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STEADY SHEAR AND DYNAMIC SHEAR RHEOLOGICAL PROPERTIES OF CARBOXYMETHYL LOCUST BEAN GUM INFLUENCING EROSION OF THE POLYSACCHARIDE COAT OF COMPRESSION COATED TABLETS

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Keywords:

Chronotherapy, Floating pulsatile release tablet, Quinapril hydrochloride, Lag time, Floating time

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ABSTRACT: Pulsatile drug delivery is one such system thereby delivering drug at the right time, right place and in right amounts and holds good promises and provides benefit to the patients suffering from chronic problems like arthritis, asthma, hypertension, *etc*. The present study investigated that optimization of quinapril hydrochloride was successfully done and batch A8 was given satisfactory results. Tablets of quinapril hydrochloride were made by direct compression method. Microcrystalline cellulose was used as direct compressing agent. Sodium starch glycolate used as disintegrating agent and croscarmellose sodium used as super disintegrating agent. The resulting powder mixtures were then compressed into tablets using KBR machine. Dry coating using different concentrations of HPMCK4M, EC, and HPMCK100M. Also magnesium stearate and spray-dried lactose. Dry coated pulsatile tablet was prepared by placing 50% pulsatile release layer in 13 mm die and core tablet was placed on it. A1 to A 5 show less lag time, less *in-vitro* buoyancy study due to less concentration of polymer. Where A 7 gave drug release after 8 hours 97.6 ± 0.05%. This formulation can be considered for floating pulsatile delivery of quinapril hydrochloride.

INTRODUCTION: The main purpose of this research study that, to develop an idea about the floating pulsatile drug delivery system for obtaining no drug release during floating and in the proximal small intestine followed by pulsed drug release in distal small intestine.

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To achieve chronotherapeutic drug release of drug which used for the treatment of rheumatoid arthritis, osteoarthritis, spondylitis, cardiovascular disease, and several hypertension syndromes which improve patient compliance.

The floating pulsatile drug delivery system is the system form in which drug release in specific sites and specific drug action at specific times. Floating drug delivery systems have bulk density less than gastric fluid and so remain buoyant in stomach for prolonged period of time releasing the drug slowly at the desired rate from the system. Floating drug delivery systems (FDDS) are system in which to

retain the drug in the stomach and are useful for drug that is poorly soluble or unstable in intestinal fluids. The underlying principle is very simple *i.e.*, to make the dosage form less dense. The basic idea behind the development of such a system was to maintain a constant level of drug in the blood plasma in spite of the fact that the drug does not undergo disintegration. The drug usually keeps floating in the gastric fluid and slowly dissolves at a pre-determined rate to release the dosage form and maintain constant drug levels in the blood [1].

The advantages of that system are that they can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in particular region of the GIT. These systems continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability. Different approaches are currently used to prolong the gastric retention time, like hydrodynamically balanced systems, swelling and expanding system, polymeric bioadhesive systems, modified shape systems, high-density systems, and other delayed gastric emptying devices. 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 [3].

Pulsatile Drug Delivery System: Diseases where constant drug levels are not preferred but need a pulse of therapeutic concentration in a periodic manner acts as a push for the development of "Pulsatile Drug Delivery Systems". In this system, there is rapid and transient release of a certain amount of drug molecules within a short time period immediately after a predetermined off release period. Various techniques are available for the pulsatile delivery like PH dependent systems, time-dependent systems, micro-flora activated systems, *etc*. This can be designed as per the physiology of disease and properties of the drug molecule. In the body several physiological functions such as metabolism sleep pattern heart attacks are regulated by pulsed or transient release of bioactive substances at a specific time and site. Therefore to mimic the function of living system it is necessary to achieve pulsed release of certain amount of bioactive compounds at predetermined intervals. Thus release pattern of such drug delivery is circadian pattern. The release of some drugs is preferred in pulses. A single dosage form provided an initial dose of drug followed by one release free interval after which second dose of drug is released, which is followed by additional release free interval and pulses of drug release. The ability to deliver a bioactive compound and therapeutic agent to a patient in pulsatile release profile is major goal in the drug delivery. This system is also called a time-controlled system because the release is independent of the environment [4, 5].

