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DEVELOPMENT AND EVALUATION OF RABEPRAZOLE GASTRORETENTIVE DRUG DELIVERY SYSTEM

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Abstract:

The present study was undertaken with an aim to design, develop and evaluate floating tablet of Rabeprazole, which release the drug in a sustained manner over a period of 12 hours. In this resesrch work used hydroxy propyl methyl cellulose(HPMC K15M), gas generating agent sodium bicarbonate and citric acid. The high level of HPMC K15M and citric acid favors preparation of floating tablet Rabeprazole. The tablets were prepared by direct compression techniques and evaluated thickness, hardness, weight variation, friability, floating lag time and In-vitro drug release studies indicated that the floating dosage form showed slower release as concentration of HPMC K15M increases. Formulation F1 was considered as optimized formulation which shows sastisfactory sustained drug release and remained buoyant on the surface of medium for more than 12 hrours. It can also concluded that floating drug delivery system of Rabeprazole can be successfully formulated as an approach to increase gastric residence time and thereby improving its bioavailability.

Keywords: *Rabeprazole, Floating Drug Delivery, Citric acid, Buoyancy, Direct compression.*

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INTRODUCTION: [1-6]

Floating system, first described by Davis in 1968, have bulk density lower than that of the gastric fluid, and thus remain buoyant in stomach for a prolonged period .While the system is floating on the gastric content ,the drug is released slowly at desired rate .this result in an increase in the GIT and a better control of fluctuations in the plasma drug concentration .Oral route is the most convenient and extensively used route for drug administration .This route has high patient acceptability ,primarily due to ease of administration .Over the years , oral dosage forms have become increasingly sophisticated with major role being played by controlled release drug delivery system. CRDDS release drug at a predetermined rate, as determined by drug pharmacokinetics and desired therapeutic concentration. This helps in achieving predictable drug plasma concentration required for therapeutic effect.

MATERIALS AND METHODS:

Materials and Instruments

Table no. 1: List of Materials.

Sr. No.	Materials	Procured from
1	Rabeprazole	Gift sample from Aristo chem. Mumbai
2	HPMC K4M	Colorcon Asia, Goa. Ltd.
3	HPMCK100M	Colorcon Asia, Goa. Ltd
4	HPMCK15M	Colorcon Asia, Goa. Ltd.
5	Sod.bicarbonate.	S.D Fine Chemicals, Mumbai.
6	Citric Acid	S.D Fine Chemicals, Mumbai
7	Lactose	S.D Fine Chemicals, Mumbai.
8	Talc	S.D Fine Chemicals, Mumbai.
9	Mg. Stearate	S.D Fine Chemicals, Mumbai

Table no. 2: List OF Instruments.

Sr. No.	Instruments	Name of company
1	Tablet compression machine	Karnavati Rimek Mini press1
2	Electronic Weighing Balance	Citizen
3	Tablet Dissolution Tester	Electro lab 8 station
4	UV/vis double beam Spectrophotometer	Shimadzu 1800 Japan
5	Friability test apparatus	Lab line
6	Tablet Hardness Tester	Monsanto/ Pfizer
7	Thickness	Screw gauge

EXPERIMENTAL DATA

Preformulation Studies:

It is extensive information to bring out good quality at high standard at which optimal dosage desired. Preformulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Solubility Studies:

Rabeprazole is slightly soluble in water, very slightly soluble in methanol, freely soluble in dichloromethane, practically insoluble in hexane, The Solubility studies were performed by taking 1gm Rabeprazole in 10ml solvent.

Determination of Melting Point:

Melting point of Rabeprazole was determined by capillary method. Fine powder of Rabeprazole was filled in glass capillary tube (previously sealed on one end). The melting point is determined by using digital melting point apparatus.

Compatibility studies:

By FTIR spectroscopy:

Compatibility with excipients was confirmed by carrying out IR studies. The pure drug and its formulations with excipients were subjected to IR studies. In the present study, the potassium bromide disc (pellet) method was employed.

Estimation of Rabeprazole:

Determination of λ Max of Rabeprazole in 0.1N Hcl.

The Scanning of Rabeprazole using 0.1N HCL.A solution of Rabeprazole containing the concentration 100µg/ ml was prepared in 0.1 N HCl and UV spectrum was taken using Shimadzu 1800 UV/Vis

double beam spectrophotometer. The solution was scanned in the range of 200 – 400.

Standard Curve:
A stock solution of Rabeprazole (100µg/ml) was prepared in 0.1N HCL. The UV spectrum was recorded 284 nm. The solutions of 2-10 µg/ml were prepared from stock solution by appropriate dilution with 0.1 N Hcl. The absorbance of each of solution was recorded using Shimadzu-1800 at wavelength of maximum absorption.

Preparation of pH 1.2 Buffer Solution (Simulated Gastric Fluid):
8.5 ml of hydrochloric acid solution was added and made up to the volume to 1000ml.

Primary Stock Solution:
10mg of Rabeprazole was accurately weighed and dissolved in pH 1.2 buffers and then made up to 100 ml a concentration of 100 µg/ml.

