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Preparation and evaluation of aceclofenac mucoadhesive microspheres

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ABSTRACT

Aceclofenac is an effective analgesic and anti-inflammatory agent with a good tolerability profile through its analgesic and anti-inflammatory properties relief in a variety of painful conditions. The objective of the present study was to prepare the mucoadhesive microspheres of aceclofenac. These were developed to reduce the side effects like gastric irritation and to increase the drug bioavailability, to reduce the frequency of dosing and to enhance patient compliance. The microspheres were prepared by orifice-ionotropic gelation method using polymers such as HPMC (K 15 M, K 100 M, 100 cps), Carbopol 940, Sodium CMC, Guar gum, Sodium Alginate, Ethyl Cellulose, Methyl Cellulose and 10% Calcium Chloride solution. Totally 16 different formulations of aceclofenac were prepared by using the above polymers in 1:1 and 9:1 ratios. Finally, the microspheres were evaluated for various characteristics like drug content, encapsulation efficiency, percent mucoadhesive strength and the in vitro release was evaluated for 10 hrs. The Microspheres were institute to be detached, spherical, free-flowing, and of the monolithic matrix type. The microspheres were uniform in size, with a mean size of 73.21 to 98.35 µm. The microencapsulation efficiency was in the range of 68% to 86%. Microspheres with a coat consisting of sodium alginate and a mucoadhesive polymer exhibited good mucoadhesive properties in the Ex Vivo wash-off test. Aceclofenac release from the microspheres was slow and depended on the composition of the coat. Release followed zero-order kinetics (R2 =0.971). The order of decreasing release rate observed with various microspheres was F9 > F7 > F1 > F2 > F3 > F10 > F11 > F4 > F12 > F14 > F13 > F5 > F8> F6 > F16 > F15. The differences in the drug release characteristics of various microspheres are due to the differences in the porosity of the coat formed and its solubility in the dissolution fluid.

Keywords: Aceclofenac, Mucoadhesive microspheres, Carbopol 940, Sodium CMC, Guar gum, Sodium Alginate, Ethyl Cellulose, Methyl Cellulose

INTRODUCTION

In recent times the novel dosage forms which can switch the release rate and target the vigorous drug molecule to a particular site have conquered a prodigious formulation interest. Microspheres are one of the novel drug delivery systems which retain pretty a lot of solicitations and are made up of various polymers. Microspheres are the carrier linked drug delivery system in which particle size ranges from 1-1000 µm range in diameter devouring a core of drug and utterly outer layers of a polymer as a coating material. Adherence of a polymeric material to biological surfaces is known as bio-adhesion or to the mucosal tissue is notorious as mucoadhesion. Mucin is the utmost imperative glycoprotein of mucus and is liable for its structure. The mucin is poised principally of flexible glycoprotein chains, which are cross-linked. The formation of non-covalent bonds such as hydrogen bonds and ionic interactions or physical entanglements between the mucus gel layer and polymers provides a good mucoadhesion[1]. A mucoadhesive controlled release expedient can expand the efficacy of the drug concentration amid the operative and toxic levels, inhibiting the dilution of the drug in the body fluids, and countenancing targeting and localization of a drug at a specific site. A drug can be incorporated into a cross-linked

polymeric device that would adhere to a mucous substrate in the body. The drug can then diffuse from the device directly into the tissues[2]. Mucoadhesion also increases the intimacy and duration of contact between a drug-containing polymer and mucous surface. The combined effects of the direct drug absorption and the decrease in excretion rate allow for increased bioavailability of drug with smaller doses and less frequent administration[3].

Aceclofenac seems to be predominantly well-abided midst the NSAIDS with a lower prevalence of gastrointestinal adverse effects. This good tolerability profile results in a reduced withdrawal rate and greater compliance with treatment. Aceclofenac is a potent inhibitor of the enzyme cyclooxygenase, which is involved in the production of prostaglandins[4]. The drugs inhibit the synthesis of the inflammatory cytokines interleukin (IL)-1 and tumour necrosis factor and prostaglandin E_2 (PGE2) production. Effects on cell adhesion molecular from neutrophils have noted. In vitro data indicate inhibition of cyclooxygenase (cox)-1 and 2 by aceclofenac in whole blood assays, with selectivity for cox–2 being evident[5].

The present study is a approach for the development of mucoadhesive microspheres of aceclofenac to enhance its oral bioavailability and efficacy.

