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FORMULATION AND *IN-VITRO* EVALUATION OF PULSATILE RELEASE TABLETS OF RITONAVIR

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Keywords:

Ritonavir, Floating drug delivery system, Pulsatile release, Superdisintegrants, Hydrophilic polymers (HPMC K100M)

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ABSTRACT: The objective of the present study was to develop a time-controlled floating pulsatile drug delivery system of Ritonavir (RIT), an antiviral drug with low oral bioavailability due to degradation by CYP3A4 enzymes, efflux by P-glycoprotein, and instability at alkaline pH. Ritonavir is primarily absorbed in the stomach; hence, a floating pulsatile release system was designed to enhance absorption and therapeutic efficacy. Core tablets of Ritonavir were prepared using different superdisintegrants and evaluated for *in-vitro* disintegration. The disintegration time varied from 21–44 seconds, with crosspovidone showing the fastest disintegration due to rapid water penetration compared with croscarmellose sodium and sodium starch glycolate. Since rapid disintegration is critical for burst release, the F3 formulation was selected for further studies. The rapid release core tablet (F3) was compression-coated with varying concentrations of HPMC K4M, HPMC K15M, and HPMC K100M (P1–P9). Formulations with HPMC K100M (P7–P9) showed a lag time of 4–4.5 hours followed by sigmoidal release, achieving 100% drug release by 10–12 hours. Among these, P9 (core 100 mg + 180 mg HPMC K100M coating) exhibited the most desirable profile. This was further formulated with floating agents (HPMC E15LV, sodium bicarbonate, citric acid), and N2 was optimized, showing buoyancy within 1 min and sustained floatability. The final optimized batch (F3P9N2) exhibited a lag time of 4 hours with complete drug release at 12 hours and demonstrated stability under accelerated conditions without significant changes. Thus, the floating pulsatile system of Ritonavir provides a promising approach for controlled gastric retention and timed drug release.

INTRODUCTION: Oral route is one of the most popular, preferable and convenient routes for drug administration. It possesses certain advantages like ease of administration, self medication, patient compliance and flexibility with a wide range of dosage form [1].

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In the present era of drug delivery, tablet is the most successful and convenient oral dosage form and preferred by patient as well as physicians [2] However with the advancement of the technologies in the pharmaceutical field, modified drug delivery systems have drawn an increasing interest.

Nowadays, the emphasis of pharmaceutical research is aimed at development of more efficacious drug delivery systems according to the requirement of body and disease state and thus achieving optimal clinical outcome with constant drug plasma concentrations [3].

In the case of certain diseases symptoms display circadian variations and hence drug release from the dosage form should also vary over time. Circadian cycles last about 24 hours, e.g. sleeping and waking patterns. The coordination of medical treatment and drug delivery with such biological clocks and rhythms is termed Chronotherapy [4].

If the peak of symptoms occurs during the daytime a conventional dosage forms can be administrated just before the symptoms are worsening. If symptoms of the disease became worse during the night or in the early morning the timing of drug administration and nature of the drug delivery system need careful consideration. In this case, modified-release dosage forms must be used [5].

The challenge of delivering drug at predetermined rate and time could be met by a wide range of newer techniques like osmotically driven pumps [6], matrices with controllable swelling [7], diffusion [8] or erosion rates [9], nonuniform drug loading profiles [10] and multi-layered matrices.

A second major challenge has been the controlled delivery of compounds in a pulsatile or staggered fashion. For this mode of delivery, it is assumed that constant plasma drug levels are not preferred and that an optimal therapeutic effect comes from a periodically fluctuating drug concentration. Two different methodologies have been broadly investigated as possible solutions to this challenge. One is the fabrication of a delivery system that releases its payload after a predetermined time delay or in pulses of predetermined sequences [11].

Controlled drug delivery systems have acquired a center stage in the arena of pharmaceutical research and development. The oral controlled release system maintains the drug concentration in the therapeutic window for a prolonged period of time, thereby ensuring sustained therapeutic action. These modified-release formulations have many advantages over immediate-release formulations. With these formulations less frequent drug administration is possible, lower peak concentrations can be obtained to avoid adverse effects, and patient compliance can be improved [12]. However, in chronological diseases like bronchial asthma, rheumatic disease, ulcer, cancer, diabetes, attention deficit syndrome, hypercholesterolemia, neurological disorder, angina pectoris, myocardial infarction and hypertension a continuous release pattern is not suitable. These conditions demand release of drug after a lag time that is a pulsatile release [13].

