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FORMULATION AND INVITRO EVALUATION OF STOMACH SPECIFIC FLOATING MICROSPHERES OF ACELCLOFENAC

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Abstract:

The aim of the present work is to study the effect of polymer characteristics on the drug release from hydrogels which were prepared using different polymers (Sodium alginate, Sodium CMC, HPMC K100 and Carbopol) by Ionotropic gelation method. The main objective of the research work is to study the drug and polymer interaction. The formulated hydrogels were characterized for their physico-chemical parameters like swelling ratio, water uptake, gel fraction, percentage yield, drug content, drug entrapment efficiency and size analysis. FTIR studies reveal the drug excipients compatibility. In-vitro drug release studies revealed that the high % drug release for F9 was 98.9% up to 14hrs. Swelling ratio and water uptake by F9 formulation was 12.6± 0.05 and found to be good swelling ratio, high water absorbing ability and high % adherence (77%). Among all formulations, F9 showed controlled drug release up to 14 hrs and considered as ideal formulation.

Keywords: *Aceclofenac, Hydrogel, Hydroxy Propyl Methyl Cellulose, Sodium alginate, Sodium carboxy Methyl Cellulose, Carbopol, Ionotrpic gelation method.*

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INTRODUCTION:

Hydrogels are defined as two- or multicomponent systems consisting of a three-dimensional network of polymer chains and water that fills the space between macromolecules or it defined as Hydrogels are polymeric networks that absorb large quantities of water while remaining insoluble in aqueous solutions due to chemical or physical cross linking of individual polymer chains [1-5].

Differing from hydrophobic polymeric networks such as PLAor PLGA which have limited water-absorption capabilities (5–10 wt %), hydrophilic hydrogels exhibit many unique physicochemical properties that make them advantageous for biomedical applications including drug delivery [2-4].

For example, hydrogels are excellent candidates for encapsulating bio macromolecules including proteins and DNA due to their lack of hydrophobic interactions which can denature these fragile species [1]. In addition, compared to commonly use hydrophobic polymers such as PLGA, the conditions for fabricating hydrogels are relatively mild.

Gel formation usually proceeds at ambient temperature and organic solvents are rarely required. In-situ gelation with cell and drug encapsulation capabilities further distinguishes hydrogels from the other hydrophobic polymers [6-8].

APPLICATIONS:

- Hydrogels because of their hydrophilic character and potential to be biocompatible have been of great interest to biomaterial scientists for many years.
- Hydrogels can also be used for cell encapsulation and encapsulation of drugs.
- Most recently used in tissue engineering as matrices for repairing and regenerating a wide variety of tissues and organs.
- Hydrogels are used for protein delivery.
- *In situ* gelling hydro gels used for pharmaceutical and biomedicalapplications.
- Hydrogels are used for sustained ophthalmic drug delivery.

The aim of the present research work is to study the effect of polymer characteristics on the drug release from Acelclofenac hydrogels to study the drug and polymer interaction and to improve the bioavailability.

Aceclofenac has higher anti-inflammatory action than conventional NSAIDs. It is a cytokine inhibitor. Aceclofenac works by blocking the action of a substance in the body called cyclo-oxygenase. Cyclo-oxygenase is involved in the production of prostaglandins (chemicals in the body) which cause pain, swelling and inflammation. Aceclofenac is the glycolic acid ester of Diclofenac.

It's having shorter half life (~4hrs). The bioavailability of Aceclofenac following oral administration is about ~40-50 % which might be due to colonic degradation by colonic bacteria. High doses produce toxicity and hence dose could be minimized. The drug is hydrophilic in nature; the hydrogel polymers and solvent are hydrophilic in nature hence drug gets easily dissolved and very much compatible for the formulation hydrogels. By entrapment of drug in the form of Hydrogels increasing the bioavailability. The minimal first pass metabolism of drug can be avoided in the form of hydrogels. Considering all the above points the Aceclofenac might be right and suitable candidate for the formulation of Hydrogels [13-15].

Hydrogels are polymeric networks that absorb large quantities of water while remaining insoluble in aqueous solutions due to chemical or physical cross linking of individual polymer chains [9-12].

METHODOLOGY:

DETERMINATION OF MELTING POINT

Melting point of Aceclofenac was determined by Capillary method. Fine powder of Aceclofenac was filled in capillary tube (previously sealed on one end). The capillary tube is inserted into melting point apparatus and observed the temperature at which the drug started to melt by using the thermometer which was already immersed into the liquid paraffin in the apparatus.

CONSTRUCTION OF CALIBRATION CURVE AT pH 1.2 HCL

1. 100 mg of Aceclofenac was accurately weighed and dissolved in 0.1N HCl[125] (pH1.2) and make up the volume up to 100 ml (Stock solution I, 1000 µg/ml).

2. From this 10 ml of stock solution was pipette out and make up the volume up to 100 ml (Stock solution II, 100µg/ml).

3. Aliquots were prepared from the stock solution II, whose concentration ranging from 5 to 50µg/ml and the absorbance were measured at 275 nm against the reagent blank.

Table 1 Calibration curve data of Aceclofenac at pH 1.2 HCl

Concentration in mcg/ml	Absorbance
0	0
5	0.196
10	0.287
15	0.399
20	0.486
25	0.562
30	0.656
35	0.76
40	0.846
45	0.996
50	1.102

CONSTRUCTION OF CALIBRATION CURVE AT pH 7.4 PHOSPHATE BUFFER

1. An accurately weighed 100 mg of Aceclofenac was dissolved in Phosphate buffer[126] (pH7.4) and make up the volume up to 100 ml (Stock solution I, 1000 µg/ml).
2. From this 10 ml of stock solution was pipette out and make up the volume up to 100 ml (Stock solution II, 100µg/ml).
3. Aliquots were prepared from the stock solution II, whose concentration ranging from 5 to50 mcg/ml and the absorbances were measured at 275 nm against the reagent blank.