Sample Solution:
From the Primary stock solution aliquots ranging from 0.2 to 1ml were pipette out and diluted to 10ml with buffer to get the concentration of 02-10µg/ml. The absorbance was measured at 284nm against blank. A standard graph was plotted by keeping the known concentration on x-axis and obtained absorbance on y-axis.

Formulation and Development of Rabeprazole [7]:
Floating tablets containing Rabeprazole were prepared by wet granulation technique using varying concentrations of polymer with sodium bicarbonate. Polymer and Rabeprazole were mixed homogeneously using glass mortar and pestle. Isopropyl alcohol was used as granulating agent. Granules were prepared by passing the wet coherent mass through a # 16 sieve. The granules were dried in hot air oven at a temperature of 45^0c. Dried granules were sieved through # 40 sieves and lubricated with magnesium stearate and talc just 4-5 min before compression. Lubricated granules were compressed into tablets by using 10 station rotary tablet machine 13 mm flat round Karnavati Minipress tablet machine.

Table no. 3: Composition of Rabeprazole floating tablets [4]

Ingredients(mg.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Rabeprazole	20	20	20	20	20	20	20	20	20
HPMCK4M	60	65	70	_	_	_	_	_	_
HPMCK15M	_	_	_	60	65	70	_	_	_
HPMCK100M	_	_	_	_	_	_	60	65	70
Sod.bicarbonate	40	40	40	40	40	40	40	40	40
Citric Acid	2	2	2	2	2	2	2	2	2
Lactose	20	15	10	20	15	10	20	15	10
Talc	3	3	3	3	3	3	3	3	3
Mg. Stearate.	5	5	5	5	5	5	5	5	5
Total Wt .(mg)	150	150	150	150	150	150	150	150	150

Pre-compression Evaluation [7]
Angle of Repose [7]:-
The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan\theta = \frac{h}{r}$$

Where,
h= height of the powder cone and r= radius of the powder cone.

Table no. 4:Standard values of angle of repose

Angle of repose	Flow property
25^0-30^0	Good
37^0-40^0	Fair
Beyond 40^0	Poor

Bulk density:-

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations.

$$LBD = \frac{\text{Weight of powder blend}}{\text{Untapped volume of the packing}}$$

$$TBD = \frac{\text{Weight of powder blend}}{\text{Tapped Volume of the packing}}$$

Compressibility index:-

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

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

Hausner's ratio (HR):-

This was calculated as the ratio of tapped density to bulk density of the sample

$$HR = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Post-Compression Evaluation of Rabeprazole Floating Tablets [7,8]'

Weight variation test:

To study weight variation twenty tablets of the formulation were weighed using a citizen electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

$$\text{Percentage Deviation PD} = \frac{WAvg - WInitial}{WAvg}$$

Where,

WAvg = average weight and
WInitial =initial weight.

Table no. 5: Standards for uniformity of weight as per I.P.

Avg. wt. of tablet	% Deviation
80 mg or < 80mg	10
> 80mg to < 250 mg	7.5
> 250mg or more	5

Uniformity of Drug content:-

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1N HCl, the drug content was determined measuring the absorbance at 284 nm after suitable dilution using a Simadzu UV- Visible double beam spectrophotometer 1800.

Hardness:-

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

Thickness:-

The thickness of the tablets was determined by using Vernier calipers. Five tablets were used, and average value was calculated.

Friability Test:-

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into Friabilator. The Friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again. The % friability was then calculated by-

$$\text{Percentage Friability} = \frac{W_0 - W}{W} \times 100$$

Where,

W0= initially weight
W= weight after friability

Percentages Friability of tablets less than 1% are considered acceptable.

In *vitro* buoyancy studies [7]

The in vitro buoyancy was determined by floating lag time method described by Dave B.S. The tablets were placed in 100ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT)

In *Vitro* drug release studies [7]

The release rate from floating tablets was determined using The United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5°C and 100 rpm. A sample (5ml) of

the solution was withdrawn from the dissolution apparatus hourly for 24h, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 284nm using a Simadzu UV-Vis double beam spectrophotometer 1800. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve.

Swelling index of Rabeprazole floating tablets [7]

The swelling index of tablets was determined by using 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

$$\text{Swelling index (SI)} = \frac{Wt - Wo}{Wo} \times 100$$

Where,

Wt = Weight of tablet at time t.

W0 = Initial weight of tablet

Drug release kinetics of Rabeprazole floating tablets [3]

To analyze the mechanism of drug release and release rate kinetics from the dosage form, the data obtained were fitted into zero order, first order, Higuchi release and Korsmeyer and Peppas release model using Graph Pad Prism 5.0 software, which is specially meant for curve fitting and statistical data analysis.

Zero-Order release kinetics

To studies the zero-order releases kinetics the release rate data are fitted to the fallowing equation.

$$F = k.t \quad \ldots\ldots (1)$$

Where, 'F' is the fraction of drug release, 'K' is the release rate constant and't' is the release Time.

First – order release kinetics

To study the first-order release kinetics the release rate data are fitted to the fallowing equation.

$$F = 100 \times (1 - e^{-kt}) \quad \ldots\ldots (2)$$

Where, 'F' is the fraction of drug release, 'K' is the release rate constant, 'e' is exponent Coefficient and t is the release time.

