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FORMULATION AND EVALUATION OF A MODIFIED RELEASE DOSAGE FORM OF BCS CLASS II DRUG

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ABSTRACT:

The purpose of the present work was to formulate and to evaluate modified release Aceclofenac tablets.The aim of the study was to prepare aceclofenac MR tablets using ethyl cellulose and cellulose acetate phthalate.Twelve different aceclofenac formulations were prepared.The preformulation studies.FTIR analysis concluded that there was no possible interaction between drug and polymer.The formulation containing only ethylcellulose showed an initial release of drug ranging from 20.30 ± 0.84 - 23.70 ± 0.63% for first 2 h and then release was sustained for 10 – 14 h. The formulations containing both EC and CAP showed 7.53 ± 0.55 - 15.42% drug release for first 2 h in gastric pH and then sustained for 14 h.The *in vitro* drug release profile of the formulations indicated variation in the release pattern on varying the concentration of EC and CAP.The above findings of the *in vitro* drug release data of all the formulations revealed that the initial release of drug was higher in the absence of CAP. As the concentration of EC and CAP increased, the initial drug release was minimal and sustained for longer duration.The *in vitro* release data of optimized formulation was fitted into various kinetic models.The most satisfactory formulation was subjected to short term stability studies by placing in varied conditions for sixty days. It was concluded that there were no significant changes in drug content or physical properties.

KEYWORDS: Aceclofenac, Ethyl Cellulose, Matrix tablets & Release kinetics.

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INTRODUCTION:

In pharmaceutical CRDDS, matrix based systems are the most commonly used type of release controlling methodology owing to their simple manufacturing process. The preparation of a tablet with the matrix involves the direct compression of the blends of drug, release retardant and other additives, in which the drug is uniformly distribute throughout the matrix core of the release retardant. Alternatively, drug-release retardant blends may be granulated to make the mix suitable for the preparation of tablets by wet granulation or beads.[1]

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system thatcould revolutionize method of medication and provide a number of therapeutic benefits.[2]

Based on intestinal permeability and solubility of drugs, *Amidon et al.*,developed biopharmaceutics classification system (BCS) Which classifies the drug into one of the four groups.

Class I drugs (High solubility/ High Permeability) are well absorbed orally since they have neither solubility nor Permeability limitation.

Class II drugs (Low solubility/ High Permeability) show variable absorption owing to solubility limitation.

Class III drugs (High solubility/ Low Permeability) show variable absorption owing to Permeability limitation.

Class IV drugs (Low solubility/ Low Permeability) are poorly absorbed orally owing to both solubility and Permeability limitation.[3]

Aceclofenac is a BCS class II drug which is a potent Nonsteroidal Anti inflammatory drug (NSAID) mainly used in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. As with most NSAIDs, irritation of the gastrointestinal (GI) tract is one of the major side effects reported after oral admistration of Aceclofenac. The GI intolerance of Aceclofenac is not only related to the inhibition of the prostaglandin synthesis but also related to the acute local contact of the drug with the gastric mucosa when it is given orally. As it possesses biological half life of 4hr, it makes up an ideal candidate for modified release dosage form.The gastric irritation can be minimized by formulating modified release matrix tablets of Aceclofenac using a combination of ethyl cellulose as a sustained release polymer and cellulose acetate phthalate as a pH dependent polymer such that intial release of drug in the gastric region is brought down and from there on to sustain it for longer period of time.[4]

MATERIALS& METHODS:

Aceclofenac was procured from Karnataka Antibiotics & Pharmaceuticals Ltd,BangaloreCellulose Acetate phthalate,Ethyl Cellulose was Procured from central drug house, New Delhi, lactose, magnesium stearate,Povidone K-30 & Talcwas procured from Karnataka Fine Chem,Bangalore.other chemicals and reagents were used are of analytical grade.

Preformulation studies:

It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included compatibility studies.

Compatibility studies

Compatibility studies were performed for aceclofenac with other additives by FTIR technique.The results were given in results and discussions.Compatibility study of drug with the excipients was determined by I.R. Spectroscopy (FTIR) using Perkin Elmer spectrum RX1 FT-IR spectrometer model. The pellets were prepared at high compaction pressure by using KBr and the ratio of sample to KBr is 1:200.The pellets thus prepared were examined and the spectra of drug and other ingredients in the formulations were compared with that of the original spectra.

FORMULATION OF ACECLOFENAC MR TABLETS:

Aceclofenac MR were prepared by using wet granulation technique, by using Ethyl cellulose and Cellulose acetate phthalate as polymers.

