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DEVELOPMENT AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF DEXRABEPRAZOLE FOR EFFECTIVE TREATMENT OF GASTRIC ULCER

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Abstract:

Absorption of drugs with a limited absorption window in the gastrointestinal tract (GIT) is low. Gastroretentive drug delivery methods provide the advantage of delaying stomach emptying time for these medicines. The goal of developing floating Dexrabeprazole tablets was to extend the stomach residence period following oral treatment in order to achieve regulated medication release. Dexrabeprazole floating tablets were made by direct compression with different grades of Hydroxyl Propyl Methyl Cellulose (HPMC) and PVP K30 utilising an effervescent process. As a gas-generating agent, sodium bicarbonate was used. Citric acid's effect on medication release profile and floating qualities was also examined. The preformulation parameters were within the limits of the pharmacopoeias. Weight uniformity, content uniformity, thickness, hardness, in vitro release experiments, buoyancy determination, and kinetic analysis of dissolving data were all used to evaluate tablets. The tablet had a 1-minute lag time and remained buoyant for 12 hours. The in-vitro drug release pattern of improved ciprofloxacin floating tablets (F8) was fitted to various kinetic models, with Higuchi order release kinetics showing the best fit (r2 = 0.984). Ciprofloxacin floating tablets had a longer gastrointestinal residence period, which improved the drug's bioavailability and therapeutic impact.

Keywords: *Dexrabeprazole, Floating drug delivery system, Hydroxy propyl methyl cellulose, Direct compression method, Buoyancy determination.*

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INTRODUCTION:

Present peroral sustained release drug delivery systems are for a maximum of 24 hours clinical effectiveness. Such systems are primarily for the drugs of short elimination half life. However, also drugs with long half-life qualify if a reduction in steady state fluctuation is desired [1]. With many drugs, the basic goal of therapy is to achieve a steady-state blood level or tissue level that is therapeutically effective and non-toxic for an extended period of time. To achieve better therapeutic action various type of drug delivery systems are available, out of which sustained release systems are gaining much importance because of their wide advantages over others like ease of administration, convenience and non-invasiveness.

Oral route is the most commonly employed route of drug administration. Although different route of administration are used for the delivery of drugs, oral route remain the preferred mode. Even for sustained release system the oral route of administration has been investigated the most because of flexibility in dosage forms design that the oral route offers [2]. The materials most widely used in preparing matrix systems, which includes both hydrophilic and hydrophobic polymers. Commonly available hydrophilic polymers include Hydroxypropyl methylcellulose (HPMC), Hydroxypropyl cellulose (HPC), Hydroxyethyl cellulose (HEC), Xanthan gum, Sodium alginate, Poly (ethylene oxide) and crosslinked homopolymers and copolymers of Acrylic acid. It is usually supplied in micronized forms because small particle size is critical to the rapid formation of gelatinous layer on the tablet surface [3-4]. Gastroretentive drug delivery systems (GRDDS) can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention time (GRT) improves bioavailability, reduce drug waste and enhance solubility for drugs that are less soluble in high pH environment.

Floating systems or Hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

Proton-pump inhibitors (PPIs) have been very efficacious for the management of a variety of acid-related disorders such as dyspepsia, peptic ulcer, gastroesophageal reflux disease, laryngopharngeal reflux, Barrett's esophagus, gastrinomas, Zollinger - Ellison syndrome. PPIs are acid-labile, weak bases that require protection from acid activation (protonation) in the stomach before they reach their principle site of absorption in the proximal small intestine. The aim of present investigation to develop floating gastroretentive tablets of Dexrabeprazole for effective treatment of peptic ulcer.

MATERIAL AND METHODS:

Method for preparation of Dexrabeprazole floating Gastroretentive tablets

Direct compression was taken after to manufacture the gas generating floating tablets of Dexrabeprazole [5]. Nine different formulations (F1, F2, F3, F4, F5, F6, F7, F8, and F9) were set up by direct compression. Every one of the polymers chose, drug and excipients were gone through strainer no. 40 preceding utilizing into plan. The sum and proportion of drug and polymers were weighed according to given in table no. 1 and all the definition were utilized for encourage assessments parameters.