Floating Drug Delivery System: Floating drug delivery systems is one of the approaches to achieve gastric retention to obtain sufficient drug bioavailability. This delivery system is desirable for drugs with an absorption window in the stomach or the upper small intestine. This has a bulk density less than gastric fluids and so remains buoyant in the stomach without affecting gastric emptying rate for a prolonged period, and the drug is released slowly as a desired rate from the system. After release of drug, the residual system is emptied from the stomach. This result in increased gastric retention time (GRT) and better control of the fluctuation in plasma drug concentration. The major requirements for floating drug delivery system are:

- It should release contents slowly to serve as a reservoir.
- It must maintain specific gravity lower than Gastric contents (1.004-1.01 gm/cm^3).
- It must form a cohesive gel barrier [6].

MATERIALS AND METHODS:

Materials: Quinapril hydrochloride was obtained as gift sample from Swapnroop drugs and Pharmaceutical, Aurangabad. Microcrystalline cellulose, Sodium Starch Glycolate, HPMCK4M, HPMCK100M, Spray-dried lactose, Ethyl Cellulose, Magnesium stearate, were gifted by S.D.Lab Chemicals Shrirampur, Hilab Chemical, Shrirampur, Ahmadnagar, Marksman's Pharma, Verna Goa, Balaji drugs, Mumbai, Cipla, Vikroli, Mumbai, Loba chemicals, Mumbai respectively.

Methods:

Preparation of Core Tablet (CT): Tablets of Quinapril Hydrochloride were made by the direct compression method. All ingredients were weighed

accurately and mix well for 15 min. microcrystalline cellulose was used as direct compressing agent. Sodium starch glycolate used as disintegrating agent and magnesium stearate was used as lubricant and polyvinyl pyrrolidine used as a binder, croscarmellose sodium used as super disintegrating agent. The resulting powder mixtures were then compressed into tablets (average tablet weight mg) using KBR machine (Diameter 8mm).

Formulations of the Floating Pulsatile Release Tablet by Direct Compression (FPRT): The optimized CT6 was used for the preparation of FPRT. Dry coating using different concentrations of HPMCK4M, EC and HPMCK 100M. Also magnesium stearate and spray Dried Lactose used for coating of core tablets which were mixed for 10 min.

Dry coated pulsatile tablet was prepared by placing 50% pulsatile release layer in 13 mm die, and the core tablet was placed on it. Then, the remaining quantity of pulsatile release layer was added in the die so as to cover RRCT and finally compressed by using KBR tablet machine (Diameter 13 mm).

Formulation of CT of Quinapril Hydrochloride is as Follows:

TABLE 1: FORMULATION OF CT OF QUINAPRILHYDROCHLORIDE

Ingredient	CT1	CT2	CT3	CT4	CT5	CT6
Drug	20	20	20	20	20	20
Microcrystalline cellulose	45	40	45	45	40	38
Sodium starch glycolate	2	3	2	3	5	2
Lactose	10	15	20	10	15	20
Crosscarmellose sodium	20	20	20	20	20	20
Magnesium stearate	3	2	3	2	5	8
PVP K30	20	20	10	20	15	12
Total	120	120	120	120	120	120

Composition of PRT of Quinapril Hydrochloride is as follows:

TABLE 2: COMPOSITION OF PRT OF QUINAPRIL HYDROCHLORIDE

Ingredients	A1	A2	A3	A4	A5	A6	A7
core tablet	120	120	120	120	120	120	120
hpmc k4m	50	55	45	50	30	45	65
hpmc k100	110	100	110	100	110	250	210
ethyl cellulose	50	45	55	50	70	55	35
lactose	165	175	165	175	165	25	65
magnesium stearate	5	5	5	5	5	5	5
total	500	500	500	500	500	500	500

RESULTS:

Micromeritic Properties:

Bulk Density, Tap Density: Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another. A quantity of accurately weighed powder (bulk) from each formula, previously shaken to break any agglomerates formed was introduced into a 10 ml measuring cylinder. After the initial volume was observed, as bulk volume. The cylinder was introduced onto a hard surface of the holly instrument. After that The Bulk and Tap densities, Hausner's ratio and Carr's Index were calculated. Each micrometric property was performed in triplicate manner and reported [7].

Carr's Index: The compressibility index of the granules was determined by Carr's compressibility index. (%) Carr's Index can be calculated by using the following formula.