MATERIALS AND METHODS

Aceclofenac (Acl), Carbopol 940P (C940p), HPMC 100 cps, HPMC K 15 M, HPMC K 100 M, Ethyl cellulose (EC), Guar gum, Methyl cellulose (MC), Sodium.CMC and Sodium alginate were received as a gift sample from Research laboratories, Hyderabad, India.

Preformulation studies

Calibration Curve of Aceclofenac

100mg of aceclofenac pure drug was dissolved in 20 to 30 ml of alcohol then make upto 100ml with pH 7.4 phosphate buffer (stock solution 1000 µg/ml), from this 10ml of the solution was taken and made up to100ml pH 7.4 phosphate buffer (100µg/ml). From this 10ml was taken and made up to 100 ml with pH 7.4 phosphate buffer (10µg/ml) and absorbance was measured at 273 nm.

Compatibility studies of drug and polymers

FTIR Studies

FTIR of Aceclofenac and other polymers was detailed with a KBr disc over the wave No. 4000 to 400 cm-1[6].

Preparation of Mucoadhesive Microspheres

All the formulations were prepared by orifice ionic gelation method. The formulas of different formulations are given in Table 1. The microspheres were prepared as per the procedure given below and the aim is to prolong the release of aceclofenac. Aceclofenac and all other polymers were individually passed through sieve no 60. Sodium alginate (1.0 g) and mucoadhesive polymer (1.0 g) were dissolved in purified water (32 ml) to form a homogenous polymer solution. The active substance, aceclofenac (1.0 g), was added to the polymer solution and mixed thoroughly with a stirrer to form a viscous dispersion.

The resulting dispersion was then auxiliary physically dropwise into calcium chloride (10 % W/V) solution (40 ml) over a syringe with a needle of size no. 18. The added droplets were retained in the calcium chloride solution for 15 minutes to complete the curing reaction and to produce spherical rigid microspheres. The microspheres was poised by decantation, and the product thus alienated and was washed frequently with water and dried at 45ºC for 12 hours. Table 1

Table 1: Composition of different formulations

F. No. (Ratio)	Acl. (mg)	HPMC 100 cps (mg)	HPMC K15M (mg)	HPMC K100M(mg)	EC (mg)	Sodium CMC (mg)	MC (mg)	Guar gum (mg)	C940p (mg)	Sodium Alginate (mg)
F1(1:1)	1000	-----	-----	-----	1000	-----	-----	-----	-----	1000
F2(1:1)	1000	-----	-----	-----	-----	1000	-----	-----	-----	1000
F3(1:1)	1000	-----	-----	-----	-----	-----	-----	-----	-----	1000
F4(1:1)	1000	-----	-----	-----	-----	-----	-----	1000	-----	1000
F5(1:1)	1000	-----	-----	-----	-----	-----	1000	-----	-----	1000
F6(1:1)	1000	-----	-----	-----	-----	-----	-----	-----	1000	1000
F7(1:1)	1000	1000	-----	-----	-----	-----	-----	-----	-----	1000
F8(1:1)	1000	-----	1000	-----	-----	-----	-----	-----	-----	1000
F9(1:1)	1000	-----	-----	1000	-----	-----	-----	-----	-----	1000
F10(1:9)	1000	-----	-----	-----	100	-----	-----	-----	-----	900
F11(1:9)	1000	-----	-----	-----	-----	100	-----	-----	-----	900
F12(1:9)	1000	-----	-----	-----	-----	-----	-----	100	-----	900
F13(1:9)	1000	-----	-----	-----	-----	-----	100	-----	-----	900
F14(1:9)	1000	-----	-----	-----	-----	-----	-----	-----	100	900
F15(1:9)	1000	-----	100	-----	-----	-----	-----	-----	-----	900
F16(1:9)	1000	-----	-----	100	-----	-----	-----	-----	-----	900

Evaluation of Microspheres

Drug content

Preparations equivalent to 50 mg was weighed accurately and transferred to 100 ml volumetric flask and dissolved in pH 7.4 phosphate buffer. The volume was made up with pH 7.4 phosphate buffer up to the mark. After suitable dilution, the absorbance of the above solution was measured at 273 nm using an appropriate blank solution. The drug content of aceclofenac was calculated using calibration curve[6].

