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Research Article

MUCOADHESIVE MICROSPHERES OF QUINAPRIL HYDROCHLORIDE FOR THE MANAGEMENT OF HYPERTENSION VIA ORAL ROUTE: AN APPROACH

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ABSTRACT

The objective of the present study is to create a new approach to design and evaluate mucoadhesive microspheres for oral controlled release. The quinapril hydrochloride microspheres with a coat consisting of alginate polymer i.e. sodium alginate in combination of mucoadhesive mineral origin chitin molecule polymer chitosan and galactomannan polymer i.e. guargum were prepared by an ionic gelation process. The microspheres were evaluated for morphological character, particle size, micromeritic properties, percentage entrapment efficiency, Swelling Index, *in-vitro* wash-off test, *in-vitro* release studies and *in vivo* mucoadhesion behavior in albino rabbits. The result of mucoadhesive microspheres were identified spherical and have free flowing properties. The percent of drug loading efficiency was 89.9 to 95.6%. The microspheres showed good mucoadhesive property during the *in vitro* wash-off test. The drug quinapril hydrochloride released from polymer matrix mucoadhesive system from these was slow and extended over 12 h duration on the composition of coat. Mucoadhesive microspheres provide the capability to adhere on the mucosal tissue of stomach. Quinapril Hydrochloriderelease mucoadhesive pulsatile multiunit dosage forms was found to be slow and extended period of time. The drug discharge ratio was dependent on the composition of polymer and stirring speed used during the formulation. The release of drug was prolonged through the matrix system produced after swelling of polymeric composition of coat within mucoadhesive polymers and sustained drug release up to 12 h duration. The result concluded that prepared mucoadhesive microspheres best suited for oral controlled release of quinapril hydrochloride for the management of hypertension via oral route.

Keywords: Quinapril Hydrochloride, Mucoadhesive microspheres, Controlled release, Oral route.

1. INTRODUCTION

Muco-adhesive drug delivery systems are very poularly applied approach for delivery of system within the lumen to enhance drug absorption in a site specific manner. Mucoadhesive drug delivery systems unite with mucin molecule present on the surface of mucin layer on mucosal epithelial layer. Such adherence nature of system increased the gastric residence time of the dosage form at the site of absorption. Such wonderful approach involved the application of mucoadhesive polymers bind with mucin molecule at mucosal epithelial layer of the stomach. Thus may increase the GRT by increasing the affinity and span of time of contact between the dosage form and the biological membrane. The cohesion nature of surface with gastric wall may increase residence time for improving bioavailability [1]. Nowdays researchers developed various mucoadhesive drug delivery systems for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effects [2]. The approach under the mucoadhesive drug delivery should be small and flexible for better acceptability to patients and cause irritation. The desired characteristics of a mucoadhesive dosage form include high drug loading capacity, controlled drug release (unidirectional release), good mucoadhesive properties, smooth surface, tastelessness, and convenient application [3].

Quinapril hydrochloride is the hydrochloride salt of quinapril, the ethyl ester of a non-sulfhydryl, angiotensin-converting enzyme (ACE) inhibitor, quinaprilat. The principal metabolite of quinapril i.e. quinaprilat, is an inhibitor of ACE activity in human subjects and animals. ACE is peptidyl dipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor, angiotensin II. The effect of quinapril in hypertension appears to result primarily from the inhibition of

circulating and tissue ACE activity, thereby reducing angiotensin II formation. Quinapril inhibits the elevation in blood pressure caused by intravenously administered angiotensin I, but has no effect on the pressor response to angiotensin II, norepinephrine, or epinephrine. Angiotensin II also stimulates the secretion of aldosterone from the adrenal cortex, thereby facilitating renal sodium and fluid reabsorption. Reduced aldosterone secretion by quinapril may result in a small increase in serum potassium. In controlled hypertension trials, treatment with quinapril alone resulted in mean increases in potassium of 0.07 mmol/L. Removal of angiotensin II negative feedback on renin secretion leads to increased plasma renin activity (PRA). Following oral administration, peak plasma quinapril concentrations are observed within one hour. During absorption, quinapril is de-esterified to its major active metabolite, quinaprilat (about 38% of oral dose), and to other minor inactive metabolites. The oral dosing of quinapril has an effective accumulation half-life of quinaprilat of approximately 3 hours, and peak plasma quinaprilat concentrations are observed approximately 2 hours post-dose. Quinaprilat is eliminated primarily by renal excretion, up to 96% of an i.v. dose, and has an elimination half-life in plasma of approximately 2 hours and a prolonged terminal phase with a half-life of 25 hours. At the recommended doses, antihypertensive effects are maintained throughout the 24-hour dosing interval in most patients. The antihypertensive effect of quinapril was maintained during long-term therapy with no evidence of loss of effectiveness. The goal of the current examination is to develop advance approach for gastroretentive medication containing quinapril HCl as a medication applicant. The approach would stay the system at the upper piece of GIT or stomach for delayed period of time. The retarding nature of system might be maximizing the medication discharge rate at the appropriate site within specified time period for enhacing the bioavailability of drug at desired site of action to give successful treatment to the patients experiencing hypertension [4].

