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FORMULATION AND EVALUATION OF DOMPERIDONE MOUTH DISSOLVING TABLET

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ABSTRACT

The aim of this study was to formulate and evaluate the mouth dissolving dosage form of domperidone drug as an anti-emetic drug. Super disintegrants were used for the preparation of mouth dissolving tablet namely sodium starch glycolate (SSG). The powder mixture was subjected to pre compression evaluation like FTIR, solubility studies and post-compression evaluation like friability, hardness, wetting time, dispersion time, disintegration time and *in vitro* dissolution rate. FTIR studies confirmed that there was no chemical interaction between the drug and excipients. The results of hardness and friability complied with the official standards. The F5 formulation showed optimum drug release of 99.5 % at the end of 25 min when compared to the other formulations.

KEYWORDS: Dosing frequency, bioavailability, drug release, disintegration, orodispersible.

INTRODUCTION

Mouth dissolving tablets are solid dosage form containing medical substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water to facilate swallowing. It is suited for tablets undergoing high first pass metabolism and is improving bioavailability with reducing dosing frequency to minimize side effect.[1]

Suitable drug candidates for Oral cavity

- The drug have good in taste.
- Primarily absorbed from mouth and oral cavity, e.g., esophagus, stomach etc.

- Drug have dissolve and disintegrated in mouth.
- Drug have absorb from mouth cavity and oral route.
- The drug will pass the first metabolic pathway.[5,6]

Mouth dissolving tablets are solid dosage form containing medical substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water to facilate swallowing. Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing. Many patients find it difficult to swallow tablets and hard gelatine capsules and do not take their medication as prescribed. It is estimated that 50% of the population is affected by this problem which results in a high incidence of non-compliance and ineffective therapy. The difficulty is experienced in particular by paediatric and geriatric patients, but it also applies to people who are bedridden and to those active working patients who are busy or travelling, especially those who have no access to water.[4]

In an effort to develop drug products that are more convenient to use and to address potential issues of patient compliance for certain product indications and patient populations, recent developments in technologies have come out with mouth dissolving tablets (MDT) that can be ingested simply by placing them on the tongue. MDT is a solid dosage form that dissolves or disintegrates within a minute in the oral cavity without the need of water and has a pleasant taste. MDT is also known as orally disintegrating tablet, fast-dissolving tablet, fast-melting tablet, mouth melting tablet or fast-disintegrating tablet[5]. Fast disintegrating dosage form has been successfully commercialized and the growing importance was highlighted recently when the European Pharmacopoeia adapted the term ‘Orodispersible Tablets’ as a tablet to be placed in the mouth where it disperses rapidly before swallowing.

MDTs are designed to disintegrate or dissolve rapidly on contact with saliva, thus eliminating the need for chewing the tablet, swallowing an intact tablet, or taking the tablet with water. Although no water is needed to allow the drug to disperse quickly and efficiently, most technologies utilize the body's own salivation. This mode of administration was initially expected to be beneficial to pediatric and geriatric patients, to people with conditions related to impaired swallowing, and for treatment of patients when compliance may be difficult (e.g. psychiatric disorders)[7] MDT has previously been distinguished as a separate dosage form because of the specific, intended performance characteristics of such products, which are

rapid oral disintegration in saliva with no need for chewing or drinking liquids to ingest these products. These characteristics which are an aid to patient use and compliance are the primary characteristics that constitute the basis for classifying a product as an MDT.

MATERIALS AND METHODS

Materials

Domperidone purchased from bioplus life science pvt. ltd., Banglore, India and avicel, magnesium stearate, talc from SD fine chem. ltd mumbai, india. Mannitol from Finar Chemical Ltd., Ahmadabad, India. Sodium starch glycolate from lafa chem. Pvt. Ltd., Mumbai, India.

Methods

Preparation of Domperidone mouth dissolving tablets

Domperidone mouth dissolving tablets were prepared by direct compression method. Each tablet containing 10 mg domperidone were prepared as per composition given in table 1. The drug and excipients passed through sieve no '20' to ensure the better mixing. Mannitol, 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 300 mg.

Formulation table for mouth dissolving tablet

Table 1: Composition of Mouth dissolving tablet of domperidone.

INGREDIENTS (mg/tablet)	F1	F2	F3	F4	F5	F6
Domperidone	10	10	10	10	10	10
Avicel	65	70	75	80	85	90
Sodium Starch Glycolate	25	30	35	40	45	50
Mannitol	100	100	100	100	100	100
Lactose	90	80	70	60	50	40
Talc	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5
Total weight (mg)	300	300	300	300	300	300

FTIR Studies

FTIR spectrum of any compound gives information about the group present in particular compound. Spectrum of drug was taken using KBr pellets method. Various peaks in spectrum of pure drug were interpreted for presence of different functional group. The spectrum was recorded using on Bruker's FTIR spectrophotometer.