Particle size analysis

Microscopic imaging analysis technique was used for the determination of particle size. Microsphere size and distribution were determined with an AXIOPALN microscope equipped with a computer-controlled image analysis system[7].

Microencapsulation Efficiency (ME)

Microencapsulation efficiency was calculated using the following formula[8]:

M E = (estimated percentage drug content/theoretical percentage drug content) × 100.

Swelling index

The swelling ability of the microspheres in physiological media was determined by swelling them to their equilibrium[7]. Precise amounts of microspheres were immersed in a little excess of Phosphate buffer (pH 7.4) and kept for 24 h. Data were presented as mean± SEM of three observations calculated at 95% confidence level (p=0.5). It was calculated using the formula:

Swelling index= (mass of swollen microspheres - a mass of dry microspheres/mass of dried microspheres) X 100.

Scanning electron microscope (SEM)

A scanning electron microscope (ESEM TMP with EDAX, Philips, and Holland) was used to characterize the surface topography of the microscope. The microspheres were retained on a metallic backing with a thin adhesive tape and microspheres were coated with gold under vacuum. The surface was scanned, and photographs were taken at 30kV accelerating voltage for the drug-loaded microspheres[9, 10].

Mucoadhesion Testing by Ex Vivo Wash-Off Test

The mucoadhesive property of the microspheres was evaluated by an in vitro adhesion testing method known as the wash-off method. Freshly excised pieces of the intestinal mucosa (2×2 cm) from sheep were mounted on to glass slides (3×1inch) with cyanoacrylate glue. Two glass slides stood allied with a seemly backing. Almost 20 microspheres remain spread onto each wet rinsed tissue specimen and proximately advanced the backing was hung onto the arm of a USP tablet disintegrating test machine[11]. When the disintegrating test machine was run, the tissue specimen was particular a relaxed, steady up-and-down movement in the test fluid at 37°C enclosed in a 1 L vessel of the machine. At the end of 30 minutes, at the end of 1 hour, and at hourly intervals up to 10 hours, the machine was stopped and the number of microspheres still adhering to the tissue was counted. The test was performed at intestinal pH (pH7.4 phosphate buffer)[12].

In Vitro Dissolution Studies

900ml 0f pH 7.4 phosphate buffer was placed in the vessel, and the USP apparatus –II (Paddle Method) was assembled. The medium was endorsed to equilibrate to the temperature of 37°C+0.5°C. Microspheres were placed in the vessel, and the vessel was covered, the apparatus was operated for 10 hrs at 50 rpm[13]. A definite time intervals of 5 ml of the dissolution fluid was withdrawn, filtered, and again 5ml blank sample was replaced. Suitable dilutions were done with dissolution fluid and analyzed spectrophotometrically at 273 nm (λ max) using a UV-spectrophotometer (Analytical).

Similarity Factor (S F (f2))

This is used for the Performance difference between the Two Identical Dosage Compounds. If the value further than 50, it is similar (f2) and less than 50 it is Dissimilar (f1). Similarity factor was calculated by using following formula

$$f2 = 50.\ \log\ \{\ [1 + (\ 1/n)\ \textstyle\sum_{t=1}^{n} (R_t - T_t)^2\ ]^{-0.5}\ .\ 100\}$$

Where 'R_t' and 'T_t' are the cumulative percentage dissolved at each of the selected n time points of the reference & test product, respectively. Whereas factor f2 is inversely proportional to the averaged squared difference between the two profiles, with emphasis on the larger difference among all the time points[14]. The similarity factor f2 and its significance, if (f2) <50 represents Test and reference profiles are dissimilar, (f2) 50 -100 represents Test and reference profiles are similar, (f2) 100 represents Test and reference profiles are identical, and if (f2) >100 represents The equation yields a negative value.

Release kinetics

To understand the mechanism and kinetics of drug release[15], the results of the *in vitro* drug release study were fitted with various kinetic equations namely zero-order (% release vs time), first-order (log% unreleased vs time), and Higuchi matrix (% release vs square root of time). To define a model which will represent a better fit for the formulation, drug release data further analyzed by Peppas equation, $Mt/M\infty=ktn$, where Mt is the amount of drug released at time t and M∞ is the amount released at time ∞, the Mt/M∞ is the fraction of drug released at time t, k is the kinetic constant and n is the diffusion exponent, and extent of the principal mechanism of drug release. Regression coefficient

(r^2) values were calculated for the linear curves obtained by regression analysis of the above plots[16].

