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Formulation and characterization of fast dissolving tablet of domperidone

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ABSTRACT

Fast dissolving drug delivery system (FDDDS) is suited for the drugs which undergo high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to mouth plasma peak levels, which in turn minimize adverse/side effects. Some drugs are absorbed well from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. The sublingual and buccal delivery of a drug via oral tablet has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.

Keywords: FDDDS, Fast dissolving tablet, Bioavailability

INTRODUCTION

Although the incredible advancement in the drug delivery system, oral route is the most preferred route of administration and tablet and capsules are the most preferred dosage form [1-3] but now they experienced several limitations like chocking and swelling discomforts in the geriatric and paediatric patients [4-5]. Among the plethora of avenues explored oral strips gain more attention as it emerging new platform for geriatric and paediatric patients [6-8].Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva. Fast dissolving tablets are useful in patients, like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules.[9] Fast dissolving drug delivery system (FDDS) was introduced in late 1970 as the alternative to conventional tablet, capsule and syrups especially for the geriatric and paediatric patients suffering from the dysphasia problem [10]. Fast dissolving tablets are the solid dosage form which disintegrates rapidly in the oral cavity without the need of water [11-12]. Some problems are associated with the OFDF like they are sometime difficult to carry, storing and handling (friability and fragility), these are prepared using the expensive lyophilisation method [13-14]. To overcome these problems oral films were developed, which are very popular now a days. The concept of oral film was come from confectionary industry [15-16]. Oral films are the recent ultra thin novel formulation of postage stamp size which contains active pharmaceutical ingredients and excipients. Domperidone is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool

in the study of dopaminergic mechanisms.Domperidone acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of Domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. Antiemetic: The antiemetic properties of Domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which among others regulates nausea and vomiting.

MATERIALS AND METHODS

Domperidone, Sodium starch glycolate, Corn starch, Sodium CMC, Crosspovidone, Mg stereate, Mannitol, Polyvinyl alcohol, Glycerin, DMSO, Electronic weighing machine, UV-VIS spectrophotometer (SHIMADZU), Friability test apparatus EF-2, Dissolution apparatus, Disintegration apparatus, Hardness tester (Pfizer type tester).

Each tablet containing 10 mg Domperidone were prepared as per composition given in Table no 3. The drug and excipients passed through sieve no '20' to ensure the better mixing. Mannitol, Crosspovidone, SSG and other excipients were used in different ratio. The powder was compressed by Direct compression machine. 50 tablets were prepared for each batch and the weight of each tablet was 350 mg.

Table no 1: Composition of fast dissolving tablet of Domperidone:

INGREDIENTS (Mg/tablet)	FT_1	FT_2	FT_3	FT_4	FT_5	FT_6
Domperidone	10.0 mg	10.0 mg	10.0 mg	10.0 mg	10.0 mg	10.0 mg
Mannitol	164.50 mg	164.50 mg	197.75 mg	197.75 mg	231.0 mg	231.0 mg
CMC	17.50 mg	17.50 mg	35.0 mg	35.0 mg	52.50 mg	52.50 mg
Crosspovidone	3.50 mg	5.50 mg	7.50 mg	9.50 mg	11.50 mg	13.50 mg
Mg stereate	3.50 mg	3.50 mg	3.50 mg	3.50 mg	3.50 mg	3.50 mg
Corn starch	10.50 mg	10.50 mg	10.50 mg	10.50 mg	10.50 mg	10.50 mg
Talc	28.0 mg	28.0 mg	28.0 mg	28.0 mg	28.0 mg	28.0 mg

CHARACTERIZATION

PRE-COMPRESSION PARAMETERS OF MOUTH DISSOLVING TABLET:

Bulk density-

It was defined as the ratio of total mass of powder to the bulk volume of powder. It was determined by pouring preseived (20 mesh) bulk drug in a graduated cylinder via a large funnel and measured the volume. Bulk density was calculated by the formula.

