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Research Article

Design, Development and Evaluation of Gastroretentive Drug Delivery System of Antacids

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Abstract

Magaldrate is an antacid have been widely used in the treatment of various gastric and duodenal disorders such as heartburn, reflux esophagitis, acid indigestion, gastritis, sour stomach, upset stomach, irritable stomach, gastric and duodenal ulcers. The conventional antacids dosage forms have a short duration of action which is about 2-3 hours due to gastric emptying process. A gastroretentive dosage form of antacid is needed since the healing of gastric ulcers occurs when gastric pH is kept above 3-4 during 24 hours. The present study was aimed at developing Gastro retentive bilayer drug delivery systems containing Magaldrate to minimize the side effect, improve the prolongation of action, to reduce the frequency of drug administration. A wet granulation technique was used to formulate 9 batches. Superdisintegrants like Polyplasdone XL-10, Ac-Di-Sol, and sodium starch glycolate was used for immediate release layer and HPMC K4 M, Ac-Di-Sol and lactose like polymers were used in floating layer. Preformulation studies were carried out to optimize the ratios required for various grades of polymers. The prepared floating tablets were evaluated for hardness, weight variation, thickness, friability, drug content uniformity, buoyancy lag time, total floating time, water uptake (swelling index), and *in vitro* dissolution studies. Successful formulation was developed having floating lag time as low as 30 sec and drug release was sustained up to 12 hrs. A biphasic drug release can be obtained by using bilayer tableting technology which involved compression of immediate and sustained release layer together. Bilayered floating tablets with release characteristics offer critical advantages such as, site specificity with improved absorption and efficacy. This technology can be inculcated to various medicaments which have stomach as the major site of absorption.

Keywords: Magaldrate, Antacid, Gastroretentive dosage form, Bilayer floating tab, Superdisintegrant

INTRODUCTION

The major disease of the stomach and duodenum are gastritis, gastric ulcer, duodenitis, and duodenal ulcer, all of which are in some way related to gastritis with injury that is mediated by acid[1]. The normal pH of the stomach is 1.2 to 1.8. During most of the day, the food stimulates the acid secretion also neutralizes it, keeping the pH between 3 and 5. However, when the stomach is empty, approximately 2 to 3 hr after eating, then the pH again drop, and ulcer patients tend to suffer pain that is relieved by consuming antacids. In general, pain only occurs when the pH is below 2[1-3]. Antacids are used widely for the relief of heartburn and dyspepsia, as well as a large variety of nonspecific gastrointestinal symptoms. The primary role of antacids in the management of peptic acid disorders is to relief pain. Another action of antacids is to prevent the conversion of gastric pepsinogen to pepsin, the active form. This is a proteolytic enzyme thought to mediate tissue injury in ulcer disease[3]. Conventional dosage form of antacids has a short duration due to the short residence time. Conventional dosage form of antacids is cleared from the empty stomach in 30 minutes due to the regulary gastric emptying. If administered while food is in the stomach, the buffering action will last for 2 hours. An additional dose 3 hours after meals will extend the buffering time by 1 hour[3, 4]. The ideal antacid should be rapid in onset and provide a continuous buffering action. The duration of buffering action is determined largely by when the antacid is administered. Healing of the peptic acid diseases occurs when the mean 24-h pH is kept above 3 to 4. The pH can be increased by either neutralizing acid (antacids) or inhibiting gastric secretion (H2-reseptor antagonists or proton pump inhibitors) [3]. Oral route is considered as the most promising route for drug delivery[5]. Development of oral controlled release systems has been a challenge to formulation scientists because of the difficulty in localizing the system in target areas of the gastrointestinal tract[6]. The real challenge in the development of an oral controlled-release drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form within the gastrointestinal tract (GIT) until all the drug is completely released at the desired period of time[7]. One of the novel approaches in the area of oral sustained release drug delivery is gastro retentive drug delivery system[8]. GRDDS can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems

help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability[9]. Extended-release dosage forms with prolonged residence time in the stomach are highly desirable for drugs with i) narrow absorption windows, ii) stability problems in the intestinal or colonic environment, iii) local action in the stomach and iv) low solubility at high pH values[10]. The biphasic system is used mostly when maximum relief needs to be achieved quickly and it is followed by a sustained release phase. It also avoids repeated administration of drug. Coronary vasodilator, antihypertensive, antihistaminic, analgesic, antipyretics and antiallergenic agents are mainly used for this system. Bilayer tablet is new era for developing a combination of two or more active pharmaceutical ingredient in single dosage form, Promoting patient convenience and compliance. Dual release tablet is a unit compressed tablet dosage form intended for oral application. It contains two layers in which one layer having conventional or immediate release part of single or multiple actives; another layer is sustained or controlled release part of single or multiple actives. They are also called as multi-layer matrix tablet. Bi-layer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose[11]. The current investigation aims at the development of gastroretentive bilayer floating tablets with different release patterns of Magaldrate. It was further planned to use optimization software for optimization of floating layer. Factorial design was planned to use for optimization. Two level factorial design having three independent and three response variable were selected for the studies.

MATERIALS AND METHODS

Magaldrate was gifted by Aurobindo Pharma Limited, Hyderabad A.P, India. HPMC K4M, Ac-Di-Sol and lactose was obtained from Mapromax, Life sciences Pvt. Ltd. Dehradun. Polyplasdone XL-10 and sodium starch glycolate obtained from Danmed Pharmaceuticals Pvt Ltd, Hyderabad. Sodium bicarbonate, magnesium stearate and Aerosil were obtained from Loba Chemical Pvt Ltd (Mumbai, India). Hydrochloric acid was obtained from S. D. Fine Chem. Ltd., Mumbai. All other chemical were purchased from Hi Media, Mumbai. Double distilled water was prepared freshly and used whenever required. All other chemicals used in this study including those stated were of analytical reagent (A.R.) grade.

Formulation development

Formulation of immediate release (IR) layer

All the ingredients except Mg stearate and aerosil were passed through the 40-mesh sieve. Mg stearate and aerosil were passed through 80-mesh sieve. Magaldrate and starch 1500 were mixed thoroughly by gentle blending for few minutes. After blending, granulation was done by sufficient quantity of water. Wet masses were first passed through the 10-mesh sieve and then dried in an oven at 50°C for 2 hour. Then the granules were passed through the 22-mesh sieve and the granule obtained were mixed with superdisintegrant and lubricated with Mg stearate and aerosil and then compressed. Hardness were tried to keep constant Table 1.

Table 1: Optimization bathes of immediate release layer

Ingredient / Batch	Magaldrate	Starch 1500	Polyplasdone XL-10	Ac-Di-Sol	Sodium starch glycolate	Mg stearate	Aerosil
AI	400	40	40	-	-	8	2
A2	400	40	20	-	-	8	2
A3	400	40	-	40	-	8	2
A4	400	40	-	20	-	8	2
A5	400	40	-	-	40	8	2
A6	400	40	-	-	20	8	2
A7	400	40	20	20		8	2
A8	400	40		20	20	8	2
A9	400	40	20		20	8	2

Optimization of the floating layer using 2^3 factorial designs

On the basis of the selection of the 2^3 factorial designs and taking a center point gives a total of nine trial batches. Nine trial batches were taken for the studies and evaluation has been done for the each batches. Excipients other than independent variable are kept constant viz. the amount of sodium bicarbonate, Mg stearate and aerosil are kept at 30mg, 10mg, and 3mg respectively Table 2-4.

Table 2: List of independent variable

Factor	Name	Units	Type	Low Actual	High Actual	Low Coded	High Coded
A	HPMC K4M	mg	Numeric	80	160	-1	+1
B	AC-DI-SOL	mg	Numeric	40	80	-1	+1
C	LACTOSE	mg	Numeric	40	80	-1	+1

Table 3: List of dependent or response variable selected for the studies

Response	Name	Units	Obs	Analysis	Model
Y1	Floating Time	Minutes	9	Factorial	3FI
Y2	Time to maintain pH above 2.5	Minutes	9	Factorial	3FI
Y3	Floating Lag time	Seconds	9	Factorial	3FI

Table 4: Trial batches and their combination of independent variables

S. No.	HPMC K4M	Ac-Di-Sol	Lactose
	mg	mg	mg
1	80	80	80
2	160	40	80
3	80	40	40
4	160	80	40
5	80	80	40
6	160	40	40
7	120	60	60
8	160	80	80
9	80	40	80