Stability studies

The persistence of stability testing is to run substantiation on exactly how the quality of a drug substance or drug product diverges with time. The impact of aspects such as temperature, humidity and light that can estimate and acclaim apt storage conditions, retest periods and shelf lives to be reputable. In the contemporary study, stability studies were conceded out at $40^0C \pm 2^0C$ / 75 ± 5 % RH for a specific period up to 30 days for the selected formulations[17]. Fig 1

RESULTS AND DISCUSSION

Preformulation studies

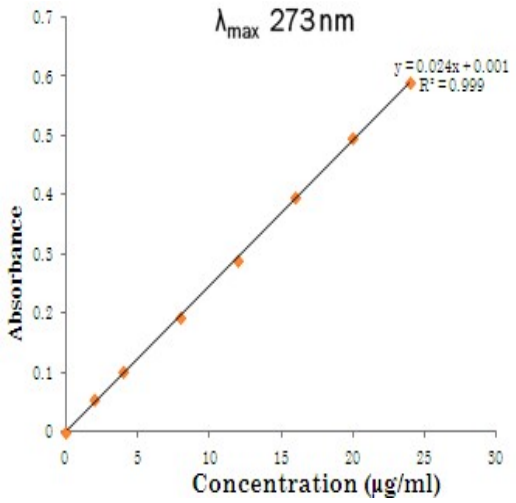
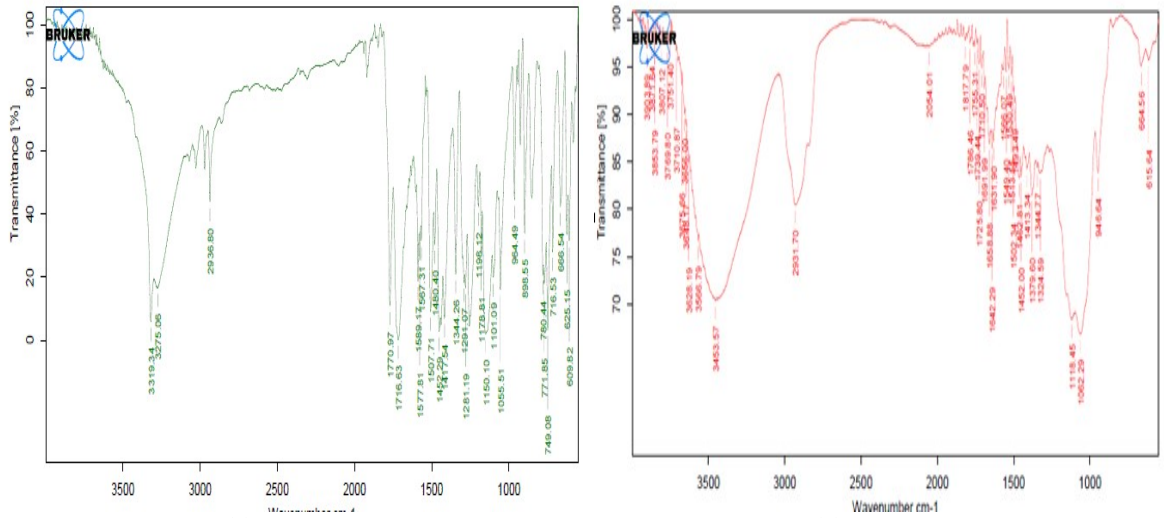


