Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 3 (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation, Development and Evaluation of The Floating Delivery Using Antiretroviral Ritonavir Tablets: A Comparative Study on Bhara Gum, Albizia Gum, Mesquite Gum as Rate Controlling Polymers

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Cite this paper as: Mohan Koteswara Rao Sandu, Beduin Mahanti, Shaik Harun Rasheed, (2025) Formulation, Development and Evaluation of The Floating Delivery Using Antiretroviral Ritonavir Tablets: A Comparative Study on Bhara Gum, Albizia Gum, Mesquite Gum as Rate Controlling Polymers. *Journal of Neonatal Surgery*, 14 (3), 303-315.

ABSTRACT

Gastroretention plays a vital role for drugs absorbed in the stomach or upper intestine, those unstable in alkaline pH, or degraded in the gut. This study evaluated natural gums (Bhara, Grewia, and Mesquite) for their physicochemical properties and potential in gastroretentive drug delivery, comparing them with synthetic polymers (HPMC K4M, K15M, K100M). Floating tablets were prepared by wet granulation and direct compression, then tested for hardness, friability, floating behavior, dissolution, stability, and in vivo pharmacokinetics.

Ritonavir formulations were studied in 0.1 N HCl for 24 hours. Bhara gum–based tablets (RTB series) showed prolonged release, with RTB2 achieving ~99% release at 24 hours, while Albizia (RTA2) and Mesquite (RTM2) reached complete release within 12–16 hours. At equal polymer levels (75 mg), Bhara gum sustained release for 24 hours, whereas Albizia and Mesquite required higher amounts to maintain extended release.

Overall, Bhara gum emerged as the most efficient natural polymer, achieving controlled release with lower concentrations and enhancing Ritonavir's gastroretentive performance.

Keywords: *Bioavailability, Gastroretentive Drug Delivery System (GRDDS), Floating lag time,Ritonavir, Total floating time.*

1. INTRODUCTION

Designing oral CRDDS for drugs with site-specific absorption is challenging, as only the portion released near the absorption window can be effectively absorbed. This limits the absorption time and compromises system efficiency. To address these issues, various oral controlled delivery systems have been developed to sustain drug release and maintain plasma levels over extended periods[1-3].

Table 1: Conventional *vs* Gastroretentive Drug Delivery System

Conventional Drug Delivery System	Gastroretentive Drug Delivery System
High risk of toxicity	Very low risk of toxicity
Less patient compliance	Improves patient compliance
Not suitable for delivery of drugs with narrow absorption window in small intestine region.	Suitable for delivery of drugs with narrow absorption window in small Intestine region.
No risk of dose dumping.	Possibility of dose dumping

Disadvantages	Advantages
Drugs having rapid absorption through GIT	Drugs acting locally in the stomach
Drugs which degrade in the colon.	Drugs which degrade in the colon.
Drugs which are poorly soluble at an alkaline pH	Drugs having rapid absorption through GIT

The limitations of conventional systems can be addressed for select drugs by extending the gastric residence time through gastroretentive drug delivery systems (GRDDS).

1.1 Need for Gastro retention:

Gastroretention is essential for enhancing the therapeutic efficacy of drugs that are primarily absorbed in the stomach or upper small intestine, have low solubility at higher intestinal pH, or are degraded in the intestinal environment. It is particularly important for drugs with a narrow absorption window or those whose absorption is influenced by gastric emptying time[4].

1.2 Approaches of Gastric Retention

Various approaches of gastroretentive drug delivery systems are:

- **Floating Drug Delivery Systems:** Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach, for a prolonged period of time, without affecting the gastric emptying rate and the drug is released slowly at a desired rate from the system[5].

a. Raft-Forming Systems:

Raft-forming systems consist of gel-forming solutions (e.g., sodium alginate with carbonates or bicarbonates) that, upon contact with gastric fluids, swell and form a viscous gel with entrapped CO_2 bubbles. This gel floats as a raft on the gastric contents, enabling sustained drug release. These formulations often include antacids like calcium carbonate or aluminum hydroxide to neutralize stomach acidity.

b. Swelling/Expanding/Unfoldable Systems[6]:

A dosage form in the stomach will withstand gastric transit if it is bigger than the pyloric sphincter, also the dosage form must be small enough to be swallowed, and must not cause gastric obstruction either singly or by accumulation. Thus, their configurations are required to develop an expandable system in order to prolong the gastric retention time (GRT):

1) A small configuration for oral intake.

2) An expanded gastroretentive form.

3) A final small form enabling evacuation following drug release from the device.

Thus, gastro retentivity is improved by the combination of substantial dimension with high rigidity of dosage form to withstand peristalsis and mechanical contractility of the stomach.

