International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304, ISSN(Online): 2455-9563
Vol.14, No.01, pp 125-132, 2021

Formulation and Evaluation of Floating Tablets of Ranolazine using Eudragit-E100 and Guar Gum

B.Sravya[1*], A.Ankarao[2], A. Seetha Devi[3]

[1] Sravya.B. M.Pharm, Department of pharmaceutics, Hindu college of pharmacy, Amaravathi Road, Guntur -522002, India

[2]Dr. A. Ankarao Ph.D, associate professor, Department of pharmaceutics, Hindu college of pharmacy, Amaravathi Road, Guntur-522002, India

[3]Dr. A. Seetha Devi, Ph.D, HOD, Department of pharmaceutics, Hindu college of pharmacy, Amaravathi Road, Guntur, India

Email Id- sravyadubai@gmail.com

Abstract: The objective was to develop gastric floating drug delivery systems of ranolazine floating tablets by using various polymers like Eudragit E-100 and Guar Gum. In the present work attempts have been made to prepare ranolazine floating tablets by direct compression method by using sodium bicarbonate, avicel, magnesium stearate, Eudragit E-100 and Guar Gum. Formulations F_1- F_9 of floating tablets of Ranolazine were prepared using variable concentrations of Eudragit and Guar Gum. The prepared formulations were evaluated for various evaluation tests like thickness, hardness, weight variation, friability, drug content and uniformity. The buoyancy lag time and total floating time was studied for all the formulations. Form all the formulations F7 of sustained release tablets of Ranolazine containing a combination of both polymers was found to be optimized formulation for 12 hours release as it fulfilled all the requirements.

Keywords: Ranolazine, sustained release floating tablets, GFDDS, Eudragit E-100.

INTRODUCTION:

Gastroretentive drug delivery system (GRDDSs) can release the drug continuously for a prolonged period of time before it reaches its absorption site and improve the controlled delivery of drugs. The drugs that are absorbed from the proximal part of the gastro intestinal tract or those are less soluble in or are degraded by alkaline pH or they encounter at the lower part of the GIT can achieve therapeutic benefits of drug by prolonging the gastric retention of the drugs [1-3].

DOI= http://dx.doi.org/10.20902/IJPTR.2021.140111

B.Sravya et al /International Journal of PharmTech Research, 2021,14(1): 125-135.

Gastro retentive systems significantly prolong the gastric residence time of drugs by remaining in the gastric region for several hours. Floating drug delivery systems (FDDS) or hydro-dynamically 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.[4]

Literature survey revealed reports on optimization of Ranolazine formulations in tablet by different methods. S.Alexandar *et. al.* and *et. al*. Md. Mofizur Rahman has reported on gastroretentive floating tablets of Ranolazine by granulation techniques using different polymer. But No methods have been reported for formulation and evaluation of gastroretentive floating tablets of Ranolazine by direct compression method using Eudragit E-100 and Guar Gum polymer. Hence, the present investigation was carried out in the view of to design sustained release floating tablet of Ranolazine by direct compression technique to improve bioavailability, therapeutic efficiency, reduce dosing frequency as it produces toxicity[5-6].

MATERIALS AND METHODS :

Ranolazine was obtained as a gift sample by Yarrow chem. Products, Mumbai. sodium bicarbonate, magnesium stearate, Eudragit E-100, Avicel and Guar Gum were procured from research lab, Mumbai, India All the materials and solvents used were of analytical grade.

METHOD OF PREPARATION :

The formulation was prepared according to the principle of effervescent technique, in which all the ingredients were weighed accurately as per the formulation table. Floating tablets containing ranolazine were prepared by direct compression technique using various polymers with sodium bicarbonate. All the powder were accurately weighed passed through 40 mesh sieve. Then except magnesium sterate all other ingredients were mixed thoroughly for 15mins. After sufficient mixing of drug as well as other components, add magnesium sterate as post lubricant and then again blend for additional 2-3mins. The final blend was compressed into tablets having average weight of 750mg using a 16-station rotary tablet punching machine.

