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DESIGN, OPTIMIZATION AND INVITRO EVALUATION OF FDDS OF RITONAVIR TABLET

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Abstract: The drug Ritonavir belongs to class II under BCS, widely prescribed as antiviral drug in the treatment of HIV/AIDS, exhibit low and variable oral bioavailability because it is practically insoluble in water and aqueous fluids and as such it possesses challenging problems in its formulation development.
This work was an attempt to increase therapeutic efficacy, reduce the frequency of drug administration, improve the bioavailability and patient compliance by developing Floating Ritonavir tablets for controlled release and to increase gastric retention time.
The Floating Ritonavir tablets were prepared by wet granulation technique by using different ratios of HPMC K4M, Xanthan gum using PVP K30, Magnesium sterate, talc, sodium bicarbonate, citric acid, lactose, Sodium Alginate & Cross carmellous sodium.
The prepared tablets were subjected to post compressional parameters such as hardness, weight variation, thickness, diameter, drug content, lag time, buoyancy time & invitro dissolution studies.
Compatibility of the drug with excipients used was checked by FTIR studies. The stability studies were conducted as per ICH guidelines.
In all the formulations, hardness test indicated good mechanical resistance. Sodium bicarbonate was added as a gas generating agent, induced carbon dioxide generating in presence of dissolution medium (0.1N HCl). The combination of sodium bicarbonate & citric acid provided desired floating ability.

Keywords: Ritonavir, HPMC, Xanthan gum, Floating Drug Delivery, FTIR

I. INTRODUCTION:

Oral controlled release dosage forms have been extensively used to improve therapy of many important medications. The bioavailability of drugs with an absorption window in the upper small intestine is generally limited with pharmaceutical dosage forms. The residence time of such systems and, thus, of their drug release into the stomach and upper intestine is often short[1]. To overcome this restriction and to increase the bioavailability of these drugs, controlled drug delivery systems, with a prolonged residence time in the stomach, can be used. Incorporation of the drug into a controlled release delivery system, which releases its payload in the stomach over a prolonged time period, can lead to significant therapeutic advantages owing to various pharmacokinetic and pharmacodynamic aspects[1]

Oral route is the most desired, convenient and preferred method of administering the drug for its systemic effect due to its ease of administration, low cost of therapy and patient compliance. Oral route of administration has received more attention in the pharmaceutical field because of more flexibility in the designing of dosage form than the other routes of drug delivery[2]. The release of drug from the delivery system may be by diffusion, dissolution or by combination of both mechanisms in a desired and controlled manner. One main prerequisite for the oral performance of the drug delivery system is that drug should have good absorption throughout the gastrointestinal tract (GIT). Floating drug delivery systems (FDDS) are aimed to retain the drug in the stomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The principle is very simple i.e., to make the dosage form less dense than the gastric fluids so that it can float on them. 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. After release of drug, the residual system is emptied from the stomach. This result an increased gastric residence time and a better control of the fluctuations in plasma drug concentration. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release[2].

Anatomy of stomach[3]: The stomach is divided into three anatomical regions: fundus, body and pylorus or antrum. The proximal stomach consists of fundus and body, which serves as a reservoir for ingested materials, whereas the distal region (pylorus) is the major site of mixing motions, acting as a pump to propel gastric contents for gastric emptying . The fundus adjusts to increased volume during eating by relaxation of fundal muscle fibers. The fundus also exerts a steady pressure on the gastric contents, pressing them towards the distal stomach. To pass through the pyloric wall into the small intestine, particles should be of the order of 1-2mm. As in figure 1.

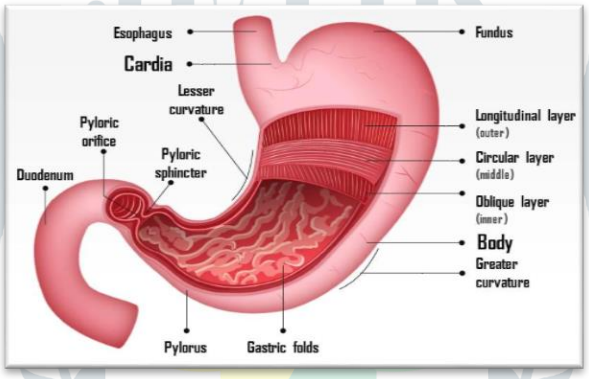

Fig 1: Anatomy of Stomach

Floating drug delivery systems [FDDS]:

FDDS is also known as hydro dynamically balanced system [HBS]. While the system is floating on the gastric contents, the drug is release is slowly at the desired rate from the systems. After release of drug, the residual system is emptied from the stomach. This result in an increased GRT and a better control of the fluctuations in plasma drug concentration.

