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Research Article

Formulation and Evaluation of Floating Microspheres of Piroxicam.

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ABSTRACT

The present study involves formulation and evaluation of floating microspheres of Piroxicam for prolongation of gastric residence time. Floating microspheres of Piroxicam were prepared by ionotropic gelation method by using Sodium alginate, HPMC, Xanthan gum as polymers. The floating microspheres were evaluated for micrometric properties, percentage yield, *in vitro* buoyancy, incorporation efficiency, drug polymer compatibility, scanning electron microscopy and *in vitro* drug release. Results show that as the concentration of polymer increases it affects the particle size, percentage yield, incorporation efficiency, *in vitro* buoyancy and *in vitro* drug release of microspheres. The micromeritic properties were found to be good and scanning electron microscopy confirmed their hollow structure with smooth surface. Formulation F9 prepared with Sodium alginate and Xanthan gum which exhibited excellent micrometric properties, percentage yield, *in vitro* buoyancy, incorporation efficiency and percentage drug release 94.95% for a period of 12 hrs. The data obtained in this study thus suggest that floating microspheres of Piroxicam are promising for sustained drug delivery, which can reduce dosing frequency and increases bioavailability.

KEYWORDS

Piroxicam, Sodium alginate, Hydroxypropyl Methyl Cellulose, Xanthan gum, Floating microspheres.

1. INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agent for their systematic effect such as patient acceptance, convenience in administration and cost effective manufacturing process.[1] Thus wide varieties of approaches of drug delivery system have been investigated for oral application. However development process is precluded by several physiological difficulties, such as inability to restrain & localize drug delivery system within desired region of GIT tract and highly variable nature of gastric emptying process. For example relatively brief gastric emptying time can result in incomplete drug release from drug delivery devices leading to diminished efficacy of administered dose. [2] Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. [3]

Floating drug delivery system (FDDS) promises to be a potential approach for gastric retention. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion, modified shape systems, or by the simultaneous administration of pharmacological agents that delay gastric emptying. [3] Piroxicam is an important analgesic and nonsteroidal anti-inflammatory drug, also with antipyretic properties. Whose mechanism of action is the reversible inhibition of cyclooxygenase, causing the peripheral inhibition of prostaglandin synthesis? Piroxicam is used in therapy of rheumatic disorder.[4] The absorption of piroxicam takes place mainly through stomach.[5]

From the conventional dosage form, absorption of Piroxicam is less due to the low gastric residence time and hence bioavailability of Piroxicam is less. So the development of floating microsphere of Piroxicam may increases the residence of dosage form in stomach ensuring its complete absorption also decrease the gastric irritation and increase the patience compliance.

2. MATERIALS AND METHODS

Piroxicam (IP) was received as a gift sample from Apex Healthcare Limited, Gujarat, Sodium Alginate (LR), Xanthan Gum (LR), Calcium Chloride (LR), Hydrochloric Acid (AR), Hydroxyl Propyl Methyl Cellulose (K4M), Sodium Bicarbonate (LR) were received as a gift sample from Research Lab, Mumbai.

2.1. Preparation of Floating Microsphere of Piroxicam [6]

Sodium alginate and sodium bicarbonate were dissolved in purified water to form a homogeneous polymer solution. The active substance, Piroxicam, was added to the polymer solution and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added manually drop wise into calcium chloride (10% w/v) solution through a 21G syringe needle. The added droplets were retained in the calcium chloride solution for 15 min to complete the curing reaction and to produce microsphere. The microsphere were collected by filtration, washed with water and dried over night at room temperature. The compositions of the microspheres formulations are listed in Table 1.

Table 1: Preparation of floating microsphere.

Ingredients (mg)	Formulation Code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Piroxicam	500	500	500	500	500	500	500	500	500
Sodium alginate	500	1000	1500	250	500	750	250	500	750
HPMC	-	-	-	250	500	750	-	-	-
Xanthan gum	-	-	-	-	-	-	250	500	750
Sodium bicarbonate	500	500	500	500	500	500	500	500	500
Calcium chloride (% w/v)	10	10	10	10	10	10	10	10	10
Acetic acid (% v/v)	2	2	2	2	2	2	2	2	2
Drug: Polymer	1:1	1:2	1:3	1:1	1:2	1:3	1:1	1:2	1:3

2.2. Evaluation of Prepared Floating Microsphere of Piroxicam

2.2.1. Drug – polymer Compatibility Studies [7]

Compatibility studies were performed in order to confirm the drug – excipients compatibility. It mainly included Fourier-transform infrared (FT-IR) Spectroscopy Study.

2.2.2. Fourier-Transform Infrared (FT-IR) Spectroscopy Study [7]

FT-IR spectra of Piroxicam sodium alginate, HPMC, Xanthan gum and physical mixtures of these polymers with drug were obtained on IR spectrophotometer (Shimadzu, FTIR-8400S, Japan) using KBr discs. The instrument was operated under dry air purge and the scans were collected at scanning speed 2 mm/sec with resolution of $4cm^{-1}$ over the region of 4000-400 cm^{-1}. The scans were evaluated for presence of principle peaks of drug, shifting and disappearance of drug peaks and appearance of new peaks due to polymer interaction.

2.2.3. Micromeritic Properties [8]

The microspheres were characterized by their micromeritic properties such as particle size, bulk density, tapped density, compressibility index, hausner ratio and angle of repose.

2.2.4. Particle Size

Particle size of each formulation was determined by optical microscope (Motic Image, Germany). 20 microsphere of each batch on glass slide and observed under optical microscope under optical lens. The size all microspheres in a field was measured.

2.2.5. Bulk Density

In this method floating microspheres are transferred to a measuring cylinder and is tapped manually till a constant volume is obtained. This volume is bulk volume and it includes true volume of the powder and the void space among the microspheres.

$$\text{Bulk density} = \frac{\text{Mass of microsphere}}{\text{Bulk volume}}$$

2.2.6.Tapped Density

In this method floating microspheres were transferred to a measuring cylinder & tapped for 100 times. After tapping volume of microspheres was visually examined. The ratio of mass of

microspheres to volume of microspheres after tapping gives tapped density floating microspheres.

$$\text{Tapped density} = \frac{\text{Mass of microsphere}}{\text{Volume of microsphere after tapping}}$$

2.2.7. Compressibility Index and Hausner Ratio

Percent Carr's index was determined by using the formula,

2.2.7.1. Carr's index (%)

Tapped density- Bulk density × 100

Tapped density

*2.2.7.2. Hausner Ratio***:**

Hausner ratio of microspheres was determined by using the equation

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

$$\text{Hausner ratio} = \frac{\text{Tapped Bulk Density}}{\text{Loose Bulk Density}}$$

2.2.8. Angle of Repose

Angle of repose (θ) of the microspheres, which measures the resistance to particle flow, was determined by a fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the blends. Accurately weighed microspheres were allowed to pass through the funnel freely on to the surface. The height and radius of the powder cone was measured and angle of repose was calculated using the following equation.