Bulk density = Weight of powder / Bulk volume

Tapped density-

It was defined as the ratio of total mass of powder to the tapped volume of the powder. Weighed 1 gm of drug which was passed through 20 mesh sieve, was transferred in 50 ml graduated cylinder. The cylinder was tapped several times primarily and the tapped volume (V1) was measured to the adjoining graduated units, the tapping was repeated an extra several times and the tapped volume (V2), was measured to the adjacent graduated units. The tapped bulk density in gm/ml was calculated by the following formula.

Tapped density = Weight of powder / Tapped volume

Angle of repose:

It was related to the flow property. The friction force can be calculated by this method. It was defined as the maximum angle made between the surface of pile of powder and the horizontal plane.

$\tan \theta = h/r$

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was calculated by measuring the height at the radius of heap of the powder form.

Table no 2: Effect of Angle of repose (ϕ) on flow property

S. No.	Angle of repose	Type of slope
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

Carr's Index or Compressibility-
It was related with the flow property. The Carr's index or Compressibility was calculated by the formula.

Carr's index (percentage) = [(TD – BD) × 100] / TD

Table no 3: Effect of Carr's index on flow property

S. No.	Carr's index or compressibility (%)	Type of Flow
1	5-12	Excellent
2	12-16	Good
3	18-21	Fair passable
4	23-35	Poor
5	33-38	Very poor
6	<40	Very very poor

Hausner's ratio:
It was defined as the indirect index of ease of powder flow. It is measured by the formula

Hausner's Ratio = TD / BD

Table no 4: Hausner's ratio

Hausner's ratio	Properties
0 – 1.2	Free flow
1.2 – 1.6	Cohesive powder

Evaluation of Mouth dissolving tablet
Weight variation:
The cause of weight variation can be divided into granules and mechanical problem. If the granule size is large, the dies will not be uniformly filled. Similarly mechanical problem can be traced of lower punches of non-uniform length[16].

Method Uncoated tablets complies this test. The average weight was determined by weighing 20 tablets. Not more than 2 tablets deviate from the average weight by a percentage greater than that given in Table no 16 and no tablet deviate by more than double that percentage. Weight variation tolerance for uncoated tablet is given in Table no 9.

Table no:5 Weight variation specification as per IP

Average wt. of Tablet	% Deviation
80mg or less	±10
More than 80mg but less than 250 mg	±7.5
250mg or more	±5

Tablet Hardness:
The strength of tablet was expressed as tensile strength (Kg/cm2). The tablet crushing load, which was the force required to break a tablet into halves by compression .It was measured using a tablet hardness tester (Pfizer Hardness Tester) [16].

Friability testing:
The friability were determined using Roche Friabilator. It was expressed in percentage (%). Ten tablets were initially weighted ($W_{Initial}$) and transferred into Friabilator. The Friabilator was operator at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weight again (W_{final}). The % friability was then calculated by,

$F=100\ (W_{Initial} - W_{Final})/\ W_{Initial}$

Wetting time:
A piece of tissue paper folded twice and placed in a small petridish containing 10 ml of water. A tablet was placed on the paper and the time for complete wetting was measured.

Water absorption ratio:
A piece of tissue paper folded twice and placed in a small petridish containing 10 ml of water. A tablet was placed on the paper and the time for complete wetting was measured. The wetted tablet was again weighted. Water absorption ratio, R, was calculated using the formula;

$R=100\ (W_{after} - W_{before})\ /\ W_{before}$

In vitro Disintegration studies:
The disintegration time was performed using USP disintegration test apparatus with 6.8 phosphate buffer solution at 37 $\pm 0.5^0$C. Disintegration time was recorded when all the fragments of the disintegrated tablet (6 tablet) passed through the screen of the basket. The time and mean value were reported.