Preparation of bilayer tablets

Immidiate release tablet granules were prepared as above. All the ingredients except Mg stearate and aerosil were passed through the 40-mesh sieve. Mg stearate and aerosil were passed through 80-mesh sieve. Floating layer tablet were prepared by wet mixing magaldrate powder with water and pass through the 20 mesh seive and then dried it in oven for 50°C for two hours. Then all the ingredients were mixed in geometric proportion. Batches consisting of 50 tablets were prepared by compresion method. All the product and process variable (other than factor chosen for optimisation studies) like amount of sodium bi carbonate, amount of lubricant and glidant, mixing time and hardness were kept as practically constant. Magaldrate and polymer were seived through 80 mesh seive and the magnesium stearate and aerosil were seived through 120 mesh seive prior to use. All the material were accurately weighed and mixed by gentle mixing for 10 minutes and subsequently compressed into tablets using capsule shaped pucnches of size 11″×22″.

Optimized batch formula

On the basis of the optimization studies the software gives the optimimum value of independent variable. On the basis of that we prepare a optimum batch and it was evluated for all the studies. The response variable anticipated by the software is cross check to the value obtained by observation Table 5.

Table 5: Formula for optimum formulation

Ingredients		Amount (mg)
Immediate Release layer	Magaldrate	400
	Starch 1500	40
	AC-DI-S0L	20
	Polyplsodone XL 10	20
	Mg Stearate	8
	Aerosil	2
	Total Weight	490
Floating layer	Magaldrate	400
	HPMC K4M	160
	AC-DI-SOL	40
	Lactose	80
	Sodium Bicarbonate	30
	Magnesium Stearate	10
	Aerosil	3
	Total Weight	723
	Grand Total	1213

Evaluation of pre-compression parameter[12]

Angle of repose (θ)

The angle of repose was determined by using fixed funnel method. The physical mixtures of drug with different excipients were prepared and the accurately weighed drug powder or its physical mixture was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the drug powder. The powder was allowed to flow through the funnel freely onto surface. The angle of repose was calculated using the following equation.

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

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

Bulk density/tapped density

Both loose bulk density (LBD) and tapped density (TBD) were determined were calculated using the following formulas.

LBD = Powder weight/volume of the packing

TBD = Powder weight /tapped volume of the packing

Compressibility index

The compressibility index of the granules was determined by Carr's compressibility index.

$$\text{Carr's index (\%)} = [(TBD - LBD)/TBD] \times 100.$$

Hausner's ratio

Hausner's ratio is an indirect index of ease of measuring the powder flow. It was calculated by the following formula [7-9].

Hausner's ratio = Tapped density/Bulk density

Evaluation of post compression parameter[13-15]

Hardness

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach) and measured in terms of kg/cm^2.

Weight variation

Twenty tablets were selected randomly from each formulation and average weight was determined. The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet.

Friability

A sample of twenty randomly selected tablets were accurately weighed and placed in a Roche friabilator. The friabilator was operated for 4 min at a speed of 25 rpm. The tablets were removed from the friabilator, de-dusted and reweighed. The percent loss in weight due to abrasion and impact was calculated as,

%Friability= (Loss in weight/ Initial weight) x 100

Disintegration test

This test was done for the immediate release tablet. The tablets were taken in a rigid basket rack assembly supporting six cylindrical glass tubes. The glass tubes were 77.5±2.5 mm long, 21.5 mm in internal diameter and with a wall thickness of about 2mm. The assembly was suspended in the liquid medium in a 1000 ml beaker. The volume of the liquid was such that, wire mesh at its lower point was at 25 mm below the surface of the liquid and its lower point was at 25 mm above the bottom of the beaker. The temperature was maintained at 37.0± 2^{o}C. The average disintegration time was finally recorded.

Drug content

Twenty tablets were weighed and finely powdered. Accurately weighed portion of the powder; equivalent to about 6 g of Magaldrate was transferred to a 200-ml volumetric flask. 100.0 ml of 2 N hydrochloric acid was added and swirled by mechanical means for 30 minutes. It was diluted with water to volume, mixed, and filtered. 100.0 ml of the filtrate was transferred to a beaker. Excess acid was titrated with 1N sodium hydroxide to a pH of 3.0, the value was potentiometrically determined. Blank determination was performed. Each ml of 2N hydrochloric acid is equivalent to 70.80 mg of $Al_5Mg_{10}(OH)_{31}(SO_4)_2$.