Higuchi release model

To study the Higuchi release model the release rate data are fitted to the fallowing equation.

$$F = K.t^{1/2} \quad \ldots\ldots (3)$$

Where,

F' is the fraction of drug release and 'K' is the release rate constant

Korsmeyer and Peppas release model

To study the Korsmeyer and Peppas release model the release rate data are fitted to the fallowing equation.

$$\frac{Mt}{M\infty} = K.t^n \quad \ldots\ldots (4)$$

Where,

Mt/M∞ is the fraction of drug release

' n' is the diffusional exponent for the drug release that is dependent on the shape of the Matrix dosage form.

RESULT:

Pre- formulation study of Rabeprazole:-

Description:

Colour-Yellowish; State- Solid; Odour-bitter.

Melting point:

Melting point of Rabeprazole was found to be 100^0c.

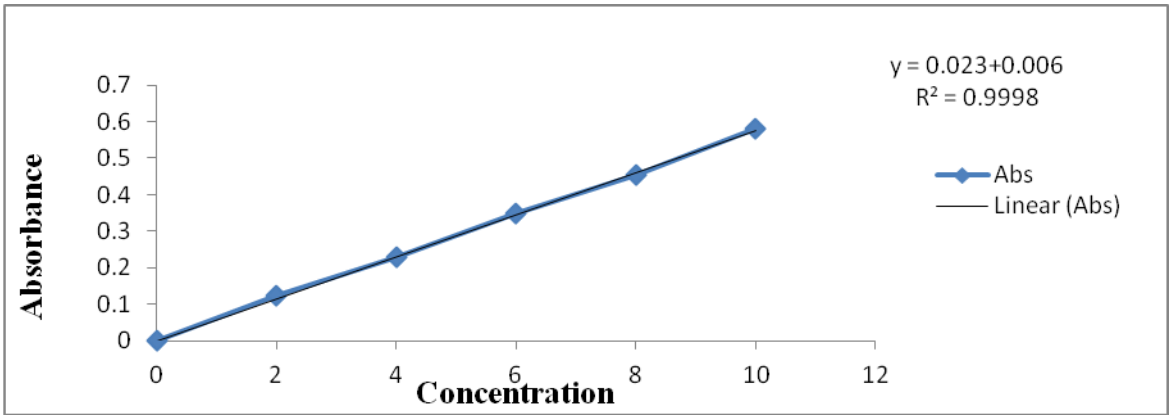
Solubility:

It is freely soluble in distilled water, methanol, ethanol.

Calibration Curve of Rabeprazole:-

Table no. 6: Calibration Curve of Rabeprazole in 0.1 N HCl (Buffer pH 1.2)

Sr. No.	Concentration(µg/ml)	Absorbance at 284 nm.
1	0	0.000
2	2	0.044
3	4	0.089
4	6	0.140
5	8	0.185
6	10	0.232



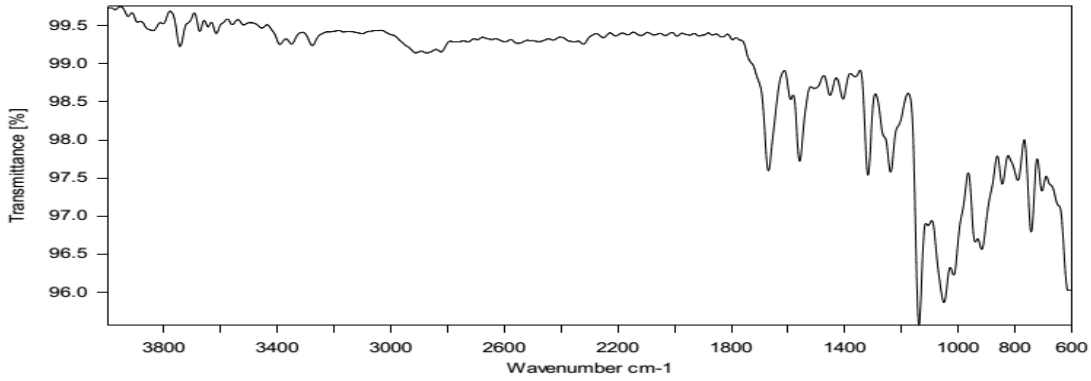
Calibration Curve of Rabeprazole in 0.1 N HCl (Buffer of pH 1.2) at 284 nm.

Table no. 7: Various Constants for Calibration Curves.

Parameters	Value for calibration curve in HCL
Slope	0.023
Intercept	0.006
R^2	0.999

