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DESIGN AND CHARACTERIZATION OF CELECOXIB FLOATING MICROSPHERES

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ABSTRACT

The purpose of the present investigation was to compare the characteristics of the bioadhesive microspheres of celecoxib prepared using different polymers : viz. Sodium alginate, Hpmc K15, Hpmc K100, HPMC K 4 M. Bioadhesive microspheres were prepared by ionotropic gelation method. Microspheres were characterized for entrapment efficiency, particle size, mucoadhesive property and in-vitro drug release was studied. The entrapment efficiency of the optimized formulation (T4)microspheres was significantly higher (88.66%) than other formulations. Particle size data was given 826 µm and In-vitro drug release studies indicated that the microspheresT4 containing Sodium alginate along with Hpmc K15as copolymer showed a maximum release of 94.66% after 12 hours. From dosage form, the in-vitro drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model.

KEYWORDS: ***Celecoxib, chitosan, cross-linking, encapsulation, microspheres***

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INTRODUCTION

For many decades, medication of an acute disease or a chronic disease has been accomplished by delivering drugs to the patients via various pharmaceutical dosage forms like tablets, capsules, pills, creams, ointments, liquids, aerosols, injectables and suppositories as carriers. To achieve and then to maintain the concentration of drug administered within the therapeutically effective range needed for medication, it is often necessary to take this type of drug delivery systems several times in a day. This results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency. This factor as well as other factors such as repetitive dosing and unpredictable absorption leads to the concept of controlled drug delivery systems[1,2]. The word new or novel in the relation to drug delivery system is a search for something out of necessity. An appropriately designed sustained or controlled release drug delivery system can be major advance toward solving the problem associated with the existing drug delivery system[3,4]. The objective of controlled release drug delivery includes two important aspects namely spatial placement and temporal delivery of drug.

1. Spatial placement relates to targeting a drug to a specific organ or tissue, while
2. Temporal delivery refers to controlling the rate of drug delivery to the target tissue[5].

In the ionotropic gelation method polysaccharid es (alginate, gellan and pectin) are dissolved in water or in weak acidic medium (chitosan). These solutions are then added drpowise under constant stirring to the solutions containing other counter ions. Due to the complexation between oppositely charge d species, polysaccharides undergo ionic gelation and precipitate to form sp herical particles.The beads are removed by filtration, washed with distilled water a nd dried. The method involves an all-aqueous system and avoids residual solvents in microspheres

Celecoxib is a newer anti-arthritic drug which is selective cyclo-oxygenase-II (COX-II) inhibitor. But, since COX-II is constitutively present in some organs and can be induced in other organs, selective COX-II inhibitors are not devoid of side effects. The side effects can be avoided by targeting the drug to the arthritic joints. One way of achieving higher concentrations in the joint for prolonged period of time is to inject the drug intra-articularly. In our pervious report [6], we have shown that post intra-articular injection, celecoxib incorporated chitosan microspheres are able to maintain significantly higher concentrations of the drug in the arthritic joint than the celecoxib solution. Thus, the present investigation was aimed to prepare an optimized formulation for use as an intra-articular injection. The effect of the different cross-linking agents on the characteristics of the microspheres was studied and a cross-linking agent which gave the desirable properties of the microspheres intended for intra-articular injection was chosen for *in-vivo* studies as reported earlier.

MATERIALS AND METHODS

The drug Celecoxib was gifted by Natco Pharma LtD.,Hyderabad, India. Sodium alginate, Hpmc K15,Hpmc K100,HPMC K 4 M was purchased from SD fine chemicals limited, India. All other chemicals and solvents were of analytical grade and used without further purification.

Method of Preparation

Ionotropic Gelation Method:

Batches of microspheres were prepared by ionotropic gelation method which involved reaction between sodium alginate and polycationic ions like calcium to produce a hydrogel network of calcium alginate. Sodium alginate and the mucoadhesive polymer were dispersed in purified water (10 ml) to form a homogeneous polymer mixture. The API, (100 mg) was added to the polymer premix and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added through a 22G needle into calcium chloride (4% w/v) solution. The addition was done with continuous stirring at 200rpm. The added droplets were retained in the calcium chloride solution for 30 minutes to complete the curing reaction and to produce rigid spherical microspheres. The microspheres were collected by decantation, and the product thus separated was washed repeatedly with purified water to remove excess calcium impurity deposited on the surface of microspheres and then air-dried.