2. MATERIAL AND METHODS

Quinapril HCl (QHL) was provided by Torrent Pharma, Gujarat, India. Sodium alginate, Guar gum and Chitosan were procured from Central Drug House, Mumbai. Other reagents used were of analytical grade. The animal study was approved by Institutional Animal Ethical Committee (Protocol No:IAEC/VCP/2019/001/5).

Various variables were selected as follows:

A. Independent variables

(a) Stirring speed (X1)
(b) Polymeric concentration (X2)

B. Dependent variables

(a) Percentage entrapment efficiency (Y1)
(b) Percentage yield (Y2)
(c) Percent mucoadhesion (Y3)
(d) Percentage of drug release (Y4)

2.1. Preparation of mucoadhesive microspheres

Quinapril Hydrochloride microspheres were prepared by ionotropic gelation method [5]. The required quantity of polymer and sodium alginate were added in combination with other polymers using chitosan and guargum in different ratios. Sodium alginate, chitosan and guargum were dissolved slowly in deionized water employing mild heat (50°C) by stirring magnetically to form a homogeneous polymer solution. The drug QHL was added to the resultant polymer solution to get a homogenous drug-polymer mixture and sonicated for 30 minutes. The dispersion was then added dropwise from #10 gauge hypodermic needle from a height of 6 cm into 100 ml aqeous 5 % solution of calcium chloride with desired various speed shown in Table 1 and 2 for 1 h using mechanical stirrer. The gelled droplets microspheres were allowed to remain in calcium chloride solution for 30 minutes for complete curing, complete reaction for producing spherical regid microspheres, the microspheres were colleceted by decantation, seperated by filteration throgh whatman filter paper #44. The prepared product was washed repeatedly with deionized water to remove excess of $CaCl_2$ that might have deposited on surface of microspheres. The microspheres were then dried at 50°C under vacuum assembly, dried and stored in dessiccator for further study.

2.2. Characterization of Microspheres

2.2.1. Particle size calculation

The particle size of Quinapril HCl loaded prepared mucoadhesive microspheres were examined by optical microscopic method. A small quantity of microspheres was dispersed in 10 mL of purified water. The dispersion was kept under sonication for about 5 mins. A small drop of resultant solution was further placed on a clean glass slide and diameters of particles were measured. Approximately 100 microspheres were counted for particle size determination using a

calibrated optical microscope. The experments were done in triplícate [6].

2.2.2. Shape and surface morphology of micro-spheres

The surface texture of drug-loaded mucoadhesive microspheres were studied using Scanning Electron Microscope (Jeol JSM- 1600, Japan) at RGPV, Bhopal, India. The samples were dried thoroughly in vacuum desiccators before mounting on brass specimen studies. A small quantity of drug-loaded microspheres was spread manually on a carbon tape and gold alloy of 120A° to an aluminum stub in Argon ambient of 8-10 Pascal with plasma voltage about 10mA for nearly 10 sec to obtain uniform coating on the sample to facilitate good quality of SEM images. Samples were analyzed by SEM with direct data capture of the image on a computer screen [7].

2.2.3. Micromeritic Properties of Microspheres

Various micromeritic properties of microspheres have been characterized [8-9]. The bulk density of the powder was determined by adding the powder sample into a measuring cylinder. The resulting bulk volume and weight of the powder are used for calculating bulk density: $\rho b = M/Vb$, where M is the weight of the powder (g) and Vb is the bulk volume (mL).

Tapped density of the powder was determined by tapping the powder containing measuring cylinder on the base platre from the height of 6 cm upto 100 times and easure the volume and calculating tapped density: $\rho t = M/Vt$, where M is the weight of the powder and Vt is the least volume occupied by the sample in a measuring cylinder (mL).