2. MATERIALS AND METHODS

2.1 Materials:

Ritonavir was procured from Gift Sample from Ajanta Pharma Ltd, Mumbai, India. HPMC K4M, HPMC K15 M, HPMC K 100M,Microcrystalline Cellulose Croscarmellose sodium, Sodium bicarbonate, Methanol Magnesium stearate, Talc and Albizia gum, Gum Bhara, Mesquite gum were procured from Yarrow chem, Mumbai, India.

2.2 Methods :

In the present study, the gums were procured from Yarrow Chem. Products, Mumbai, and subjected to a series of evaluations including solubility, phytochemical screening, powder characterization, moisture content determination, pH measurement, swelling index, volatile acidity and rheological analysis.

2.2.1 Organoleptic evaluation and solubility behavior[7]

Organoleptic properties, including color and odour, were assessed, and adulteration was evaluated through solubility studies in water, methanol, ethanol, acetone, and ether.

2.2.2 Determination of purity and identification tests for gums[8]

Identification of the obtained gums was performed using RGI and RGII reagents, as per AOAC (1984) guidelines (Sydney Williams, 1984). RGI was prepared by dissolving 3 g of iodine in 100 ml of alcohol, while RGII was formulated by dissolving 8 g of ruthenium red in 10 ml of lead acetate solution. One gram of gum was treated with 5 ml of each reagent. In accordance with FAO specifications (1991), the gums were also evaluated for swelling in ethanol and subjected to color reactions with concentrated HCl, 5N NaOH, aqueous methylene blue, and concentrated sulphuric acid.

2.2.3 Determination of powder properties[9-10]

- Bulk density
- Tapped density
- Bulkiness
- Compressibility index (I) and Hausner ratio
- Determination of Moisture content

$$\%\text{Moisture content} = \frac{\text{Volume of the KF reagent} \times \text{Water equivalent}}{\text{Sample weight (mg)}} \times 100$$

- Determination of swelling index and water retention capacity:

$$\text{Swelling index (SI)} = \frac{X_t - X_o}{X_o} \times 100$$

- Differential scanning calorimetry (DSC)
- Determination of rheological properties of gums
- Microbiological studies on gums

Microbial analysis was conducted as per the IP to detect aerobic bacteria, fungi, and specific pathogens. Viable counts were determined using the plate count method—liquefied agar for bacteria and potato dextrose agar for fungi. A gum solution (1 g/10 ml) were mixed with sterile agar, poured into Petri dishes, solidified at 5–10°C for 1 h, and incubated at 37°C for 18 h (bacteria) or 20–25°C for 5 days (fungi), followed by colony counting.

2.3 Preparation of floating tablets using synthetic and natural polymers[11-12]:

Tablets containing HPMC of different viscosity grades (K4M, K15M, and K100M) and natural polymers (Gum Bhara, Albizia gum, and Mesquite gum) were prepared by wet granulation at various drug-to-polymer ratios as per the composition tables 2, 3 for RTV Microcrystalline cellulose was used as diluent and sodium bicarbonate as gas-generating agent. The wet mass was formed, passed through a #20 sieve, dried at 60 °C for 1 h, sifted through #22 sieve, and lubricated with magnesium stearate and talc (#80 mesh). Granules were compressed using a Karnavati R&D tablet press with B-type tooling.

Table 2: Formulation of Ritonavir floating tablets using synthetic polymers

c. Ingredients (mg)	d. RTS1	e. RTS2	f.	g. RTS4	h. RTS5	i. RTS6	j. RTS7	k. RTS8	l. RTS9	m.	n. RTS11	o. RTS12
p. Ritonavir	q. 394	394	394	394	394	394	394	394	394	394	394	394
r. HPMCK4M	s. 23.75	t. 47.5	u.	v. 95	w. -	x. -	y. -	z. -	aa. -	bb.	cc. -	dd. -
ee. HPMCK15	ff. -	gg. -	hh.	ii. -	jj. 23.7	kk. 47.5	ll. 71.2	mm. 95	nn. -	oo.	pp. -	qq. -