Dissolution study

The method was a modification of an RIGO and used USP dissolution test apparatus 2 with a stirring rate of 125 rpm in combination with a burette connected to a peristaltic pump. The test solution was 250 ml 0.02 M HCl. A total of 20 min after addition of an antacid to the test solution titration was started at a constant speed of 2.0 ml/m in 0.1 M HCl. The proposed acceptance criteria was: pH after 4 min not less than 2.5 to ensure a rapid onset of effect, pH after 20 min not exceeding 7.0 to ensure that the pH in the stomach remains within physiological values.

Floating time and floating lag time

These evaluations were part of the dissolution study. Floating time indicates the time for which the tablet remains floating on the surface of the dissolution medium and floating lag time is the time required to reach the surface of the dissolution medium.

RESULTS AND DISCUSSIONS

The powdered blends of different formulations of immediate release layer were evaluated for angle of repose, bulk density (BD), tapped density (TBD) and compressibility index. The results of pre-compression parameter of immediate release layer are summarized in Table 6. The value shows that the powder has compressibility index vary from 11.53 to 13.72 and hausner's ratio varies from 1.13 to 1.20. This shows good compressibility, whereas angle of repose varies from 31º to 34º which ensure good flow properties of powder. The formulation of immediate release tablet prepared by using the superdisintegrants exhibited the LBD, TBD, angle of repose, compressibility index and Hausner's ratio of within the range, which shows good flow properties of the powdered blend. The prepared tablets were evaluated for different physico-chemical properties and the results are summarized in Table 7. Results of pre-compression and post-compression parameters of floating layer were given in Table 8&9. The Table 10 trial batches were selected according to the 2^3 factorial design of design expert software and their evaluation has been done. The results obtained were feeded in the software. The Constriants are selected on the basis of the requirement of the formulation in which, the independent variable and dependent variable are kept in the range except the time to maintain pH above 2.5 were maximize. Which shown in the table 11. Table 12 shows that the formulation should not only prolong the action of the antacids but it should kept pH in the physiological range. F1, F3,F5, and F9 shows the case of dose dumping in which the pH after 20 rise above unphysiological pH . Formulation F2, F4, F6, F7, and F8 shows the well control over the rise of pH. All formulation passes the initial criteria of above pH 2.5 after 4 minutes. The coefficient of polynomial equation generated for the floating time, time to maintain pH above 2.5 and floating lag time and polymer

blend were studied . seven coefficients (β_o to β_{23}) were calculated where β_o as the intercept. The coefficients β_1 to β_{23} were represent various quadratic and interaction terms, but are denoted as such in below equation due to their simplicity. Table 13 shows the values of coefficient for the polynomial equations for various response variable of the bilayer tablet formulation of magaldrate.

$$Y= \beta_o+\beta_1X_1+ \beta_2X_2+ \beta_3X_3+\beta_{12}X_1X_2+\beta_{13}X_1X_3+\beta_{23}X_2X_3$$