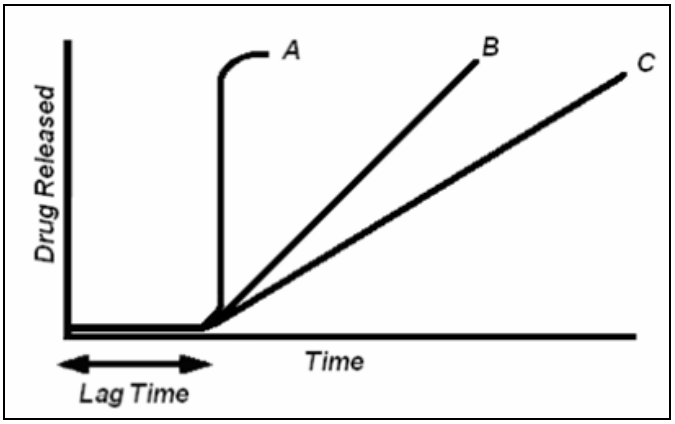

FIG. 1: DRUG RELEASE PROFILE OF PULSATILE DRUG DELIVERY SYSTEM A: IDEAL SIGMOIDAL RELEASE B&C: DELAYED RELEASE AFTER INITIAL LAG TIME

Floating Drug Delivery System: There are numerous approaches to prolong gastric retention, floating drug delivery system is the most widely used technique and offers a simple practical approach to increased gastric residency through inherent buoyancy.

Floating systems significantly extend the period of time, over which drug may be released and prolong dosing intervals and increase patient compliance. These systems retain in stomach and improve the absorption window and thus enhance the bioavailability [26].

Floating drug delivery systems or hydrodynamically balanced systems were first described by Davis (1968). Floating system also known as dynamically controlled systems low density systems that have sufficiently 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 **Fig. 2.**

This results in an increased gastric retention time and a better control of the fluctuations in plasma drug concentration. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hallow Microspheres [27].

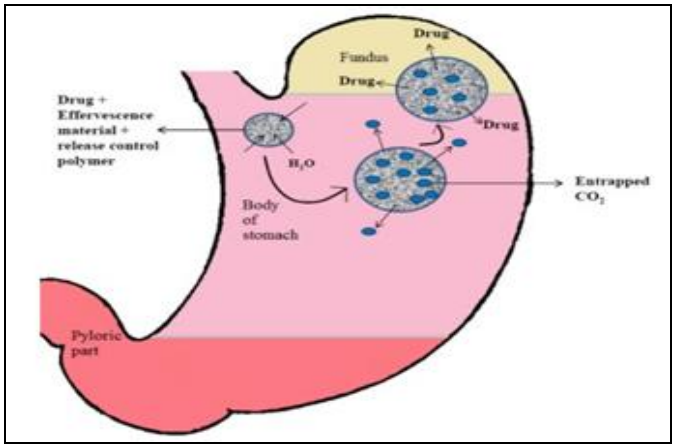

FIG. 2: FLOATING DRUG DELIVERY SYSTEM IN STOMACH

MATERIALS AND METHODOLOGY:

Preparation of Floating Pulse Release Tablets [60]: A pulsatile–floating drug delivery system consists of three different parts, a core tablet, containing the active ingredient, an erodible outer shell, and a top cover buoyant layer. Floating pulsatile release tablet of RIT was prepared by compression with different composition ratio of erodible coating (press-coated systems). Rapid release core tablet (RRCT) of RIT was first prepared and optimized. RRCT was then press coated with polymers in two steps to formulate Pulsatile release tablet (PRT). Finally, PRT were compressed with effervescent floating layer to prepare floating pulsatile released tablets (FPRT).

Preparation of the Rapid Release Tablet (RRCT) [61-62]: Core tablets containing Ritonavir were prepared by using direct compression method. All the ingredients were passed through 60# mesh sieve separately and collectively. Different preliminary batches of core tablets were prepared by mixing all ingredients with different superdisintegrants. Powder mixture of RIT, Crospovidone, crosscarmellose sodium, Sodium Starch Glycolate and MCC were dry blended for 20min followed by addition of magnesium stearate. The mixtures were then further blended for 10 min and resultant powder blend was compressed using rotary tablet machine with a 6mm punch and die to obtain the core tablet containing 25mg of RIT. For the above batches disintegration study was conducted from which optimized batches were selected and only that batch was conducted for further study **Table 1.**

TABLE 1: COMPOSITION OF RAPID RELEASE CORE TABLET OF RIT

Ingredients (mg)	Formulation code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Ritonavir	100	100	100	100	100	100	100	100	100
Crospovidone	3.0	4.0	5.0	—	—	—	—	—	—
Cross Carmellose Sodium	—	—	—	3.0	4.0	5.0	—	—	—
Sodium starch glycolate	—	—	—	—	—	—	3.0	4.0	5.0
MCC	39	38	37	39	38	37	39	38	37
Magnesium stearate	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Talc	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Total Tablet weight	150	150	150	150	150	150	150	150	150

Preparation of Pulsatile Release Tablet (PRT) [62]: The optimized RRCT (F3) was taken as core for the preparation of PRT. For dry coating of F3 formulation 250mg coatings of HPMC K4M, Na CMC, HPMCE14 and Magnesium stearate were used with two steps: In the first 125mg coatings were filled into the die (11.8mm in diameter), followed by RRCT placed in the center of die, and slightly pressed to fix the coatings around and under the core, and then the rest of the coatings were filled and compressed **Table 2.**

TABLE 2: COMPOSITION OF PULSATILE RELEASE TABLETS

Ingredients (mg)	Formulation code								
	P1	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**
HPMC K4M	25	50	75	-	-	-	-	-	-
HPMC K15M	-	-	-	25	50	75	-	-	-
HPMCK100M	-	-	-	-	-	-	25	50	75
MCC	220	195	170	220	195	170	220	195	170
Magnesium stearate	5	5	5	5	5	5	5	5	5
Total Tablet weight	250	250	250	250	250	250	250	250	250