Table 2: Calibration curve data of Aceclofenac at pH 7.4 phosphate buffer

Concentration in mcg/ml	Absorbance
0	0
5	0.132
10	0.198
15	0.256
20	0.348
25	0.546
30	0.635
35	0.748
40	0.832
45	0.993
50	1.114

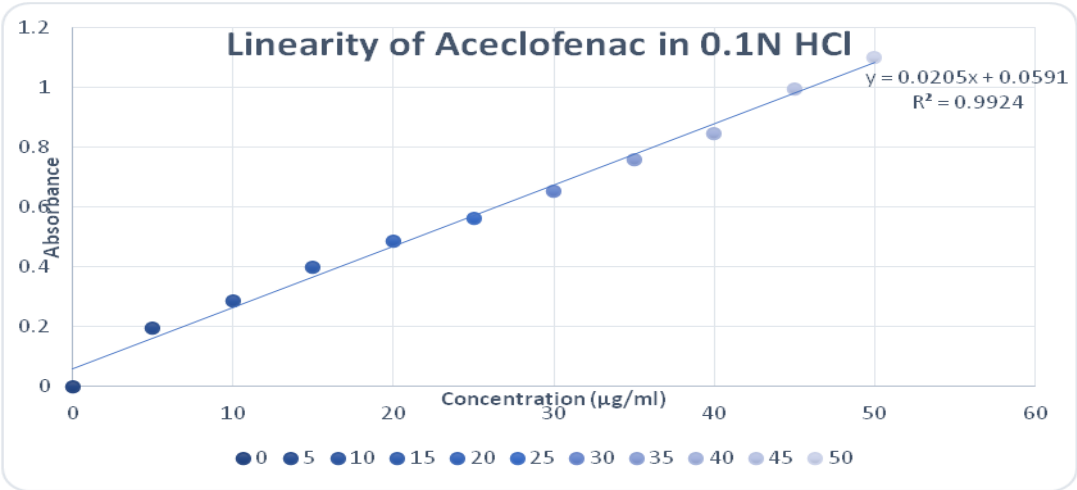

Fig.1: Linearity of Aceclofenac in 0.1NHCl

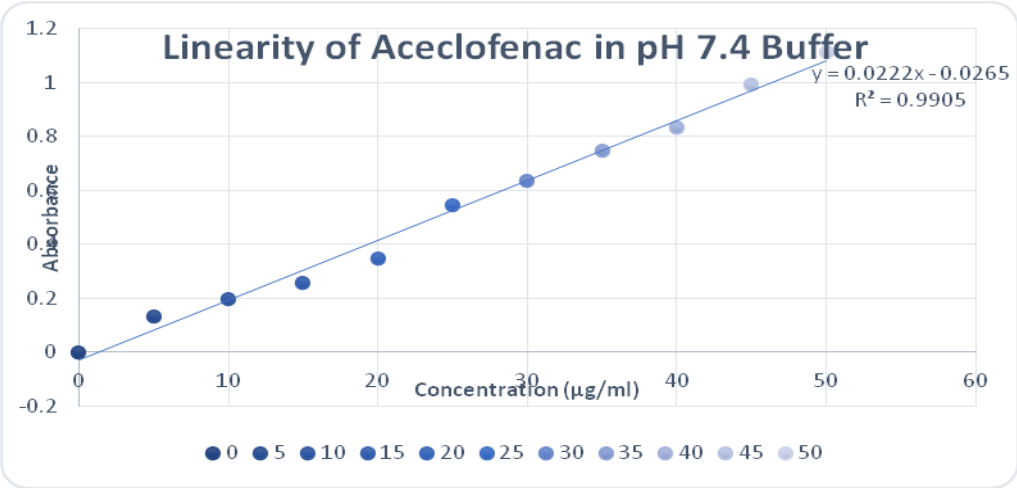

Fig. 2: Linearity of Aceclofenac in pH 7.4 buffer

FORMULATION OF PLACEBO HYDROGELS

The Hydrogels were prepared by the method of physical crosslinking (ionotropic gelation technique). An accurately weighed quantity of sodium alginate,HPMC - K100, SCMC and carbopol were dissolved in required quantity of distilled water and this solution is being homogenized at 500 rpm for 30 min. This solution was sonicated for 30 min to remove air bubbles thus the solution was dropped into2 % $CaCl_2$ solution (crosslinking agent) using a syringe fitted with a 21G needle and the formed hydrogels were cured for 30 min. These hydrogels were washed with distilled water and dried atroom temperature over night.

FORMULATION OF ACECLOFENAC HYDROGELS

The Hydrogels were prepared by the method of physical crosslinking method(ionotropic gelation technique). An accurately weighed quantity of sodium alginate, HPMCK100, SCMC, carbopol and Aceclofenacas per table: 5 were dissolved inrequired quantity of distilled water and this solution is being homogenized at 500 rpmfor 30 min. This solution was sonicated for 30 min to remove air bubbles. Thus the solution was dropped into 2 % $CaCl_2$ (crosslinking agent) solution using a syringe fitted with a 21G needle and the formed hydrogels were cured for 30 min. These hydrogels were washed with distilled water and dried at room temperature.

Table 2: Compositions of Aceclofenac hydrogel formulation

Formulation	Drug %w/v	Polymers			
		Sodium alginate %w/v	SCMC %w/v	carbopol %w/v	HPMC K100 %w/v
F1	1	2	1	-	-
F2	1	2	2	-	-
F3	1	2	3	-	-
F4	1	2	-	1	-
F5	1	2	-	2	-
F6	1	2	-	3	-
F7	1	2	-	-	1
F8	1	2	-	-	2
F9	1	2	-	-	3

DRUG - POLYMER COMPATIBILITY STUDIES BY FTIR:

Drug and polymer compatibility studies[128,129] were performed by Fouriertransform infra red spectroscopy (FTIR) spectroscopy. It is very important to study the interaction between the drug and polymers in order to confirm that the entrapmentof drug within the polymeric systems involving the physical process and no interaction. The FTIR spectra of pure drug, individual polymers and the combination were shows no significant interaction so that the polymers and drug were chosen having well suitable for the formulation of hydrogels.

PHYSICOCHEMICAL EVALUATION

Swelling ratio

Swelling of hydrogels was carried out in triplicate by gravimetric method. Known weight of hydrogels were taken and immersed in pH 7.4 phosphate buffer solution at 37ºC. Then the hydrogels were removed at particular time intervals, wiped with tissue paperto remove excess of solvent and weighed immediately. The difference in weight has given the amount of pH 7.4 phosphate buffer solution uptake by hydrogels after definite time intervals (60 min).