Advantage of FDDS [4,5,6,7]

1. Controlled delivery of drugs.
2. Improve drug absorption, because of increased gastro retentive and more time spent by the dosage form at its absorption site.
3. Delivery of drugs for local action in the stomach.
4. Minimizing the mucosal irritation due to drugs, by releasing slowly at controlled rate.
5. Treatment of gastrointestinal disorders such as gastro-esophageal reflux
6. Ease of administration and better patient compliance.
7. Site-specific drug delivery.

Limitations of FDDS[8,9,10,11]

• Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
• Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
• High variability in gastric emptying time due to its all or non-emptying process.
• Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore, patients should not be dosed with floating forms just before going to bed.

Drugs that are required to be formulated into gastro retentive dosage forms include[12,13,14]

• Drugs acting locally in the stomach.
• Drugs that are primarily absorbed in the stomach.
• Drugs those are poorly soluble at alkaline pH.
• Drugs with a narrow window of absorption.
• Drugs rapidly absorbed from the GI tract and
• Drugs that degrade in the colon.

Mechanism of Floating System: FDDS has a bulk density less than gastric fluids so that they remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time[14].
Mechanism of Action: Ritonavir binds to the protease active site and inhibits the activity of the enzyme. This inhibition prevents cleavage of the viral polyproteins resulting in the formation of immature non-infectious viral particles.

II. MATERIALS AND METHOD:

Materials:

Table 1: Materials used for the preparation of tablets

Name of chemicals	Received from
Ritonavir	Hetero drugs limited (unit-IX), A.P.
HPMC K4M	AstraZeneca Pvt Ltd Bangalore
PVP K30	S.D. Fine chemicals Mumbai
Magnesium state	S.D. Fine chemicals Mumbai
Talc	S.D. Fine chemicals Mumbai
Sodium bicarbonate	S.D. Fine chemicals Mumbai
Citric acid	S.D. Fine chemicals Mumbai
Lactose	S.D. Fine chemicals Mumbai
Xanthan Gum	Hi Media Chem. Pvt. Ltd. Mumbai
Sodium alginate	S.D. Fine chemicals, Mumbai
Crosscarmellose sodium	Rajesh chemicals, Mumbai

Method[15]**:**

Drug and polymers were mixed in a poly bag and the mixture was passed through a mesh No. 60. Granulation was done with a solution of PVP K30 in sufficient isopropyl alcohol. The wet mass was passed through mesh No. 12. The wet granules were dried at 60º for about 4 hours. The dried granules were sized

by a mesh No. 18 and mixed with sodium bicarbonate, citric acid, magnesium stearate and talc. Granules thus obtained weighing equivalent to required weight were compressed into tablets.

Table 2: FDDS Ritonavir Tablet Formulations Table

Ingredients	RF1	RF2	RF3	RF4	RF5	RF6	RF7	RF8	RF9	RF10	RF11	RF12
Ritonavir	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg
HPMC K4m	200 mg	150 mg	100 mg	50 mg	-	-	-	-	50 mg	50 mg	100 mg	100 mg
PVP K30	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Mg Stearate	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Talc	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Sod Bicarbonate	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg	80 mg
Citric acid	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Lactose	10 mg	60 mg	110 mg	160 mg	85 mg	135 mg	185 mg	235 mg	120 mg	70 mg	70 mg	20 mg
Xanthan gum	-	-	-	-	200 mg	150 mg	100 mg	50 mg	50 mg	100 mg	50 mg	100 mg
Sodium Alginate	-	-	-	-	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg
Cross carmellous Sodium	-	-	-	-	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
Total weight	**650 mg**	**650 mg**	**650 mg**	**650 mg**	**765 mg**	**765 mg**	**765 mg**	**765 mg**	**700 mg**	**700 mg**	**700 mg**	**700 mg**

III. RESULTS AND DISCUSSION:

PRE-COMPRESSIONAL PARAMETERS:

Compatibility of drug-polymer studies were conducted using FTIR spectrophotometer by KBr pellet technique, suggesting that the drug as well as excipient are in the unreacted from. FTIR spectra are in Figure 2.