Table no :1 composition of formulations of Ranolazine

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ranolazine	500	500	500	500	500	500	500	500	500
Guar gum	50	100	150	--	--	--	50	100	50
Eudragit E-100	--	--	--	50	100	150	50	50	100
Sodium bicarbonate	45	45	45	45	45	45	45	45	45
Avicel	147.5	97.5	47.5	147.5	97.5	47.5	97.5	47.5	47.5
Magnesium stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Total	750	750	750	750	750	750	750	750	750

EVALUATION OF FLOATING TABLETS OF RANOLAZINE

PHYSICAL EVALUATION :

The formulated floating tablets of Ranolazine were evaluated for physical characteristic viz., thickness, hardness, weight variation, friability and drug content and uniformity.

FLOATING EVALUATION:

The formulated Ranolazine floating tablets were evaluated for buoyancy lag time, total floating time, and effect of hardness on buoyancy lag time.

THICKNESS:

The thickness uniformity studies were carried out by using vernier caliper from prepared formulation randomly selected ten tablets for thickness uniformity studies and denoted in millimeters. The data obtained was used to calculate mean and standard deviation.

HARDNESS:

Hardness indicates the ability of a tablet to withstand mechanical shocks while handiling. The hardness of tablet was determined by using Monsanto hardness tester. The prepared five floating tablets were used for hardness uniformity studies. The hardness data was used to calculate mean and standard deviation and % friability. It was expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.

FRIABILITY:

The friability of tablets was determined using rochefriabilator. It is expressed in percentage(%). Ten tablets were initially weighed (initial)and transferred into friabilator. The friabilator was run up to 100 revolutions or operated at 25 rpm for 4min. The tablets were weighed again (final).

The friability was then calculated by

Friability = [(initial weight – final weight)/ (initial weight)] ×100

WEIGHT VARIATION:

Ten tablets were selected randomly from each batch and weighed individually to check for weight initial variation. A little variation was allowed in the weight of a tablet by U.S. pharmacopiea. The following percentage deviation in weight variation was allowed shown in table[7].

$$\% \text{ weight variation} = 100 \times (W_A - W)/W$$

CONTENT UNIFORMITY:

Twenty tablets were taken and amount of drug present in each tablets was determined. The tablets were crushed using mortar and pestle and the powder equivalent to 100 mg of drug was transferred to a standard flask. The powder was dissolved in a suitable solvent and made up to the final volume with suitable buffer solution. The sample was mixed thoroughly and filtered using a 0.45µ membrane filter. The drug content was determined by Shimadzu UV-1800 at wave length of 276nm after a suitable dilutions with 0.1N HCL.

CONSTRUCTION OF STANDARD PLOT OF RANOLAZINE:

The absorbance of the solution was measured at 272nm using the spectrophotometer with methanol as blank. The values are shown in graph of absorbance vs. concentration was plotted in concentration range of 10-50µg/ml.

Table no :2 standard calibration curve of ranolazine in 0.1N HCL

s.no	Conc.in mcg/ml	absorbance
1	0	0
2	10	0.049
3	20	0.101
4	30	0.160
5	40	0.209
6	50	0.271