Preparation of Floating Pulsatile Release Tablets (FPRT) [61]: On the basis of drug release profile of PRTs best formula composition (F3P9) was selected for the preparation of FPRT **Table 3**. Floating tablets were prepared by placing 50% of pulsatile release layer in 11.8 mm die and optimized RRCT was placed on it. Further remaining quantity of pulsatile release layer was added in cavity so as to cover the RRCT and finally pre-compressed it with lower compression pressure (hardness, 3-4 kg/cm^2) by using single punch tablet machine. The weighed amount (100 mg) of floating layer powder composition was kept on pre-compressed tablet (PRT) in die, and then finally compressed it to give certain hardness (6-7Kg/cm^2). The total weight of each FPRT tablet was adjusted to 500mg.

TABLE 3: COMPOSITIONS OF THE BUOYANT LAYER

Ingredients (mg)	Formulation code		
	N1	N2	N3
HPMC E15LV	40	50	60
Sodium Bicarbonate	20	20	20
Citric acid	10	10	10
Lactose	30	20	10
Total weight	100	100	100

Evaluation of Floating Pulsatile Release Tablet:

Hardness [63]: Hardness (Kg/cm^2) of RRCT and FPRTs were determined by Monsanto hardness tester. Tablet hardness testing is the test to determine the breaking point and structural integrity of a tablet "under conditions of storage, transportation, and handling before usage".

Friability (F) [63]: RRCT and FPRT formulations (20) were weighed and placed in the Roche Friabillator that revolves at 25 rpm for 4 minutes dropping them from a distance of six inches with each revolution. After the operation the tablets were de-dusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable. The % friability was then calculated by the following formula:

F = Initial Weight - Final weight / Initial weight × 100

Weight Variation Test [63]: FPRT formulations [20] were individually weighed, calculated the average weight, and compared the individual tablet weights to the average. The tablets met the IP tests that were not more than 2 tablets were outside the percentage limit and no tablets differed by more than 2 times the percentage limit. The maximum percentage difference allowed is 5% for the average weight of tablets more than 250mg **Table 4.**

TABLE 4: SPECIFICATIONS OF % WEIGHT VARIATION ALLOWED IN TABLETS

S. no.	Average Weight of tablet	% Deviation
1.	80 mg or less	10
2	More than 80 but less than 250 mg	7.5
3	250 mg or more	5

Disintegration Time [63]: USP disintegration test apparatus was used to determine the disintegration time of RRCT formulation. To test the disintegration time of tablets, one tablet was placed in each tube, and the basket rack was positioned in a 1-liter beaker containing 0.1N HCl at 37°C ± 1°C such that the tablet remains 2.5 cm below the surface of the liquid. The time taken for the complete disintegration of the tablets was noted.

Drug Content [64]: Total 10 tablets were weighed and powder equivalent to 25 mg of RIT was weighed and dissolved in 0.1N HCl then filtered through Whatman filter paper. Solution was analysed for RIT content by UV Spectrophotometer at 246 nm using 0.1N HCl as blank.

Floating Lag Time [63-64]: The floating lag time is determined in order to assess the time taken by the dosage to float on the top of the dissolution medium, after placing the dosage form in the medium. Floating characteristics of the prepared formulations were determined using USP paddle apparatus at a speed of 50 rpm in 900ml of 0.1N HCl solution. The time required to float is noted.

Floating Time [63-64]: Floating time of the prepared formulations were determined using USP paddle apparatus at a speed of 50 rpm in 900ml of 0.1N HCl solution at 37±0.2°C for 24 hours. The time during which the dosage form remains buoyant (floating duration) was measured.

***In-vitro* Dissolution Studies of PRT & FPRT Tablets [64]:** Dissolution studies on PRT & FPRT tablet of RIT were performed under gastric conditions. The test was performed using the USP dissolution apparatus type II at 50 rpm. A tablet containing 25mg of RIT was placed in a dissolution

vessel containing 900mL of 0.1N HCl maintained at 37±0.5°C. At predefined time intervals, samples from the dissolution medium were withdrawn, filtered and concentration of RIT was determined spectrophotometrically at λ_{max} 246nm.

Stability Studies [64]: Stability studies were performed to determine the changes on the final formulation at different storage conditions. In the present study the selected formulation (F3P9N2) exposure up to 3 months stability studies at accelerated condition. Initial drug content was considered as 100 percent and drug content at each time interval was determined.

RESULT AND DISCUSSION:

Preformulation Studies:

Organoleptic Properties: Identification studies showed that the drug supplied by Arysta Life science India Limited, Indore, matched with the official standard as prescribed **Table 5.**

TABLE 5: PHYSICAL IDENTIFICATION TESTS OF RITONAVIR

Parameters	Ritonavir	Results
Appearance	White hygroscopic powder	Complies
Odor	Odorless	Complies

Determination of Wavelength Maxima (λ_{max}): UV spectrum of drug was obtained by scanning drug solutions (10µg/ml) showed maximum absorption at 246 nm. Reported λmax of RIT is 246nm **Fig. 3.** So it can be concluded that the given drug was Ritonavir.

