

FORMULATION AND EVALUATION OF MUCOADHESIVE MICROSPHERES OF PIROXICAM

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<p>*For Correspondence: Pharmaceutics department, Ashokrao Mane College of Pharmacy, Peth-Vadgaon. Tal-Hatkanangale, Dist-Kolhapur, Maharashtra, India, 416111.</p>	<p>ABSTRACT Oral route for administration of the drug is the most convenient route, but oral route for administration has certain disadvantages because of inability to localize the drug at sites of absorption such as gastrointestinal tract. Mucoadhesive microspheres are one of the novel drug delivery systems which can cause localization of the drug at site of absorption. Bioadhesion is a phenomenon in which two materials are held together which each other biologically by interfacial forces. Mucoadhesion is very useful phenomenon because it can improve bioavailability as well as increase patient compliance. A microsphere was prepared by non-aqueous emulsification solvent evaporation method by using different polymers such as carbopol 974-P, HPMC K100M .Particle size of all microspheres was in the range suitable for administration by GI route. Also the mucoadhesion properties of all microspheres were good. Carbopol has higher mucoadhesion, swelling property as well as higher entrapment efficiency as compared to HPMC. Whereas HPMC containing batches show higher drug release as compared to carbopol.</p> <p>KEY WORDS: Piroxicam, Mucoadhesive microspheres, Different polymers, evaluation.</p>
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INTRODUCTION

Gastric residence time is an important parameter which may affect drug bioavailability of dosage forms. Many drug suffer from low bioavailability because of short gastric emptying time. Gastro retentive systems are the current approach to overcome the problem of gastric residence time (Chaturvedi, 2012). Among the number of approaches mucoadhesive drug delivery system is one of the promising delivery system which adhere to the mucous layer of the stomach and thus remains in the stomach for long period of time (Foda, 2011). Nonsteroidal anti-inflammatory drugs (NSAIDs) are amongst

the most commonly prescribed medications in the world. The common side effect of antiinflammatory drugs is the gastric irritation. A trend in NSAID development has been to improve therapeutic efficacy and reduce the severity of GI (Gastric Intestinal) side effects through altering dosage forms by modifying release of the formulations to optimize drug delivery (Shivanand, 2010, Ravindran, 2012). One such approach is using polymeric microspheres as carriers of drugs. Microspheres can be defined as solid, approximately spherical particles ranging from 1 to 1000 μm they are made up of polymeric, waxy or other protective materials. The short residence time of the microspheres at the site

of absorption can be overcome by coupling bioadhesion characters to the microspheres and developing bioadhesive microsphere (Andrews, 2009, Carvalho, 2010, Mikos, 1989). Mucoadhesive microspheres helps to overcome the relatively short GI residence time and to improve localization of oral controlled or sustained release drug delivery system by intimate contact with the mucous layer and by specific targeting of drug to the absorption site. Piroxicam is the member of oxicam group of NSAIDs. Their mechanism is inhibition COX2. They are indicated in long term management of osteoarthritis as well as rheumatoid arthritis. But long term use is also associated with various adverse effects such as GI tract bleeding, ulceration. Developing mucoadhesive microspheres of Piroxicam will provide constant and prolonged therapeutic effect, which will reduce the dosing frequency and thereby improve the patient compliance. Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects. Thus the aim of the research is to formulate mucoadhesive microspheres of Piroxicam and carry out its evaluation (Harding 2003, Garg, 2012, Kaurav, 2012).

MATERIALS AND METHODS

Piroxicam was obtained as a gift sample from Marksans Pharma Ltd. Carbopol 974-P was obtained as a gift sample from Encube Ethics, Goa. HPMC K100M was purchased from Loba Chemicals, Mumbai. Methanol and Light liquid paraffin was purchased from Research Lab Fine Chem Industries. Dichloromethane and Span 80 was purchased from Molychem Pvt. Ltd.

FORMULATION OF MUCOADHESIVE MICROSPHERES OF PIROXICAM:

The mucoadhesive microspheres of piroxicam were prepared by non-aqueous emulsification solvent evaporation method. In this method the solvents used were methanol +

dichloromethane while the polymers used were carbopol 974-P, HPMC K100M or combination of Carbopol and HPMC K100M. The accurately weighed amount of polymer was dissolved in the methanol + dichloromethane. Then drug was added to above solution. It was sonicated for 15 min in sonicator. The above solution was extruded through syringe in the beaker containing 50ml of light liquid paraffin containing 2% Span 80 as suspending agent. Then stirring was performed in the propeller stirrer at 1000 RPM for period of 60 min to allow the solvent to evaporate completely. Then the microspheres were collected by filtration. Microspheres were washed with petroleum ether to remove the oil completely. Then they obtained microspheres were dried overnight (Singh, 2011).