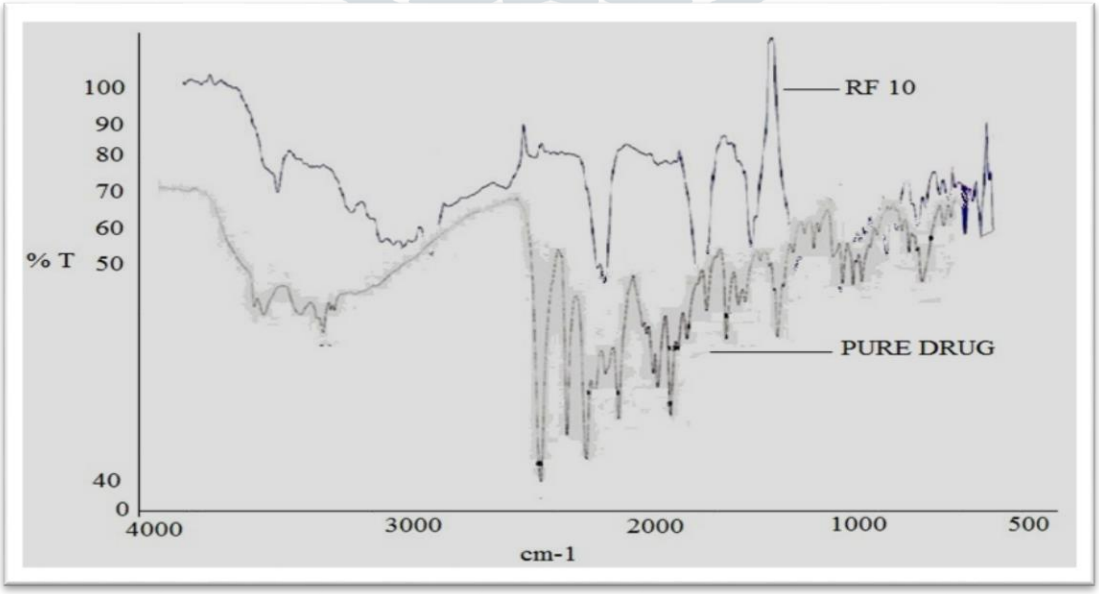

Fig 2: FTIR of Pure Ritonavir & RF 10

PRE-COMPRESSIONAL PARAMETERS: Bulk density depends on particle size, shape and tendency of particles to adhere together, may influence compressibility, porosity, dissolution and other properties.
The bulk density and tapped density of powder blend was found between 0.567 ± 0.04 to 0.790 ± 0.05gm/cm^3 and 0.642 ± 0.05 to 0.929 ± 0.02gm/cm^3, which indicates good packing capacity of powder blend.
Data are shown in table 3.

Carr's index was found to be between 13.56 ± 0.01 to 25.90 ± 0.03. Hausner's ratio method used to evaluate stability of powder column and to estimate the flow properties, it was found between 1.13 ± 0.04 to 1.28 ± 0.09. Low range observed of Hausner's ratio which indicates good flow ability. The angle of repose of all the formulations were found to be within the range of 25.35 ± 0.11 to 31.43 ± 0.17 which showed that, granules were of good flow properties. Data are shown in table 3.

Table 3: Precompressional Parameters

Formulations	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Hausner Ratio	Angle of repose (θ)
RF1	0.780 ±0.06	0.720 ± 0.02	24.20 ± 0.14	1.19 ± 0.07	27.32 ± 0.10
RF2	0.620 ±0.04	0.845 ± 0.03	15.32 ± 0.06	1.16 ± 0.06	29.55 ± 0.12
RF3	0.640 ± 0.05	0.800 ± 0.05	13.56 ± 0.01	1.27 ± 0.01	29.48 ± 0.10
RF4	0.668 ± 0.02	0.862 ± 0.02	23.62 ± 0.09	1.23 ± 0.04	28.10 ± 0.12
RF5	0.710 ± 0.09	0.901 ± 0.08	23.73 ± 0.02	1.22 ± 0.02	25.37 ± 0.17
RF6	0.670 ± 0.02	0.699 ± 0.01	25.90 ± 0.03	1.13 ± 0.04	30.11 ± 0.13
RF7	0.759 ± 0.02	0.721 ± 0.03	20.17 ± 0.13	1.28 ± 0.09	31.43 ± 0.17
RF8	0.712 ± 0.04	0.834 ± 0.05	23.70 ± 0.11	1.22 ± 0.11	29.56 ± 0.15
RF9	0.790 ± 0.05	0.642 ± 0.05	21.44 ± 0.10	1.18 ± 0.01	30.44 ± 0.10
RF10	0.567 ± 0.04	0.929 ± 0.02	22.08 ± 0.09	1.19 ± 0.04	27.09 ± 0.13
RF11	0.699 ± 0.09	0.834 ± 0.04	16.18 ± 0.13	1.24 ± 0.03	29.37 ± 0.13
RF12	0.700 ± 0.03	0.742 ± 0.04	24.55 ± 0.11	1.23 ± 0.06	25.35 ± 0.11

POSTCOMPRESSIONAL PROPERTIES:

TABLET THICKNESS, DIAMETER AND HARDNESS: Thickness was in range of 4.2 ± 0.02 to 4.4 ± 0.06. The hardness of tablets was measured by Pfizer hardness tester. The hardness was in range of 6.4 to 9.1 Kg/cm^2. Tablet hardness reflects differences in tablet density and porosity, which showed results in difference release patterns of the drug by affecting the rate of penetration in the dissolution medium at the surface of the tablet. The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The present study of tablets is within the limit and the slight variation in seen in friability because of the variation in compression force applied and its total weight. The friability of tablets also depends on type of filler and moisture contents present in it. The friability was found to be in the range of 0.23 ± 0.014 to 0.76 ± 0.087. Data are in table 4.