Fig. 1: Calibration Curve of Aceclofenac

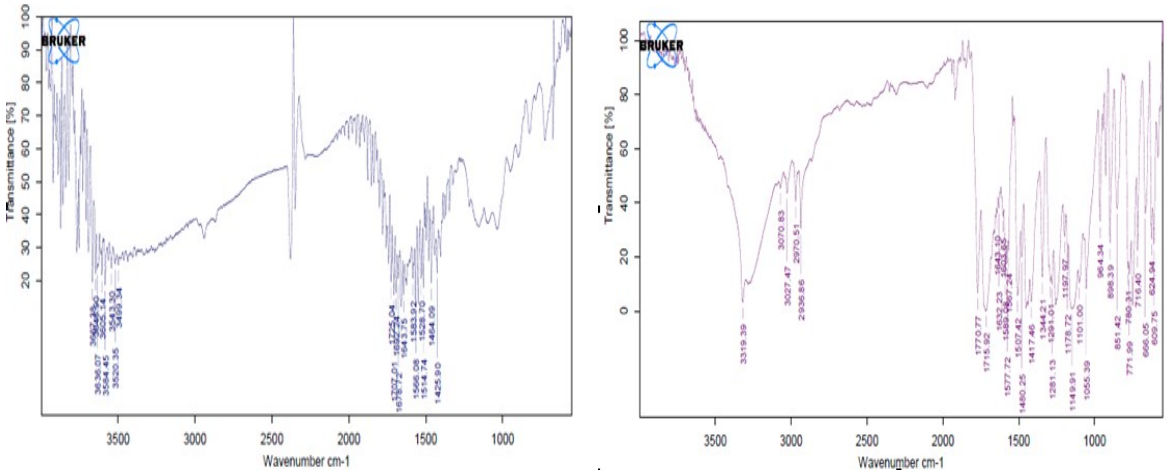
Compatibility studies of drug and polymers

FTIR Studies

From the infrared spectra, it is evident that there was no interaction of the drug. IR Spectrum of the pure drug shows the characteristic peaks at 3319.34 cm-1, 1770.97 cm-1 and 1716.63 cm-1. The IR Spectrum of Drug and polymer exhibited peaks at 3319.39 cm-1, 1770.77 cm-1 and 1715.92 cm-1. This confirms the undisturbed structure of the drug in the formulation. This proves the fact that there is no potential incompatibility of the drug with the polymers used in the formulations. Hereafter, the formula for preparing aceclofenac mucoadhesive microspheres can be replicated deprived of any dread of probable drug-polymer interactions. Fig 2



(a) **(b)**



(c) **(d)**

Fig.2: IR spectra of (a)-Aceclofenac (b)-HPMC K 15 M (c)-sodium alginate (d)-physical mixture

Evaluation Parameters

Drug content

It was in the range of 34-43% and represented in Table 2. F15 shows great drug content, among other formulations.

Particle size

The handling variables such as a drug to polymer ratio, stirring speed, stabilizer concentration affect the particle size of microspheres. The drug to polymer ratio seemed to impact on the particle size distribution of microspheres. When drug to polymer ratio was amplified from 1:1 to 1:9, the proportion of greater particles designed became advanced, which may be due to upsurge in viscosity of the solvent with an upsurge in polymer to drug ratio. The mean particle size ranged from 73.21 to 98.35 µm, as shown in Table 2

Table 2: Evaluation Parameters of Aceclofenac Mucoadhesive Microspheres

Formulation	Mean particle size(µm)	Percent Drug content	Microencapsulation Efficiency (%)	Swelling Index	% Mucoadhesive strength
F1	79.08±1.03	38.66±0.82	77.32±0.82	0.581±0.04	65
F2	81.07±1.35	36.0±0.68	72.0±0.68	0.673±0.07	70
F3	84.11±1.17	35.73±0.96	71.46±0.96	0.693±0.03	60
F4	86.09±1.09	37.2±0.98	74.4±0.98	0.671±0.02	65
F5	82.29±0.99	39.33±0.57	78.66±0.57	0.591±0.01	55
F6	88.25±1.11	34.0±0.66	68.0±0.66	0.598±0.05	75
F7	80.03±0.79	38.4±0.78	76.8±0.78	0.610±0.09	50
F8	88.15±1.01	39.06±1.12	78.12±1.12	0.701±0.02	70
F9	83.21±1.16	39.86±1.22	79.72±1.22	0.700±0.08	65
F10	98.35±1.21	38.53±0.68	77.06±0.68	0.691±0.04	60
F11	91.41±1.33	40.13±0.82	80.26±0.82	0.607±0.09	65
F12	98.15±1.11	38.4±0.54	76.8±0.54	0.670±0.09	65
F13	90.13±0.79	40.13±0.66	80.26±0.66	0.681±0.02	50
F14	88.75±1.01	38.93±0.78	77.86±0.78	0.690±0.08	65
F15	73.21±1.16	43.06±0.44	86.12±0.44	0.771±0.04	75
F16	97.25±1.21	42.13±0.68	84.26±0.68	0.607±0.09	70

*Mean ± SD, (n=3)

Microencapsulation Efficiency

The microencapsulation efficiency within microspheres produced using orifice-ionotropic gelation method. The microencapsulation efficiency was in the range of 68% to 86%, as shown in table 2. The low entrapment efficiency may be due to solubility of the drug in the solvent, and the drug may be migrated to the processing medium.

