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Floating microspheres of prazosin hydrochloride: Formulation, characterization and *in-vitro* evaluation

Sudhir Singh*, Ajay Kumar Tiwari

Department of Pharmaceutics, School of Pharmaceutical Sciences,
Jaipur National University, Jaipur, Rajasthan, India.

ABSTRACT

Prazosin Hydrochloride, a selective alpha-adrenergic receptor blocking agent, was loaded in the hollow microspheres to improve bioavailability and patient compliance by prolonging the residence time in the gastrointestinal tract. The hollow microspheres of Prazosin HCl were prepared by solvent evaporation diffusion method using Eudragit RS 100 and ethyl cellulose as a release controlled polymer, HPMC as a matrix former. The present study involves preparation and evaluation of floating microspheres with Prazosin Hydrochloride as model drug for prolongation of gastric residence time. Prazosin Hydrochloride is a BSC class-II having short biological half-life (2 to 3 hours) with low bioavailability (40-60%). The sustain release gastro retentive dosage form offer many advantages for Prazosin Hydrochloride drug. Gastro retentive dosage form improves the bioavailability and reduces the side effect of Prazosin hydrochloride. The microspheres were prepared by the emulsification solvent diffusion method using polymers Eudragit RS100, Hydroxypropylmethyl cellulose K4M and Ethylcellulose. The shape and surface morphology of prepared microspheres were characterized by optical microscopy. In-vitro drug release studies were performed and drug release kinetics was evaluated using the linear regression method.

Keywords: *Gastroretentive; Prolonged release; Prazosin HCl; Floating microspheres; Ethyl cellulose; Hydroxypropyl methyl cellulose; Eudragit.*

INTRODUCTION

The oral route is the most common and preferable route for the delivery of drugs. This may be due to ease of administration, patient compliance, and flexibility in formulation. [1]

Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. [2] Moreover, first-pass metabolism of drugs in the intestinal wall and liver has also been a limiting factor for exploring the potential of oral dosage forms. These problems can be overcome by using oral controlled release (CR) formulations that provide controlled release of the drugs in GIT, maintain a constant drug concentration in the serum for longer periods of time, and provide better bioavailability, therapeutic efficacy, and possible reduction of the dose size. The dissolution rate of the slightly or poorly water soluble drugs can be successfully increased by increase gastric retention time (GRT). Prolonged gastric retention helps to retention of drug in the stomach for a longer time in a predictable manner. [2]

During the past decade, several approaches have been utilized to increase the gastric retention time, i.e. floating systems, mucoadhesive dosage forms, high-density systems, superporous hydrogel, swelling and expanding systems, and magnetic systems. These systems have more flexibility in dosage design than conventional dosage forms. [3-5]

The multiple unit system has been developed to identify the merit over a single unit dosage form because the single unit floating systems are more popular but have a disadvantage owing to their "all-or-nothing" emptying process, leading to high variability of the gastrointestinal transit time.

Kawashima et al. prepared hollow microspheres or microballoons of ibuprofen by the emulsion-solvent diffusion method using acrylic polymers. [6] The microspheres exhibited good in-vitro floatability and drug release decreased drastically with increasing polymer concentration. This method has been the most widely used since it is known to be simple and able to be produced in a small batch size. [7, 8] In this method, dispersion of drug in the solution of polymer in organic solvent is stabilized in an external phase containing surfactant stabilizer. Polyvinyl alcohol (PVA) is most widely used as a surfactant stabilizer and appears to most effective for formation of microparticles. [8]In final stage, the microspheres are normally obtained after organic solvent evaporation and solidification of polymer droplets.

Eudragit RS 100 is an anionic copolymerization product of methacrylic acid and methyl methacrylate and preferably used as a sustained release polymer. [9] It is a low density polymer (0.83–0.85 g/cm^3) and soluble in intestinal fluid (pH > 7). Dichloromethane (methylene chloride) is the most widely used organic solvent because it possesses high volatility (boiling point of 41^{0}C) and can be evaporated during production, resulting in a round cavity inside microspheres. The microspheres with a round cavity, called hollow microspheres, yield low density microspheres that can float in GI fluids for longer times. [2]

Prazosin Hydrochloride [1-(4-amino - 6, 7 - dimethoxy - 2 - quinazolinyl) - 4 - (2 - fur-anylcarbonyl)-monohydrochloride] is indicated in the treatment of mild to moderate hypertension. It is slightly soluble in water, very slightly soluble in alcohol, and has an apparent pKa of 6.5 in 1:1 water and ethanol solution. [10]It is readily absorbed after oral administration. Peak serum levels are attained in 2-3 h and it has a half-life of 4-5 h. [11] Its average dosing is 1-2 mg three times a day. Thus, its short half-life and increased dosing frequency suggest the need for a controlled delivery of Prazosin Hydrochloride for better patient compliance.

The objective of this study is to develop a simple uncomplicated and easy to manufacture floating microspheres that is capable of delivering Prazosin Hydrochloride at a prolong release rate of delivery.

MATERIALS AND METHODS

Materials: Prazosin Hydrochloride was obtained from Tokyo Chemical Industry Co. Ltd., (Japan). Ethylcellulose and HPMC were obtained from Colorcon Asia Pvt. Ltd. (India). Eudragit RS100 was obtained from Evonik degussa Pvt. Ltd., Mumbai, India. Distilled water was used throughout the experiments. All other chemicals/reagents used were of analytical grade and used without further modification.

Preparation of Microballoons of Prazosin HCl: [13] Prazosin HCl and different polymers with different proportion were dissolved in ethanol: dichloromethane mixture (3:2 v/v, 15 ml) at room temperature. The drug solution was poured slowly as a thin stream into 200 ml of water containing 1.0 % w/v polyvinyl alcohol. The solution was kept at constant temperature while stirring at 300 rpm. The finely dispersed/emulsified droplets of the polymer solution of drug were solidified in the aqueous phase via diffusion of the solvent. After agitating the mixture for 2 h, the microspheres were filtered, washed several times with water to remove traces of polyvinyl alcohol and dried overnight at 40°C. During drying, microspheres cavity became hollow resulting in floating drug delivery system. Emulsion solvent evaporation method has been successfully used to encapsulate lipophilic drugs into micro particles.