Swelling ratio=W_t–W_O/W_O

Where, W_t = weight of hydrogels at time.

W_o = initial weight of hydrogels.

Water uptake

Known weight of hydrogels for were taken and immersed in excess of distilled water at 37ºc. Then the hydrogels were removed at particular time intervals, wiped with tissue paper to remove excess of solvent and weighed immediately. The difference in weight has given the amount of water uptake by hydrogels for definite period of time.

Water uptake= W_S/W_D

Where, W_S = weight of swollen hydrogels.

W_D = weight of dried hydrogels.

Gel fraction

To extract the insoluble parts of hydrogels (i.e., the gelled part), the prepared hydrogels were soaked in water for 48 h. Then they were taken out and washed with hot water to remove soluble part, dried and weighed. Gel fraction was determined from equation given below

Gel fraction=$W_e/ W_o \times 100$

Where, w_o = weight of dried hydrogel after crosslinking.

w_e= weight of Sample after extraction of soluble parts

***IN VITRO* DRUG RELEASE STUDIES**

In Vitro drug release studies of Aceclofenac were performed using USP dissolution test apparatus (paddle method).

Dissolution medium: 900 ml of pH 1.2HCL buffer and 900 mlof pH 7.4 phosphate buffer

Temperature of 37±1ºC and stirred at rate of

RPM: 50

Volume withdrawn & replaced: 5ml every 60 minutes.

λ_{max}: 275nm

In each formulation100 mg Aceclofenac equivalent hydrogels were taken and immersed in 900 ml of pH 1.2HCL buffer for first two hours. Then acidic buffer is replaced with fresh buffer of 900 mlof pH 7.4 phosphate buffer which mimic stomach and intestinal pH conditions.

Thealiquots of 5 ml were withdrawn at one hour time interval and replaced with equal volume of dissolution medium in order to maintain the sink condition throughout the study. Then the samples were filtered and analyzed spectrophotometrically at 275 nm after a suitable dilution. The cumulative amount of drug release was calculated.

***IN-VITRO* MUCOADHESION TEST**

In-vitro muco adhesion test was performed by using *in vitro* Wash- Off test. 100particles of hydrogels were counted and placed on strip of goat intestine which was adhered to glass slide by using cyano acrylate glue. Then this slide consisting of particles was placed in disintegration apparatus for eight hours of time. After eight hours number of particles being adhered was counted and % of Adherence was calculated by using the formula.

$$\mathbf{Na = (N/No) X 100}$$

Where,

Na = is the adhesion number

No = is the total number of applied particles

N = number of particles attached to the substrate.

MECHANISM OF DRUG RELEASE

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as

i. Cumulative percentage drug released Vs Time (*In-vitro* drug release plots)
ii. Cumulative percentage drug released Vs Square root of time (Higuchi's plots)
iii. Log cumulative percentage drug remaining Vs Time (First order plots)
iv. Log percentage drug released Vs Log time (Peppas plots)

Higuchi release model

To study the Higuchi release kinetics, the release rate data was fitted to the following equation.

$$\mathbf{F = K_H t_{1/2}}$$

Where, 'F' is the amount of drug release,

'K_H' is the release rate constant, and

't' is the release time

When the data is plotted as a cumulative percentage drug release versus square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to 'K'.

Korsmeyer and Peppas release model

The release rate data were fitted to the following equation,

$$\mathbf{Mt/M\infty = K_M .t^n}$$

Where, Mt / M∞ is the fraction of drug release,

'K_M' is the release constant,

't' is the release time,

'n' is the diffusional exponent for the drug release that dependent on the shape of the matrix dosage form.

When the data is plotted as log percentage release versus log time, yields as straight line with a slope equal to 'n' and the 'K' can be obtained from Y – intercept. For non- Fickian release the 'n' values falls between 0.5 and 1.0 while for Fickian (case I) diffusion n= 0.5 and zero order release (case II transport) n= 1.0.

Zero order release rate kinetics

To study the zero-order release kinetics the release rate date are fitted to the following equation.

$$\mathbf{F = K_0 .t}$$

Where 'F' is the fraction of drug release,

'K_0' is the release rate constant and

't' is the release time.

When the data is plotted as cumulative percentage drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K_0.

First order model

This model has also been used to describe absorption and/or elimination of some drugs. The release of the drug which followed first order kinetics can be expressed by the equation:

$$\mathbf{LogC = LogC_0 - K_1 t/2.303}$$

Where, C_0 is the initial concentration of drug,

k is the first order rate constant, and

t is the time .

The data obtained are plotted as log cumulative percentage of drug remaining *vs*. time which would yield a straight line with a slope of -K/2.303.

RESULTS AND DISCUSSION:

Hydrogels of Aceclofenac were formulated by physical cross linking method i.e ionotropic gelation technique by using different polymers like sodium alginate, HPMCK100, SCMC ans carbopol. The solvent used as distilled water and 2 % Calcium chloride serves as a crosslinking agent. The formulated hydrogels were characterized for their physico-chemical parameters like swelling ratio, water uptake, gel fraction,% yield, drug content, drug entrapment efficiency and size analysis.

Melting Point

Melting Point of Aceclofenac was found to be 150-155°C

Determination of Melting Point

Table 3: Determination of Melting Point

S. No	Observed melting point (°C)	Average Melting point (°C)	Reference Melting Point (°C)
1	153	153.3	152-154
2	155		
3	152		

Drug –polymer compatibility studies by FTIR

The physicochemical compatibility of the drug and the polymer was established through FTIR studies. The FTIR spectra of Aceclofenac, Sodium Alginate SCMC, HPMC, CP, and the combination of drug and polymers were shows no significant interaction between drug and polymer. The FTIR spectra's of Aceclofenac, Sodium Alginate SCMC,HPMC, CP and mixture of drug along with polymers.