Figure 1(A) depicts a quite linear increasing trend in the values of floating time with increase in the amount of HPMC. Whereas increasing the amount of croscarmellose the floating time decreases. Here the effect of HPMC is more prominent than croscarmellose. Figure1 (B) reveals that the increase in amount of HPMC and lactose leads to increase in floating time. But the influence of HPMC is more prominent than lactose. Figure 1(C) depicts that the floating time is increase by decrease in croscarmellose whereas floating time increase by increasing amount of lactose but the effect of lactose is more prominent than lactose. Figure 2(A) depicts a quite linear increasing trend in the values of time to maintain pH above 2.5 with increase in the amount of HPMC. Whereas increasing the amount of croscarmellose the time to maintain pH above 2.5 is decreases. Here the effect of HPMC is more prominent than croscarmellose. Also increase in lactose leads to decrease in floating time. Figure 2(B) reveals that the increase in amount of HPMC and lactose leads to increase in time to maintain pH above 2.5. But the influence of HPMC is more prominent than lactose. Figure 2(C) depicts that the time to maintain pH above 2.5 is increase by decrease in croscarmellose whereas "time to maintain pH above 2.5" increase by increasing amount of lactose but the influence of lactose is more prominent than croscarmellose. Figure 3(A) depicts a quite linear increasing trend in the values of floating lag time with increase in the amount of HPMC and croscarmellose. Here the influence of HPMC is more prominent than croscarmellose. Figure 3(B) reveal that the increase in amount of HPMC and lactose leads to increase in floating lag time. But the influence of HPMC is more prominent than lactose. Figure 3(C) depicts that the floating lag time is increase by increase in croscarmellose and lactose. But the effect of croscarmellose is more prominent than lactose. The three batch of optimum formula were prepared and their powder and tablet were evaluated. Their evaluations were shown in table 14. It was found that the all batches have good compressibility as well good flow properties. The tablets were passes the weight variation and friability test. The drug content was found to be satisfactory. Further responses of three optimum batches were taken and it shown in table 15. Here it shows a good correlation between the observed responses with that of the anticipated value predicted by software hence the optimization method was validated the optimization tool. Table 16 list the dissolution parameter of marketed formulation studied viz. Ulgel (Dabur), containing 400mg of Magaldrate. The results of table shows that the developed formulation is long acting in comparison to existing normal dose of marketed products and also when the dose of marketed formulation is increased then the pH after 20 minutes rises above the physiological pH. Hence the prepared formulation is long acting as well as safe and effective.

Table 6: Result of pre-compression properties of immediate release layer

Parameters	A1	A2	A3	A4	A5	A6	A7	A8	A9
Bulk density (g/cc)	0.44	0.47	0.46	0.46	0.47	0.45	0.45	0.46	0.46
Tapped density (g/cc)	0.51	0.54	0.53	0.52	0.54	0.52	0.52	0.53	0.52
Compressibility index (%)	13.72	12.96	13.20	11.53	12.96	12.13	13.46	13.20	11.53
Hausner's ratio	1.16	1.15	1.15	1.13	1.15	1.20	1.15	1.15	1.13
Angle of repose	31°	32°	32°	32°	33°	34°	32°	34°	31°

Table 7: Results of post-compression parameters of immediate release layer

B. No.	Average weight (mg) Mean ± SD	Disintegration time (Seconds)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
A1	507.19 ± 23.39	44	5.0±1.0	0.62	100.39
A2	476.76 ± 12.92	65	5.0±1.0	0.28	100.82
A3	496.76 ± 24.12	50	5.0±1.0	0.54	98.54
A4	482.02 ± 13.48	74	5.0±1.0	0.89	98.25
A5	507.60 ± 9.67	102	5.0±1.0	0.72	97.80
A6	475.57 ± 17.51	120	5.0±1.0	0.68	97.95
A7	493.97 ± 8.10	22	5.0±1.0	0.32	98.42
A8	498.60 ± 10.80	35	5.0±1.0	0.65	98.95
A9	501.23 ± 23.12	43	5.0±1.0	0.46	100.10

Table 8: Result of pre-compression properties of floating layer

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (g/cc)	0.44	0.43	0.43	0.46	0.43	0.45	0.44	0.44	0.44
Tapped density (g/cc)	0.50	0.51	0.49	0.52	0.52	0.51	0.50	0.51	0.52
Compressibility index (%)	12.00	15.68	12.24	11.53	17.30	11.76	12.00	13.72	15.38
Hausner ratio	1.13	1.18	1.14	1.13	1.21	1.13	1.13	1.16	1.18
Angle of repose	34^0	35^0	33^0	33^0	34^0	34^0	35^0	35^0	33^0

Table 9: Results of post-compression parameters of Magaldrate floating tablets

B. No.	Average weight (mg) Mean ± S.D	Hardness (kg/cm^2)	Friability (%) (Average)	Drug Content (%) (Average)
F1	1185.24 ± 35.49	9.0 ± 1.0	0.82	97.49
F2	1226.62 ± 25.46	9.0 ± 1.0	0.45	98.82
F3	1103.32 ± 42.26	9.0 ± 1.0	0.64	96.95
F4	1222.42 ± 24.53	9.0 ± 1.0	0.87	98.90
F5	1142.52 ± 15.64	9.0 ± 1.0	0.73	98.45
F6	1185.87 ± 27.54	9.0 ± 1.0	0.88	98.75
F7	1182.67 ± 38.20	9.0 ± 1.0	0.48	97.80
F8	1265.60 ± 20.80	9.0 ± 1.0	0.85	98.95
F9	1145.23 ± 23.12	9.0 ± 1.0	0.76	100.05