Swelling index

As shown in table 2 swelling behaviour was found to be a variable depending on the nature of polymers used their surface charges, degree of interaction to form complex, available porosity after swelling etc. The swelling index was in the range from 0.581 to 0.771, and F15 shows great swelling index.

Scanning Electron Microscopy

From SEM study, it was found that microspheres were spherical and rough, as shown in figure 3. The study of drug-loaded microspheres spectacles the incidence of drug particles on the surface. The Microspheres were institute to be isolated, spherical, free-flowing, and of the monolithic matrix type. **Fig 3**

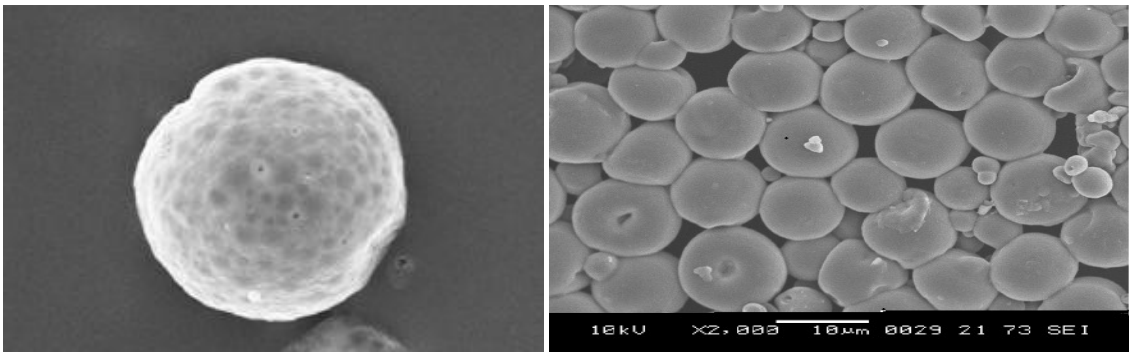


Fig 3: SEM photographs of microspheres

Mucoadhesion Testing by Ex Vivo Wash-Off Test

Mucoadhesive property of microspheres being explored for targeting purpose is considered as a prime parameter for evaluation of performance as mucoadhesion and its durability both can predict the degree of sustainability and duration of drug availability at the desired site. Present in vitro wash-off study also determined the effect of variation in polymer concentration in formed complex on their mucoadhesive nature. Microspheres with a coat consisting of sodium alginate and a mucoadhesive polymer exhibited good mucoadhesive properties in the Ex Vivo wash-off test, as shown in table 2.