FTIR SPECTRA OF ACECLOFENAC

IR spectral analysis of Aceclofenac showed the peaks at wave numbers as follows

Table 4: FTIR Spetra of Aceclofenac

S.No	Peaks	Functional groups
1	3256.27, 3191.01	Associated N-H Stretching
2	3101.00	C-H Asymmetric Stretching
3	2945.11, 2558.80, 2509.32, 2466.15	Ring Stretching
4	1568.60	NO_2 Asymmetric Stretching
5	1226.15, 1190.50, 1128.81, 1072.07, 1042.61	C-N Stretching
6	803.74, 759.45, 697.73	N-H Bending out of plane
7	759.45, 697.73	C-S Stretching

From the above peaks in IR spectrum confirming the purity of drug with standard.

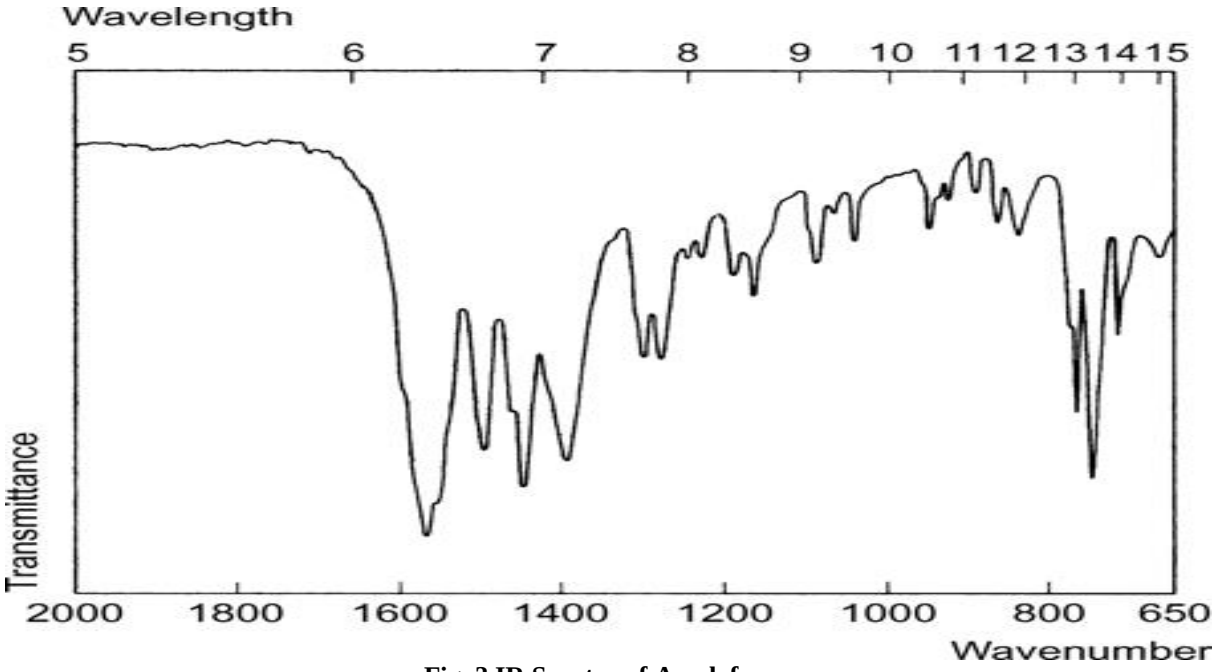

Fig. 3 IR Spectra of Aceclofenac

FTIR SPECTRA OF ACECLOFENAC WITH POLYMERS

In the physical mixture of Aceclofenac with SODIUM ALGINATE, SCMC, HPMC, CP the major peaks of Aceclofenac:

Table 5: IR Spectra of drug with Polymers

S.No	Peaks	Functional groups
1	3258.73, 3193.75	Associated N-H Stretching
2	3103.94	C-H Asymmetric Stretching
3	2944.84, 2560.78, 2511.30, 2469.05	Ring Stretching
4	1570.17	NO2 Asymmetric Stretching
5	1222.45, 1192.92, 1131.40, 1072.30, 1045.07	C-N Stretching
6	802.96, 760.46, 698.45	N-H Bending out of plane
7	760.46, 698.45	C-S Stretching
8	3259.380	Associated N-H Stretching
9	3108.73	CH Asymmetric Stretching
10	2559.67, 2512.56, 2467.58	Ring Stretching
11	1572.54	NO2 Asymmetric Stretching
12	1223.74, 1192.26, 1130.35, 1070.83, 1045.47	C-N Stretching
13	803.57, 759.97, 698.04	N-H Bending out of plane
14	759.97, 698.04	C-S Stretching

However, additional peaks were absorbed in physical mixtures which could be due to presence of polymers and indicated that there was no chemical interaction between Aceclofenac and other excipients.