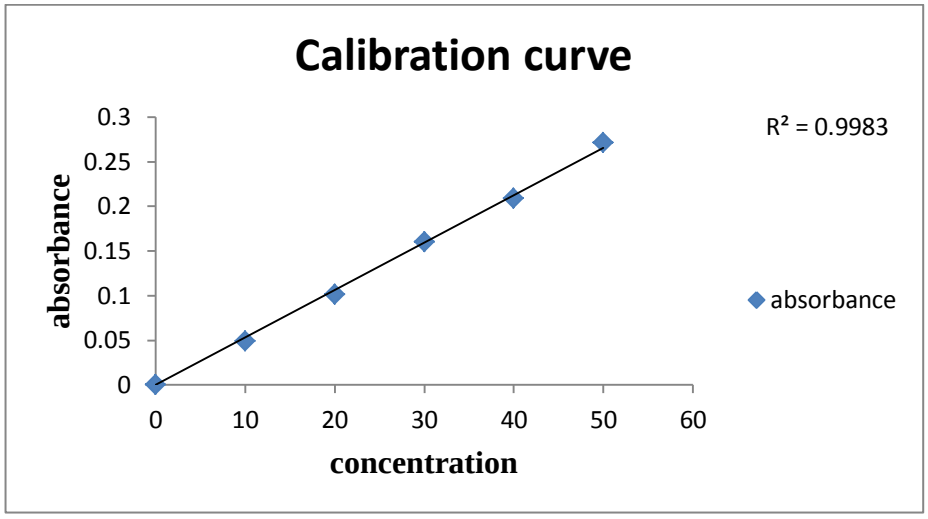

Figure no: 1 Standard calibration graph

DETERMINATION OF FLOATING PARAMETERS:

***IN-VITRO* BUOYANCY TEST:**

The Buoyancy test of floating tablet was studied by placing them in 500mL beaker containing 0.1HCl.Then tablet from same batch were placed in dissolution test apparatus containing 0.1 HCl, maintained at 37±0.100C and agitated at 100rpm. The floating onset time (time period between placing tablet in the medium and buoyancy beginning) and floating duration of tablet were determined by visual observation[8].

SWELLING INDEX:

The swelling behaviour of the dosage form was measured by studying the weight in grams. The dosage form was placed in basket of dissolution apparaturs which is filled with dissolution medium (stimulated gastric fluid or 0.1N HCl at 37±0.5C) and rotated at 50rpm. At specific time intervals tablets were removed from basket and lightly blotted with tissue paper to remove excess water and weighed.

Swelling index calculated by using the following formula.

Swelling index : $WU = (Wt-w0) \times 100 / W0$

Wt = weight of dosage form at time t.

W0 = initial weight of dosage form.

FLOATING LAG TIME AND FLOATING TIME:

In vitro buoyancy was determined by measuring floating lag time and duration of floating. The tablets were placed in a 250 mL glass beaker containing 0.1 N HCl. The floating lag time was determined by the time required for the tablet to rise to the surface . The total floating time was determined by duration in which the tablet remains floating[9].

RESULTS :

WEIGHT VARIATION,THICKNESS,HARDNESS AND FRIABILITY :

From the obtained results it was showed that weight variation, thickness were lying within limits. There was a slight variation in hardness of tablets. By increasing the concentration of polymers the hardness of the tablets was found to be increased. The friability loss was found to be within the limits in all the friability tablet was found to mechanically strong.

Table no: 3 post compression parameters of all the formulations

Formulation code	Thickness	Avg. wt(mg)	Hardness (kg/cm^2)	Friability (%)	Assay (%)
F1	3.3	750±1.50	4.87±0.20	0.36%	98.15
F2	3.7	748±0.07	4.5±0.11	0.28%	98.97
F3	3.9	749±0.05	5.00±0.21	0.48%	100.5
F4	4.0	745±0.10	4.97±0.15	0.39%	99.32
F5	3.8	751±1.25	4.0±0.63	0.42%	99.75
F6	3.6	750±0.20	4.2±0.63	0.36%	100.99
F7	3.9	748±0.03	4.5±0.11	0.40%	98.5
F8	3.5	749±0.24	4.72±0.12	0.21%	99.22
F9	3.45	745±0.21	4.4±0.45	0.37%	98.50

***IN-VITRO* DISSOLUTION STUDIES:**

The release rate of Ranolazine from floating tablets(n=3) was determined using the United states Pharmacopiea (USP) dissolution testing apparatus 11(paddle method). The dissolution test test was performed using 900ml of 0.1N HCl, at 37±0.5 C at 50rpm. A sample of 5 ml of the solution was withdrawn from the dissolution apparatus at an interval of 1,2,3,4,5,6,7,8,9,10,12, hrs and the samples were replaced with fresh dissolution medium. Absorbance of these solutions was measured at using Shimadzu UV 1800 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obatined from a standard curve[10].

