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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE ACECLOFENAC TABLETS

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Abstract: The purpose of this research was to develop a matrix type tablets containing drug Aceclofenac with different ratios of hydrophilic (hydroxyl propyl methyl cellulose) and hydrophobic (ethyl cellulose) polymers. The physicochemical compatibility of the drug and the polymers studied by infrared spectroscopy suggested absence of any incompatibility. Formulated sustained release Aceclofenac tablets were physically evaluated with regard to thickness, weight variation, drug content, friability, hardness. All prepared formulations indicated good physical stability. In-vitro dissolution studies of formulations were performed by using USP-I dissolution apparatus. The results followed the release profile of Aceclofenac followed zero order kinetics. However, the release profile of the optimized formulation F2 has r^2 value 0.998 for zero order. To conclude, hydroxy propyl methyl cellulose at a concentration ratio of 4: 3 is suitable for preparing sustained release matrix tablets of Aceclofenac.

Key words: Aceclofenac, sustained release, hydroxyl propyl methyl cellulose, *in-vitro* dissolution

Introduction:

SRDDS include any drug delivery system that achieves slow release of drug over an extended period of time. This leads to increase in duration of effect so that therapeutic effect is sustained[1]. The basic concept underlying the design of oral sustained release the drug delivery system is to maintain a steady therapeutic drug level over a period of 12-24 hrs. Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption[2]. Such immediate-release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. However, after absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached, another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms. In recent years, various modified-release drug products have been developed to control the release rate of the drug and/or the time for drug release[4].

Aceclofenac is a drug which is having low half life (less than 2 hours). In the present study, Aceclofenac was formulated as sustained release matrix tablets in order to increase the retention time of the drug in the body to have better sustained action and to reduce the dose frequency.

Materials and Methods:

Materials:

Aceclofenac was selected as model drug for sustained release drug delivery. To deliver the drug for prolonged time some polymers are used in the formulation. In this formulation we selected HPMC K100, ethyl cellulose and Carbopol 934 to deliver the drug for long time. And PVP K30 was selected as a binder to prepare granules. Isopropyl alcohol was used as a solvent for the preparation of binder solution. Lactose was selected as a diluent and magnesium stearate as a lubricant and talc was selected as a glidant.

Methods:

1. **Investigation of Compatibility of Drug with Polymers:**

The physicochemical compatibility between ACF and polymers used in the tablets was studied by using Fourier transform infrared spectroscopy by using potassium bromide. The results are indicated that there was no chemical incompatibility between drug-polymer, polymer-polymer, and polymer-excipients.

2. **Preparation Of Sustained release Aceclofenac Tablets**

Aceclofenac, polymers (HPMC K100M, CP, EC 45cps), lactose were triturated well and allowed to pass through sieve no.30 and mixed thoroughly (Table 1). Polyvinylpyrolidine K-30 dissolved in Isopropyl alcohol was used as binder; the granules

were prepared by wet granulation method after passing through sieve no.16. The granules thus obtained were dried. The dried granules were received and are added with the lubricants like talc, magnesium stearate .The granules were compressed to get tablets of average weight 500 mg using punching machine.

Table 1: Composition of Aceclofenac tablets

S. No	Ingredients	FI	FII	FIII	FIV	FV	FVI	FVII	FIIX	FIX
1	Aceclofenac	200	200	200	200	200	200	200	200	200
2	HPMC(k-100)	100	150	200	_	_	_	_	_	_
3	Ethyl cellulose	_	_	_	150	200	250	_	_	_
4	Carbopol 934	_	_	_	_	_	_	50	100	150
5	PVP(K-30)	10	10	10	10	10	10	10	10	10
6	Lactose	180	130	80	130	80	30	230	180	130
7	Purified talc	4	4	4	4	4	4	4	4	4
8	Magnesium stearate	6	6	6	6	6	6	6	6	6
9	Isopropyl alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
10	Total	500	500	500	500	500	500	500	500	500

3. Evaluation tests for tablets:

The formulated tablets were evaluated for the following physico chemical characteristics.