Table No1: Formula for Aceclofenac MR tablets

INGREDIENTS	E1 (mg)	E2 (mg)	E3 (mg)	E4 (mg)	E5 (mg)	E6 (mg)	E7 (mg)	E8 (mg)	E9 (mg)
Aceclofenac	100	100	100	100	100	100	100	100	100
Ethyl Cellulose (14 Cps)	10	10	10	15	15	15	20	20	20
Cellulose Acetate Phthalate	2.5	5	7.5	2.5	5	7.5	2.5	5	7.5
Povidone K-30	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8
Purified Water	5	5	5	5	5	5	5	5	5
Lactose	32.85	30.35	27.85	27.85	25.35	22.85	22.85	20.35	17.85
Magnesium Stearate	0.61	0.61	0.61	0.61	0.61	0.61	0.61	0.61	0.61
Talc	1.22	1.22	1.22	1.22	1.22	1.22	1.22	1.22	1.22

Total Weight/tablet	150	150	150	150	150	150	150	150	150

RESULTS AND DISCUSSION

PREFORMULATION STUDIES: Compatibility studies:

FTIR STUDY: the FTIR spectra of aceclofenac and aceclofenac with other additives were given below.

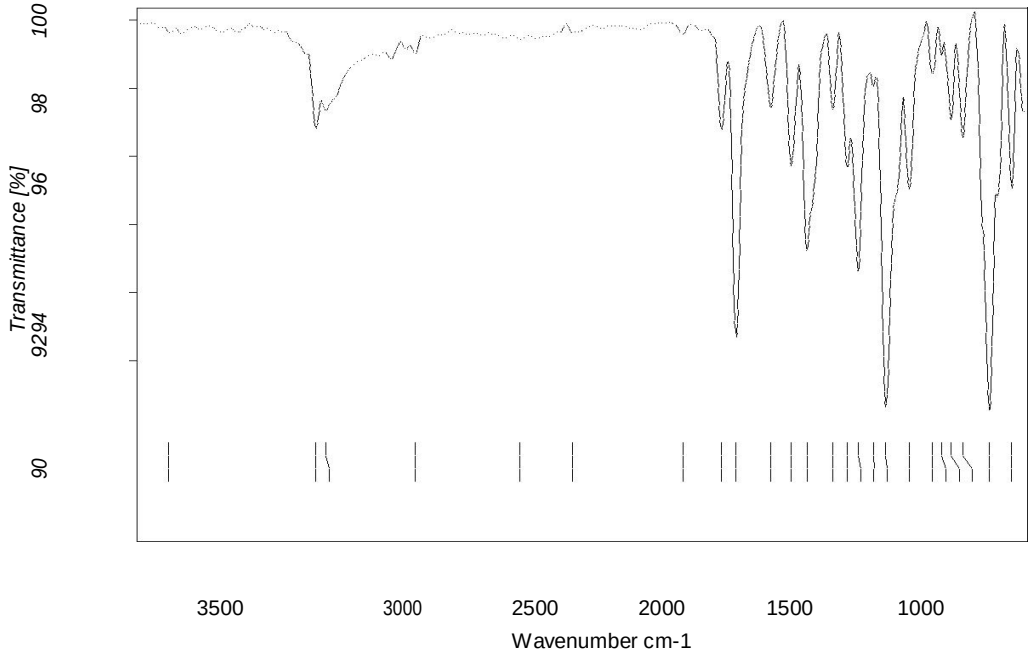
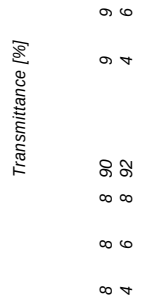