M					5		5					
rr. HPMCK100M	**ss.** -	**tt.** -	**uu.**	**vv.** -	**ww.** -	**xx.** -	**yy.** -	**zz.** -	**aaa.** 23.75	**bbb**	**ccc.** 71.25	**ddd.** 95
eee. Microcrystalline cellulose	**fff.** 106.25	**ggg.** 2.5	**hhh**	**iii.** 35	**jjj.** 106.25	**kkk.** 82.5	**lll.** 58.75	**mmm.** 5	**nnn.** 106.25	**ooo**	**ppp.** 58.75	**qqq.** 35
rrr. Sodium Bicarbonate	**sss.** 30	30	30	30	30	30	30	30	30	30	30	30
ttt. PVP K30	**uuu.** 10	10	10	10	10	10	10	10	10	10	10	10
vvv. Talc	**www.**	**xxx.**	**yyy**	**zzz.**	**aaaa.**	**bbbb.**	**cccc.**	**dddd.**	**eeee.**	**ffff**	**gggg.**	**hhhh.**
iiii. Magnesium stearate	**jjjj.** 4	**kkkk**	**llll.**	**mmm**	**nnnn.**	**oooo.**	**pppp.**	**qqqq.**	**rrrr.** 4	**ssss**	**tttt.** 4	**uuuu.**
vvvv. Total weight	**wwww 70**	**xxxx. 70**	**yyy**	**zzzz. 70**	**aaaaa. 70**	**bbbbb 70**	**ccccc. 70**	**ddddd 70**	**eeeee. 70**	**ffff**	**ggggg. 70**	**hhhhh 70**

Table 3: Formulation of Ritonavir floating tablets using natural polymers

iiiii. Ingredients (mg)	jjjjj. TB1	kkkkk. TB2	lllll. TB3	mmm TB4	nnnn TA1	ooooo TA2	pppp TA3	qqqqq TA4	rrrrr TM1	sssss TM2	ttttt. RTM3	uuuu TM4
vvvvv. itonavir	www 94	394	394	394	394	394	394	394	394	394	394	394
xxxxx. hara Gum	yyyy 3.75	zzzzz. 7.5	aaaa 1.25	bbbb 5	ccccc	dddd	eeeee	ffffff.-	ggggg	hhhh	iiiiii. -	jjjjjj.
kkkkkk lbizia gum	llllll.	mmmm	nnnn	ooooo	pppp 3.75	qqqq 7.5	rrrrr 1.25	ssssss. 5	ttttt.	uuuu	vvvvvv	www
xxxxxx. esquite gum	yyyy	zzzzzz.	aaaa	bbbb	ccccc	dddd	eeeee	fffffff.	ggggg 3.75	hhhh 7.5	iiiiiii. 71.25	jjjjjjj 5
kkkkkk icrocrystalline cellulose	lllllll 06.25	mmmm 2.5	nnnn 8.75	ooooo 5	pppp 06.25	qqqq 2.5	rrrrr 8.75	sssssss 5	ttttttt 06.25	uuuu 2.5	vvvvvv 8.75	www 5
xxxxxxx odium Bicarbonate	yyyy 0	30	30	30	30	30	30	30	30	30	30	30
zzzzzzz. VPK30	aaaa 0	10	10	10	10	10	10	10	10	10	10	10
bbbbbb alc	ccccc	ddddd	eeeee	fffffff	ggggg	hhhh	iiiiiiii	jjjjjjjj	kkkk	lllllll	mmmm	nnnn
ooooooo agnesium stearate	pppp	qqqqq	rrrrr	ssssss	ttttttt	uuuu	vvvv	wwww	xxxxx	yyyy	zzzzzzz	aaaaa
bbbbbb otal weight	ccccc 70	ddddd 70	eeeee 70	fffffff 70	ggggg 70	hhhh 70	iiiiiiii 70	jjjjjjjj 70	kkkk 70	lllllll 70	mmmm 70	nnnn 70

3. RESULTS& DISCUSSION:

Organoleptic evaluation is a crucial step in developing oral dosage forms, as it directly impacts patient compliance. Sensory analysis was conducted to assess the colour and odour of the gum powders. These characteristics, along with solubility behavior, are summarized in tables 3-5.

Table 3: Organoleptic evaluation and solubility behavior of gums

Parameter	**Observation**		
	Bhara gum	**Albizia gum**	**Mesquite Gum**
Color	Yellow to dark brown	Pale yellow to light brown	Amber to brownish yellow
Odor	Odorless	Odorless	Odorless
Solubility in water	Soluble, forming colorless mucilage	Swells significantly when added to water	Soluble, forming mucilage
Solubility in solvents (chloroform and methanol)	In soluble	In soluble	In soluble

Table 4: Identification test for gums

Test	**Observation**		
	Bhara gum	**Albizia gum**	**Mesquite gum**
Swelling by ethanol solution	Swelling is observed	80% of swelling	60% of Swelling
Color reaction with Conc. HCl	Brownish yellow color is observed	darker yellow to amber or light brown	light reddish-brown
Color reaction with 5N NaOH	Light yellow to yellowish-brown coloration	yellow or brown coloration is observed	Pale yellow to brownish-yellow is observed
Aqueous methylene blue stain	Deep blue or bluish-purple	Deep blue	Moderate blue
Conc. sulphuric acid	brown to black is observed	Reddish-brown to black	Moderate charring