Optimization of Gastro retentive floating tablets of Dexrabeprazole

Optimization of formulation carried out on the basis of OVAT (One variable at time) using amount of excipient used like Excipients like HPMC K4, HPMC K15, Carbopol 940 P, and PVP K30.

Table 1: Various formulations of Dexrabeprazole Gastroprotective tablets

Excipients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dexrabeprazole	10	10	10	10	10	10	10	10	10
HPMC K4	70	90	120	-	-	-	35	45	70
HPMC K15	-	-	-	70	90	120	35	45	70
Carbopol 940 P	-	-	-	-	-	-	10	10	10
PVP K30	20	20	20	20	20	20	20	20	20
Citric acid	5	5	5	5	5	5	5	5	5
$NaHCO_3$	10	10	10	10	10	10	10	10	10
$Mg(C_{18}H_{35}O_2)_2$	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Lactose	120	100	70	120	100	70	110	90	40
Total Weight	250	250	250	250	250	250	250	250	250

Evaluation of Precompression Parameter [6-7]

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated 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:-

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

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

$$\text{Housner's ratio} = \frac{\text{Tapped bulk density}}{\text{Loose Bulk density}}$$

Hausner's ratio value <1.25 shows better flow properties

Evaluation of tablets

All the tablets were evaluated for following various parameters which includes;

General Appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -).

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated [8].

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined [9]. The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of 0.1 N

HCl and made up to volume with of 0.1 N HCl. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at λ_{max} of 256 nm using of 0.1 N HCl as blank.

Hardness
For each formulation, the hardness of five tablets was resolved utilizing the Monsanto hardness tester.

Friability
The friability of a sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated [10].

Uniformity of weight
Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

***In vitro* buoyancy studies:**
In vitro buoyancy was determined by floating lag time as per the method described by Rosa *et al.* The tablets were separately in a 100 ml glass beaker containing simulated gastric fluid, pH 1.2 as per USP. The time necessary for the tablet to increase to the outside and float was determined as floating lag time [11].

Dissolution rate studies
In vitro drug release of the sample was done using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was set into the dissolution flask maintaining the temperature of 37±0.5°C and rpm of 75. One prepared Dexrabeprazole tablet was set in every container of dissolution apparatus. The mechanical assembly was permitted to keep running for 10 hours. Sample measuring 5 ml were pulled back after each 1 hour up to 10 hours using 10ml pipette. The new disintegration medium (37°C) was supplanted each time with a similar amount of the sample and takes the absorbance at 256nm using UV/Visible spectroscopy.

RESULTS AND DISCUSSION:

Different formulation of gastroretentive sustain release floating tablets containing Dexrabeprazole were prepared and evaluated for pre compression and post compression parameters. The loose bulk density (LBD) and Tapped bulk density (TBD) of the powders of different formulations were evaluated before the compression of powders in to tablets. The bulk density and the tapped density for all the formulations varied from 0.342 to 0.385gm/cm^3 and 0.458 to 0.485gm/cm^3 respectively.

The values obtained lies within the acceptable range. The difference exists between the bulk density and tapped density found to be very few. This result helps in calculating the % compressibility of the powder. The result of Hausner's ratio of all formulations ranges from 1.242 to 1.398. which indicates that the flow ability of all the formulation.

The results of the Compressibility index of all the formulations ranges from 24.156% to 39.769%. Results clearly showed that the flow ability of all the formulations was good and also the powder had good compressibility.