Fig No 1 : FTIR SPECTRA OF DRUG ACECLOFENAC



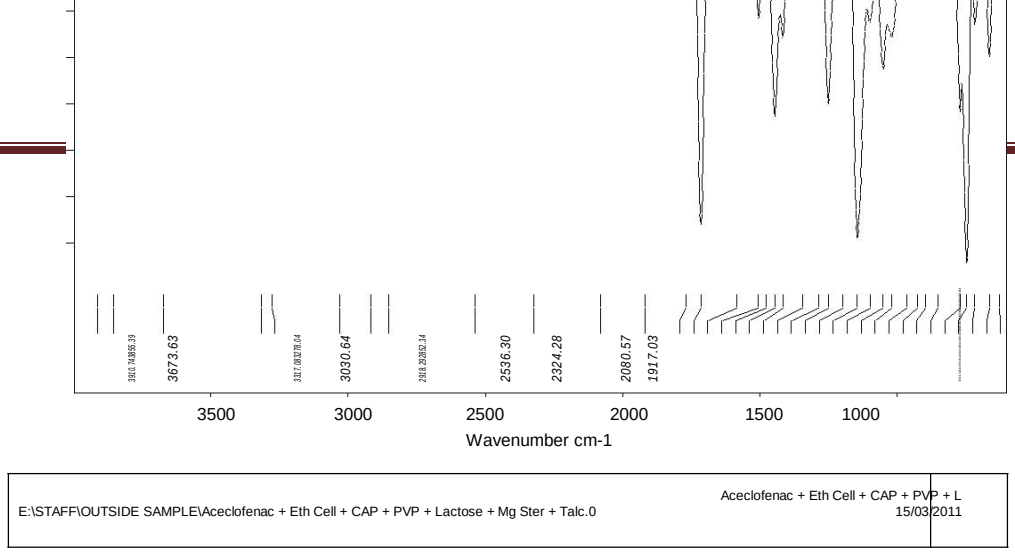


Fig No 2: FTIR SPECTRA OF DRUG – POLYMER MIXTURE

From the above spectras it was found that there is no interaction between aceclofenac and other additives. The presence of peaks at the expected range confirms that the materials taken for the study are genuine.

Table No 2:Flow property characterization of Aceclofenac blend

s.no	Formulation	Angle of Repose (°)	Compressibility Index(%)	Hausners Ratio
1	E1	29.40±0.28	12.5±4.3	1.14±0.05
2	E2	29.03±0.80	22.08±00	1.29±0
3	E3	29.56±1.54	26±7.03	1.35±0.12
4	F1	37.91±0.43	11.23±6.05	1.13±0.07
5	F2	38.15±1.68	11.23±6.05	1.13±0.07
6	F3	33.13±1.46	23.33±2.88	1.33±0.04
7	F4	27.01±1.21	17.77±1.92	1.21±0.02
8	F5	34.37±1.29	27.77±0	1.38±0.15
9	F6	30.39±1.11	12.77±6.30	1.5±0.08
10	F7	30.66±1.71	29.25±1.28	1.41±0.02
11	F8	33.49±0.86	24.52±4.30	1.32±0.07
12	F9	30.11±1.42	23.73±0.35	1.31±0.06

Table No 3: EVALUATION OF ACECLOFENAC MR TABLETS

PHYSICAL EVALUATION:

The weight variation, Friability, Hardness and Content uniformity were found to be within acceptable limits. All the physical properties of the formulation were conforming to the specifications of USP limits.

s.no	Formulation Code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Average weight(mg)	Drug content(%w/w)
1	E1	5.86±0.3	3.58±00	0.53	149.2±0.53	98.4
2	E2	6.66±0.7	3.56±00	0.44	149.3±0.46	99.85
3	E3	6.73±1.84	3.52±0.04	0.39	148.95±0.7	98.00
4	F1	4.76±0.37	3.5±0.03	0.47	150.2±0.13	99.20
5	F2	5.86±1.10	3.57±0.01	0.36	150.2±0.28	98.80
6	F3	7.86±0.23	3.57±00	0.46	150.2±0.14	98.00
7	F4	6.06±0.13	3.58±00	0.35	151.82±1.2	98.40
8	F5	6.83±0.58	3.5±00	0.35	152.2±1.53	98.40
9	F6	6.6±1.10	3.58±00	0.32	150.9±0.64	99.20
10	F7	6.26±0.41	3.58±00	0.25	150.5±0.36	98.00
11	F8	6.4±0.8	3.57±00	0.40	151.1±0.7	98.80
12	F9	7.33±0.50	3.55±00	0.29	149.71±0.19	98.00

Evaluation of Aceclofenac MR tablets

Tablet Dimensions:

The dimensions determined for formulated tablets were given in Table No 3. Tablets mean thickness was found to be in the range of 3.5± 0.03 mm to 3.58±0.01mm.

Hardness Test:

The measured hardness of tablets of each batch ranged between 4.76±0.37 to 7.86±0.23 $kg/cm^2$and was shown in the Table No 3.

Friability Test:

The value of % Friability of each batch was found to be in the range of 0.25 to 0.53%. The values of friability test are given in Table No 3.

Weight variation test:

The percentage weight variations for all formulations are shown in Table No 3. All the formulated (F1 to F9) tablets passed weight variation test as per the pharmacopoeias limits of±7.5%. The weights of all the tablets were found to be uniform with low standard deviation values.