A. General appearance:

The formulated tablets were assessed for its general appearance.

B. Thickness:

Thickness of the formulated matrix tablets were measured by using Vernier Calipers.

C. Weight variation:

The formulated tablets were tested for weight uniformity. 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with the average weight to ascertain whether it is within permissible limits or not[7] (Table 2).

Table 2: Standard weight variation limits (IP)

S No.	Average mass	Percentage deviation
1.	130mg or less	±10
2.	More than 130 mg and less than 324 mg	±7.5
3.	324 mg or more	±5

D. Hardness:

Hardness of the tablets was determined using the Monsanto hardness tester. The lower the plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along the gauge in the barrel to indicate the force[3].

E. Friability:

The Roche friability test apparatus was used to determine the friability of the prepared tablets. 20 pre-weighed tablets were placed in the apparatus, which was given 100revoluations. After which the tablets were re-weighed. The percentage friability was calculated[3].

F. Drug content:

Twenty tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 200mg of Aceclofenac was transferred into a 100ml volumetric flask and extracted with distilled water. Then it was filtered and suitable dilutions were made and absorbance was measured by using Shimadzu UV-Visible spectrophotometer (UV-1601) at 275nm[3].

G. In-vitro drug release:

The in-vitro drug release of prepared tablets was estimated by dissolution study. It was done by using paddle type dissolution test apparatus up to 12 hours. The temperature was maintained at 37 ± 0.5 ^{o}C. At each sampling point,

5 ml of sample was withdrawn and the same amt was replaced with fresh buffer. The collected samples were analyzed in UV-visible spectrophotometer at 275 nm.

Table 3: Weight variation, thickness, friability, hardness and drug content of tablets

S.no.	Formulation	Thickness (mm)	Hardness (Kg/cm^2)	Percentage Friability	Weight Variation	Drug content in %
1	F-I	4.3±0.22	8.5±1.5	0.36	498±3.1	96
2	F-II	4.6±0.32	8.9±0.9	0.41	496±2.8	95
3	F-III	4.9±0.44	7.1±1.2	0.45	499±3.1	97.8
4	F-IV	4.5±0.28	8.2±1.4	0.38	500±1.5	94.7
5	F-V	4.4±0.65	8.8±2	0.42	495±4	201
6	F-VI	4.0±0.33	8.4±1.7	0.54	496±2.4	99.2
7	F-VII	5.0±0.76	8.5±.54	0.48	498±3.4	96
8	F-VIII	4.3±0.55	8.9±1.1	0.42	494±2.2	96.8
9	F-IX	4.3±0.32	7.5±0.42	0.49	495±4.5	98.2

Results and Discussion:

1. Weight variation, thickness, hardness, friability and drug content:

Weight variation was found with in specifications of I.P limits and the values shown in table 3. Thicknesses of all fabricated formulations are in the range of 4.3-5mm and the values shown in table 3. The hardness of all fabricated formulations was in the range of 7.5 - 8.9kg/cm^2. Friability for all the formulations was in the range of 0.36-0.54% (Table 3). The value of hardness and percent friability indicates good handling property of prepared tablets. The results for the above parameters were found to be in the recommended range.

2. In-vitro drug release

FI released more than 75% of drug at 12^{th} hour, where as FII released more than 80% of drug at 12^{th} hour and FIII released more than 70% of drug at 12^{th} hour. In case of formulations containing ethyl cellulose FIV and FV released more than 65% of drug at 12^{th} hour. FVI releases more than 64% of drug at 12^{th} hour. In case of formulations containing Carbopol FVII and FVIII drug release was more than 76% of drug at 12^{th} hour. Whereas, FIX releasing more than 69% of drug at 12^{th} hour (Table 4 and figure 1).