Excipients Compatibility Studies:-

FTIR Study



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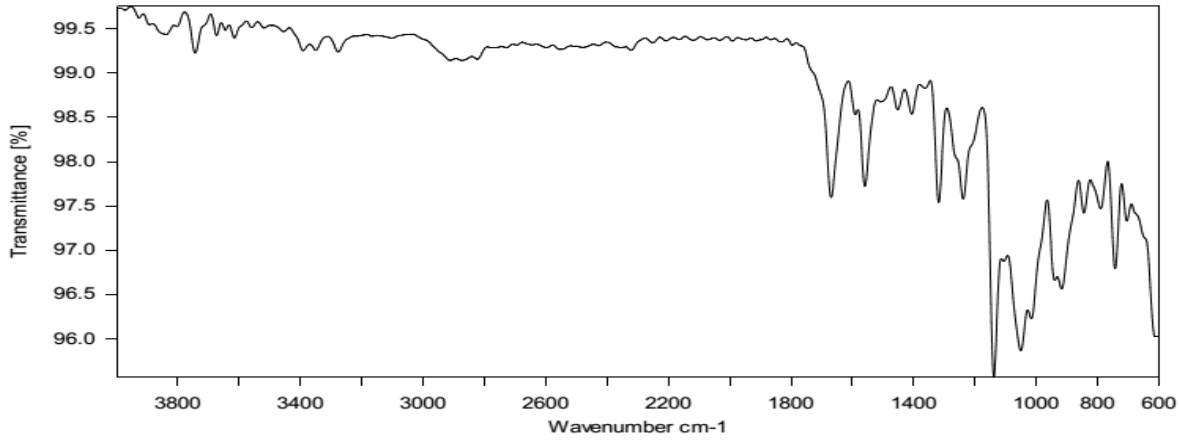
FTIR Spectra of Rabeprazole



FTIR Spectra of Rabeprazole and Excipient

Data obtained from FTIR Spectra:-

Table no. 8: Interpretation of FTIR Spectra.

Sr. No	Functional Group	Standard Value	Obtained Value
1	C=C group	1600-1475 cm^{-1}	1474cm^{-1}
2	C-N group	1350-1000 cm^{-1}	1091cm^{-1}
3	C-O group	1000-1300 cm^{-1}	1008 cm^{-1}
4	S=O group	1050 cm^{-1}	1049 cm^{-1}
5	C-H group	2850-3000 cm^{-1}	2922.57 cm^{-1}
6	N-H group	3300-3500 cm^{-1}	3428.18 cm^{-1}

Pre-Compression Evaluations Parameters.

Table no. 9:Flow properties of granules prepared by different techniques:

Batch Code	Angle of repose (θ)	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Hausner's ratio (HR)	Carr's index (CI)
FT-1	27·44±0.13	0.523±0.062	0.680±0.014	1.27±0.034	16.77±0.04
FT-2	28.18±0.20	0.458±0.052	0.652±0.053	1.05±0.073	17.50±0. 51
FT-3	24.77±0.19	0.474±0.053	0.524±0.062	1.08±0.033	21.88±0.65
FT-4	25.68±0.13	0.464±0.017	0.565±0.017	1.13±0.061	16.82±0.56
FT-5	24.27±0.28	0.443±0.014	0.456±0.023	1.26±0.045	19.01±0.42
FT-6	26.56±0.16	0.525±0.031	0.552±0.031	1.12±0.034	21.85±0.09
FT-7	27.50±0.90	0.558±0.012	0.487±0.019	1.18±0.055	10.90±0.23
FT-8	25.72±0.15	0.448±0.018	0.488±0.073	1.07±0.029	13.77±0.45
FT-9	23.75±0.89	0.430±0.018	0.0545±0.054	1.10±0.026	12.56±0.24

Post-Compression Evaluations Parameters.

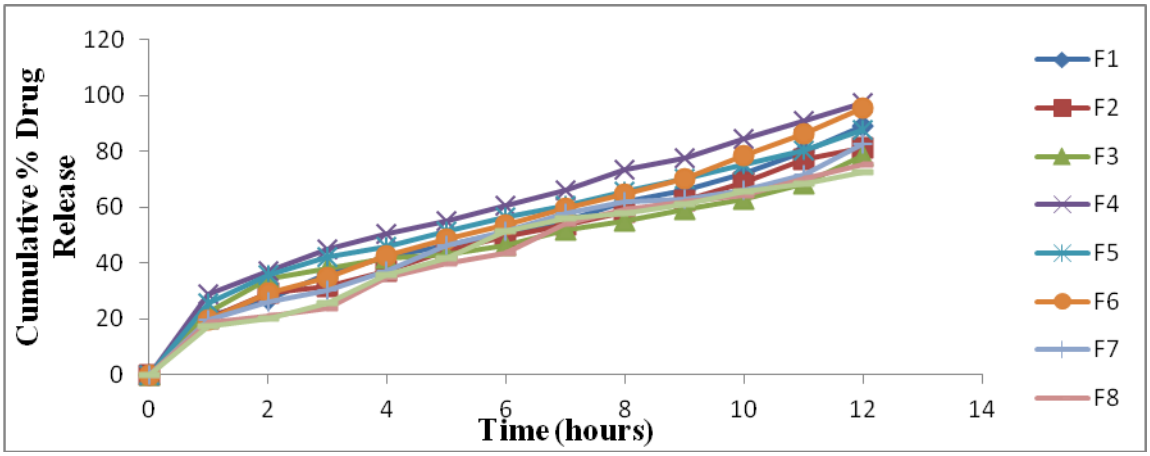
Table no. 10:Post-Compression Evaluation Parameters.

