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

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ABSTRACT: The present investigation deals with development of fast dissolving tablets of Domperidone to produce the intended benefits. Domperidone is an antiemetic and a prokinetic medicine. Domperidone is water insoluble drug with problems of variable bioavailability and bio-inequivalence. 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 using *Plantago ovata* mucilage as a natural super disintegrant. The tablets were prepared by Direct Compression using microcrystalline cellulose as a directly compressible vehicle. Tablets were evaluated for their physicochemical properties and *In-vitro* dissolution study. The evaluation studies were performed such as Weight Variation, Thickness, Hardness, Disintegrating Time, Wetting Time, and *In-vitro* Drug release study. The Disintegration time of Fast Dissolving tablets were increased by the addition of concentration of Super disintegrants.

INTRODUCTION: Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. The most popular solid dosage forms are tablets and capsules. Sometimes people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis.

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For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention [1].

Fast disintegrating dosage forms are the drug delivery systems that disintegrate in the patient's oral cavity within less than a minute without the intake of water. Thus, these tablets are easily swallowed and have high patient compliance [2]. The fast disintegrating tablets are synonymous with fast dissolving tablets; melt in mouth tablets, rapimelts, Porous tablets, Orodispersible, quick dissolving or rapidly disintegrating tablets.

Domperidone is selected as the model drug which comes under anti-emetic class. Domperidone is optimized suits for preparation of FDT as it has longer half-life and in case of vomiting it required

quick release. This drug is effective in all the categories i.e. pediatrics, adults, geriatrics. Domperidone blocks the action of dopamine. It has strong affinities for the D_2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone (CTZ) located just outside the blood brain barrier, which regulates nausea and vomiting [3].

MATERIALS AND METHODS:

Materials: Domperidone was obtained as a gift sample from Sherrington's Formulations, Hyderabad. Mannitol, Lactose, Talc, Magnesium stearate were also obtained from Sherrington's Formulations, Hyderabad. All the chemicals and solvents were of analytical grade.

Methods:

1. **Extraction of *Plantago ovata* mucilage:** 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. Then squeeze the mucilage through muslin cloth for filtering and separate out marc. Then equal volume of acetone was added to the filtrate so as to precipitate the mucilage. The separated mucilage was dried in oven at temperature < 60^o c, powdered, sieved and stored in desiccator until use.

2. **Preparation of Domperidone Fast Dissolving Tablets:** Different fast dissolving tablet formulations were prepared by direct compression method. All the materials were passed through 80 # screens prior to mixing. Domperidone, *Plantago ovata* mucilage, lactose, Mannitol, talc and magnesium stearate 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**.

TABLE 1: FORMULA FOR DOMPERIDONE FAST DISSOLVING TABLETS

Ingredients (mg)	F1 (2.5%)	F2 (5%)	F3 (7.5%)	F4 (10%)	F5 (12.5%)
Domperidone	10	10	10	10	10
Plantago ovata mucilage	5	15	20	20	25
Mannitol	100	100	100	100	100
Lactose	75	70	65	60	55
Talc	5	5	5	5	5
Mg. stearate	5	5	5	5	5

Evaluation of Domperidone Fast Dissolving Tablets:

Pre-Compression Parameters: Angle of repose, Bulk density and Tap density, Powder Compressibility (Carr's compressibility index) and Hausner's ratio were determined. The results were shown in **Table 2.**

TABLE 2: PRE-COMPRESSION PARAMETERS OF DOMPERIDONE POWDER BLEND

Formulation code	Angle of repose (Θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	19.02	0.65	0.76	14	1.16
F2	19.93	0.64	0.79	18	1.23
F3	19.52	0.64	0.74	13	1.16
F4	18.92	0.63	0.77	18	1.22
F5	18.26	0.63	0.71	11	1.13

Post Compression Parameters:

1. **Uniformity of weight:** Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of the tablet was determined from the collective weight.

TABLE 3: STANDARD PERCENTAGE DEVIATION IN WEIGHT

Average weight of tablets (mg)	Maximum allowable percentage difference
130 or less	10
130-324	7.5
More than 324	5

2. **Content uniformity:** Ten tablets were taken and amount of drug present in each tablet was determined as follows: Tablet was crushed in mortar and transferred to 100 ml flask. The powder was dissolved in pH 3.2.The sample was mixed by using Remi mixer for 5 minutes, after which it was filtered through Whatman filter paper. The filtered solutions after appropriate dilution (1 to 10 ml) with 0.1 N HCl were analyzed by validated UV spectrophotometric method at λ_{max} 284 nm [4].

3. **Hardness:** The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. It is now designated as either the Monsanto or Stokes hardness tester. The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10kg; however, hypodermic and chewable tablets are usually much softer (3 kg) and some sustained release tablets are much harder (10-20 kg) [5].

4. **Friability (F):** Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25rpm and dropping a tablet at l height of 6 inches in each revolution. Preweighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de-dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.[5]

$$F = \frac{W_{initial} - W_{final}}{W_{final}} X\ 100$$

% Friability of tablets less than 1% is considered acceptable. Thus, it is necessary that this parameter should be evaluated and the results are within bound limits (0.1-0.9%).

