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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF DOMPERIDONE USING FENUGREEK SEED MUCILAGE AS NATURAL SUPERDISINTEGRANT BY DIRECT COMPRESSION METHOD.

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ABSTRACT

The demands for fast dissolving tablets have received ever increasing day to day during the last 2-3 decades. In the present designed in-vitro study, the effect of natural superdisintegrant was compared with synthetic super disintegrants and conventional super disintegrants in the of fast dissolving tablet formulation of Domperidone. Dopamine is an antiemetic drug which used for the management of the vomiting treatment, and cancerous nausea. In the present work 9 formulations of FDT (Fast dissolving tablet) of Domperidone were prepared by using isolated mucilage of the fenugreek seed (Mucilage) was evaluated and compiles with the official parameters and specifications. Various formulations were prepared using four different superdisintegrsnts namely- fenugreek seed mucilage, sodium starch glycolate, cross carmelose sodium with three concentrations (2%, 4%, 6%) by direct compression method. The blend was evaluated for pre-compression parameters like Angle of repose, bulk density, tapped density and then tablet evaluated post-compression parameters like thickness, drug content, hardness, weight variation, wetting time, friability, disintegration time, dissolution time, drug release study. Formulation 8 showed the lowest disintegration time and invitro dissolution studies recorded that formulation 8 showed 99.50% drug release at the end of 3 minutes. The best formulations were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline.

KEYWORDS: Antiemetic, fenugreek seed mucilage, sodium starch glycolate, Domperidone, Gastric antrum, dissolution time.

INTRODUCTION

The tablet is most generally used dosage for because of its convenience in term of self-administration, compactness, correct dose and ease in manufacturing. Over this one disadvantage of conventional tablet is difficulty in swallowing by paediatric and geriatric patients.

To beat these problems the scientists have developed novel drug delivery system that known as fast dissolving tablet. The fast dissolving tablets that dissolving in few seconds within the mouth when they come with contact saline without requirement of additional water. The advantage of FDT (Fast dissolving tablet) is onset of action, higher patient acceptance, and enhanced bioavailability.[1]

Domperidone is a peripherally selective dopamine D2 and D3 receptor antagonist. It's no clinically important interaction with the D1 receptor, not like metoclopramide. The drug provides relief from nausea by block receptors at the chemoreceptor trigger zone at the ground of the ventricle (a location the brain). It increases motility in the upper epithelial duct to a moderate degree and increases lower esophageal sphincter muscle pressure by block dopamine receptors within the gastric antrum and the small intestine.

Domperidone is absorbed orally, but bioavailability is only 15% due to first pass metabolism. It completely biotransformed and metabolites are excreted in urine.[2,3]

MATERIAL AND METHOD

MATERIAL

Domperidone was received as gift sample by Ultra Drugs Pvt. Ltd., Solan H.P. (by the reference Reckon Animal Health Care) fenugreek seed mucilage, Magnesium stearate, Lactose used were procured from Rescue laboratories, Jaipur, Asparteme used was procured from Gsweet Biotech, China and other reagents and chemicals used were of analytical grade.

METHOD

Fast dissolving tablet of Domperidone were prepared by direct compression method. Pure drug and excipients were separately passed through # 60 No. seive mesh, Required amount of drug and excipients were taken for every formulation as according the table no.1 formula.

The powdered drug, lactose and Mannitol were mixed uniformly with continuous trituration using mortar and pestle. Then required quantity of super disintegrates as sodium starch glycolate, croscarmellose and aspartame taken for each formulation and mixed, finally talc powder and magnesium stearate were added and mixed well.

The mixed blend of drug and excipients were compressed using 10 station tablet punching machine. (Shakti pharmaceuticals**) 4** Mm punch. A Batch of 100 tablets of each formulation was prepared for all the entired formulation. Before the tablet preparation /punch (Before Compression) the mixture blend of all designed formulations were subjected to compatibility studies (IR) and pre-compression parameters like- Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.[4,6]

Pre-formulation studies

Angle of Repose (θ)

Angle of repose is defined as the calculation of the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder blend. When more quantity of the powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force.[7]

The angle of repose is determined by the funnel method suggested by the scientist Newman. Angle of repose is determined by the following formula

$\text{Tan } \theta = h/r$

$\theta = \text{Tan}^{-1}\ h/r$

Where θ = Angle of repose

r = Radius of the cone

h = height of the cone

Bulk Density

Density of powder is defined as weight per unit volume. Bulk density is defined as the mass of the powder that divided by the bulk volume of powder and is expressed as gm/ cm^3. The bulk density of a powder primarily depends on its particle shape, size, distribution and the adhering properties of particles to adhere together. There are two types of bulk density.[8]

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density.