Ingredients	Batch code								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Prazosin Hydrochloride(mg)	100	100	100	100	100	100	100	100	100
Eudragit RS100 (mg)	100	200	300	-	-	-	50	133	225
Ethylcellulose (mg)	-	-	-	100	200	300	-	-	-
HPMC K4M (mg)	-	-	-	-	-	-	50	67	75
Ethanol (ml)	8	8	8	8	8	8	8	8	8
DCM (ml)	5	5	5	5	5	5	5	5	5
IPA (ml)	2	2	2	2	2	2	2	2	2
Stirring Speed (rpm)	600	600	600	300	300	300	600	600	600

Characterization of Prepared Microballoons:

Interaction studies: The IR spectra of pure drug, drug: eudragit RS100, drug: ethyl cellulose, drug with mixture of polymer (eudragit RS100: HPMC K4M) were obtained in KBr pellets at moderate scanning speed 4000-400 per cm by using SHIMADZU (8400S) FTIR Spectroscope.

Micrometric Properties [14, 18]
The floating microspheres are characterized by their micromeritic properties such as particle size, tapped density, carr's index and angle of repose.

Particle size: Particle Size of floating microspheres was performed with the help of optical microscope for randomly selected samples of all the formulation. [12]

Percent Yield of Microspheres: The prepared microballoons were collected and weighed. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microballoons.

% Yield = (Actual weight of product / Total weight of excipient and drug) × 100

Determination of Percent Drug Entrapment: Floating microspheres equivalent to 20 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1 N HCl of pH 1.2 repeatedly (3X10ml). The extract was transferred to a 100 ml volumetric flask and the volume was made upto 100 ml using 0.1 N HCl of pH 1.2. The solutions were filtered and the absorption was measured after suitable dilution spectrophotometrically (UV- Shimadzu1800 double beam) at 247 nm against appropriate blank. Each determination was made in triplicate. [18]

The percentage drug entrapment was calculated as follows:

% Drug entrapment = (Calculated drug conc. / Theoretical drug content) × 100

Percentage Buoyancy: Floating microspheres (equivalent to 50 mg) were dispersed in 900ml of 0.1 N hydrochloric acid solution (pH 1.2) containing tween 80 (0.01 w/v %) at 37°C. The mixture was stirred with a paddle at 100 rpm and after 12 hr, the layer of buoyant microspheres (W_f) was pipetted and separated by filtration simultaneously sinking microsphere (W_s) was also separated. Both microspheres type were dried at 40°C overneight. Each weight was measured and buoyancy was determined by the weight ratio of the floating microsphers to the sum of floating and sinking microsphers. [18]

$$\% \text{ Buoyancy} = \frac{\text{Weight of floating microspheres } (W_f)}{\text{Initial weight of microspheres } (W_f + W_s)} \times 100$$

Where W_f and W_s are the weights of the floating and settled microspheres, respectively. All the determinations were made in triplicate.

In-Vitro Drug Release Study: Drug release study from the hollow microspheres is complicated because the hollow microspheres float and hence adhere to the inside surfaces of the dissolution basket while the dissolution experiments are in progress, which leads to the nonparticipation of the hollow microspheres or their surface in the release study. Hollow microspheres have the propensity to exhibit a buoyancy effect in-vivo, but the development of a dissolution method as a quality control tool with the simulated buoyant condition is difficult.

The drug release rate from floating microspheres was determined using USP XXIII basket type dissolution apparatus. A weighed amount of floating microspheres equivalent to 20 mg Prazosin Hydrochloride was taken for dissolution study. Simulated gastric fluid (SGF, pH 0.1N HCl) (900 ml) containing Tween 20 (0.02 w/v %) was used as the dissolution medium and maintained at 37^0C at a rotation speed of 100 rpm. 5 ml sample was withdrawn at 1 hr interval and analyzed spectrophotometrically at 247 nm to determine the concentration of drug present in the dissolution medium. The initial volume of the dissolution fluid was maintained by adding 5 ml of fresh dissolution fluid after each withdrawal.

Kinetic Assessment: [15, 16, 17]

Drug release from the prepared microspheres made of eudragit RS100, Ethylcellulose and mixture of two polymers were kinetically evaluated to fit to zero order, first order, Higuchi kinetic, Hixon-crowell and Korsemeyer-peppas models.
The release data of Prazosin Hydrochloride from various floating microspheres was fitted to various mathematical models like:

$$Q_1 = Q_0 + K_0 t \quad \text{-------Zero order kinetic}$$

Where, Q is the amount of drug dissolved in time t, Q is the initial amount of drug in the solution (most times, Q 50) and *K* is the zero order release constant.

$$\ln Q_t = \ln Q_0 - k_1 t \quad \text{--------First order kinetics}$$

Where, Qt is the amount of drug released in time t, Q_0 is the initial amount of drug in the solution and *K* is the first order release constant.

$$Q_t = K_H t^{1/2} \quad \text{---------- Higuchi model}$$

Where, Q_t is amount of drug released in time t and K_H is release rate constants.

$$W_0^{1/3} - Wt^{1/3} = K_s t \quad \text{---------Hixon crowell model}$$

Where, W is the initial amount of drug in the pharmaceutical dosage form, W is the remaining amount of drug in the pharmaceutical dosage form at time t and K is a constant incorporating the surface–volume relation.
Korsmeyer et al. (1983) developed a simple, semiempirical model, relating exponentially the drug release to the elapsed time (*t*). An equation that can be described in the following manner:

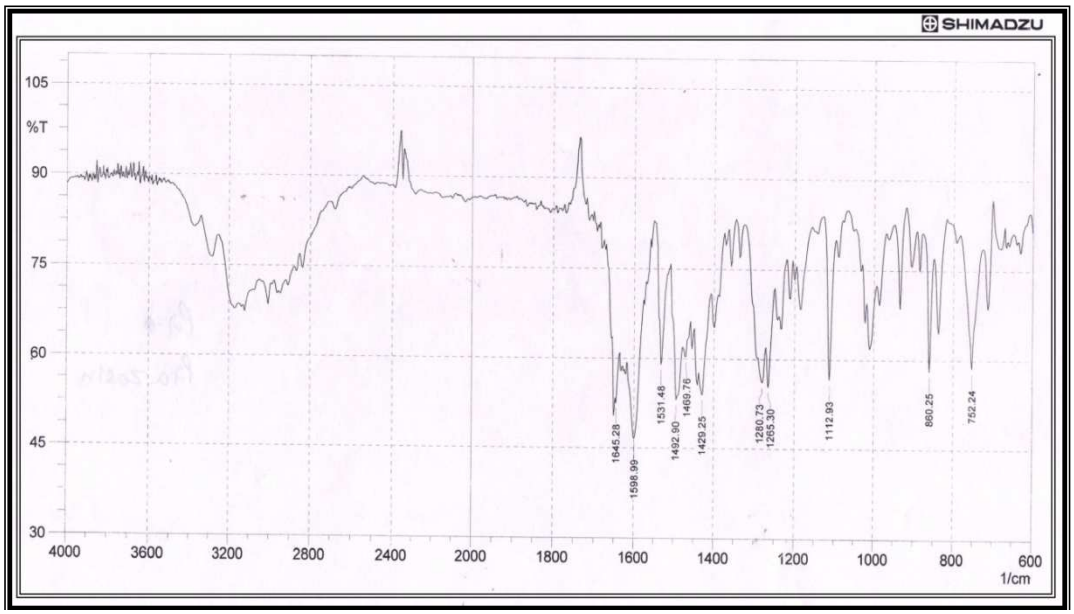
$$Mt / M\infty = at^n \quad \text{---------Korsmeyer–Peppas model}$$