Drug content:
For the drug content 10 tablets were powdered and the blend was equivalent to 100 mg of Domperidone was weighted and dissolved in 100 ml of pH 6.8 phosphate buffer solution, stirred for 15 minutes and filtered. 1 ml of filtrate was diluted upto 100 ml with 6.8 pH phosphate buffer. Absorbance of this solution was measured at 287 nm using 6.8 pH phosphate buffer as blank and content of drug was estimated.

In vitro Dissolution studies:
It was carried out in 100 ml of pH 6.8 phosphate buffer in dissolution apparatus at 50 rpm. A measured 5 ml amount of dissolution medium was withdrawn at regular interval and diluted up to 10 ml with 6.8 PBS. An equal volume of phosphate buffer was added to maintain the sink condition. Absorbance was measured at 287 nm [17].

RESULT AND DISCUSSION

PREFORMULATION STUDIES:
Drug Identification-

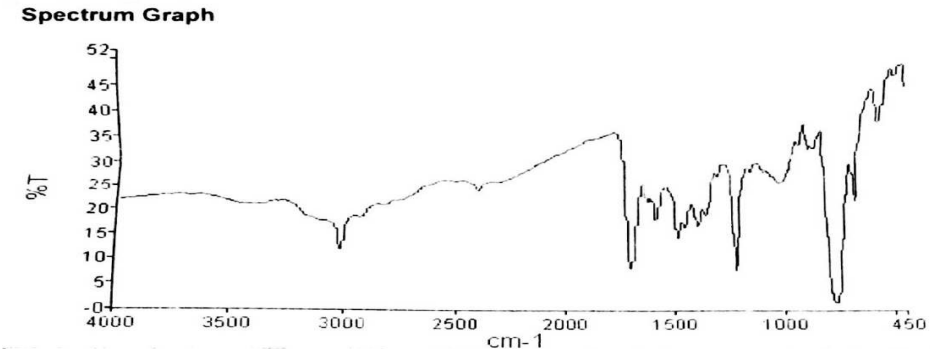

Fig no 1: FT IR spectra of Domperidone

COMPATIBILITY STUDY-
The compatibility studies were performed using IR spectrophotometer.

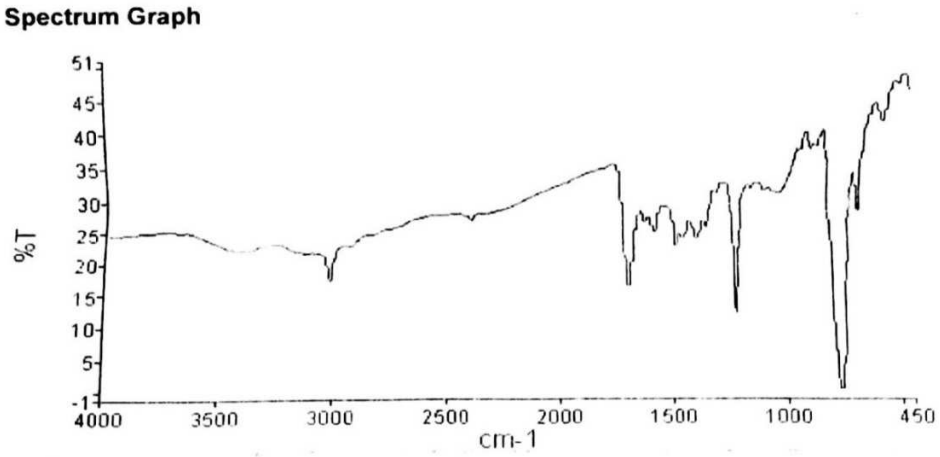

Fig no 2: FT IR spectra of Domperidone + Crosspovidone

All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

CHARACTERIZATION OF PRE-COMPRESSION PARAMETERS OF MOUTH DISSOLVING TABLET:
Bulk density: The bulk density was shown in Table no 6. The bulk density ranged from (0.299 – 0.431) which indicated the good properties of powder blend.

