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Research Article

DESIGN AND EVALUATION OF FLOATING MICROSPHERES OF RABEPRAZOLE SODIUM

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ABSTRACT

In recent years oral dosage form for gastric retention(floating drug delivery systems) have drawn more and more attention for their theoretical advantage in permitting control over time and site of drug release. The aim of the present study was to develop floating microspheres of Rabeprazole sodium(RPS), which belong to class of proton pump inhibitor. Floating microspheres of Rabeprazole were prepared by emulsion solvent evaporation method using HPMC K15M and ethyl cellulose as polymer. Six different formulations were developed. The floating microsphere was evaluated for angle of repose, particle size, percentage yield, in vitro buoyancy, incorporation efficiency, drug polymer compatibility (IR study), scanning electron microscopy, drug release and DSC(Differential Scanning colorimetry), X-Ray Diffraction(XRD) of microsphere. Results show that as the concentration of polymer increases it affects the particle size, percentage yield, in vitro buoyancy and drug release of microsphere. Formulations prepared with HPMC K15M exhibited excellent Micromeritic properties, percentage yield, in vitro buoyancy, incorporation efficiency and percentage drug release when compared to ethyl cellulose polymer. Results of our present study suggest that floating microsphere of Rabeprazole sodium can be successfully designed to develop controlled drug delivery which can reduce dosing frequency thus this formulation can be considered as an alternative to conventional dosage forms.

Keywords: Floating drug delivery systems, Rabeprazole sodium (RPS), Incorporation efficiency, Dosing frequency, Micrometric properties, DSC (Differential Scanning colorimetry) X-Ray Diffraction (XRD).

INTRODUCTION

The real challenge in the development of controlled drug delivery system is not just to sustain the drug release but also to prolong the release of drug over an extended period of time. The oral route is considered as the most promising route of drug delivery.Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day. This results in a significant fluctuation in drug levels. Recently, several technical advancements have led to the development of several novel drug delivery systems (NDDS) that could revolutionize method of medication and provide a number of therapeutic benefits. The most important objectives of these new drug delivery systems are: First, it would be single dose, which releases the active ingredient over an extended period of time. Second, it should deliver the active entity directly to the site of action, thus, minimizing or eliminating side effects[1]. To overcome the limitations of conventional drug delivery system, floating drug delivery systems have been developed. Drugs that have narrow absorption window in the gastrointestinal tract (GIT) will have poor absorption. For these drugs, gastroretentive drug delivery systems offer the advantages in prolonging the gastric emptying time.

Floating drug delivery systems are among the several approaches that have been developed in order to increase the gastric residence time of the dosage frms[2,3,4] .The floating drug delivery systems have been extensively used to improve therapy with several drugs. However during development process several difficulties are faced such as inability to restrain and localize the system within desired region of the GIT and its variable as per gastric emptying process. The variability may cause unpredictable bioavailability and time to achieve peak plasma levels. On the other hand, incorporation of the drug in a controlled release gastroretentive dosage forms (CR-GRDF) which can remain in the gastric region for several hr would significantly prolong the gastric residence time of drugs and improve bioavailability, reduce drug waste, and enhance the solubility of drugs that are less soluble in high pH environment [5]. This FDDS provides local delivery of drug in the form of microspheres to specific region like stomach and also shows better bioavailability and improved therapeutic activity and substantial benefits to patients.

Floating microspheres are gastro- retentive drug delivery systems based on non- effervescent approach. Hollow microspheres are in strict sense, spherical empty particles without core. These microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, ideally having a size range less than 200 micrometer. Gastroretentive floating microspheres are low density systems that have sufficient buoyancy to float over a gastric content and remain buoyant for prolonged period of time. The drug is released slowly at a desired rate resulting in increased gastric retention with reduced fluctuations in plasma drug concentration. Floating microspheres to improve patient compliance by decreasing dosing frequency, better therapeutic effect of short half –life drugs can be achieved [6].

The present study involves formulation and in-vitro evaluation of floating microspheres of Rabeprazole Sodium under gastro retentive drug delivery system for improving bioavailability by prolonging gastric retention time. In the present work Rabeprazole sodium was chosen as the drug to be incorporated into the individual polymer like HPMC K15 M and EC. Rabeprazole sodium is a drug prescribed to treat disorders caused by excess stomach acid. Available as the brand AcipHex. Rabeprazole is a proton pump inhibitor similar to Prevacid and Prilosec. PPIs block an enzyme in the stomach from producing acid, significantly reducing gastric acid levels and allowing acid-related disorders to heal, as well as alleviating symptoms of chronic conditions drug that has been widely used in treating gastric and duodenal ulceration and also in Zollinger Ellison syndrome and reflux esophagitis [7]. It is poorly absorbed from the lower GIT and has a short elimination half-life (2 h). The Rabeprazole has an oral bioavailability of approximately 52% [8]. Rabeprazole is less susceptible to the influence of genetic polymorphisms for CYP2C19, resulting in minor influence on its pharmacokinetics and pharmacodynamics [9, 10].

MATERIALS AND METHODS

Rabeprazole sodium was obtained from Reddies lab Hyderabad. India as gift sample, HPMC K15 was provided by Shreeji chemicals, Mumbai. Ethyl cellulose was purchased from Rolex chemicals, Mumbai. Ethanol was obtained from S D fine chemical Ltd, Mumbai, Span 80, dichloromethane also obtained from S D fine chemical Ltd, Mumbai. All other ingredients were of analytical grade.

Selection of vehicle

The solubility of Rabeprazole sodium was checked in various solvents like water and methanol, ethanol, chloroform and ethyl acetate, ether and n-hexane. Studies revealed that Rabeprazole sodium was Rabeprazole sodium was found to be very soluble in water and methanol, freely soluble in ethanol, chloroform and ethyl

acetate and insoluble in ether and n-hexane [7]. The solubility was confirmed by analysing the sample by quantitative determination by UV spectroscopy. Wavelength scan was done from 400-200 nm and maximum absorbance was found at 275.43nm.

Drug polymer interaction (FTIR) study [11]

FTIR spectroscopy was performed on Fourier transformed infrared spectrophotometer (IR-Affinity-1, Shimadzu, Japan). The pellets of drug and potassium bromide were prepared by compressing the powders at 20 psi for 10 min on KBr-press and the spectra were scanned in the wave number range of 4000- 600 cm^{-1}. FTIR study was carried on RPS, physical mixture of RPS and polymers.