where a is a constant incorporating structural and geometric characteristics of the drug dosage form, n is the release exponent, indicative of the drug release mechanism, and the function of t is M /M∞ (fractional release of drug).

Stability Studies: A study of stability of pharmaceutical product is essential. These studies were designed to increase the rate of chemical and physical degradation of the drug substance or product by using exaggerated storage condition. Optimized formulations were packed in amber colored bottles, which were tightly plugged with cotton and capped. They were then stored at 40oC/ 75%RH for 3 months and evaluated for the physical appearance and drug content, %buoyancy and entrapment efficiency at specific interval of time. Finally, at the end of 3 months and *in-vitro* release studies were also conducted.

RESULTS AND DISCUSSION

Hollow microspheres were prepared by using dichloromethane, ethanol and isopropanol as the organic solvents32. Microspheres were prepared in order to increase gastric residence time of the drug, by making them hollow with excellent buoyancy, which can be retained in the upper part of GIT for a longer period of time.



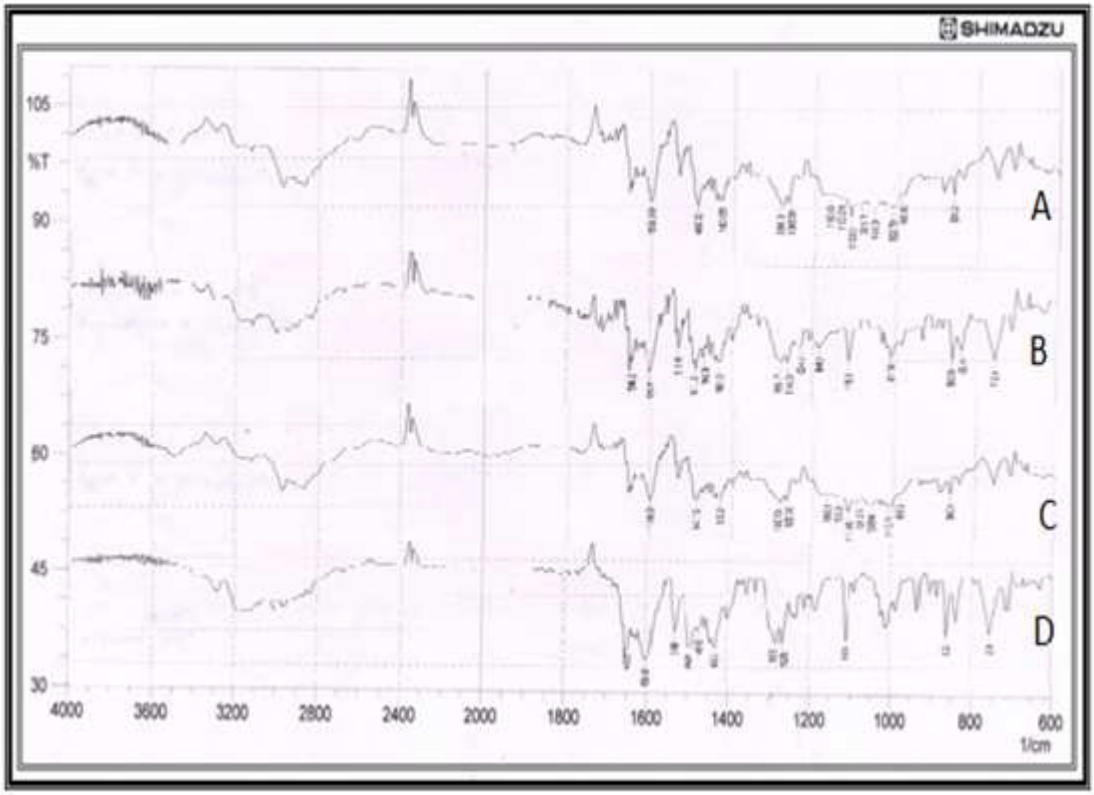
IR Spectra of Pure drug e.g. Prazosin Hydrochloride

Characteristic Peaks Found in IR Spectra of Drug sample	
3198-3295 cm^{-1}	Broad peak shows that stretching of C-H.
1645.28 cm^{-1}	Characteristic peak for stretching of C=O.
1598.99 cm^{-1}	Stretching vibration of C=N in aci-nitro group of nitronic acid
752.24 cm^{-1}	Characteristic sharp peak for the α form of Prazosin Hydrochloride

Solubility of Prazosin HCl was found 0.6 mg/mL in water thus a significant amount of drug was diffused from emulsion droplets into external aqueous phase during evaporation of dichloromethane. In the present work, an attempt is made to reduce the drug loss after the solvent evaporation from the aqueous phase by modifying external aqueous phase.

Drug excipient compatibility study by FTIR spectroscopy

From IR spectra of Prazosin Hydrochloride and different polymers, it can be seen that there is no significant change in IR spectra i.e., it is nearly same to that of plain compounds. IR Spectra of pure drug and physical mixture ofdrug with polymer is shown in figure.



Comparative Drug Excipients compatibility study by IR Spectroscopic Method
(A: Drug+Eudragit+HPMC K4M, B: Drug+Ethyl cellulose, C: Drug+Eudragit RS100, D: Pure drug.)

As seen in the above figure all the characteristic peaks of Prazosin Hydrochloride did not deviate significantly. So there was no major sign of incompatibilities seen in the interaction studies and thus all excipients can be used for the formulation.