The thickness of the tablets was reported in the micrometer (mm).The thickness of tablet indicates that, die fill was uniform. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (250mg). The average weight of each formulation was recorded in shown in Table no 8.2. The value of thickness ranges between 3.1±0.2 to 3.4±0.2mm. Friability determines the strength of the tablets. The friability for all the formulations was below 1% indicating that the friability was within the prescribed limits. The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.652±0.032 to 0.774±0.014. The hardness value ranges from 6.1±0.2 to 6.5±0.1kg/cm^2.

Twenty tablets were randomly selected from each formulation and evaluated. The obtained data were almost uniform. The values of tablets average weight ranging from 243±5 to 258±7mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5% of the weight. The % drug content of all the formulated tablets were found within the limit. % drug content value of Dexrabeprazole was within 98.45±0.12% to 99.85±0.14%.The results within the range indicate uniform of mixing. The Table no 8.2 shows the % drug content in each formulation. The *in vitro* drug release was carried out for formulation (F1, F2, F3, F4, F5, F6, F7, F8 and F9 Formulation and release kinetics was calculated for optimized formulation F8. When the regression coefficient values of were compared, it was observed that 'r^2' values of higuchi was maximum i.e. 0.984 hence indicating drug release from formulations was found to follow higuchi release kinetics.

Table 2: Result of pre-compression properties of Dexrabeprazole

Formulation Code	Bulk density(gm/ml)	Tapped density(gm/ml)	Compressibility index	Hausner ratio
F1	0.345	0.465	34.783	1.348
F2	0.385	0.478	24.156	1.242
F3	0.374	0.482	28.877	1.289
F4	0.365	0.477	30.685	1.307
F5	0.347	0.485	39.769	1.398
F6	0.365	0.478	30.959	1.310
F7	0.342	0.458	33.918	1.339
F8	0.345	0.469	35.942	1.359
F9	0.365	0.478	30.959	1.310

Table 3: Results of post compression properties of Dexrabeprazole FGR tablets

Formulation code	Thickness (mm)	Hardness (kg/cm2) n=3	Weight variation (mg) n=3	Friability (%) n=3	Drug content (%) n=3	Total floating duration (h)
F1	3.1±0.2	6.1±0.2	255±4	0.658±0.025	98.45±0.12	>12
F2	3.2±0.1	6.2±0.3	245±5	0.652±0.032	98.65±0.25	>12
F3	3.3±0.3	6.3±0.2	258±6	0.698±0.041	98.74±0.12	>12
F4	3.2±0.1	6.4±0.1	243±5	0.754±0.032	98.65±0.32	>12
F5	3.2±0.2	6.5±0.1	246±8	0.698±0.014	99.12±0.14	>12
F6	3.3±0.3	6.2±0.2	247±4	0.685±0.025	98.85±0.25	>12
F7	3.4±0.2	6.1±0.1	252±5	0.674±0.032	98.87±0.32	>12
F8	3.3±0.1	6.1±0.2	250±6	0.712±0.025	99.85±0.14	>12
F9	3.4±0.2	6.2±0.2	258±7	0.774±0.014	99.12±0.15	>12

Table 4: Results of *in-vitro* buoyancy study of floating gastroretentive tablet

S. No.	Formulation Code	Floating lag times (sec)
1.	F1	68±2
2.	F2	62±5
3.	F3	63±6
4.	F4	55±4
5.	F5	45±5
6.	F6	43±6
7.	F7	45±4
8.	F8	35±7
9.	F9	49±3

Table 5: *In-vitro* drug release study of FGR tablets

Time	% Cumulative Drug Release								
(hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	35.65	32.45	29.98	36.65	32.25	29.98	25.65	18.54	13.25
1	45.65	41.74	35.65	48.85	42.21	39.95	35.45	22.25	28.85
1.5	55.65	53.32	48.85	52.12	55.65	45.58	43.32	36.65	33.36
2	78.85	69.98	65.12	69.98	65.25	62.25	55.65	48.85	45.58
3	89.98	82.32	78.85	88.12	85.65	78.85	69.98	65.45	53.32
4	98.12	89.98	83.32	98.65	98.45	87.98	78.28	73.32	65.54
6	-	98.14	91.12	-	98.85	90.25	93.32	85.65	73.32
8	-	-	98.85	-	-	99.45	98.85	92.45	79.98
12	-	-		-	-	-	-	99.12	85.65