Evaluation of Precompression Parameter

Pre-compression parameters like angle of repose, bulk density, carr's compressibility index, Hausner's ratio were evaluated for the granules according to the standard procedures.

Evaluation of post compression Parameter

Post-compression parameters like friability, hardness, thickness, weight variation, content uniformity, disintegration tests were evaluated for the tablets according to the standard procedures.

In-vitro dissolution study

The prepared tablets were evaluated for in vitro drug release. The drug release studies were carried out using USP XXII paddle type Dissolution test apparatus. The dissolution study was carried out in 900 ml dissolution medium which was stirred at 75 rpm maintained at 37±0.2□C. A tablet placed in dissolution media (900 ml) at 37±0.2□C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 10 ml Phosphate buffer pH 6.8. The samples withdrawn were assayed spectrophotometrically at 287 nm using uv-visible spectrophotometer. The release of drug was calculated with the help of standard curve of domperidone

Stability studies

The reason of stability testing is to provide evidence on how the quality of drug formulation varies with time under the influence of various environmental conditions such as temperature, humidity, light. From this study we know about recommended storage condition, re-test periods and shelf-life of the drug can be established. Stability of a drug has been defined as the ability of a particular formulation in a specific condition, to remain within its physical, chemical, therapeutical and toxicological specifications.

RESULT AND DISCUSSION

Solubility

Table 2: Solubility profile of drug.

S. No.	Solvents	Solubility
1.	Water	insoluble (+)
2.	Methanol	Soluble (+++)
3.	Ethanol (95%)	Slightly soluble
4.	Chloroform	Sparingly soluble (++)
5.	0.1 N HCl	Soluble
6.	pH 6.8 phosphate buffer	Soluble

Partition Coefficient

Table 3: Partition Coefficient

Material	Observation
Domperidone	2.527

Results of loss on drying (%)

Results: Results of loss on drying of Domperidone was found 0.175±0.005%.

Melting point determination

Table 4: Melting point of drug.

Material	Observation
Domperidone	240 – 245 ^{O}C

Ultra-Violet (UV) spectroscopy

Determination of λ_{max} of Domperidone

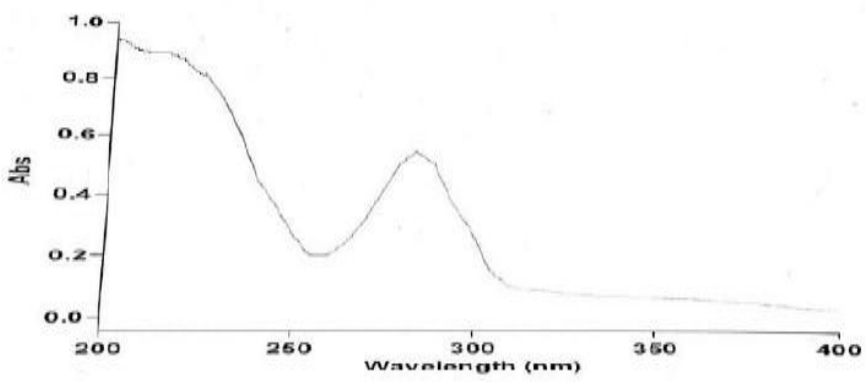

Fig. 1: UV Spectrogram of domperidone standard drug.

Calibration curve in pH 6.8 phosphate buffer

Table 5: Calibration data of drug in standard phosphate buffer (pH 6.8).

S. No.	Concentration (µg/ml)	Absorbance
1	0.2	0.103
2	0.4	0.185
3	0.6	0.282
4	0.8	0.370
5	1.0	0.454

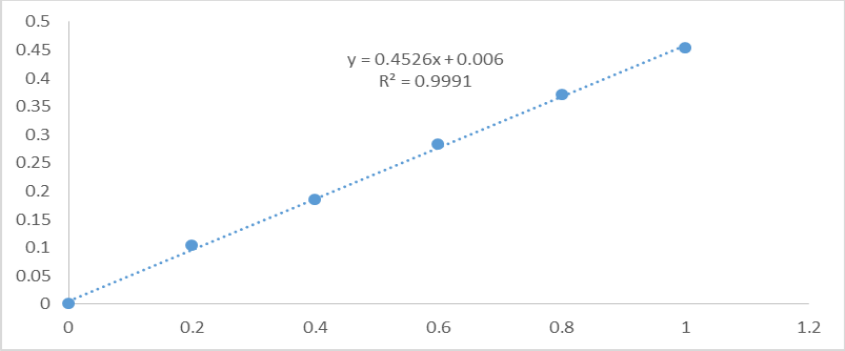

Fig. 2: Standard curve of drug in phosphate buffer pH 6.8.