Carr's Index = (Tapped density-Bulk density) / (Tapped density) × 100

Grading of the Powders for their Flow Properties According to Carr's Index is Follows:

TABLE 3: GRADING OF THE POWDERS FOR THEIR FLOW PROPERTIES

S. no.	Consolidation index (Carr's index %)	Flow
1	5-15	Excellent
2	12-16	Good
3	18-21	Fair to passable
4	23-35	Poor
5	33-38	Very poor
6	>40	Very very poor

Hausner's Ratio: Hausner's Ratio of powder was determined by comparing the tapped density to bulk density using the equation: [8]

Hausner's Ratio = (Bulk density) / (Tapped density) × 100

Determination of Angle of Repose: The flowability was determined by the angle of repose () using fixed funnel method. The angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The angle of repose has been used as indirect methods of qualifying powder flowability, because of their relation with inter particular friction. The frictional force in a loose powder can be measured by angle of repose [9].

Formula for Calculating Angle of Repose Given as Follows:

$$\text{Tan } \theta = h / r$$

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

Where,

Θ is the angle of repose,
H: height of pile,
R: radius of the base of pile

Different Ranges of Flow Ability in Terms of Angle of Repose are given below:

TABLE 4: DIFFERENT RANGES OF FLOW ABILITY IN TERMS OF ANGLE OF REPOSE

S. no.	Flow Property	Angle of Repose (Degrees)
1	Excellent	25-30
2	Good	31-35
3	Fair-aid not needed	36-40
4	Passable-may hang up	41-55
5	Poor-must agitate, vibrate	46-55
6	Very poor	56-65
7	Very, very poor	>66

Uniformity of Thickness: The thickness of individual tablets may be measured with a micrometer, which permits accurate measurements and provides information on the variation between tablets. The thickness of a tablet is determined by the diameter of die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material, and the force or pressure applied during compaction. The tablet thickness was measured using vernier caliper [10].

Hardness Test: Tablets require a certain amount of strength or hardness, and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. In addition, tablet should be able to withstand reasonable abuse when in hands of consumer. The relationship between hardness to disintegration and perhaps to drug dissolution release rate has become apparent. The hardness of tablet was determined using apparatus Pfizer Hardness tester. It is expressed in kg/cm^2. Five tablets were randomly selected from each formulation and the mean and standard deviation values were calculated [11].

Friability Test: It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche Friabilator. It is expressed in Percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by using the following formula [12]

$$F = (Wi_{nitial} - W_{final}) / (W_{initial}) \times 100$$

% Friability of tablets less than 1% is considered acceptable

Weight Variation Test: The weight variation test would be a satisfactory method of determining the drug content uniformity of tablets if the tablets were all or essentially all (90 to 95%) active ingredients, or if the uniformity of drug distribution in the powder form which tablets were made perfect. Ten tablets were taken and their weight was determined individually and collectively by using single pan electronic balance. The average weight of the tablets was determined from collective weight.

From the individual tablets weight, the range and percentage standard deviation were calculated. Not more than 2 tablets should deviate from the average weight of tablets and the maximum percentage of deviation allowed. In direct compression of tablet, uniform weight of tablets represents appropriate powder flow and uniform die filling [13, 14].

Weight Variation Test Limit as Per USP is Given Below:

TABLE 5: WEIGHT VARIATION TEST LIMIT AS PER USP

Average weight of a tablet	Percentage deviation
30 mg or less	10%
More than 130 mg and less than 324 mg	7.5%
324 mg or more	5%

Drug Content Uniformity: The tablets were randomly selected from each batch of formulation and subjected for content uniformity test. The tablets were taken and milled separately by using glass mortar and pestle then powder equivalent to 10 mg of drug was accurately weighed and transfer 50 ml of 0.1N HCl solution and stir to mix properly. The resulting solution was filtered through Whatman filter paper and the final volume adjusted with 0.1N HCl up to 100 ml. Then the suitable dilutions were prepared and samples were analyzed by using validated UV Visible Spectrophotometer (Agilent Technologies Cary 60 UV-visible double beam spectrophotometer) at 214 nm using 0.1N HCl as blank [15].

***In-vitro* Disintegration Time:** The process of breakdown of a tablet into smaller particles is called as disintegration. The disintegration of tablet was generally occurring due to water uptake by tablet *via* capillary action, which results in swelling, and thus tablet gets disintegrated. It was also reported that increased compaction force may increase or decrease disintegration time. In the present study disintegration test was carried out on six tablets using the apparatus specified in IP (disintegration apparatus IP). The phosphate buffer at 37 ºC ± 2 ºC was used as a disintegration media and time in minute taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured [16].

