Int. J. Chem. Sci.: 10(3), 2012, 1521-1528
ISSN 0972-768X
www.sadgurupublications.com

FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF DOMPERIDONE BY USING *PLANTAGO OVATA* MUCILAGE

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ABSTRACT

In the presence study, fast disintegrating tablets of domperidone were prepared to enhance patient compliance by direct compression method. In the presence study, to prepare fast disintegrating tablets of the drug using, *plantago ovata* mucilage and crospovidone were used as superdisintegrants (2.5 to 10 % w/w) along with microcrystalline cellulose (20 to 60 % w/w) and directly compressible mannitol (pearlitol SD 200) to enhance mouth feel. The prepared tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio and *in vitro* dispersion time. Based on *in vitro* dispersion time (approximately 10 s), the two formulations were tested for the *in vitro* drug release, short term stability (at 40^0/75% RH for 3 months) and drug excipient interaction (IR spectroscopy). Among the two promising formulations, the formulations prepared by using 10% w/w of *plantago ovata* mucilage and 60% w/w of MCC as emerged as the overall best formulation ($t_{50\%}$ 2.75 min.) compared to conventional commercial tablets formulation ($t_{50\%}$ 10.20 min). Short-term stability studies on the formulations indicated that there are no significant changes in drug content and *in vitro* dispersion time ($p < 0.05$).

Key words: Domperidone, *Plantago ovata* mucilage, Crospovidone, Fast disintegrating tablets.

INTRODUCTION

Mucilage is most commonly used as adjuvant in the manufacturing of different pharmaceutical dosage forms. They possess a variety of pharmaceutical properties, which include binding, disintegrating, suspending, emulsifying and sustaining properties at different proportion in different pharmaceutical dosage forms[1-4]. Natural mucilages are preferred over semi-synthetic and synthetic materials due to their non-toxic, low cost, free availability, emollient and non-irritating nature[5,6]. Ispaghula mucilage consists of epidermis

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of the dried seeds of *Plantago ovata*. The present work was carried out to study the disintegrant property of *Plantago ovata* mucilage in comparison with crospovidone by formulating fast disintegrating tablets of Domperidone.

Many patients express difficulty in swallowing tablets and hard gelatin capsules, tending to non-compliance and ineffective therapy[7]. Recent advances in novel drug delivery systems (NDDS) 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 fast disintegrating tablets[7-10]. Domperidone is an antidopaminergic drug. Domperidone does not readily cross the blood brain barrier. Domperidone is therefore more advantageous than any other anti-emetic drug. Domperidone is also prescribed for the treatment of gastroparesis, a stomach motility condition. The bioavailability of domperidone is about 90% in intramuscular and 13 to 17% in oral. The low systemic bioavailability of the oral form of domperidone is likely due to first pass hepatic metabolism and gut wall metabolism % and significantly affected by the presence of food. The elimination hale life of domperidone is reported to be 7.5 hours following IV administration of 10 mg.

Materials and methods

Domperidone was obtained as gift sample from Man Pharmaceuticals Ltd., Mehsana. Crospovidone was gift sample from Wockhardt Reserch Centre, Aurangabad. Directly compressible mannitol (Pearlitol SD 200), Microcrystalline cellulose (MCC, PH-101), all were obtained as generous gifts from Strides Arcolabs, Bangalore. All the other chemicals were of analytical grade.

Isolation of mucilage[11]

The seeds of *Plantago ovata* were soaked in distilled water for 48 hours and then boiled for few minutes so that mucilage was completely released into water[6]. The material collected was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate so as to precipitate the mucilage. The separated mucilage was dried (in oven at temperature less than 60^{o}C), powdered, sieved (#80) and stored in a desicator until use.

Preparation of fast disintegrating tablets of domperidone

Fast disintegrating tablets of domperidone were prepared by direct compression method[12] according to the formulae given in Table 1. All the ingredients were passed through #60 mesh separately. The drug and MCC were mixed by taking small portion of both each time and blending it to get a uniform mixture and kept aside. Then the other

ingredients were weighed and mixed in geometrical order and tablets were compressed using 6 mm round flat punches to get tablets of 100 mg weight on a 10-station rotary tablet machine (Clit, Ahmedabad). A batch of 60 tablets was prepared for all the designed formulations.