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

Where, θ - Angle of repose

h - Height of granules above the flat surface

r - Radius of the circle formed by the granule heap.

2.2.9. In vitro Buoyancy **[9,10,11,12]**

Floating microspheres (equivalent to 100 mg) were dispersed in 900 ml of 0.1 N hydrochloric acid solution (pH 1.2) containing tween 80 (0.01 W/V%) tween 20 (0.02 W/V%) to simulate gastric fluid at 37°. 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 over night. Each weight was measured and buoyancy was determined by the weight ratio of the floating microspheres to the sum of floating and sinking microspheres.

$$\textbf{Buoyancy (\%)} = \frac{W_f}{W_f + W_s} \times 100$$

Where W_f and W_s are the weights of the floating and settled microspheres, respectively.

2.2.10. Production Yield and Incorporation Efficiency of Microsphere **[9, 10, 11, 12]**

Microsphere were dried at 50°C, then weighed and the yield of microsphere preparation was calculated using the formula

$$\text{Production yield (\%)} = \frac{\text{Practical mass (microballoons)}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

Microsphere were crushed and powdered by using a mortar. Accurately weighed of this powder was extracted in ethanol. The solution was then filtered, a sample of was withdrawn from this solution and assayed spectrphotometrically to determine the Piroxicam content of the microsphere. A calibration curve based on standard solutions of Piroxicam in ethanol was used to calculate the Piroxicam concentration.

The incorporation efficiency (%) was calculated by using following equation

$$\text{Incorporation efficiency} = \frac{\text{M actual}}{\text{M theoretical}} \times 100$$

Where M actual is the actual Piroxicam content in weighed quantity of powder of microsphere and M theoretical is the theoretical amount of Piroxicam in microsphere.

2.2.11. In vitro Release Studies **[9, 10, 11, 12]**

The *in vitro* dissolution of microsphere was determined with a USP rotating paddle method (900 ml 0.1 N HCl; 100 rpm; 37^0c; n =3). At present time intervals aliquots were withdrawn and replaced by an equal volume of dissolution medium to maintain constant volume. After suitable dilution, the samples were analyzed spectrphotometrically at 335 nm for the 0.1 N HCl.

The *in vitro* release data obtained was treated to Zero-order kinetic, First-order kinetic, Higuchi equation, Korsmeyer-Peppas model to know precisely the mechanism of drug release from floating microsphere.

2.2.12. Characterization of Optimized Formulation **[4,12]**

2.2.12.1. Scanning electron microscopy

Scanning electron microscopy was carried out for formulation F9. Dry microspheres were placed on an electron microscope brass stub coated with gold in an ion sputter. Then picture of microsphere were taken by random scanning of the stub. The SEM analysis of the microspheres was carried out by using JEOL – 6360A analytical scanning electron microscope. The microspheres were viewed at an accelerating voltage of 20KV.

2.2.12.2. FT-IR spectrum of optimized formulation

FT-IR spectra of optimized formulation F9 were obtained on IR spectrophotometer (Shimadzu, FTIR-8400S, Japan) using KBr discs. The instrument was operated under dry air purge and the scans were collected at scanning speed 2 mm/sec with resolution of $4cm^{-1}$ over the region of 4000-400 cm^{-1}. The scans were evaluated for presence of principle peaks of drug, shifting and disappearance of drug peaks and appearance of new peaks due to polymer interaction.

2.2.12.3. DSC of optimized formulation

The DSC study was carried out for pure Piroxicam, and optimized formulation. The DSC patterns were recorded on a METTLER TOLEDO (Star SW 920). Each sample (2-4mg) was heated in crimped aluminum pans with a pierced lid at a scanning rate of 10^0C/min in an atmosphere of nitrogen flow (40mL/min) using the range of 40-200^0C. The DSC was calibrated for baseline using empty pans, and for temperature and enthalpy using indium. The DSC thermo grams are carefully observed for the possibility of interaction.

2.2.13. Stability studies of optimized formulation

Stability of a pharmaceutical product may be defined as the capability of a particular formulation, to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications.

The optimized formulation sealed in aluminum packaging coated inside with polyethylene; samples were kept in the humidity chamber maintained at 40°C and 75% RH for 3 months. At the end of studies, samples were analyzed for organoleptic properties, % entrapment efficiency and % cumulative drug release, total floating time and surface and appearance.

3. RESULTS AND DISCUSSION

3.1. Compatibility Study of Drug and Excipients

The Drug–Excipients compatibility studies were performed in order to confirm the compatibility of drug with the used excipients in the formulation floating microsphere.

This study mainly includes FTIR studies.

3.2. Compatibility Study of Drug and Excipients by FT-IR Spectroscopy

IR spectrums of physical mixture of Piroxicam with sodium alginate, HPMC, and xanthan gum were recorded in figure 2, 3, 4 respectively.

A) FT-IR Spectrum of Piroxicam:

IR spectra of Piroxicam are shown in figure 1 and table 2**.**

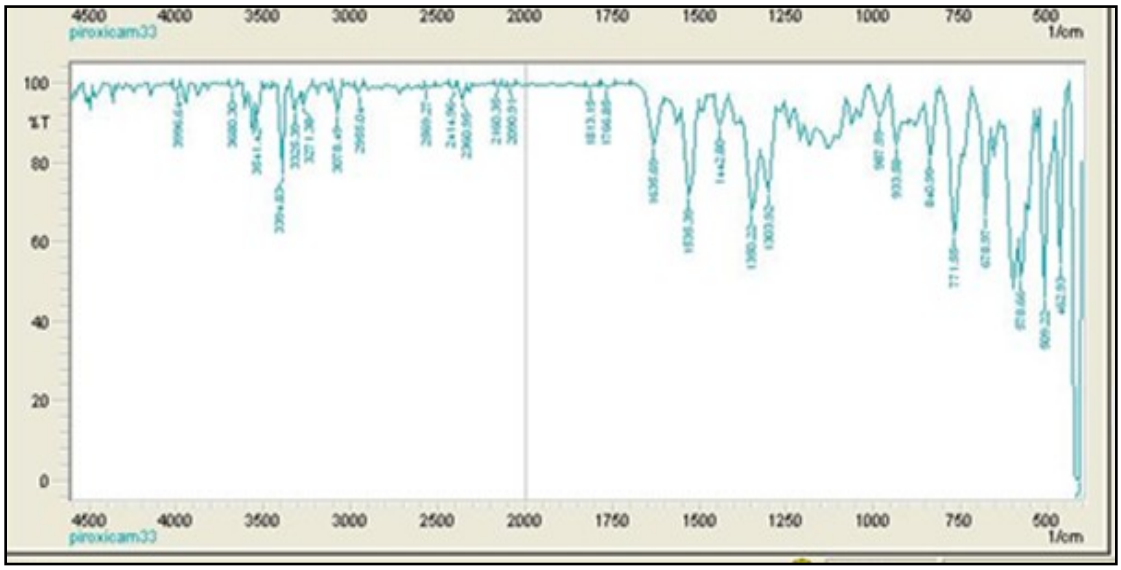

Figure 1: FT-IR spectrum of Piroxicam.