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Table 1: Prepared formulation of Biooadhesive Microspheres

S.No.	Formulation code	Drug : Polymer ratio	Polymer Ratio
1	T_1	1:2.5	Na alginate:Hpmc K15 (1.5:0.5)
2	T_2	1:3	Na alginate:Hpmc K15 (2:1)
3	T_3	1:3.5	Na alginate:Hpmc K15 (2.5:1)
4	T_4	1:4	Na alginate:Hpmc K15 (3:1)
5	T_5	1:2.5	Na alginate:Hpmc K100 (1.5:0.5)
6	T_6	1:3	Na alginate:Hpmc K100 (2:1)
7	T_7	1:3.5	Na alginate:Hpmc K100 (2.5:1)
8	T_8	1:4	Na alginate:Hpmc K100 (3:1)
9	T_9	1:2.5	Na alginate:HPMC K 4M (1.5:0.5)
10	T_{10}	1:3	Na alginate:HPMC K 4 M (2:1)
11	T_{11}	1:3.5	Na alginate:HPMC K 4 M (2.5:1)
12	T_{12}	1:4	Na alginate:HPMC K 4 M (3:1)

Characterization of Microspheres:

Fourier Transform Infrared Spectroscopy (FT- IR):

In order to check the integrity (Compatibility) of dr ug in the formulation,FT-IR spectra of the formulations along with the drug and other exci pients were obtained and compared using Shimadzu FT-IR 8400 spectrophotometer.

In the present study, Potassium bromide(KBr) pellet method was employed. The samples were thoroughly blended with dry powdered potassium bromide crystals. The mixture was compressed to form a disc. The disc was placed in the spectrophotometer and the spectrum was recorded.The FT-IR spectra of the formulations were compared with the FT-IR spectra of the pure drug and the polymers.

Percentage Yield [7]:

The percentage of production yield was calculated from the weight of dried microsphe-res recovered from each batch and the sum of the initial weight of starting materials. The percentage yield was calculated using the following formula:

$$\% \text{ Yield} = \frac{\text{Practical mass (Microspheres)}}{\text{Theoretical mass (Polymer + Drug)}} \times 100$$

Drug entrapment efficiency [8]:

Microspheres equivalent to 15 mg of the drug Dulaxetine HCl were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres. The powder was transferred to a 100 ml volumetric flask and dissolved in 10ml of methanol and the volume was made up using simulated gastric fluid pH 1.2 . After 24 hours the solution was filtered through Whatmann filter paper and the absorbance was measured after suitable dilution spectrophotometrically at 269 nm. The amount of drug entrapped in the microspheres was calculated by the following formula,

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Experimental Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Particle size analysis [9]:

Samples of the microparticles were analyzed for particle size by optical microscope. The instrument was calibrated and found that 1unit of eyepiece micrometer was equal to 12.5µm. Nearly about 100 Microparticles sizes were calculated under 45x magnification.

The average particle size was determined by using t he Edmondson's equation:

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

Where,

n – Number of microspheres observed

d – Mean size range

Swelling study:

Swelling ratio of different dried microspheres were determined gravimetrically in simulated gastric fluid pH 1.2 .The microspheres were removed periodically from the solution, blotted to remove excess surface liquid and weighed on balance. Swelling ratio (% w/v) was determined from the following relationship:

$$\text{Swelling ratio} = \frac{(Wt - W0)}{(W0)} \times 100$$

Where W0 & Wt are initial weight and Final weight of microspheres respectively.

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Evaluation of mucoadhesive property:

The mucoadhesive property of microspheres was evaluated by an in vitro adhesion testing method known as wash-off method. Freshly excised pieces of goat stomach mucous were mounted on to glass slides with cotton thread. About 20 microspheres were spread on to each prepared glass slide andluble drugs. immediately thereafter the slides were II tablet disintegration test, when the test apparatus was operated, the sample is subjected to slow up and down movement in simulated gastric fluid pH 1.2 at 37 ^{0}C contained in a 1-litre vessel of the apparatus. At an interval of 1 hour up to 8 hours the machine is stopped and number of microspheres still adhering to mucosal surface was counted.

$$\% \text{ Mucoadhesion} = \frac{\text{Number of microspheres adhered}}{\text{Number of microspheres applied}} \times 100$$

In vitro drug release study:

The dissolution studies were performed in a fully calibrated eight station dissolution test apparatus (37 ± 0.5^{0}C, 50 rpm) using the USP type – I rotating basket method in simulated gastric fluid pH 1.2 (900ml). A quantity of accurately weighed microspher- es equivalent to 15mg Dulaxetine HCl each formulation was employed in all dissolution studies. Aliquots of sample were withdrawn at predetermined intervals of time and analyzed for drug release by measuring the absorbance at 269nm. At the same time the volume withdrawn at each time intervals were replenished immediately with the same volume of fresh pre- warmed simulated gastric fluid pH 1.2 maintaining sink conditions throughout the experiment.

In-Vitro Drug Release Kinetics

The release data obtained was fitted into various ma thematical models.The parameters ‘n’ and time component ‘k’,the release rate constant and ‘R’,the regression coefficient were determined by Korsmeyer- Peppas equation to understand the release mechanis m.

a. Zero Order

$$\% R = kt$$

This model represents an ideal release in order to achieve prolonged pharmacological action.

