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Research Article

PREPARATION AND *IN VITRO* EVALUATION OF MOUTH DISSOLVING TABLETS OF DOMPERIDONE

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ABSTRACT

The aim of this study was to prepare mouth dissolving tablets of Domperidone by using pertinent disintegrants. The tablets were prepared using mannitol and lactose along with two different levels of disintegrant by direct compression method. The superdisintegrants used in this study were Sodium starch glycolate (SSG) and Cross-carmillose sodium (CCS). The tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time (DT) and dissolution study. Using the same excipients, the tablets were prepared, without disintegrants and were evaluated in the similar way. From the results obtained, it can be concluded that the tablet formulation (batch F4) showed Disintegration time of 27±3.0 seconds *in vitro*. Also the hardness, friability and dissolution rate of prepared tablets (batch F4) were found to be acceptable according to standard limits.

Keywords: Mouth dissolving tablets, Domperidon, In vitro evaluation

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. For the past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency, and the production of more cost-effective dosage forms[1].

However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as "melt in mouth" or "mouth dissolve (MD)" or sometimes "dispersible" tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bed-ridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market[2].

Evaluation of Domperidone mouth dissolving tablets

Uniformity of weight

The weights were determined to within ±1mg by using Sartorious balance (Model CP- 224 S). Weight control is based on a sample of 20 tablets. Determinations were made in triplicate.

Tablet thickness

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness

The hardness of the tablets was determined by diametral compression using a dial type hardness tester (Model no 1101, Shivani Scientific Ind). A tablet hardness of about 4-5 kg is considered adequate for mechanical stability. Determinations were made in triplicate.

Domperidone is widely used anti-emetic drug acting by an inhibition of the dopaminergic receptor. Domperidone does not cross blood brain barrier. Domperidone is also effective in gastro paresis, pediatrics gastro esophageal reflux (infant vomiting). Domperidone after oral dosing undergoes extensive gastric and hepatic first pass metabolism resulting in low bioavaibility (15%) which therefore, may not minimize the rate of vomiting[3]. In context of the above principles, a strong need was recognized for the development of mouth dissolving tablets of Domperidone to improve its bioavailability for relief on nausea and vomiting.

MATERIALS AND METHODS

Domperidone was a gift from Mann Pharmaceutical Industries (Mehsana, India). Croscarmellose sodium (CCS) used was analytical reagent (AR) grade procured from Loba Chemie, Mumbai and Sodium Starch Glycolate (SSG) used was procured from Merck Limited, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of mouth dissolving tablets of Domperidone

All the materials were passed through 60 # screens prior to mixing. Domperidone, Croscarmellose sodium (CCS), Sodium Starch Glycolate (SSG), and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a Rimek- rotary tablet machine[4]. The composition of the batches is shown in Table 1.

Tablet friability

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W_0) 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.

$$\% \text{ Friability} = \frac{W_0 - W}{W_0} \times 100$$

Wetting time

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a Petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Table 1: Formulation of Domperidone MDT

Ingredients	Batch codes				
	F1	F2	F3	F4	F5
Domperidone	10	10	10	10	10
Crosscarmellose sodium	80	80	90	90	-
Sodium starch glycolate	30	40	30	40	-
Mannitol	100	100	100	100	100
Lactose	70	60	60	50	180
Talc	5	5	5	5	5
Magnesium stearate	5	5	5	5	5
Total (mg)	300	300	300	300	300

Water absorption ratio (%)

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following Equation.

$$\text{Water absorption ratio (R)} = \frac{W_a - W_b}{W_b} \times 100$$

Where, W_b is the weight of the tablet before water absorption and W_a is the weight of the tablet after water absorption.

***In-vitro* disintegration test**

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 no palable mass remaining in the apparatus was measured in seconds.

***In-vitro* dissolution study**

The release rate of Domperidone from mouth dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl (PH=1.2), at 37± 0.5ºC and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 5, 10, 15, 20, 25 and 30min. 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 284 nm using a Shimadzu UV-1700 UV/Vis spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

RESULTS AND DISCUSSION

The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. The results of tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study as show in Table 2.

Using the same excipients, the tablets were prepared, without these superdisintegrants 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. Prepared mouth-dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Figure 1 show the cumulative percentage of Domperidone released from formulated tablet with different concentration of CCS and SSG.

It is clear that the dissolution of domperidone has improved considerably in formulation F4 as compared to formulation F1, F2, F3 and F5. The tablets of the batch F4 showed good dissolution efficiency and rapid dissolution. The study shows that the dissolution rate of Domperidone can be enhanced to a great extent by direct compression technique with the addition of superdisintegrants, which gives quick relief from emesis.

Table 2: Evaluation of Domperidone MDT

Batch	Weight variation (%)	Thickness (mm)	Hardness n=10 (kg/cm²)	Friability (%)	Wetting time (sec)	Water absorption ratio (%)	Disintegration time (sec)
F1	301±1.45	4.1	2.7±0.13	0.39	41	73.57	35±2.6
F2	300±2.98	4.3	3.2±0.12	0.40	37	78.45	31±3.1
F3	298±1.33	4.2	3.6±0.17	0.37	32	82.12	33±2.4
F4	299±3.09	4.5	3.7±0.21	0.32	27	91.34	27±3.0
F5	299±2.06	4.1	2.5±0.27	0.31	61	62.99	51±2.0

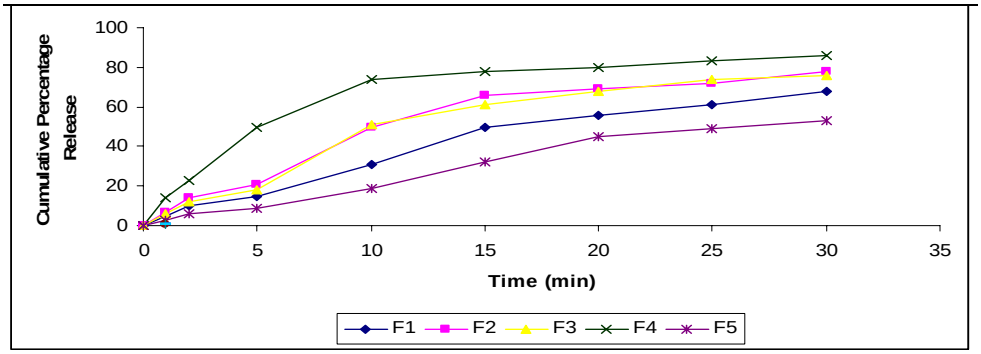

Fig. 1: Drug release profile of Domperidone MDT from various batches

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