Table 2: Interpretation of FTIR spectrum of Piroxicam.

Functional Group	Reference peak wave number(cm^{-1})	Observed peak wave number(cm^{-1})
Aromatic C-H stretching	3100-3000	3078
C=O stretching	1870-1540	1766
Asymmetric $S(=O)_2$	1350-1430	1303

stretching		
Symmetric $S(=O)_2$ stretching	1160-1120	1149
Secondary amine N-H stretching	3350-3310	3325
OH stretching	3650-3584	3680

B) FT-IR spectrum of physical mixture of Piroxicam and sodium alginate:

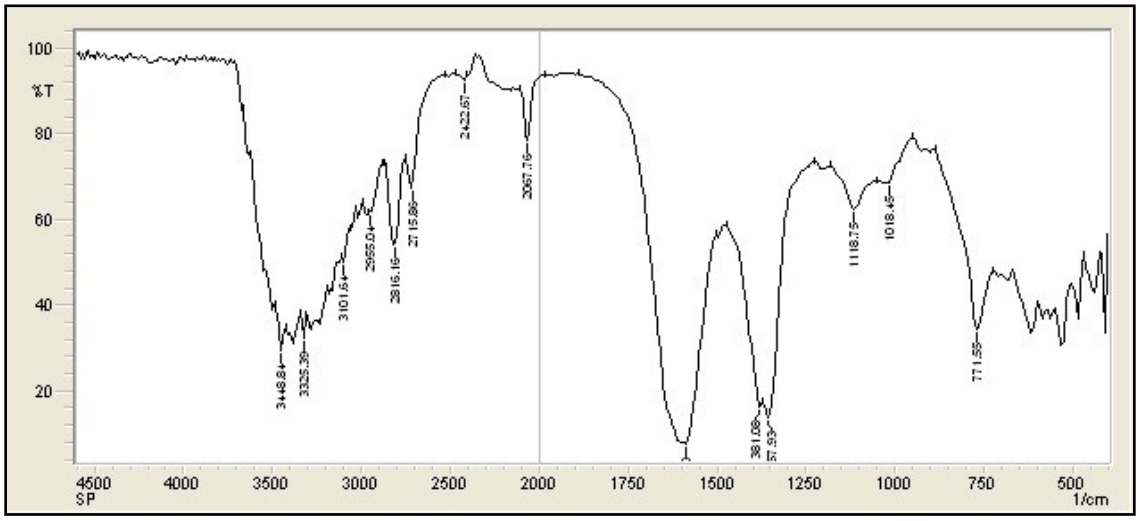

Figure 2: FT-IR spectra of physical mixture Piroxicam and sodium alginate.

C) FT- IR spectrum of physical mixture of Piroxicam and HPMC:

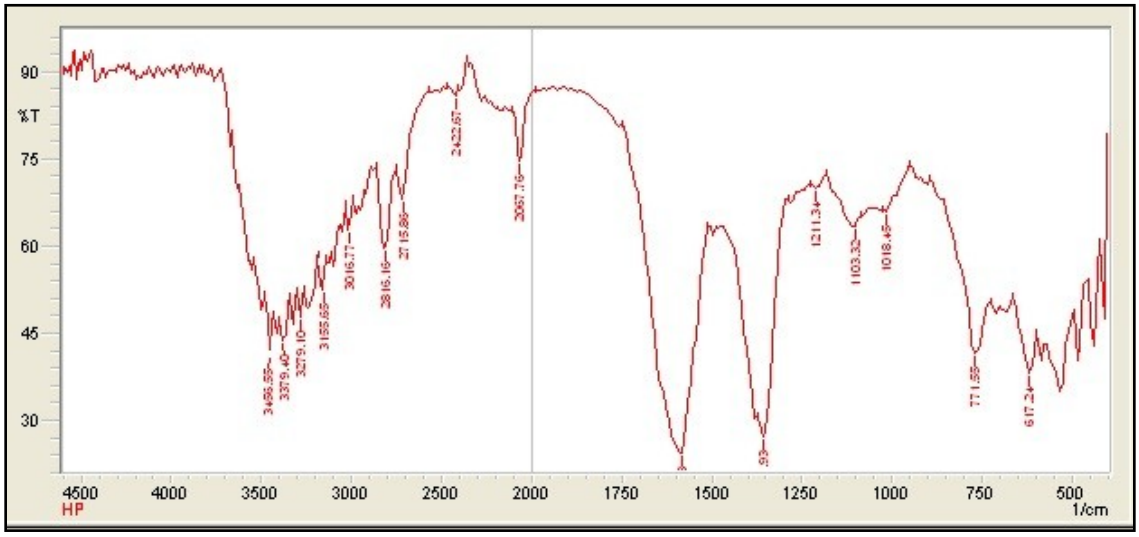

Figure 3: FT-IR spectra of physical mixture Piroxicam and HPMC.

D) FT-IR Spectrum of Physical Mixture of Piroxicam and Xanthan Gum

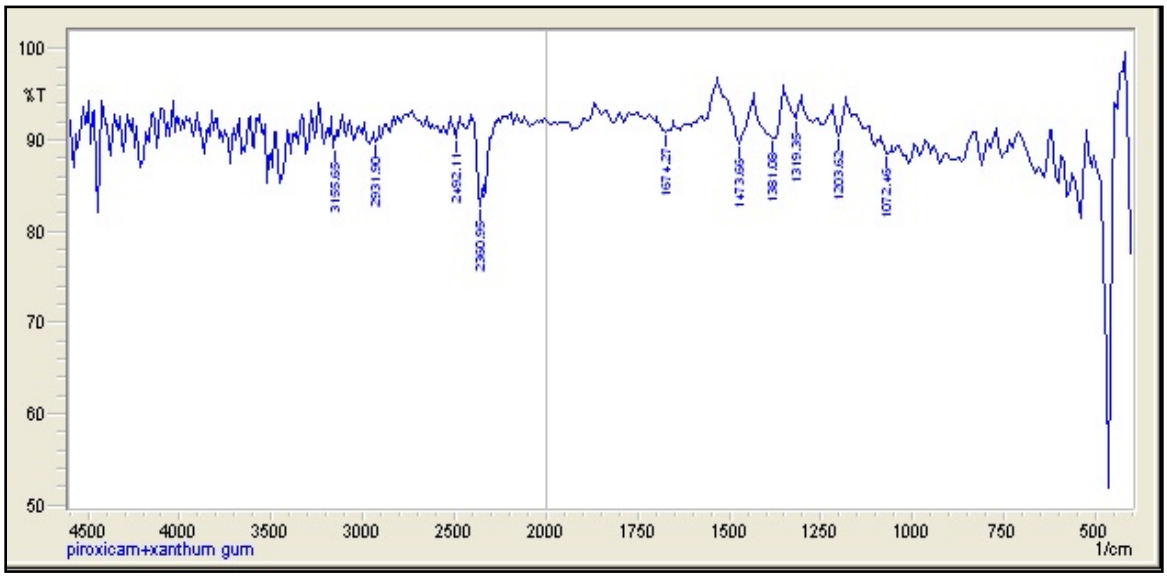

Figure 4: FT-IR spectra of physical mixture Piroxicam and Xanthan gum.