Table 1: Composition of different batches of Fast disintegrating tablets of Domperidone

Ingredients (mg/tablet)	Formulation Code								
	DC_0	**DCP_1**	**DCP_2**	**DCP_3**	**DCP_4**	**DPM_1**	**DPM_2**	**DPM_3**	**DPM_4**
Domperidone	10	10	10	10	10	10	10	10	10
Cross-povidone	-	2.5	5.0	7.5	10	-	-	-	-
Plantago Ovata mucilage	-	-	-	-	-	2.5	5.0	7.5	10
Microcrystalline cellulose	-	-	20	40	60	-	20	40	60
Aspartame	3	3	3	3	3	3	3	3	3
Sod stearyl fumarate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Banana flavour	1	1	1	1	1	1	1	1	1
Mannitol qs (Pearlitol SD 200)	82	79.5	57	34.5	12	79.5	57	34.5	12

DC_0 = Control formulation without superdisintegrant
DCP = Formulation containing crosspovidone as a superdisintegrant,
DPM = Formulation containing *plantago ovata* mucilage as superdisintegrant

Evaluation of tablets

Twenty tablets were selected at random and weighed individually. The individual weights were compared with the average weight for determination of weight variation[13]. Hardness and friability of the tablets were determined by using Monsanto Hardness Tester and Roche friabilator, respectively. For content uniformity test, ten tablets were weighed and powdered. The domperidone content was determined by measuring the absorbance at 283 nm. The drug content was determined using the standard calibration curve. The mean

percent drug content was calculated as an average of three determinations[14]. For determination of wetting time and water absorption ratio[15], a piece of tissue paper folded twice was placed in a small Petri dish (internal diameter of 5 cm) 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. Water absorption ratio 'R' was calculated using the equation: $R = 100 \times (W_a - W_b)/W_a$, where W_a is weight of tablet after water absorption and W_b is weight of tablet before water absorption. *In vitro* dispersion time was performed by apparatus specified in USP at 50 rpm. Phosphate buffer 3.2, 900 mL was used as disintegration medium, and the temperature of which maintained at 37 ± 2°C and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds[16]. IR spectra of domperidone and its formulations were obtained by KBr pellet method using Perkin-Elmer FTIR series (Model 1615) spectrophotometer in order to rule out drug-carrier interactions.

Evaluation of *in vitro* dissolution studies[10]

In vitro dissolution study was performed by using USP type II Apparatus (Paddle type) [Electrolab (ETC-11L) Tablet Dissolution Tester] at 50 rpm. Phosphate buffer pH 3.2, 900 mL was used as dissolution medium which maintained at 37 ± 0.5°C. Aliquot of dissolution medium (5 mL) was withdrawn at specific time intervals and was filtered. The amount of drug dissolved was determined by UV spectrophotometer (Shimadzu, Japan) by measuring the absorbance of the sample at 283 nm. Three trials for each batch were performed and average percentage drug release with standard deviation was calculated and recorded.

Stability testing

Short-term stability studies on the promising formulations (DCP_4 and DPM_4) were carried out by storing the tablets in an amber coloured rubber stoppered vial at 40°/75% RH over a 3 months period. At an interval of 1 month, the tablets were visually examined for any physical changes, changes in drug content and *in vitro* dispersion time.

RESULTS AND DISCUSSION

Fast disintegrating tablets of domperidone were prepared by direct compression method employing *Plantago ovata* mucilage and crospovidone as super-disintegrants in different ratios along with microcrystalline cellulose. Directly compressible mannitol (Pearlitol SD 200) was used as a diluent to enhance mouth feel.

A total of eight formulations and a control formulation DC_0 (without super-disintegrant) were designed. As the blends were free flowing (angle of repose < 30°, and Carr's index < 15%) tablets obtained were of uniform weight (due to uniform die fill), with acceptable variations as per IP specification i.e., below ± 10%. Drug content was found to be in the range of 95 to 100%, which is within acceptable limits. Hardness of the tablets was found to be about 2.63 Kg/cm^2. Friability below 1% was an indication of good mechanical resistance of the tablets. Among all the designed formulations, two formulations, viz., DPM_4 and DCP_4 were found to be promising and displayed an *in vitro* dispersion time ranging from 10 to 12 s, which facilitates their faster dispersion in the mouth. Overall, the formulation DPM_4 containing 10% w/w of *Plantago ovata* mucilage and 60% w/w of microcrystalline cellulose was found to be promising and has shown an *in vitro* dispersion time of 10 s, wetting time of 11 s and water absorption ratio of 87% when compared to control formulation (D_0) which shows 234 s, 257 s and 50% values, respectively for the above parameters (Table 2). The dissolution profiles depicted in Fig. 1. This data reveals that overall, the formulation DPM_4 has shown more than five-fold faster drug release ($t_{50\%}$ 2.75 min) when compared to the commercial conventional tablet formulations of domperidone ($t_{50\%}$ 10.20 min.). IR spectroscopy studies indicated that the drug is compatable with all the excepients. Short-term stabilities studies of the above formulations presented in Tables 3 and 4 indicated that there are no significant changes in drug content and *in vitro* dispersion time at the end of 3 months period ($p < 0.05$).