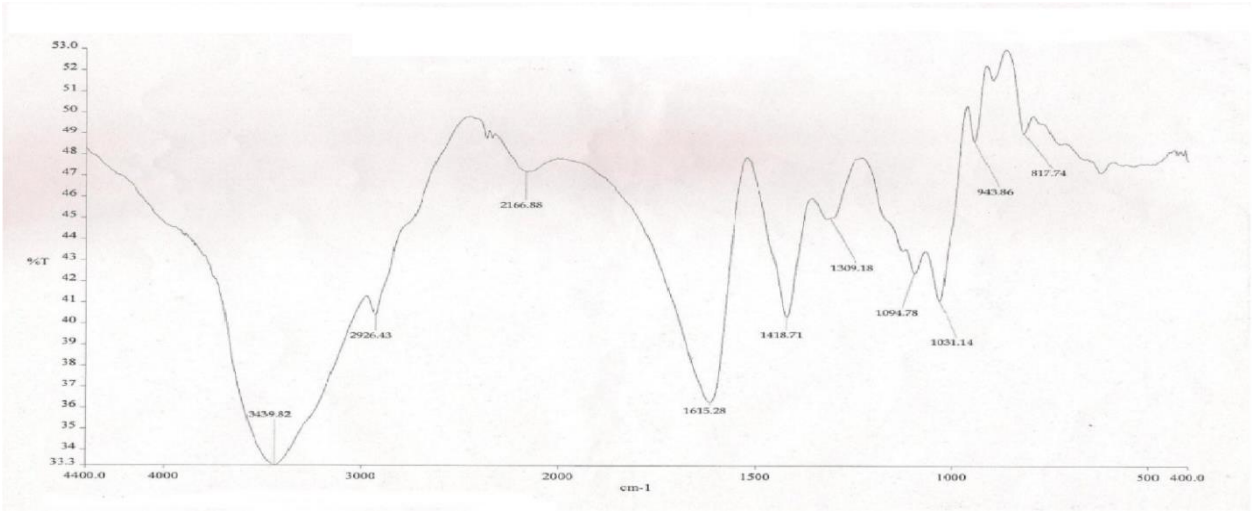

Fig.4 FTIR Spectra of Sodium Alginate

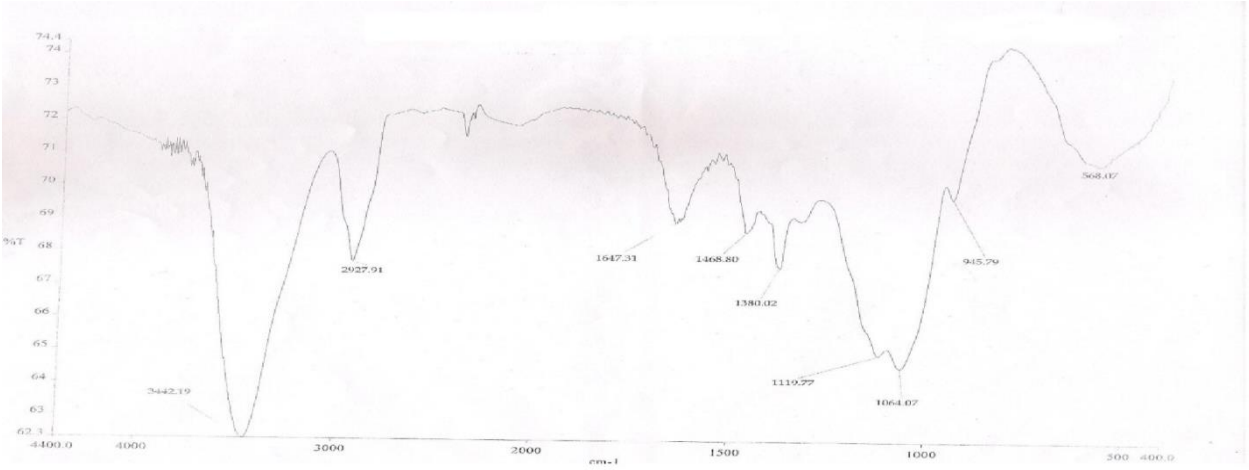

Fig.5 FTIR Spectra of HPMCK100

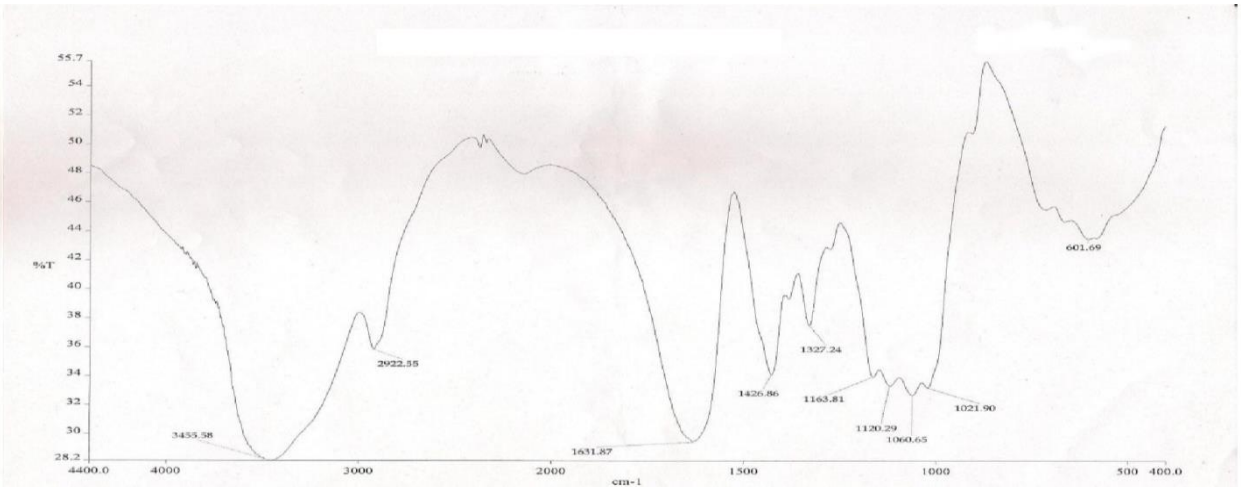

Fig.6 FTIR Spectra of Sodium Carboxy Methyl Cellulose

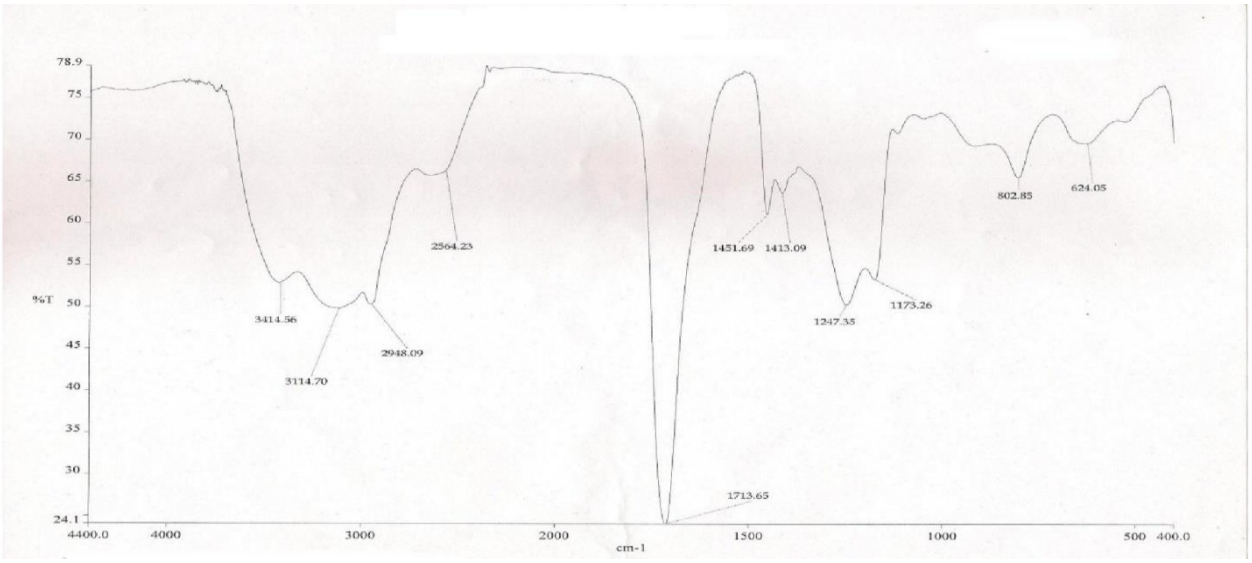

Fig.7 IR Spectra of Carbopol 934

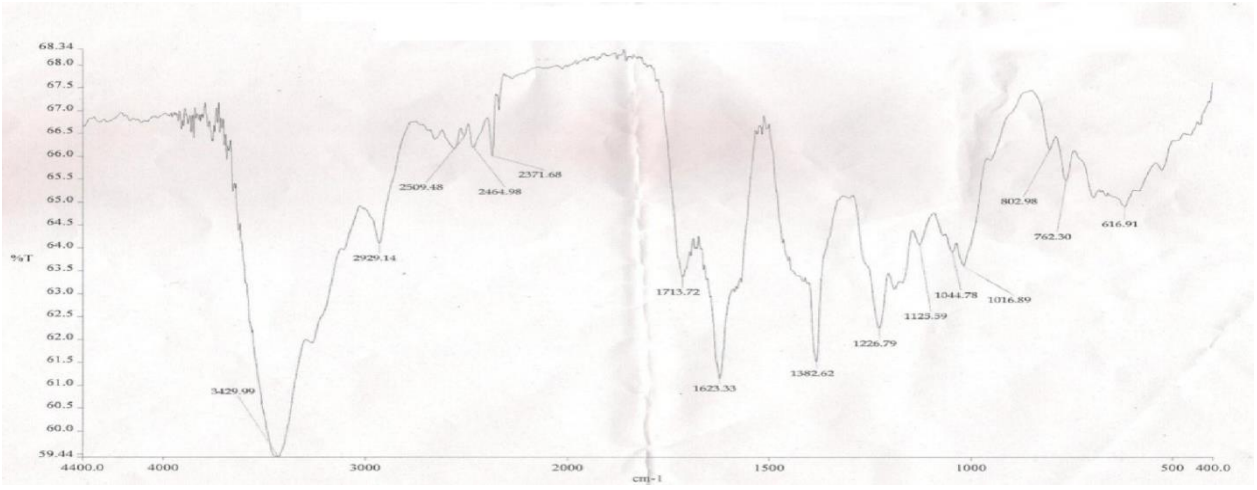

Fig.8 IR Spectra of Aceclofenac+Sod.Alginate+Carbopol+HPMCK100+SCMC

Swelling ratio

Swelling studies was done in triplicate using phosphate buffer. The prepared Aceclofenac hydrogels showed good swelling properties. The observed swelling ratio for formulations ***F1,F2,F3,F4,F5,F6,F7,F8,F9*** are as follows ***7.6± 0.05, 8.2 ±0.05, 10.7± 0.05, 6.6± 0.05, 7.3± 0.11, 9.6± 0.05, 9.6±0.05, 10.6± 0.05, 12.6± 0.05*** respectively. The results found