As per the IR spectrum, the result showed that there was no evidence of Piroxicam & excipients interaction which allows us to formulate the formulation with this excipients & drug.

Micromeritic Properties

The formulation of floating microsphere of

Piroxicam were prepared by ionic gelation method and evaluated by following parameter like Particle size, Bulk density, Tapped density, Hausner ratio, Angle of repose, Percentage yield, *In vitro* buoyancy, Incorporation efficiency, *In-vitro* drug release etc.

Table 3: Micromeritic properties of floating microsphere of Piroxicam.

Formulation	Particle Size(µm)	Bulk Density (g/mL)	Tapped Density(g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of Repose(***θ***)
F1	586±0.26	0.108±0.62	0.123±0.47	12.19±0.94	1.13±0.33	21.37±0.65
F2	602±0.34	0.116±0.41	0.141±0.19	17.73±0.23	1.21±0.31	22.94±0.14
F3	610±0.54	0.132±0.29	0.155±0.22	14.83±0.63	1.17±0.25	20.45±1.32
F4	592±0.13	0.118±1.25	0.129±0.69	8.52±0.75	1.09±0.39	26.19±0.36
F5	642±0.69	0.138±0.84	0.159±0.85	13.20±0.43	1.15±0.55	25.45±1.23
F6	644±0.72	0.143±0.52	0.161±0.63	11.18±0.71	1.12±0.59	25.33±1.02
F7	545±0.96	0.165±0.58	0.181±0.94	8.83±0.45	1.09±0.67	20.39±1.46

F8	568±0.17	0.127±0.87	0.143±0.84	11.18±0.69	1.12±0.07	29.54±0.75
F9	655±0.24	0.156±0.32	0.169±0.68	7.69±0.89	1.08±0.46	21.80±2.44

All values are represented as mean ± standard deviation (n=3)

The mean particle size of the microspheres formulation F1 to F9 containing sodium alginate, HPMC, xanthan gum was in range 545±0.96 to 655±0.24 respectively (as shown in table 3).The effect of polymer concentration on the particle size of microspheres was determined. The mean particle size of the microspheres was found to increase with increasing concentration of polymers (as shown in table 3). The viscosity of the medium increases at higher concentration of polymers resulting in enhanced interfacial tension. Shearing efficiency is also diminished at higher viscosities. This results in the formation of larger particles.

The bulk density values ranged from 0.108±0.62 g/ml to 0.165±0.58 g/ml, tapped density was determined by tapping method.

The tapped density values of microsphere ranged from 0.123±0.47 g/ml to 0.181±0.94 g/ml the density of microsphere was found to be ≥ 1 therefore the floating of microsphere observed. The compressibility index which was in range of 8.52±0.75% to 17.73± 0.23% to indicate excellent and or good flow characteristics of floating microsphere. Hausner ratio value ranged from 1.9±0.39 to 1.21±0.31 which was within normal acceptable range. Angle of repose of microsphere was in range of 20.39±1.46 to 29.54±0.75. All formulation showed good flowability as expressed in terms of angle of repose ($\leq 40^0$). The better flow property of microsphere indicates that the floating microsphere produced was non aggregated.

Table 4: Percentage yield, in vitro buoyancy and incorporation efficiency of floating microspheres of Piroxicam.

Formulation code	Production yield (%)	In vitro buoyancy (%)	Incorporation efficiency (%)
F1	61.53±0.34	75.30±0.15	65.96±0.89
F2	74.28±0.81	81.25±0.39	85.13±0.34
F3	81.33±1.23	82.71±1.13	78.99±1.04
F4	70.32±0.56	71.83±1.18	74.33±1.16
F5	90.44±0.49	90.81±2.11	90.00±0.38
F6	92±0.16	88.54±0.91	89.5±1.96
F7	64.61±0.98	78.72±0.76	63.76±0.63
F8	77.33±0.22	72.5±0.89	80.00±1.94
F9	84.28±0.53	92.63±1.09	94.26±1.63

All values are represented as mean ± standard deviation (n=3)

Production Yield

The percentage yield of floating microsphere formulation F1 to F9 containing sodium alginate, HPMC, xanthan gum was in range of 61.53±0.34 to 92±0.16% (as shown in table 4). There is no significant effect of concentration of polymers on the production yield.

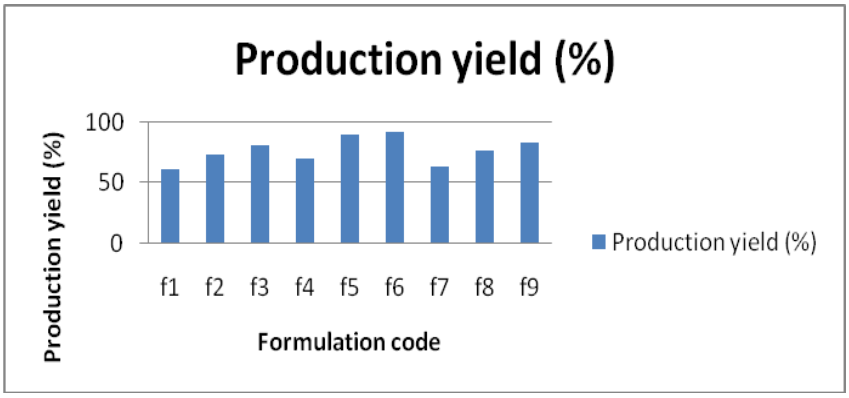

Figure 5: Production yield.

Incorporation Efficiency:

The incorporation efficiency of formulation F1 to F9 containing sodium alginate, HPMC, xanthan gum was in range 63.76±0.63 to 94.26±1.63 respectively (as shown in table 4) Among all formulation F5 and F9 was found to be highest incorporation efficiency Results demonstrated that increase in concentration of HPMC and Xanthan gum increased the entrapment of the drug. The drug entrapment efficiency was found to be good in all the formulation.