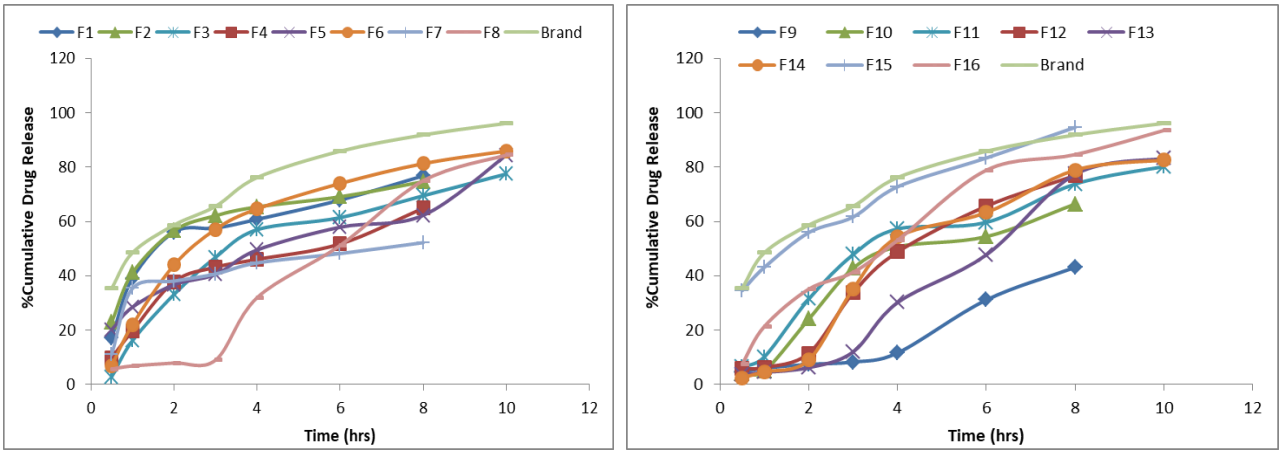
In-vitro release study

Aceclofenac release from the microspheres was studied in phosphate buffer (pH 7.4) for 10 hours. Aceclofenac release from the microspheres was slow and depended on the composition of the coat. The differences in the drug release characteristics of various microspheres are due to the differences in the porosity of the coat formed and its solubility in the dissolution fluid. Aceclofenac release from alginate-HPMC K 15M (F15) was slow and extended over a period of 10 hrs, and these microspheres were found suitable for oral controlled release formulations. The order of decreasing of drug release with various microspheres was observed F9 > F7 > F1 > F2 > F3 > F10 > F11 > F4 > F12 > F14 > F13 > F5 > F8> F6 > F16 > F15.

Table 3a: Cumulative percentage drug release of Formulations from F1-F8

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	Brand
0.5	17.19±0.92	22.95±0.66	2.79±0.57	9.84±1.42	20.16±0.88	6.89±1.22	11.04±1.22	5.7±0.98	35.4±0.89
1	39.02±1.12	41.07±0.98	16.06±0.66	19.73±1.23	28.45±0.98	21.93±0.96	35.31±1.32	6.81±1.65	48.49±0.94
2	56.12±0.87	56.6±0.78	33.12±1.24	37.81±0.86	36.71±1.24	43.95±0.58	38.05±1.42	7.89±1.42	58.66±0.68
3	57.54±0.95	62.09±0.57	46.8±1.20	43.15±0.88	40.52±0.57	57.10±0.84	40.66±0.86	8.96±1.38	65.58±1.14
4	60.78±1.22	65.35±0.78	56.96±0.84	46.05±0.68	49.51±0.66	64.61±0.92	44.73±0.98	31.95±1.06	76.15±1.22
6	67.87±0.86	69.09±0.98	61.4±0.92	51.71±0.78	57.88±1.33	73.97±0.93	48.19±1.54	51.18±0.98	85.86±0.84
8	76.79±0.58	74.64±1.25	69.46±1.32	64.89±1.44	62.25±1.45	81.27±1.56	52.20±1.64	75.01±1.96	91.83±0.98
10	76.31±0.88	76.84±1.45	77.49±1.18	80.39±0.98	84.4±1.25	85.92±1.42	71.99±1.08	84.43±0.64	96.12±1.55
S F (f_2)	39.18	38.80	41.69	36.84	46.52	41.62	37.86	33.91	65.30

*Mean ± SD, (n=3)



(a) **(b)**

Fig.4: Cumulative percentage drug release of Formulations from (a)-F1-F8 (b)-F9-F16

Table 3b: Cumulative percentage drug release of Formulations from F9-F16

Time (hrs)	F9	F10	F11	F12	F13	F14	F15	F16	Brand
0.5	4.59±1.56	3.96±1.74	6.36±1.46	5.82±1.88	3.66±1.88	2.49±1.04	34.5±1.02	7.53±1.90	35.4±0.89
1	5.96±1.42	4.88±1.48	10.14±1.28	6.27±1.44	4.43±1.48	4.63±1.96	43.09±1.28	21.33±1.65	48.49±0.94
2	7.4±1.24	24.04±1.28	31.44±1.78	11.46±1.28	6.19±1.56	9.03±0.96	55.92±1.65	35.09±1.53	58.66±0.68
3	8.25±0.88	42.78±1.46	47.81±0.98	33.73±0.68	11.98±1.48	35.18±0.56	61.63±1.12	41.30±1.23	65.58±1.14
4	11.59±1.82	50.66±1.28	57.24±0.64	48.76±1.64	30.14±0.98	54.28±0.68	72.77±1.42	53.07±0.76	76.15±1.22
6	31.10±1.42	54.41±1.44	59.65±0.62	65.62±0.96	47.71±0.88	63.28±0.98	83.37±1.54	78.87±0.62	85.86±0.84
8	43.11±1.28	66.39±1.28	73.78±1.57	76.89±1.98	77.37±0.66	78.93±1.48	94.63±1.24	84.60±0.92	91.83±0.98
10	59.85±1.06	77.85±1.76	80.19±1.66	80.57±0.92	83.20±1.12	82.57±1.54	97.57±0.88	93.5±1.24	96.12±1.55
S F (f_2)	44.21	41.32	39.86	42.41	38.71	46.63	65.48	48.12	65.30

*Mean ± SD, (n=3)

Similarity factor (f2)

The dissolution profiles of the developed dosage form are considered to be similar to a theoretically developed profile when F2 value is 50 to 100. The similarity factor value for F15 is 65%, so its profile is identical to the reference profile.

