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Formulation and Evaluation of Gastroretentive Floating Tablets of Domperidone

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ABSTRACT

In the present study gastroretentive anti-emetic floating tablets of Domperidone was formulated by using HPMC K15M and Microcrystalline cellulose as polymers. The FTIR studies shows the drug is compatible with the polymer used in the formulation. The prepared tablets were evaluated for physical characters such as weight variation, hardness, friability, disintegration.

The Invitro studies were carried out in pH 1.2 for 8 hours. The studies shows that increased concentration of polymers shows decreasing rate of drug release from the formulation.

KEYWORDS

Domperidone, HPMC K15M and Microcrystalline cellulose, FTIR studies and In-vitro release and study.

I. INTRODUCTION

The oral route of drug administration is the most important method of administering drugs for systemic effects. However, this route has several physiological problems which includes an unpredictable Gastric Emptying Rate. The process of gastric emptying occurs both in fasting as well as fed status. Nevertheless, the pattern of motility diffuses markedly in the two status. In case of fasted state an inter digestive series of electrical events occurs in cyclic manner both through the stomach and a small intestine every 2-3hrs. This activity is called the inter digestive myo electric cycle or migrating myo electric complex (MMC). In fed state, the gastric emptying rate is slowed since the onset of MMC is delayed. Gastric retention time is affected by several factors including size and shape of dosage form, density, concentration in take of food and drugs such as Anti cholinergic agents (eg: atropine, propanthelin), Prokinetc agents (eg: cisapride, methoclopramide) and opiates (eg: codeine). Floating properties of FDDS that enables them to be retained in stomach for prolonged period of time is usually acquired due to low density of the HBS dosage form. In general for a HBS dosage form to be in stomach, it should have the density less than the gastric content (1.004g/cm^3). Studies on FDDS demonstrated that GRT of 4-10hrs could be achieved after a fat and protein meal.

II. MATERIAL AND METHODS

Domperidone was gifted sample form Kniss Laboratories, Hydroxypropylmethylcellulose K15M, Microcrystalline cellulose, Talc, Sodium bicarbonate, Magnesium stearate, Isopropyl alcohol from Fine chemie. All the chemical used were analytical grade.

Preparation of Calibration curve for Domperidone

A stock solution of Domperidone was prepared by dissolving 100mg of the drug in 100ml of Buffer pH 1.2 to get 1 mg/ml solution (stock solution) from this 10ml of solution was pipetted out and diluted to 100ml using Buffer pH -1.2 to produce 100µg/ml (working stock solution), from this 0.5 ml of solution was diluted to 10ml using Buffer pH – 1.2 to 5µg/ml from the working stock solution, dilution were made with Buffer pH-1.2 to produce 10, 15, 20 and 25 µg/ml and the absorbance was measured at 284 nm using UV spectrophotometer.

COMPATIBILITY STUDIES

A physical mixture (1:1) of drug and polymer was prepared and analyzed by FTIR. The IR spectrum of the physical mixture was compared with those of pure drug and polymers and matching was done to detect any appearances or disappearance of peaks.

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Preparation of Granules

The granules were prepared by wet granulation technique and Isopropyl alcohol was used as granulating agent. Accurately weighed quantities of the ingredient were passed through sieve no-60 and mixed. Required quantity of Isopropyl alcohol was added and kneaded to get cohesive mass. Cohesive mass was passed through British Standard Sieve (BSS) No. 44 mesh. The granules were collected and allowed to air dry.

Evaluation of Granules

Angle of Repose

The angle of repose of the prepared granules was measured by funnel method. A dry clean funnel was kept on a burette stand at particular height (2-3cm). A graph paper was placed on the flat surface and a sufficient quantity of the granules was allowed to flow slowly through the funnel until the heap touched the tip of the funnel. The circumference of the heap was drawn and the midpoint was located and its radius was measured. The angle of repose was calculated using the formula

$\Theta = \tan^{-1} h/r$

Where, h- height of pile

r- Radius of the base of the pile and

Θ- Angle of repose

Bulk density

The bulk density of the prepared granules was measured by bulk density apparatus. A weighed amount of granules was introduced into a graduated measuring cylinder. The cylinder was fixed on the bulk density apparatus and the timer knob was set for hundred tapping. Then the bulk density was calculated using the formula

Bulk density = Wt. of sample (g) / Final volume (cc)

Compressibility

Tapped density is determined by placing a graduated cylinder containing a known mass of drug or formulation on a bulk density apparatus which is operated for a fixed number of taps (100) until the powder bed volume has reached a minimum. Using weight of the drug in cylinder and minimum be calculated. Initially without performing the taps the fluff density is calculated percentage compressibility can be calculated by the formula.