Preparation of Rabeprazole sodium floating microspheres [12, 13, 14, 15]

Method used**:** Emulsification – solvent evaporation method

Floating microspheres were prepared by solvent evaporation technique accurately weighed drug and individual polymer like HPMC K15 M and EC were dissolved in ethanol and dichloromethane (1:1) to form a homogenous polymer solution. This solution is poured in 100 ml light liquid paraffin containing 0.01% span 80 maintained at 30-40^{0}C subsequently stirred at ranging agitation speed for 30 min to allow the volatile liquid to evaporate. The microspheres formed were filtered, washed with petroleum ether and dried in vacuum. The microspheres were then stored in a desiccator over fused calcium chloride.

Formulation Design

Formulation design for Rabeprazole Sodium floating microspheres using different ratios of drug and polymers. (**1, 2 & 3** HPMC K15M & **4, 5&6** Ethyl Cellulose) shown in table1.

Table 1: Formulation design of RPS floating microspheres

S. No.	Batch code	Drug: Polymer	Organic solvent system(1:1)
1	RPS-1	1:1	Dichloromethane: Ethanol
2	RPS-2	1:2	Dichloromethane: Ethanol
3	RPS-3	1:3	Dichloromethane: Ethanol
4	RPS-4	1:1	Dichloromethane: Ethanol
5	RPS-5	1:2	Dichloromethane: Ethanol
6	RPS-6	1:3	Dichloromethane: Ethanol

Evaluation of Rabeprazole Sodium Floating Microspheres

Drug polymer interaction (FTIR) study

FTIR spectroscopy was performed on Fourier transformed infrared spectrophotometer (IR-Affinity-1, Shimadzu, Japan). The spectra were scanned in the wave number range of 4000- 600 cm^{-1}. FTIR study was carried on RPS loaded microspheres.

Micromeritic properties

Angle of repose

Angle of repose of different formulations was measured according to fixed funnel standing method (n = 3) θ = tan-1h / r where θ is the angle of repose, r is the radius, and h is the height

Scanning electron microscopy (S.E.M)

Scanning electron microscopy has been used to determine particle size distribution, surface topography, texture, and to examine the morphology of fractured or sectioned surface. SEM is probably the most commonly used method for characterizing drug delivery systems, owing in large to simplicity of sample preparation and ease of operation. SEM studies were carried out by using JEOL JSM T-330A scanning microscope (Japan). Dry RPS floating microspheres were placed on an electron microscope brass stub and coated with in an ion sputter. Picture of RPS floating microspheres were taken by random scanning of the stub.

Particle size analysis

Determination of average particle size of RPS floating microspheres was carried out by optical microscopy in which stage micrometer was employed. A minute quantity of RPS floating microspheres was spread on a clean glass slide and average size of 300 RPS floating microspheres was determined in each batch.

Percentage yield

The percentage yield of prepared RPS floating microspheres was determined by using the formula.

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Buoyancy percentage

Fifty milligrams of the floating microspheres were placed in 0.1M HCL, 100 ml containing 0.02 w/v%span 80. The mixture was stirred at 100 rpm in a magnetic stirrer. After 12 hrs, the layer of buoyant microspheres was pipette and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both types were dried in a desiccators until constant weight.

$$\text{Buoyancy}(\%) = \frac{Wf}{Wf + Ws} \times 100$$

Where, Wf and Ws are the weights of the floating and settled microspheres, respectively.

Determination of percentage drug entrapment (PDE) [16, 17]

Efficiency of drug entrapment for each batch was calculated in terms of percentage drug entrapment as per the following formula.

$$\text{PDE} = \frac{\text{Practical drug loading}}{\text{theoretical drug loading}} \times 100$$

Preparation of standard calibration curve of Rabeprazole sodium in 0.1M HCL

Scanning of Rabeprazole sodium by UV-spectrophotometer in 0.1M HCL

I Stock: 100 mg of RPS was accurately weighted into 100 ml volumetric flask, dissolved in 0.1M HCL and volume was made up with 0.1M HCL. II Stock: Pipette 1ml of above solution into another 10 ml volumetric flask and the volume was made with 0.1M HCL.

Procedure for calibration of Rabeprazole sodium in 0.1M HCL at λ_{max} 275.43nm

From the RPS standard stock solution (1000µg/ml), 1ml solution was diluted to 10 ml using 0.1M HCL solution to get concentrations of 100 µg/ml. from this solution, aliquots of, 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, 2.5 ml, 3.0 ml from standard drug solution were diluted to 10 ml with 0.1M. The absorbance of these solutions was measured at 275.43nm 0.1M HCL as a blank.

- **Theoretical drug content**

Theoretical drug content was determined by calculation assuming that the entire RPS present in the polymer solution used gets entrapped in RPS floating microspheres, and no loss occurs at any stage of preparation of RPS floating microspheres

- **Practical drug content**

Procedure: Practical drug content was analyzed by using the following procedure, weighed amount of RPS floating microspheres

equivalent to eight mg of RPS floating microspheres was dissolved in 100 ml of 0.1 M HCL. This solution was kept overnight for the complete dissolution of the RPS floating microsphere in 0.1M HCL. This solution was filtered and further diluted to make a concentration of 10 µg/ml solution. The absorbance of the solutions was measured at 275.43nm using double beam UV-Visible spectrophotometer against 0.1M HCL solution as blank and calculated for the percentage of drug present in the sample.

***In Vitro* dissolution studies**

Calibration curve of Rabeprazole sodium in 0.1M HCL

The procedure for the calibration of Rabeprazole sodium is same as mentioned under determination of percentage drug entrapment.

Procedure for In vitro dissolution study

The release rate of RPS floating microspheres was determined by employing USP XXIII apparatus by rotating basket method. The dissolution test was performed using 900 ml 0.1M HCL, in 37 ± 0.5°C at 50 rpm. RPS floating microspheres equivalent to 20 mg were placed in a basket to avoid floating of microspheres. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 12 hrs, and the samples were replaced with fresh dissolution medium. The samples were passed through Whatman filter paper and the absorbance of these solutions was measured at 275.43nm. Dissolution profiles of the formulations were analyzed by plotting drug release versus time plot. Data obtained was also subjected to kinetic treatment to understand release mechanism.

Kinetics of drug release

To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order (Q v/s t), first order [Log(Q_0-Q) v/s t], Higuchi's square root of time (Q v/s $t^{1/2}$) and Korsemeyer Peppas double log plot (log Q v/s log t) respectively, where Q is the cumulative percentage of drug released at time t and (Q_0-Q) is the cumulative percentage of drug remaining after time t.