that the formulations showed good swelling ratio required for hydrogels which may affect the drug release and also mucoadhesive nature of hydrogels.

Table 6: Swelling ratio data for all formulations

Formulation Code	Time in mins					
	60	120	180	240	300	360
F1	1.2±0.05	2.6± 0.1	4.5 ±0.1	5.4± 0.15	7.2± 0.05	7.6± 0.05
F2	2.2± 0.05	3.6 ±0.05	4.4 ±0.05	6.4± 0.05	7.3± 0.05	8.2 ±0.05
F3	2.7± 0.11	4.3± 0.05	6.2± 0.11	7.5± 0.1	10.7± 0.05	10.7± 0.05
F4	0.5± 0.15	2.6± 0.15	3.6± 0.05	4.3± 0.05	6.6± 0.05	6.6± 0.05
F5	1.3± 0.1	3.4± 0.15	4.7± 0.05	5.4± 0.05	7.3± 0.11	7.3± 0.11
F6	1.7 ±0.1	4.6± 0.1	6.5± 0.15	7.5± 0.05	9.6± 0.05	9.6± 0.05
F7	1.0±0.1	2.6± 0.1	5.3 ±0.11	9.4± 0.05	9.6 ±0.05	9.6±0.05
F8	1.6 ±0.1	3.3± 0.15	7.4± 0.05	8.2± 0.05	10.6± 0.05	10.6± 0.05
F9	2.5 ±0.1	4.7± 0.05	7.5 ±0.05	9.5± 0.05	12.6± 0.05	12.6± 0.05