Tapped density: The tapped density was shown in Table no 6 ranged from (0.32– 0.50). The results of tapped density indicated good flow properties of powder blend.

Angle of repose: The values obtained for angle of repose for all (FT_1- FT_2) batches was shown in Table no 6. The values were found to be in range from 21.9 – 32.6. This indicated good flow properties of blend.

Carr's Index: The values obtained for Carr's index for all batches was shown in Table no 6. Compressibility value ranged from 2.23 – 30.43 indicated good flow properties of batches FT_2 ,$FT_3$and FT_5 and passable flow properties of batches FT_1 and FT_6.
Hausner's ratio: The values obtained from for Hausner's ratio for all batches was shown in Table no 6, ranged from 1.02 – 1.30 indicated that all batches having good flow properties.

Table no 6: Pre-compression evaluation parameters for Mouth dissolving tablet

Formulation	Bulk density (gm/cm^3)	Tappeddensity (gm/cm^3)	Angle of Repose (θ)	Carr's index (%)	Hausner's Ratio (%)
FT_1	0.299	0.39	26.8	30.43	1.30
FT_2	0.313	0.32	28.3	2.23	1.02
FT_3	0.398	0.41	21.9	3.83	1.03
FT_4	0.401	0.47	30.2	17.20	1.17
FT_5	0.431	0.50	32.6	16.00	1.16
FT_6	0.367	0.39	24.9	6.26	1.06

CHARACTERIZATIONOF POST COMPRESSION STUDIES OF DOMPERIDONE MOUTH DISSOLVING TABLET
Shape of the tablet
Microscopic examination of all batches of formulation showed circular shape without any cracks.

Hardness test
The measured hardness of tablets of each batch was shown in Table no 7 and the range between 2.8 kg/cm^2 to 4.0 kg/cm^2. The hardness was increased with the compression force. This ensures good handling characteristics of all batches.

Friability test:
The values of friability test were shown in Table no 7. The friability range was between 0.60 % to 0.94 %.The friability values was not more than 1% in all the formulation which ensuring that the tablets were mechanically stable.

Wetting time:
The wetting time of the tablets was given in Table no 7. The wetting time obtained from the direct compression method was in range of 24 – 32 sec. These result shows that the disintegration time was good.

Water absorption ratio:
The water absorption ration was given in Table no 7. The water absorption ration from the direct compression method was between 9.1 – 12.3 %. This method shows that the water absorption ratio was within limit.

Weight variation:
The percentage weight variation for all formulation was within Pharmacopoeia limits. The limit was ±5%. All the formulations passed weight variation test as per I.P limits. The weights of all the tablets were found to be uniform.

Disintegration time:
The in-vitro disintegration time of the tablet was given in the Table no-7. The in-vitro disintegration time obtained from direct compression method was between 33 – 38sec. The formulation showed that the disintegration time was within the limit particular in Pharmacopoeia.

Drug content:
The percentage of drug content was found to be in range of 88.3 – 98.4 of Domperidone, which was within acceptable limits. Table no 7 showed the results of drug content uniformity in each batch.

In-vitro drug release:
The in-vitro dissolution time was 25 minutes in which 98.5 % drug was released for formulation F_5. Therefore formulation no F_5 showed better in-vitro drug release within 25 minutes.