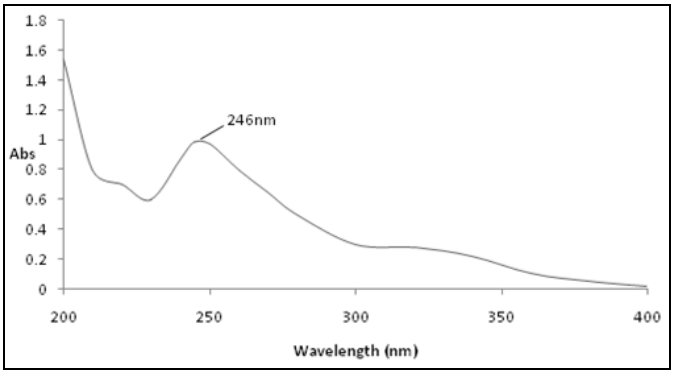

FIG. 3: UV SCAN OF RITONAVIR DRUG SAMPLE

FTIR Spectroscopy of Drug: FTIR spectra of RIT was obtained and compared with reference IR spectra for identification and confirmation of various functional groups. Interpretation of FTIR spectra of RIT suggests that the observed peak list meets with that of the reference peak list **Table 6** and **Fig. 4**. The observation confirms that the drug obtained is pure. At cm 3131, 3417.

TABLE 6: IMPORTANT BAND FREQUENCIES IN IR SPECTRUM OF RIT

Characteristic Group	Practical Peaks (CM^{-1})
Ether stretching	3417
-OH Stretch	3131
N-H Stretch	2301
C-O	1715
phenyl nucleus skeletal stretching	1527

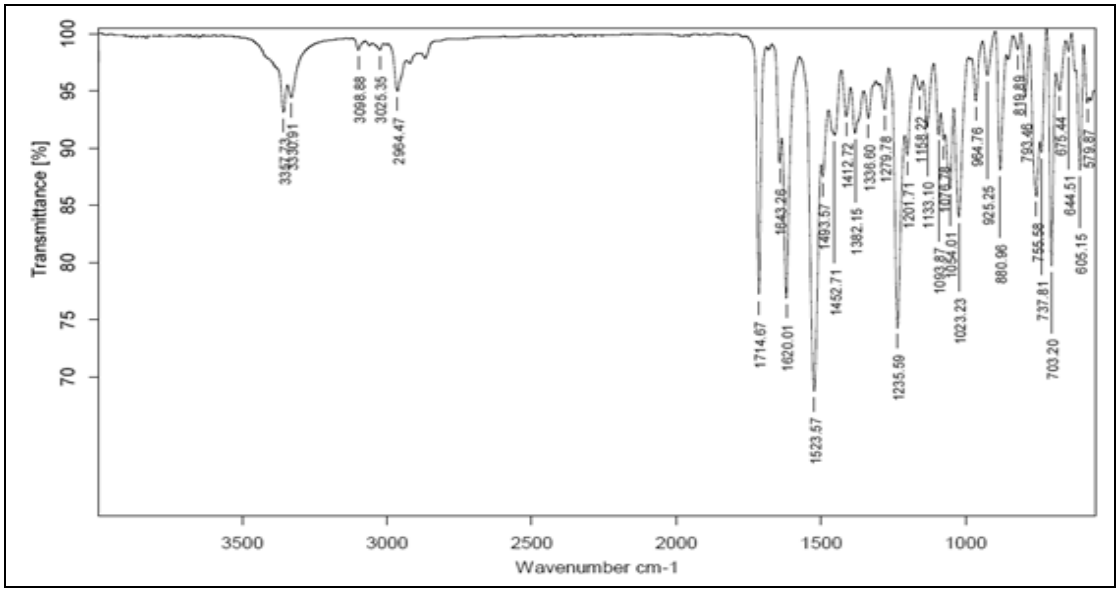

FIG. 4: FTIR SPECTRUM OF RIT

Melting Point of Drug: A capillary melting point method was used to determine the melting point of the drug. It was observed that the melting point of Ritonavir was found to be similar to the reported value which proved that the received drug samples meet the reported properties **Table 7.** Any impurity, if present, will cause variation in the melting point of a given drug substance. From the above test it was found that the sample drug complies with the standard test of Ritonavir.

TABLE 7: MELTING POINT OF RITONAVIR

S. no.	Reported melting point	Observed melting point
1	120-122 °C.	119±0.2 °C
2	120-122 °C.	121±0.5 °C
3	120-122 °C.	122±0.3 °C

Solubility Studies: The solubility profile of RIT shows its hydrophillic nature as it was found to be freely soluble in water, 0.1N HCl, PBS pH 7.4 and ethanol. However, it is slightly soluble in acetone and insoluble in ether **Table 8.**

TABLE 8: SOLUBILITY OF RIT IN DIFFERENT SOLVENTS

Solvents	Solubility (RIT)
Distilled Water	Sparingly Soluble
0.1 N HCl	Soluble
PBS pH 7.4	Sparingly Soluble
Ethanol	Soluble
Methanol	Soluble