Micrometric Properties and Morphology

Formulation No.	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr`s Index (%)	Hausner Ration	Angle of repose (^{0})	Shape of Particle
F_1	0.314	0.353	11.04%	1.12	23.10^0	Spherical
F_2	0.340	0.386	11.90%	1.13	25.22^0	Spherical
F_3	0.410	0.463	11.44%	1.12	24.15^0	Spherical
F_4	0.385	0.436	11.69%	1.13	25.00^0	Spherical
F_5	0.441	0.491	10.18%	1.11	21.15^0	Spherical
F_6	0.362	0.429	15.61%	1.18	23.35^0	Spherical
F_7	0.358	0.402	10.94%	1.12	26.62^0	Spherical
F_8	0.365	0.417	12.47%	1.14	23.20^0	Spherical
F_9	0.395	0.458	15.59%	1.18	25.50^0	Spherical

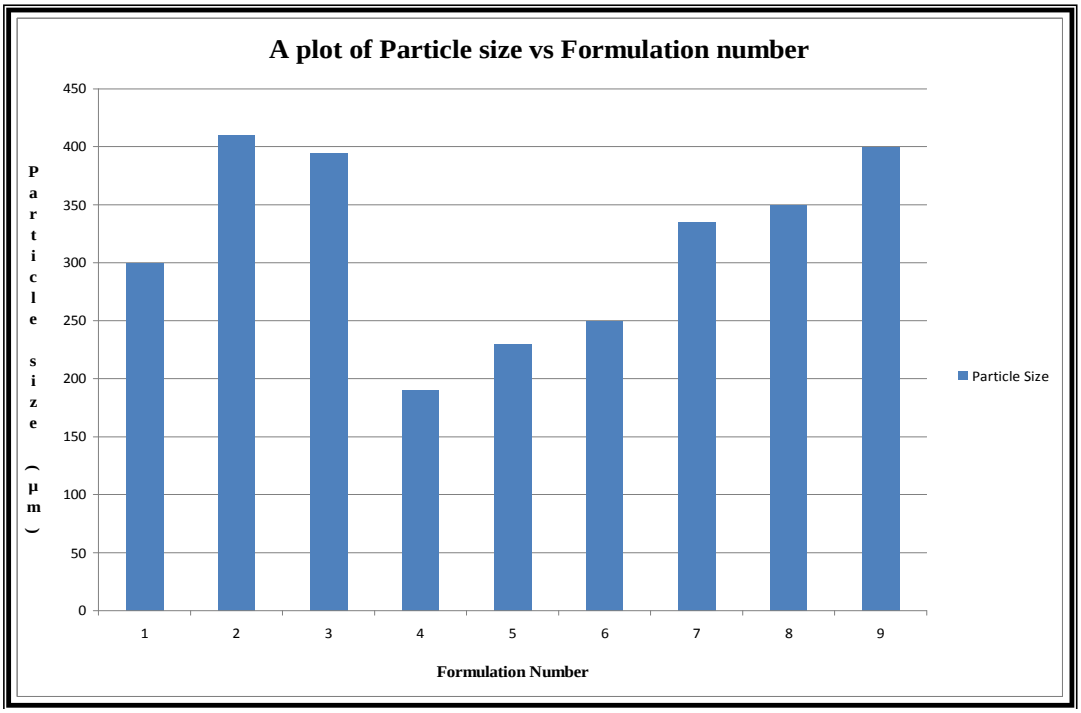
Prepared microspheres were subjected to various micromeritic property evaluations such as bulk density, Carr's index, Hausner's ratio, true density, and particle size analysis.

The flow properties of all formulation were found out by measuring the angle of repose and compressibility index. The results are shown in table 47. The values were found in the range of 21.15 to 26.62 which are within the normal acceptable range of 20^0 to 40^0. Thus porous microspheres showed reasonable good flow potential.

The value of Compressibility Index was in the range 11.04 to 15.59, indication good flow characteristics of microspheres. This also implies that the microspheres are non-aggregated.

The particle size was analyzed by optical microscopy and expressed in terms of geometrical mean diameter.

Formulation No.	Particle Size (µm)	Shape
F_1	300±25	spherical
F_2	410±15	spherical
F_3	395±35	spherical
F_4	190±15	spherical
F_5	230±30	spherical
F_6	215±45	spherical
F_7	335±25	spherical
F_8	350±20	spherical
F_9	400±35	spherical

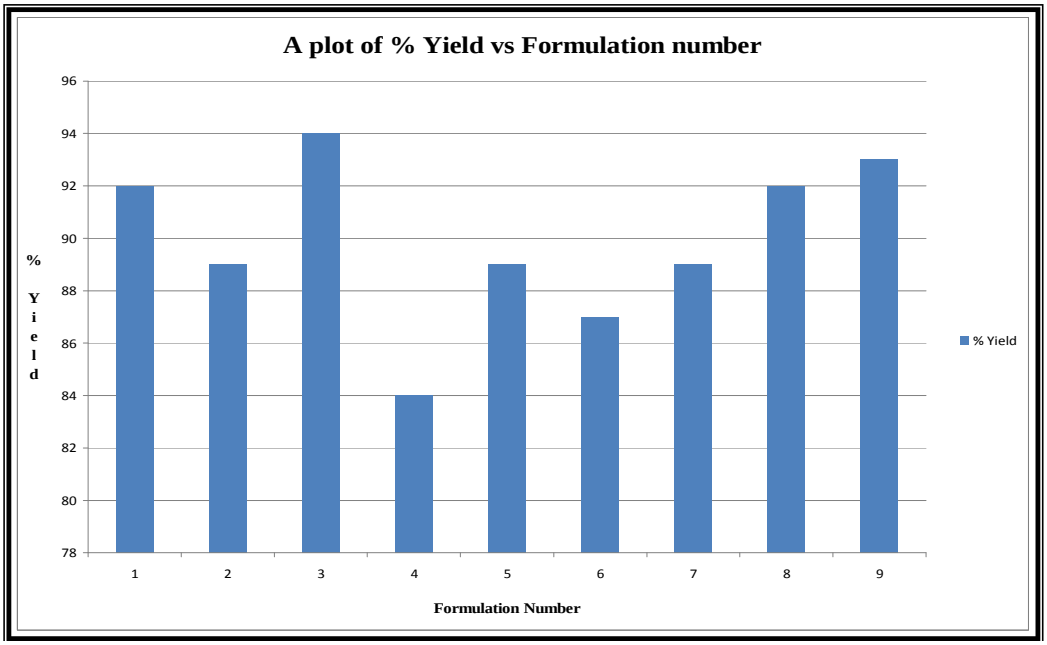


A plot of particle size Vs Formulation number

As the concentration of polymer increases, Particle size of microspheres increases. Particle size was found in the range of 190 to 410 µm.