Table no: 4 *In-vitro* dissolution studies

Time (hrs)	% drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0.5	20.85±0.54	19.81±0.66	19.42±0.54	16.25±0.46	15.92±0.81	15.5±0.71
1	25.36±0.52	22.09±0.65	20.85±0.45	23.27±0.06	20.56±0.65	19.78±0.15
2	33.94±0.51	31.50±0.31	28.71±0.82	27.36±0.52	25.34±0.56	23.34±0.56
3	38.24±0.56	36.50±0.51	33.62±0.76	36.24±0.46	34.27±0.15	32.23±0.51
4	47.72±0.70	43.34±0.19	39.83±0.12	45.72±0.78	42.59±0.90	38.19±0.70
5	59.36±0.35	54.61±0.13	48.61±0.15	52.36±0.85	49.53±0.67	45.53±0.19
6	67.44±0.44	65.35±0.03	58.29±0.50	59.39±0.18	56.6±0.89	54.83±0.13
7	79.49±0.65	76.10±0.17	65.33±0.52	66.96±0.34	64.8±0.78	60.82±0.03
8	87.27±0.25	84.10±0.38	76.56±0.17	70.89±0.45	68.99±0.14	65.16±0.17
9	98.62±0.02	90.67±0.75	83.46±0.40	79.38±0.53	75.58±0.78	73.31±0.38
10	--	97.36±0.06	93.62±0.02	86.50±0.12	84.82±0.24	80.82±0.35
12	--	--	95.32±0.01	93.96±0.19	90.57±0.85	87.57±0.67

Table no: 5 In-vitro dissolution studies

Time (hrs)	%drug release		
	F7	F8	F9
0	0	0	0
0.5	23.29±0.79	26.81±0.06	20.81±0.48
1	30.83±0.51	31.81±0.95	29.44±0.54
2	39.32±0.3	39.50±0.83	35.46±0.98
3	45.32±0.14	45.09±0.11	40.34±0.56
4	54.48±0.60	53.26±0.65	45.32±0.74
5	65.51±0.94	58.33±0.91	56.21±0.31
6	70.74±0.25	66.67±0.17	62.62±0.53
7	75.76±0.82	72.67±0.94	67.35±0.49
8	80.12±0.91	79.71±0.57	70.63±0.58
9	87.67±0.21	84.69±0.15	77.10±0.17
10	93.32±0.86	89.12±0.04	80.12±0.38
12	98.69±0.04	94.26±0.50	87.54±0.07

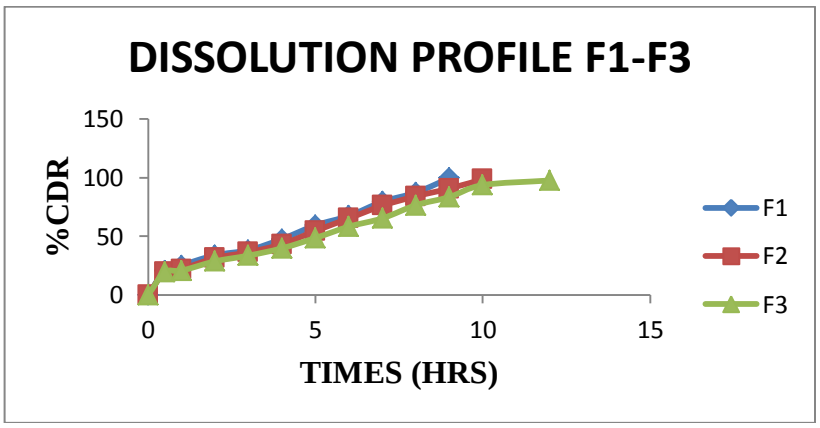

Figure no: 2 *Invitro* drug release profile (F1-F3)