Partition Coefficient: The partition coefficient of RIT was determined in n-octanol: water system. The partition coefficient of RIT was found to be 4.15 which shows its diffusion in oil phase. This value is close to that of the literature citation **Table 9.**

TABLE 9: PARTITION COEFFICIENT OF RIT IN N-OCTANOL: DISTILLED WATER

Drug	Amount of Drug (mg)		Partition coefficient ($Po_{/w}$)	
	Aqueous Phase	n- Octanol	Theoretical	Practical
RIT	1.94	8.06	4.30	4.15

Calibration Curve of Drug: Calibration curve was prepared in 0.1N HCl at 246nm and linearly regressed. The correlation coefficient for standard curves was found to be very near to one which indicates good co-linear correlation between concentration 2-10 µg/ml **Table 10** and **Fig. 5**. Hence, drugs are following Beer Lambert Law in the above range **Table 11.**

TABLE 10: CALIBRATION CURVE OF RIT AT 246NM

Concentration (µg/ml)	Absorbance
2	0.0924
4	0.1768
6	0.2713
8	0.3664
10	0.4572

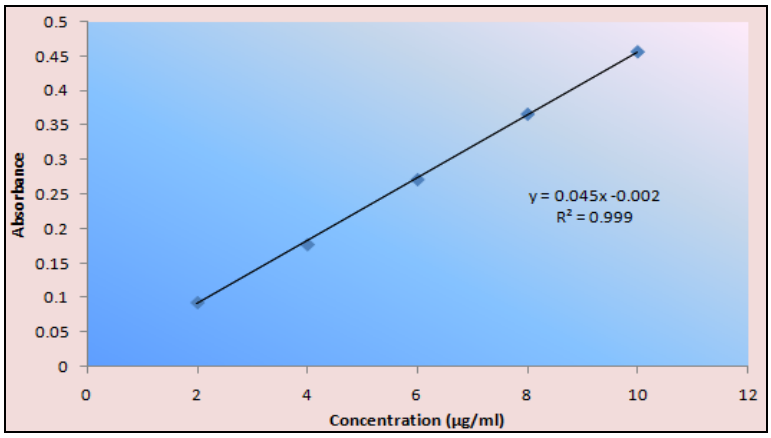

FIG. 5: CALIBRATION CURVE OF RIT AT 246 NM

TABLE 11: REGRESSION ANALYSIS OF RITONAVIR IN 0.1N HCL

S. no.	Parameters	Result
1.	Regression equation	y = 0.045x -0.002
2.	Correlation coefficient	R^2 = 0.999
3.	Calibration curve range	2-10 (µg/ml)

Drug-Excipients Compatibility Study: This study was performed to determine any physical change in the drug when kept in contact with various formulation excipients. Drug excipient compatibility studies were performed for drug and

physical mixtures. Drug excipients compatibility study showed no change in physical appearance as well as color of the contents which indicates that there is no interaction between drugs and excipients **Table 12.**

TABLE 12: DRUG EXCIPIENTS COMPATIBILITY STUDY FOR 4 WEEKS

Name of drug/ excipients	Initial Description	Test parameters		
		Refrigerator (2-8°C)	Room temperature	40°C±75%RH
RIT drug	White Powder	No Change	No Change	No Change
RIT + HPMC	White Powder	No Change	No Change	No Change
RIT + MCC	White Powder	No Change	No Change	No Change
RIT + PVPK30	White Powder	No Change	No Change	No Change
RIT + Na CMC	White Powder	No Change	No Change	No Change
RIT + Mg Stearate	White Powder	No Change	No Change	No Change
RIT + HPMC + MCC + PVP + NaCMC + Mg Stearate	White Powder	No Change	No Change	No Change

TABLE 13: POST-COMPRESSION EVALUATION OF RAPID RELEASE CORE TABLET

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Hardness ($Kg/cm^{2)}$	2.8±0.01	2.7±0.03	2.8±0.05	3.1±1.3	2.9±2.0	2.9±1.5	3.0±2.2	2.8±0.8	2.7±1.2
(%) Weight variation	2.2±0.4	2.2±0.7	0.8±0.06	2.6±0.2	1.5±0.4	1.8±0.9	0.8±1.2	1.4±0.6	2.5±0.7
Thickness (mm)	1.6±0.03	2.0±0.15	1.8±0.19	2.2±1.2	2.0±0.7	2.0±1.2	1.9±0.8	1.8±0.06	2.0±1.12
Friability (%)	0.68±2.0	0.66±2.4	0.62±2.8	0.67±1.17	0.66±2.0	0.62±1.2	0.68±2.0	0.65±1.12	0.63±2.0
% Drug Content	95.20±1.2	98.84±1.4	98.84±1.4	98.15±2.0	98.02±3.4	98.26±2.5	97.58±2.7	98.18±3.1	98.37±3.0
Disintegration Time (Sec)	36	26	21	44	31	24	30	28	25