In short, the results obtained from *in vitro* release studies were plotted in four kinetics models of data treatment as follows.

- Cumulative percentage drug release Vs. Time (zero order rate kinetics)
- Log cumulative percentage drug retained Vs. Time (first order rate kinetics)
- Cumulative percentage drug release Vs. √T (Higuchi's classical diffusion equation)
- Log of cumulative percentage drug release Vs. log Time(Peppas exponential equation)

Differential Scanning Calorimetery (DSC)

The physical state of drug in the RPS floating microspheres was analyzed by DSC. The thermograms of RPS, RPS floating microspheres with different polymers were obtained at a scanning rate of 10°C/min conducted over a temperature range of 25–350ºC, respectively.

X-Ray power Diffractometry (XRD) study [18]

X-ray diffractometry of the RPS and RPS microspheres were performed by a diffractometer using model (Joel JDX-8030, Japan) equipped with a graphite crystal monochromator (Cu-Kα) radiations to observe the physical state of RPS in the microspheres

RESULTS AND DISCUSSION

Drug polymer interaction (FTIR) study

From the spectra of RPS, physical mixture of RPS and individual polymer, RPS loaded microspheres it was observed that all characteristic peaks of RPS were present in the combination spectrum, thus indicating compatibility of the RPS and polymer IR Spectra shown in Figure 1 to 5.