Infrared spectroscopy (FT-IR)

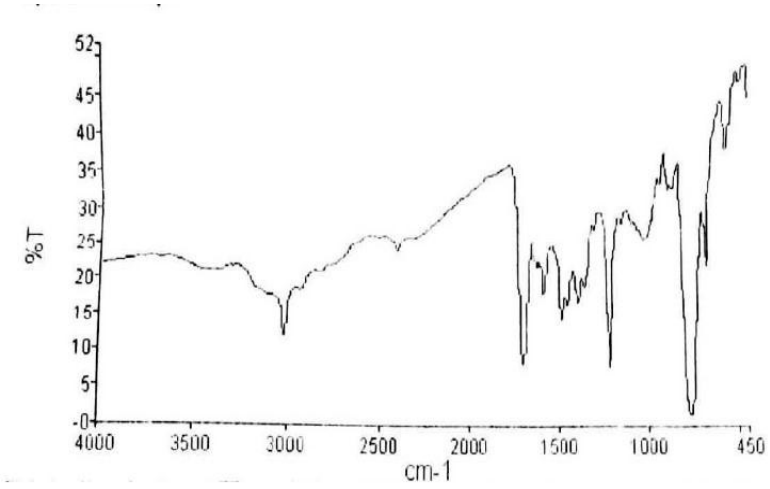

Fig. 3: Infrared spectrum of drug sample.

Table 6: Interpretation of peaks for presence of functional group.

S. No.	Characteristics bands	Observed in study cm-1	Literature values cm-1
1	N-H stretching	3072.60	3100-3500
2	C=O stretch, sharp	1681.90	1640-1690
3	C-Cl bending, sharp	731.02	600-800

Compatibility Study

The compatibility studies were performed using FTIR spectrophotometer.

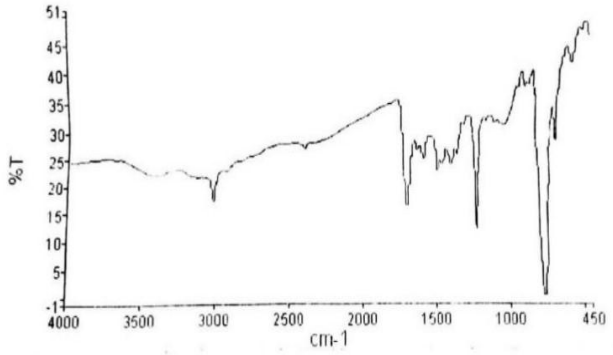

Fig. 4: FT IR spectra of Domperidone + Crosspovidone.

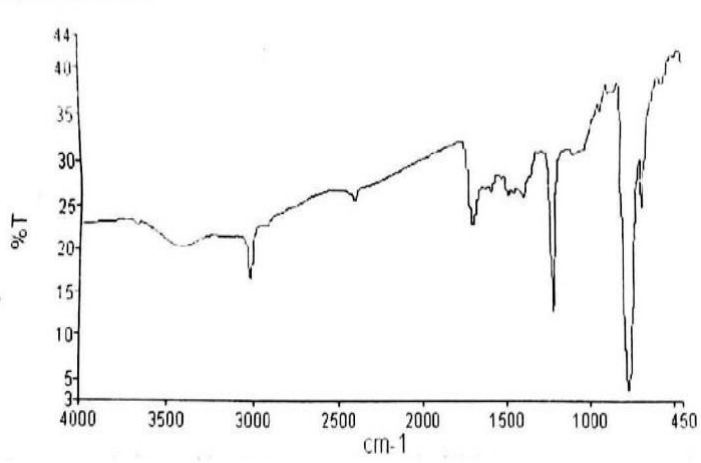

Fig. 5: FT IR spectra of Domperidone + Talc.

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.

Evaluation of Pre-Compression Parameters of Mouth Dissolving Tablet

Table 7: Pre-compression evaluation parameters for Mouth dissolving tablet.

Formulation	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of Repose (θ)	Carr's index (%)	Hausner's Ratio (%)
F1	0.303	0.40	27.9	19.2	0.86
F2	0.321	0.32	28.3	13.1	0.62
F3	0.418	0.28	22.4	13.6	1.14
F4	0.402	0.46	30.2	19.4	1.93
F5	0.428	0.52	32.8	15.7	1.87
F6	0.378	0.37	25.6	20.7	1.12

Evaluation of Post Compression Studies Of Domperidone Mouth DissolvingTablet

Table 8: Physical properties of all formulation of Mouth dissolving tablet (F1 – F6).