TABLE 14: POST COMPRESSION CHARACTERIZATION OF PULSATILE RELEASE TABLETS

Parameter	P1	P2	P3	P4	P5	P6	P7	P8	P9
Hardness (Kg/cm^2)	3.4±0.02	3.4±0.06	3.2±0.9	3.5±0.2	3.8±0.7	4.4±1.2	3.2±2.0	3.6±2.0	3.2±0.9
Friability (%)	0.40±0.01	0.37±0.05	0.35±1.5	0.46±1.2	0.38±0.7	0.32±1.7	0.45±1.8	0.38±2.6	0.31±0.03
Uniformity of weight (mg)	494	498	498	402	498	498	499	404	499

TABLE 15: DISSOLUTION STUDY OF PULSATILE RELEASE TABLETS

Time (hr)	Percentage Drug Release								
	P1	P2	P3	P4	P5	P6	P7	P8	P9
0.5	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0
4	6.26	5.42	5.15	6.88	5.3	5.64	5.22	6.84	2.56
6	35.86	30.26	27.65	31.35	34.38	28.53	35.37	32.4	28.58
8	68.42	76.14	61.36	74.45	70.9	69.54	75.57	71.68	68.8
10	99.88	98.65	86.23	99.42	100.3	91.48	95.61	96.52	90.36
12			88.03			95.32			99.85

TABLE 16: POST COMPRESSION EVALUATION OF FLOATING PULSATILE RELEASE TABLET

Parameter	N1	N2	N3
Hardness (Kg/cm^2)	6.6±0.03	6.8±0.8	7.2±1.3
Thickness (mm)	4.0±0.5	4.2±0.4	4.2±1.0
Friability (%)	0.72±0.01	0.54±0.6	0.65±0.3
Uniformity of weight (mg)	500	501	502
Floating Lag Time (sec)	54	26	45
Floating Time (hr)	10	12	17

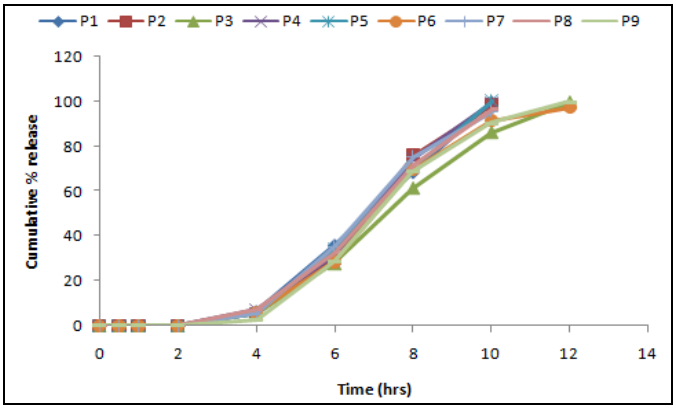

FIG. 6: CUMULATIVE % RIT RELEASE FROM PULSATILE RELEASE TABLETS (P1-P9)

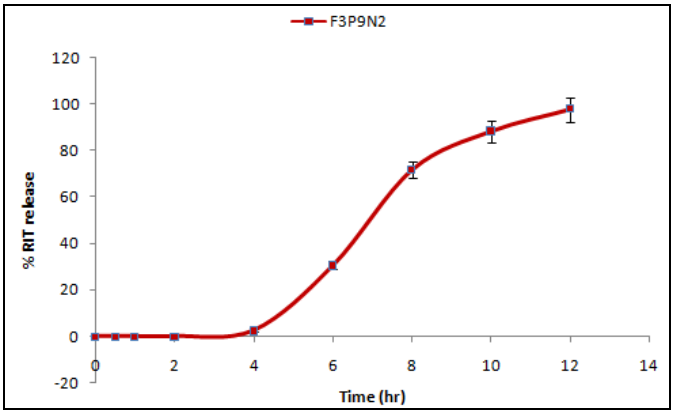

FIG. 7: CUMULATIVE % RIT RELEASE FROM FLOATING PULSATILE RELEASE TABLETS

TABLE 17: *IN-VITRO* RELEASE PROFILE OF OPTIMIZED FLOATING PULSATILE RELEASE TABLETS (F3P9N2)

Time (hr)	Cumulative % drug release
0.5	0
1	0
2	1.05±0.16
4	2.56±0.68
6	30.58±1.82
8	71.86±3.44
10	88.36±4.65
12	97.85±5.28

Value represent mean ± SD (n=3)

Stability Studies: It was found that the percent drug content after a period of 3 months for RIT was 99.29±1.6% at 40±2°C & 75±5% **Table 18**.

Stability studies on final formulation demonstrated its better stability profile at 4.0 °C and 25°C however it was found a little unstable at higher temperature and humidity conditions.

TABLE 18: STABILITY STUDIES AT DIFFERENT CONDITIONS

Storage Conditions	Observations on storage for Drug content (%) (F3P9N2)			
	Initial	1 months	2 months	3 months
40±2°C and 75±5%	100	99.82±3.7	99.63±3.1	99.29±1.6

Values are mean± SD (n=3).

CONCLUSION: The present work was based on the floating pulsatile drug delivery of Ritonavir. The core containing crosspovidone disintegrates the tablet within a short time due to easy and high-water penetration ability of as compared to Cross Carmellose Sodium and Sodium starch glycolate. The PRT containing buoyant material, such as HPMC E15LV, $NaHCO_3$, and citric acid achieved a satisfactory buoyant force *in-vitro*, whereas the floating onset time was less than 1 min. The pulsatile releasing mechanism of PRT is based on the exploitation of the peculiar interaction between hydrophilic polymeric coating and the aqueous gastrointestinal fluids.