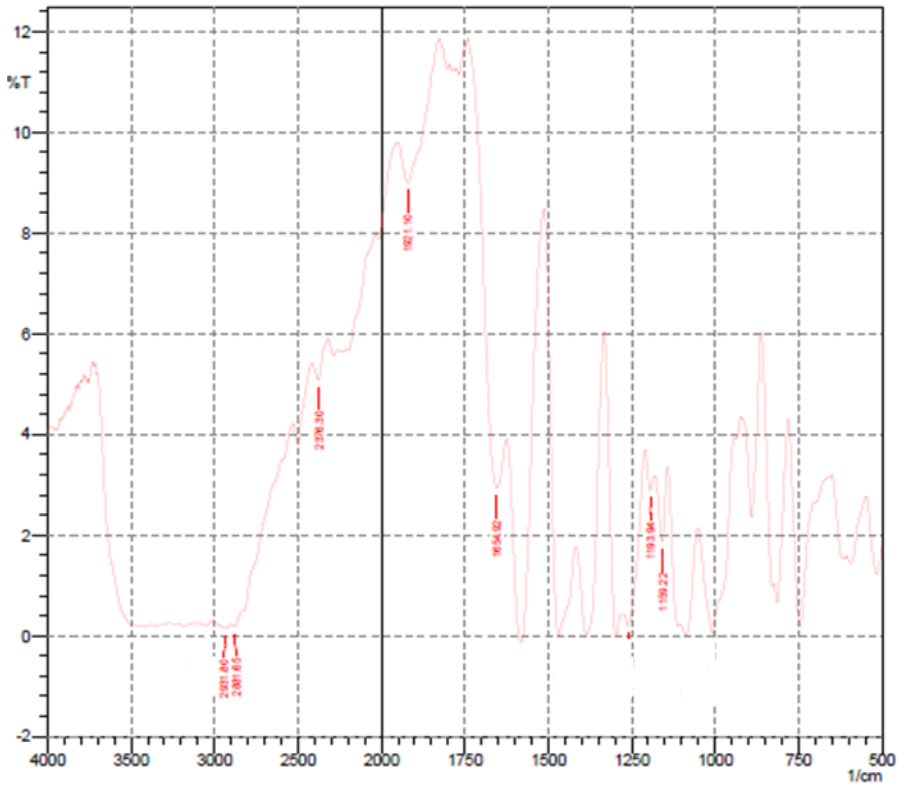

Fig. 1: IR spectra of RPS

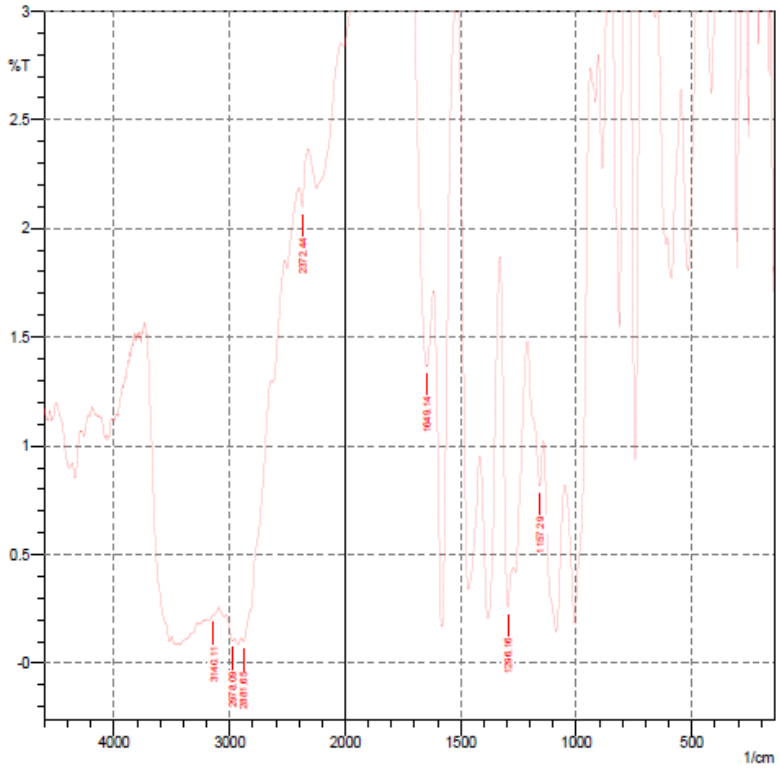

Fig. 2: IR spectra of physical mixture of Rabeprazole sodium and hpmc K15 M

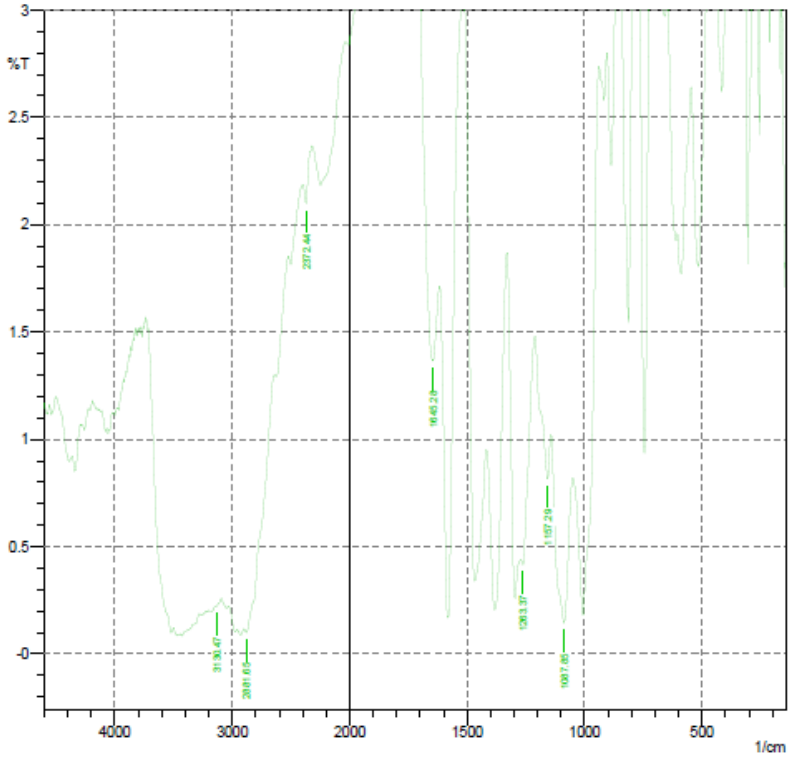

Fig. 3: IR spectra of physical mixture of Rabeprazole sodium and ethyl cellulose

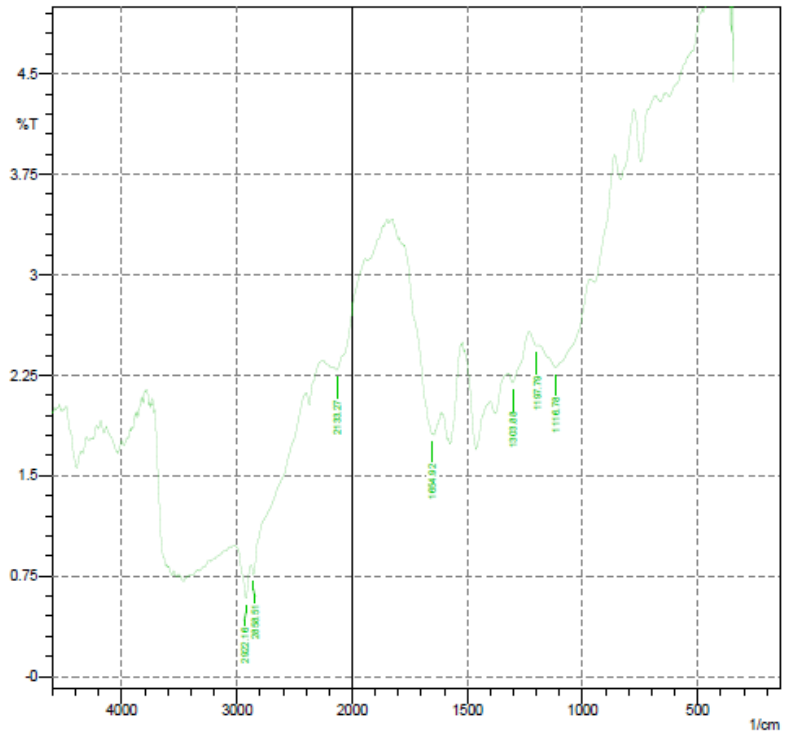

Fig. 4: IR spectra of formulation of drug with HPMC K15 M

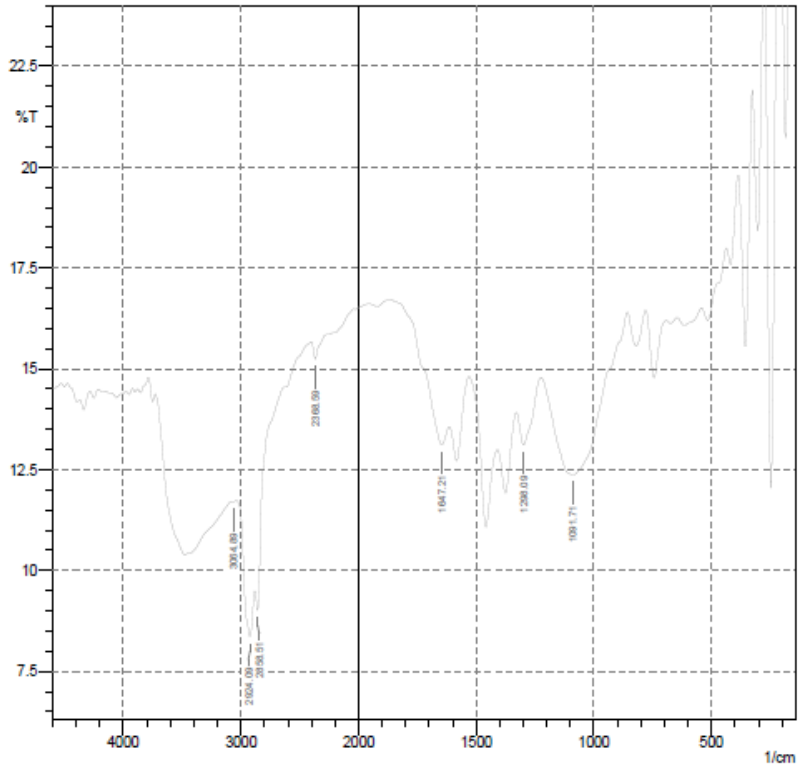

Fig. 5: IR spectra of formulation of drug with ethyl cellulose

Angle of repose

The formulations with HPMC K15 M and EC show angle of repose value in the range of $21^0.17'$to $29^0.23'$ given in Table5.3 i.e., less than 30 ,which shows good flow properties of the formed microparticles which was given in table 2.

Surface morphology of Rabeprazole Sodium microspheres (SEM)

The surface morphology of the RPS floating microspheres was studied by SEM. SEM photographs of the various formulations were shown in the Figure 6. Surface smoothness of the RPS floating microspheres was increased by increasing the polymer conc., which was confirmed by SEM.

