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Research Paper

Formulation and Evaluation of Aceclofenac Matrix Tablet

Pharma

KEYWORDS : Aceclofenac, Matrix tablets, Wet granulation.

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ABSTRACT

The aim of the study was to develop matrix tablets of Aceclofenac by wet granulation using hydrophilic polymer like Hydroxy propyl methyl cellulose K -100. Hydroxy propyl methyl cellulose K -15 Hydroxy propyl methyl cellulose K -4M The drug excipient mixtures were subjected to preformulation studies. The tablets were subjected to physicochemical studies, in- vitro drug release, kinetic studies and stability studies. FTIR studies shown there was no interaction between drug and polymer. The physicochemical properties of tablets were found within the limits. Aceclofenac is a non steroidal anti-inflammatory agent used in treatment of rheumatoid arthritis, osteoarthritis and spondylitis. The drug release from optimized formulations was extended for a period of 12 hrs. The kinetic treatment of selected formulation (F5) showed that the release of drug follows zero order models. The optimized formulations were subjected to stability studies for three month at 45° temperature with RH 75±5% and showed there were no significant changes in drug content, physicochemical parameters and release pattern. Results of the present study indicated the suitability of hydrophilic polymers in the preparation of matrix based sustained release formulation of Aceclofenac.

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are considered to be the first-line drugs in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and spondylitis, Aceclofenac is one of them[1]. It is a newer derivative of Diclofenac with low gastrointestinal complications. The short biological half-life (3- 4h) and dosing frequency more than one per day make Aceclofenac an ideal candidate for sustained release. To reduce the frequency of administration and to improve patient compliance, a once-daily sustained release formulation of Aceclofenac is desirable[2]. Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in designing a sustained release system. The present study aims to develop sustained release matrix tablets using hydrophilic matrix materials[2], such as HPMC- K 15, HPMC- K4M and HPMC- K 100 along with drug in varying proportions by wet granulation method. For sustained release systems, the oral route of drug administration has received the most attention as it is natural, uncomplicated, convenient and safer route[3] Matrix tablets were prepared by either wet granulation or direct compression method. Currently available sustained matrix tablets are generally prepared by wet granulation method. The aim of the present work was to prepare sustained release matrix tablets of Aceclofenac and to study the effect of *in-vitro* release characteristics, kinetics of the prepared formulations and stability studies [4].

Materials

Aceclofenac, Hydroxy propyl methyl cellulose K-100 and, Hydroxyl propyl methyl cellulose K-15 were obtained as gift samples from concept pharmaceuticals ltd, Aurangabad, India. Lactose, Mannitol, Povidone (PVP K-30) were purchased from loba chemicals Mumbai, All other chemicals used were of analytical grade.

Methods

Preformulation studies

Micromeritic properties

The physical mixtures were prepared by triturating drug and excipients in a dried mortar for 5 min. The angle of repose of Aceclofenac and its Physical mixtures with other excipients were determined by fixed funnel method. The angle of repose, Compressibility index, Degree of compression (c) and the Hausner's ratio were calculated [5] using following equations. The result was shown in table no: 1

Drug-excipient compatibility studies

Infrared (IR) spectroscopy was conducted using a FTIR Spectrophotometer (Aglient Cary 630ATR) and the spectrum was recorded in the wavelength region of 4000 to 400 cm−1. The procedure consisted of dispersing a sample (drug alone or mixture of drug and excipients)

Preparation of tablets

Tablets weighing 320mg were prepared containing 100 mg of Aceclofenac and Lactose, Mannitol and HPMC. Polyvinyl pyrrolidone (3%) was used as binder. Magnesium stearate and Talc (1.8%) was added as lubricant prior to compression. Different tablet formulations were prepared by wet granulation technique. All the powders were passed through sieve no 24. Required quantity of drug, diluents and polymers were mixed thoroughly and a sufficient quantity of binding agent was added slowly. After enough cohesiveness was obtained, the mass was sieved through sieve no 16. The granules were dried at 50ºC for 45minuts and were mixed with talc and magnesium stearate. The tablets were compressed using multiple punch tablet compression machine (Cemach Pvt. Ltd). The different formulations were shown in table no: 2

Evaluation of physical properties of matrix tablets

All prepared matrix tablets were evaluated for uniformity of weight and drug content, as per I.P. Friability was determined using roch friabilator. Hardness was measured by using Pfizer hardness tester. Diameter and thickness were measured by Vernier caliper [6]. The result was shown in table no: 3

Dissolution studies

The in vitro dissolution study was carried out using USP Type II dissolution apparatus. The study was carried out in 900 ml of 0.1N HCl (pH 1.2) for first 2hours and then 900 ml of phosphate buffer (pH 6.8) from 2nd to 12 hr. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37±0.50C. Basket rotation was adjusted to 50 rpm. At definite intervals, 5 ml sample was withdrawn and analyzed spectrophotometricaly at 274 nm for the drug release. At each time of withdrawal, 5 ml of fresh corresponding medium was replaced into the dissolution flask [7].