Drug Content Uniformity:

The percentage of drug content for F1 to F9 was found to be 98.45% to 98.94 % of Aceclofenac. The results are shown in Table No 4

s.no	TIME (min)	E1	E2	E3
2	30	7.15	6.79	7.15
3	60	11.29	10.80	11.45
4	90	15.91	14.94	16.88
5	120	23.70	20.30	22.73
6	180	33.07	30.27	32.46
7	240	45.12	44.01	40.99
8	300	55.24	51.95	46.62
9	360	62.09	62.69	55.77
10	420	70.54	70.04	63.60
11	480	82.14	79.58	73.38
12	540	90.61	85.49	79.64
13	600	99.20	91.05	84.59
14	660	----	95.15	87.96

15	720	----	99.38	92.06

s.no	TIME (min)	F1 (%CDR± SD)	F2 (%CDR± SD)	F3 (%CDR± SD)	F4 (%CDR± SD)	F5 (%CDR± SD)	F6 (%CDR± SD)	F7 (%CDR± SD)	F8 (%CDR± SD)	F9 (%CDR±SD)

16	780	----	----	95.68
17	840	----	----	99.18

2	30	3.51	1.16	3.339	2.30	1.09	1.57	1.69	1.70	1.82
3	60	4.25	6.18	5.58	4.24	4.85	4.12	2.62	3.65	3.88
4	90	8.3	8.01	7.53	8.74	6.80	5.95	6.43	6.94	4.98
5	120	15.42	12.39	9.11	13.95	12.51	8.74	9.11	8.77	7.53
6	180	30.37	35.70	28.66	23.81	25.38	22.71	22.71	32.16	32.54
7	240	48.12	50.18	49.56	43.25	44.83	43.12	45.5	45.71	43.74
8	300	59.70	59.82	67.09	55.56	57.7	54.09	55.91	54.89	49.25
9	360	68.50	69.11	75.90	64.84	67.39	64.95	66.17	65.67	55.85
10	420	75.37	76.35	85.09	73.04	76.93	72.42	72.55	71.71	60.65
11	480	83.71	88.69	93.92	82.23	86.36	80.88	80.64	80.80	65.93
12	540	98.73	99.22	98.51	90.20	93.25	88.61	84.61	84.17	70.49
13	600	----	----	-----	94.19	94.81	94.41	87.25	87.07	77.25
14	660	----	----	----	99.27	98.92	98.52	88.81	89.35	82.55
15	720	----	----	----	----	-----	-----	92.06	91.89	88.83
16	780	----	----	-----	----	----	----	95.07	93.94	94.27
17	840	----	----	-----	-----	-----	-----	99.06	98.91	99.35

Table No :5 COMPARITIVE RELEASE PROFILES OF F1 to F9 MODIFIED RELEASE ACECLOFENAC TABLETS

Dissolution profile of formulation E1 to E3

In-vitro drug release Studies:

All the formulations E1 to E3 are subjected to *invitro* release studies in 900 ml 0.1N Hcl (pH 1.2) using dissolution apparatus, at 50 rpm at 37±0.5˚C, and the results are recorded as shown in Table No 5 and the comparative drug release of E1-E3 was shown in Fig No 3

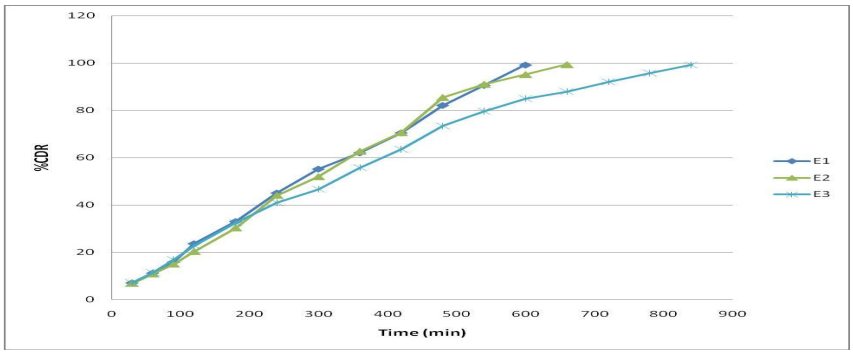


Fig No 3: Comparative drug release profile of E1, E2 and E3 modified release Aceclofenac tablets