At lower polymer conc. (1:1) rough and wrinkled surface of RPS floating microspheres was obtained. Fig6 and at higher polymer concentration (1:3) the RPS floating microspheres with smooth surface was obtained Fig6. Microspheres with HPMC K15M contain smooth surface and smaller in size compare to the microspheres with ethyl cellulose.

Table 2: Angle of repose

S. No.	Pure drug	RPS1	RPS2	RPS3	RPS4	RPS5	RPS6
Angle of repose	$33^0.39'$	$25^0.42'$	$23^0.26'$	$21^0.17'$	$29^0.23'$	$27^0.45'$	$24^0.13'$

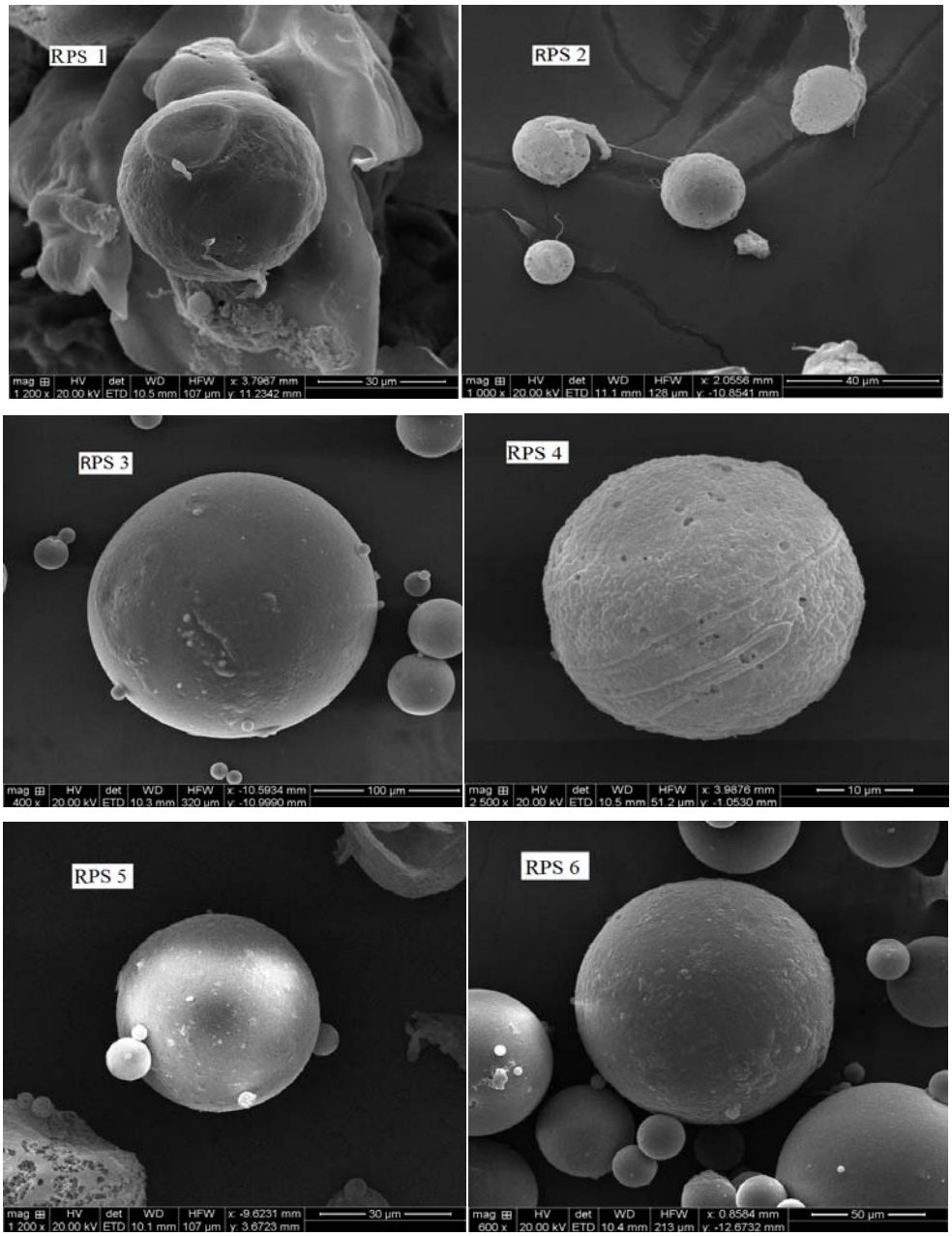

Fig. 6: SEM photographs of RPS floating microspheres

RPS1, RPS2, RPS3, RPS4, RPS5 and RPS6 refers to RPS floating microspheres prepared by using HPMC K15 M and EC with drug: polymer ratio 1:1, 1:2, 1:3, 1:4, 1:5 and 1:6.(HPMC K 15M 1,2,3& ethyl cellulose 4,5,6)

Determination of Average particle size

As the RPS to polymer ratio was increased, the mean particle size of RPS floating microspheres was also increased Table 3. The significant increase may be because of the increase in the viscosity of the droplets (may be due to the increase in concentration of polymer solution). RPS floating microspheres with HPMC K15M having a size range less when compared to that of ethyl cellulose which was shown in table 3.

Table 3: Average diameter of Rabeprazole Sodium floating microspheres

S. No.	Formulation code	Average size (µm)
1	RPS1	73.32
2	RPS2	74.41
3	RPS3	78.52
4	RPS4	86.26
5	RPS5	90.83
6	RPS6	93.57

Buyounancy percentage

The microspheres floated for prolonged time over the surface of the dissolution medium without any apparent gelation. As the polymer concentration increases the buoyancy time increases. The results obtain are given in table 4.