Table 4: Post-Compressional Properties

Formulations	Average weight (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)
RF1	644 ± 0.03	4.4 ± 0.01	11.8 ± 0.06	8.5 ± 0.02	0.41 ± 0.022
RF2	669 ± 0.03	4.4 ± 0.01	11.8 ± 0.04	7.2 ± 0.03	0.48 ± 0.035
RF3	634 ± 0.03	4.4 ± 0.02	11.7 ± 0.06	6.4 ± 0.05	0.41 ± 0.033
RF4	649 ± 0.03	4.4 ± 0.01	11.9 ± 0.03	9.1 ± 0.07	0.44 ± 0.076
RF5	770 ± 0.03	4.4 ± 0.02	12.8 ± 0.04	8.8 ± 0.02	0.29 ± 0.023
RF6	768 ± 0.06	4.4 ± 0.03	12.6 ± 0.02	8.1 ± 0.08	0.27 ± 0.067
RF7	764 ± 0.03	4.3 ± 0.06	12.4 ± 0.03	8.3 ± 0.05	0.76 ± 0.087
RF8	746 ± 0.03	4.3 ± 0.04	12.7 ± 0.09	8.5 ± 0.03	0.23 ± 0.014
RF9	701 ± 0.03	4.3 ± 0.02	12.3 ± 0.08	7.5 ± 0.01	0.25 ± 0.086
RF10	653 ± 0.03	4.4 ± 0.06	11.9 ± 0.04	7.8 ± 0.04	0.57 ± 0.032
RF11	699 ± 0.03	4.2 ± 0.04	12.9 ± 0.04	7.8 ± 0.07	0.27 ± 0.044
RF12	695 ± 0.03	4.2 ± 0.02	12.5 ± 0.06	8.2 ± 0.03	0.38 ± 0.051

PHYSICO-CHEMICAL PROPERTIES:

DRUG CONTENT: Drug content was in range of 96.21 ± 0.15 to 99.67 ± 0.13, which reflects good drug content uniformity in all the prepared formulations. The reading complies as per I P. which indicates drug was uniformly distributed throughout the tablet compressed. Results are in Table 5.

SWELLING INDEX (WATER UPTAKE STUDY): The % of swelling of RF5 and RF12 were higher due to increase in the concentration. The swelling index was in range 51.80 ± 0.22 to 71.20 ± 0.56. RF6 formulation has higher swelling index. The reason for higher swelling index values are due channelling agent, allows more permeation of water into the gel layer and it enhances the water retention property also. This could be the reason for more moisture uptake by formulations of RF6, RF7 and RF11. Results are in Table 5.

Table 5: Physico-Chemical Properties

Formulations	Drug content (%)	Swelling index (%)
RF1	98.32 ± 0.12	61.82 ± 0.24
RF2	96.21 ± 0.15	58.75 ± 0.78
RF3	99.45 ± 0.19	60.40 ± 0.21
RF4	99.67 ± 0.13	61.80 ± 0.27
RF5	98.51 ± 0.22	69.01 ± 0.34
RF6	97.79 ± 0.11	71.20 ± 0.56
RF7	99.50 ± 0.15	70.80 ± 0.41
RF8	97.50 ± 0.24	68.50 ± 0.50
RF9	98.45 ± 0.27	69.38±0.47
RF10	97.21 ± 0.14	58.60 ± 0.32
RF11	99.33 ±0.20	69.99 ± 0.56
RF12	99.58 ±0.32	68.50 0.12

INVITRO BUOYANCY AND LAG TIME: The floating lag time for all the formulations were found to be less than 130 seconds, the floating time duration was found to be up to 24 hrs. The tablet floated with less lag time due to high concentration of gas generating agent. It was observed that paddle speed affected the floating properties of tablet. As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent ($NaHCO_3$) increases the drug release increases and at the same time floating lags time decreases.