EVALUATION OF MUCOADHESIVE MICROSPHERE:

a) % Practical yield:

% Practical yield is determined by using following formula.

$$\% \text{ Practical yield} = \frac{\text{Weight of Microsphere}}{\text{Weight of Drug} + \text{Weight of Polymer}} \times 100$$

b) Determination of particle size of microspheres:

Particle sizes of different batches of microspheres were determined by optical microscopy. Then the particle sizes of various batches are compared. The average particle size was determined by using the Edmondson's equation (Swamy, 2012).

$$D_{\text{mean}} = \frac{\sum nd}{\sum n}$$

Where,

n= number of microspheres observed

d= mean size range

c) Determination of morphology of microspheres by SEM:

The shape and surface characterization of microspheres were examined by scanning electron microscopy (SEM).

d) Determination of flow properties of microspheres:

i) Angle of repose: Angle of repose is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Angle of repose (θ) of the microspheres, which measures the resistance to particle flow, was determined by a fixed funnel method. The height and diameter of the powder cone was measured and angle of repose was calculated using the following equation (Khanam, 2011)

$$\theta = \tan^{-1} \frac{h}{r}$$

Where,

h- Height of the heap in cm,

r- Radius of the heap in cm.

ii) Determination of bulk density and tap density: Bulk density and tapped density were measured by using 10 ml of graduated cylinder. The sample poured in the cylinder was tapped mechanically for 100 times, and then the tapped volume was noted down. Bulk density and tapped density were calculated by using following formula

$$\text{Bulk Density} = \frac{\text{Weight of Microsphere}}{\text{Bulk Volume}}$$

$$\text{Tap Density} = \frac{\text{Weight of Microsphere}}{\text{Tap Volume}}$$

iii) Carr's Index:

Carr's index value of microparticles was calculated by using following formula,

$$\text{Carrs Index(\%)} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}}$$

iv) Hausner's Ratio:

Hausner's ratio of micro particles was determined by comparing the tapped density to the bulk density using the equation,

$$\text{Hausners Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

e) Determination of entrapment efficiency:

To determine the total drug content of microspheres entrapment efficiency is studied. Accurately weighed amount (10mg) of the microsphere formulations were dispersed in 10 ml

of 0.1N HCl and then stirred for 15 minutes in sonicator. After 24hrs the solution was filtered and analyzed spectrophotometrically at 334nm by diluting appropriately with 0.1N HCl. Theoretical drug loading was determined by entire drug present in the polymer solution in the microsphere. The entrapment efficiency is determined by following formula (Natarajan, 2011).

$$\text{Entrapment Efficiency} = \frac{\text{Practical Drug Loading}}{\text{Theoretical Drug Loading}} \times 100$$

f) DSC of formulation:

DSC of formulation is carried out to check the various properties conversion of crystalline form to amorphous form due to combination of drug and polymers. Also the type of reaction taking place is determined such as endothermic or exothermic reaction. The instrument was calibrated by using Alumina as reference. 10 mg of sample was used for DSC study. The sample was kept on Aluminum pans. Then it was heated at the rate of 10°C/min. The probe was heated from 30°C to 300°C (Prajapati, 2011, Kumar)

g) Determination of swelling index:

Swelling ability of microspheres in physiological media was determined by swelling them to their equilibrium. Accurately weight 1000mg of microspheres were dissolved in little excess of 0.1N HCl and kept for 24 hrs. The excess surface-adhered liquid drops were removed by blotting and the swollen microspheres were weighed. The microspheres were then dried in an oven at 60°C for 5 hours until there was no change in the dried mass of the sample. The swelling index is determined by following formula (Prajapati, 2011, Swamy, 2012).

$$\text{Swelling Index} = \frac{\text{Mass of Swollen Microspheres} - \text{Mass of Dried Microsphere}}{\text{Mass of Dried Microsphere}} \times 100$$

h) In vitro mucoadhesion test:

In this strip of goat intestinal mucosa was mounted on a glass slide and accurately weighed mucoadhesive microspheres in dispersion form was placed on the mucosa of the intestine. This glass slide was incubated for 15 min in a desiccator at 90% relative humidity to allow the polymer to interact with the

membrane and finally placed in the cell that was attached to the outer assembly at an angle 45°. 0.1 N HCl previously warmed to 37±0.5 °C, was circulated to the cell over the microspheres and membrane at the rate of 1 ml/min. Washings were collected at different time intervals and microspheres were separated followed by drying at 50 °C. The weight of microspheres (washed out) was taken and percentage mucoadhesion was calculated by (Dhaliwal, 2008, Nallaswamy, 2010, Swamy, 2012)

$$\text{Percentage Mucoadhesion} = \frac{W_a}{W_l} \times 100$$

Where,

W_a- weight of microspheres applied;

W_l- weight of microspheres leached out.

i) In vitro drug release study:

Dissolution studies are carried out for all the formulations employing USP apparatus (paddle method) at 37 ± 0.5°C rotated at constant speed of 100rpm using 900ml of 0.1 N HCl as the dissolution medium for 12hours. A sample of 100 mg of microspheres is used in each test. An aliquot of the sample is periodically withdrawn at 1 hr time interval and the volume is replaced with fresh dissolution medium in order to maintain the sink condition. The samples were suitably diluted and analyzed at 334nm using 0.1 N HCl as blank using double beam UV Visible spectrophotometer (Singh, 2010).

RESULT AND DISCUSSION

1. Compatibility study by FTIR:

The FTIR study was carried out to check the compatibility of drug with excipients. Peaks of pure drug and physical mixture were observed. Pure drug piroxicam shows peaks due to various functional groups at 3338.18, 1629.53, 1576.57, 1528.31, 1038.48 and 1350cm⁻¹ such as Alcohols & phenols, Alkenes, Aromatic ring, 20 amide, Sulphoxide and 30 amide respectively. Peaks of physical mixture and pure drug revealed that most of peaks of pure drug were retained in the FTIR of physical mixture. Hence we can say that given drug Piroxicam is compatible with polymers.

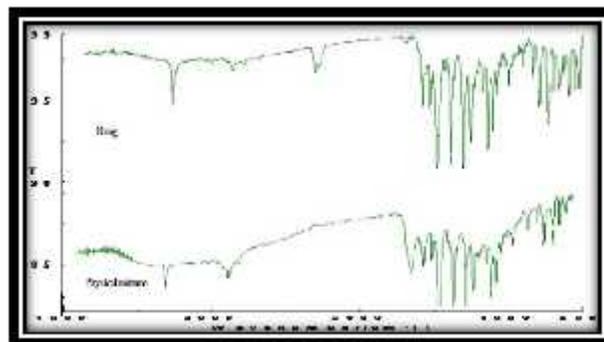


Figure 1: FTIR compatibility of polymer and drug

2. Formulation of mucoadhesive microspheres of piroxicam:

Mucoadhesive microspheres were formulated by emulsification solvent evaporation method using two polymers such as carbopol 974-P, HPMC K100M. Solvent used was methanol +dichloromethane and Span 80 as suspending agent in liquid paraffin which constitute oily phase. Total 17 batches were prepared. RPM was kept constant at 1000 rpm whole stirring time was 45-60 minutes.

Table 1: Formulation Table

Sr No	Formulation Code	Piroxicam (mg)	Carbopol 974-P (mg)	HPMC K100M (mg)
1	F1	100	25	
2	F2	100	25	100
3	F3	100	50	
4	F4	100		
5	F5	100		50
6	F6	100	50	
7	F7	100	50	50
8	F8	100		
9	F9	100		100
10	F10	100	150	
11	F11	100		
12	F12	100		150
13	F13	100	150	
14	F14	100	150	150
15	F15	300	300	
16	F16	300		
17	F17	300		300

Evaluation of mucoadhesive microspheres:

3.1. % Practical yield and particle size: % Practical yield of all the batches was found to be very good. %Practical yield was in the range of 83% to 99.31%. Particle size was measured by optical microscope. Particle size of all batches of piroxicam

was in the range of 189.72 μm for F13 to 506.22 μm for the F17 batches. The microspheres were in size range suitable for GI mucoadhesive drug delivery.