% Compressibility = ρt-ρo /ρt x 100

Where, ρt- Tapped density, ρo- Bulk density

Evaluation of Tablets:

The prepared tablets were subjected for various quality control tests in order to characterize them.

Weight variation

The weight variation test of the tablets was done as per the guidelines of Indian Pharmacopoeia. Ten tablets from each batch were weighed in digital balance and average weight was determined and standard deviation was calculated. Weight variation limits as per USP.

Friability

The weight of 10 tablets was noted and placed them in Roche Friabilator. The device subjects the tablets to the combined effect of shock and abrasion by utilizing a plastic chamber, which revolves at 25rpm, dropping the tablets a distance of 6 inches with the revolution. The pre-weighed tablet sample is removed after 100 revolutions, dusted and reweighed. Tablets that loose less than 0.5 to 1 percent in weight are generally considered acceptable.

Friability (%) = (Initial wt. of 10 tablets – Final wt. of 10 tablets) / Initial wt. of 10 tablets x 100

Hardness

The apparatus used for finding Hardness was Monsanto hardness tester. It consist of a base containing a compressible spring, held between two ends. The lower plunger was placed in contact with the tablet by clockwise rotation of string and zero reading is forced towards a spring by a threaded belt tube until the tablet fractures, as the spring was compressed. The force of fracture as recorded and then reading was detected from it.

Swelling and Erosion studies

Matrixes were introduced into the dissolution apparatus under the standard set of condition as specified for drug release rate studies. The tablets were removed using small basket and the swollen weight of each tablet was determined. To determine the matrix erosion, swollen tablets were dried in a vacuum oven at 45ºC to a constant weight.

Swelling Index = (Mt-Mo) / Mo x 100

Where, Mt – weight of tablet at time 't'

Mo- weight of tablet at time t=0.

Erosion studies = Original weight – Remaining dry weight / Original weight x 100

Assay

10mg tablets were accurately weighted and crushed in a mortar, a quantity of powder equivalent to label claim was disperse in methanol, shake and diluted to 100ml with methanol and dichloromethane and filtered. 20ml of the filtrate

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was diluted to 100ml with methanol. Absorbance was measured at 284nm in UV spectrophotometer.
Calculations:

% Drug content = Drug content / Label claim x 100

DISSOLUTION TEST

Dissolution studies were performed using USP XXIII type II dissolution apparatus at 37±0.5ºC. The tablet was placed in 900ml of dissolution medium and rotated at 50rpm. The dissolution media used was 0.1N HCl (pH – 1.2) the samples were withdrawn at specific time intervals of 0.5, 1, 2, 4, 6 and 8 and 24 hours after each withdrawal some volume of fresh dissolution medium was added to maintain sink conditions. The samples were analyzed spectrophotometrically by cyber lab UV 286nm.

III. RESULT AND DISCUSSION

Table no. 1: CALIBRATION CURVE OF DOMPERIDONE IN 0.1N HCl (pH – 1.2)

Concentration (µg/ml)	Absorbance at 284nm
10	0.214
15	0.423
20	0.619
25	0.811
30	1.02