Table 5: Physico-chemical properties of gums

Property	**Bhara gum**	**Albizia gum**	**Mesquite gum**
Bulk density (gm/cc)	0.612±0.01	0.535±0.33	0.608±0.41
Tapped density (gm/cc)	0.655±0.01	0.675±0.13	0.652±0.15
Bulkiness	1.43±0.04	1.55±0.13	1.57±0.36
Compressibility index (%)	9.82±1.34	8.76±0.68	10.01±0.6
Hausner's ratio	1.02±0.054	1.10±0.21	1.00±0.62

Angle of repose (º)	28.20±1.28	25.12±0.36	26.60±0.45
Moisture content	15.2±1.12	10.11±0.12	11.22±0.32
pH	4.8	4.0	4.2
Swelling index (%)	115±10.00	120±8	113±6
Water retention capacity (ml)	14±1.67	17±0.12	13±0.36

3.1 Preformulation studies :

3.1.1 Melting point method

It was found by the capillary tube method in the laboratory. Result for a melting point found is reported in table 6.1 as follows:

Table 6: Melting point of drugs

Drug	Melting point(^{0}c)
Ritonavir	121

3.1.2 Determination of wavelength:

To determine the wavelength of the selected drugs 10 mg of the drug RTV was dissolved in 100 ml of methanol, a standard solution (100 µg/ml) was prepared and scanned over a range of 200 to 400 nm. Maximum absorption was observed at 238 nm for RTV (Figure 1) respectively.

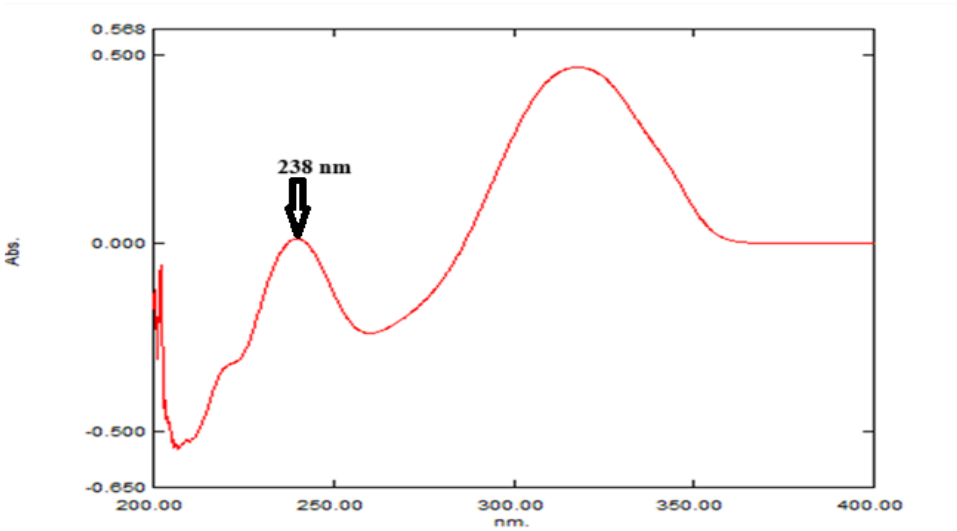


Fig 1: Wavelength of RTV at 238 nm

3.1.3 Calibration curve using solvent 0.1N HCl: Standard plot was constructed using 0.1N HCl as solvent. Concentrations ranging from 10 µg to 50 µg was prepared.

