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DESIGN AND EVALUATION OF ORODISPERSIBLE TABLETS OF DOMPERIDONE

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Abstract:

The aim of this study was to design and evaluate the mouth dissolving dosage form of domperidone drug as an anti-emetic drug. The orodispersible tablets of domperidone were prepared by direct compression method. Formulation of tablets was carried out using different types of super disintegrating agents and excipients. The obtained calibration curve was straight line. The curve was obtained in pH 6.8 at the maximum wavelength of 287 nm. The calculation of in-vitro drug release study was based on the calibration curve. The Mouth dissolving tablet are beneficial for geriatric and pediatric patients. 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. About 98.5% drug was released within 5 minutes. The disintegration time and in-vitro drug release is good. The percent drug release of Mouth dissolving tablet (F_5) was 98.5 % at the end of 5 minutes.

Keywords: *Friability, Hardness, Disintegration, compression, drug release*

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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.

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.
- 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.
- 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 tech nologies 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.

Need to Formulate Mouth Dissolving Tablets:

The need for non-invasive drug delivery systems continues due to patient's poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses coupled with high cost of disease management. MDT is one such dosage form which is useful for

i) Geriatric patients mainly suffering from conditions like hand tremors and dysphasia.
ii) Paediatric patients who are unable to swallow easily because their central nervous system and internal muscles are not developed completely.
iii) Travelling patients suffering from motion sickness and diarrhoea who do not have easy access to water.
iv) Patients with persistent nausea for a long period of time are unable to swallow. Especially cancer patients after taking their chemotherapy are too nauseous to swallow the H_2 blockers, which are prescribed in order to avoid gastric ulceration.
v) Mentally challenged patients, bedridden patients and psychiatric patients.

It is suited for tablets undergoing high first pass metabolism and is improving bioavailability with reducing dosing frequency to minimize side effect.

MATERIALS AND METHODS:

5.1 Materials

Table no. 1 List of chemicals used

S. No.	Materials	Supplier
1.	Domperidone	Bioplus life science
2.	Methanol	S.D. Fine Pvt. Ltd.
3.	Ethanol	Jiangsu Huaxi International
4.	Chloroform	Avantor materials india Ltd
5.	Hydrochloric acid	RFCL Ltd.
6.	KH_2PO_4	S.D. Fine Pvt. Ltd.
7.	NaOH	RFCL Ltd.
9.	Sodium starch glycolate	Loba Chemie Pvt Ltd
10.	Croscarmellose Sodium	Loba Chemie Pvt Ltd
11.	Citric acid	Loba Chemie Pvt Ltd
12.	Crospovidone	Loba Chemie Pvt Ltd

METHODS: -

Preformulation Study

Preformulation testing is the first step in the rational development of dosage forms of a drug substance.

Physical Characteristics

Colour: A small quantity of drug powder was taken on butter paper and viewed in well-illuminated place.

Taste and odour: Very less quantity of drug was used to get taste with the help of tongue as well as smelled to get the order.

Solubility: A qualitative determination of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of drug.

Partition Coefficient: First 25 µg/ml solution of pure drug in octanol was prepared. Then the mixture of octanol and water were mixed in ratio of 1:1.

Loss on drying (%): Loss on drying is the loss of weight expressed as percentage w/w resulting from water and volatile matter of any kind that can be driven off under specified conditions 57.

Melting Point: The Melting point was determined by the capillary method using Digital Melting point apparatus.

Ultra-Violet (UV) spectroscopy: Organic molecules when exposed to light in UV region they absorb light of particular wavelength depending on the type of electron transition associated with the absorption.

Determination of λ_{max} of Domperidone

10 mg of drug sample was weighed accurately and dissolved in 10 ml of methanol in 10 ml of volumetric flask and stock solution was prepared.

Calibration curve in pH 6.8 phosphate buffer

Preparation of the phosphate buffer 6.8 media: 10 mg drug was weighed accurately and transferred to 100 ml volumetric flask.