Figure NO. 1: Calibration curve

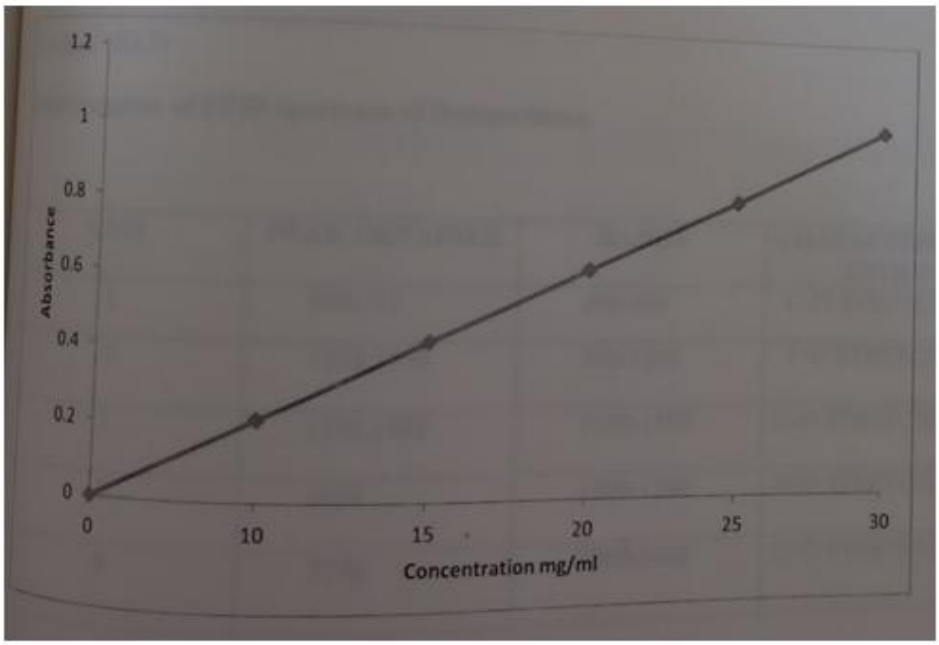

Figure NO.2: IR Spectrum of Domperidone

TABLE NO. 2:
Interpretation of FTIR spectrum of Domperidone.

S.No	PEAK OBTAINED	RANGE	CHARACTERISTIC GROUP
1	606,731	600-800	C-Cl STRETCHING
2	1103,1150	800-1200	C-C STRETCHING
3	1384,1488	1300-1500	C-H STRETCHING

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4	1634	1500-1700	N-H STRETCHING
5	2386	2000-2400	C=O STRETCHING

FIGURE NO. 3: IR SPECTRUM OF HPMC

TABLE NO.3:
INTERPRETATION OF FTIR SPECTRUM OF HPMC:

S.NO	PEAK OBSERVED	RANGE	CHARACTERISTIC GROUP
1	3468,3332	3300-3600	C=O STRETCHING
2	3173	3000-3700	NH STRETCHING
3	2992	2700-3300	C-H STRETCHING

FIGURE NO.:4 IR SPECTRUM OF MICROCRYSTALLINE CELLULOSE

TABLE NO.4:
INTERPRETATION OF FTIR SPECTRUM OF MICROCRYSTALLINE CELLULOSE

S.NO	PEAK OBTAINED	RANGE	CHARACTERISITC GROUP
1	668	600-900	C-Cl STRETCHING
2	1021, 1060, 1112, 1162	900-1300	C-C STRETCHING
3	1361, 1424	1200-1500	C-H STRETCHING
4	1545, 1700, 2357	1600-1700	N-H STRETCHING

FIGURE NO. 5: IR SPECTRUM OF DOMPERIDONE + HPMC + MCC

TABLE NO. 5:
INTERPRETION OF FTIR SPECTRUM OF DOMPERIDONE + HPMC + MCC

S.NO	PEAK OBTAINED	RANGE	CHARACTERISITC GROUP
1	731	600-800	C-Cl STRETCHING
2	2356	2000-2400	C=O STRETCHING
3	1100	800-1200	C-C STRETCHING
4	1377, 1487	1300-1500	C-H STRETCHING
5	1698	1500-1700	N-H STRETCHING

The IR Spectra of physical mixture shows all characteristic peaks (C-C stretching at 1688.58, O-H bending at 1226.64, 1349.11, 1433.01) same as the spectrum of Domperidone (C-C stretching at 1655, OH bending at 1226, C-H stretching at 1349, 1433).

TABLE NO.6: Evaluation of granules:

S.No	Parameters	F1	F2	F3	F4	F5
1	Angle of repose	23º31'±1.21	24º16'±1.39	25º19'±1.32	24º21'±1.53	24º14'±1.92
2	Bulk density	0.894	0.723	0.615	0.549	0.526
3	Compressibility index	9%	8%	9%	8%	8%

The prepared granules are evaluated for Angle of repose, Bulk density and Compressibility according to I.P. Angle of repose was in the range of 21 to 25 percentage compressibility less than 10. All these values indicate good flow property of the granules prepared.