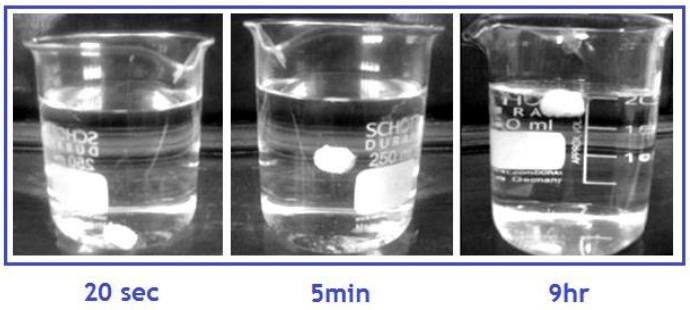

Fig 3: In-vitro Buoyancy Study of Floating Tablet

INVITRO DISSOLUTION STUDES: Invitro dissolution studies were performed for all the batches of Floating tablets of Ritonavir using USP XXIII dissolution test apparatus-II at 50rpm, 900ml of 0.1N HCl used as dissolution media. Results are shown in Tables from 6 to 8 & figures from 4 to 6

Table 6: Invitro release data of Floating Tablets of Ritonavir-RF1, RF2, RF3 & RF4

Timings	RF1	RF2	RF3	RF4
30min	25.90±0.45	23.26±0.70	17.50±0.18	18.74±0.22
1 hr	32.37±0.33	29.89±0.40	27.53±0.23	29.69±0.34
2 hr	40.58±0.31	37.47±0.98	42.57±087	43.42±0.11
3 hr	48.06±0.85	46.52±0.11	50.90±0.36	51.26±0.35
4 hr	55.49±0.49	57.63±0.74	61.97±0.47	63.80±0.25
5 hr	63.21±0.53	60.98±0.46	69.81±0.12	71.74±0.18
6 hr	69.45±0.82	66.45±0.58	77.83±0.69	78.47±0.87
7 hr	76.37±0.73	74.41±1.10	85.80±0.23	86.36±0.05

8 hr	83.83±0.45	82.98±0.87	92.40±0.14	93.78±0.40
9 hr	89.40±0.78	91.57±0.69	99.90±0.78	99.90±0.50
10 hr	99.99±0.78	99.99±0.41	99.90±0.78	99.90±0.50
11 hr	99.99±0.78	99.99±0.41	99.90±0.78	99.90±0.50
12 hr	99.99±0.78	99.99±0.41	99.90±0.78	99.90±0.50

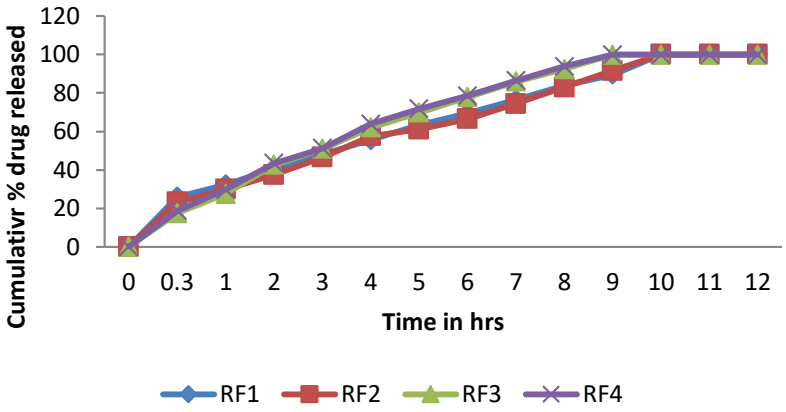

Fig 4: Invitro release of Floating Tablets of Ritonavir-RF1, RF2, RF3 & RF4

Table 7: Invitro release data of Floating Tablets of Ritonavir-RF5, RF6, RF7 & RF8

Timings	RF5	RF6	RF7	RF8
30min	4.23 ± 0.77	5.19 ± 0.63	8.30 ± 0.21	10.00 ± 0.10
1 hr	9.56 ± 0.25	10.32 ± 0.23	17.01 ± 0.88	18.11 ± 0.34
2 hr	14.48 ± 0.34	16.56 ± 0.83	23.96 ± 0.10	24.66 ± 0.39
3 hr	20.36 ± 0.50	21.90 ± 0.30	31.68 ± 0.32	32.89 ± 0.63
4 hr	31.89 ± 0.63	33.89 ± 0.41	39.90 ± 0.43	42.14 ± 0.48
5 hr	38.10 ± 0.41	39.63 ± 0.44	47.83 ± 0.44	48.22 ± 0.66
6 hr	50.73 ± 0.65	53.12 ± 0.78	54.69 ± 0.65	55.50 ± 0.74
7 hr	62.76 ± 0.76	64.89 ± 0.43	65.70 ± 0.67	66.96 ± 0.96
8 hr	71.15 ± 0.49	73.63 ± 0.51	74.00 ± 0.12	75.14 ± 0.41
9 hr	83.79 ± 0.38	85.67 ± 0.77	83.76 ± 0.78	84.78 ± 0.52
10 hr	91.86 ± 0.59	93.54 ± 0.17	94.90 ± 0.98	95.50 ± 0.80
11 hr	100.00 ± 0.01	100.00 ± 0.03	99.99 ± 0.00	99.99 ± 0.00
12 hr	100.00 ± 0.01	100.00 ± 0.03	99.99 ± 0.00	99.99 ± 0.00