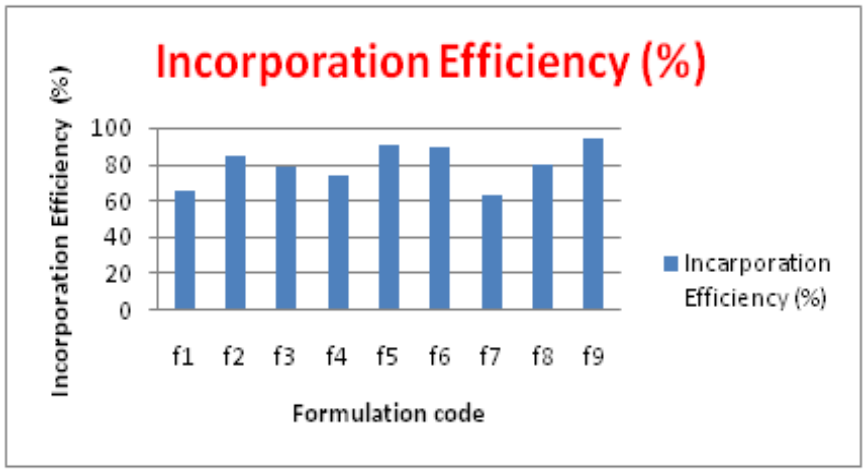

Figure 6: Incorporation efficiency.

In vitro Buoyancy

The purpose of preparing floating microspheres was to extend the gastric residence time of a drug. The buoyancy test was carried out to investigate the floatability of the prepared microspheres. The microspheres were spread over the surface of a simulated gastric fluid and the fraction of microspheres buoyant and settled down as a function of time was quantitated. The *in vitro* buoyancy of formulation F1 to F9 containing, sodium alginate, HPMC, xanthan gum was in range 71.83±1.18 to 92.63±1.09 % respectively (as shown in table 4). Among all formulation F5 and F9 was found to be highest *in vitro* buoyancy. The results also showed a tendency that the larger the particle size, the longer floating time.

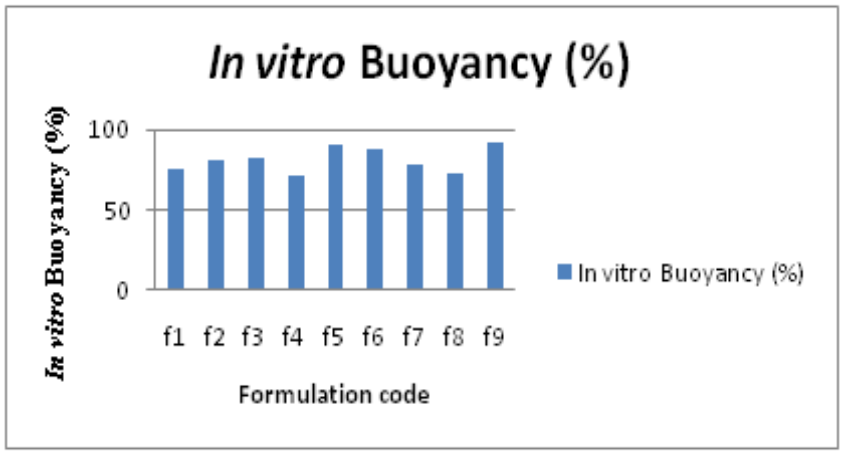

Figure 7: *In vitro* buoyancy.

Figure 8: *In vitro* buoyancy F1. F2. F3.

Figure 9: *In vitro* buoyancy F4. F5. F6.

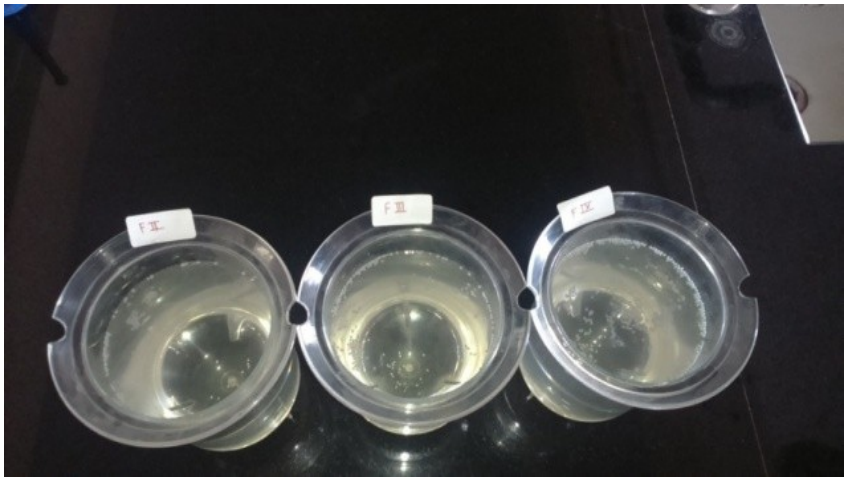

Figure 10: *In vitro* buoyancy F7. F8. F9.

3.3. In vitro drug Release Studies of Floating Microspheres Piroxicam in 0.1 N HCl

In-vitro Drug Release

In vitro drug release studies of Piroxicam from floating microspheres were performed in pH 0.1 N HCl for 12 hr using USP Type I dissolution test apparatus. It was found that *in vitro* drug release of formulation F1 to F9 containing, sodium alginate, HPMC, xanthan gum as follows.

F1, F2, F3, F4, F5, F6, F7, F8, F9 show percentage drug release 72.9 to 94.95 at end of 12 hour. Formulation F9 show percent drug release 94.95 ± 0.90 at end of 12 hr. (as shown in table 5) Among all formulations, F9 was found to be the best formulation as it release Piroxicam 94.95 % in a sustained manner with constant fashion over extended period of time (after 12 hr). It was observed as the concentration of sodium alginate and xanthan gum was increased percent release of Piroxicam formulation. The increase in concentration of sodium alginate and xanthan gum leads to the increased density of polymer matrix into the microspheres which result in sustain release.

Table 5: *In vitro* drug release studies of floating microspheres Piroxicam formulation.