Stability studies

Accelerated stability study was carried out to observe the effect of temperature and relative humidity on selected formulation (F5), by keeping at 40°± 2°C, in air tight high density polyethylene bottles for three months, at RH 75±5%. Physical evaluation and *in-vitro* drug release was carried out in each month [8].

Results and Discussion

Micromeritic properties

The results of Micromeritic properties were performed. The results of indicate that the Aceclofenac raw material showing passable flowability with the angle of repose values ranging from 29.64^0 to 33.18^0. All granules ready for compression showing fair to good flowability with the angle of repose values ranging from 25.62^o to 29.56^o. According to angle of repose graph readings and are better than that of powder drug. The bulk density, tapped density, compressibility index and Hausner ratio were observed. It reveals that all the formulation blend having

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good flow characteristics and flow rate than raw material. Degree of compression is characteristic of compression capability of the granules and the results obtained exhibited good compression capability of the granules.

Drug Excipient Compatibility Studies

Drug excipient compatibility studies were carried out by IR spectrophotometer. The IR spectra of pure Aceclofenac and its polymers were shown there was no interaction between drug and polymer.

Evaluation of prepared tablets

The results of physical evaluation of tablets were given in Table no: 3. The tablets of different batches were found uniform with respect to hardness within the range of 5-7 kg/cm². Another measure of a tablet's strength is friability. Conventional compressed tablets that lose Less than 1% of their weight are generally considered acceptable. The diameter of all Diameter of all formulation was in the range of 3.73- 3.93 cm. In weight variation test, the pharmacopoeial limit for percentage deviation for tablets of more than 250 mg is ±5% and all the formulations were found to comply with the specifications given in I.P. for weight variation test. Good uniformity in drug content was found among the formulations, and percentage of drug content was more than 95%. All the tablet formulations showed acceptable pharmaco technical properties.

In - vitro drug release study

The release profile of Aceclofenac from different batches of formulated matrix tablets were illustrated in Table no: 4 and plotted in Figure no: 3. All the formulations showed very low drug release in 0.1N HCl (pH 1.2). This was due to the very low solubility of Aceclofenac at pH 1.2. The final formula (F5) complies with all the release limits and giving 97.78% in 12th hr. Hence formulation 8 was selected as best formula. Formulation F5 containing HPMC- K100was found to release the drug in sustained manner up to 12 hour and was considered optimum for stability studies.

Stability studies

The results of accelerated stability studies carried out according to ICH guidelines indicated that the tablets did not show any physical changes (color change, friability and hardness), assay and dissolution characteristics during the study period.

Study of drug release kinetics Mechanism of drug release from hydrophilic Matrices

The kinetic treatment reflected that release data of selected formula F5 showed r2 value of 0.991which is close to 1, indicating that release of drug follows zero order kinetics. The in vitro drug release of F4 was best explained by Higuchi's equation, as the plots showed the highest linearity (r2 =0.9534). The drug release significantly follows a zero order kinetic model for formulation F5. As the plot showed the highest linearity (r2 = 0.9891). The slope values of selected formulations (F5) for Korsemeyer and Peppa's diffusion model was >1 (0.6168) and exhibited as release mechanism of drug through polymeric membrane was found through diffusion and rate of diffusion is controlled by swelling of polymer.

Table no: 1 Result of study of physical parameters of Aceclofenac and Formulatoion F1-F8

Formulation	Loose bulk density (g|cm2)	Tapped density (gm|cm2)	Carr's index (%)	Hausner's ratio	Angle of repose
F1	0.486	0.539	9.83	1.109	33⁰18
F2	0.469	0.50	7.37	1.078	29⁰64
F3	0.482	0.515	6.40	1.068	30⁰53
F4	0.480	0.512	6.04	1.064	29⁰64
F5	0.466	0.528	11.74	1.133	32⁰82
F6	0.434	0.498	12.85	1.147	32⁰26
F7	0.443	0.508	12.79	1.146	31⁰02
F8	0.414	0.462	10.38	1.115	32⁰45
F9	0.488	0.522	6.51	1.065	29⁰75

Table No: 2 Various formulation of Aceclofenac sustained release tablets.

	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aceclofenac	100	100	100	100	100	100	100	100	100
Corn starch	50	75	87.5	50	75	87.5	50	75	87.5
HPMCK4M	50	25	12.5	--	--	--	--	--	--
HPMC K100M	--	--	--	50	25	12.5	--	--	--
HPMC K15M	--	--	--	--	--	--	50	25	12.5
PVP	3	3	3	3	3	3	3	3	3
Magnesium stearate	1	1	1	1	1	1	1	1	1
Silicon dioxide	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Table No: 3 : Evaluation of un coated Sustained release matrix tablets.