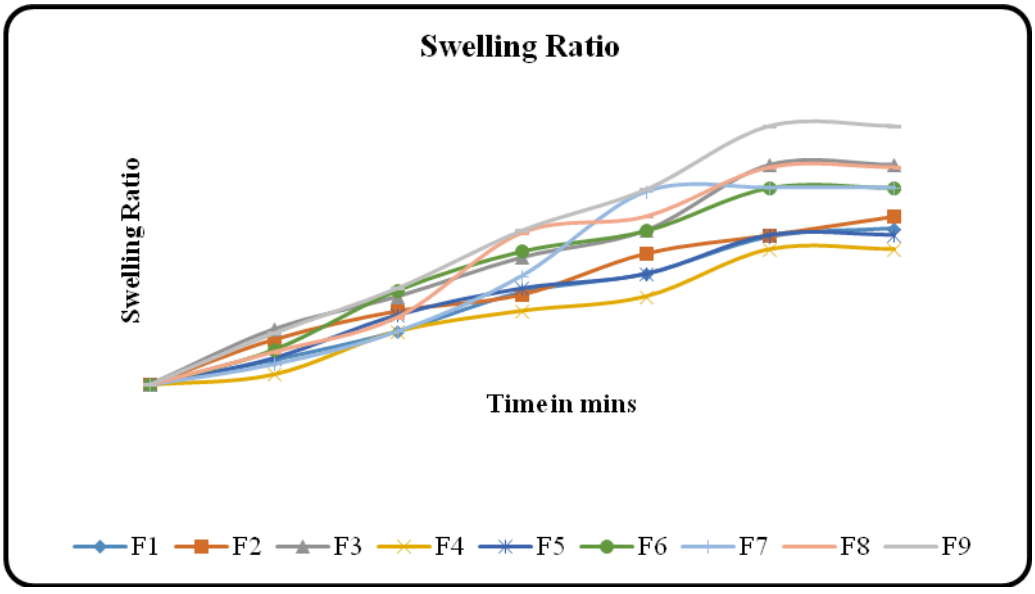

Fig. 9 Swelling ratio

Water uptake

The ability of hydrogels to absorb water and swell without losing its structure is done by water uptake studies. Among all formulations the best water uptake was observed for F9 and F3 this is due to high swelling ability of HPMC and SCMC. The increasing order of formulation was found in order of ***F9>F3>F8>F6>F7>F2>F1>F5>F4*** (i.e)***13.6±0.05, 11.8±0.57, 11.6±0.05, 10.6±0.05, 10.5±0.05, 9±0.05, 8.5±0.05, 8.3±0.11, 7.6±0.05*** due to high water absorbing ability of HPMC and SCMC, hence the formulation containing HPMC and SCMC have high water up taking property than other formulations.

Table: 7 Water uptake data for all formulations

Formulation code	Time in mins					
	60	120	180	240	300	360
F1	2.2±0.05	3.7± 0.1	5.6± 0.1	6.6 ± 0.05	8.3± 0.05	8.5± 0.05
F2	3.3±0.05	4.5 ±0.05	5.4± 0.05	7.2± 0.05	8.6± 0.05	9± 0.05
F3	3.7 ±0.11	5.3± 0.05	7.3± 0.11	8.3± 0.1	11.8± 0.57	11.8± 0.57
F4	1.6± 0.15	3.6± 0.15	4.4± 0.05	5.3± 0.05	7.6± 0.05	7.6± 0.05
F5	2.3± 0.1	4.5± 0.15	5.8± 0.05	6.4± 0.05	8.3± 0.11	8.3± 0.11
F6	2.7± 0.1	5.6± 0.1	7.6± 0.15	8.5± 0.05	10.6± 0.05	10.6± 0.05
F7	2.1± 0	3.7± 0.1	6.4± 0.11	10.5± 0.05	10.5± 0.05	10.5± 0.05
F8	2.5± 0.1	4.3± 0.15	8.6± 0.05	9.2± 0.05	11.6± 0.05	11.6± 0.05
F9	3.5 ±0.1	5.6± 0.05	8.5± 0.05	10.5± 0.05	13.6 ± 0.05	13.6± 0.05

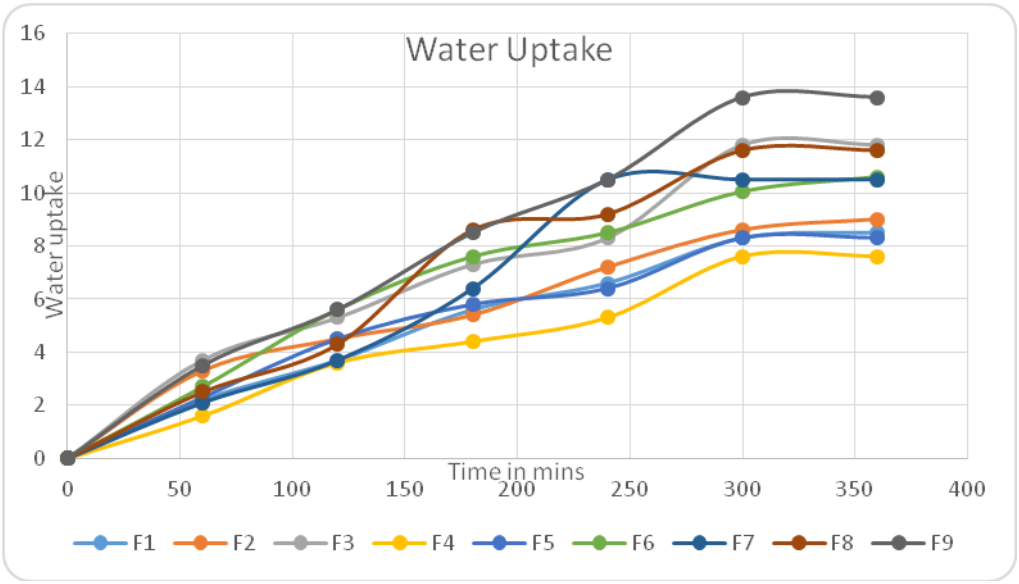

Fig. 10 Water uptake

Gel fraction

Gel fraction is the amount of insoluble parts of polymer obtained after formulation. The obtained results were in the range of ***99.83±0.05 to 98±0.1.***

***In Vitro* release studies**

In vitro drug release studies were performed using 1.2 pH HCL buffer for first two hours and after the release studies were continued in 7.4 pH phosphate buffersolution. The drug concentration were measured UV spectrophotometrically at 275nm. The studies were performed upto 14 hrs.

- The graphs were plotted by taking cumulative % drug release Vs time
- The % drug release was observed in formulation ***F9*** after 14 hrs was found to be ***98.9%*.**
- The cumulative % drug release was observed in the formulation ***F3 and F8*** after 12 hours were found to be ***98.3% and 97.9%*** respectively.
- The cumulative % drug release was observed in formulation ***F6 and F2*** after 11 hrs was found to be ***95.8 % and 95.2%*** respectively.
- The cumulative % drug release was observed in formulation ***F5*** after 10 h was found to be ***94.8%*** respectively.
- The cumulative % drug release was observed in formulation ***F1 and F7*** after 9 hours were found to be ***94.6% and 87.3%*** respectively.
- The cumulative % drug release was observed in formulation ***F4*** after 8 hours was found to be ***93.5%*** respectively.

The observed results were indicating that the maximum percentage of drug release characteristics was observed for the formulations containing sodium alginate along with HPMC and SCMC because both of the polymers have high gelling and swelling abilities these are the parameters which are mainly useful for retardation of drug release from the formulations for about 14 to 12 hrs release. Among all formulations ***F9*** showed retarded release rate and have achieved the controlled release characteristics.