***In-vitro* Dissolution Studies:** *In-vitro* dissolution study of CT and Pulsatile Tablet was carried out using VDA-8DR, USP, Veego dissolution test apparatus [17, 18].

***In-vitro* Dissolution Study of Core Tablet (CT):** Tablet was introduced into the basket of the Electro lab TDT-08L USP dissolution test apparatus and the apparatus was set in motion and rotated with 100 rpm and 5ml of sample was withdrawn for first half-hour at 5 min intervals. And dilute to 10ml with 0.1 N HCl. Samples withdrawn were analyzed by UV spectrophotometer for the presence of drug-using 0.1N HCl solution as blank.

General Dissolution Conditions for Core Tablet (CT) are given as follows:

TABLE 6: GENERAL DISSOLUTION CONDITIONS FOR CORE TABLET (CT)

S. no.	Parameter	Specification
1	Dissolution medium	900 ml of 0.1N HCl
2	Temperature	37º ± 0.5 ºC
3	Rotation Speed	75 RPM
4	Volume Withdrawn	5ml
5	Λ max	214
6	Time Interval	5 min
7	Beer's range	5-25µg/ml

***In-vitro* Dissolution Study of Pulsatile Release Tablet (PRT):** Different coating compositions were evaluated for providing pulsatile drug delivery of quinapril hydrochloride. Initially, tablets were coated with HPMCK4M, HPMCK100M and EC, as well as spray-dried lactose and magnesium stearate, which are used for compressed coating tablets. And form pores through which buffer Penetrate in EC coated layer.

Because of the penetration of the buffer into the inner coating layer, HPMC of inner coating layer swells and it ruptures the EC coated layer and drug release takes place after 8 h. HPMC coated tablets were coated with different proportion of ethylcellulose:

Summary of General Dissolution Conditions for Pulsatile Release Tablet (PRT) is Given as Follows:

TABLE 7: SUMMARY OF GENERAL DISSOLUTION CONDITIONS PULSATILE RELEASE TABLET (PRT)

S. no.	Parameter	Specification
1	Dissolution Medium	900 ml of 0.1N HCl
2	Temperature	37º ± 0.5 ºC
3	Rotation Speed	75RPM
4	Volume Withdrawn	5 ml
5	Time interval	1 h
6	Max	214
7	Beer's range	5-25 µg/ml
8	Dilution factor	2 ml

***In-vitro* Buoyancy Studies:** The time between the introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remains buoyant were measured. The time taken for dosage form to emerge on surface of medium called floating Lag Time (FLT) or Buoyancy Lag Time (BLT) the *in-*

vitro buoyancy was determined by floating lag time as per the method described. The tablets were placed in a 100 ml glass beaker containing simulated 0.1N Hydrochloric acid, as per USP. The time required for the tablet to rise to the surface and float was determined as the floating lag time [19].

Total Floating Time (TFT): The duration of time at which the dosage form constantly remained on the surface of the medium was determined as the total floating time (TFT). The Total Floating Time was determined by as per the method described. The tablets were placed in a 100ml glass beaker containing simulated 0.1N Hydrochloric acid, as per USP. And Time when the tablet burst and core tablet is out of press coating.This is considered a predetermined off-release period that is total floating time [20].

Effect of Outer Polymer Concentration and Water Uptake Performance: To study the effect of outer polymeric layer concentration on lag time, core tablets were coated with different levels of Ethylcellulose, HPMC, Lactose spray-dried and magnesium stearate. The % water uptake capacity of tablets (Wo) was determined before the test, and then the tablet was put into the basket and immersed in 900 ml phosphate buffer. The basket was rotated at 100 rpm in the dissolution apparatus. Tablets were removed from containers at predetermined regular intervals, blotted with tissue paper, weighed (Wt). The % water uptake was calculated using the formula [20].

$$\% \text{ Water uptake} = (Wt-Wo) / Wo \times 100$$

DISCUSSION:

Preformulation: Compatibility Study:

FTIR Spectroscopy: The IR spectrum of pure drug and the physical mixture was as given in fig. it was observed that there were no changes in the IR spectra of a mixture of drugs and polymers. This indicates no physical interactions. Because of some bond formation between drugs and polymers. This indicates that the drug was compatible with the formulation components. Hence drugs and excipients are compatible with further use.