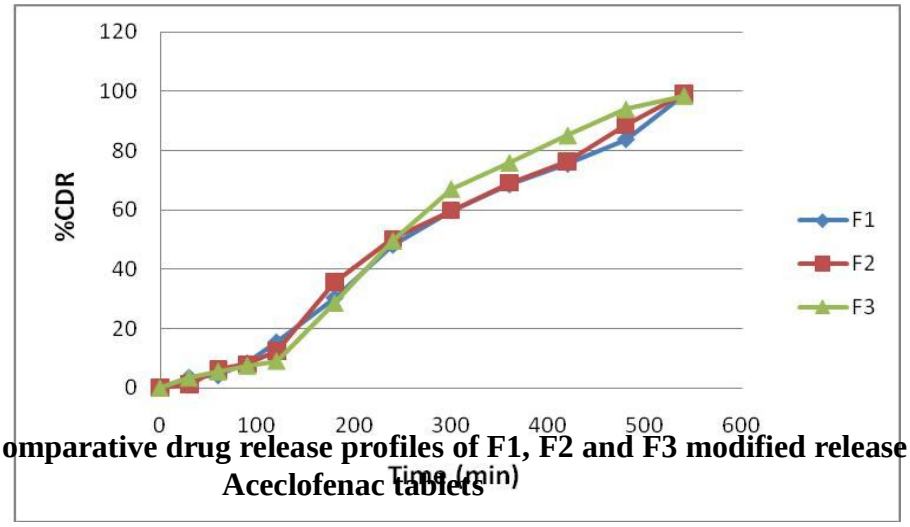


Fig No 4: Comparative drug release profiles of F1, F2 and F3 modified release Aceclofenac tablets

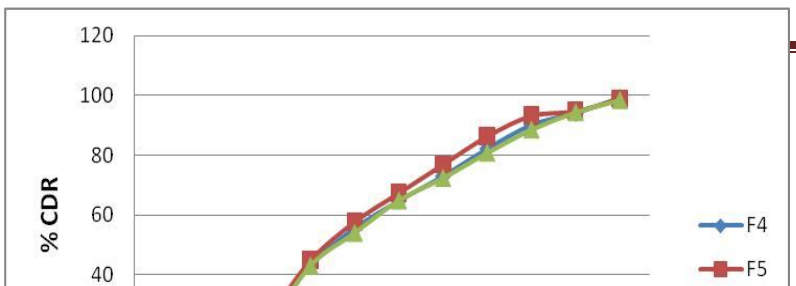


Fig No:5 Comparative drug release profiles of F4, F5 and F6 modified release Aceclofenac tablets

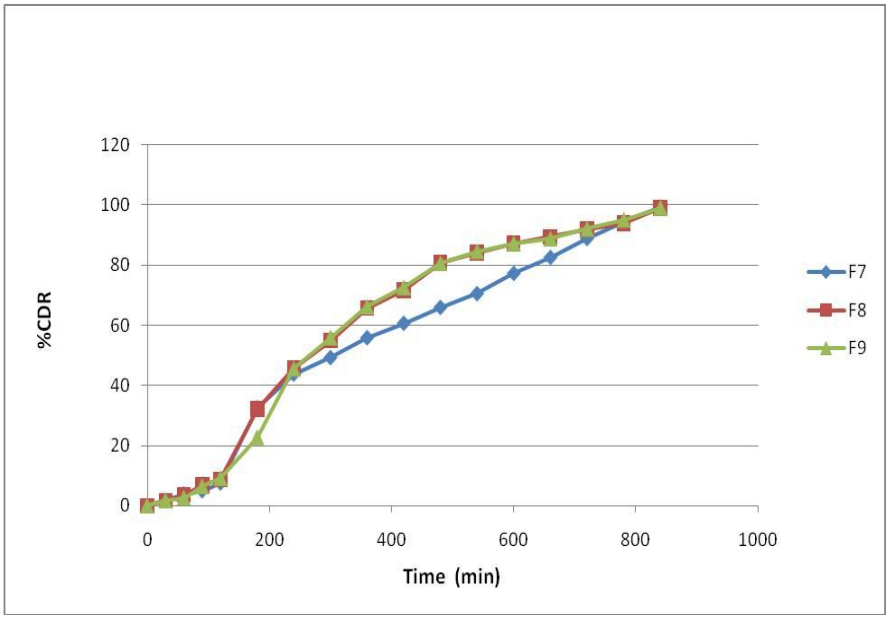


Fig No 6: Comparative drug release profiles of F7, F8 and F9 modified release Aceclofenac tablets

KINETIC MODELLING OF DRUG DISSOLUTION PROFILES

The regression coefficient (R^2) values of release data of all formulations obtained by curve fitting method for zero-order, first-order, Higuchi and Krosmeyer-Peppas model are reported in Table No:6.The *in vitro* release data of formulation F9 was fitted into various kinetic models. Correlation coefficients of formulation F9 batch showed higher correlation with zero order plots than First order, Higuchi model and Peppas model. The 'n' value was found to be 0.848 which corresponds to Non-Fickian release. So, predominant drug release mechanism was found to be of controlled and Non-Fickian type.