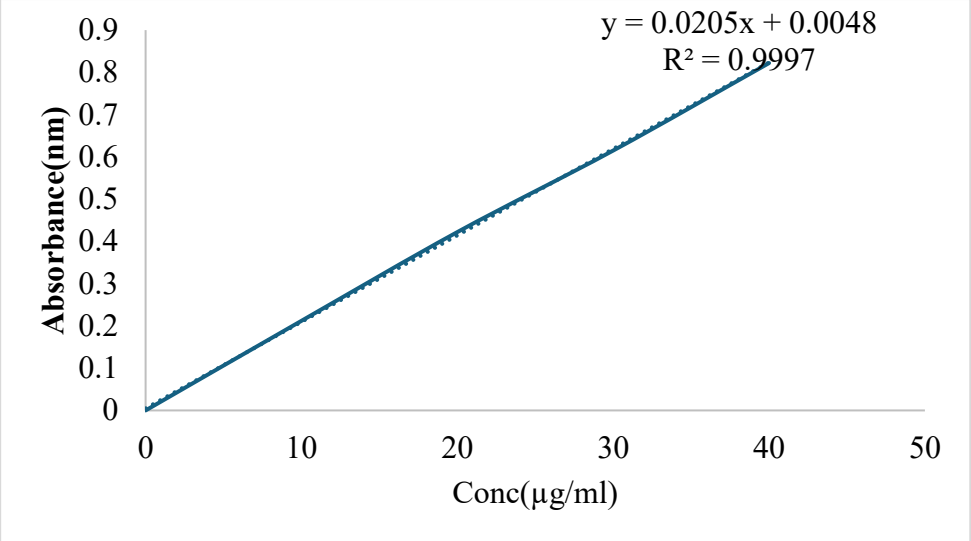


Fig 2: Calibration curve of Ritonavir using 0.1 N HCl

3.1.4 Post-compression physicochemical evaluation of floating tablets

The formulated floating tablets were subjected for post compressional evaluation such as hardness, weight variation, friability, uniformity of drug content, *in vitro* buoyancy, swelling, *in vitro* dissolution and stability. The results are summarized in Tables 7, 8.

Table 7: Post compression parameters of Ritonavir floating tablets by using synthetic polymers

Formula tion	Hardness (kg/cm²) *	Weight variation (mg)*	Friability (%)*	Drug content (%)*	Floating Lag time (min)*	Total floating time (h)*
RTS1	5.6±0.11	570.12±0.33	0.59±0.01	99.35±0.16	1.7	9
RTS2	5.7±0.13	569.69±0.77	0.59±0.02	99.33±0.15	1.5	19
RTS3	5.8±0.04	571.71±0.98	0.53±0.01	99.85±0.16	1.0	23
RTS4	5.9±0.05	570.61±0.02	0.59±0.01	99.12±0.16	1.0	25
RTS5	5.0±0.07	569.51±0.66	0.56±0.02	97.33±0.35	1.1	15
RTS6	5.3±0.04	571.23±0.76	0.63±0.02	98.15±0.23	1.5	25
RTS7	5.5±0.03	570.11±0.94	0.59±0.01	99.33±0.61	1.3	27
RTS8	5.6±0.04	570.93±0.28	0.61±0.01	100.17±0.97	1.4	29
RTS9	5.3±0.06	570.08±0.16	0.58±0.02	99.33±0.36	1.9	21
RTS10	5.4±0.02	570.05±0.85	0.56±0.01	99.17±0.81	1.30	27
RTS11	5.5±0.04	570.30±0.05	0.59±0.02	99.17±0.19	1.08	29
RTS12	5.6±0.02	569.90±0.10	0.60±0.018	98.66±0.17	1.00	31

*Data is expressed as mean ±SD (n=10)

Table 8: Post compression parameters of Ritonavir floating tablets by using natural polymers

Formulation	Hardness (kg/cm^2)*	Weight variation (mg)*	Friability (%)*	Drug content (%)*	Floating Lag time (min)*	Total floating time (h)*
RTB1	5.8±0.021	570.32±0.24	0.33±0.04	99.14±0.13	2.05	12
RTB2	5.9±0.025	569.65±0.28	0.36±0.015	100.78±0.15	1.19	20
RTB3	6.0±0.032	568.83±0.39	0.21±0.020	99.56±0.17	2.10	22
RTB4	6.1±0.011	569.23±0.13	0.37±0.013	99.33±0.12	2.14	24
RTA1	5.9±0.022	570.12±0.18	0.35±0.020	99.35±0.11	2.05	6
RTA2	6.0±0.016	570.66±0.23	0.24±0.012	99.70±0.17	1.44	10
RTA3	6.1±0.015	569.21±0.15	0.39±0.005	99.784±0.13	2.17	12
RTA4	6.2±0.008	568.18±0.12	0.44±0.011	99.74±0.10	2.20	16
RTM1	6.0±0.012	568.86±0.13	0.38±0.011	99.55±0.13	1.66	12
RTM2	6.1±0.01	568.16±0.11	0.41±0.008	99.19±0.11	2.19	14
RTM3	6.2±0.013	568.12±0.19	0.39±0.010	99.70±0.14	2.15	16
RTM4	6.3±0.010	570.73±0.09	0.33±0.0075	99.91±0.09	1.5	18

*Data is expressed as mean ±SD (n=10)

The Ritonavir tablets formulated with semi-synthetic and natural polymers exhibited good mechanical strength and adequate hardness. The measured hardness ranged from 5.0 to 6.3 kg/cm^2, and it was observed that hardness increased as the polymer concentration increased. The weight variation of the prepared RTV formulations ranged from 569.90 ± 0.10 to 571.71 ± 0.98 mg, all tablet batches complied with the weight variation test requirements.