Formulation No.	% Yield	% Drug Loading	% Entrapment Efficiency
F_1	92.40	37±0.12	91±0.06
F_2	89.75	31±0.32	85±0.12
F_3	94.82	35±0.31	89±0.16
F_4	84.46	32±0.10	87±0.09
F_5	89.19	34±0.04	91±0.03
F_6	87.53	38±0.23	89±0.12
F_7	89.75	38±0.21	93±0.20
F_8	92.35	37±0.19	87±0.14
F_9	93.22	36±0.17	90±0.10

±Mean standard deviation where n=3



A plot of % Yield of formulations F_1 to F_9

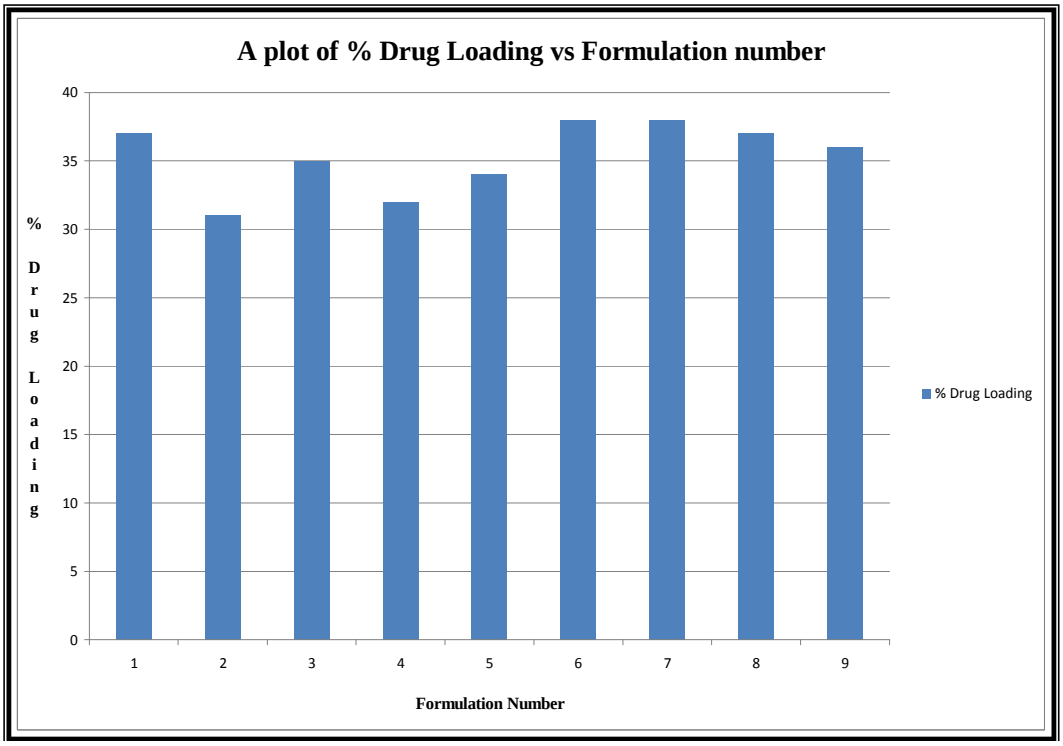


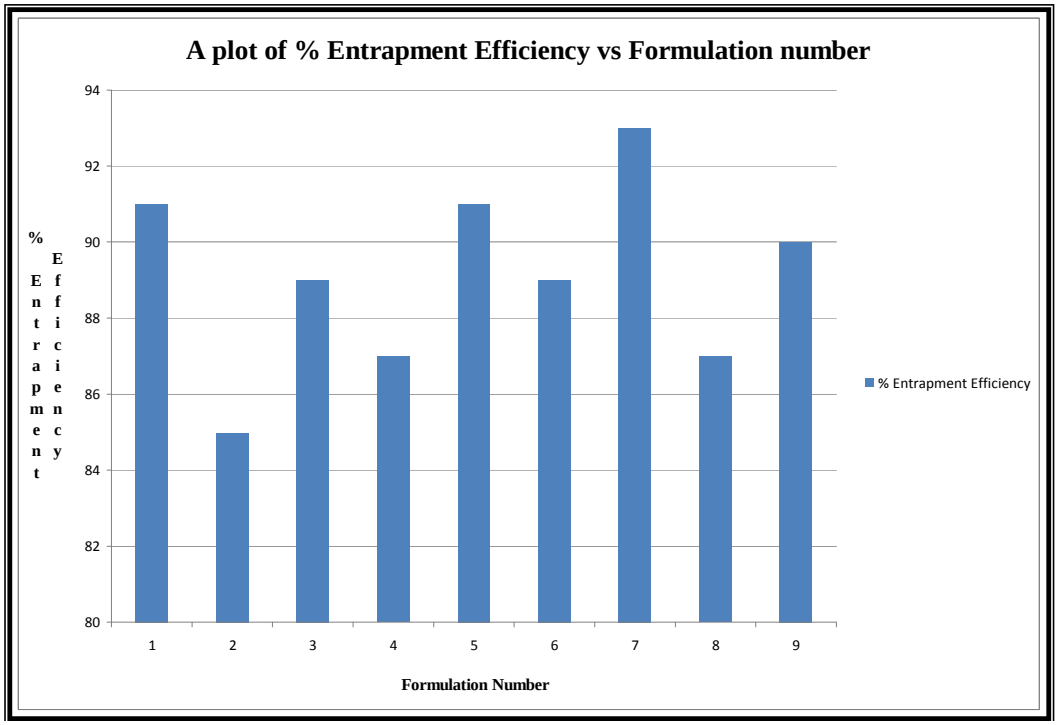
Figure : A plot of % drug loading of formulations F_1 to F_9

Percentage yield

The percentage yield of floating microspheres was varied according to concentration of polymer. The percentage yield of floating microsphere for formulations (F_1–F_9) shown in below Table.