Carr's index (IC) $IC = \rho t - \rho b / \rho t * 100$.

The angle of repose (Θ) was determined by the funnel method where powders were allowed to pass through the funnel, which was vertically raised to a maximum height (h) of the cone, and the radius (r) of the cone was measured.

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

2.2.4. Percentage Entrapment efficiency

The 25 mg of pure drug equivalent containing prepared mucoadhesive microspheres were crushed in pestle mortar. The crushed microspheres were transferred into a 50 mL of volumetric flask containing 10 mL of ethanol with 40 mL of 0.1N HCL (SGF). The mixture sonicated with ultrasonicator upto 1 h, and such mixture was filtered throughout with whatman filter paper (#44). The resultant solution was analyzed by UV spectrophotometrically at 214 nm. The percent drug entrapment was determined by following equation:

Drug efficiency (%) = Amount of drug present in microspheres / Theoretical amount of drug x 100

2.2.5. Swelling Index

The swelling characteristics of mucoadhesive microspheres were resolved correctly in the 0.1 N HCl (pH 1.2). Microspheres of known weight (50 mg) from different batches were placed in the dissolution medium (0.1 N HCl pH 1.2) for 24 hours and swollen microspheres were accumulated in a centrifuge. The swollen microsphere weight or mass was found out by first blotting the microsphere with filter paper to eradicate water which was absorbed on surface and after that undergone taking weight instantly in an electric balance.

2.2.6. In-vitro wash-off test

Freshly excised pieces of intestinal mucosa (5 x 2 cm) from sheep were mounted onto glass slides (3 x 1 inch) with adhesive material [9]. About 100 number of microspheres were spread onto each wet rinsed tissue specimen, and immediately thereafter the support was hung onto the arm of a USP tablet disintegrating test apparatus. The disintegrating test machine was operated with tissue specimen, cylinder was regular moved up and down in the test fluid at 37°C. At each one hour time intervals up to 12 h regularly check machine, after completion of experiment the machine was stopped and the number of microspheres still adhering to the tissue was counted [12].

Mucoadhesive Property (% mucoadhesion) = No. of Mucoadhesive adhered/No. of Microspheres applied x 100

2.3. *In-vitro* drug release of microspheres

The *in vitro* dissolution studies of prepared mucoadhesive microspheres (equivalent to 25 mg drug) were performed by using the USP type I dissolution testing apparatus for 24 h. The dissolution medium used for the study was 900 mL 0.1N HCl; temperature 37±0.5°C with stirring speed at 100 rpm to maintain the sink conditions. At predetermined time intervals, 1 mL of samples were withdrawn periodically, which replaced with prewarmed fresh medium. The sample was diluted with dilution medium, passed through a membrane filter (#5mm), and analyzed spectrophoto-

metrically using a UV spectrophotometer (Shimadzu UV-1800, Japan) at 214 nm with triplicate study and average data were considered for the analysis [13].

2.4. *In vivo* mucoadhesive Study

In vivo mucoadhesion behaviour of the prepared microspheres was observed through X-ray images. The microspheres containing barium sulphate as placebo material other tan API was used as a diagnostic agent or as a core material for the justification of mucoadhesion behaviour. The microspheres was prepared placebo without addition of drug with barium sulphate kept in empty gelatine capsular shell. Microspheres in gelatine capsules were administered with 10 ml of water to an albino rabbit after a light meal. The source of the X-ray machine and the animal were kept uniform throughout the procedure, and finally, images of the gastric region were captured at 0, 1, 3, 6 and 12 h to observe the mucoadhesion of microspheres [14]. This experimental design was conducted at the RKDF University, Bhopal and approved by the Institutional Animal Ethics Committee (Registration No. IAEC/VCP/2019 /001/5).

2.5. Statistical analysis

Experimental results were performed in triplicate (n=3) and expressed as mean±S.D. One-way analysis of variance (ANOVA) was applied to check significant difference in drug release from different formulations. Differences were considered to be significant at $P<0.05$.

3. RESULTS AND DISCUSSION

The prepared mucoadhesive microspheres were charcterized by various parameters i.e. particle size calculation, shape and surface morphology, micromeritic properties, percentage entrapment efficiency, swelling index, *in-vitro* wash-off test, *in vitro* dissolution studies and *in vivo* mucoadhesion behaviour. The experimental results were performed in triplicate (n=3) and expressed as mean ± S.D. One-way analysis of variance (ANOVA) was applied to check significant difference in drug release from different formulations. Differences were considered to be significant at $P<0.05$.