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TABLE NO.7: Evaluation of tablets:

S.No.	Parameters	F1	F2	F3	F4	F5
1	Weight variation	1.84±0.1	1.76±0.1	1.89±0.1	1.93±0.1	1.96±0.1
2	Thickness	4mm	4mm	4mm	4mm	4mm
3	Hardness	3.5±0.1kg/cm$_2$	3.8±0.3kg/cm$_2$	4.7±0.1kg/cm$_2$	5.9±0.1kg/cm$_2$	6.8±0.1kg/cm$_2$
4	Friability	0.3±0.2	0.2±0.1	0.2±0.1	0.1±0.1	0.1±0.1
5	Drug content	98%±0.32	99%±0.46	98%±0.73	97%±0.81	97%±0.65
6	Swelling index	72.3%	85.9%	91.8%	95.7%	98.3%
7	Buoyancy time	7min	5min	4min	3min	2min
8	Floating time	10±1.7hrs	10±1.2hrs	12±0.2hrs	12±0.7hrs	12±0.8hrs

± Standard Deviation for 3 Batches

The average percentage weight variation was within the pharmacopeia limit of 5%. The weight of all formulation was to be uniform with less standard deviation. The thickness was found to be 4mm. The hardness was found 3.2±0.42 to 6.7±0.1 kg/cm square. Friability value was found to be 0.1±0.1 to 0.3±0.2. The values are satisfactory within the IP limit 0.1-0.9%.

FIGURE NO.6: Floating of Tablet

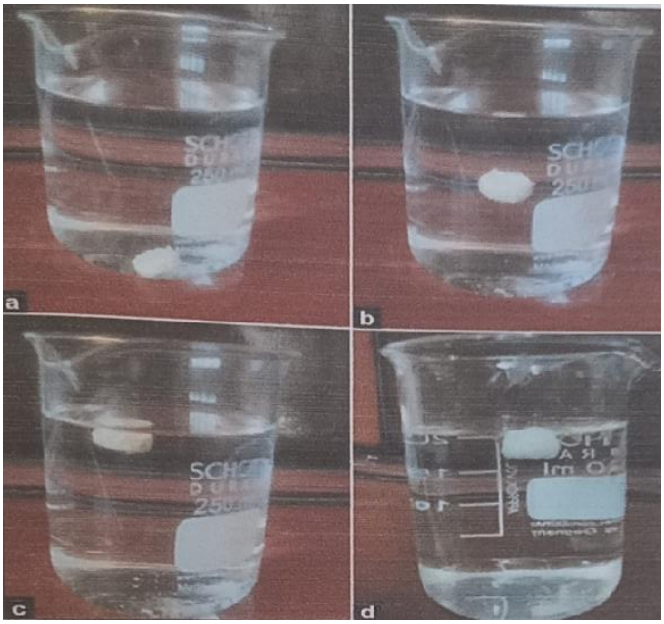

TABLE NO.8: In vitro Dissolution Study

S.No	Time (h)	PERCENTAGE OF DRUG RELEASE				
		F1	F2	F3	F4	F5
1	0	0.00	0.00	0.00	0.00	0.00
2	0.50	19.32	17.48	13.61	9.53	5.39
3	1.00	51.63	41.75	37.82	24.43	13.96

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4	2.00	86.41	69.88	78.32	59.16	28.47
5	4.00	86.41	69.88	78.32	59.16	28.47
6	6.00	95.74	71.16	87.91	72.34	39.16
7	8.00	97.08	89.58	90.65	78.95	51.43
8	24.00	98.32	95.67	94.24	87.18	69.82

FIGURE NO.7: In vitro Dissolution Curve

IV. CONCLUSION

An anti-emetic drug delivery of Domperidone was successfully prepared using HPMC K15M as swellable polymer. From the FTIR studies it was confirmed that Domperidone is compatible with the polymers used in the formula. The prepared granules were evaluated for Angle of repose, Bulk density, and Compressibility index and the values were within the limits specified in the Indian Pharmacopoeia. The compressed tablets were evaluated for weight variation (1.84 to 1.96), thickness (4mm), hardness(3.5 to 6.8), friability (0.3-0.1), Drug content (97 to 99%), swelling index (72 to 98%) buoyancy time(2 to 7min) and floating time (10 to 12 hrs.). From the dissolution studies, the percentage of drug release was found to be F1 (97.08%), F2 (89.58%), F3 (90.65%), F4 (78.95%) and F5 (51.43%) at 8 hours. An increase in the concentration of HPMC K15M showed a delay in the drug release from the formulation. From the results it was concluded that the Formula F5 was optimized since the drug release was 51.43% at 8 hours. The percentage drug release at 24 hours was found to be F1 (98.32%), F2 (95.67%), F3 (94.24%), F4 (87.18%) and F5 (69.82%).

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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