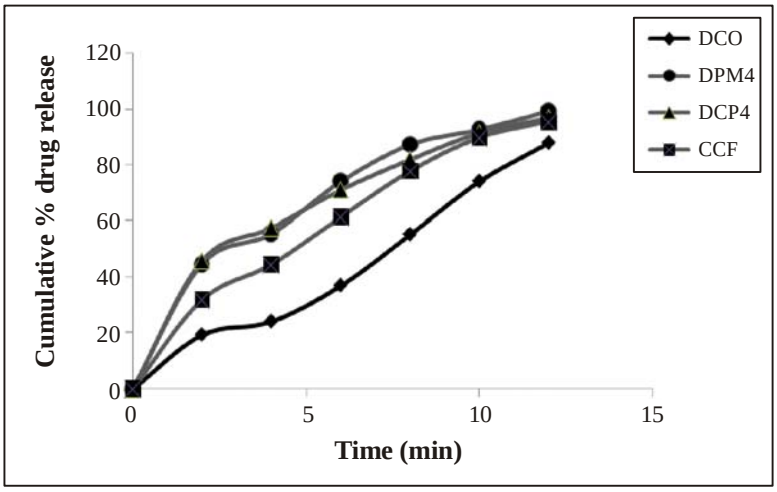

Fig. 1: Plot showing % cumulative drug release of promising domperidone formulations in pH 3.2 Phosphate buffer. DCO (Controlled drug formulations), DPM4 (Formulation containing plantago ovate mucillage), DCP4 (Formulation containing Cross povidone), CCF (Commercial controlled formulation)

Table 2: Evaluation of fast disintegrating tablets

Parameters	Formulation code								
	DC_0	**DCP_1**	**DCP_2**	**DCP_3**	**DCP_4**	**DPM_1**	**DPM_2**	**DPM_3**	**DPM_4**
Hardness (Kg/cm^3) ± S.D	2.6 ± 0.10	2.53 ± 0.15	2.5 ± 0.1	2.63 ± 0.11	2.53 ± 0.11	2.63 ± 0.057	2.66 ± 0.15	2.63 ± 0.15	2.56 ± 0.057
Thickness (mm)	2.9	2.83	2.86	2.93	2.7	2.86	2.8	2.63	2.76
Friability (%)	0.45	0.40	0.48	0.45	0.5	0.46	0.52	0.42	0.48
***In vitro* dispersion time (s) ± S.D**	234.73 ± 2.20	46.97 ± 1.69	40.48 ± 0.95	21.02 ± 0.14	11.02 ± 0.48	39.07 ± 0.8	30.06 ± 0.18	16.29 ± 0.58	10.13 ± 0.34
Wetting time (s) ± SD	235.84 ± 2.93	48.92 ± 1.59	43.03 ± 1.86	23.36 ± 2.08	12.02 ± 0.83	42.69 ± 1.30	32.04 ± 2.45	18.78 ± 1.04	11.68 ± 0.78
Water absorption ration (%) ± S.D	50.63 ± 0.97	57.02 ± 0.14	64.04 ± 0.25	72.86 ± 0.64	86.22 ± 0.24	61.46 ± 1.03	69.09 ± 0.64	77.99 ± 0.13	87.18 ± 0.2
Percent drug content (%) ± S.D	95.41 ± 1.13	96.96 ± 1.93	99.78 ± 0.90	98.6 6 ± 1.86	99.90 ± 0.73	99.78 ± 0.46	100.09 ± 0.9	100.05 ± 0.9	99.28 ± 0.9
Weight Variation (%)	(97-105 mg) with in the IP limits of ±10%								

*Average of three determinations, formulations DCP_4 and DPM_4 were selected as the promising and used in further studies

Table 3: Stability data of DCP_4 formulation at 40^oC/75% RH

Time in days	Physical changes	Percent drug content ± SD*	In vitro dispersion time*
1st day (initial)	-----	99.90 ± 0.73	11.02 ± 0.48
30th day (1 month)	No changes	99.86 ± 0.104	11.13 ± 0.102
60th day (2 month)	No changes	99.73 ± 0.109	11.17 ± 0.041
90th day (3 month)	No changes	99.64 ± 0.090	11.23 ± 0.052

*Average of three determinations, Mean percent drug content on the first day was 99.90 ± 0.73, on day 90 was 99.64 ± 0.090 with a difference between day 90 and the first day being 0.26 ± 0.64

Table 4: Stability data of DPM_4 formulation at $40^oC/75\%$ RH

Time in days	Physical changes	Percent drug content ± SD*	In vitro dispersion time*
1st day (initial)	-----	99.64 ± 0.090	10.13 ± 0.344
30th day (1 month)	No changes	99.33 ± 0.047	10.16 ± 0.032
60th day (2 month)	No changes	99.37 ± 0.041	10.17 ± 0.015
90th day (3 month)	No changes	99.42 ± 0.049	10.20 ± 0.030

*Average of three determinations, Mean percent drug content on the first day was 99.28 ± 0.98, on day 90 was 99.42 ± 0.049 with a difference between day 90 and the first day being 0.22 ± 0.041

ACKNOWLEDGMENT

The authors are thankful to Man Pharmaceutical Ltd., Mehsana for providing gift sample of Domperidone. They also wish to express their gratefulness to the Principal, Dr. Samuel George Institute of Pharmaceutical Sciences, Markapur for providing the necessary facilities for the study.

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Revised : 28.05.2012 *Accepted : 30.05.2012*