Table 1: The different variables parameters for the 3^2 factorial study as independent Variables and Their Levels

Levels	Stirring speed (rpm) X1	Polymer concentration (mg) X2
-1	250	50
0	500	100
1	750	150

Table 2: Formulation of Various Batches of Mucoadhesive Microspheres of Quinapril Hydrochloride

S. No.	Formulation Code	Drug (mg)	Sodium Alginate (mg)	Chitosan (mg)	Guargum (mg)	Deionized wáter (ml)	Calcium chloride (% w/v)	Stirring speed (rpm)
1	FM1R1	25	150	100	50	100	5	250
2	FM1R2	25	150	100	50	100	5	500
3	FM1R3	25	150	100	50	100	5	750
4	FM2R1	25	150	50	100	100	5	250
5	FM2R2	25	150	50	100	100	5	500
6	FM2R3	25	150	50	100	100	5	750
7	FM3R1	25	100	50	150	100	5	250
8	FM3R2	25	100	50	150	100	5	500
9	FM3R3	25	100	50	150	100	5	750
10	FM4R1	25	100	150	50	100	5	250
11	FM4R2	25	100	150	50	100	5	500
12	FM4R3	25	100	150	50	100	5	750
13	FM5R1	25	50	150	100	100	5	250
14	FM5R2	25	50	150	100	100	5	500
15	FM5R3	25	50	150	100	100	5	750
16	FM6R1	25	50	100	150	100	5	250
17	FM6R2	25	50	100	150	100	5	500
18	FM6R3	25	50	100	150	100	5	750

3.1. Physical characterization of microspheres

The microspheres were found to be discrete, spherical and free-flowing. The effects of alginate concentrations and polymer ratios on the average particle size and % drug entrapment of microspheres are shown in tables 3 and 4. The mean particle size increased with increase in polymer concentration which might be due to the fact that as polymer concentration increases it produces a significant increase in the viscosity, leading to an increase of the emulsion droplet size and finally a higher microsphere size. The % entrapment efficiency for the different formulations significantly increased with increasing polymer content ($p<0.05$). The mucoadhesive microspheres (FM6R2) with SA:CH:GG in 1:2:3 ratio produced the highest percent drug entrapment efficiency of 93.73±1.44%. An increase in polymer concentration resulted in formation of larger microspheres entrapping greater amount of drug with médium stirring speed at 500 rpm. The size of the microspheres increased with increase in the alginate concentration which may be due to the increase in viscosity, resulting in increase in droplet size during addition of the polymer dispersion to the harvesting medium. The SEM of prepared microspheres (FM6R2) is shown in fig.1. Formation of cracks on the surface of the microspheres were observed which may be due to the penetration of the dissolution medium into the microspheres and the subsequent dissolution of the drug and hence its diffusion through the polymer matrix.

3.2. Micromeritic properties of microspheres

The physical study parameters like angle of repose, tapped density, bulk density and packing properties (Tables 3-4) confirms better good to excellent flow properties of the prepared microspheres. All the formulation showed angle of repose value within the range of 20° to 31° (n=3), which is an appreciable limit for microspheres to show flow property during the packing in capsular shell as complete dosage form.

3.2.1. Swelling index

The swelling index of mucoadhesive microspheres was found to be in the range of 1.08±0.62 to 1.93±0.94. Swelling studies showed that the amount of polymer plays an important role in solvent transfer. It can be concluded that upon increasing the polymer concentration, the swelling index also increased. When increasing ratio of the polymer which could be due to more amount of polymer present in the microspheres may also be responsible for higher swelling. It was indicated that the stirring speed showed a positive effect on the Swelling index i.e., with an increasing the stirring speed there was improved Swelling Index.

3.2.2. In-vitro wash-off studies

The mucoadhesion test was performed on both simulated gastric pH (0.1N HCl, pH 1.2) for 12h. The results are given in tables 3-4. The result of wash-off test was found to be adhered the microspheres the at intestinal pH due to highly swelling nature of composition of polymers at this pH. So, increase the adhesive strength and retarded the drug release of best composition of SA:CH:GG in the ratio of 1:2:3 (FM6R2). Guargum is a highly viscous material having a property of more swelling nature due to presence of galactommannan constituent. Thus, poor mucoadhesion of FM1R1 formulation was shown due to having reducing amount of guargum. Although chitosan was also playing the important role on the mucoadhesion as hydrophilic functional group's presence in polymer. Thus, the microspheres having specific ratio of chitosan could form hydrogen bonds with mucus molecules, thus producing some adhesive force of this polymer.