This is applicable to dosage forms like transderm al systems, coated forms, osmotic systems, as well as Matrix tablets containing lowso hung to USP

b. First Order

$$log (fraction\ unreleased) = kt/2.303$$

The model is applicable to hydrolysis kinetics a nd to study the release profiles of pharmaceutical dosage forms such as those containing water soluble drugs in porous matrices.

c. Matrix (Higuchi Matrix)

$$\% R = kt^{0.5}$$

This model is applicable to systems with drug disp ersed in uniform swellable polymer matrix as in case of matrix tablets with water solubl e drug.

d. Peppas Korsmeyer Equation

$$\% R = kt^{n}$$
$$log \% R = logk + nlogt$$

This model is widely used when release mechanism is well known or when more than one type of release phenomenon could be involved.

RESULTS AND DISCUSSION

Compatibility Studies

Drug polymer compatibility studies were carried out using Fourier Transform Infra Redspectroscopy to establish any possible interaction of Celecoxib with the polymers used in the formulation. The FT- IR spectra of the formulations were compared with the FTIR spectra of the pure drug. The results indicated that the characteristic absorption peaks due to pure Celecoxib have appeared in the formulated microspheres, without any significant change in their position after successful encapsulation, indicating no chemical interaction betweencelecoxib and Polymers results were shown in figures 1-4.

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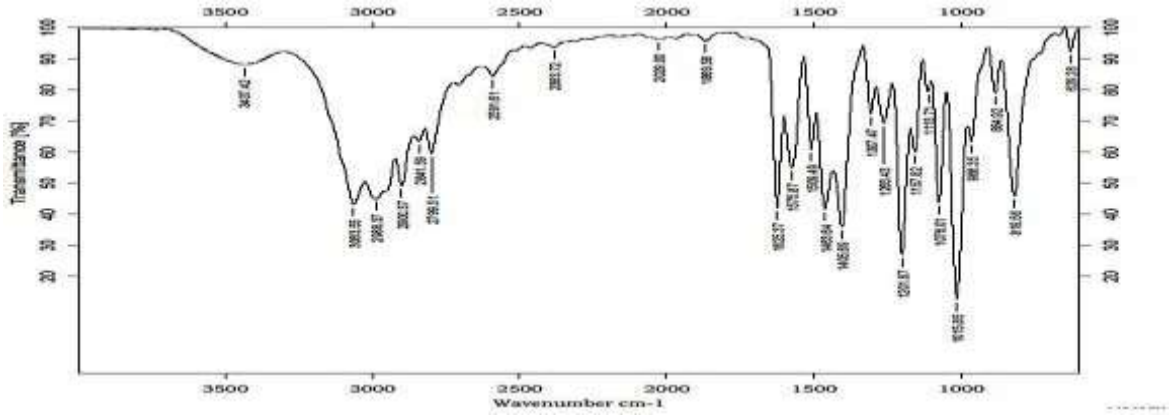