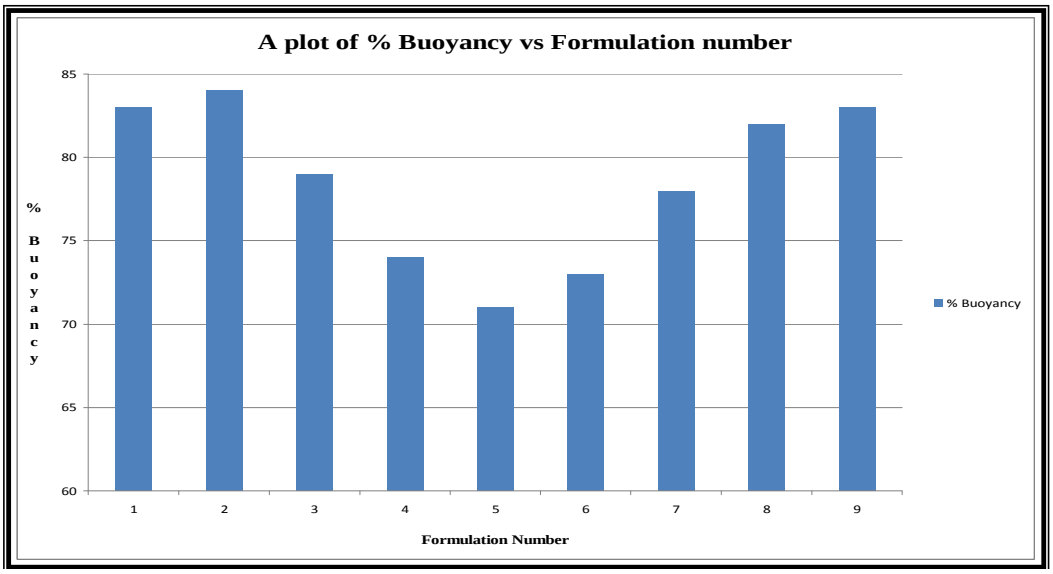
Percentage Drug Loading and Drug Entrapment Efficiency:

The percentage buoyancy and drug entrapment efficiency of formulation F_1–F_9 are shown in below Tables, respectively.



A plot of Percentage Entrapment of formulations F_1 to F_9

The results of different formulations are shown in table. % Yield was found in the range of 84.46% to 94.82%. % Drug loading was found in the range of 31% to 38%. High % drug loading was found with lower concentration of polymer. As the concentration of polymer increases, the % drug loading was decreased. Entrapment efficiency was found in the range of 85% to 93%.



A plot Percentage buoyancy Vs formulation number

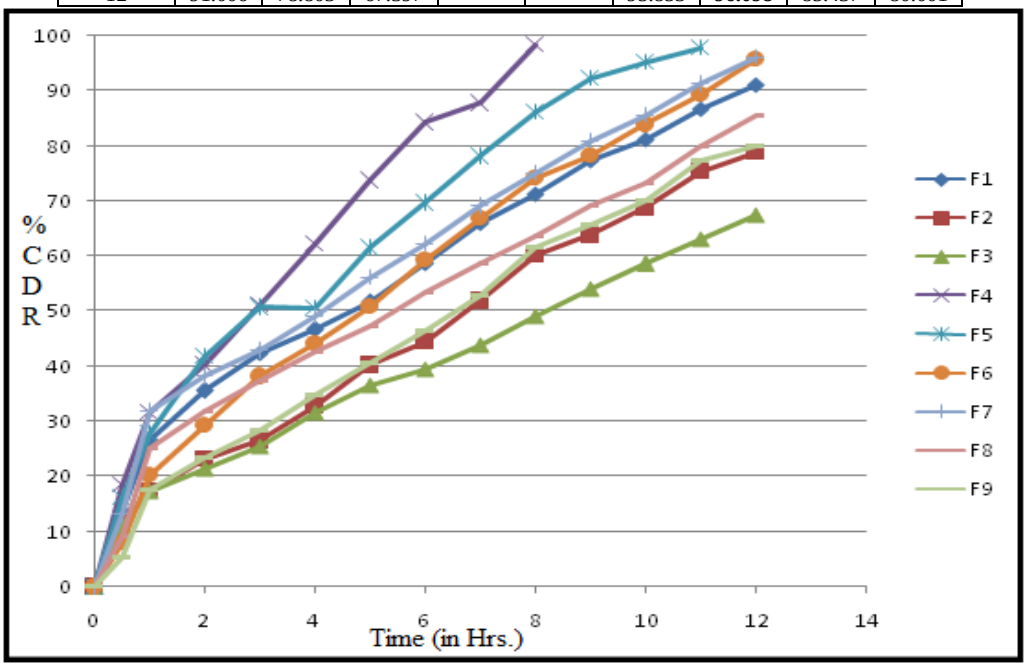
Percentage Buoyancy:

Formulation No.	% Buoyancy
F_1	83.34
F_2	84.53
F_3	79.92
F_4	74.46
F_5	71.67
F_6	73.13
F_7	78.68
F_8	82.45
F_9	83.68

The % buoyancy of the prepared floating microspheres was found 71.67 to 84.53. The % buoyancy of prepared floating microspheres of Ethyl cellulose was less as compared to Eudragit RS100 polymer as well as HPMC K4M.

In-vitro Drug Release Study and Release Kinetics: The in vitro drug release of Prazosin Hydrochloride form different formulation (F_1 to F_9) was performed in the USP dissolution apparatus type I at 37±0.5^{0}C and following data were obtained.

Time (hr)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
0	0	0	0	0	0	0	**0**	0	0
0.5	13.843	11.306	11.065	18.546	16.185	7.981	**13.130**	8.991	5.296
1	26.568	17.229	17.358	31.575	27.618	20.165	**31.795**	25.263	17.428
2	35.520	23.047	21.306	40.250	41.743	29.212	**38.138**	31.820	23.498
3	42.383	26.471	25.488	51.093	50.714	38.188	**42.876**	37.431	28.342
4	46.626	32.847	31.647	62.225	50.521	44.102	**49.029**	42.701	34.776
5	51.575	40.176	36.524	73.789	61.521	50.853	**56.112**	47.195	40.679
6	58.653	44.516	39.409	84.267	69.646	59.400	**62.261**	53.489	46.402
7	65.954	51.879	43.855	87.787	78.138	66.835	**69.044**	58.744	52.933
8	71.182	60.087	49.093	98.429	86.082	74.144	**75.058**	63.766	61.610
9	77.401	63.784	54.062	--	92.235	78.249	**80.927**	69.315	65.685
10	81.272	68.749	58.530	--	95.216	83.904	**85.474**	73.198	69.948
11	86.746	75.361	63.095	--	97.720	89.282	**91.202**	80.082	77.335
12	91.006	78.803	67.397	--	---	95.853	**96.098**	85.437	80.001



Comparative release profile of formulation F_1-F_9

Formulations F_1, F_2, and F_3 containing drug and Eudragit RS100 prepared at a drug-polymer ratio of 1:1, 1:2 and 1:3 and % cumulative drug released 91.01%, 78.80% and 67.40% of Prazosin Hydrochloride in 12 hrs respectively. Formulations F_4, F_5, and F_6 containing drug and Ethyl cellulose prepared at a drug-polymer ratio of 1:1, 1:2 and 1:3 and % cumulative drug released 98.43%, 97.72% and 95.85% of Prazosin Hydrochloride in 8, 11, 12 hrs respectively. % cumulative drug release of formulation F_4, F_5, and F_6 was found more than 90% at 12 hr. Formulations F_7, F_8, and F_9 containing drug and Eudragit RS100 plus HPMC K4M prepared at a drug-polymer ratio of 1:1, 1:2 and 1:3. The % cumulative drug release of formulation F_7, F_8 and F_9 at 12 hr was found 96.10%, 85.44% and 80.00%. %cumulative drug release of formulation F7 was found 96.10% at 12 hr

Formulation coded by F_7 was fulfilled the criteria for optimized formulation and released for 12 hrs. So, F_7 was considered as the optimized formulation.