Table 4: Buyounancy percentage of Rabeprazole Sodium floating microspheres

S. No.	Formulation code	% Buoyancy time
1	RPS1	78.40 ± 1.02
2	RPS2	83.45 ± 1.8
3	RPS3	91.15 ± 1.01
4	RPS4	67.30 ± 1.01
5	RPS5	74.32 ± 1.69
6	RPS6	79.300 ± 1.60

Percentage drug entrapment efficiency

Entrapment efficiency increases with increase in the polymer concentration. From the results it can be inferred that there is a proper distribution of RPS in the microspheres and the deviation is within the acceptable limits. A maximum of 89.60% drug entrapment efficiency was obtained in the RPS floating microspheres which were prepared by using HPMC K15 M. A maximum of 83.22% drug entrapment efficiency was obtained in the RPS floating microspheres which were prepared by using Ethyl cellulose. It was further observed that the drug entrapment was proportional to the RPS: polymer ratio and size of the RPS floating microspheres. By increasing the polymer concentration, the encapsulation efficiency was increased. Results shown in table 5

Table 5: Drug entrapment efficiency of Rabeprazole Sodium floating Microspheres

Formulation Code	Percentage yield	Drug content (%)	Entrapment efficiency (%)
RPS1	85.02	18.65	70.80±1.10
RPS2	89.67	15.95	78.88±0.98
RPS3	93.88	13.57	89.60±1.12
RPS4	70.00	32.29	53.74±1.02
RPS5	77.01	29.96	66.12±1.11
RPS6	82.33	25.44	83.22±2.25

***In Vitro* dissolution studies**

The *in vitro* performance of RPS floating microspheres showed prolonged and controlled release of RPS. The results of the *in vitro* dissolution studies shows controlled and predictable manner as the polymer concentration increases the drug release from the floating microsphere decreases. The formulations with HPMC K15M i.e.RPS1 95.25% to RPS3 78.35% are shown in Table 6and Figure 7. The formulations with Ethyl cellulose i.e.RPS4 86.48% to RPS6 64.35% are shown in Table 7 and Figure 8.

Table 6: *In vitro* release data of Rabeprazole Sodium floating microspheres with HPMC K15M

S. No.	Time (h)	% Cum. drug release		
		RPS1 ± SD	RPS2 ± SD	RPS3 ± SD
1	0	0	0	0
2	1	17.38± 0.32	13.47± 0.10	12.35± 0.13
3	2	25.47± 0.22	17.52± 0.16	18.37± 0.20
4	3	32.49± 0.12	28.31± 0.11	24.31± 0.10
5	4	39.43± 0.16	32.36± 0.29	30.31± 0.04
6	5	46.55± 0.13	41.81± 0.23	36.34± 0.26
7	6	55.32± 0.16	51.27± 0.24	42.33± 0.41
8	7	64.92± 0.33	56.68± 0.22	48.37± 0.16
9	8	76.13± 0.26	70.1± 0.12	54.36± 0.07
10	9	87.77± 0.14	75.62± 0.21	60.37± 0.16
11	10	92.26± 0.24	83.74± 0.27	66.39± 0.16
12	11	93.07± 0.42	85.95± 0.18	72.39± 0.36
13	12	95.25± 0.37	88.98± 0.26	78.35±0.43

SD=Standard deviation (n=3)

Table 7: *In vitro* release data of Rabeprazole Sodium floating microspheres with Ethyl Cellulose

S. No.	Time (h)	% Cum. drug release		
		RPS4 ± SD	RPS5 ± SD	RPS6 ± SD
1	0	0	0	0
2	1	21.44±0.60	10.52 ± 0.64	7.64 ± 0.50
3	2	28.60±0.49	15.63 ± 0.57	13.38 ± 0.54
4	3	33.50±0.69	21.50 ± 0.60	17.78 ± 0.60
5	4	38.69±0.68	27.37 ± 0.62	23.57 ± 0.68
6	5	45.60±0.67	32.56 ± 0.59	28.45 ± 0.60
7	6	53.68±0.60	38.40 ± 0.56	34.01 ± 0.58
8	7	60.46±0.67	43.68 ± 0.60	38.65 ± 0.60
9	8	67.54±0.58	49.43 ± 0.56	44.44 ± 0.69
10	9	75.63±0.68	54.62 ± 0.64	49.52 ± 0.73
11	10	80.43±0.56	60.49 ± 0.52	54.54 ± 0.66
12	11	84.45±0.59	66.33 ± 0.60	59.56 ± 0.56
13	12	86.48±0.53	71.55 ± 0.56	64.35 ± 0.66

SD=Standard deviation (n=3)

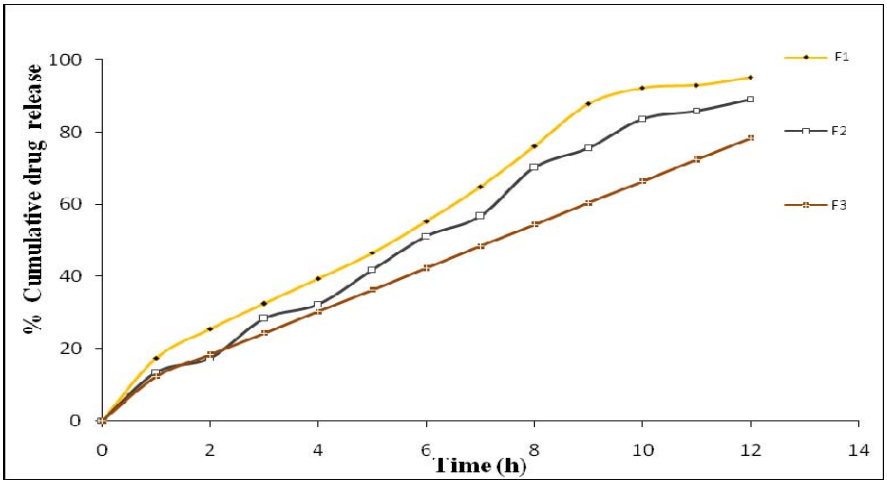

Fig. 7: Comparative *in vitro* release profile of RPS floating microspheres with HPMC K15M

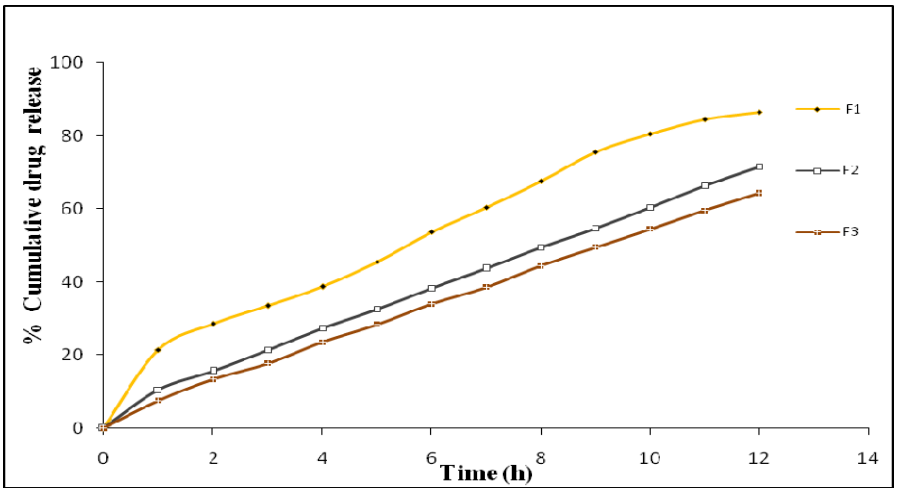

Fig. 8: Comparative *in vitro* release profile of RPS floating microspheres with Ethyl Cellulose

Kinetics of Drug Release

The slopes and the regression co-efficient of determinations (r^2) were listed in Table 8. The co-efficient of determination indicated that the release data was best fitted with zero order kinetics. Higuchi equation explains the diffusion controlled release mechanism. The diffusion exponent 'n' values of Korsemeyer-Peppas model was found to be in the range of 0.5 to 1 for the RPS floating microspheres prepared with HPMC K15 M and EC indicating Non-Fickian of drug through RPS floating microspheres.

