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Formulation and Evaluation of Domperidone Fast Dissolving Tablets.

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Abstract: Domperidone, an antiemetic drug, has been used as an add-on treatment in adults and children. As precision of dosing and patient's compliance become important prerequisite for quick relief from emesis, there is a need to develop a formulation for this drug which overcomes problems such as difficulty in swallowing, inconvenience in administration while traveling and better compliance. Hence, the present research work was held to develop a fast dissolving tablet of domperidone, prepared with Avicel PH 102 and Sodium Starch Glycolate by direct compression method. All formulations were evaluated for characteristics such as hardness, friability, disintegration time and Dissolution rate. An effective, pleasant tasting formulation was found to have a good hardness of 3 kg/cm^2, disintegration time of 27$\pm$1 seconds and in vitro drug release of not less than 95% within 30 minutes. The drug release was found to be comparable with the marketed dispersible tablet.
Keywords: Domperidone, SSG, FDT

Introduction

A fast dissolving system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in form of liquid. Recently fast dissolving formulation is popular as NDDS because they are easy to administer and lead to better patient compliance. Pediatric and geriatric patient have difficulty in swallowing the conventional dosage forms. Fast dissolving and fast dispersing drug delivery system may offer a solution to these problems. Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of noncompliance and ineffective therapy.[1] Fast-disintegrating tablets are gaining prominence as new drug-delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing.[2] 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 gastroparesis, paediatric gastroesophageal reflux (infant vomiting). Domperidone after oral dosing undergoes extensive gastric and hepatic first pass metabolism resulting in low bioavaibality (15%) which therefore, may not minimize the rate of vomiting.[3] The formulated tablets will be characterized for various parameters like hardness, friability, disintegration, wetting and in vitro dissolution.

Materials and Methods

Domperidone was a gift from Mann Pharmaceutical Industries (Mehsana, India), and Avicel PH 102 and SSG were gifted from Colorcon Asia Pvt Ltd (Mumbai). All other reagents and chemicals used were of analytical grade.

Preparation of domperidone fast dissolving tablets

All the materials were passed through 80 # screens prior to mixing. Domperidone, Avicel PH 102, 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. The composition of the batches is shown in Table 1.

Evaluation of domperidone fast dissolving tablets

1. Uniformity of weight[4]

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

2. Tablet hardness[5]

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.

3. Tablet friability[5]

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.

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

4. In-vitro disintegration test[6]

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.

5. Wetting time[6]

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.

6. Tablet thickness[5]

Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Varnier calipers. The thickness was measured by placing tablet between two arms of the Varnier calipers.

7. In-vitro dissolution study

The release rate Domperidone from fast 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 ($_P$H=1.2), at 37± 0.5^{0}C 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-1601 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

8. Accelerated stability study of best batch (F4)[7, 8, 9]

In order to determine the change in *in-vitro* release profile on storage, stability study of batch F5 was carried out at 40^0 C in a humidity chamber having 75% RH. Sample were withdrawn after three month interval and evaluated for change in in-vitro drug release pattern, hardness and disintegration time.

Result and Discussion

The use of superdisintegrants for preparation of fast-dissolving tablets is highly effective and commercially feasible. 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 fast-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 Avicel PH 102 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 and marketed preparation F4 tablet 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 1: Formulation of Domperidone FDT

Ingredients	Batch codes				
	F1	**F2**	**F3**	**F4**	**F5**
Domperidone	10	10	10	10	10
Avicel PH 102	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

Table 2: Evaluation of Domperidone FDT.

Batch	Disintegration time (sec)	Wetting time (sec)	Hardness (n=10) kg/cm^2	Friability (%)	Weight variation	Q_{30} (%)
F_1	35	39	3.5 ±0.122	0.36	300±3.09	82.64
F_2	30	32	3.3±0.122	0.39	301±2.64	90
F_3	29	31	3.3±0.365	0.40	299±1.56	91.54
F_4	27	29	3.0±0.211	0.32	299±1.56	96
F_5	47	52	3.9±0.270	0.31	298±1.33	50

Table 3: Comparision of parameters for Batch F4 Initial and after three months

Parameters	Batch F4 (Initial)	Batch F4 (After three months)
Disintegration time	27 sec	30 sec
Wetting time	29 sec	34 sec