The *in-vitro* release profiles of RIT from pulsatile release tablet prepared using HPMC K100M as retarding polymer are characterized by a predetermined lag time (4 hr), the duration of which depends on the kind and amount of the polymeric layer applied on the cores as well as type of superdisintegrant in core tablet. The developed system offers a simple and novel technique for pulse release of drugs. From the results it is concluded that the pulsatile release tablet we prepared could achieve a rapid release after a lag time of 4hr with relatively low variability.

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CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Baker K & Hoare T: Inject able palatial drug delivery hydro gels: how do we get to the clinic? Expert Opinion on Drug Delivery 2025; 22(4): 447-453.
2. Kantar Y, Ahmad S, Halifax HAEW, Hendy AS, Yusuf BAA & I dress, R: Numerical investigation of drug delivery mechanisms in pulsatile flow with machine learning approach. Inter J of Thermophys 2025; 46(3): 44.
3. Wei X, Wang Y, Hu H, Sheng T, Yao Y, Chen C & Gu Z: Wirelessly controlled drug delivery systems for translational medicine. Nature Reviews Electrical Engineering 2025; 1-19.

4. Mohanavel D: Response of intensive and thermophysical properties of a pulsatile blood through stenosed artery subject to drug delivery. Heliyon 2025; 11(4).
5. Jyothirmayi P, Bharathi A & Reddy DRS: Formulation And Evaluation Of An Oral Timed Pulsatile Drug Delivery For Alleviating Pain In Rheumatoid Arthritis. Int J App Pharm 2025; 17(1): 316-322.
6. Zhang Y, Liu X & Li X: Development and advantages of drug delivery systems. In Drug Delivery To Tumors: Recent Strategies and Techniques 2025; 35-60. Singapore: Springer Nature Singapore.
7. Sailaja R, Lakshmi DL, Kalyani KN, Avinash KU & Madhulatha K: A time adjustable pulsatile release system of ketoprofen by combination of floating drug delivery and a novel natural pulsatile polymer. Magnesium 2025; 5(5): 5.
8. Hu J, Zhang J, Hou Y, Li C, Yang W, Fu J & He Y: Digital electronics-free implantable drug delivery system for on-demand therapy. Chemical Engineering Journal 2025; 504: 158763.
9. Rajput A, Pingale P, Telange D, Musale S & Chalikwar S: A current era in pulsatile drug delivery system. Drug Journey Based On Chronobiology. Heliyon 2024.
10. Neupane S & Kharel P: Pulsatile drug delivery system: a review. Asian Journal of Pharmaceutical Research 2024; 14(3): 309-314.
11. Bodke V, Tekade BW, Badekar R, Phalak SD & Kale M: Pulsatile Drug Delivery Systems the Novel Approach 2024.
12. Sawale AV, Jajoo VS & Deshmukh AA: Formulation and evaluation of pulsatile drug delivery system for the treatment of arthritic pain. Research Journal of Science and Technology 2024; 16(3): 193-202.
13. Sivaneswari S, Senthilkumaran K & Sambathkumar R: Chronomodulated drug delivery systems for the treatment of hypertension: an overview. Intelligent Pharmacy 2024; 2(1): 155-160.
14. Deepan P, Bharathi M, Vaikumdam K, Senthilkumar K & Rajalingam D: Advancements in Pulsatile Drug Delivery Systems: A 2024.
15. Butler CT, Rodgers AM, Curtis AM & Donnelly RF: Chrono-tailored drug delivery systems: recent advances and future directions. Drug Delivery and Translational Research 2024; 14(7): 1756-1775.
16. Kurapati P & Chinni S: Pulsatile drug delivery systems of esomeprazole: optimization through quality by design. Indian Journal of Pharmaceutical Education & Research 2024; 58(2).
17. Anusha V, Umashankar MS & Kumar YG: Pulsatile drug delivery system an innovative method to treat chronotherapeutic diseases by synchronizing drug delivery with circadian rhythm. Journal of Applied Pharmaceutical Science 2023; 13(12): 066-078.
18. Gomathi J, Veeralakshmi B & Farzana AM: Pulsatile drug delivery: a strategy for treating chronotherapeutic ailments. Int J Curr Pharm Res 2023; 15(4): 1-8.
19. Yadav R, Jha M, Jat D & Jain DK: Present scenario of pulsatile drug delivery system. International Journal of Comprehensive and Advanced Pharmacology 2023; 7(4): 171-8.
20. Graf TP, Qiu SY, Varshney D, Laracuente ML, Euliano EM, Munnangi P & Mchugh KJ: A scalable platform for fabricating biodegradable microparticles with pulsatile drug release. Advanced Materials 2023; 35(22): 2300228.
21. Gandhi R, Sharma BK & Khanduri U: Electromagnet hydrodynamics casson pulsatile nanofluid flow through a bifurcated stenosed artery: magnetically targeted drug delivery. Journal of Applied Physics 2023; 134(18).