Table 10: Optimization trial batches and their responses

S. No.	HPMC K4M (mg)	Ac-Di-Sol (mg)	Lactose (mg)	Floating Time Mean ± S. D. (Minutes)	Time to maintain pH above 2.5 Mean ± S. D. Minutes	Floating Lag time Mean ± S. D. Seconds
1	80.00	80.00	80.00	83.33 ± 5.77	253.33 ± 5.77	43.00 ± 7.09
2	160.00	40.00	80.00	616.66 ± 5.77	276.66 ± 5.77	33.00 ± 2.64
3	80.00	40.00	40.00	116.66 ± 5.77	246.66 ± 11.54	25.00 ± 5.00
4	160.00	80.00	40.00	1066.66 ± 15.27	160.00 ±10.00	20.00 ± 5.00
5	80.00	80.00	40.00	56.66 ± 5.77	226.66 ± 5.77	23.66 ± 1.52
6	160.00	40.00	40.00	1170.00 ± 10.00	150.00 ± 10.00	50.00 ± 5.00
7	120.00	60.00	60.00	690.00 ± 10.00	253.33 ± 5.77	22.33±2.51
8	160.00	80.00	80.00	730.00 ± 10.00	226.66 ± 5.77	55.00 ± 5.00
9	80.00	40.00	80.00	26.66 ± 5.77	233.33 ± 5.77	40.00 ± 5.00

Table 11: Constriants given to the system

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
HPMC K4M	is in range	80	160	1	1	3
Ac-Di-Sol	is in range	40	80	1	1	3
Lactose	is in range	40	80	1	1	3
Floating Time	is in range	20	1200	1	1	3
Time to maintain pH above 2.5	maximize	140	280	1	1	3
Floating Lag time	is in range	15	80	1	1	3

Table 12: Dissolution data of optimization batches

Batch	pH after 4 minutes	pH after 20 minutes
F1	4.02	6.55
F2	3.80	5.05
F3	4.40	6.05
F4	4.19	4.86
F5	4.56	6.22
F6	3.35	4.46
F7	4.06	5.43
F8	4.20	5.06
F9	4.16	6.52

Table 13: Polynomial coefficient values for response variables

Coefficient code	Polynomial coefficient values for response variables		
	Floating Time	Time to maintain pH above 2.5	Floating Lag time
β_o	+484.17	+221.67	+35.79
β_1	+411.67	-18.33	+2.88
β_2	+0.000	-5.00	-0.37
β_3	-120.00	+25.83	+6.13
β_{12}	+2.50	-5.00	-0.79
β_{13}	-102.50	+22.50	-2.46
β_{23}	+42.50	-2.50	+7.46

Table 14: Powder and tablet evaluation of optimum batches

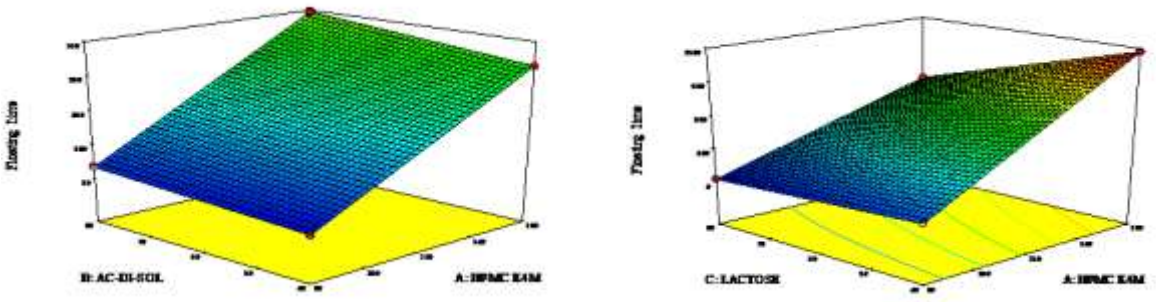
Parameters	Batch O I	Batch O II	Batch OIII
Bulk density	0.44	0.45	0.44
Tapped density	0.51	0.52	0.52
Compressibility index	13.72	13.46	15.38
Hausner ratio	1.16	1.15	1.18
Angle of repose	34	35	34
Weight variation	1222.62 ± 25.54	1218.56 ± 21.42	1226.87 ± 25.46
Hardness test	9.0±1.0	9.0±1.0	9.0±1.0
Friability test	0.55	0.45	0.47
Drug content	99.67	99.52	99.23