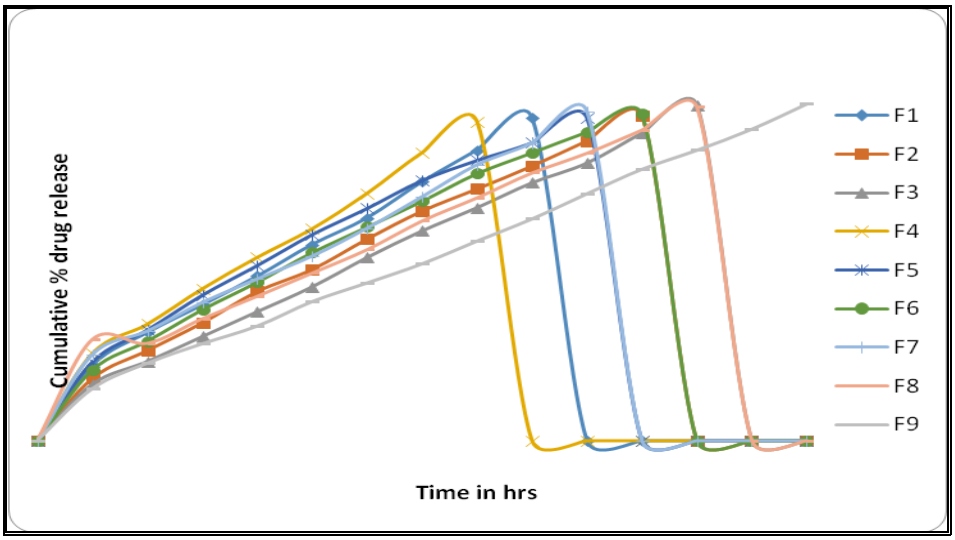

Fig. 11 In vitro drug release data for Formulation F1-F9

***In-vitro* muco adhesion test**

In-vitro mucoadhesion test was performed by using *in vitro* Wash- Off test. The % Adherence was in the range of ***62 % to 77%*.**

Table 8: *In-vitro* muco adhesion test

Formulation code	% Adherence
F1	72%
F2	74%
F3	75%
F4	62%
F5	63%
F6	66%
F7	73%
F8	74%
F9	77%

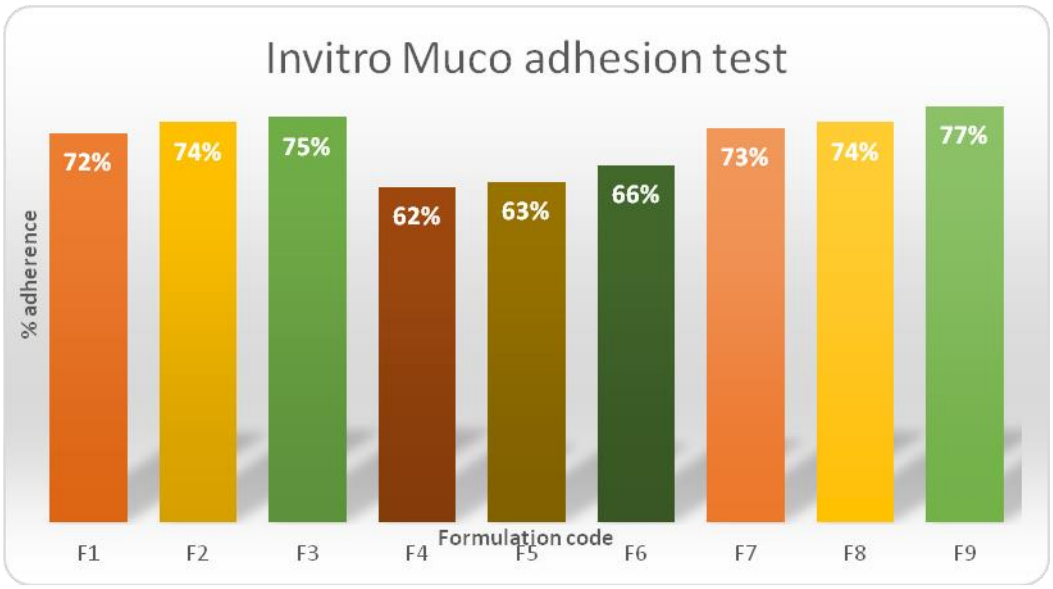

Fig. 12 In vitro Muco adhesion test

Release kinetics and mechanism

The release mechanism of drug and kinetics of Aceclofenac can be knownby fitting them in to mathematical models and n, r^2 values forzero order, First order, Higuchi and Peppas models are represented in ***Table No.9.*** When the release mechanism is not well known or more than one type of release could be involved the peppas model is widely used.

Table 9: Release kinetics data of Aceclofenac hydrogel formulations

Formulation code		Mathematical models (Kinetics)			
	Zero order	Fisrt Order	Higuchi	Peppas model	
	R^2	R^2	R^2	R^2	n
F1	0.985	0.855	0.962	0.986	0.666
F2	0.988	0.857	0.966	0.984	0.708
F3	0.994	0.771	0.95	0.988	0.746
F4	0.985	0.892	0.967	0.982	0.634
F5	0.968	0.930	0.986	0.996	0.629
F6	0.979	0.913	0.978	0.994	0.661
F7	0.976	0.854	0.967	0.973	0.598
F8	0.985	0.790	0.97	0.987	0.634
F9	0.994	0.751	0.948	0.987	0.723

Table 10: Diffusion Exponent Drug Release Mechanisms

S.No	Diffusion exponent value (n)	Drug release mechanism
1	<0.45	Fickian release
2	0.45-0.89	Non-fickian transport
3	0.89	Case II transport
4	>0.89	Super case transport

CONCLUSION:

The results found that formulations containing **HPMC** showed good swelling ratio,water uptake, Percentage yield, Drug content and Drug entrapment efficiency due its high water absorbing ability and high viscosity nature required for hydrogels which may effect the drug release and also mucoadhesive nature of hydrogels.

So the choice of Aceclofenac might be a right and suitable candidate for the formulation of hydrogels and for therapeutic use.

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