Time (hr)	**Drug Release (%)**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	11.16 ±0.55	6.75±0.97	7.78±1.10	7.56±1.46	15.70±1.27	10.89±1.00	6.70±1.77	8.23±1.1	13.99±1.1
2	15.25 ±0.56	14.44±0.97	16.42±0.41	13.54±1.14	28.70±1.25	16.2±1.22	13.95±2.25	17.1±0.8	19.21±0.1
3	18.11 ±1.43	29.25±0.24	24.66±1.5)	23.94±0.50	31.59±0.95	18.36±0.96	23.4±0.90	17.55±1.8	26.86±1.0
4	23.85 ±0.62	33.88±1.32	33.34±1.36	33.21±0.73	45.01±0.82	26.46±1.36	33.3±3.28	27.5±1.2	34.11±0.9
5	26.95 ±0.81	39.96±0.92	40.05±0.92	37.89±1.00	48.6±1.20	27.46±2.38	37.8±1.700	35.50±5.9	44.66±0.7

6	33.75 ±1.40	45.45± 0.53	46.35± 0.88	49.05± 1.36	55.8±0. 70	31.1±0. 84	45.45± 1.49	36.49± 09	49.97± 0.9
7	40.59 ±0.78	60.75± 0.88	59.85± 1.13	54.45± 1.86	61.65± 1.07	44±0.9 1	59.4±0. 93	40.45± 0.6	72.45± 1.5
8	42.84 ±0.54	66.6±1. 13	71.18± 1.18	62.55± 1.16	71.55± 3.16	49.6±1. 20	70.65± 1.8	44.95± 0.5	81.9±1 .9
9	49.05 ±1.86	71.18± 1.18	76.5±1. 13	64.8±2. 80	79.2±1. 29	62.2±1. 4	73.38± 1.42	55.35± 0.8	87.75± 0.7
10	62.11 ±2.73	75.6±1. 38	78.75± 1.18	67.95± 0.20	80.55± 1.01	75.6±1. 30	74.7±1. 14	74.25± 0.6	90.45± 1.1
11	76±1. 43	77.85± 1.21	81.9±1. 38	71.4±0. 45	83.7±1. 10	76.95± 1.50	78.3±1. 3	80.55± 0.8	93.15± 1.6
12	76.95 ±0.52	79.65± 1.53	84±1.1 2	72.9±1. 15	90.90± 0.96	84.15± 1.02	79.65± 1.50	83.7±0 .5	94.95± 0.9

All values are represented as mean ± standard deviation (n=3)

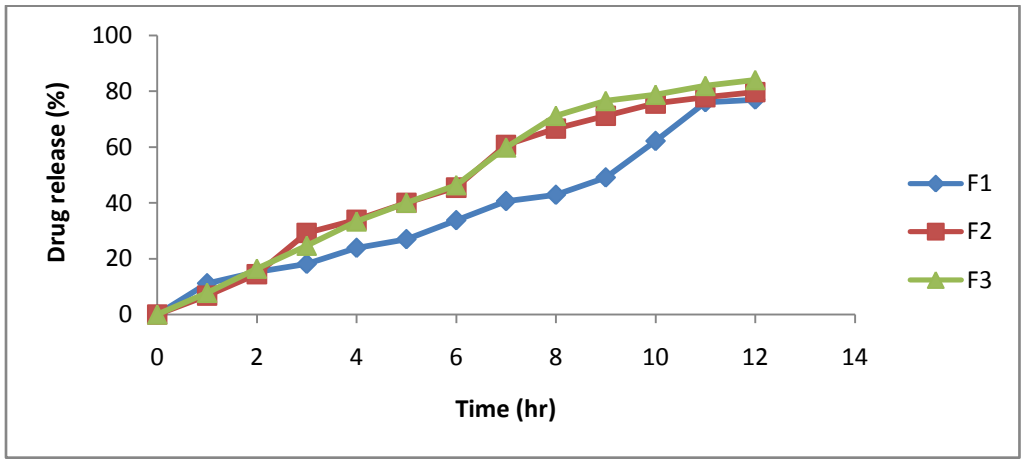

Figure 11: *In vitro* drug release profile of formulation F1 to F3.

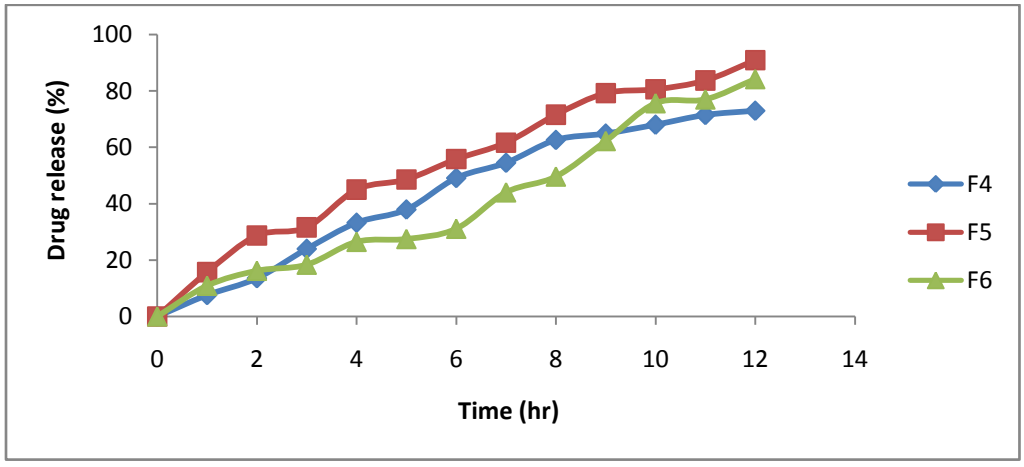

Figure 12: *In vitro* drug release profile of formulation F4 to F6.

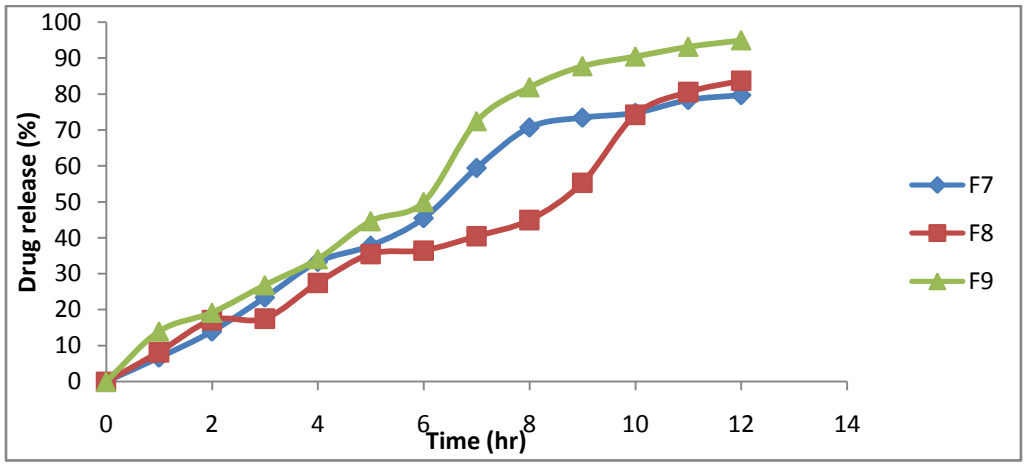

Figure 13: *In vitro* drug release profile of formulation F7 to F9.

3.4. Dissolution kinetics study

Table 6: Dissolution kinetics of formulations F1 to F9.