Batch Code	Weight variation Average wt in (mg) ±SD	Hardness (kg/cm2) ±SD	Thickness (mm) ±SD	Friability (%)	Drug Content Uniformity (%)±SD
FT-1	150±3.19	5.2±0.20	4.3±0.11	0.718	97.33±1.15
FT-2	150±3.21	5.4±0.20	5.2±0.12	0.832	96.00±1.73
FT-3	150±2.27	5.5±0.10	6.3±0.17	0.804	97.00±1.00
FT-4	150±3.06	5.7±0.15	5.2±0.20	0.852	97.00±1.00
FT-5	150±2.57	5.8±0.11	6.1±0.18	0.822	97.00±1.73
FT-6	150±3.37	5.8±0.05	6.4±0.10	0.934	97.00±2.64
FT-7	150±2.75	5.6±0.17	5.4±0.13	0.703	96.33±1.15
FT-8	150±2.58	5.6±0.20	6.2±0.15	0.815	97.66±2.30
FT-9	150±2.76	5.7±0.17	6.7±0.19	0.914	95.66±2.08

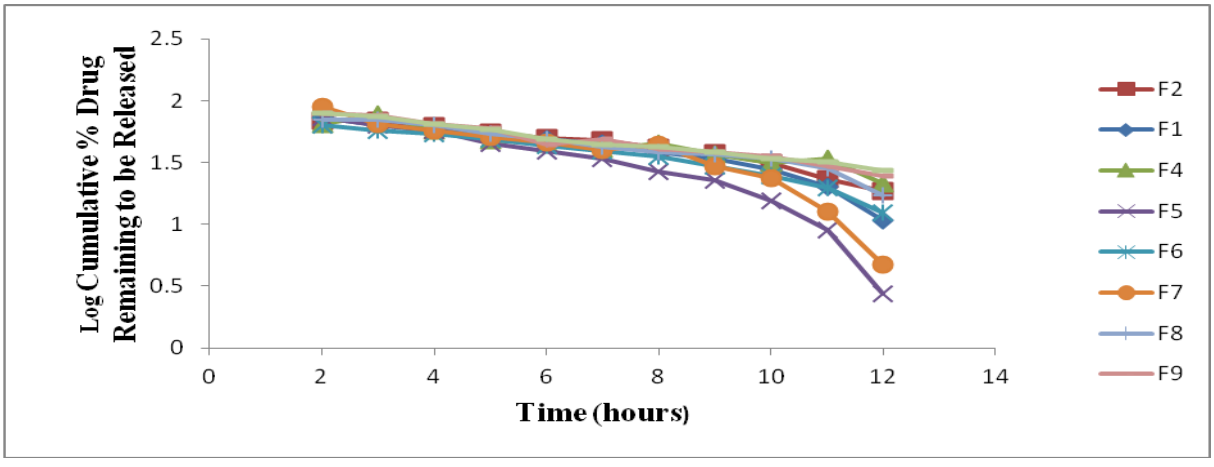
***In-vitro* Drug Release Studies:**

Table no. 11: *In-Vitro* Drug Data Batches F1-F9.

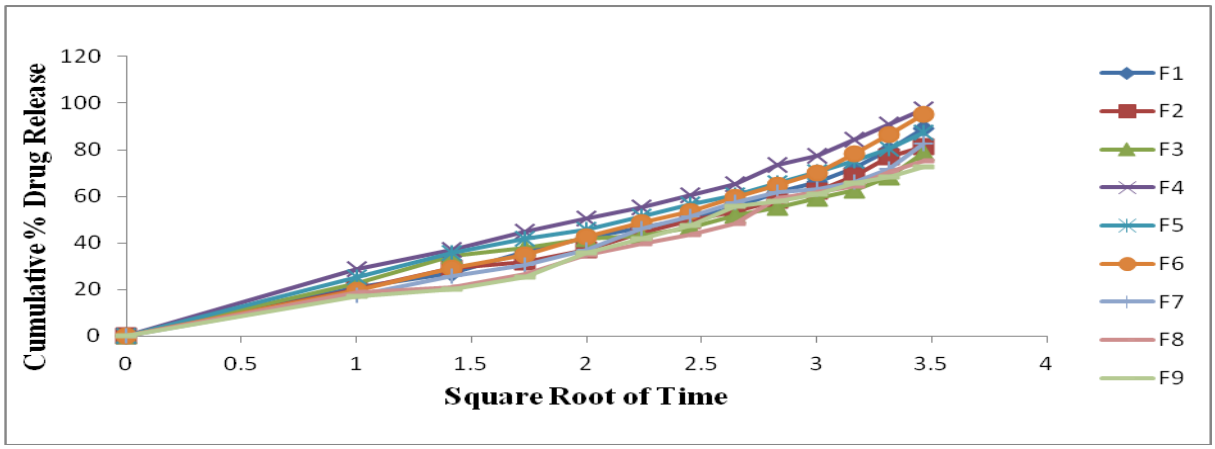
Time (Hours)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1	21.128	20.217	22.608	28.782	25.436	19.673	19.565	18.695	17.133
2	27.127	29.339	34.565	36.923	35.912	29.215	25.869	21.085	20.000
3	36.304	31.635	37.826	44.787	41.956	35.041	30.434	23.695	25.434
4	42.173	37.211	41.739	50.531	45.717	42.724	36.956	34.78	35.652
5	46.434	44.35	43.26	55.175	51.304	48.695	46.086	39.782	41.739
6	50.695	49.651	46.521	60.68	56.478	53.735	51.521	43.43	51.304
7	55.217	53.552	51.956	66.134	60.704	59.824	57.605	54.347	55.869
8	61.95	58.154	55.217	73.335	65.645	64.678	61.869	59.347	57.826
9	66.086	62.336	59.347	77.425	70.356	70.167	63.043	61.739	61.086
10	72.173	68.687	62.826	84.543	75.174	78.345	66.086	64.347	65.652
11	79.826	76.956	68.26	90.756	80.39	86.456	71.739	70.434	68.26
12	89.173	81.304	78.695	97.234	87.608	95.307	82.826	75.217	72.608