Table 15: Responses of the optimized batch

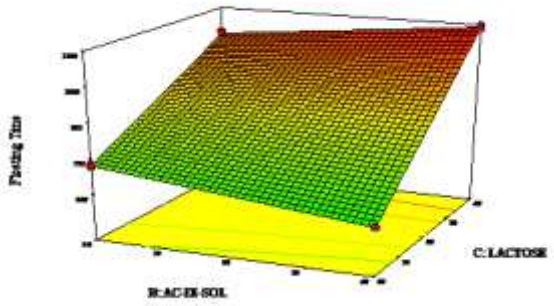
Response	Predicted by software	Obtained by evaluation of optimized batches		
		Batch O I	Batch O II	Batch OIII
Floating Time (minutes)	617	610	610	620
Time to maintain pH above 2.5 (minutes)	277	280	270	280
Floating Lag time (seconds)	30	30	35	34

Table 16: Dissolution parameter for optimized batch and popular marketed batch

Marketed Products	pH after 4 minutes	pH after 20 minutes	Time to maintain pH above 2.5 (minutes)
Ulgel (2 tablets)	3.63	4.13	140
Ulgel (4 tablets)	4.05	7.05	250
Optimized batch formula (2 tablets)	3.80	4.65	280

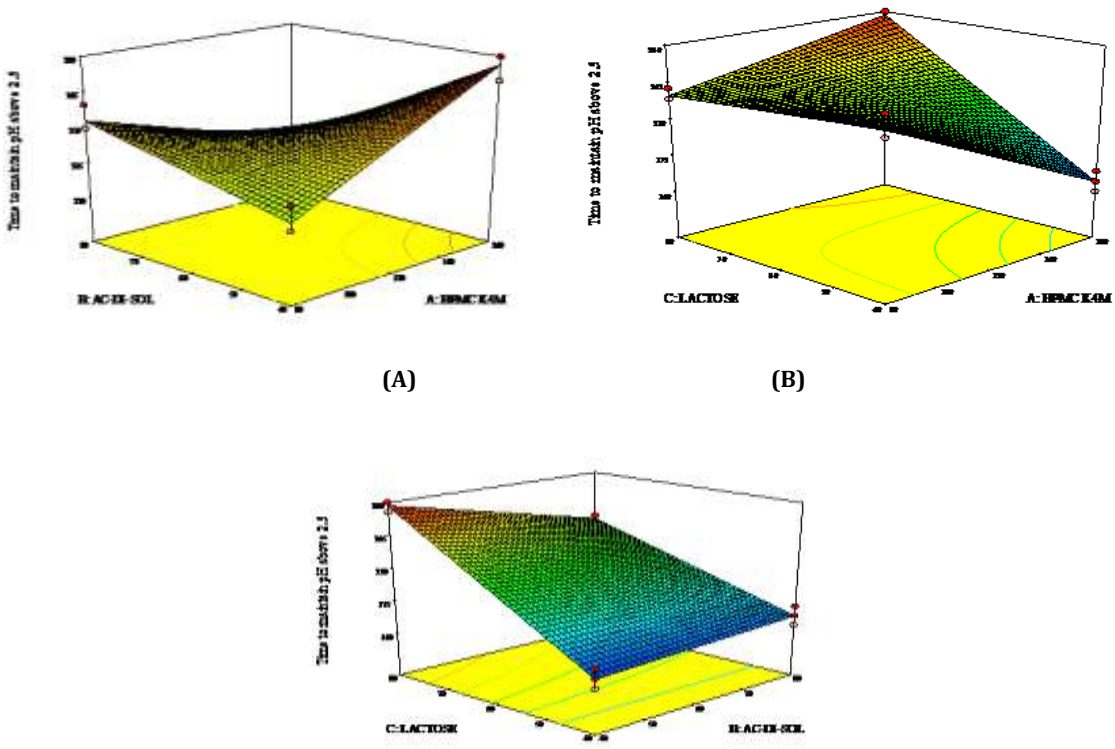


(A) **(B)**



(C)