Formulation code	Zero order		First order		Higuchi plot r		Korsemeyer & peppas	
	r^2	k	r^2	k	r^2	k	r^2	N
F9	0.96	0.12	0.78	0.001	0.958	3.98	0.848	0.834

TABLE 6:DRUG RELEASE KINETICS

STABILITY STUDIES

Table No 7 : Physicochemical parameters of most satisfactory formulation F9 during stability studies

Time (Days)		Formulation F9	
		Hardness(kg/cm^2)	Drug content (%)
0		7.33	98.00
30	**A**	7.1	98.44
	B	7.3	97.60
60	**C**	6.93	98.29
	D	7.1	98.20

A, C = 30 ± 2°C / 65 ± 5% RH

B, D = 40 ± 2°C / 75 ± 5% RH

Table No 8: Drug release profile for most satisfactory formulation F9 during stability studies

TIME (min)	AFTER 30 DAYS		AFTER 60 DAYS	
	A	B	C	D
	F9 (%) ± SD	F9 (%) ± SD	F9 (%) ± SD	F9 (%) ± SD
30	1.82 ± 0	1.82 ± 1.02	1.63 ± 0.25	1.27 ± 0.25
60	3.82 ± 0.25	4 ± 1.03	3.64 ± 0.0002	4.00
90	4.73 ± 0.51	4.92 ± 1.28	4.73 ± 0.51	5.64 ± 1.81
120	7.83 ± 0.25	7.11 ± 0.16	7.47 ± 0.25	7.65 ± 0.002
180	31.14 ± 0.77	37.87 ± 1.80	30.05 ± 0.77	32.60
240	43.01 ± 1.03	42.46 ± 3.35	41.91 ± 0.51	43.74
300	48.51 ± 0.51	47.79 ± 1.55	48.33 ± 0.77	47.43
360	55.12 ± 1.02	54.21 ± 1.81	55.30 ± 0.77	53.48
420	59.19 ± 1.54	57.55 ± 1.81	59.91 ± 0.51	58.64
480	65.08 ± 1.54	63.98 ± 1.55	65.62 ± 0.77	63.07
540	70.06 ± 1.28	68.97 ± 1.81	70.24 ± 1.03	70.42
600	76.88 ± 0.51	76.14 ± 1.56	75.24 ± 2.83	77.05
660	81.87 ± 1.29	80.96 ± 1.05	82.24 ± 0.78	80.96
720	88.15 ± 0.76	88.15 ± 0.79	86.88 ± 1.03	87.60 ± 3.6
780	93.17 ± 1.53	93.70 ± 0.79	91.71 ± 0.52	95.35
840	99.09 ± 0.51	99.29 ± 0.79	98.91 ± 0.78	98.73

All values are mean of 3 readings.