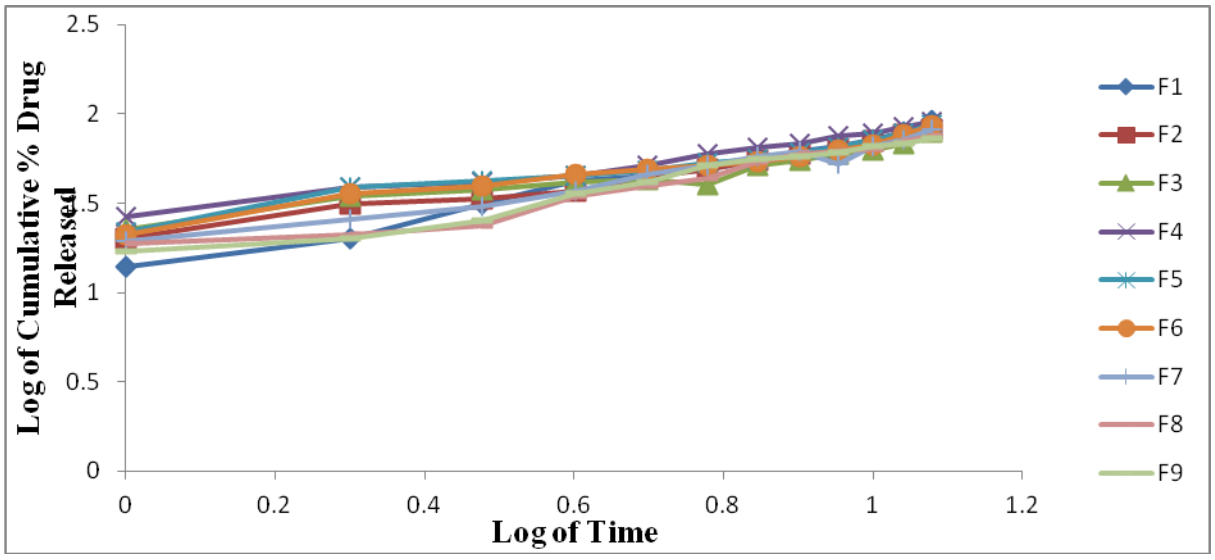
Comparative *In-vitro* Release Profile of Rabeprazole Tablet According to Zero Order Kinetics for Formulation F1-F9



Comparative In-vitro Release Profile of Rabeprazole Tablet According to First Order Kinetics for Formulations F1-F9



Comparative In-vitro Release Profile of Rabeprazole Tablet According to Higuchi Matrix Kinetics for Formulations F1-F9.



Comparative In-vitro Release Profile of Rabeprazole Tablet According to Korsmeyer- Peppas Kinetics for Formulations F1-F9

***In-vitro* buoyancy study:-**

Table no. 12: Floating Properties of Rabeprazole Floating tablets.

Formulation	Floating Lag Time (seconds)	Matrix Integrity	Floating Duration (hours)
F1	40	✓	> 12
`F2	60	✓	> 12
F3	44	✓	> 12
F4	48	✓	> 12
F5	55	✓	> 12
F6	57	✓	> 12
F7	50	✓	> 12
F8	62	✓	> 12
F9	55	✓	> 12

Kinetic Data

Table no. 13:Drug Release Kinetic Model

Formulation Code	Zero Order (R^2)	First order (R^2)	Higuchi Matrix Model (R^2)	Korsmeyer Peppas Model (R^2)	Best Fit Model
F1	0.9967	0.8556	0.9295	0.9878	Zero order
F2	0.9198	0.9799	0.9916	0.9916	Korsmeyer- Peppas
F3	0.8228	0.9615	0.9923	0.9898	Hiuchi Matrix
F4	0.8534	0.9686	0.9899	0.9665	Higuchi Matrix
F5	0.9734	0.7923	0.9734	0.9576	Korsmeyer-Peppas
F6	0.7614	0.9491	0.9864	0.9858	Matrix
F7	0.9491	0.9352	0.9770	0.9864	Peppas
F8	0.9531	0.9950	0.9849	0.9915	1st Order
F9	0.9427	0.9943	0.9886	0.9940	1st Order