3.3. *In-vitro* drug release of microspheres

Solubility of QHL depends on pH medium of dissolution media. The drug showed maximum absorption expected with increasing solubility in acid environment. It is known that microspheres constitute multiple unit dosage forms which have many advantages as compared to tablets. They spread more evenly in the stomach which leads to a decreased risk of high local concentration at the specific site for better effect. The *in-vitro* release studies were carried out in 0.1 N HCl (pH 1.2), which indicated a slow and controlled release of drug for all the formulations. The drug release of the microspheres (FM1R1-FM6R3) were shown in Fig. 2 (a, b), respectively. Drug release from the mucoadhesive microspheres was slow, extended and dependent on the composition of galactomannan concentration of polymer and stirring speed during formulation used. The differences in the drug release characteristics of various microspheres might be due to the differences in the porosity of the coat formed and swelling and adhesion nature of coat and its solubility in the dissolution fluid. Drug release from FM6R2 was slow and extended over a period of 12 h and these microcapsules were found suitable for oral controlled release formulations (Tables 3-4).

Table 3: 3^2 Factorial Design for MucoadhesiveMicrospheres of Quinapril Hydrochloride

F Code	Independent variables				Dependent variables			
		X2			Y1	Y2	Y3	Y4
	X1	Sod. Alginae (mg)	Chitosan (mg)	Guar gum (mg)	% entrapment	% yield	% mucoadhesion	% of drug release
FM1R1	-1	1	0	-1	86.4	83.51	73.25	94.24
FM1R2	0	1	0	-1	88.9	87.12	76.81	91.06
FM1R3	1	1	0	-1	81.18	83.14	80.14	95.24
FM2R1	-1	1	-1	0	88.05	83.81	79.06	88.41
FM2R2	0	1	-1	0	87.14	87.83	83.21	84.14
FM2R3	1	1	-1	0	87.17	86.16	80.05	88.25
FM3R1	-1	0	-1	1	90.14	87.24	83.05	85.14
FM3R2	0	0	-1	1	88.81	89.12	90.13	80.13
FM3R3	1	0	-1	1	85.04	90.22	81.18	82.11
FM4R1	-1	0	1	-1	90.11	92.17	80.09	91.15
FM4R2	0	0	1	-1	87.41	94.11	81.13	88.15
FM4R3	1	0	1	-1	85.16	92.15	81.18	90.17
FM5R1	-1	-1	1	0	86.18	91.96	80.06	87.04
FM5R2	0	-1	1	0	85.27	97.12	89.03	84.16
FM5R3	1	-1	1	0	87.35	95.25	82.38	86.17
FM6R1	-1	-1	0	1	90.25	96.17	90.05	85.18
FM6R2	0	-1	0	1	93.73	98.97	94.12	74.21
FM6R3	1	-1	0	1	91.09	95.15	91.06	81.15

X1 = stirring speed; X2=concentration of SA:CH:GG; Y1=percentage entrapment efficiency; Y2=percentage yield; Y3=percent mucoadhesion; Y4 = percentage of drug release.