Batch	Thickness	Hardness	Friability	Content uniformity	Wt variation
F1	3.73±0.22	5.4±0.16	0.84±0.018	97.54±0.24	Passes
F2	3.97±0.18	5.5±0.20	0.92±0.014	98.74±0.18	Passes
F3	3.81±0.20	5.8±0.14	0.90±0.012	98.12±0.32	Passes
F4	3.75±0.11	4.9±0.11	0.79±0.020	99.12±0.11	Passes
F5	3.89±0.17	5.8±0.19	0.88±0.014	100.13±0.14	Passes
F6	3.65±0.15	5.4±0.12	0.82±0.012	98.4±0.28	Passes
F7	3.85±0.18	4.8±0.14	0.86±0.015	97.4±0.21	Passes
F8	3.91±0.28	6.1±0.17	0.79±0.017	97.5±0.25	Passes
F9	3.95±0.27	5.0±0.13	0.85±0.012	98.3±0.18	Passes

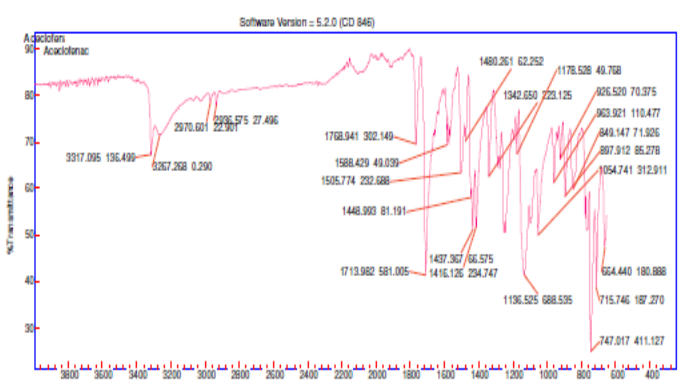

Figure 1. FTIR Spectra of aceclofenac

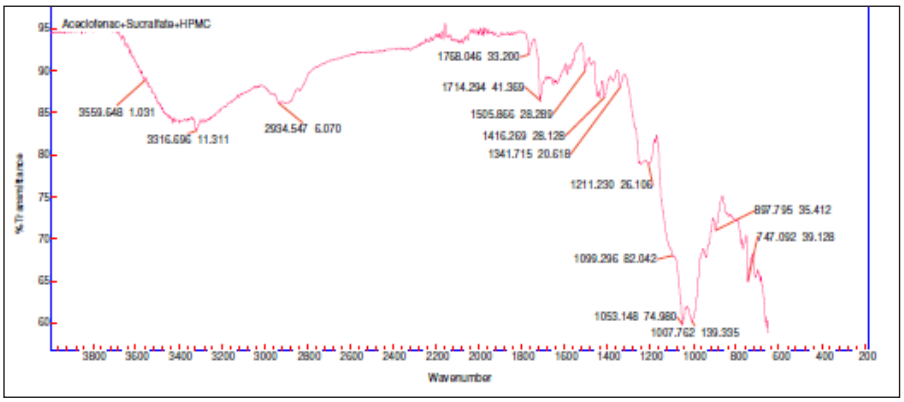

Figure 2; FTIR Spectra ofpremixture

Table No: 4 Data for dissolution profiles of various formulations F1-F8.
Percentage cumulative drug release from various Formulations.

Timein hours	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	16.07	18.89	20.57	14.69	18.12	20.96	18.44	20.94	23.62
2	20.87	24.29	26.89	19.18	23.64	27.47	23.89	25.71	29.92
3	26.56	28.76	31.72	23.93	28.26	37.63	27.21	30.34	34.59
4	35.37	36.12	35.45	35.37	37.14	43.72	38.37	37.24	39.35
5	38.58	41.47	40.37	47.73	49.13	54.19	41.6	43.61	49.58
6	42.67	46.67	49.45	56.76	56.68	63.15	45.15	54.81	56.61
7	51.92	54.42	58.64	67.34	68.52	76.81	52.06	59.45	61.89
8	63.18	66.37	67.53	74.56	76.12	84.72	63.17	66.56	68.75
9	76.25	77.07	82.83	83.07	81.42	87.3	72.82	77.27	78.26
10	78.74	83.27	88.02	86.27	88.4	90.19	81.32	85.06	86.56
11	83.67	86.71	97.44	88.63	90.49	98.49	87.24	89.78	97.54
12	86.95	90.62		93.49	97.78		89.64	93.29	

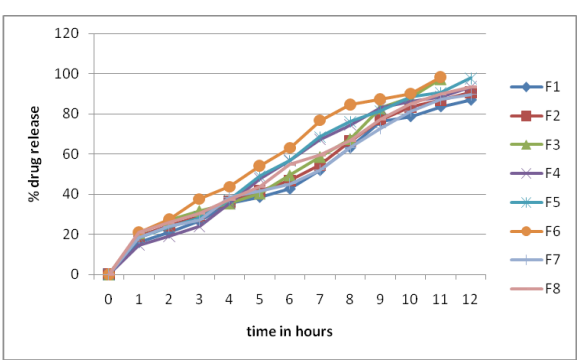

Figure 3: Comparative dissolution profiles for various formulations F1-F8

Conclusion

The study was undertaken with the aim to Formulation and evaluation of Aceclofenac matrix tablet using HPMC grade of polymer as retarding agent. From the above results and discussion, it is concluded that the formulation of sustained release tablet of Aceclofenac containing HPMC K100, corn starch which is taken as ideal or optimized formulation of sustained release tablet for 12 hours release as it fulfills all the requirement of sustained release tablet

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