Table 8: Pharmacokinetic release of Rabeprazole Sodium floating microspheres with HPMC K15M and EC

Formulation	Zero order	First order	Higuchi Matrix	Peppas plot	
				r^2 value	'n' value
RPS1	0.9795	0.9244	0.9473	0.9821	0.7420
RPS2	0.9884	0.9532	0.9376	0.9819	0.8361
RPS3	0.9959	0.9671	0.9764	0.9928	0.7628
RPS4	0.9747	0.9704	0.9721	0.9751	0.6046
RPS5	0.9971	0.9773	0.9454	0.9936	0.7942
RPS6	0.9988	0.9854	0.9378	0.9979	0.8682

DSC Thermograms

In order to confirm the physical state of RPS in the microspheres, DSC of the RPS, RPS loaded floating microspheres with individual polymers were carried out and shown in Fig 9 to 11. The DSC trace of RPS showed a sharp endothermic peak at 141.89°C, its melting point. RPS floating microspheres with HPMC K15M and EC showed the same thermal behavior 147.18°C and 147.32°C respectively indicating that there was no interaction between the RPS and the polymer in the solid state. The melting point range of RPS is between 140-142°C, thus indicating there is no change of RPS in pure state. The absence of endothermic peak of the RPS at 141°C in the DSC of the RPS floating microspheres suggests that the RPS existed in an amorphous or disordered crystalline phase as a molecular dispersion in polymeric matrix.