Table 4: In vitro drug release data of formulations

Time (hrs)	FI	FII	FIII	FIV	FV	FVI	FVII	FVIII	FIX
1	19.64	17.65	16.12	21.66	18.05	17.66	30.01	25.66	20.20
2	26.62	25.96	22.60	27.31	24.1	22.60	37.14	29.80	25.68
3	32.85	30.61	27.31	32.7	28.69	27.20	41.52	34.88	29.56
4	39.76	36.17	32.38	37.61	32.44	32.49	45.29	41.53	34.29
5	44.39	42.12	37.81	42.97	34.61	38.33	49.47	46.90	39.26
6	49.68	48.78	42.99	46.12	39.56	43.63	53.44	51.29	43.17
7	53.83	54.16	47.75	52.34	45.69	47.84	57.75	58.60	48.20
8	58.87	60.31	54.59	58.17	49.16	50.21	62.69	64.68	52.17
9	64.7	66.12	58.32	62.31	53.28	53.55	66.04	69.36	56.37
10	68.31	72.31	64.46	65.96	56.52	56.54	72.97	72.32	62.09
11	72.1	76.12	68.09	68.45	61.55	61.69	76.40	74.28	66.02
12	75.68	82.12	70.12	71.45	66.36	64.52	80.30	76.50	69.80

Marketed sustained release formulation (Hifenac SR) the drug release is 79.56% in 12 hours, where as our selected formulation FII releases 82.12% of drug in 12 hours. Hence formulation FII was selected as optimized formulation.

The release kinetic analysis was studied for formulation FII for first order, zero order, and Higuchi and Peppas kinetics. The results were plotted graphically. From the graph it was found that dissolution profile of formulation FII follows zero order kinetics.

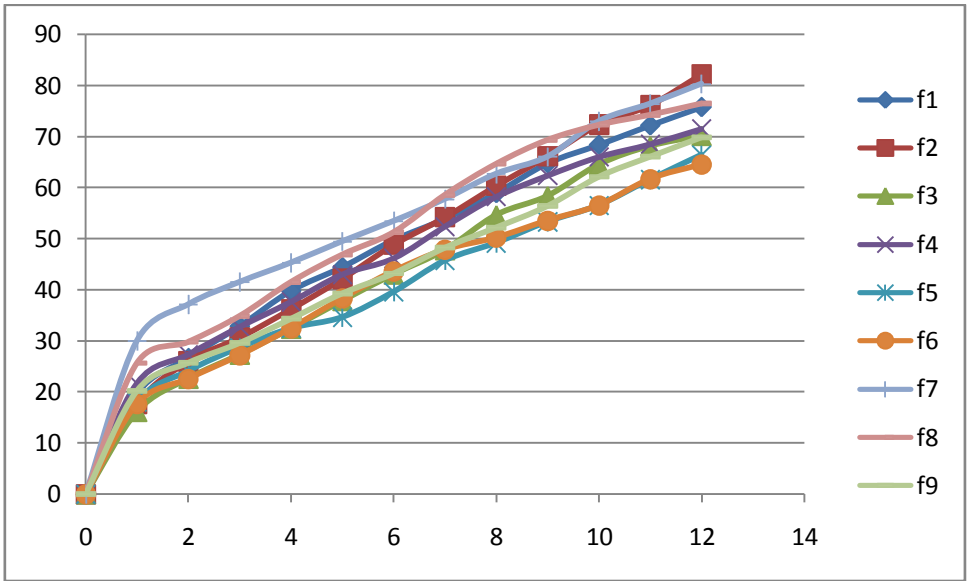

Figure 1: In vitro drug release profile of formulation

Conclusion:

From the results and discussions, amongst the 9 different formulations designated as FI ,FII ,FIII, FIV, FV ,FVI, FVII, FVIII, FIX the formulation FII was found to be the better formulation in terms of sustained release and maximum percentage drug release and results are comparable with that of the marketed formulation . It can be concluded that hydroxyl propyl methyl cellulose at a concentration ratio of 4: 3 is suitable for preparing sustained release matrix tablets of Aceclofenac.

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