Table 2: % Practical yield and particle size

Sr. No.	Formulation	% Practical	Particle size
1	F1	95.95 \pm 0.40	507.22 \pm 8.48
2	F2	98.45 \pm 0.79	426.92 \pm 7.75
3	F3	84.12 \pm 1.18	265.86 \pm 22.72
4	F4	89.81 \pm 0.46	361.42 \pm 6.35
5	F5	88.33 \pm 0.81	348.3 \pm 10.02
6	F6	98.49 \pm 0.73	509.56 \pm 8.75
7	F7	99.423 \pm 0.52	488.65 \pm 9.89
8	F8	98.96 \pm 0.65	445.82 \pm 9.69
9	F9	99.31 \pm 0.46	383.14 \pm 12.86
10	F10	99.29 \pm 0.68	529.72 \pm 6.32
11	F11	99.29 \pm 0.51	331.87 \pm 12.95
12	F12	98.50 \pm 1.01	354.79 \pm 8.42
13	F13	98.86 \pm 0.47	190.72 \pm 7.65
14	F14	95.77 \pm 0.88	278.15 \pm 8.86
15	F15	94.22 \pm 0.71	496.66 \pm 11.95
16	F16	99.23 \pm 0.60	395.59 \pm 7.84
17	F17	97.66 \pm 0.52	303.15 \pm 9.94

3.2. Evaluation of morphology by SEM:

The external surface of microsphere was found to be scattered with crystals and pores. The crystals adsorbed on surface of microsphere cause burst release. The photograph also shows the dense and porous nature of microsphere.

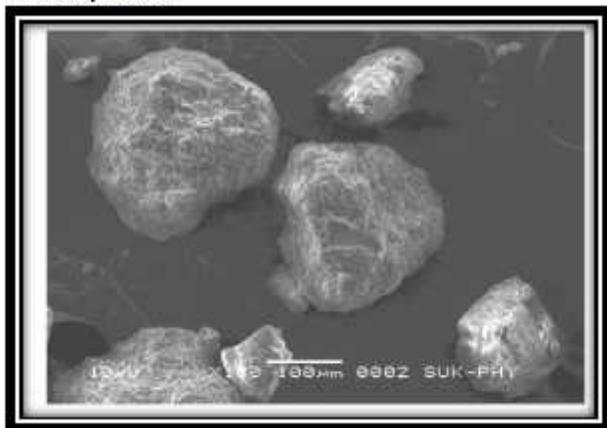


Figure 2: SEM photograph of formulation

3.4. DSC analysis of mucoadhesive microspheres: DSC of drug shows endothermic peak at 142.20c. While DSC of formulation shows peak at 64.80c and 206.60c. The characteristic endothermic peak of pure drug

is not visible in the DSC of both formulations. The disappearance of peak corresponding to melting point of piroxicam may indicate that drug is dissolved in the polymer as a solid solution or that the drug is dispersed in the polymer in a metastable molecular dispersion. So we can conclude that crystalline drug is probably converted to amorphous form.