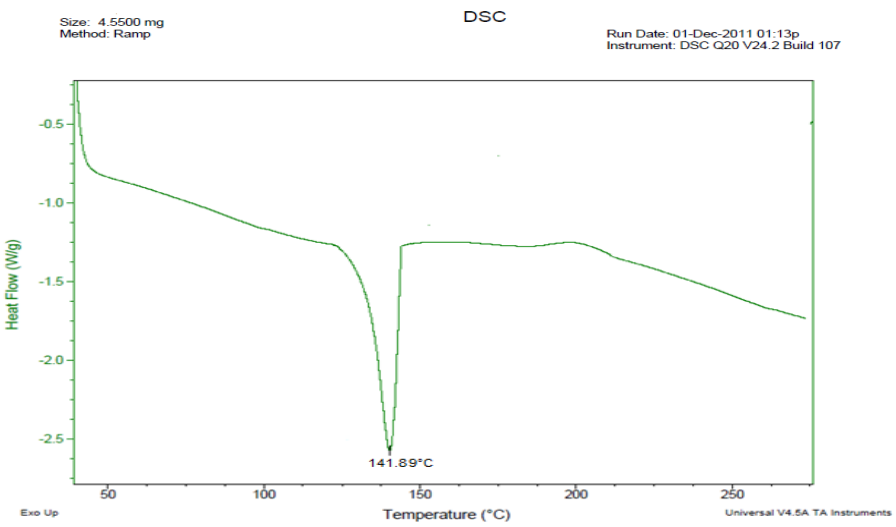

Fig. 9: DSC of pure drug rabeprazole sodium

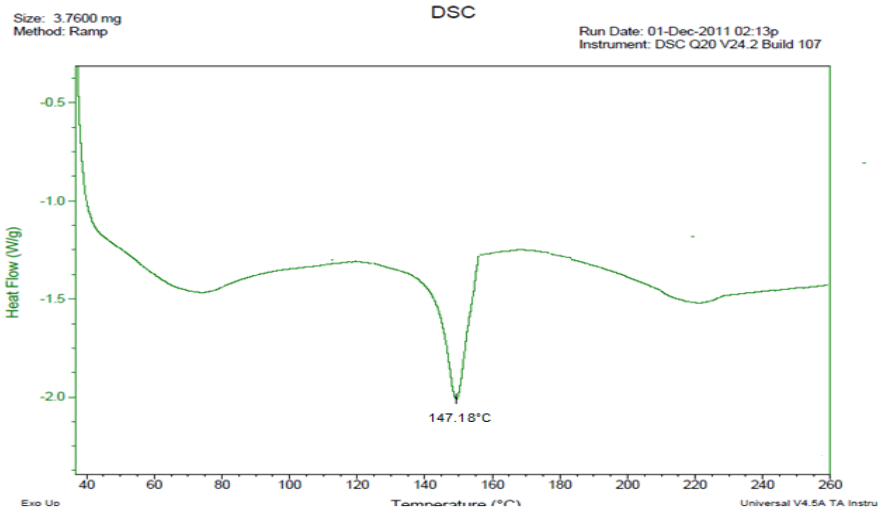

Fig. 10: DSC of Formulation with HPMC K15 M

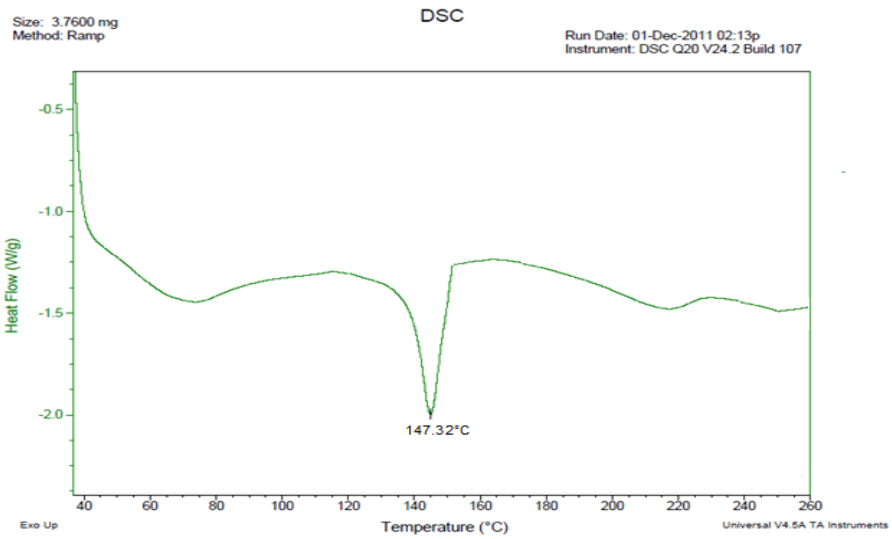

Fig. 11: DSC of formulation with ethyl cellulose

X-Ray Diffraction Thermograms

In order to confirm the physical state of the RPS in the microspheres, powder X-ray diffraction studies of the RPS, RPS microspheres with individual polymers were carried out. X-ray diffractograms were shown in Figure 12 to 14 and showed that the RPS is still present in its lattice structure where it is completely amorphous inside the RPS microspheres. This may be due to the conditions used to prepare the RPS microspheres lead to cause complete drug amorphization.

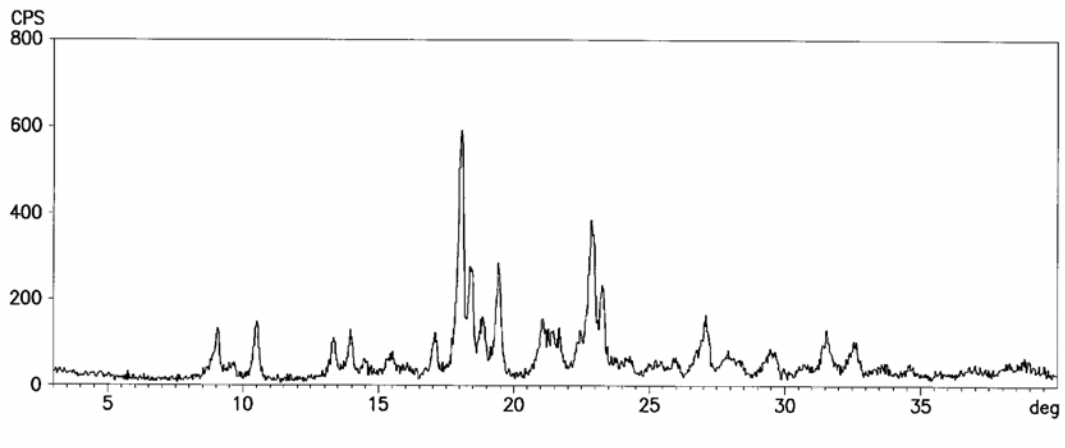

Fig. 12: XRD thermogram of RPS

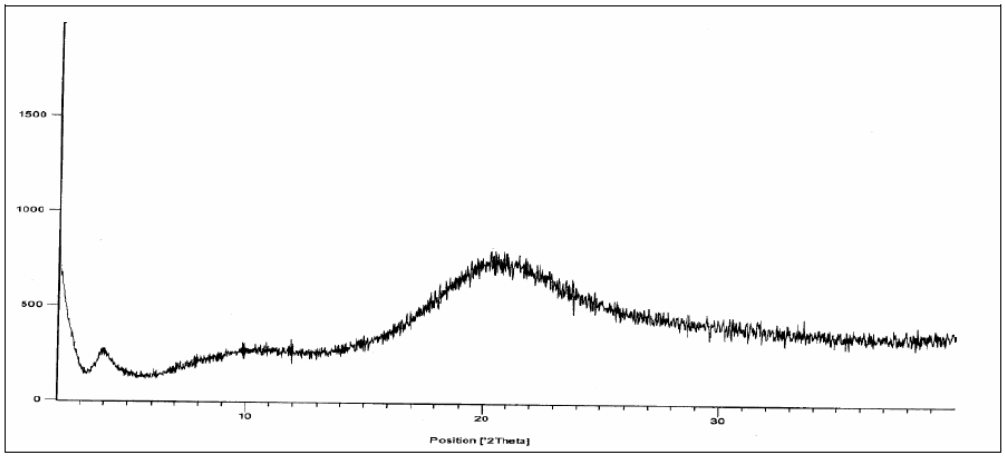

Fig.13: XRD thermogram of RPS formulation with HPMC K15 M

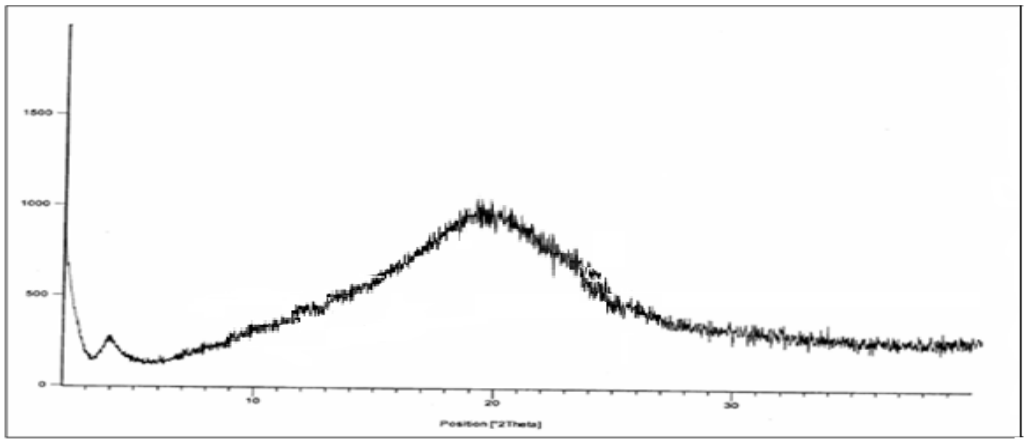

Fig. 14: XRD of formulation of RPS with EC

CONCLUSION

The concept of formulating floating microspheres containing RPS offers a suitable, practical approach to achieve a prolonged therapeutic effect by continuously releasing the medication over extended period of time. floating microspheres of RPS were prepared successfully by emulsion solvent evaporation method using the different concentration of individual polymers like HPMC K15 M, and EC by means of prolonging its gastric retention thus improving the oral bioavailability of the drug. It would be faster and more economical to alter beneficially the properties of the existing drugs than developing new drug entities hence this formulation will be boon to novel drug dosage forms.

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