Figure 1: Comparision of CPR of formulated batches and marketed preparation

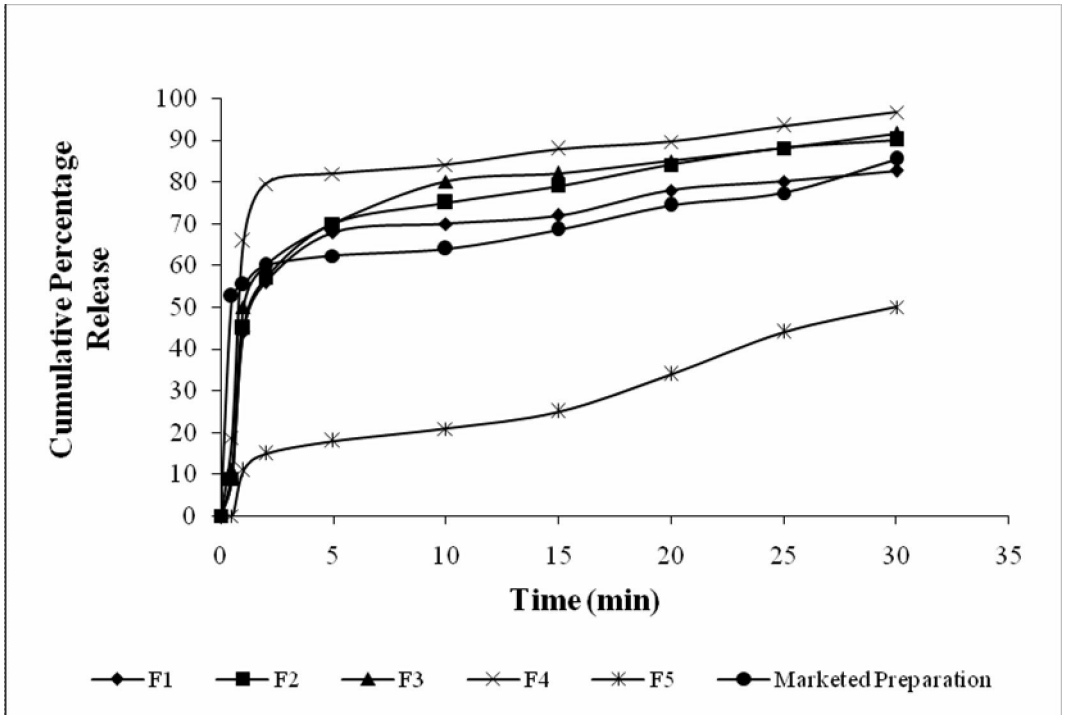
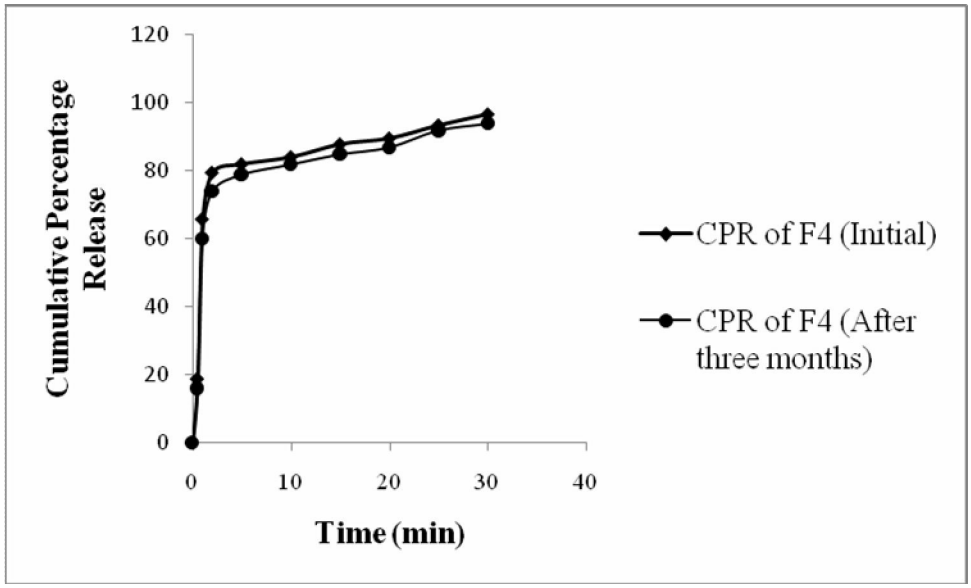


Figure 2: Drug release profile of Domperidone FDT before and after stability study of best batch F4



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