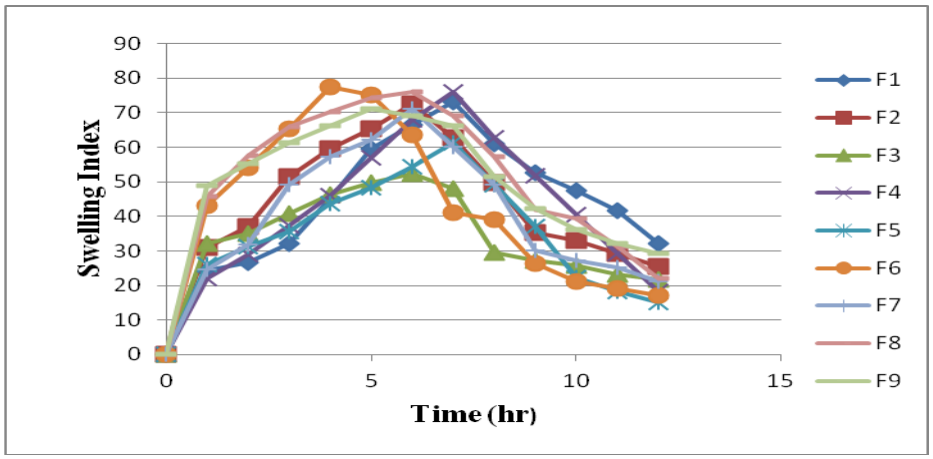
Table no. 14: Interpretation of diffusion release mechanisms.

Sr. No.	Release exponent	Drug transport mechanism
1	0.5	Fickian diffusion
2	0.5 < n < 1	Anomalous (Non-Fickian)Transport
3	1.0	Case II Transport
4	Higher than 1.0	Super case II transport

Swelling Index Study (Water uptake study)

Table no. 15: Swelling Characeristics (Water uptake Study)

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	24.32	31.04	32.21	22.06	26.03	43.01	24.49	45.65	48.87
2	26.52	37.06	34.95	28.96	31.25	54.05	31.77	57.47	55.11
3	32.05	51.49	40.78	37.38	35.73	65.25	49.15	66.07	61.24
4	45.07	59.55	46.37	46.02	43.66	77.51	57.23	70.22	66.21
5	59.51	65.23	49.65	56.92	48.22	75.23	62.12	74.18	71.22
6	66.51	72.55	52.33	67.94	54.30	63.51	71.23	76.19	69.19
7	73.21	62.7	48.06	75.97	61.32	41.23	60.22	69.23	66.13
8	60.96	49.9	29.60	62.85	49.23	39.12	49.12	57.18	51.41
9	52.66	35.38	27.33	51.78	37.12	26.23	30.12	42.03	42.13
10	47.55	32.96	25.72	40.49	22.21	21.12	27.23	39.28	36.23
11	41.61	29.14	23.13	29.22	18.18	19.12	25.12	31.22	32.24
12	32.22	25.49	21.74	18.21	15.16	17.11	21.21	22.01	29.25



Relationship between swelling index and time

DISCUSSION:

In the present study, GFDDS of Rabeprazole were prepared by using polymer hydroxy propyl methyl cellulose (HPMC K15M), and using sodium bicarbonate as gas generating agent and Lactose as binder. GFDDS tablets were prepared by wet granulation technique. Formulation was optimized by using different ratios of polymers and lactose. The prepared GFDDS tablets were evaluated for its hardness, friability, uniformity of weight, uniformity of drug content, drug-polymer interaction studies, in vitro floating studies, and in vitro dissolution studies.

Preformulation Studies:

Melting Point Determination:

Melting point of Rabeprazole was determined by capillary method. The melting point of Rabeprazole was found to be in the range 99-100 ^{0} C, which complied with IP standards, indicating purity of the drug sample.

Solubility:

Rabeprazole very soluble in water, methanol, freely soluble in dichloromethane, and practically insoluble in hexane.

Compatibility studies:

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymers were studied. Drug-excipients interactions play a vital role with respect to release of drug from the formulation amongst others. FTIR techniques have been used here to study the physical and chemical interaction between drug and excipients used. In the present study, it has been observed that there is no chemical interaction between Rabeprazole and the polymer used. It was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers. The peaks obtained in the spectra's of each polymer correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components.

Standard Calibration Curve of Rabeprazole:-

The scanning of drug solution in UV region (200–400 nm) to find out the wavelength of maximum absorption (λ max). The λ max was found to be at 284nm. So the Standard calibration curve of Rabeprazole was developed at these wavelengths. The calibration curve was linear between 02-10µg/ml concentration ranges. The standard calibration curve of Amoxicillin trihydrate was determined in 0.1N HCl, by plotting absorbance against concentration at 284 nm; The R^2 were found to be 0.999 in 0.1 N HCl.

Angle of Repose (θ):

The angle of repose for the formulated blend was carried out and the results were shown in table. It concludes all the formulations blend was found to be in the range 23.75±0.89 to 28.18±0.20. The lower angle of repose 23.75±0.89 was shown by formulation F9. Formulation containing HPMC K15M showed good angle of repose.

Compressibility Index:

Carr's index below 15 % usually shows good flow characteristics, but above 25% indicate poor Flowability. Compressibility index was carried out, it found between 10.90% and 21.88% indicating the powder blend has the required flow property for compression.

Hausner's Ratio:

Hausner's ratio is simple method to evaluate stability of powder column and to estimate flow properties. Low range was observed for Hausner's ratio that indicates good flow ability. Many different types of angular properties have been employed to assess Flowability. The Hausner's ratio was found between

1.05 and 1.27.All formulation showed acceptable flow properties.