Preparation of calibration curve of domperidone in phosphate buffer pH 6.8: From above stock solution various dilutions were prepared to get desired concentration.

Selection of method for compression: There are number of compression technology available in pharmaceutical industry on these bases granulation process can be divided as: Dry granulation method, Direct compression, Wet granulation.

Preparation of Domperidone mouth dissolving tablets: 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 300 mg.

FORMULATION TABLE FOR MOUTH DISSOLVING TABLET:

Table no 2: 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

Evaluation of Precompression Parameter

Angle of repose (θ): The frictional forces in a loose powder or granules can be measured by the angle of repose.

$$\tan \theta = h/r$$

$$\theta = \tan^{-1} (h/r)$$

Where, θ is the angle of repose, h is the height, r is the radius.

Table no. 3: Relationship between Angle of Repose (θ) and flow properties

S. No.	Angle of Repose (θ) (degrees)	Flow
1.	<25	Excellent
2.	25-30	Good
3.	30-40	Passable*
4.	>40	Very poor

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined by using following formulas.

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Packing}}$$

Carr's Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula:

$$\text{Carr's Index \%} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

Table no. 4: Grading of the powders for their flow properties according to Carr's index

S. No.	Carr's Compressibility index	Flow
1	5 – 15	Excellent
2	12 – 16	Good

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation

Hausner's ratio = Tapped bulk density/Bulk density

Hausner's ratio value <1.25 shows better flow properties

EVALUATION OF POST COMPRESSION PARAMETER

Shape and colour of tablets: Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Thickness Test: The tablet thickness was measured using dial-caliper.

Weight Variation Test: Twenty tablets were selected randomly from each formulation and average weight was determined. The following percentage deviation in weight variation is allowed.

Table no. 5: Percentage deviations in weight variation

S. No.	Average weight of a tablet	Percentage deviation
1	130 mg or less	10
2.	More than 130 mg and less than 324 mg	7.5
3	324 mg or more	5

FRIABILITY TEST

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The friability was determined as the mass loss in percent according to equation:-

$$\%\text{Friability} = (\text{Loss in weight}/\text{Initial weight}) \times 100$$

The test complies if tablets not loss more than 1% of their weight.

UNIFORMITY OF DRUG CONTENT:

The test is mandatory for tablets with 10 mg or less weight of active ingredient. Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered.

In-vitro Dissolution rate studies

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.

Stability studies:

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:

Preformulation Study

Physical Characteristics

Table 6: Organoleptic and physical properties of drug

Test	Observations
Colour	Light yellowish powder
Taste	Bitter
Odour	Odourless

7.1.2 Solubility

Table 7: 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 Po4 buffer	Soluble

Partition Coefficient:

Table 8: Partition Coefficient

Material	Observation
Domperidone	2.527

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

Melting point determination

Table 9: Melting point of drug

Material	Observation
Domperidone	240 – 245 ^{O}C

Ultra-Violet (UV) spectroscopy

Determination of λ_{max} of Domperidone

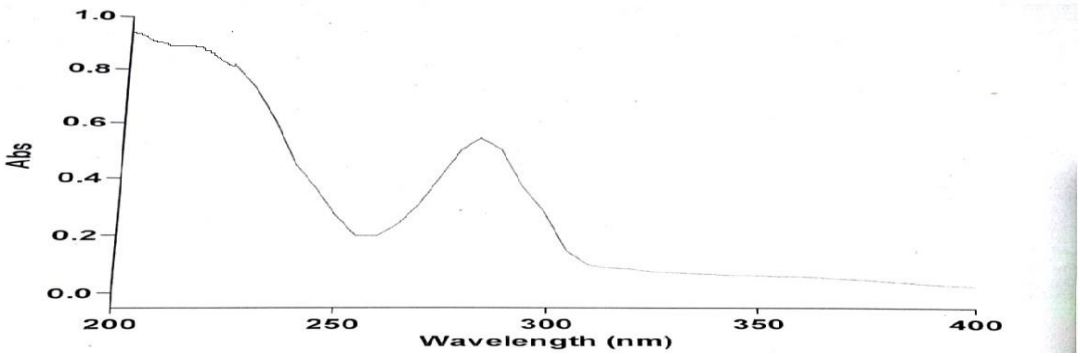

Fig. 1: UV Spectrogram of domperidone standard drug

Calibration curve in pH 6.8 phosphate buffer

Table 10: Calibration curve of drug in standard phosphate buffer (pH 6.8)

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	0.2	0.103
3	0.4	0.185
4	0.6	0.282
5	0.8	0.370

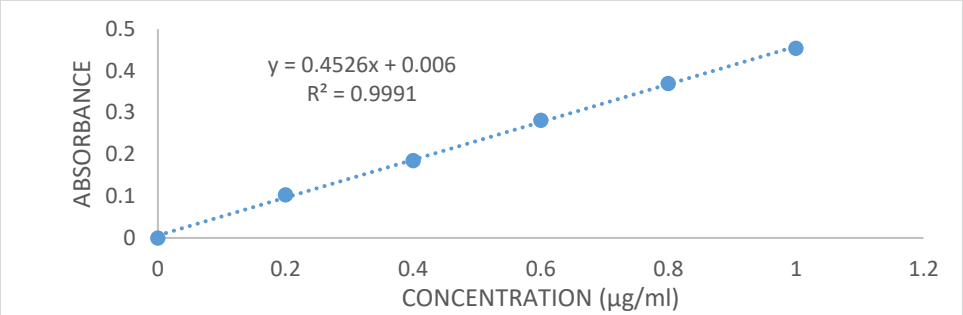

Fig. 2: Standard curve of drug in standard phosphate buffer pH 6.8

EVALUATION OF PRE-COMPRESSION PARAMETERS OF MOUTH DISSOLVING TABLET

Table 11: 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 DISSOLVING TABLET

Table 12: Physical properties of all formulation of Mouth dissolving tablet (F_1 – F_6)