The friability loss of the prepared tablets, determined using a Roche friabilator, ranged from 0.21% to 0.62%. All batches met the requirement of less than 1%, indicating good mechanical stability. The drug content uniformity of the prepared tablets, evaluated according to I.P. specifications, was found to be compliant. The formulations showed drug content ranging from 97.31 ± 0.11% to 101.33 ± 0.25%, confirming uniform drug distribution. All individual values were within the I.P. acceptance range of 90% to 110% of the average content.

3.1.5 *In vitro* buoyancy

Floating tablets were formulated with sodium bicarbonate as the gas generator to achieve minimal floating lag time and 24 h buoyancy. In 0.1 N HCl, CO_2 release caused effervescence, pore formation, and rapid polymer hydration, lowering density (<1 g/ml) for floatation. Low-viscosity HPMC K4M showed the fastest lag time (1–1.7 min), while higher-viscosity grades (K15M, K100M) increased lag but extended floating duration. Polymer type, viscosity, and concentration influenced buoyancy and drug release, with RTS3 optimized for 24 h float and complete release.

Among natural polymers, Bhara gum performed best, giving shortest lag time with RTB2 (1.19 min). All natural polymer formulations (Bhara, Albizia, Mesquite gums) contained sodium bicarbonate, and higher polymer content prolonged float time.

Fig 3A: Photograph taken immediately after placing the tablet into the beaker

3B: Photograph taken during the intermediate stage of tablet floating

3C: Photograph taken immediately after the tablet floated onto the surface indicating the floating lag time

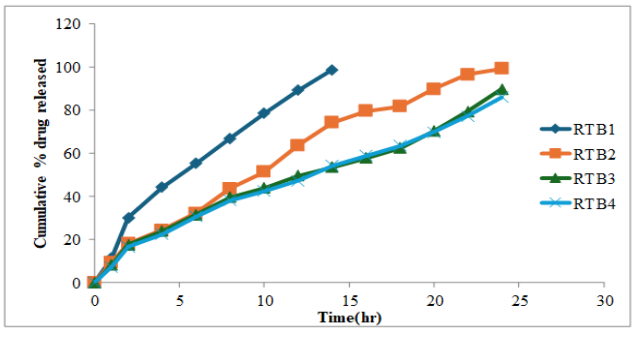
Table 9: Swelling studies of Ritonavir floating tablets formulated with different natural polymers

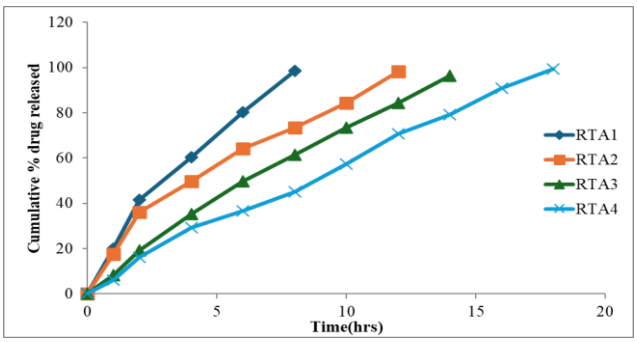
Formulation	Swelling index		
	After 1 h	After 2 h	After 8 h
RTB1	67.44	90.53	160.74
RTB2	70.55	103.06	182.89
RTB3	73.22	110.16	168.73
RTB4	75.79	108.24	156.5
RTA1	63.34	88.49	155.5
RTA2	68.36	97.7	162
RTA3	72.66	108.06	170.84
RTA4	74.47	113.72	174.8
RTM1	64.42	91	153.79
RTM2	66.79	98.72	163.17
RTM3	68.44	104.14	174.93
RTM4	70.53	106.34	176.76

3.1.6 *In vitro* dissolution of Ritonavir floating tablets: was carried out in 0.1 N HCl for 24 h. Drug release from formulations containing three natural polymers—Bhara gum, Albizia gum and Mesquite gum—were compared. The release profiles of RTB1–RTB4, RTA1–RTA4, RTM1–RTM4, were tabulated and plotted as cumulative release vs. time curves.

Floating drug delivery prolonged release and improved bioavailability. Ritonavir formulations with Bhara gum (RTB series) showed slower release as polymer concentration increased. RTB2 achieved nearly complete release (99.11 ± 0.48%) at 24 h. Comparable formulations with Albizia gum (RTA2) and Mesquite gum (RTM2) released ~100% by 12 and 16 h, respectively. At 75 mg polymer, Bhara gum-maintained release for 24 h, whereas Albizia and Mesquite required higher concentrations to sustain release beyond 18–20 h.