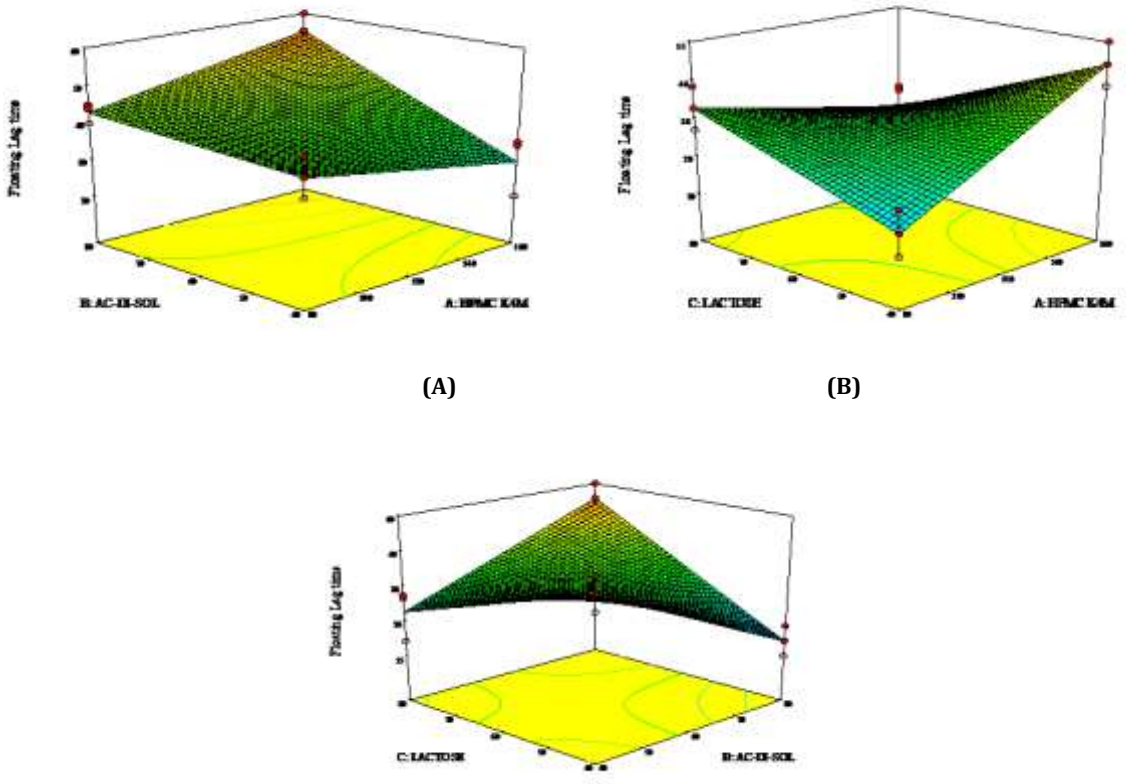
Figure 1: Response surface plot (A) showing the influence of HPMC K4M and Ac-Di-Sol, (B) HPMC K4M and Lactose, (C) Lactose and Ac-Di-Sol on the floating time



(A) (B)

(C)

Figure 2: Response surface plot (A) showing the influence of HPMC K4M and Ac-Di-Sol, (B) HPMC K4M and Lactose, (C) Lactose and Ac-Di-Sol on the time to maintain pH above 2.5



(A) (B)

(C)

Figure 3: Response surface plot (A) showing the influence of HPMC K4M and Ac-Di-Sol, (B) HPMC K4M and Lactose, (C) Lactose and Ac-Di-Sol on floating lag time of tablet

CONCLUSION

In present study we developed a bilayer formulation having one layer as immidiate release and other layer as floating layer which gives the long duration action of antacids. Hence for the optimisation of the floating layer 2 level factorial design has been selected. The design expert software 7.2.3 version has been used. A very good correlation between the observed value of optimized batch and the anticipated value of software was found. Also formulation was compared with the marketed product and it was found that the present formulation is safe and effective as well as long acting.

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