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* DISSOLUTION STUDIES:**

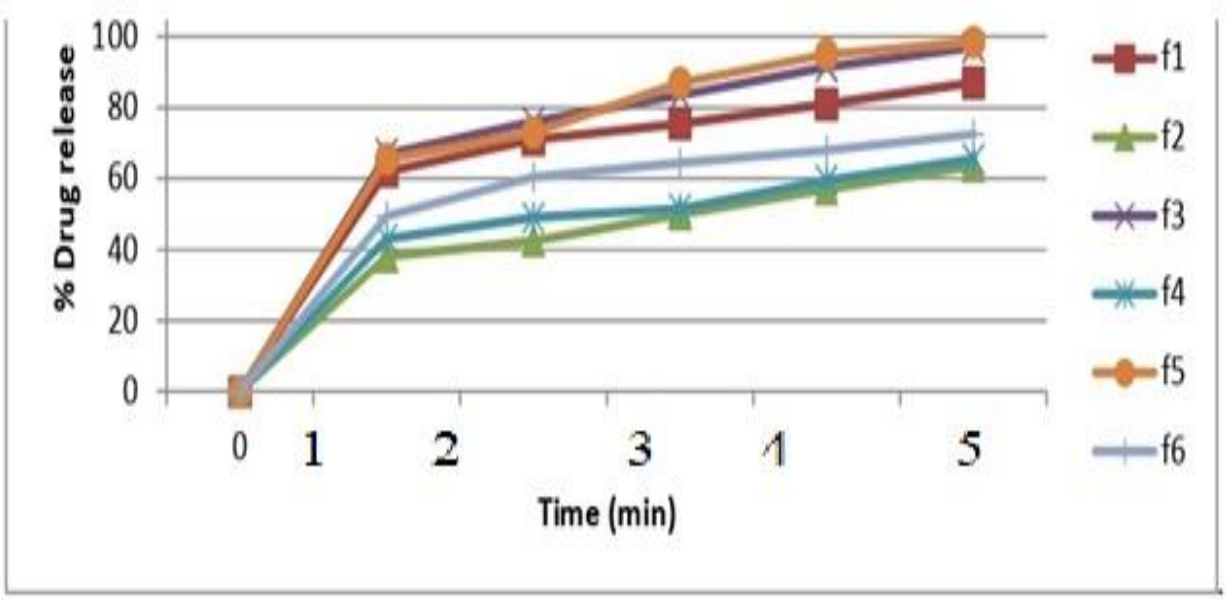

Fig 3: Dissolution data from F1-F6

STABILITY STUDIES:

Table 13: Results of stability studies for formulation F_4 stored at 25ºC/60% and45ºC/75% RH

Storage Period	Stored at 25ºC/60% RH Formulation F_2		
	HardnessKg/cm^2	% friability	% CDR
Initial	7.0	0.57	99.77
After 1month	6.8	0.6	99.3
After 2 Month	6.7	0.61	98.7
After 3 months	6.6	0.62	98.1
Storage Period	Stored at 40ºC/75% RH Formulation F_2		
	HardnessKg/cm^2	% friability	% CDR
Initial	7.0	0.57	99.77
After 1month	6.7	0.62	99.1
After 2 Month	6.6	0.64	98.3
After 3months	6.4	0.65	97.8

SUMMARY AND CONCLUSION:

Formulation of tablets was carried out using different types of super disintegrating agents and excipients. The optimization of concentration of excipients and super disintegrants 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. The curve was obtained in pH 6.8 at the maximum wavelength of 287 nm. The slope,

intercept and regression coefficient were obtained from the graph. The calculation of in-vitro drug release study was based on the calibration curve. The aim of this study was to Fabricate and Evaluate the mouth dissolving dosage form of Domperidone drug as an anti-emetic drug. The direct compression method was used for the formulation of Mouth dissolving tablet of Domperidone. 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. About 98.5% drug was released within 5 minutes by direct compression method. The disintegration time and in-vitro drug release is good. The percent drug release of Mouth dissolving tablet (F_5) was 98.5 % at the end of 5 minutes.

REFERENCES:

1. Virely P, Yarwood R.Zydis - a novel, fast dissolving dosage form.Manuf Chem. 1990; 61:36–37.
2. Pebley WS, Jager NE, Thompson SJ. Rapidly disintegrating tablet. US Patent 5, 1994 March 29, 298, 261.
3. Watanabe Y. New compressed tablet rapidly disintegrating in the mouth using crystalline cellulose and a disintegrant. Biol Pharm Bull. 1995; 18: 1308–1310.
4. Myers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product there from. PCT Patent WO 95/34293-A1.1995 Dec 21.
5. Elan Corporation, plc. Orally disintegrating tablets (ODT) Nanomelt TM ; http://www.elan.com/EDT/nanocrystal%5Ftechnology/orally_disintegrating_tablet.asp.
6. Liang AC, Chen LH. Fast-dissolving intraoral drug delivery systems. Expert Opin Ther Pat. 2001; 11:981-986
7. Koizumi KI, Watanabe Y, Morita K, Utoguchi N, Matsumoto M., New method for preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int J Pharm. 1997; 152: 127–131.
8. Bess WS, Kulkarni N, Ambike SH, Ramsay MP. Fast dissolving orally consumable solid film containing a taste masking agent and pharmaceutically active agent at weight ratio of 1:3 to 3:1. US Patent 7067116. 2006 Jun 27.
9. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian J Pharm. 2008; 2: 2–11.
10. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull. 1996; 44: 2121–2127.340