Table 4: Characteristics of Formulated Mucoadhesive Microspheres

Formulation code	Bulk density[a] (g/cm^3)	Tapped density[a] (g/cm^3)	Carr's index[a] (%)	Angle of repose[a] (h°)	Mean particle size[b] (µm)	Percent entrapment	Percentage yield	Swelling index	Percent mucoadhesion	Percentage of drug release
FM1R1	0.36±0.021	0.43±0.011	19.44±0.11	31.22±1.98°	288.12±3.25	86.4±1.21	83.51±1.98	1.15±0.45	73.25±2.11	93.23±1.18
FM1R2	0.42±0.011	0.47± 0.012	10.63±0.13	24.25±1.23°	266.28±3.38	88.9±2.01	87.12±1.65	1.36±0.75	76.81±2.16	90.65±1.05
FM1R3	0.36±0.028	0.42±0.007	14.28± 0.25	25.22±1.16°	251.16±3.16	81.18±1.25	83.14±1.44	1.48±0.33	80.14±1.99	94.11±1.22
FM2R1	0.37±0.021	0.44±0.021	15.90±1.07	25.12±1.60°	249.84±2.17	88.05±1.14	83.81±1.52	1.24 ±0.44	79.06±1.85	86.11±1.13
FM2R2	0.40±0.017	0.45±0.012	11.11±0.97	24.91±1.20°	241.14±2.67	87.14±1.12	87.83±1.65	1.64 ±0.32	83.21±2.89	82.12±1.02
FM2R3	0.38±0.014	0.43±0.024	11.62±1.15	23.21±1.11°	240.12±3.18	87.17±1.05	86.16±1.32	1.79 ±0.55	80.05±2.09	86.31±1.06
FM3R1	0.39±0.023	0.45± 0.011	13.33±1.18	25.91±1.17°	256.12±2.87	90.14±1.14	87.24±1.84	1.38±0.21	83.05±1.99	83.11±1.24
FM3R2	0.41±0.028	0.46± 0.026	10.86±0.95	22.16±1.67°	249.01±2.05	88.81±1.09	89.12±1.69	1.55±0.43	90.13±2.45	80.03±1.21
FM3R3	0.38±0.015	0.44± 0.018	13.63±0.85	22.98±1.01°	251.11±2.81	85.04±1.36	90.22±1.78	1.76±0.62	81.18±3.04	81.08±1.15
FM4R1	0.43±0.028	0.49±0.019	12.24±0.12	22.12±1.03°	245.13±2.65	90.11±2.04	92.17±1.96	1.08±0.62	80.09±2.89	90.05±1.16
FM4R2	0.44±0.011	0.50±0.011	12.01±0.38	22.04±1.01°	241.03±2.98	87.41±1.11	94.11±2.01	1.32±0.25	1.59 ±0.55	1.59 ±0.55
FM4R3	0.42±0.021	0.48±0.024	12.51±0.27	23.01±1.11°	255.13±2.51	85.16±1.89	92.15±1.88	1.49±0.23	1.78 ±0.21	1.78 ±0.21
FM5R1	0.41±0.004	0.47±0.017	12.76± 0.39	23.18±1.08°	244.02±2.11	86.18±.74	91.96±1.96	1.34±0.64	1.25 ±0.43	1.25 ±0.43
FM5R2	0.44±0.012	0.50±0.014	12.01± 0.99	22.99±1.13°	251.18±2.63	85.27±1.41	97.12±1.63	1.56±0.11	1.08 ±0.62	1.08 ±0.62
FM5R3	0.43±0.011	0.49±0.021	12.24± 0.18	23.25±1.02°	259.08±2.11	87.35±1.21	95.25±2.01	1.73±0.54	1.59 ±0.55	1.59 ±0.55
FM6R1	0.44±0.012	0.49± 0.017	10.20±0.34	21.80±0.92°	246.16±2.02	90.25±1.31	96.17±1.98	1.31±0.22	1.78 ±0.21	1.78 ±0.21
FM6R2	0.46±0.016	0.51± 0.027	9.87±0.88	20.10±0.72°	259.11±2.62	93.73±1.44	98.97±1.63	1.68±0.31	94.12±2.85	71.19±1.72
FM6R3	0.43±0.017	0.49± 0.021	12.24±0.18	22.22±1.22°	261.26±2.35	91.09±1.46	95.15±1.99	1.93±0.94	91.06±2.43	78.18±1.99

[a]Mean SD, n = 3; [b]Mean SD, n = 100. CDR, cumulative drug release; SD, standard deviation.

3.4. *In vitro* mucoadhesive study

In vitro mucoadhesive study was further selected by the radiological technique to justify the increased residency time in the stomach. The mucoadhesion capacity of dried mucoadhesive microspheres was evaluated in simulated gastric fluid. FM6R2 containing SA:CH:GG

(1:2:3) exhibiting good responce. X-ray images taken at different time intervals for the mucoadhesive study (Fig. 3) indicate the gastro- retentive property of microspheres, emphasizing a significant gastric residence time for optimum release and absorption of the drug due to the porous nature of mucoadhesive microspheres.