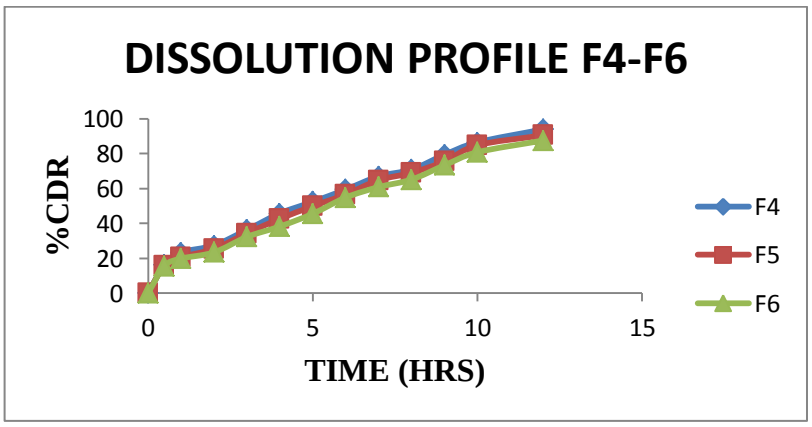

Figure no: 3 *Invitro* drug release profile (F1-F3)

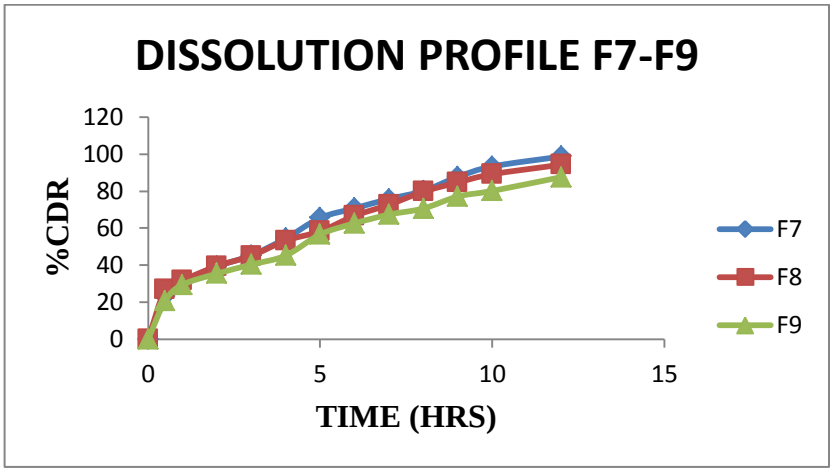

Figure no: 4 *Invitro* drug release profile (F1-F3)

BUOYANCY AND TOTAL FLOTATION TEST :

Floating lag time and total floating time was determined by using 0.1N HCL. The formulation contains sodium bicarbonate as gas generating agent. The polymers used are Eudragit E-100 and Guar Gum. The floating lag time of all the formulations (F1-F9) were found to be in the range of 27-120 sec. The best formulation is F7 is 26sec. The total floating time of all the formulations (F1-F9) were found to be in the range of 9-12hrs. The best formulation F7 is 12hrs[11].

Table no : 6 Floating characteristics of formulations

Formulation code	Floating lag time (sec)	Total floating time (hrs)	Swelling index
F1	27	>12	1.251±0.23
F2	50	>10	1.523±0.14
F3	90	>12	1.312±0.23
F4	45	<12	1.520±0.14
F5	74	<10	1.220±0.80
F6	120	<12	1.620±0.80
F7	26	>12	1.316±0.65
F8	60	>12	1.923±0.86
F9	70	>12	1.515±0.56

Table no : 7 Stability studies

Parameters	After 30 days	After 60days	After 90 days
Physical appearance	No change	No change	No change
Weight variation (mg)	750±1.6	750±2.70	748±1.30
Thickness (mm)	3.9±1.87	3.9±2.86	3.9±3.98
Hardness (kg/cm^2)	4.5±0.23	4.49±0.64	4.49±0.99
Friability (%)	0.40±0.05	0.40±0.08	0.40±0.06
Drug content (mg/Tab)	98.34±0.34	98.21±0.29	98.01±0.87
Buoyancy lag time (sec)	6±0.78	6±2.8	6±3.10
Duration of buoyancy (hrs)	>12	>12	>12