Tapped Density (Dt)

It was the ratio of total mass of the powder to tapped volume of the powder. Volume was represented by tapping the powder for 500 times and the tapped volume was recorded, if the difference between these two volumes was less than 2%. If it more than 2%, then tapping was continued for 750 times and tapped volume was noted. Tapping was continued until the difference between volumes was less than 2% in bulk density apparatus. It was expressed in g/ml and was given as following,

Dt= M/Vt

Where, M is the mass of powder

Vt is the tapped volume of the powder.[9]

Carr's index (or) % compressibility

Carr's index indicates powder flow properties. It is expressed by percentage and is given by:

I=Dt−Db/Dt×100

Where, Dt denotes the tapped density of the powder

And

Db is the bulk density of the powder.[9,10]

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow properties. It is calculated by the following formula:

Hausner ratio=Dt/Db

Where, Dt show the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).[11]

EVALUATATION OF TABLET

All prepared tablets of Domperidone were evaluated for the following parameters as per IP guideline; all the calculations are represented in the table No.2.

WEIGHT VARIATION

Twenty tablets of Domperidone formulation were selected randomly sampled from each of the formulation and weighted individually by using Citizen Digital Balance for their weight data. The average weight of the tablets as well as percentage deviation was calculated.[12]

HARDNESS

Hardness of the Domperidone tablet was measured with the tablet hardness testing apparatus known as Monsanto tablet harness tester.[13]

THICKNESS

The thickness of the tablet Domperidone was measured in mm by the Vernier Calipers for all the designed formulation batches.[14]

FRIABILITY

The friability of the Domperidone is measured by using 20 tablets as sample is measured by using USP type Roche Friabilator. The tablets were dusted reweighed and percentage weight-loss was calculated.[15]

%Friability= Initial Weight−Final Weight * 100/ Initial Weight

Water absorption ratio

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation,

$$\mathbf{R = \{(Wa - Wb) / Wa\} \times 100}$$

Where, Wa and W_b were weights of the tablets after and before study.[16]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time

taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.[17]

DISINTEGRATION STUDY

Disintegration time study was carried out by selecting 6 tablets of Domperidone and performed disintegration test (Lab India) using 900 ml distilled water at temperature ($37^0C \pm 2^0C$).[18]

DISSOLUTION STUDY

The In-vitro for the dissolution study was carried out in the USP (United state pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at 37 ± 0.5^0C. The speed of the paddle was set at RPM 50, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was replenished to the dissolution medium. The calculations of the Concentration were calculated by absorbance base. The release of the drug was performed in replicates of three.[19,20]

Table No. 1:- Formulation of fast dissolving tablet of Domperidone.

Ingredients(mg)	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Domperidone	20	20	20	20	20	20	20	20	20
Cross carmellose Sodium	3	6	9	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	3	6	9	-	-	-
Fenugreek seed mucilage	-	-	-	-	-	-	3	6	9
Aspartame	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Mannitol	40	40	40	40	40	40	40	40	40
Lactose	50	50	50	50	50	50	50	50	50
MCC	31	28	25	31	28	25	31	28	25
TOTAL	150	150	150	150	150	150	150	150	150

RESULT AND DISCUSSION

Table No. 2:- Pre-compression parameters for Domperidone FDTs.

Formulation Code	Angle of repose (°) (±SD) n=3	Bulk density (gm/ml) (±SD) n=3	Tapped density (gm/ml) (±SD) n=3	Carr's index (%)* (±SD) n=3	Hausner's ratio* (±SD) n=3
FD1	25.18±1.32	0.55±0.13	0.52±0.12	15.29±1.11	1.17±0.03
FD2	24.35±1.34	0.59±0.15	0.59±0.67	11.81±1.29	1.16±0.02
FD3	28.44±1.45	0.57±0.17	0.51±0.55	17.28±1.25	1.15±0.19
FD4	25.59±0.57	0.51±0.11	0.61±0.23	13.86±1.52	1.11±0.18
FD5	26.19±1.21	0.54±0.02	0.49±0.28	14.97±1.68	1.13±0.14
FD6	27.11±1.87	0.56±0.18	0.56±0.26	12.82±1.87	1.12±0.55
FD7	30.20±0.16	0.52±0.16	0.62±0.11	15.01±0.22	1.16±0.07
FD8	28.28±0.23	0.58±0.04	0.48±0.14	16.19±0.56	1.14±1.00
FD9	29.31±1.15	0.49±0.10	0.57±0.19	17.27±1.58	1.10±1.11

Table No. 3:- Post-Compression parameters of Domperidone FDTs.