Table 6: *In-vitro* drug release data for optimized formulation F8

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	18.54	1.268	81.46	1.911
1	1.000	0.000	22.25	1.347	77.75	1.891
1.5	1.225	0.176	36.65	1.564	63.35	1.802
2	1.414	0.301	48.85	1.689	51.15	1.709
3	1.732	0.477	65.45	1.816	34.55	1.538
4	2.000	0.602	73.32	1.865	26.68	1.426
6	2.449	0.778	85.65	1.933	14.35	1.157
8	2.828	0.903	92.45	1.966	7.55	0.878
12	3.464	1.079	99.12	1.996	0.88	-0.056

Table 7: Regression analysis data of Dexrabeprazole Floating sustain release tablets

Batch	Zero Order	First Order	Higuchi	Peppas
	R^2	R^2	R^2	R^2
F8	0.811	0.984	0.929	0.941

CONCLUSION:

In our study, our observation shows that the dexrabeprazole gastroretentive tablets extends the release rate of drug for a prolong period of time at least 12 hrs and shows to increase the bioavailability and simultaneously decrease the dosing interval. The

sustained release floating gastroretentive tablets of dexrabeprazole shown better, efficacy and potency.

REFERENCES:

1. Howard C. Ansel, NIcholos G. Popvich, lyold V. Allen, pharmaceutical dosage forms and Drug Delivery system. 1st ed.; 1995.p.78.4.
2. Jain N.K and Sharma S.N. A text book of professional pharmacy. 1st ed.; 1995.p.78.5.
3. Qiu Y, Zhang G, Wise DL. Handbook of Pharmaceutical Controlled Release Technology. New York: Marcell Dekker; 2000:465-503.
4. Kamboj S, Gupta GD. Matrix Tablets: An Important Tool for Oral Controlled-Release Dosage Forms, Pharmainfo.net.; 2009:7(6).
5. Vijay D. Gulkari, Suparna S. Bakhle, Leena S. Yelane. Development and evaluation of ofloxacin floating tablets using natural polymer: *Sterculia foetida* Linn. gum. International Journal of Pharmacy and Pharmaceutical Sciences. 2016; 8(5): 356-360.
6. Wasnik S, Parmar P, Singh D, Ram A. Preparation and characterization of floating drug delivery system of azithromycin. Acta Pol Pharm 2012; 69:515-22.
7. Kadivar A, Kamalidehghan B, Javar HA, Davoudi ET, Zaharuddin ND, Sabeti B, et al. Formulation and in vitro, in vivo evaluation of effervescent floating sustained release imatinib mesylate tablet. PLOS One 2015; 10: 1-23.
8. Rahim SA, Carter PA, Elkordy AA. Design and evaluation of effervescent floating tablets based on hydroxyethyl cellulose and sodium alginate using pentoxifylline as a model drug. Drug Des Dev Ther 2015; 9:1843-57.
9. Taghizadeh DE, Ibrahim NM, Kadivar A, Kamalidehghan B, Farjam AS, Akbari Javar H. Preparation and characterization of a gastric floating dosage form of capecitabine. Biomed Res Int 2013; 1-8. Doi.org/10.1155/2013/495319.
10. Pawar HA, Gharat PR, Dhavale RV, Joshi PR, Rakshit PP. Development and evaluation of gastroretentive are floating tablet of an antihypertensive drug using hydrogenated cottonseed oil. ISRN Pharm 2013; 1-9. Doi:10.1155/2013/137238.
11. Meka VS, Nali SR, Songa AS, Kolapalli VR. Characterization and in vitro drug release studies of natural polysaccharide *Terminalia Catappa* Gum (Badam Gum). AAPS PharmSciTech 2012; 13: 1451-64.