Fig 1: FT-IR spectra of Celecoxib

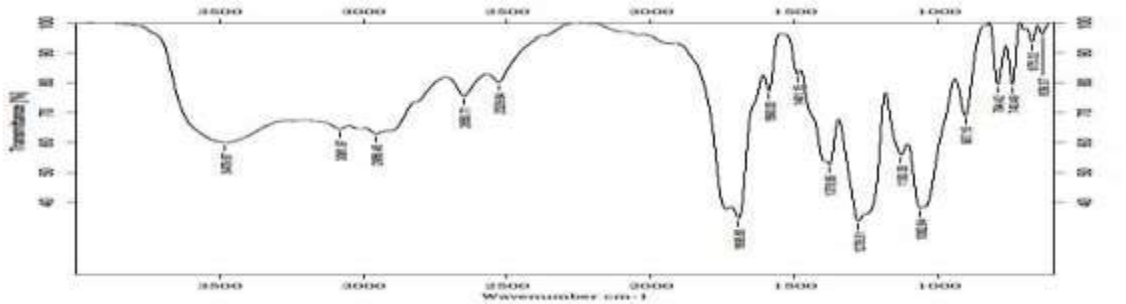

Fig 2: FT-IR spectra of Celecoxib +Sodium alginate

Fig 3: FT-IR spectra of Celecoxib +Hpmc K15

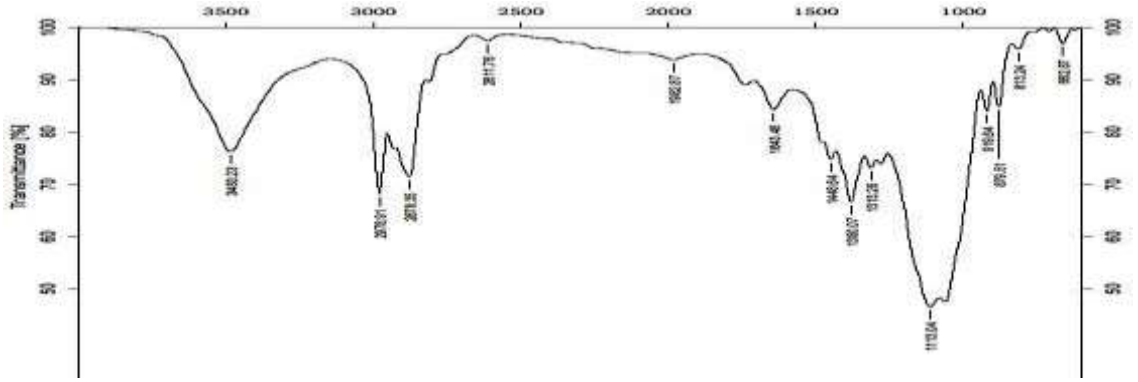

Fig 4: FT-IR spectra of Celecoxib +Hpmc K15+Sodium alginate

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Evaluation and Characterisation of Microspheres Percentage Yield

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug- polymer solution, adhesion of polymer solution to the magnetic bead and microspheres lost during the washing process. The percentage yield was found to be in the range of 80 to 88% for microspheres containing sodium alginate along with Hpmc K15 as copolymer,

62.22 to 87% for microspheres containing sodium alginate along with Hpmc K100 as copolymer and 80 to 87.5% for microspheres containing sodium alginate along with HPMC K 4 M as copolymer. The percentage yield of the prepared microspheres is recorded in Table 6.3 and displayed in Figures 6.7 to 6.9.

Percentage Drug entrapment efficiency of Celecoxib ranged from 82.66 to 88.66% for microspheres containing sodium alginate along with Hpmc K15 ascopolymer, 53.2 to 76.66% for microspheres containing sodium alginate along with Hpmc K100 as copolymer and66.73 to 79.2% for microspheres containing sodiumalginate along with HPMC K 4 M as copolymer. The drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higherentrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 2.

Drug Entrapment Efficiency

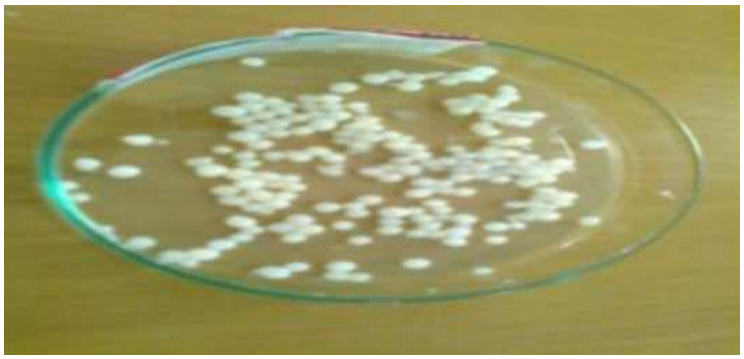

Fig 5: Photograph of prepared microsphere

Table 2: Percentage yield and percentage drug entrapment efficiency of the prepared microspheres

S.No.	Formulation code	% yield	Drug Content (mg)	% Drug entrapment efficiency
1	T_1	80	12.40	82.66
2	T_2	83.33	12.66	84.4
3	T_3	85	12.70	84.66
4	T_4	88	13.29	88.66
5	T_5	62.22	8.07	53.2
6	T_6	80	8.25	55
7	T_7	80	10.33	68.86
8	T_8	87	11.5	76.66
9	T_9	80	10.01	66.73
10	T_{10}	86	10.5	70
11	T_{11}	86.66	11.25	75
12	T_{12}	87.5	11.88	79.2

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Particle Size Analysis

The mean size increased with increasing polymer concentration which is due to a significant increase in the viscosity thus leading to an increased droplet size and finally a higher microspheres size. Microspheres containing sodium alginate along with Hpmc K15 as copolymer had a size range of 512µ m to 826µm, microspheres containing sodium alginate along with Hpmc K100 as copolymer exhibited a size range between 517µ m to 834µm and microspheres containing sodium alginate along with HPMC K 4 M as copolymer had a size range of 664µ m to 903µm. The particle size data is presented in Tables 6.4 to 6.15 and displayed in Figure 6.10 to 6.12. The effect of drug to polymer ratio on particle size is displayed in Figure 6.13 . The particle size as well as % drug entrapment efficiency of the microspheres increased with increase in the polymer concentratio n results were shown in figure 6..