Formulation	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (sec)	Water absorption ratio (%)	Wetting Time (sec)	Drug Content (%)
F1	3.8	0.77	35	11.2	25	93.6
F2	3.2	0.75	38	12.3	29	96.8
F3	3.6	0.95	33	12.1	24	95.1
F4	2.9	0.74	37	11.3	32	92.7
F5	4.1	0.61	32	9.1	22	98.4
F6	3.3	0.76	41	10.7	30	88.3

In-vitro drug release: The in-vitro dissolution time was 25 minutes in which 99.5 % drug was released for formulation F_5. Therefore formulation no F_5 showed better in-vitro drug release within 25 minutes.

Dissolution Profile for Mouth Dissolving Tablet.

Time (Min)	Cumulative % drug release					
	F1	F2	F3	F4	F5	F6
2	22.2	20.80	18.34	15.29	28.80	26.54
4	34.5	35.72	30.60	28.20	40.51	39.21
6	45.1	46.32	47.72	48.91	51.72	50.26
8	62.6	63.64	66.56	67.34	68.48	67.45
10	75.7	76.42	74.78	75.67	81.30	80.37
15	80.4	82.95	84.43	86.40	87.92	86.56
20	84.0	83.83	86.90	87.24	93.25	92.41
25	92.61	93.29	95.32	97.70	99.50	96.21

Dissolution profile for formulation F1-F6

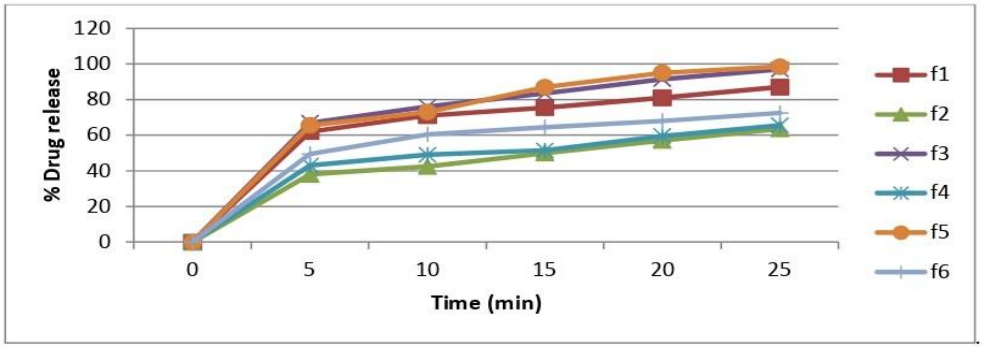

Fig. 4: In-vitro drug release profiles of all the formulations (F1-F6).

Stability studies

Based on the results of *in-vitro* drug release best formulations F_5 was selected for three month stability studies at 25ºC/60% RH and at 45ºC/75% RH. The selected formulations were

evaluated for physical appearance, hardness, friability, and drug content and *in-vitro* drug release. Three months of stability studies revealed that; there was no any significant degradation of the drug. Thus prepared formulations were physically and chemically stable.

Table 9: Results of stability studies for formulation F_5 stored at 25ºC/60% and 45ºC/75% RH.

Storage Period	Stored at 25ºC/60% RH Formulation F_5		
	HardnessKg/cm^2	% friability	% CDR
Initial	4.1	0.61	99.5
After 1month	4.0	0.6	99.4
After 2Month	4.0	0.6	99.3
After 3month	4.0	0.6	99.3
Storage Period	Stored at 40ºC/75% RH Formulation F_5		
	HardnessKg/cm^2	% Friability	% CDR
Initial	4.1	0.61	99.5
After 1month	4.0	0.60	99.4
After 2 Month	4.0	0.6	99.3
After 3month	4.0	0.6	99.3

CONCLUSION

The mouth dissolving tablets of domperidone were prepared by direct compression method. Taste and odour was acceptable for both types of patient like geriatric and pediatric. The obtained calibration curve was straight line. The curve was obtained in pH 6.8 at the maximum wavelength of 287 nm.

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.

The sodium starch glycolate as superdisintegrant shows better results for mouth dissolving tablet. Therefore F_5 formulation is the best formulation of mouth dissolving tablet among all formulations.

The disintegration time and in-vitro drug release is good. The percent drug release of mouth dissolving tablet (F_5) was 99.5% at the end of 25 minutes. Therefore on the basis of percentage drug release and disintegration times of drug produce rapid action and provide relief in case of nausea and vomiting.

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