A, C = 30 ± 2°C / 65 ± 5% RH

B, D = 40 ± 2°C / 75 ± 5% RH

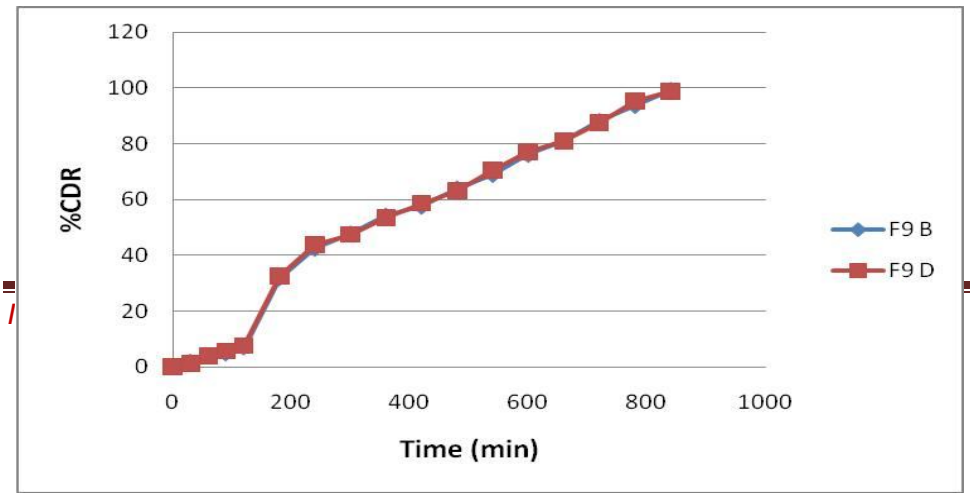


Fig No 7: *In vitro* drug release of F9B and F9D

RESULTS AND DISSCUSSION

In the present study, Aceclofenac modified release tablets were prepared by using Ethylcellulose as a sustained release polymer and CAP as a pH dependent polymer. A total of 12 formulations were prepared by wet granulation technique. The preformulation studies such as bulk density, tapped density, angle of repose, compressibility index and Hausner ratio were evaluated which were found to be within prescribed limits and indicated good to poor flowing property. The data obtained from physicochemical parameters such as hardness, friability, weight variation, drug content and *in vitro* drug dissolution are shown in Table No (2,3,4,5)

Preformulation studies:

Estimation of Aceclofenac was carried out by using SHIMADZU-1700 UV spectrophotometer at λ_{max} 268 nm in 0.1N HCl (2% SLS) and in phosphate buffer at 275 nm (pH 6.8). The linear coefficients were found closer to 1. By using the regression coefficient equation, the drug content and % CDR were calculated.

UV spectrum analysis of Aceclofenac:

Aceclofenac showed maximum absorption at a wavelength of 268 nm in 0.1 N HCl and 275 nm in phosphate buffer (pH 6.8). Standard calibration curve when subjected to regression analysis, the value of regression coefficient was found to be 0.998 and 0.999 which showed linear relationship between concentration and absorbance Any formulation development work has to be preceded by preformulation studies. This preformulation study includes drug polymer compatibility study and analytical investigation of the drug. FT-IR studies showed that there was no interaction between drug and polymer. So, the drug and polymers were found to be compatible.

Formulation studies:

Various formulations of modified release tablets were developed by using Povidone (PVP) in water as the granulating fluid which is mixed with Aceclofenac, lactose, EC, CAP followed by drying and milling of the granules and then blending with magnesium stearate and talc.

Micromeritic properties:

Angle of repose:[5]

The results of angle of repose ranged between 27.01 ± 1.21 to 38.15 ± 1.6º (Table No 2) which indicates good to fair flow properties of granules.

Compressibility index and Hausner ratio:

The compressibility index values were found to be in the range of 11.23 ± 6.05 to 29.25 ± 1.28% and the Hausner ratio was found to be in the range of 1.13 ± 0.07 to 1.5 ± 0.08 (Table 2). These findings indicated that the mixture of all batches of formulation exhibited good to poor flow characters.

Evaluation of physicochemical parameters[6,7,8]

Tablet hardness:

Hardness of the developed formulations varied from 4.76 ± 0.37 to 7.86 ± 0.23 kg/cm^2 (Table 3) in all the formulation indicating good mechanical strength with an ability to withstand physical and mechanical stress condition while handling.

Tablet thickness:

Thickness of the developed formulations varied from 3.5 ± 0.03 mm to 3.58 ± 0.01mm (Table 3) in all the formulations and the average thickness was within the range of ± 5%. Each sample was analyzed in triplicate.

Friability:

The loss in total weight of the tablets due to friability was in the range of 0.25 to 0.53% (Table 3) in all the formulation and the friability value was less than 1% which ensured that formulated tablets were mechanically stable.

Weight variation:

The maximum % deviation of all the formulations is shown in Table 3. As none of the formulation showed a deviation of more than ± 7.5% (IP limit) for any of the tablets tested, the prepared formulations comply with the weight variation test, thus it fulfills the IP requirements.

Uniformity of drug content:

The drug content in different tablet formulations was uniform and in the range of 98.0 to 99.2 (Table 3). The drug content was found within the limits specified by IP.

***In vitro* drug dissolution study:**

The *in vitro* release study of Aceclofenac from modified release tablets of all formulations were carried out in 0.1 N HCl (2% SLS) for first 2 h and then in phosphate buffer (pH 6.8). From *in vitro* dissolution profile of Aceclofenac modified release tablet, it was found that the formulation F9 containing 20 mg EC and 7.5 mg CAP, gave initial drug release of 7.53 ± 0.55% for first 2 h which was less compared to other formulations and eventually complete release of the drug was found to be within 14 h which was longer than other formulations. This was mainly due to higher concentration of EC and CAP.

Kinetic modelling of drug dissolution profiles:[9,10,11]

The *in vitro* release data obtained were fitted into various kinetic models. Correlation coefficients of formulation F9 batch showed higher correlation with zero order plots than First order, Higuchi model and Peppas model. The 'n' value was found to be0.848 which corresponds to Non-Fickian release. So, predominant drug release mechanism was found to be of controlled and Non-Fickian type.