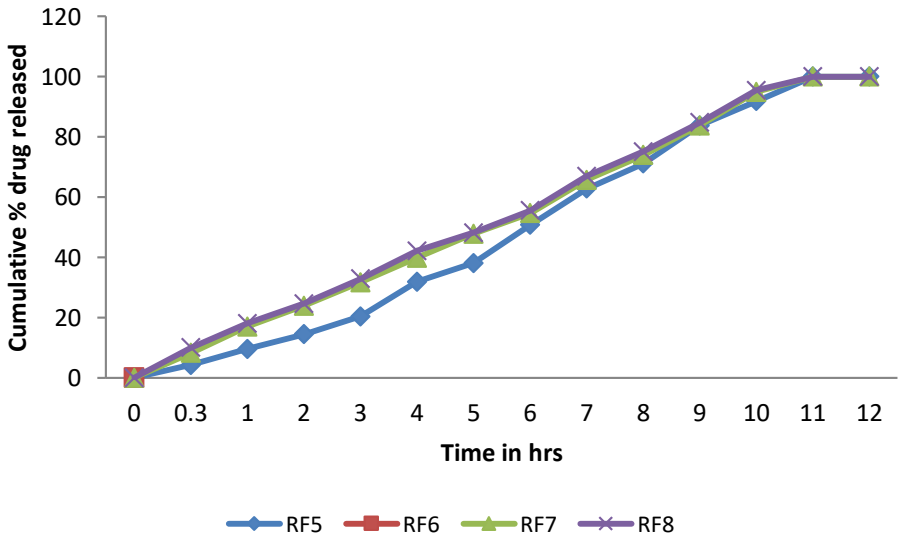

Fig 5: Invitro release of Floating Tablets of Ritonavir RF5, RF6, RF7 & RF8

Table 8: Invitro release data of Floating Tablets of Ritonavir-RF9, RF10, RF11 & RF12

Timings	RF9	RF10	RF11	RF12
30min	10.17 ±0.23	8.81±0.76	7.10 ±0.68	6.43 ±0.22
1 hr	29.16±1.15	16.08±0.48	17.00±1.33	13.30±0.45
2 hr	45.41±0.64	25.83±0.66	23.83±1.30	19.56±0.78
3 hr	53.91±0.38	37.11±0.70	29.95±0.80	25.93±0.14
4 hr	62.19±0.76	44.22±0.56	37.03±0.68	31.31±0.45
5 hr	65.86±0.33	54.26±0.58	47.48±0.71	36.29±0.78
6 hr	71.34±0.73	68.10±0.54	54.99±0.42	42.66±0.60
7 hr	78.93±0.65	75.30±0.31	60.94±0.71	47.49±0.12
8 hr	87.11±0.73	81.90±0.79	67.40±0.67	54.46±0.88
9 hr	99.84±0.82	86.43±0.34	73.65±0.80	62.43±0.98
10 hr	99.84±0.82	90.19±0.91	79.49±0.66	68.76±0.34
11 hr	99.84±0.82	99.91±0.85	90.36±0.65	77.39±0.75
12 hr	99.84±0.82	99.91±0.85	98.41±0.96	83.42±0.98