Overall, Bhara gum proved most effective in extending drug release with comparatively lower polymer concentration.





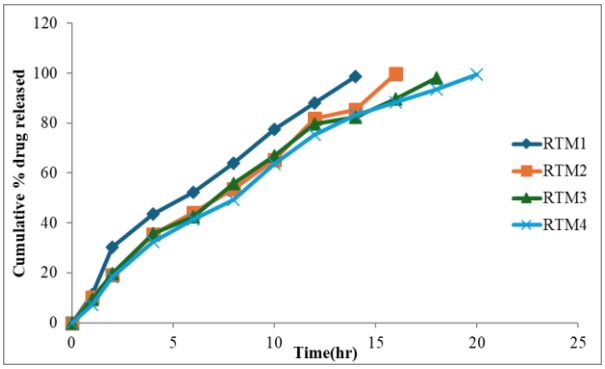


Fig 4: Comparison of Ritonavir Cumulative % drug released using natural polymers

3.1.7 Drug release kinetics: The drug release mechanism of the prepared formulations was assessed by evaluating the correlation coefficients of different kinetic models, namely zero-order, first-order, Higuchi, and Korsmeyer–Peppas, based on the release data of each formulation. The kinetic study results are summarized in the table 10. In most cases, the correlation coefficient values for the Korsmeyer–Peppas and zero-order models were closer to unity compared to the other models, suggesting that the release pattern predominantly followed these two mechanisms.

An inverse relationship was noted between the zero-order release constant and the drug-to-polymer ratio. With an increase in polymer concentration, the release rate declined, showing a strong correlation. This clearly indicated that natural polymers exhibited superior performance compared to synthetic ones.

For the optimized formulations, the 'n' values obtained from the Korsmeyer–Peppas model were within the range of 0.68–0.89. Hence, the release behavior was best explained by non-Fickian (anomalous) diffusion.

Table 10: Correlation Coefficient (r^2) Values of formulations using natural polymers

Formulation	Correlation Coefficient (r^2) Values				
	Zero order	First order	Higuchi's	Peppas's	n value
ooooooooo. RTB1	**0.9691**	0.8205	0.9625	**0.9733**	0.76
ppppppppp. RTB2	**0.9791**	0.8329	0.9617	**0.9908**	0.73
qqqqqqqqq. RTB3	**0.9803**	0.7014	0.9502	**0.9815**	0.68
rrrrrrrrr. RTB4	**0.9814**	0.7233	0.9587	**0.9881**	0.71
sssssssss. RTA1	**0.9735**	0.8527	0.9712	**0.9814**	0.74
ttttttttt. RTA2	**0.9622**	0.8128	0.9441	**0.9814**	0.67
uuuuuuuuu. RTA3	**0.9905**	0.8631	0.9562	**0.9952**	0.89
vvvvvvvvv. RTA4	**0.9933**	0.7317	0.9419	**0.9843**	0.85
wwwwwwwww. RTM1	**0.9681**	0.8207	0.9733	**0.9536**	0.76
xxxxxxxxx. RTM2	**0.9894**	0.7263	0.9512	**0.9911**	0.80
yyyyyyyyy. RTM3	**0.9833**	0.8402	0.9612	**0.9914**	0.82
zzzzzzzzz. RTM4	**0.9769**	0.8435	0.9709	**0.9912**	0.83

Based on the studies conducted with synthetic polymers (HPMC K4M, HPMC K15M, HPMC K100M) and natural polymers (Bhara gum, Albizia gum, Mesquite gum) using Ritonavir the most effective formulations were obtained with HPMC K4M and Bhara gum. These were further studied for stability and *in vivo* studies were performed.

3.1.8 Stability studies

In the present study, samples were stored under accelerated conditions (40 ± 2 °C/75% RH) in accordance with ICH guidelines, and withdrawn at predetermined intervals (0, 1, 2, 3, and 6 months).

The optimized formulations (RTS3, RTB2) were subjected to accelerated stability testing, and the results pertaining to floating behavior and drug release profiles are presented in the respective table 11 and figures.

