lactose. Sodium Saccharine was used to enhance mouth feel. A total eight formulation and a control formulation (with out superdisintegrant) were designed. As the blends were free flowing tablets obtained were of uniform weight, with acceptable variation as per IP specification i.e., below ± 7.5%. Drug content was found to be in the range to 95 to 101%, which is within acceptable limit. Hardness of tablet was 4.33 Kg/ Cm^2. Friability of below 1% indicates good mechanical resistant of the tablets. Water absorption ratio and wetting time, which are important criteria for understanding capacity of disintegrant to swell in presence of little amount of water were found to be in the range of 55-83% and 21-55 s, respectively. Among all the design formulation two formulation F3 and F9 were found to be promising and displayed an *In Vitro* dispersion time ranging from 15 to 18 s, which facilities their faster dispersion in the mouth.

Table: 3 *In vitro* Dissolution Data

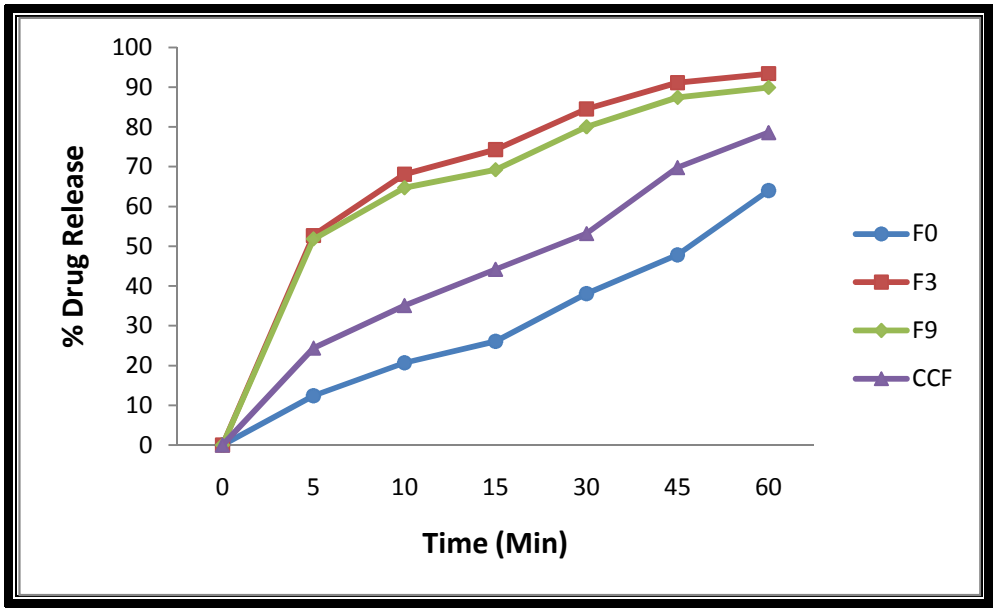
Time	F0	F3	F9	CCF
0	0	0	0	0
5	12.4	52.7	51.8	24.4
10	20.7	68.1	64.7	35.1
15	26.1	74.3	69.2	44.2
30	38.1	84.5	80.0	53.2
45	47.8	91.1	87.4	69.8
60	64.0	93.4	89.9	78.6

F0*: control formulation,* ***CCF****: conventional commercial formulation*

Overall, the formulation F3 containing 8% w/w of SSG was found to be promising and has show an in vitro dispersion time 15 s, wetting time of 18 s and water absorption ratio of 83% when compared to control formulation (F0) which shows 212 s, 217 s and 56% values respectively for the above parameter. The experimental data also shows that the results obtained from SSG are comparable and even slightly better then those of crospovidone.

In vitro dissolution studies on the promising formulation (F3 and F9), the control (F0) and commercial conventional formulation (CCF) were carried out in pH 6.8 phosphate buffers, and various dissolution profiles of F0, F3, F9 and CCF were shown in figure 1. This data revels that overall, the Formulation F3 shows faster drug release when compared to a commercial conventional tablet of PCZM.

Fig: 1 *In vitro* Percent Drug release Vs. time Profile



Acknowledgement
The Author is thankful to kiwi Labs. LTD. Por GIDC, Vadodara, for providing gift sample of prochlorperazine maleate. They are also thankful to Kap Tab Pharmaceutical Pvt. Ltd. Vadodara. They are also wish to their gratefulness to the principal, Department of Pharmacy, Sumandeep Vidyapeeth, vadodara for providing the necessary facility for the study.

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