Formulation Code	Weight Variation (%) (±SD) n=3	Thickness (mm) (±SD) n=3	Hardness (kg/cm^2) (±SD) n=3	Friability (%) (±SD) n=3
FD1	140±0.51	2.85±0.24	3.50±0.18	0.63
FD2	160±0.76	2.49±0.16	3.19±0.06	0.60
FD3	145±0.12	1.94±0.38	4.24±0.92	0.45
FD4	147±0.25	1.86±0.82	4.10±0.14	0.48
FD5	148±0.19	2.30±0.20	3.28±0.07	0.89
FD6	154±0.10	2.21±0.29	3.00±0.15	0..95
FD7	153±0.13	2.13±0.23	2.85±0.09	0.55
FD8	150±0.04	2.55±0.25	3.31±0.01	0.52
FD9	155±0.27	2.61±0.27	3.40±0.20	0.49

Table No. 4:- Disintegration, Wetting time, Water absorption ratio, and Drug content of Domperidone FDTs.

Formulation Code	In-vitro Dispersion Time (Sec.) (±SD) n=3	Wetting time (sec) (±SD) n=3	Water absorption Ratio (±SD) n=3	Drug Content (±SD) n=3
FD1	62±1.35	50±1.54	60±1.25	89.48±1.12
FD2	60±1.15	48±1.49	59±1.56	91.85±1.25
FD3	65±1.54	53±1.31	61±1.35	88.12±1.31
FD4	47±1.52	41±1.24	57±1.64	93.58±1.56
FD5	45±1.25	39±1.97	55±1.15	94.54±1.15
FD6	50±1.37	43±1.71	58±1.51	92.65±1.35
FD7	42±1.02	37±1.12	52±1.41	97.98±1.01
FD8	40±1.46	35±1.28	51±1.62	99.50±1.56
FD9	43±1.58	38±1.35	53±1.58	96.14±1.25

RESULTS AND DISCUSSION

Bulk density and tapped density of powder blend has been evaluated. The angle of repose for the formulations blend was found to be in the range 24.35 to 30.20°. Formulations with Crosscarmelose Sodium (FD1-FD3) as a disintegrant showed angle of repose values ≤ 28.44^o. Other the formulation Sodium Starch Glycolate containing (FD4-FD6) was showed angle of repose values <27.11^o and last one formulation with Fenugreek seed mucilage (FD7-FD9) was showed angle of repose values ≤ 30.20^o indicating fair flow properties of powder blend. Compressibility index was found to be in the range 11.81% to 17.27%. All formulations showed good flow properties. Hausner‟s ratio was found to be in the range 1.10 to 1.7 and that indicated that all formulation has good flow properties. The formulation FD7 showed low hardness (2.85±0.09) and FD3 higher (4.24±0.92kg/cm2). Higher friability FD6 (.95%) and low friability FD3 (0.45%). All parameters show weight variation, thickness, Disintegration time (sec) within standard limit. All formulation was subjected to dissolution. From all the above observations it was concluded that the formulation FD1 contain

Fenugreek seed mucilage 4% found to be better formulation in terms of rapid dissolution (62%) and but maximum percentage drug release was found 99.50 of formulation FD8, with fenugreek 4%.

Table 5: Calibration Curve Data of Domperidone.

Concentration	Absorbance (263 nm)
0.0	0
2.0	0.165
4.0	0.325
6.0	0.475
8.0	0.625
10.0	0.759
12.0	0.875

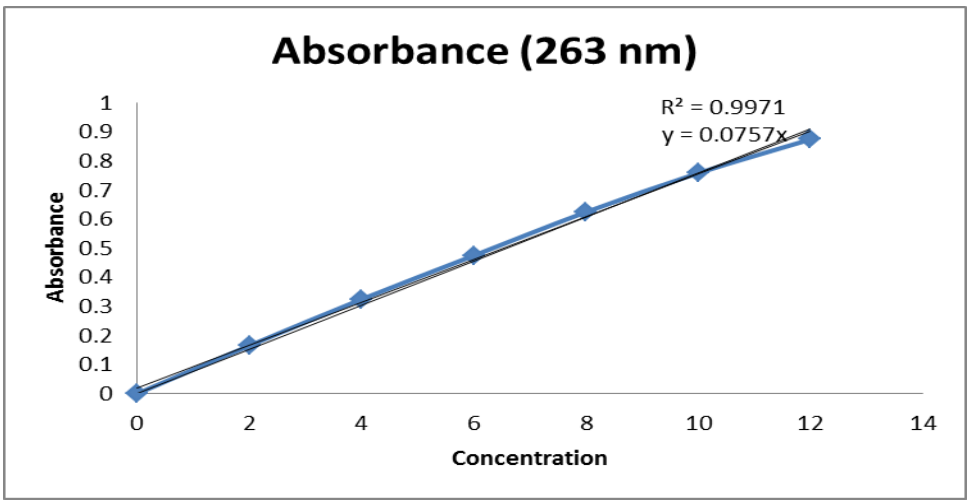

Figure: Calibration Curve of Domperidone.