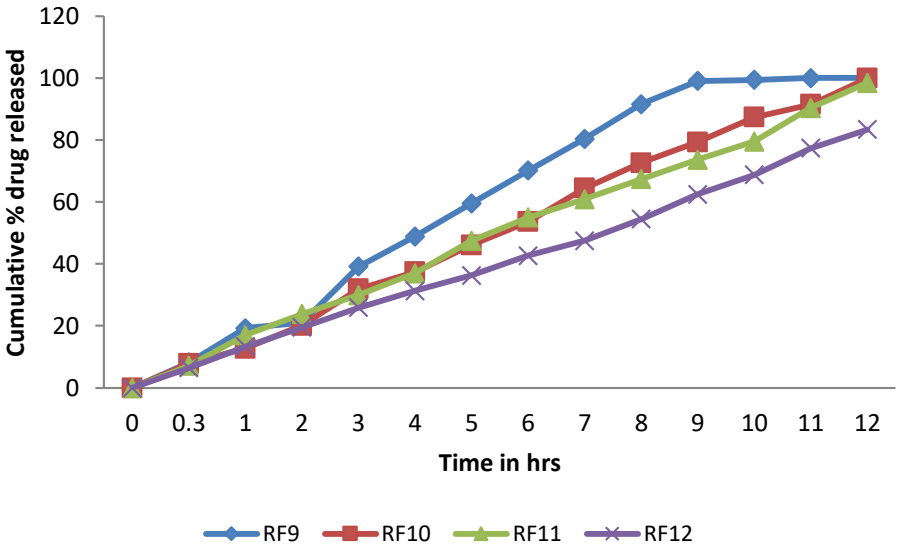

Fig 6: Invitro release of Floating Tablets of Ritonavir RF9, RF10, RF11 & RF12

Formulation RF10 containing Xanthan gum in combination with HPMC K4M showed a drug release of 99.91% in 11 hours. The release profiles of formulation in terms of dissolution t_{50} and t_{90} values, It was observed t_{90} for RF10=10hours exhibited shorter dissolution times. Data are shown in table 9 & in figure 7.

Table 9: Dissolution of t_{50} and t_{90} values of various formulations

Formulations	t50	t90
RF1	3.2	9
RF2	3.5	8,5
RF3	3	7.7
RF4	2.5	5.5
RF5	6	9.5
RF6	5.4	9.4
RF7	5.3	9.4
RF8	5.3	9.3
RF9	2.5	8.3
RF10	4.5	10
RF11	4.3	11
RF12	7.3	12.3

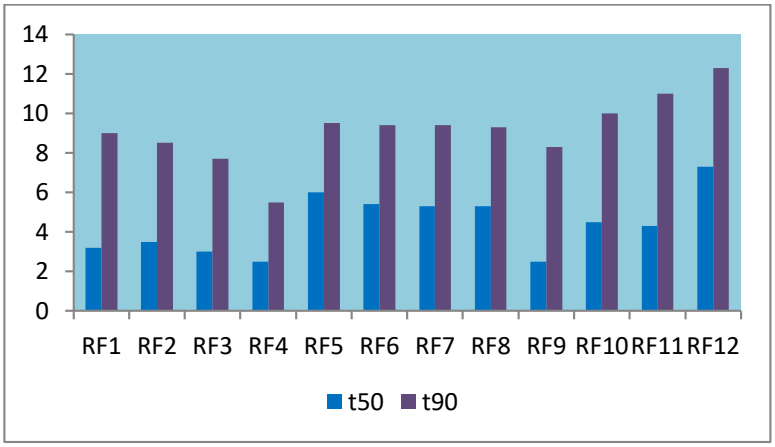

Fig 7: Dissolution of t_{50} and t_{90} values of various formulations

IV. STABILITY STUDIES: Short term stability study was performed for formulation RF10 at $40^0 \pm 2^0$ C / 75 ± 5 % RH for 3 months. The samples were analysed for percent drug content, invitro floating ability and invitro drug release studies. The results are given in table 10 & 11 and figures 8. No appreciable difference was observed for the above parameters.

Table 10: Stability studies of Formulation RF10

Time in days	Physical changes	Mean ± SD (40^0±2°C)
01	--	97.88±1.76
30	No Change	98.30±0.34
60	No Change	98.11±0.66
90	No Change	99.10±0.42

Table 11: InVitro Drug Release data of the formulation RF10

Sl. No.	Time (Hrs)	Cumulative Percent drug released ± SD	
		40^0±2°C & 75%±5% RH	
		1st Day	90th Day
1.	01	19.24±1.86	18.10±1.10
2.	02	25.22±0.90	24.09±1.89
3.	03	35.80±0.71	34.39±0.80
4.	04	44.67±1.53	43.71±0.40
5.	05	60.60±0.13	58.19±1.75
6.	06	66.11±0.43	63.87±0.29
7.	07	74.26±0.77	72.09±1.18
8.	08	85.98±0.64	83.47±0.95
9.	09	90.35±0.90	89.22±1.32
10.	10	96.90±1.23	95.01±1.09
11.	11	97.66±0.75	96.03±0.07
12.	12	98.74±1.90	97.00±1.19