Swelling Ratio

The swelling ratio is expressed as the percentage of water in the hydrogel at any instant during swelling. Swell ability is an important characteristic as it affects mucoadhesion as well as drug release profiles of polymeric dru g delivery systems. Swell ability is an indicative parameter for rapid availability of drug solution for diffusion with greater flux. Swell ability data revealed that amount of polymer plays an important role in solvent transfer.It can be concluded from the data shown in Table 3 that with an increase in polymer concentration, the percentage of swelling also increases. Thus we can say that amount of polymer directly affects the swelling ratio.As the polymer to drug ratio increased, the percentage of swelling increased from 28to 85%formicrospheres containing sodium alginate along with Hpmc K15 as copolymer, 24 to 64% for microspheres containing sodium alginate alongwith Hpmc K100 as copolymer and 31 to 85 for microspheres containing sodium alginate along with HPMC K 4 M as copolymer.

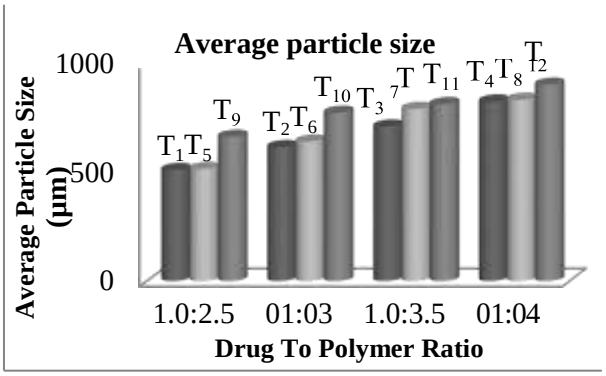

Fig 6: Comparison of average particle size of prepared microspheres

Table 3: Percentage swelling of the prepared microspheres

S.NO.	Formulation Code	Initial (wt)	Final (wt)	Percentage Swelling
1	T_1	10	12.8	28
2	T_2	10	14.2	42
3	T_3	10	16.2	62
4	T_4	10	18.5	85
5	T_5	10	12.4	24
6	T_6	10	13.9	39
7	T_7	10	15.5	55
8	T_8	10	16.4	64
9	T_9	10	13.1	31
10	T_{10}	10	15.3	53
11	T_{11}	10	16.7	67
12	T_{12}	10	18.5	85

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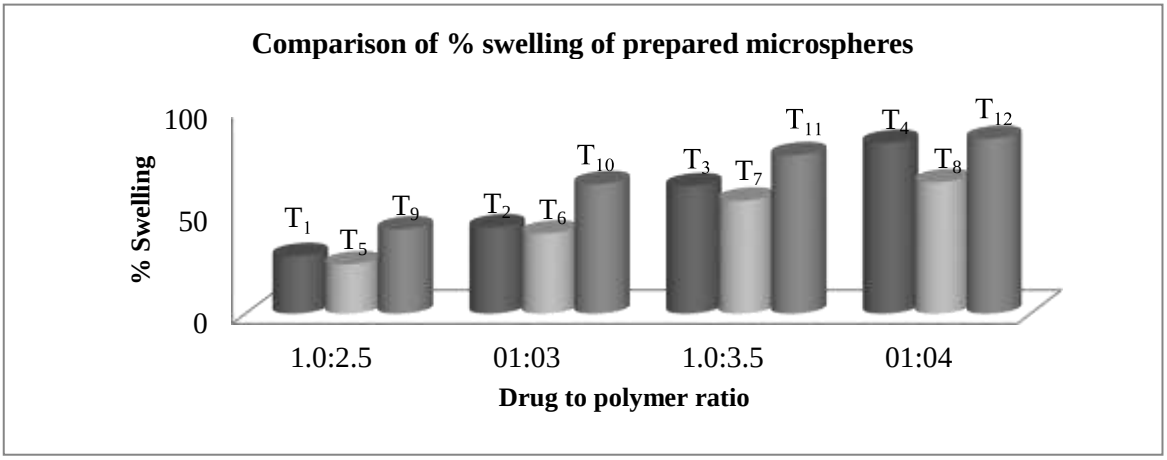

Fig 7: Comparison of % swelling of prepared microspheres

***In-Vitro* Mucoadhesion Test**

As the polymer to drug ratio increased, microspheres containing sodium alginate along with Hpmc K15 as copolymer exhibited % mucoadhesion ranging from 65 to 85%, microspheres containing sodium alginate along with Hpmc K100 as copolymer exhibited % mucoadhesion ranging from 60 to 75% and microspheres containing sodium alginate along with HPMC K 4 M as copolymer exhibited % mucoadhesion ranging from 60 to 80%.

The rank of order of mucoadhesion is Hpmc K15 > HPMC K 4 M > Hpmc K100. The results of *in-vitro* mucoadhesion test are compiled in Table 4. Effect of polymer proportion on % mucoadhesion is depicted in Fig. 6.20 to 6.22 and comparative depiction of % mucoadhesion is depicted in Figure 8.