Models / Parameter	R^2 values for formulations F1 toF9				
	Zero order	First order	Higuchi	Korsmeyar-Peppas	Hixson-Crowell
F1	0.954	0.860	0.950	0.963	0.899
F2	0.906	0.675	0.969	0.984	0.767
F3	0.947	0.747	0.957	0.997	0.834
F4	0.913	0.716	0.981	0.994	0.794
F5	0.886	0.729	0.981	0.986	0.790
F6	0.943	0.855	0.903	0.947	0.896
F7	0.943	0.736	0.953	0.995	0.827
F8	0.850	0.690	0.971	0.972	0.751
F9	0.973	0.881	0.901	0.952	0.926

Where R2 = correlation coefficient for the korsmeyer-peppas, zero order, higuchi models, first order, and hixon-Crowell model.

The dissolution data of batches F1 to F9 was fitted to zero order, first order, higuchi, korsemayer-Peppas and hixon-crowell models. The coefficient of determination (R2) value was used as criteria to choose the best model to describe drug release from the microsphere. The R2 values of various models are given in Table 6. In case of majority of formulations the R2 values were much higher for korsemayer-peppas model and higuchi model indicating that the drug release from the formulation followed korsemayer-peppas model and higuchi model kinetics. The R2 value (R2>0.956) obtained for fitting the drug release data to the korsemayer-peppas model and higuchi model indicating that the drug release mechanism from these microsphere was diffusion and or anomalous release. The values higuchi model also indicated that all the formulations followed diffusion controlled release mechanism; this indicated that the drug release is controlled by diffusion.

3.5. Characterization of Optimized Formulation

Scanning Electron Microscopy (SEM)

Morphology study of optimized formulation was examined by scanning electron microscopy. The view of the microspheres showed a hollow spherical structure with a smooth surface morphology. Some of the microspheres showed a dented surface structure but they showed good floating ability on the surface of the medium, indicating intact surface. The outer surface of the microspheres was smooth and dense, while the internal surface was porous. The shell of the microspheres also showed some porous structure

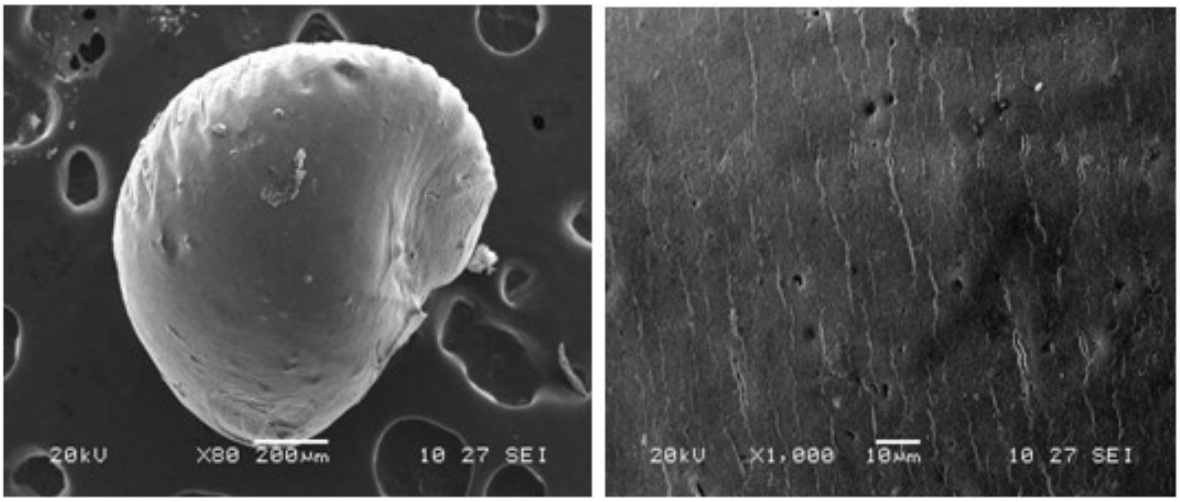

Figure 14: Morphology of optimized formulation.

FT-IR Spectrum of Optimized Formulation

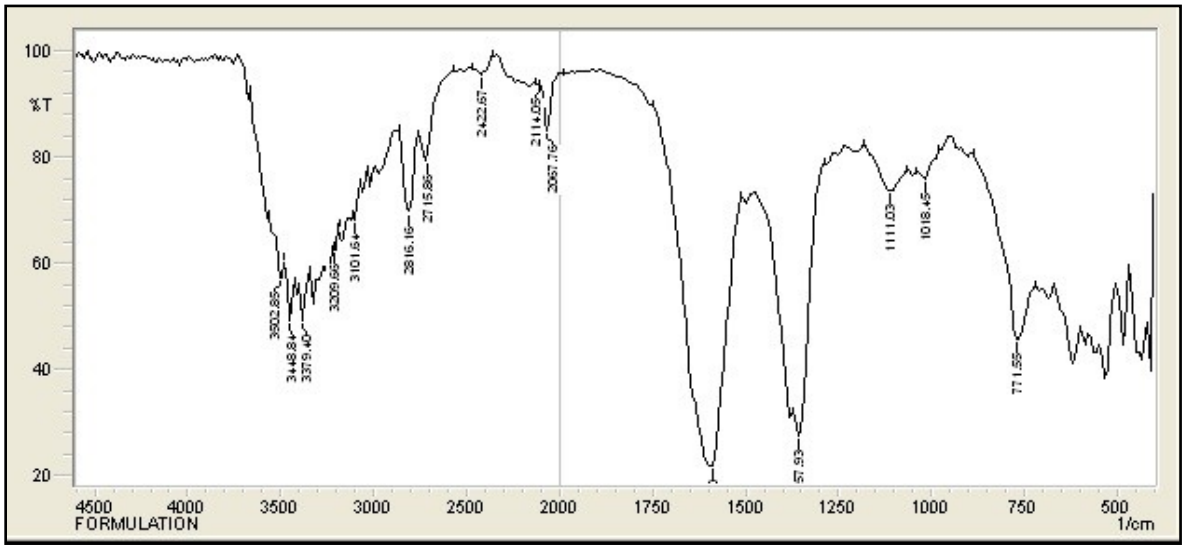

Figure 15: FTIR spectrum of optimized formulation.

Table 7: Interpretation of FT-IR spectra peak of Piroxicam.