Table 11: Floating characteristics before and after Storage

Formulations	Floating characteristics			
	Before Storage		After Storage	
	Floating Lag time (min)	Floating time (hr)	Floating Lag time (min)	Floating time (hr)
RTS3	1	23	1	23
RTB2	1.19	20	1.19	20

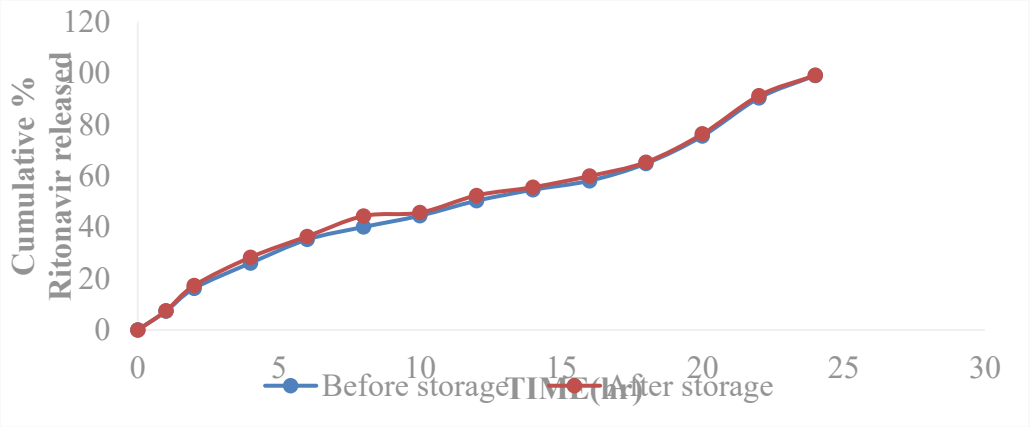


Fig 5: *In vitro* dissolution data of optimized Ritonavir floating tablets (RTS3) tested at 40±2^0 C/75±5% RH for 3 months

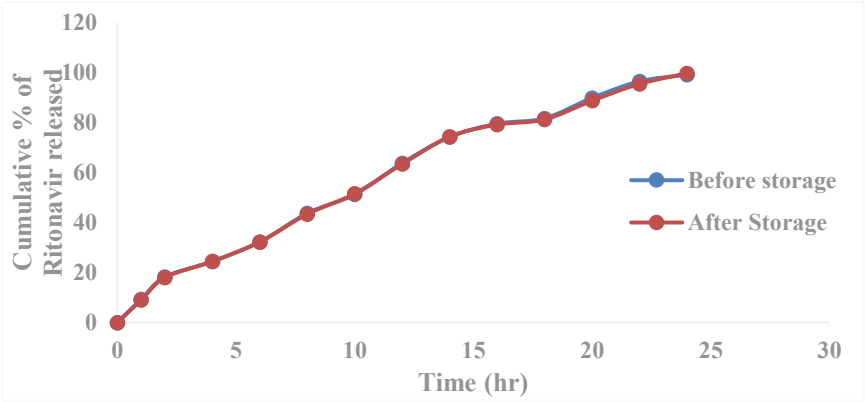


Fig 6: *In vitro* dissolution data of optimized Ritonavir floating tablets (RTB2) tested at 40±2^0 C/75±5% RH for 3 months

3.1.9 Pharmacokinetic evaluation of optimized formulations of Ritonavir

The *in vitro* dissolution studies confirmed the sustained release performance of the optimized formulations of Ritonavir (RTB2) over a 24-hour period. Consequently, these formulations were chosen for in vivo evaluation against the pure drug, since no controlled-release commercial products are currently available at rabbit-equivalent doses. The human doses of Ritonavir were adjusted to the rabbit scale, and floating tablets containing the optimized dose (RRTB2 and RNFB3) were developed accordingly.

4. CONCLUSION

The work aimed to evaluate natural polymers such as Bhara gum, Grewia gum, and Mesquite gum for their properties (viscosity, swelling index, microbial load, etc.) and their applications in designing GRDDS tablets. We also compared these natural gums with synthetic polymers like HPMC K4M, K15M, and K100M. The release profiles for RTB1–RTB4, RTA1–RTA4, RTM1–RTM4 were tabulated and plotted as cumulative release versus time curves. Our findings indicate that floating drug delivery prolonged release and improved bioavailability. For Ritonavir, formulations with Bhara gum (RTB series) showed slower release as polymer concentration increased. Specifically, RTB2 achieved nearly complete release (99.11 ± 0.48%) at 24 hours. Comparable formulations with Albizia gum (RTA2) and Mesquite gum (RTM2) released approximately 100% by 12 and 16 hours, respectively. At 75 mg polymer, Bhara gum-maintained release for 24 hours, whereas Albizia and Mesquite gums required higher concentrations to sustain release beyond 18–20 hours. With an increase in polymer concentration, the release rate declined, showing a strong correlation. This clearly indicated that natural polymers exhibited superior performance compared to synthetic ones.

For the optimized formulations, the 'n' values obtained from the Korsmeyer–Peppas model were within the range of 0.68–0.89. Hence, the release behavior was best explained by non-Fickian (anomalous) diffusion.

Acknowledgement

None.

Conflict of Interest

Authors have no conflict of interest to declare.

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