In-vitro drug release study indicated that release of Prazosin Hydrochloride depends on the concentration of polymer. Increase in the amount of polymer showed decrease in drug release.

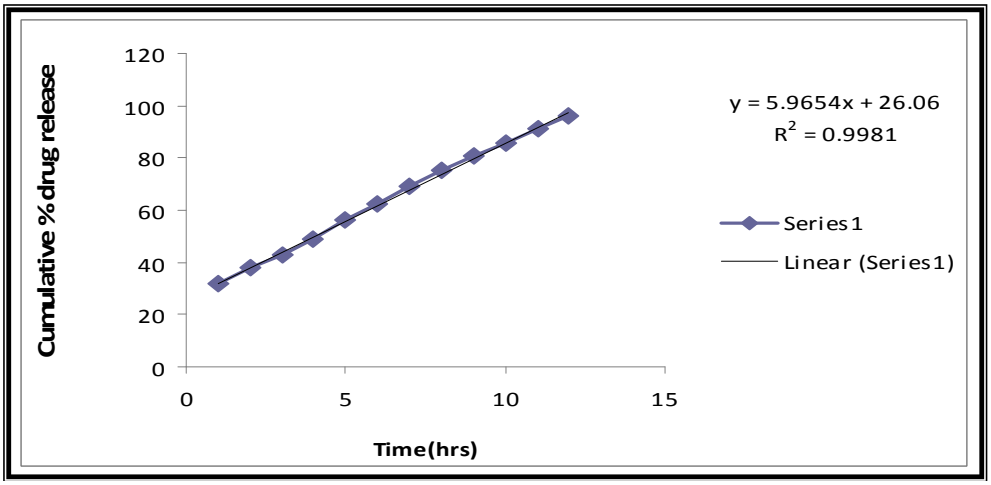
Kinetics modeling of drug dissolution profile: The *in-vitro* release data obtained were fitted in to various kinetic equations. Correlation coefficients of individual batch with applied equation. All batches showed higher correlation

with Higuchi plot & zero order than first order so predominant drug release pattern follow zero order with mechanism is Diffusion controlled release.

Formulation	R^2						
	Zero order	First order	Higuchi model	Hixon-crowell model	Korsmeyer-peppas model	n	Release mechanism
F_1	0.9952	0.9512	0.9867	0.9841	0.9861	0.5085	Diffusion controlled
F_2	0.9962	0.9720	0.9727	0.9861	0.9721	0.6496	Diffusion controlled
F_3	0.9988	0.9834	0.9751	0.9915	0.9733	0.5731	Diffusion controlled
F_4	0.9795	0.9040	0.9908	0.9781	0.9859	0.5565	Diffusion controlled
F_5	0.9658	0.9482	0.9947	0.9922	0.9969	0.5657	Diffusion controlled
F_6	0.9933	0.9627	0.9915	0.9682	0.9965	0.642	Diffusion controlled
F_7	**0.9981**	**0.8910**	**0.9802**	**0.9604**	**0.9673**	**0.4731**	**Diffusion controlled**
F_8	0.9991	0.9491	0.9791	0.9781	0.9777	0.5019	Diffusion controlled
F_9	0.9965	0.9715	0.9766	0.9866	0.9810	0.6475	Diffusion controlled

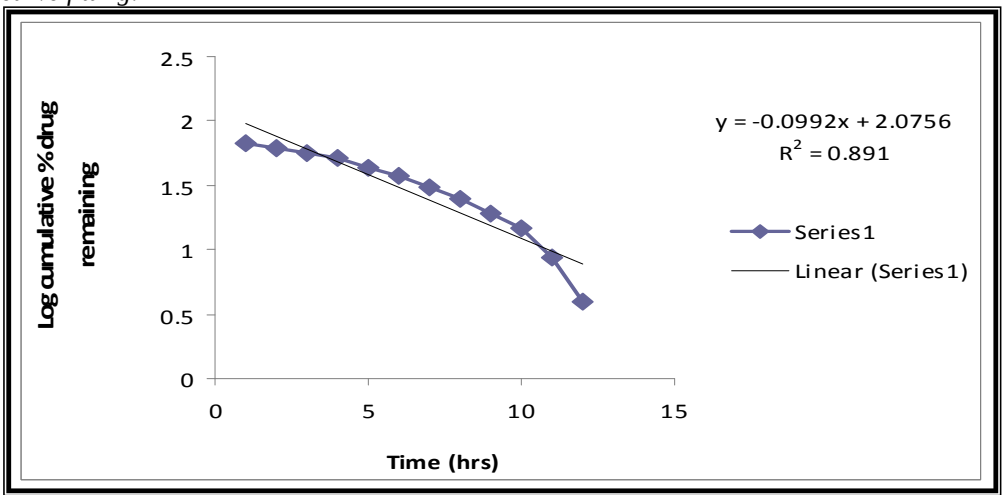
Kinetic plots of optimized formulation (F_7)

Zero order curve fitting:



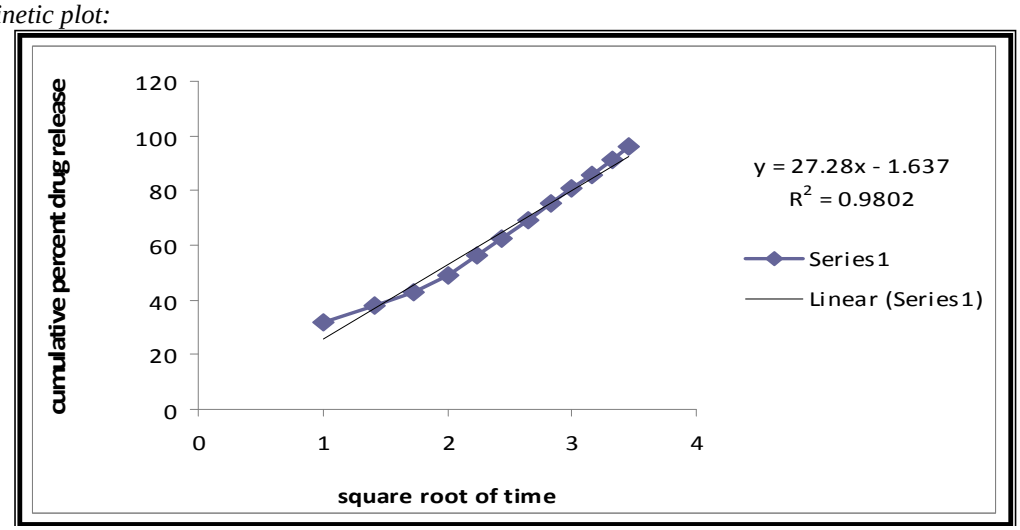
Zero order plot of Formulation F_7

First order curve fitting:



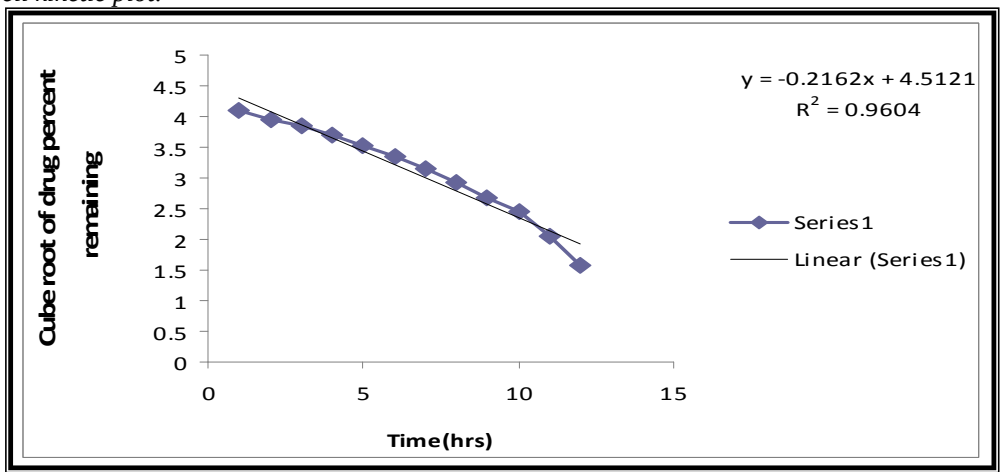
First order plot of Formulation F_7

Higuchi kinetic plot:



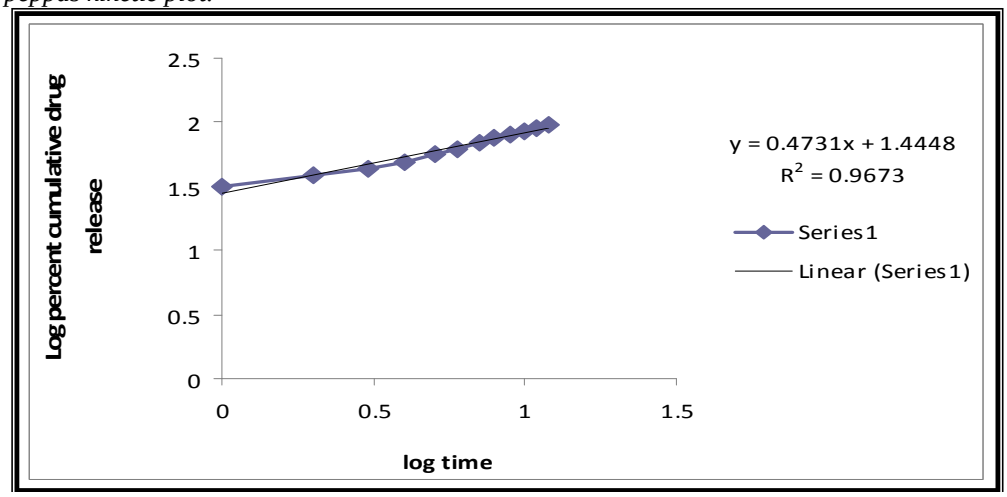
Higuchi plot of formulation F_7

Hixon crowell kinetic plot:



Hixon crowell plot of formulation F_7

Korsmeyer peppas kinetic plot:



Korsmeyer-peppas plot of formulation F_7

Stability Studies: It was done only for those selected formulations F_7 as per procedure given in material and method section. The results illustrated in tables.

Storage conditions: $40^0C \pm 2^0C$ / 75 % RH±5 % & Room temperature $25^0C \pm 2^0C$ /65% RH±5.

Parameter	$40^0C \pm 2^0C$ / 75 % RH ± 5 %		Room Temperature $25^0C \pm 2^0C$ /65% RH±5.	
	At 0 days	At 90 days	At 0 days	At 90 days
Drug Loading (%)	38%	37%	38%	37%
Entrapment Efficiency (%)	93%	91%	93%	93%
% Buoyancy	78%	76%	78%	78%

Formulation F_7	$40^0C \pm 2^0C$ / 75 % RH ± 5 %		Room Temperature $25^0C \pm 2^0C$ /65% RH±5.	
	At 0 days	At 90 days	At 0 days	At 90 days
1st hr	31.80	28.94	31.80	32.35
3rd hr	42.88	39.63	42.88	41.91
6th hr	62.26	61.45	62.26	62.49
9th hr	80.93	73.92	80.93	78.27
12th hr	96.10	94.82	96.10	95.79

Stability studies was performed after 3 months by keeping the formulations in stability chamber at $40^0C \pm 2^0C$ /75%RH±5 and $25^0C \pm 2^0C$ /65% RH±5. Stability study data revealed that there was no significant change in appearance and change in % drug content and in-vitro release. The optimized formulation F_7 was stable at 40^0C± /75% RH±5 and $25^0C \pm 2^0C$ /65% RH±5.

CONCLUSION

In-vitro data obtained for floating microspheres of Prazosin HCl prepared by solvent evaporation diffusion method showed excellent floatability, good buoyancy and prolonged drug release. Microspheres of different size and drug content could be obtained by varying the formulation variables. Diffusion was found the main release mechanism. Thus, the prepared floating microspheres may prove to be potential candidates for multiple-unit delivery devices adaptable to any intragastric condition.

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