Table 4: Percentage mucoadhesion of the prepared microspheres

S.NO.	Formulation Code	No. Of microspheres		Percentage Mucoadhesion
		Initial	Final	
1	T_1	20	13	65
2	T_2	20	14	70
3	T_3	20	15	75
4	T_4	20	17	85
5	T_5	20	12	60
6	T_6	20	13	65
7	T_7	20	14	70
8	T_8	20	15	75
9	T_9	20	12	60
10	T_{10}	20	14	70
11	T_{11}	20	15	75
12	T_{12}	20	16	80

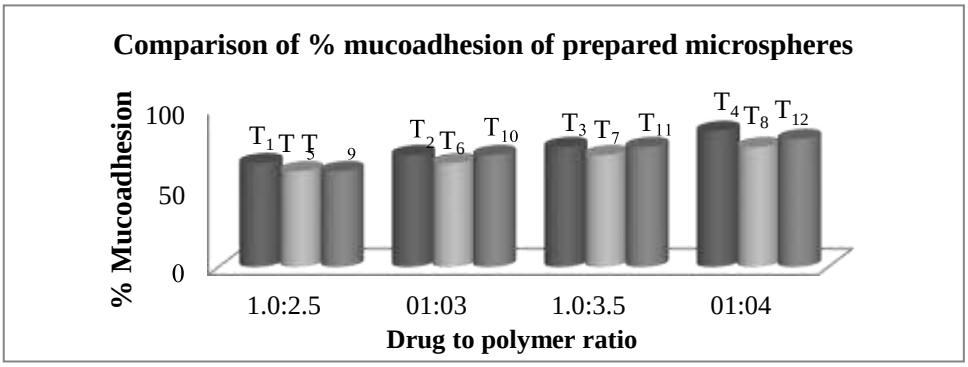

Figure 8: Comparison of percentage mucoadhesion of prepared microspheres

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In-Vitro Drug Release Studies

Dissolution studies of all the formulations were carr ied out using dissolution apparatus USP type I. The dissolution studies were conducted by using dissolution media, pH 1.2. The results of the in-vitro dissolution studies of formulations T_1 to T_4, T_5 to T_8 and T_9 to T_{12} are shown in table 5,6,7 and 8. The plots of Cumulative percentage drug release Vs Time. Figure 6.24 shows the comparison of % CDR for formulations T_1 to T_4, figure 6.25 for formulations T_5 to T_8 and figure 6.26 for formulations T_9 to T_{12}. Korsmeyer-Peppas plots of Celecoxib microspheres formulations T_1 to T_{12} are displayed in figures 9,10 and 11. The formulations T_1, T_2, T_3 and T_4 containing Sodium alginate along with Hpmc K15 as copolymer showed a maximum release of 92.66% after 9 hours, 90.66% after 10 hours, 90.6%after 11 hours and 94.66% after 12 hours respectively. The formulations T_5, T_6, T_7 and T_8 containing Sodium alginate along with Hpmc K100 as copolymer showed a maximum release of 92.22% after 9 hours, 91.33% after 10 hours,

89.55% after 11 hours and 90.66% after 12 hours respectively. The formulations T_9, T_{10}, T_{11} and T_{12} containing Sodium alginate along with HPMC K 4 M as copolymer showed a maximum release of 92.6% after 9 hours, 91.3% after 10 hours, 90% after 11 hours and 92.44% after 12 hours respectively. This shows that more sustained release was observed with the increase in percentage of polymers. As the polymer to drug ratio was increased the extent of drug release decreased. A significant decrease in the rate and extent of drug release is at tributed to the increase in density of polymer matrix that results in increased diffusion path length which the drug molecules have to traverse. The releaseof the drug has been controlled by swelling control release mechanism. Additionally, the larg er particle size at higher polymer concentration also restricted the total surface area re sulting in slower release.

TIME (h)	Cumulative Precent Of Drug Released			
	T_1	T_2	T_3	T_4
0	0	0	0	0
1	24.88	21.11	18.66	15.88
2	31.55	31.55	25.11	24.22
3	42.44	39.77	35.44	32.66
4	53.55	47.77	40.66	39.33
5	62	56.66	52	47.55
6	74.66	62.44	57.33	55.77
7	83.55	69.55	63.11	61.77
8	89.33	75.33	69.11	69.55
9	92.66	84.66	75.33	77.55
10	85.55	90.66	82.66	85.55
11	80.22	84.22	90.66	90.66
12	78.88	80.88	89.55	94.66

Table 5: *In-Vitro* drug release data of Celecoxib microspheres containing sodium alginate along with Hpmc K15 as copolymer