22. Kumar PP, Anjali T, Nandyala S, Vanitha P, Srihitha T, Saraswathi MY & Nikitha N: Pulsatile Drug Delivery Systems-A Review. World J Pharm Res 2023.
23. Khadka B, Lee B & Kim KT: Drug delivery systems for personal healthcare by smart wearable patch system. Biomolecules 2023; 13(6): 929.
24. Alam MN: Pulsatile release drug delivery system based on compression-coated tablets (Doctoral Dissertation) 2023.
25. Mashiku LR & Shaw S: Unsteady nano-magnetic drug dispersion for pulsatile darcy flow through microvessel with drug elimination phenomena. Physics of Fluids 2023; 35(10).
26. Campbell S, Preciado Rivera N, Said S, Lam A, Weir L, Gour J & Hoare T: Injectable on-demand pulsatile drug delivery hydrogels using alternating magnetic field-triggered polymer glass transitions. ACS Applied Materials & Interfaces 2023; 15(42): 48892-48902.
27. Jumana KK, Geetha VS, Farsana T & Mubashira NP: Development and evaluation of floating pulsatile drug delivery system for chronotherapy of hypertension 2023.
28. Parekh K, Thakkar V, Joshi A, Sojitra C, Dalwadi S & Rana H: Optimizing pulsatile release of febuxostat for managing gout flares: a chronotherapeutic approach. Future Journal of Pharmaceutical Sciences 2023; 9(1): 89.
29. Srikrishna S, Sadhana K & Sri SR: Formulation and evaluation of bosentan pulsatile drug delivery system by using Press Coated Technique 2023.
30. Khalifa AZ, Zyad H, Mohammed H, Ihsan K, Alrawi L, Abdullah M & Akram O: Recent advances in remotely controlled pulsatile drug delivery systems. Journal of Advanced Pharmaceutical Technology & Research 2022; 13(2): 77-82.
31. Hussein M & Nathir I: Pulsatile Drug Delivery System Utilizing Innovative Technology. Pakistan Journal of Medical & Health Sciences 2022; 16(06): 601-601.
32. Dash SK, Sahoo RK, Padhan A, Khan A, Karna N, Nanda N & Dash S: Pulsatile Drug Delivery System (Pdds): A Cronotherapeutic Approach For Optimum Therapy. J Pharm Res Int 2022; 34: 28-45.
33. Habeeb F & Mohammed S: A review on pulsatile drug delivery system. International Journal of Pharmacy Research & Technology 2022; 12(2): 10-23.
34. Aldawsari HM, Naveen NR, Alhakamy NA, Goudanavar PS, Rao GK, Budha RR & Badr-Eldin SM: Compression-Coated Pulsatile Chronomodulated Therapeutic System: Qbd Assisted Optimization. Drug Delivery 2022; 29(1): 2258-2268.
35. Pal S, Monika M & Singh M: Circadian rhythms regulated pulsatile drug delivery system. International Journal of Health Sciences 2022; 6(4): 7944-7965.
36. Amritha R, Sivakumar R & Haribabu Y: A review on pulsatile drug delivery system: drug scheduling based on biological rhythm. Research Journal of Pharmacy and Technology 2022; 15(3): 1359-1364.
37. Mahajan KR, Gorle AP & Khalane VS: Overview on pulsatile drug delivery system. Int J Sci Res Arch 2022; 5: 110-8.
38. Rashid R, Zaman M, Ahmad M, Khan MA, Butt MH, Salawi A & Sarfraz RM: Press-Coated aceclofenac tablets for pulsatile drug delivery: formulation and *in-vitro* evaluations. Pharmaceuticals 2022; 15(3): 326.
39. Thakur G, Wani SUD & Gautam SP: A review on recent advancement in pulsatile drug delivery systems. International J of Current Pharmaceutical Res 2021; 6-10.

40. Bagade OM, Sutar SS & Doke PE: A concise insight on pulsatile drug delivery system: an outlook towards its development. International Journal of Pharmaceutical Sciences and Nanotechnology 2021; 14(5): 5577-5587.
41. Anandan D: Design and development of floating pulsatile drug delivery system of carvedilol doctoral dissertation, Cl Baid Metha College of Pharmacy, Chennai 2021.
42. Kumar BP, Venkatachalam A & Bhaskar RK: Formulation and *in-vitro in-vivo* pharmacokinetic evaluation of cardiovascular drug-loaded pulsatile drug delivery systems. Int J App Pharm 2021; 13(6): 144-151.
43. Roy SK, Das P, Mondal A, Mandal A & Kuotsu K: Design, formulation and evaluation of multiparticulate time programmed system of ramipril for pulsed release: an approach in the management of early morning surge in blood pressure. Journal of Drug Delivery Science and Technology 2021; 62: 102344.
44. Ahmed SF: Pulsatile drug delivery systems and their methodologies. Journal of Cardiovascular Disease Research 2021; 12(5): 1501-1514.
45. Ugurlu T & Ilhan E: Development and *in-vitro* evaluation of a novel pulsatile drug delivery system containing dexketoprofen trometamol. Journal of Pharmaceutical Innovation 2021; 16: 371-383.

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