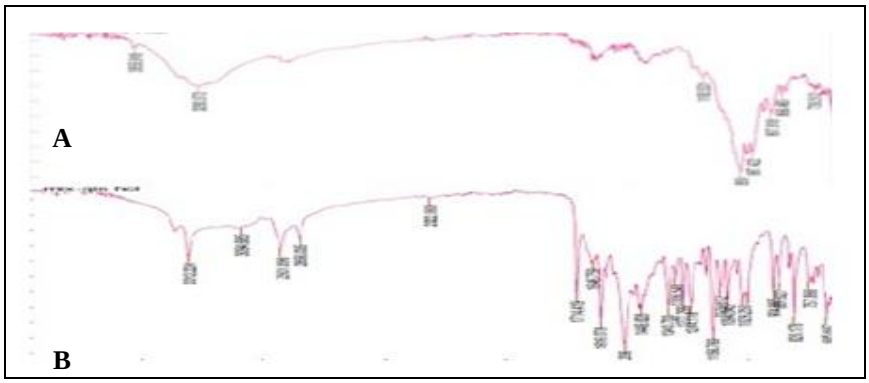

FIG. 1: FTIR SPECTRA OF (A) PURE DRUG QUINAPRIL HYDROCHLORIDE AND (B) DRUG AND HPMC K4M, HPMC K100, ETHYL CELLULOSE

Calibration Curve of Quinapril Hydrochloride in 0.1N HCl: In preformulation studies, it was found that the estimation of Quinapril hydro-chloride by spectrophotometric method at 219 nm in Phosphate buffer and 0.1 N HCl, at the concentration between 10-100 µg/ml. Correlation between concentration coefficient was found 0.998 & 0.999 for both phosphate buffer and 0.1 N HCl and slope for phosphate buffer and 0.1 N HCl was found 0.008 and 0.039 respectively.

Calibration curve of quinapril hydrochloride in 0.1 N HCl was found to be linear in the range of µg/ml and coefficient was found to be 0.999

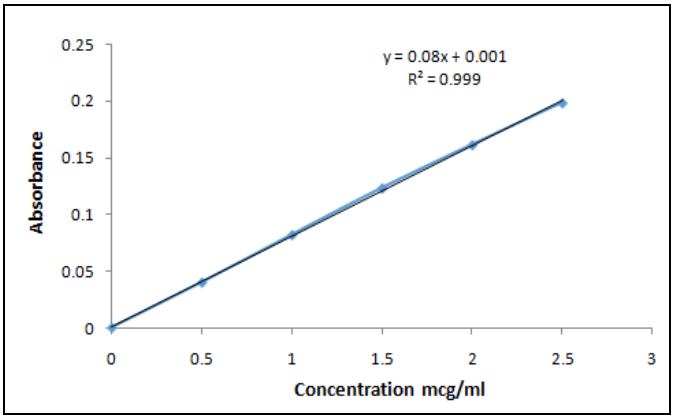

FIG. 2: CALIBRATION CURVE OF QUINAPRIL HYDROCHLORIDE IN 0.1 N HCl

Calibration Curve of Quinapril Hydrochloride in Phosphate Buffer pH 6.8: Calibration curve of quinapril hydrochloride in phosphate buffer pH 6.8 was found to be linear in the range of µg/ml and coefficient was found to be 0.999.

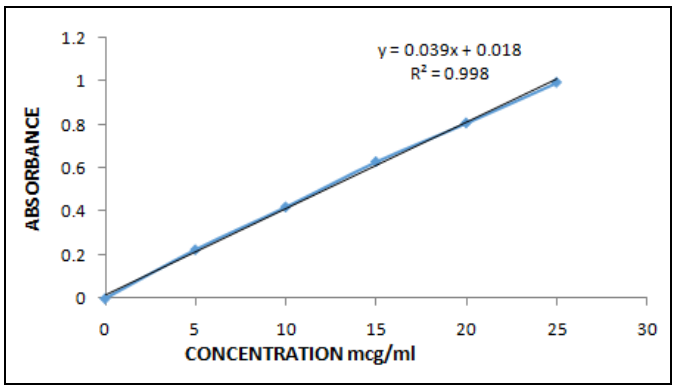

FIG. 3: CALIBRATION CURVE OF QUINAPRIL HYDROCHLORIDE IN PHOSPHATE BUFFER pH 6.8

Evaluation of Tablet:

Pre-compression Parameter of Tablet:

TABLE 8: PRECOMPRESSION PARAMETER OF TABLET

Batch code	Bulk density gm/cm^3	Tapped density	Hausner's ratio	Carr's index (%)	Angle of repose (Θ)
A1	0.33 ± 0.08	0.49 ± 0.003	1.16 ± 004	13.89 ± 0.2	22.01 ± 0.50
A2	0.37 ± 0.05	0.65 ± 0.004	1.2 ± 0.02	22.21 ± 0.3	28.18 ± 1.09
A3	0.31 ± 0.10	0.60 ± 0.006	1.2 ± 0.05	16.6 ± 0.3	29.22 ± 1.19
A4	0.39 ± 0.09	0.53 ± 0005	1.14 ± 0.03	13.25 ± 0.2	21.19 ± 0.30
A5	0.40 ± 1.0	0.61 ± 0.006	1.24 ± 005	12.5 ± 0.3	26.19 ± 0.25
A6	0.32 ± 0.08	0.51 ± 0.003	1.16 ± 0.07	22.21 ± 0.24	20.17 ± 0.40

Post-compression Parameter of CT:

TABLE 9: POSTCOMPRESSION PARAMETER OF CT

Batch code	Weight variation (mg)	Diameter (mm)	Thickness (mm)	Hardness	Friability
A1	120 ± 2.08	8.16 ± 0.10	1.83 ± 0.10	2.89 ± 0.01	0.51 ± 0.21
A2	119 ± 1.0	8.33 ± 0.05	180 ± 0.09	1.91 ± 0.11	0.60 ± 0.32
A3	119 ± 2.64	8.33 ± 007	1.82 ± 0.10	2.12 ± 2.12	0.59 ± 0.31
A4	117 ± 5.56	8.16 ± 0.10	1.78 ± 0.21	2.10 ± 020	0.46 ± 0.26
A5	118 ± 0.9	8.25 ± 0.11	1.80 ± 0.09	1.99 ± 0.19	0.69 ± 0.08
A6	119 ± 0.60	8.16 ± 0.14	1.79 ± 0.05	1.98 ± 0.10	0.44 ± 0.41

Evaluation of Core Tablet:

TABLE 10: EVALUATION OF CORE TABLET

Batch code	*In-vitro* disintegration time	Drug content
A1	609.1 ± 0.07	97.33 ± 0.76
A2	586.2 ± 1.21	97.19 ± 0.09
A3	522.4 ± 0.79	98.11 ± 1.12
A4	499.6 ± 1.23	98.99 ± 1.21
A5	449.9 ± 0.67	98.44 ± 0.65
A6	300.3 ± 0.45	99.21 ± 034

In-vitro Dissolution of Core Tablet as Follows:

TABLE 11: *IN-VITRO* DISSOLUTION OF CORE TABLET

Time in (min)	CT 1	CT 2	CT 3	CT 4	CT 5	CT 6
5	19.70 ± 1.36	21.45 ± 3.87	21.88 ± 2.56	25.21 ± 2.13	43.43 ± 2.95	68.89 ± 2.65
10	27.46 ± 2.12	29.53 ± 2.43	29.34 ± 3.42	37.15 ± 3.19	59.12 ± 3.25	98.02 ± 3.87
15	31.88 ± 2.89	39.78 ± 2.34	33.26 ± 2.22	41.29 ± 2.86	71.19 ± 2.32	-
20	46.12 ± 3.49	42.11 ± 2.78	49.11 ± 2.89	69.52 ± 3.74	93.52 ± 3.65	-
25	55.23 ± 2.45	52.45 ± 3.54	61.32 ± 3.71	90.61 ± 2.63	-	-
30	65.34 ± 3.54	76.19 ± 3.97	84.45 ± 1.54	-	-	-

Pre Compression Parameter of PRT:

TABLE 12: PRECOMPRESSION PARAMETER OF PRT

Batch code	Bulk density gm/cm^3	Tapped density	Hausners ratio	Carrs index (%)	Angle of repose (Θ)
C1	0.53 ± 0.05	0.76 ± 0.23	1.10 ± 0.43	15.5 ± 0.04	16.12 ± 0.45
C2	0.58 ± 0.06	0.34 ± 0.021	1.14 ± 0.32	10.4 ± 0.05	14.23 ± 0.32
C3	0.60 ± 0.08	0.65 ± 1.4	1.13 ± 0.22	16.3 ± 0.05	15.42 ± 0.32
C4	0.48 ± 0.86	0.56 ± 0.15	1.23 ± 1.21	15.2 ± 0.03	12.2 ± 0.53
C5	0.76 ± 0.55	0.65 ± 2.4	1.09 ± 0.43	17.2 ± 0.06	16.2 ± 0.43
C6	0.65 ± 1.51	0.74 ± 0.23	1.87 ± 0.32	14.4 ± 0.04	16.4 ± 0..2
C7	0.75 ± 0.034	0.24 ± 1.22	1.043 ± 0.21	14.2 ± 0.02	17.2 ± 0.03
C8	0.71 ± 1.22	0.45 ± 1.20	1.24 ± 0.11	15.2 ± 0.05	16.4 ±0.43
C9	0.45 ± 1.54	0.52 ± 0.03	1.15 ± 1.23	13.3 ± 0.04	20.3 ± 0.53
C10	0.65 ± 1.34	0.53 ± 0.54	1.18 ± 1.32	15.7 ± 0.01	12.54 ± 0.12

Evaluation of PRT:

TABLE 13: EVALUATION OF PRT

Batch code	Weight variation (mg)	Diameter (mm)	Thickness (mm)	Hardness	Friability
A1	220 ± 2.01	13.6 ± 0.10	2.83 ± 0.10	5.89 ± 0.01	0.68 ± 0.21
A2	239 ± 1.4	13.3 ± 0.05	380 ± 0.09	4.91 ± 0.11	0.63 ± 0.32
A3	279 ± 2.64	12.4 ± 007	3.82 ± 0.10	6.12 ± 2.12	0.51 ± 0.31
A4	227 ± 3.56	12.6 ± 0.10	2.78 ± 0.21	4.10 ± 020	0.46 ± 0.26
A5	218 ± 4.9	12.25 ± 0.11	2.80 ± 0.09	6.99 ± 0.19	0.69 ± 0.08
A6	231 ± 0.60	12.6 ± 0.14	3.79 ± 0.05	4.98 ± 0.10	0.44 ± 0.41
A7	213 ± 0.43	13.5 ± 0.14	2.43 ± 0.12	4.35 ± 0.14	0.64 ± 0.43
A8	222 ± 042	13.2 ± 0.23	2.13 ± 0.23	5.32 ± 0.012	0.65 ± 0.43
A9	243 ± 0.52	13.5 ± 0.23	3.12 ± 0.34	4.53 ± 0.24	0.54 ± 0.34
A10	232 ± 0.6	12.9 ± 0.43	3.11 ± 0.54	5.43 ± 0.43	0.56 ± 0.23

In-vitro Dissolution Study:

% Drug Release Profile of PRT Tablet:

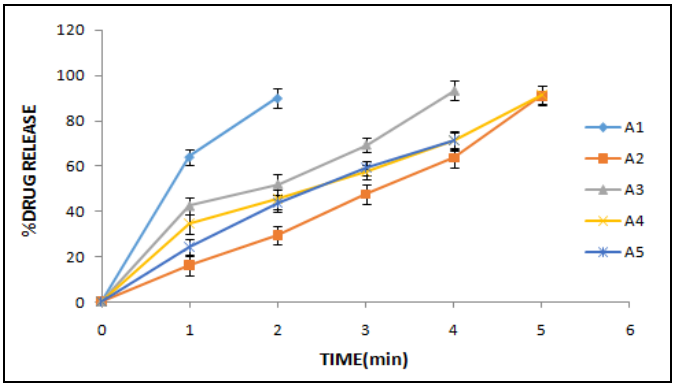

FIG. 4: % DRUG RELEASE A1 TO A5

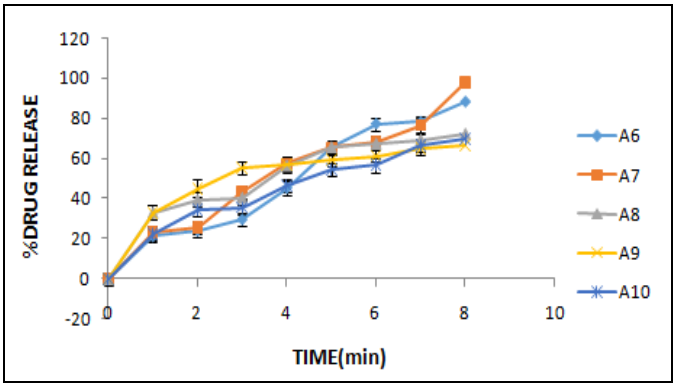

FIG. 5: % DRUG RELEASE A6 TO A10

Evaluation of PRT:

TABLE 14: EVALUATIONS OF PRT

Batch code	Percentage Purity	*In-vitro* buoyancy Studies	Total floating time	Water Uptake study
A1	98.45	55	3	85
A2	97.66	50	4	83
A3	96.44	51	5	82
A4	98.43	48	5	76
A5	97.54	47	6	74
A6	98.76	48	4	63
A7	97.77	53	5	64
A8	98.56	62	7	62
A9	96.66	45	8	56
A10	98.87	21	8	47

% Water Uptake Study of PRT:

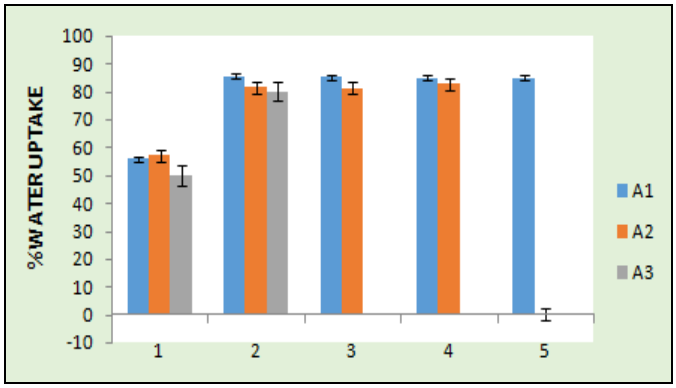

FIG. 6: % SWELLING INDEX FROM A1 TO A3

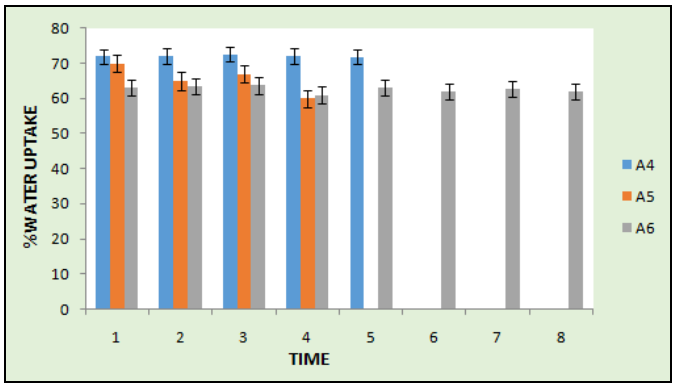

FIG. 7: % SWELLING INDEX FROM A4 TO A6

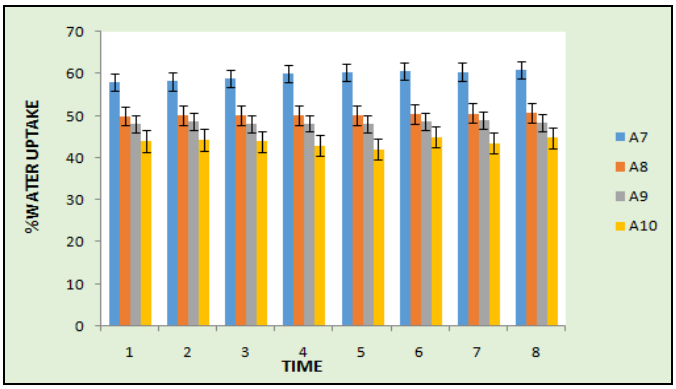

FIG. 8: % SWELLING INDEX FROM A7 TO A10

CONCLUSION: The present study investigated that optimization of quinapril hydrochloride was successfully done and batch A8 was given satisfactory results. As a concentration of HPMC increases the floating lag time increases. Pulsatile drug delivery is one such system thereby delivering drug at the right time, right place and in right amounts and holds good promises and provides benefit to the patients suffering from chronic problems like arthritis, asthma, hypertension, *etc*. Floating pulsatile drug delivery system shall be gifted in future by enhancing patient compliance, providing optimum drug delivery to the target site, and minimize the undesired effects.

A1 to A 5 show less lag time, less *in-vitro* buoyancy study due to less concentration of polymer. Where A 7 gave drug release after 8 h 97.6 ± 0.05%. This formulation can be considered for floating pulsatile delivery of quinapril hydrochloride.

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CONFLICTS OF INTEREST: None

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