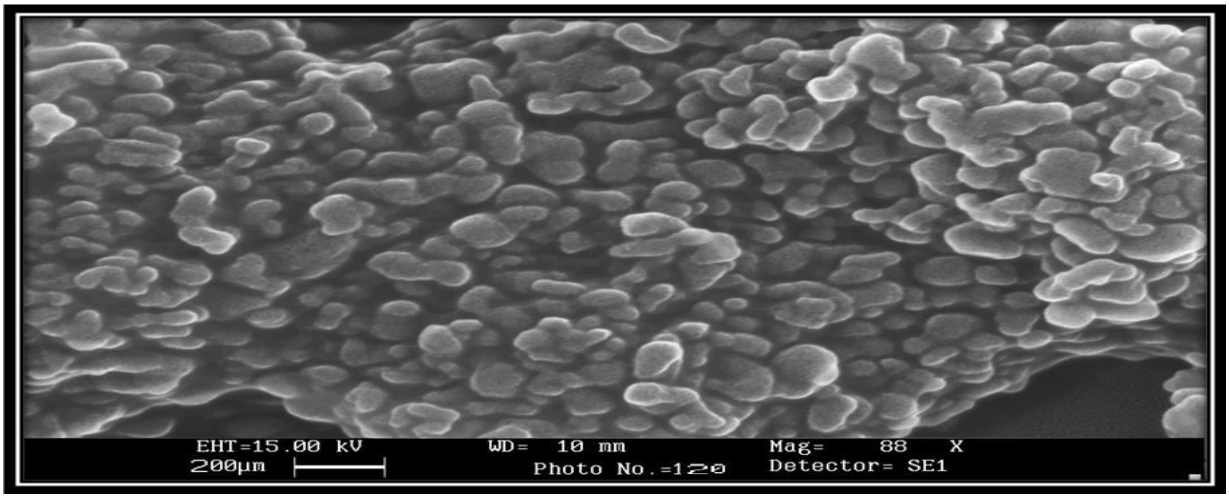
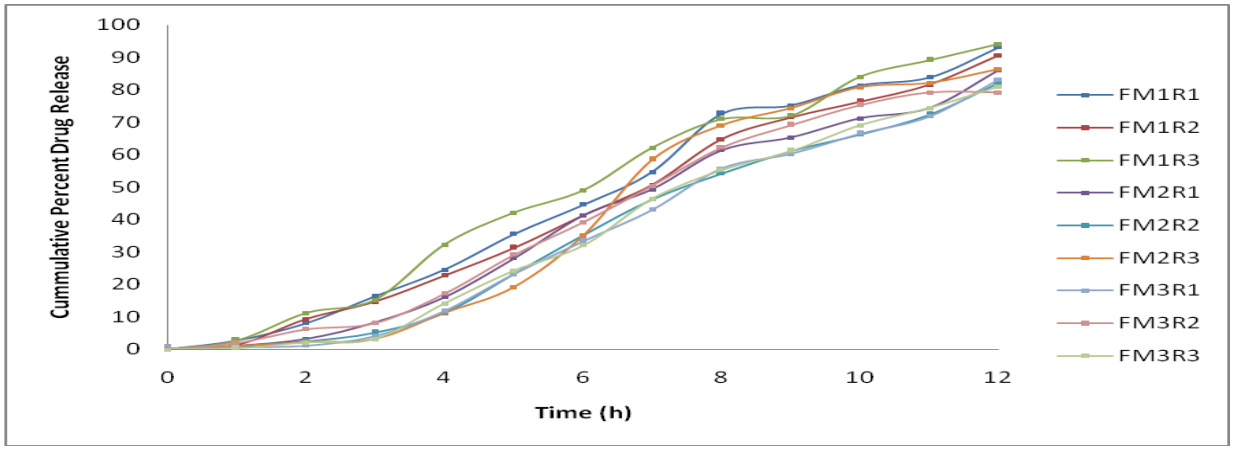
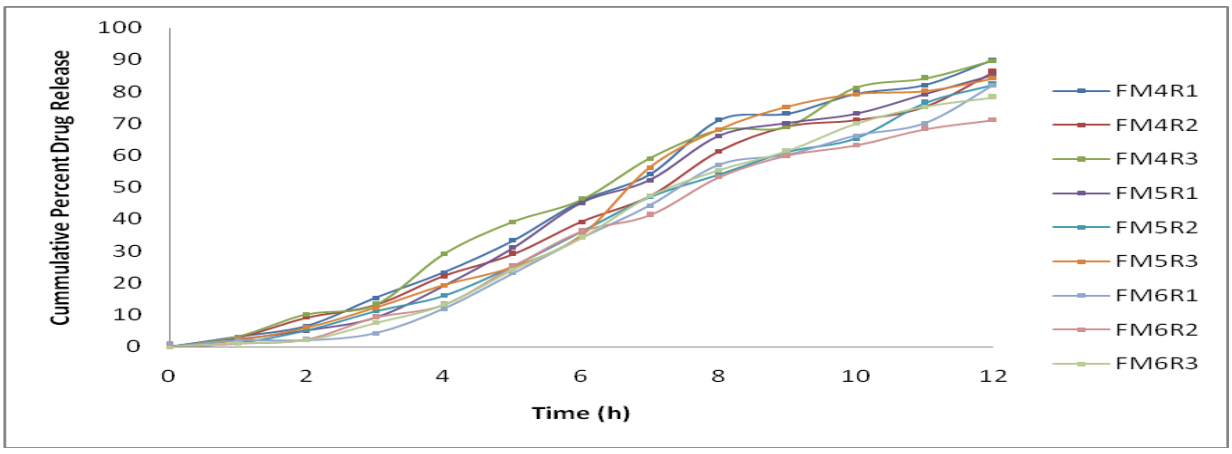