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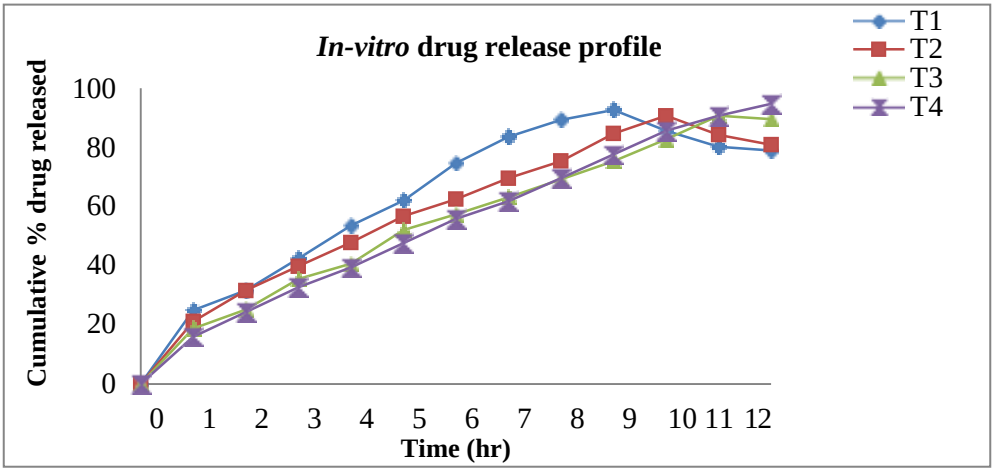

Fig 9: Comparison of *In-Vitro* drug release profile of Celecoxib microspheres containing sodium alginate along with Hpmc K15 as copolymer

Table 6: *In-Vitro* drug release data of Celecoxib microspheres containing sodium alginate along with Hpmc K100 as copolymer

Time (h)	Cumulative Precent Of Drug Released			
	T_5	T_6	T_7	T_8
0	0	0	0	0
1	27.77	22.44	18.44	17.11
2	36.44	32.22	29.33	26.44
3	43.77	40.88	39.55	37.55
4	54.66	48.66	45.55	46.88
5	64.01	57.55	57.33	55.77
6	75.77	63.55	65.33	63.55
7	84.65	70.44	71.55	71.33
8	90	76.55	77.56	75.77
9	92.22	85.55	81.55	79.77
10	84.88	91.33	83.33	82.44
11	79.55	85.77	89.55	86.88
12	77.55	81.11	87.55	90.66

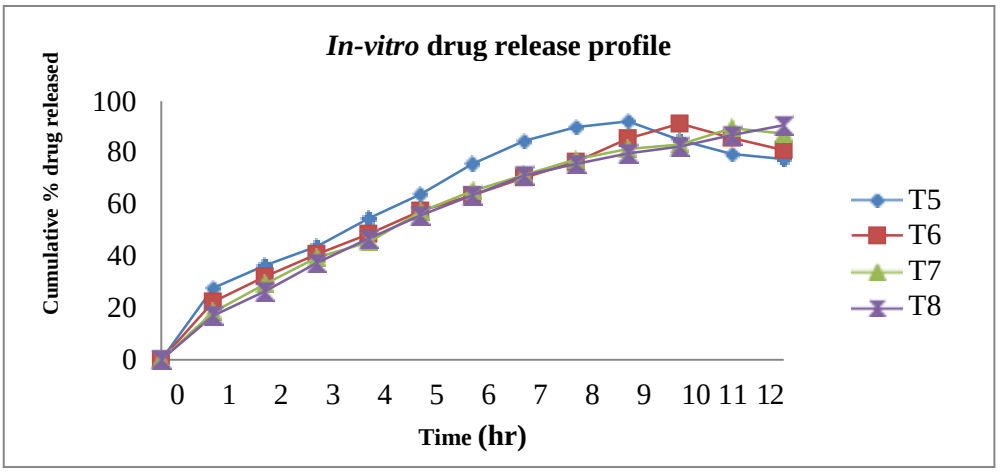

Fig 10: Comparison of *In-Vitro* drug release profile of Celecoxib microspheres containing sodium alginate along with Hpmc K100 as copolymer

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Table 7: *In-Vitro* drug release data of Celecoxib microspheres containing sodium alginate along with HPMC K 4 M as copolymer

Time (h)	Cumulative precent of drug released			
	T_9	T_{10}	T_{11}	T_{12}
0	0	0	0	0
1	25.77	21.55	18.66	16.44
2	35.33	31.77	26.55	27.11
3	43.55	40.44	36.55	36.44
4	54	48.44	43.66	45.55
5	63.55	57.11	54.55	55.33
6	75.33	63.11	62.33	63.11
7	84	70.22	67.68	71.55
8	89.77	76	73.55	76.44
9	92.66	85.11	78.55	80.66
10	85.11	91.33	83	85.55
11	80.66	85.33	90	89.55
12	78	81.11	87.55	92.44