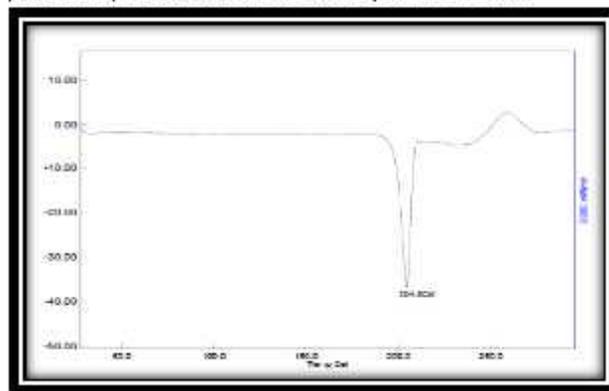


Figure 3: DSC thermogram of drug

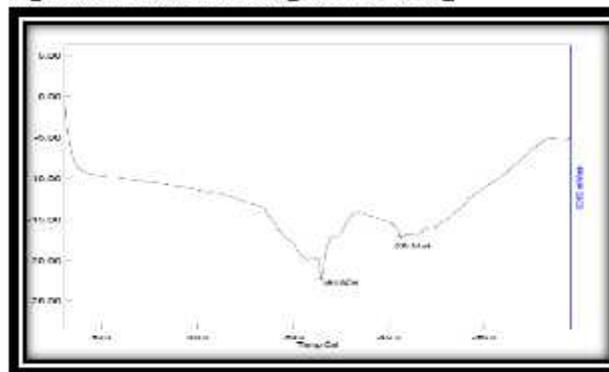


Figure 4: DSC thermogram of formulation

3.5. Flow properties of microspheres:

Flow properties of microspheres were studied by determining bulk density and tap density, and then Hausner's ratio and Carr's index. The Hausner's ratio of all the batches was found in the range of 1.14 – 1.19 which indicated good flow property for all the batches. Whereas the Carr's index value of all the batches was in the range of 10.99 – 14.65 which also indicated good flow properties of all microspheres. Angle of repose is one of the parameter which shows the resistance to flow. Angle of repose was lowest for batch F11 which is 18.540 whereas highest was for batch F2 which is 27.740. Angle of repose of all the batches indicated good flow property.

Table 3: Flow property of formulations

Sr. No.	Formulation Code	Bulk density (gm/cm ³)	Tap density (gm/cm ³)	Hausner's Ratio	Carr's Index	Angle of repose (θ)
1	F1	0.71 ±0.004	0.82 ±0.007	1.1655±0.004	12.463±0.31	26.47±0.38
2	F2	0.69 ±0.006	0.80 ±0.007	1.1684±0.004	12.677±0.36	27.74±0.14
3	F3	0.67 ±0.002	0.79 ±0.001	1.1877±0.003	14.053±0.26	26.42±0.35
4	F4	0.76 ±0.003	0.87 ±0.003	1.1529±0.005	12.033±0.95	25.27±0.43
5	F5	0.72 ±0.003	0.85 ±0.004	1.1931±0.009	14.473±0.7	25.98±0.18
6	F6	0.66 ±0.003	0.78 ±0.004	1.1956±0.007	14.657±0.54	21.96±0.09
7	F7	0.72 ±0.001	0.83 ±0.001	1.1667±0.003	12.554±0.28	25.47±0.19
8	F8	0.65 ±0.004	0.77 ±0.007	1.1856 ±0.01	13.936±0.79	24.30±0.12
9	F9	0.61 ±0.005	0.73 ±0.004	1.1927±0.004	14.449±0.32	23.73±0.17
10	F10	0.68 ±0.003	0.79 ±0.003	1.1776±0.009	13.356±0.71	27.89±0.91
11	F11	0.73 ±0.003	0.83 ±0.003	1.1463 ±0.01	10.997±0.82	18.54±0.55
12	F12	0.68 ±0.002	0.77 ±0.001	1.1772±0.003	13.329±0.22	22.42±0.49
13	F13	0.70 ±0.003	0.82 ±0.003	1.1781 ±0.01	13.214±0.50	24.95±0.99
14	F14	0.71 ±0.003	0.86 ±0.001	1.1678±0.006	12.632±0.51	23.72±0.44
15	F15	0.73 ±0.002	0.84 ±0.004	1.1699 ±0.01	12.777±0.78	23.83±0.02
16	F16	0.78 ±0.01	0.89 ±0.004	1.157 ±0.01	11.809±1.16	20.93±0.47
17	F17	0.74 ±0.003	0.87 ±0.001	1.1890±0.004	14.188±0.35	22.89±0.20

3.6. Entrapment efficiency, Swelling index and In-vitro mucoadhesion study:

Higher entrapment value indicate higher drug loading. Entrapment efficiency value ranges from 23.13 to 72.22%. Entrapment efficiency value indicate that batches containing carbopol show higher drug loading while HPMC containing batches show lower entrapment efficiency. Thus carbopol has higher drug loading capacity than HPMC. Swelling indicates the ability of swelling of the mucoadhesive polymer in the fluid of GI tract. Higher swellability indicate rapid availability of drug solution for diffusion with greater flux. Carbopol 974-P shows higher swelling than HPMC K100M. This is because carbopol swells 1000 times of its volume as well as it has hydrophilic nature. The porous nature of carbopol is responsible for hydrophilicity

which also results in higher swelling than HPMC. Mucoadhesion study indicates the ability of the polymer to adhere to the GI mucosa when it is continuously washed by GI fluid. Mucoadhesive study indicated that % mucoadhesion was higher for batches containing carbopol whereas lowest for batches containing HPMC K100M. It was highest for F15 i.e. 97.36% and lowest for F7 i.e. 81.24%. The higher mucoadhesion for carbopol is due to free carboxyl group (-COOH) which has ability to form covalent bonding with the mucin ion present in mucous membrane whereas HPMC contains hydroxyl (-OH) group. Hydroxy group also shows mucoadhesion but the hydroxy group in HPMC is less polar as compared to free carboxyl group of carbopol. Hence carbopol shows higher mucoadhesion as compared to HPMC.