Release kinetics

Release followed zero-order kinetics, and R2 value is 0.971(table 4). Higuchi plot of F15 showed an R2 value of 0.997 (table 4). From the result, it suggests that diffusion plays an essential role in the controlled release formulations. The data were fitted to korse meyer peppas equation, and the value of diffusional exponent 'n' is 0.47 (table 4) indicated that the drug release shows non-fickian diffusion

.Table 4: Release kinetics of Aceclofenac Mucoadhesive microspheres

F.No.	Zero order	First order	Higuchi's	Peppa's	n	K0 (mg/ L/hr)	K1 (h-1)	T50 (hrs)	T75 (hrs)	T90 (hrs)
F1	0.920	0.926	0.967	0.956	0.313	3.75	0.172	1.5	7.8	>10
F2	0.931	0.936	0.952	0.933	0.184	2.72	0.092	1.5	8.5	>10
F3	0.948	0.961	0.955	0.919	0.774	13.75	0.138	3.2	9.3	>10
F4	0.925	0.938	0.963	0.926	0.612	6.42	0.161	5.5	9.3	>10
F5	0.963	0.933	0.958	0.923	0.455	5.83	0.092	4.2	9.4	>10
F6	0.929	0.972	0.940	0.916	0.413	11.11	0.283	2.5	6.5	>10
F7	0.937	0.942	0.948	0.912	0.214	2.70	0.046	7.0	>10	>10
F8	0.958	0.936	0.937	0.904	1.275	11.03	0.246	5.8	8.0	>10
F9	0.945	0.912	0.943	0.919	1.253	5.30	0.020	9.0	>10	>10
F10	0.901	0.969	0.964	0.940	0.741	6.00	0.155	4.0	9.0	>10
F11	0.944	0.969	0.958	0.932	0.441	6.92	0.230	3.3	8.5	>10
F12	0.932	0.981	0.957	0.917	0.982	10.90	0.200	4.2	7.7	>10

F13	0.966	0.931	0.904	0.946	1.123	11.42	0.142	6.4	7.9	>10
F14	0.917	0.978	0.951	0.994	0.752	10.52	0.184	3.8	7.6	>10
F15	0.971	0.948	0.997	0.971	0.472	5.45	0.241	1.5	4.5	7.5
F16	0.966	0.940	0.987	0.991	0.931	10.00	0.267	3.8	5.6	7.5
Brand	0.901	0.995	0.978	0.991	0.340	6.12	0.257	1.2	4.0	8.0

Stability studies

In the present study, stability studies were carried out for formulation F15 at 40^0C / 75 % RH for a specific period up to 30 days for the selected formulation. Stabilities studies of Aceclofenac Mucoadhesive Microspheres, as shown in table 10.

Table 5: Stability studies of Aceclofenac Mucoadhesive microspheres (F15)

Formulation	Tested after time (days)	Microencapsulation Efficiency (%)	Cumulative % Drug Released
Stored at 25°C/ 60% RH			
F3	30	87.10	97.57
Stored at 40°C/ 75% RH			
F3	30	89.15	98.15

CONCLUSION

The main objective is to prepare the mucoadhesive microspheres to enhance the bioavailability. Microspheres were prepared by orifice Ionotropic gelation method using polymers. Totally 16 different formulations of aceclofenac were prepared in 1:1 & 1:9 ratios and evaluation is done for drug content, encapsulation efficiency, and the *in vitro* drug release was evaluated for 10 hrs in phosphate buffer solution PH 7.4. The release followed zero-order kinetics, and R2 value is 0.971. Aceclofenac release from Alginate, HPMC K15m (F15) was slow and extended throughout 10 hrs, and their microspheres were found suitable for opal controlled release formulations. In the *in vitro* evaluations, SODIUM Alginate: HPMC K15m 9:1 ratio (F 15) microsphere could sustain the drug release over a10hrs period. The mucoadhesive microspheres are then suitable for oral controlled release of aceclofenac.

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