Functional Group	Reference peak wave number(cm^{-1})	Observed peak wave number(cm^{-1})
Aromatic C-H stretching	3078	3101.64

C=O stretching	1766	1589.40
Asymmetric $S(=O)_2$ stretching	1303	1357.93
Symmetric $S(=O)_2$ stretching	1149	1111.03
Secondary amine N-H stretching	3325	3379.40
OH stretching	3680	3448.84

9.4.3. Diff erential Scanning Calorimetry:

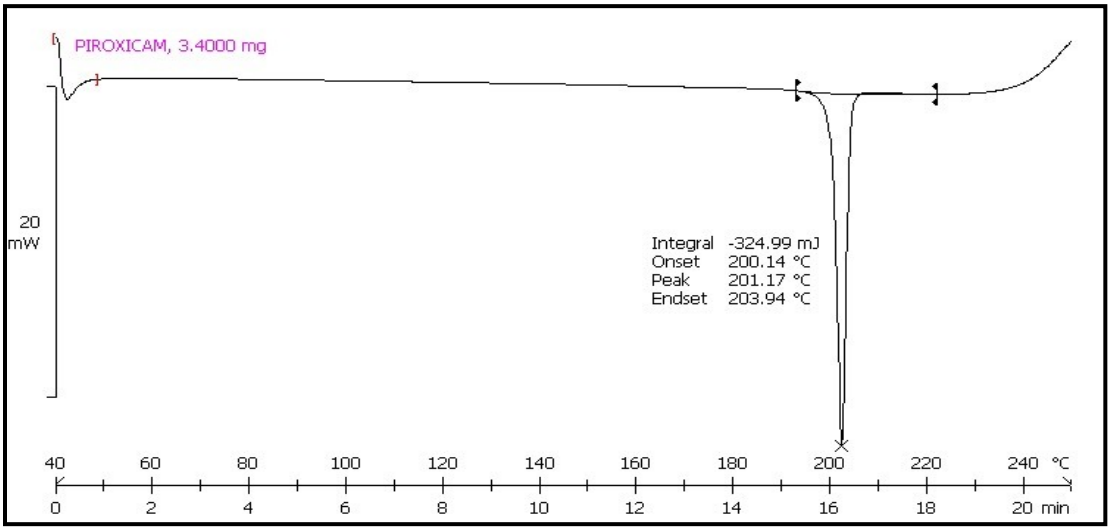

Figure 16: DSC thermogrm of Piroxicam.

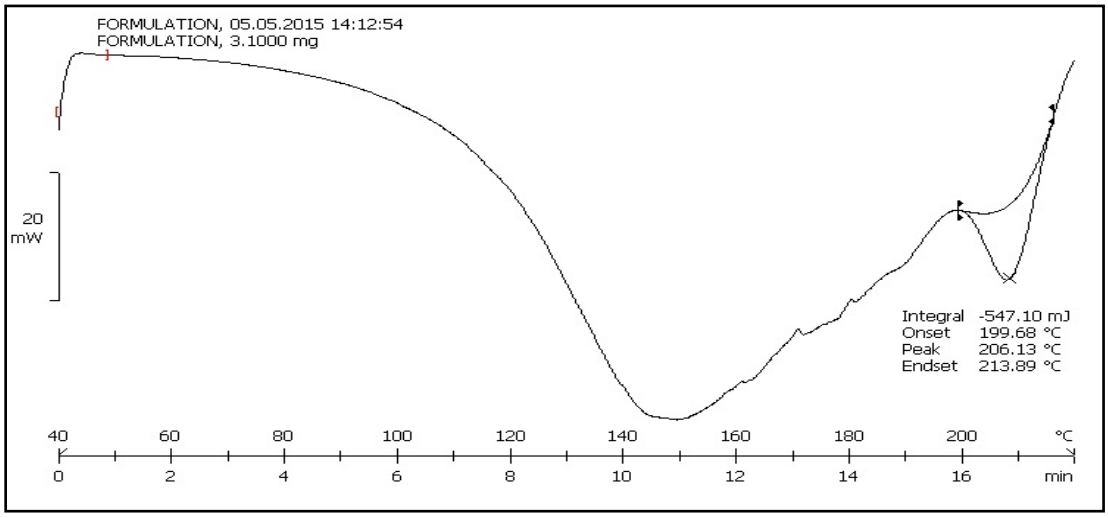

Figure 17: DSC of optimized formulation.

When DSC thermogram of optimized formulation and DSC of Piroxicam, is compared, the Piroxicam showed a characteristic sharp endothermic peak at 201.17^0c indicating the melting point of drug. The obtained DSC curve of optimized formulation shows the endothermic peak at 206.13^0c of Piroxicam. The results of DSC study are revealed that there was no any interaction between Piroxicam and polymers in final formulation.

3.6. Stability Studies

Short term stability testing was carried out for the optimized formulation. The results of stability testing were reported in table 8

Short term accelerated stability data obtained for optimized formulation revealed that organoleptic characteristics, % entrapment efficiency, % cumulative drug release and *in vitro* buoyancy were within acceptable limit. Thus the formulation can be said to be stable.

Organoleptic characteristics, % Entrapment efficiency, % Cumulative drug release and in vitro Buoyancy

Table 8: Stability study of optimized floating microsphere formulation (F9).

Initial	**Appearance**	**An off white to light yellow powder.**
	% Entrapment efficiency	94.26±1.63
	% Cumulative drug release	94.95±0.90
	In vitro Buoyancy	92.63±1.09
After 3 months	Appearance	An off white to light yellow powder
	% Entrapment efficiency	93.32 ± 0.48
	% Cumulative drug release	92.11 ± 0.45
	In vitro Buoyancy	91.39±0.55

4. CONCLUSION

Floating microspheres have a bulk density less than gastric fluids and thus it remains buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. Also floating microspheres provide a constant and prolonged therapeutic effect which will reduce dosing frequency. The data obtained from the study of "Formulation and evaluation of floating microspheres of Piroxicam reveals following conclusion:

- Floating microspheres of Piroxicam can be successfully prepared using Sodium alginate HPMC, Xanthan gum as polymers by inotropic gelation method.
- The percent yield of all floating microspheres formulation was more than 60% suggesting that the methods used for encapsulation was effective. The percent yield was significantly increased as the amount of polymer was increased in each preparation method.
- The entrapment efficiency was good in all the cases. This suggested that optimized parameters were used in the method of preparations.
- The *in vitro* buoyancy was more than 70% after 12 hours indicated satisfactory performance of proposed formulations.

  The percent buoyancy increased significantly in some formulation. The results showed a tendency that larger the particle size, the longer floating time.

- The mean particle size of microspheres was in the range of 545(±0.96) to 655(±0.24) μm depending upon the type of polymer used. The particle size increased significantly as the amount of polymer increased.
- The flow properties of all the prepared microspheres were good as indicated by angle of repose and compressibility index. The good flow properties suggested that the microspheres produced were non-aggregated.
- *In vitro* release of floating microspheres of Piroxicam was found to be in following order. F9>F5>E6>f3 Among all formulations, F9 was found to be the best formulation as it release Piroxicam 94.95 % in a sustained manner with constant fashion over extended period of time (after 12 hr). The curve fitting data indicated that the formulation followed korsmeyer-Peppas model and higuchi model of dissolution suggesting that the mechanism of drug release was dominated by diffusion.
- The surface morphology of the prepared floating microspheres was studied using scanning electron microscopy. The prepared floating microspheres also characterized by FTIR spectroscopy and DSC and stability study to find out any chemical interaction between Piroxicam and polymers used.

  Hence, finally it was concluded that the prepared floating microspheres of Piroxicam may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency.

5. ACKNOWLEDGEMENT

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