Table 4: Entrapment efficiency and Swelling index of formulations

Sr	Formulation code	Entrapment efficiency	Swelling index	% Mucoadhesion
1	F1	69.44 ±0.54	0.86 ±0.18	87.28 ±1.27
2	F2	70.34 ±0.79	0.97 ±0.14	83.57 ±0.65
3	F3	50.71 ±0.66	0.83 ±0.05	88.70 ±1.70
4	F4	42.46 ±1.11	0.65 ±0.04	82.47 ±0.40
5	F5	44.23 ±0.51	0.76 ±0.11	80.42 ±0.37
6	F6	70.01 ±0.77	1.06 ±0.09	86.56 ±1.00
7	F7	72.40 ±0.72	0.94 ±0.18	81.24 ±1.21
8	F8	64.52 ±0.72	0.78 ±0.06	86.32 ±0.51
9	F9	71.05 ±0.63	0.93 ±0.09	82.10 ±0.78
10	F10	73.22 ±0.68	1.44 ±0.12	92.70 ±1.01
11	F11	63.72 ±1.52	0.95 ±0.10	90.21 ±2.48
12	F12	70.85 ±0.79	0.98 ±0.05	89.03 ±2.01
13	F13	65.89 ±1.44	0.96 ±0.19	93.42 ±0.48
14	F14	70.17 ±1.16	1.06 ±0.12	90.36 ±0.58
15	F15	32.52 ±2.12	1.24 ±0.10	97.36 ±1.11
16	F16	24.13 ±1.47	0.65 ±0.07	88.19 ±1.36
17	F17	26.33 ±2.64	0.93 ±0.08	82.69 ±1.38

3.7. In-vitro drug release study:

The in-vitro drug release study was carried out in USP rotating paddle apparatus operated at 100 rpm at temp 37±0.50c. The drug release ranges from 64.05% for F10 to 99.81% for F9. Drug release study indicates that HPMC shows higher drug release as compared to Carbopol. Also higher the concentration of carbopol lesser the drug release from formulation. Hence the optimized combination HPMC and Carbopol 974-P is necessary to achieve proper drug release. Also it was observed that increase in drug to polymer ratio resulted in decreased drug release. This is due to increase in density of polymer matrix which causes increase in diffusion path length. The drug release was initially very rapid or burst release which was important for achieving initial therapeutic plasma concentration of the drug.

Table 5: a) % Drug release of batches F1-F6

Time (Hour)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	13.91 ±0.55	12.26 ±0.44	16.33 ±0.39	19.76 ±0.29	18.17 ±0.25	18.18 ±0.45
2	20.83 ±0.71	19.87 ±0.84	28.20 ±0.32	27.44 ±0.32	26.62 ±0.24	28.05 ±0.24
3	28.88 ±0.61	27.03 ±0.59	35.85 ±0.32	39.82 ±0.31	37.88 ±0.29	33.90 ±0.19
4	35.04 ±0.81	36.62 ±0.66	46.74 ±0.34	47.63 ±1.12	46.50 ±0.37	42.51 ±0.32
5	40.39 ±0.27	45.87 ±0.47	53.57 ±0.35	54.63 ±0.38	51.51 ±0.21	50.67 ±0.58
6	44.82 ±0.74	50.63 ±0.52	64.58 ±0.31	66.13 ±0.59	64.28 ±0.30	59.32 ±0.31
7	54.11 ±0.56	60.10 ±0.28	71.70 ±0.40	67.44 ±0.26	70.81 ±0.51	64.42 ±0.41
8	60.23 ±0.20	67.91 ±0.89	72.52 ±0.31	71.62 ±0.17	72.47 ±0.18	66.62 ±0.24
9	65.96 ±0.71	76.86 ±0.52	74.55 ±0.39	79.98 ±0.46	76.99 ±0.84	70.37 ±0.29
10	72.86 ±0.49	81.15 ±0.52	75.61 ±0.25	80.73 ±0.51	83.31 ±0.42	74.27 ±0.30
11	76.84 ±0.48	86.49 ±0.37	77.12 ±0.13	83.58 ±0.16	89.68 ±0.32	77.53 ±0.29
12	81.57 ±0.34	92.53 ±0.57	83.35 ±0.37	90.62 ±0.33	96.59 ±0.16	83.54 ±0.13