DISCUSSION :

To encourage the gastric retention of an oral dosage form Various approaches have been followed. Due to low bulk density of the floating systems they can float on the gastric juice in the stomach. In the present study, floating tablets of Ranolazine were prepared by direct compression method using Ranolazine with polymers like Eudragit E-100 and Guar Gum in variable concentrations. The prepared Ranolazine floating tablets were subjected to various evaluation studies done like weight uniformity test, hardness, thickness, friability, content uniformity, *in vitro* buoyancy study, swelling index disintegration studies and *in vitro* dissolution studies.

From the obtained results it was showed that weight variation, thickness were lying within limits. As the proportion of polymers increases, the hardness of the tablets was found to increases. The friability loss was found to be within the limits in all the samples and the tablets were found to mechanically strong. The buoyancy lag time and the total floating time were studied for all the formulations. From the preformulation studies for drug excipients compatibility, it was observed that there was no compatibility problem with the excipients used in study. The drug release from the formulations shows the Fickian diffusion. All formulations possessed good floating properties with total floating time between 8-12 hrs.

CONCLUSION :

The result of the present research work demonstrate that the combination of both hydrophilic and hydrophobic polymers successfully employed for formulating the sustained release tablets of Ranolazine. The optimum concentration of each polymer in combination was able to produce desired formulation which release complete drug in 12 hours was observed. The mechanism of drug release has observed the combined effect of diffusion and erosion for sustained release of drug. So F7 is the optimized formulation having ratio of Eudragit E-100 and Guar gum polymers (1:1) best for effervescent floating tablets.

REFERENCES :

1. Sing B.N., Kim K.H., Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J. Cont. Rel., 2000,63, 235-59.
2. Sungthongjeen S., Paeratakul O., Limmatvapirat S., Puttipupathachorn S, Preparation and in-vitro evaluation of multiple-unit floating drug delivery system based on gas formation technique. Int. J. Pharm., 2006, 324, 136-43.
3. Sangekar S., Evaluation of effect of food and specific gravity of the tablets on gastric retention time. Int. J. Pharm., 1985,35, 34-53.
4. Pahwa R., Garg R., Nanda S., Formulation and Evaluation of Floating Multiparticulate Drug Delivery System of Glipizide. Der Pharmacia Sinica. 2011,2 (5), 110-120.
5. Md.Mofizur rahman ., Sayeed Hasan., Formulation and evaluation of ranolazine sustained release matrix tablets using Eudragit and HPMC. Int Jpharma Biomed Res 2011,1(5), 172-177
6. S.Alexandar , M.Kumar., formulation and evaluation of buoyant type of gastro retentive dosage form of ranolazine tablets J.pharma. Sci.&Res. Vol. 9(2), 2017,145-149.
7. Leon L., Herbert A., Liebermann J., Kanig L., The Theory And Practice Of Industrial Pharmacy, 3rd ed., 2003, pp.298-302.
8. Sigal S., Amir R., Rachel B., Yishai K., Gastrointestinal tracking and gastric emptying of solid dosage forms in rats using X-rays imagining. Int. J. Pharm., 2010, 388,190-195.
9. Dorozynski P, Jachowicz R, Kulinowski P, Kwiecinski S, Szybinski K, Skorka T,Et.Al. The Marcomolecular Polymers For The Preparation Of Hydrodynamically Balanced Systems-Methods Of Evaluation. Drug Dev.Ind Pharm 2004; 30:974-57.
10. Kiortsis S, Kanchrimanis K, Broussali T And Malamataris S.Drug Release From Tableted Wet Granulations Comprising Cellulosic (HPMC OR HPC) And Hydrophobic Component. Eur.J. Pharm. Biopharm 2005: 59 73-83.
11. Burns S.J., Corness D., Hay G., Studies on Formulation and evaluation Ranitidine floating Tablet. Ind. J. Pharm.Sci., 2005, 67(6), 703-709.

*****