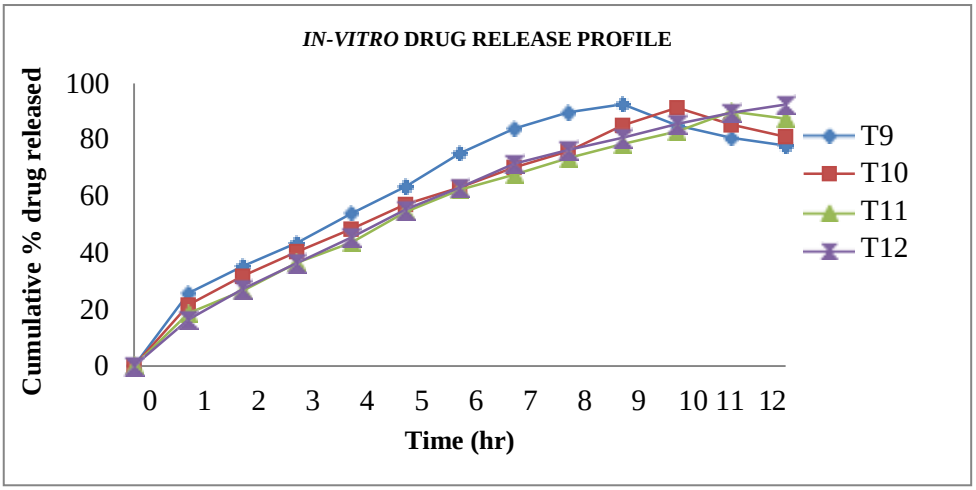

Fig 11: Comparison of *In-Vitro* drug release profile of Celecoxib microspheres containing sodium alginate along with HPMC K 4 M as copolymer

In-Vitro Drug Release Kinetics

For understanding the mechanism of drug release a nd release rate kinetics of the drug from dosage form, the in-vitro drug dissolution data obtained was fitted to va rious mathematical models such as zero order, First order, Higuchi mat rix, and Krosmeyer-Peppas model. The values are compiled in Table 6.21. The coefficient of determination (R^2) was used as an indicator of the best fitting for each of the models considered. The kinetic data analysis of all the formulations reached higher coefficient of determination with the Korsmeyer-Peppas model (R^2 = 0.914 to 0.996) whereas release exponent value (n) ranged from 0.498 to 0.743. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows Korsmeyer-Peppas model along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion.

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Table 8: Release Kinetics Studies of The Prepared Formulations

Formulation code	Release model								
	Zero order		First order		Higuchi matrix		Koresmeyer-peppas		
	K	R^2	K	R^2	K	R^2	n	K	R^2
T_1	21.6	0.797	1.923	0.720	-0.313	0.912	0.556	1.388	0.925
T_2	16.39	0.908	1.991	0.890	-3.945	0.970	0.595	1.326	0.983
T_3	10.45	0.976	2.062	0.945	-8.966	0.975	0.673	1.233	0.991
T_4	7.434	0.990	2.118	0.914	-12.25	0.962	0.743	1.171	0.996
T_5	24.34	0.768	1.897	0.689	2.624	0.903	0.498	1.442	0.914
T_6	17.19	0.904	1.990	0.885	-3.333	0.971	0.579	1.346	0.981
T_7	14.53	0.936	2.018	0.985	-6.239	0.983	0.655	1.278	0.990
T_8	13.06	0.948	2.032	0.991	-7.587	0.984	0.690	1.241	0.991
T_9	23.20	0.783	1.909	0.704	1.336	0.909	0.526	1.418	0.925
T_{10}	16.73	0.906	1.992	0.885	-3.771	0.970	0.591	1.334	0.982
T_{11}	12.50	0.957	2.036	0.974	-7.640	0.982	0.667	1.253	0.993
T_{12}	11.94	0.959	2.061	0.982	-8.986	0.981	0.712	1.226	0.995

CONCLUSION

In the present work, bioadhesive microspheres of Celecoxib using Sodium alginate along with Hpmc K15, Hpmc K100, HPMC K4M as copolymers were formulated to deliver Celecoxib via oral route. FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers and copolymers used. Micromeritic studies revealed that the mean particle size of the prepared microspheres was in the size range of 512-903µm and are suitable for bioadhesive microspheres for oral administration. Increase in the polymer concentration led to increase in % Yield, % Drug entrapment efficiency, Particle size, % swelling and % Mucoadhesion. The *in-vitro* mucoadhesive study demonstrated that microspheres of Celecoxib using sodium alginate along with Carbopol934 as copolymer adhered to the mucus to a greater extent than the microspheres of Celecoxib using sodium alginate along with Hpmc K100 and HPMC K4M as copolymers. The *invitro* drug release decreased with increase in the polymer and copolymer concentration. Analysis of drug release mechanism showed that the drug release from the formulations followed non-Fickian diffusion and the best fit model was found to be Korsmeyer-Peppas. Based on the results of evaluation tests formulation coded T_4 was concluded as best formulation. The optimsied Formulation microspheres were packed in hard gelatin capsule shells.

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