Fig. 1: SEM image of the optimized mucoadhesive microsphere formulation, FM6R2



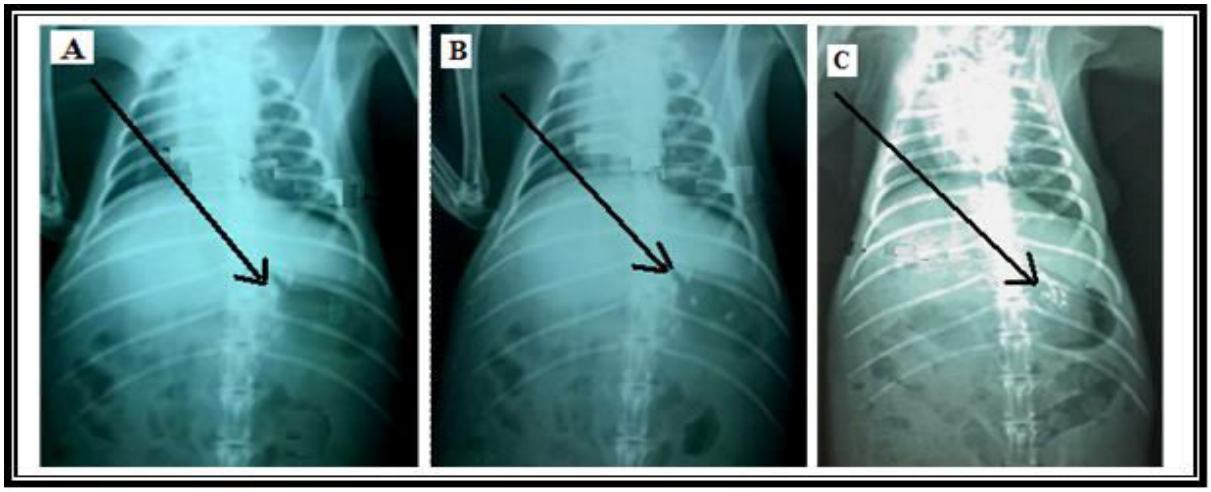
(a)



(a) Mucoadhesive microspheres. (FM1R1–FM3R3) (b) Mucoadhesive microspheres (FM4R1–FM6R3)

(b)

Fig. 2: In vitro drug release of all formulations.



The insets indicate the in vivo adhesive behavior of Sodium alginate:Chitosan:Guargum based Quinapril Hydrochloride microspheres upto 12 h intervals.

Fig. 3: X-ray images of formulation FM6R2 in the gastric region of an albino rabbits at (A) 0 h (B) 6 h (C) 12 h.

4. CONCLUSION

Mucoadhesive microspheres offer a unique carrier system owing to its capability to adhere to any mucosal tissue. This ionic gelation method produced spherical and free flowing microspheres. Quinapril Hydrochloride release was found to be slow and extended period of time. The release depends on the type and composition of polymer and stirring speed used. The release of drug was prolonged when incorporated within mucoadhesive polymers. The mucoadhesive microspheres prepared by ionotropic gelation technique gave sustained drug release up to 12 h duration. Microspheres have best reproducible results, would prove to be promising carrier for oral delivery of Quinapril Hydrochlorideand thereby help in the management of hypertension with oral route.

Disclosure statement

All authors disclose that there is no institutional or commercial conflict of interest regarding the publication of a manuscript.

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