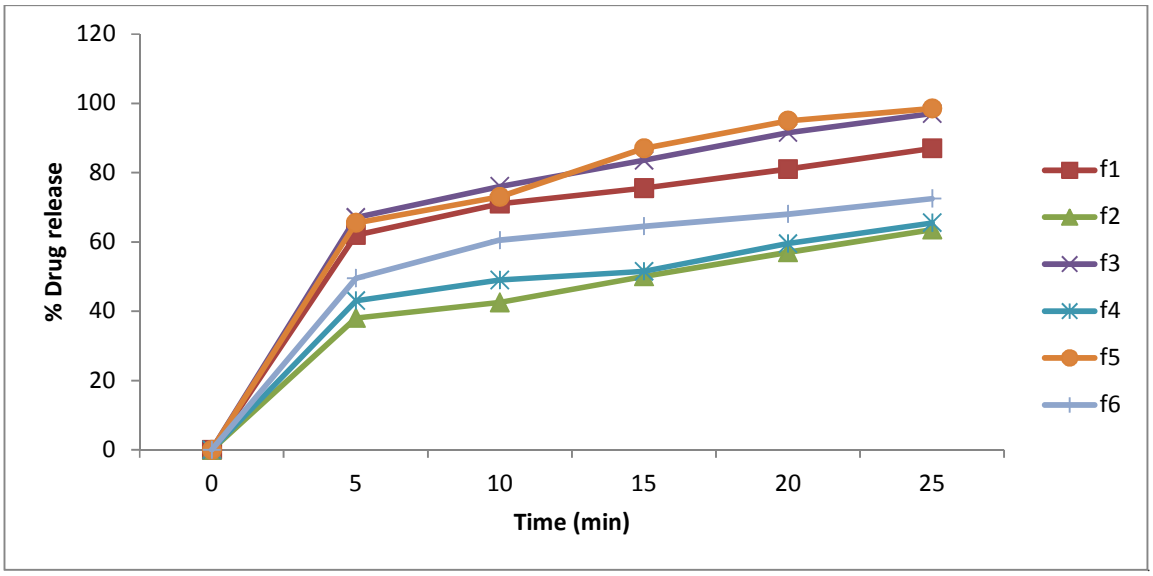

Fig no 3; Comparative percentage Drug release vs. Time for all batches of MDT

The comparative percentage Drug release was shown in Fig no 3. Among all the formulation, F_5 formulation achieved maximum percentage drug release at the end of 25 minutes. Therefore formulation F_5 was the best formulation for Mouth dissolving tablet of Domperidone.

Table no 7: Physical properties of all formulation of Mouth dissolving tablet (FT_1 – FT_6)

Formulation	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (sec)	Water absorption ratio (%)	Wetting Time(sec)	Drug Content (%)
FT_1	3.7	0.76	36	11.2	25	93.6
FT_2	3.1	0.74	39	12.3	29	96.8
FT_3	3.5	0.94	34	12.1	24	95.1
FT_4	2.8	0.73	38	11.3	32	92.7
FT_5	4.0	0.60	33	9.1	22	98.4
FT_6	3.2	0.75	42	10.7	30	88.3

The Mouth dissolving tablets of Domperidone were prepared by Direct compression method. Formulation of tablets was carried out using different types of superdisintegrating agents and excipients. The optimization of concentration of excipients and superdisintegrants was carried out for hardness of the tablet to give the least disintegration time and get greatest drug release. The taste and odour was acceptable for the geriatric and pediatric patients. Domperidone drug was used as an anti-emetic drug because of best relief in the nausea and vomiting.Compatibility studies of Domperidone with different excipients and polymer were carried out prior to the preparation. All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

CONCLUSION

The aim of this study was to prepare a formulation and characterization the Fast dissolving tablet of Domperidone drug as an anti-emetic drug. The direct compression method was used for the formulation of Mouth dissolving tablet of Domperidone. The Mouth dissolving tablet is beneficial for geriatric and pediatric patients. The Crosspovidone as Superdisintegrants have shown better results in compare to Sodium starch glycolate for Mouth dissolving tablet. Therefore FT_5 formulation is the best formulation of Mouth dissolving tablet among all formulations. The disintegration time and in-vitro drug release is good. About 98.5% drug was released within 25 minutes by direct compression method. The percent drug release of Mouth dissolving tablet (FT_5) was 98.5 % at the end of 25 minutes and disintegration time was 32 seconds. Therefore on the basis of percentage drug release and disintegration times the Fast dissolving Tablet of Domperidone was produce rapid action and provide relief in case of nausea and vomiting.

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