Table 6: b) % Drug release of batch F7 – F12

Time (Hour)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
1	10.86 ±0.32	12.75 ±0.21	16.89 ±0.44	14.28 ±0.64	17.82 ±0.63	16.20 ± 0.79
2	19.32 ±0.26	24.37 ±0.59	31.12 ±0.67	22.25 ±0.34	29 ±0.51	21.76 ± 0.34
3	27.76 ±0.17	33.4 ±0.57	45.01 ±0.58	26.62 ±0.47	37.43 ±0.60	33.57 ± 0.29
4	38.49 ±0.06	41.66±0.19	58.27 ±0.23	32.51 ±0.36	41.93 ±0.35	43.24 ± 0.64
5	45.84 ±0.22	49.36 ±0.45	70.17 ±0.38	40.41 ±0.39	49.44 ±0.45	49.59 ± 0.19
6	56.56 ±0.41	54.85 ±0.09	77.51 ±0.49	45.72 ±0.44	53.12 ±0.56	56.30 ± 0.53
7	67.74 ±0.53	60.41 ±0.21	84.68 ±0.19	48.59 ±0.61	58.98 ±0.62	60.94 ± 0.89
8	73.44 ±0.17	64.99 ±0.25	89.22 ±0.68	54.04 ±0.25	59.40 ±0.45	63.48 ± 0.22
9	75.87 ±0.27	70.58 ±0.09	90.40 ±0.13	56.56 ±0.46	63.55 ±0.39	65.01 ± 0.78
10	78.28 ±0.16	75.47 ±0.51	96.55 ±0.23	57.72 ±0.55	65.18 ±0.33	69.13 ± 0.62
11	80.51 ±0.24	79.08 ±0.16	98.60 ±0.27	59.40 ±0.26	69.39 ±0.32	71.78 ± 0.21
12	88.68 ±0.20	86.43 ±0.47	99.81 ±0.30	64.05 ±0.54	74.55 ±0.43	77.15 ± 0.06

Table 7: c) % Drug release of batches F13 – 17:

Time (Hour)	F13	F14	F15	F16	F17
0	0	0	0	0	0
1	12.72 ±0.26	14.17 ±0.33	23.53 ±0.33	19.69 ±0.46	18.85 ±0.34
2	19.43 ±0.49	22.67 ±0.15	25.30 ±0.23	26.56 ±0.27	31.41 ±0.26
3	30.10 ±0.23	29.64 ±0.19	33.41 ±0.17	36.40 ±0.34	39.87 ±0.39
4	39.32 ±0.12	36.43 ±0.34	34.79 ±0.08	47.35 ±0.50	45.71±0.11
5	44.41 ±0.34	42.61 ±0.54	36.92 ±0.15	54.22 ±0.40	53.63 ±0.36
6	48.55 ±0.70	45.40 ±0.40	38.65 ±0.50	56.72 ±0.33	54.44 ±0.39
7	51.81 ±0.46	53.61 ±0.43	41.86 ±0.27	57.38 ±0.34	57.33 ±0.30
8	54.38 ±0.43	55.59 ±0.37	48.76 ±0.36	61.31 ±0.23	58.87 ±0.31
9	56.38 ±0.23	56.48 ±0.35	51.26 ±0.52	63.73 ±0.44	62.74 ±0.19
10	57.40 ±0.40	60.44 ±0.45	56.54 ±0.38	66.70 ±0.30	64.57 ±0.41
11	59.39 ±0.24	63.52 ±0.35	57.36 ±0.46	67.51 ±0.34	67.22 ±0.32
12	64.77 ±1.11	66.73 ±0.36	58.84 ±0.37	69.34 ±0.16	72.13 ±0.10