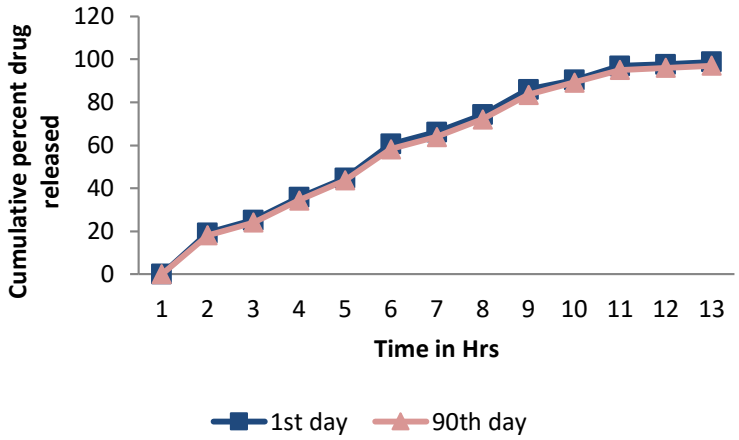

Fig 8: Invitro Drug Release of the stability formulation RF10

V. CONCLUSION:

From the present study, the following conclusions can be drawn:

- From study it is evident that, the formulation retained for longer periods of time in the stomach and provides controlled release of the drug.
- Floating tablets of Ritonavir can be developed to increase gastric residence time and thereby increasing its bioavailability.
- All the prepared tablet formulations were found to be good without capping and chipping.
- Formulated FDDS tablets gave satisfactory results for various post-compressional parameters like hardness, friability, thickness, weight variation and content uniformity.
- As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent (NaHCO3) increases the drugs releases increases and at the same time floating lag time decreases.
- $NaHCO_3$ has predominant effect on the buoyancy lag time, while HPMC K4M, has predominant effect on total floating time and drug release.
- Sodium alginate and Xanthan gum has given extra adhesion property and helped to maintain the integrity of the tablet.
- Swelling index has a significant effect on the drug release.
- Short term stability studies of formulation RF10 Indicates there are no significant changes in the drug content and dissolution parameter value at stable at 40^0C and 75% RH for a period of 3 Months.

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VII. REFERENCES:

1. Mohamed HGD, Khan FN. Gostroretentive drug delivery system: A patent perspective. Int J Health Res 2009;2:23-44.
2. Jain N K. Progress in controlled and Novel drug delivery system 1st edition, New Delhi,CBS publishes, 2004; pg no: 76.
3. Sunil Firangi & Dr S.N.Hiremath. Formulation and Invitro Evaluation of Floating Tablets of Antiritroviral Drug: Acyclovir. IJPRA 2023; 8(5): 343-353.
4. Khan AD, BajpaiM. Floating Drug Delivery System: An Overview. International Journal of PharmTech Research 2010; 2(4): 2497-2505.
5. Sharma N, Agarwal D, Gupta MK, Khinchi MA Comprehensive Review on Floating Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(2): 428-441.
6. Ikechukwu UR, John Francis DE, Ambi AA. Development and evaluation of Ritonavir hollow microballoons for floating drug delivery. Universal Journal of Pharmaceutical Research, 2017; 2(2): 8-11.

7. Rathod H, Patel V, Modasia M. Floating Drug Delivery System: Innovative Approach of Gastroretention. International Journal of Pharmaceutical Sciences Review and Research, 2010; 4(3): 183-192.
8. Dixit N. Floating Drug Delivery System. Journal of Current Pharmaceutical Research 2011; 7(1): 6-20.
9. Shaikh SC, Sanap D, Bhusari DV, Jain S, Kochar PP, Sanchati VN. Formulation and evaluation of Ibuprofen gastro-retentive floating tablets. Universal Journal of Pharmaceutical Research 2018; 3(4): 19- 23.
10. Nakagawa M, Ichikonda S, SasaiY, KuzuyaH. Preparation of Floating Drug Delivery System By Plasma Technique. Chemical and Pharmaceutical Bulletin (The Pharmaceutical Society of Japan) 2006; 54: 514-518.
11. Dorozynski P, Kulinowski P, Wicz RJ, Jasinski A. Development of a System for Simultaneous Dissolution Studies and Magnetic Resonance Imaging of Water Transport in Hydrodynamically Balanced Systems: A Technical Note. AAPS Pharm SciTech 2007; 8(1): E1-E4.
12. Dr. Jose Gutierrez-Rocca., Hossein Omidian and Khalid Shah.,Progress in Gastroretentive Drug Delivery Systems, Pharmatech 2003:152-160.
13. Sunil Firangi1 and SN Hiremath. Development And Characterization Of Floating Drug Delivery System For Antiretroviral Drug: Ritonavir. RJPBCS 2023; 14(5): 40-50.
14. Saliya Parveen, R. B. Nawale, Sadhana Shahi, Nityanand S. Zadbuke and Shehla Khan. Floating Bilayer Tablet: A Review. European Journal of Pharmaceutical and Medical Research, 5(1), 2018.
15. The United States Pharmacopoeial Convention Inc., CD-2004; USP27-NF-22.