EVALUATION OF TABLETS

Tablet dimensions:-

The thickness of the tablet is depends upon the diameter of die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material and the force applied during compression.

Hardness and friability:

Thus, the tablets found to be of good tensile strength to withstand the handling stress without break. Tablets hardness is a determining factor, with regard to the buoyancy of the tablets. Tablet hardness reflects differences in tablet density and porosity, which are supposed to result in difference release patterns of the drug by affecting the rate of penetration of the dissolution fluid at the surface of the tablet. The hardness of the prepared GFDDS of Rabeprazole was found to be in the range of 5.2 to 5.8 kg/cm^2. It ensures that the tablets can withstand mechanical impacts during packing, transportation and other processing operations. The present study of tablets is in within the limit and the slight variation in friability because of the variation in compression force applied and its total weight. The friability of tablets is also depends on moisture contents in it. The friability of all the tablets was to be less than 1% i.e. in the range of 0.718 to 0.934 % .

Uniformity of weight:

All the prepared GFDDS tablets were evaluated for weight variation. The percent deviation from the average weight was found to be within the prescribed official limits.

Uniformity of drug content:

The drug content uniformity was examined as per I.P specification. All the batches of tablets were found to comply with uniformity of content test and results are mentioned. Drug content was in range of 95.66±2.08to 97.66±2.30 in the prepared formulation.

Tablet density:

When tablet contacts the test medium, tablet expanded (because of swellable polymers) and there was liberation of CO2 gas (because of effervescent agent NaHCO3). The density decreased due to this expansion and upward force of CO2 gas generation. This plays an important role in ensuring the floating capability of the dosage form. To provide good floating behavior in the stomach, the density of the tablets should be less than that of the gastric contents the density below (1.004g/cm3) than of gastric fluid. For formulation F1-F9 density were found to be less than that of the gastric content.

In vitro Buoyancy:

The gas generated is trapped and protected within the gel, formed by hydration of polymer, thus decreasing the density of the tablet. As the density of the tablet falls below 1, the tablet became buoyant. reveled that HPMC K15M produced tablets with good gel strength, entrapping CO_2 gas and imparting stable and persistent buoyancy. Floating lag time was in range of 40 sec to 62sec.

All the factorial design batches showed good *in vitro* buoyancy, also the tablet remained buoyant for 12 hours, but the tablet actually floated throughout the entire study. The above photograph of in vitro buoyancy study the optimized batch F4 tablet at initial 0 min seen at the bottom of beaker, at the 48 sec the tablet was seen at center of the beaker that is the floating lag time and at 1 min the tablet was seen at surface of the beaker.

Swelling Study:

The swelling indexes of batches F1 to F9 . Polymer matrices representing swellable matrix drug delivery systems are porous in nature. When these matrices come in contact with water or aqueous gastrointestinal fluid, the polymer absorbs the water and undergoes swelling or hydration. The rapid formation of a viscous gel layer upon hydration suggests that swelling is associated with polymer chain relaxation with volume expansion. The liquid diffuses through the polymer matrix at a constant velocity, and the rate of diffusion of the liquid and that of macromolecular relaxation of the polymer are almost of the same magnitude or, possibly, the rate of diffusion of the liquid is relatively higher than that of relaxation of the polymer segment.

This mechanism gives the idea regarding the water uptake study of various grades of polymer. This phenomenon is attributes to that the swelling is more due to water uptake and then gradually decreased due to erosion. Swelling measurement was performed separately in order to collect on the basis of weight increase over time. The swelling is due to presence of hydrophilic polymer, which gets wetted and allows water uptake leads to increase in its weight.

The swelling index was calculated with respect to time. As time increase, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration. Later on, it decreased gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The direct relationship was observed between swelling index and HPMC K15M increase, swelling index was increased.

In vitro dissolution study:

Besides the satisfactory buoyancy, the matrix tablets are required to release Rabeprazole gradually over prolonged period. Hence, they were tested for release kinetics by conducting in-vitro dissolution test.

The results obtaining in In-Vitro release studies were plotted in different model of data treatment as follows:

- Cumulative percent drug released vs. time (zero order kinetics)
- Log Cumulative percent drug retained vs. time (First order rate kinetics)
- Log Cumulative percent drug released vs. square root of time (Higuchi's classical diffusion equation)
- Log Cumulative percent drug released vs. log time (Peppas Exponential equation)

Dissolution data of batch F1 to F9, From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling, and drug diffusion. It was observed that all the tablets ascended to the upper one third of the dissolution vessels within a short time, and remained floated until the complete of release studies. The drug release study was carried out up to 12 hrs. The percentage drug release from batch F1 to F9 vary from 97.282 to 72.362 % because of increase in concentration of polymer (HPMC K15M). High drug release is observed in F4 batch because of low concentration of polymer (HPMC K15M). Large concentration of high viscosity polymer induces the formation of strong viscous gel layer that slowed down the rate of water diffusion into the tablet matrix, which may result in the retardation or decreases the drug release. Being water soluble polymers, they dissolve and form pores filled liquid in which drug can there after diffuse in dissolution medium. All the formulations were designed as dosage form for 12 hrs.

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling and drug diffusion.

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