5. **Tablet thickness:** Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Vernier callipers. The thickness was measured by placing tablet between two arms of the Vernier callipers [1].

TABLE 4: RESULT OF EVALUATION PARAMETERS OF DOMPERIDONE FAST DISSOLVING TABLETS

Formulation code	Weight variation	Content uniformity (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)
F1	pass	98.91	3.9	0.32	4.3
F2	pass	98.28	3.5	0.36	4.5
F3	pass	98.86	3.3	0.39	4.2
F4	pass	99.28	3.4	0.40	4.1
F5	pass	99.85	3.0	0.31	4.1

6. ***In-vitro* Disintegration test**: The disintegration time was measured using disintegration test apparatus. One tablet was placed in each tube of the basket. The basket with the bottom surface made of a stainless steel screen (mesh no. 10) was immersed in water bath at 37 ± 2^0C. The time required for complete disintegration of the tablet in each tube was determined using a stop watch. To be complied with the Pharmacopoeial standards, dispersible tablets must disintegrate within 3 min when examined by the disintegration test for tablets [1].

7. **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 [6].

8. ***In vitro* dispersion time:** Tablet was added to 10 ml of 0.1N HCl at 37± 0.5°C. Time required for complete dispersion of tablet was measured [7].

9. ***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 0.45µ 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 drug release was calculated using an equation obtained from a standard curve. [6]

TABLE 5: DISINTEGRATION TIME, WETTING TIME, IN VITRO DISPERSION TIME OF DOMPERIDONE FAST DISSOLVING TABLETS

Formulation code	Disintegration time (sec)	Wetting time (sec)	In vitro dispersion time (sec)
F1	47	43	57
F2	45	41	53
F3	35	32	42
F4	30	29	39
F5	28	22	32

TABLE 6: DRUG RELEASE PROFILE OF DOMPERIDONE FAST DISSOLVING TABLETS

Time (mins)	Cumulative percentage of Domperidone release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
3	15.37	16.51	21.47	47.02	47.93
6	23.96	25.32	28.03	56.95	72.35
9	47.25	48.83	52.68	73.93	86.37
12	72.12	73.93	87.95	93.37	100
15	85.52	87.50	98.57	100	-
18	100	100	100	-	-

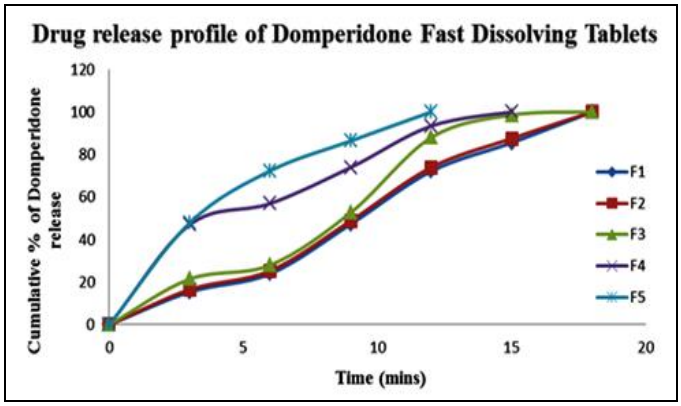

FIG. 1: DRUG RELEASE STUDY OF DOMPERIDONE FAST DISSOLVING TABLETS OF DIFFERENT BATCHES IN pH 6.8 PHOSPHATE BUFFER

RESULTS AND DISCUSSION: The present study was undertaken with an aim to formulate and evaluate Fast Dissolving tablets of Domperidone using direct compression method with the addition of Plantago ovata mucilage as a natural super-disintegranting agent. Tablets each containing 10 mg of domperidone were prepared by employing different proportions of super-disintegrant at five different concentrations of 2.5%, 5%, 7.5%, 10% and 12.5%. The two most important attributes for the direct compression formula are good flow and good compressibility.

The values obtained for bulk density and tapped density does not affect the compression of tablets. The angle of repose gives information about the flow characteristics of powder mixture. The angle of repose < 30^o indicates free flowing material and > 40^o with poor flow properties.

Values of angle of repose were found in the range of 18.26^o to 19.93^o showing that the blend of powder was free flowing can be used for direct compression. The value for Carr's index was in between 10-15% indicating that all the batches of powder blends were having good compressibility. Thickness was observed between 4.1-4.5 mm, hardness of the tablet was in the range of 3.0-3.9 kg/sq cm, and weight loss in the friability was less than 1% in all the cases.

Among all the formulations of domperidone F5 (12.5%) was found to have less disintegration time, wetting time, in vitro dispersion time i.e. 28 sec, 22 sec and 32 sec respectively and this formulation shows 100% drug release at 12 min and the remaining formulations like F1, F2, F3 and F4 were shown 100% drug release at 18 min, 18 min, 15 min, 18 min respectively.

CONCLUSION: Domperidone requires quick action for relieving emesis so it is suitable for fast dissolving tablet. From the study results reveal that F5 (12.5%) exhibits faster disintegration i.e. 28 sec and faster dissolution i.e. for 12 min compared to other formulations, since it was found to be better formulation than F1, F2, F3 and F4.

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