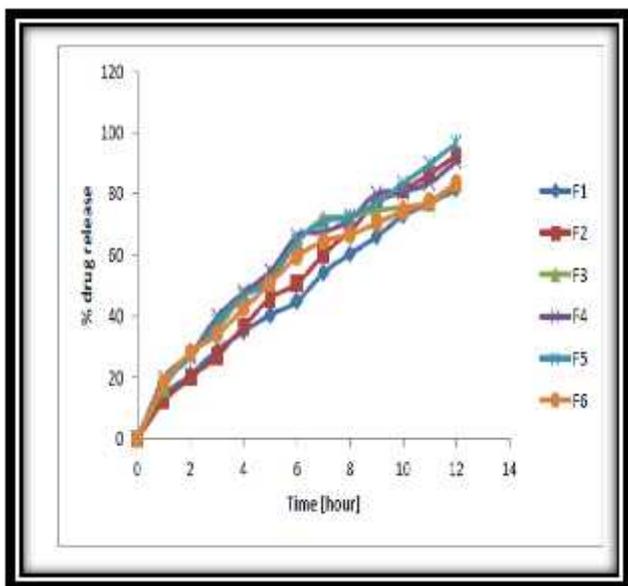


Figure 6: In-vitro drug release of batches F1-F6

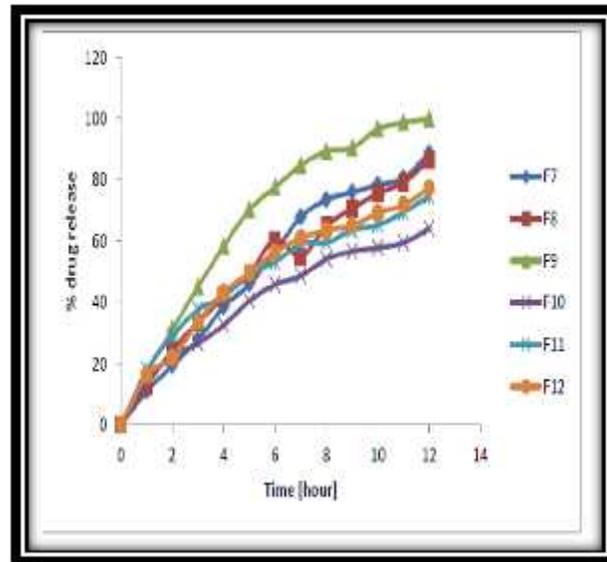


Figure 7: In-vitro drug release of batches F7-F12

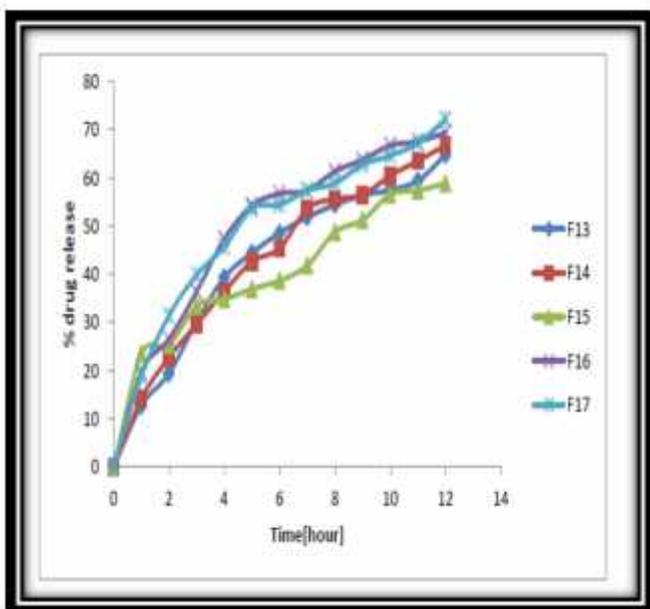


Figure 8: In-vitro drug release of batches F13-F17.

CONCLUSION

From the above study it was concluded that, carbopol 974-P, HPMC K100M were compatible with piroxicam based on the results obtained from compatibility studies and hence are suitable for formulation of mucoadhesive microspheres. Particle size of all microspheres was in the range suitable for administration by GI route. Also the mucoadhesion properties of all microspheres were good. Carbopol has higher mucoadhesion, swelling characters as well as higher entrapment efficiency as compared to HPMC. Whereas HPMC containing batches show higher drug release as compared to Carbopol. Finally it can be concluded that the mucoadhesive microspheres can be formulated successfully formulated by using Carbopol, HPMC K4M, HPMC K100M.

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