Stability studies:

Stability studies were carried out for the most satisfactory formulation F9 at 30 ± 2°C / 65 ± 5%

RH and 40 ± 2°C / 75 ± 5% RH for 60 days to assess their long term stability.At various time intervals of 30 days and 60 days, samples were evaluated. There was no significant difference in the physicochemical parameters evaluated like hardness, drug content and *in vitro* dissolution pattern at the various sampling points. There was no statistically significant difference between the initial values and the results obtained during stability studies.

CONCLUSION

The micromeritic evaluation such as angle of repose, compressibility index and Hausner ratio showed good to poor flow properties. The physicochemical evaluations of different formulations were carried out as per IP and the results obtained were in accordance with IP limits. The formulation containing only ethylcellulose showed an initial release of drug ranging from 20.30 ± 0.84 - 23.70 ± 0.63% for first 2 h and then release was sustained for 10 – 14 h. The formulations containing both EC and CAP showed 7.53 ± 0.55 - 15.42% drug release for first 2 h in gastric pH and then sustained for 14 h.

The *in vitro* drug release profile of the formulations indicated variation in the release pattern on varying the concentration of EC and CAP. Among 12 formulations, formulation F9 containing 20% of EC and 7.5% of CAP (core weight of the tablet) showed 7.53 ± 0.55% of initial drug release in 2 h in gastric pH and eventually complete drug release over a period of 14 h.

The above findings of the *in vitro* drug release data of all the formulations revealed that the initial release of drug was higher in the absence of CAP. As the concentration of EC and CAP increased, the initial drug release was minimal and sustained for longer duration.

The *in vitro* release data of formulation F9 was fitted into various kinetic models. Correlation coefficients of formulation F9 batch showed higher correlation with zero order plots than First order, Higuchi model and Peppas model. The 'n' value was found to be 0.848 which corresponds to Non-Fickian release. So, predominant drug release mechanism was found to be of controlled and Non-Fickian type.

The most satisfactory formulation F9 was subjected to short term stability studies by placing in varied conditions for sixty days. It was concluded that there were no significant changes in drug content or physical properties. The *in vitro* drug release of formulation F9 showed no noticeable changes confirming that the formulation was stable after a periodofperiod60days.

REFERENCES:

1. Colombo P, Bettini R and Massimo G.Drug diffusion front movement is important in drug release control from swellable matrix tablets. J Pharm Sci. 1995;84(8):991-997.
2. Chien YW. Novel drug delivery systems.2nd ed. New York, Marcel Dekker, Inc. 1992.
3. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetics a treatise. 2nd

ed. New Delhi: Vallabh Prakashan; 2009. p. 345.
4. Vaishali AK, Nidhi PS, Jasmine GA, Bharti DS. Development and characterization of enteric-coated immediate-release pellets of aceclofenac by extrusion/spheronization technique using *κ*-carrageenan as a pelletizing agent. AAPS Pharm Sci Tech 2010;11(1):336-43.
5. Powder flow properties [online] 2010 Oct.[cited on 2011 Feb 18]; Available from: URL: http://www.pharmacopeia.cn/v29240/usp29nf24s0c1174.html.
6. Indian Pharmacopoeia. 6th ed. Ghaziabad: The Indian pharmacopoeia commission; 2010. p. 185-95, 392, 559. vol I.
7. Mutalik S, Krishnan M, Reddy MK, Kushtagi P, Usha AN, Parambil A *et al*. Chitosan and enteric polymer based once daily sustained release tablets of aceclofenac: *in vitro* and *in vivo* studies. AAPS Pharm Sci Tech 2008;9(2):651-9.
8. Shoaib MH, Tazeen J, Hamid A. Evaluation of drug release kinetics from ibuprofen matrix tablets. Pak J Pharm Sci 2006;19(2):119-24.
9. Grassi M, Grass G. Mathematical modelling and controlled drug delivery: matrix systems. Curr drug del. 2005;2:97-118.
10. Gauforian T, Safari A, Khosro A, Parviz F, Nokhodchi A. A drug release study from hydroxypropylmethylcellulose (HPMC) matrices using QSPR modeling. J. Pharm. Sci. 2007;96(12):3334-351.
11. Ghosh TK, Jasti BR. Theory and practice of contemporary pharmaceutics. London: CRC press; 2005. p. 146-47, 217-25, 242-8, 334-39.

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