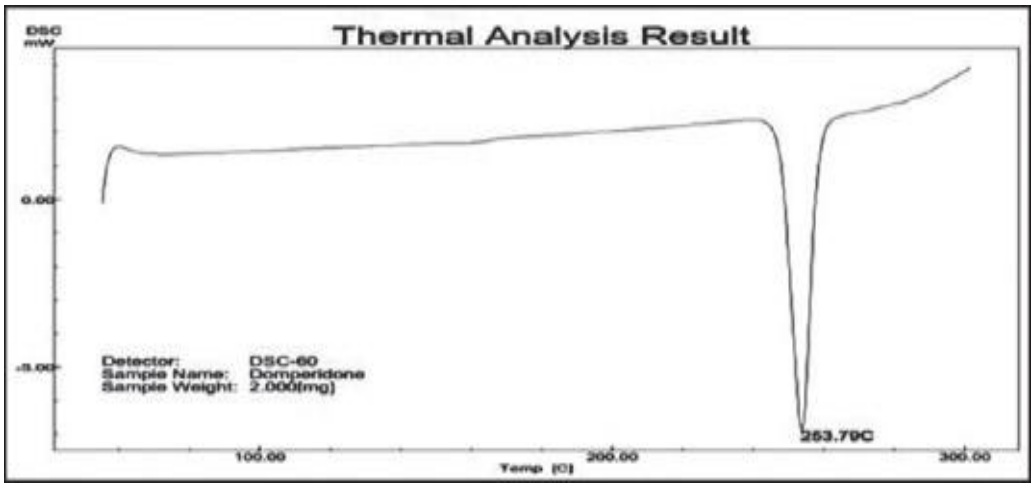

Figure: DSC Thermogram of Domperidone.

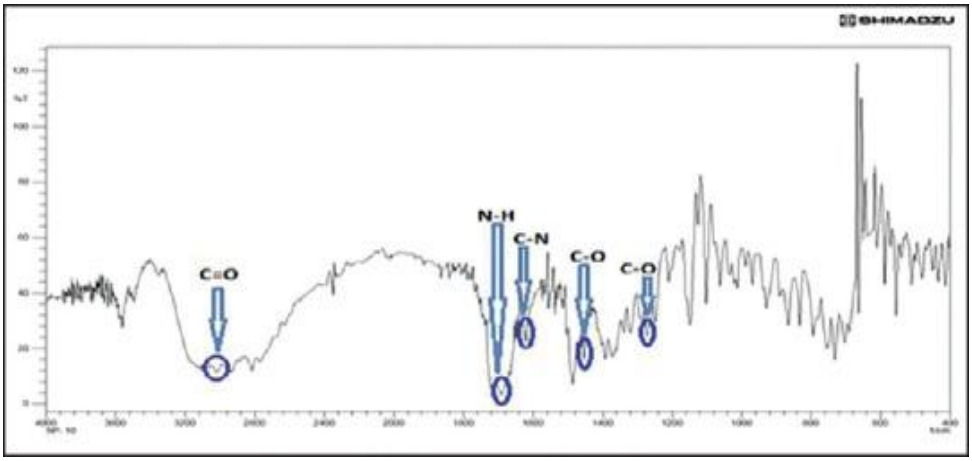

Figure: FTIR Spectra of Domperidone.

CONCLUSION

It can be concluded from the whole study that fast dissolving tablets of Domperidone drug. Natural Superdisintegrants can be used as pharmaceutical excipients for oral drug delivery. So natural superdisintegrant like fenugreek exhibited faster drug dissolution which leads to improve bioavailability, effective therapy (Therapeutic ratio), improve patient compliance, and satisfies all the standards as fast dissolving tablet. It was concluded formulation FD8 maximum percentage drug release was found 99.50, with fenugreek seed mucilage 4%.

From the study, it was concluded that Natural Super disintegrate like Fenugreek seed mucilage showed better disintegrating property over the synthetic super disintegrate like, SSG(Sodium starch glycolate) and CCS (Crosscarmelose Sodium).

Hence the fenugreek mucilage can be used at higher concentration at it has advantage of being non-toxic, low cost, biodegradable and biocompatible with no side effect.

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