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STUDIES ON SUSTAINED RELEASE TABLETS OF ACECLOFENAC: FORMULATION AND *IN VITRO* EVALUATION

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ABSTRACT

The objective of the present study was to develop a sustained release matrix tablets of aceclofenac. The tablets were prepared with different ratios of hydroxypropylmethylcellulose K100 M and ethylcellulose by wet granulation technique.The granules were evaluated for angle of repose, bulk density and compressibility index. The prepared tablets were evaluated for hardness, friability, weight variation and drug content. The *in vitro* release of the matrix tablets were carried out using USP XXI apparatus with simulated gastric fluid (SGF, pH 1.2) followed by simulated intestinal fluid (SIF, pH 6.8) as the dissolution medium. The tablet properties complied with the official limits. The release of aceclofenac from tablets containing hydroxypropylmethylcellulose K100 M was completed within 12 h.

Key words: Aceclofenac, Sustained release, Hydroxypropylmethylcellulose K100M, Ethylcellulose

INTRODUCTION

Sustained release dosage forms are becoming increasingly important, either to achieve the desired level of therapeutic activity required for a new drug entity or to extend life cycle of an existing drug through improved performance or patient compliance. The drug candidate selected under the present study is aceclofenac, a synthetic NSAID[1,2] used in treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. It is almost rapidly and completely absorbed from the gastrointestinal tract after oral administration[3]. It is reported to have plasma half life 4 hours , time of peak plasma concentration occurs about 1.25 to 3 hours after an oral dose. It is reported to have considerable first pass metabolism. Aceclofenac is usually administered as conventional tablet, containing 100 mg, two times daily. These bio–pharmaceutical and physiochemical properties reveal that aceclofenac is an ideal candidate to develop the oral sustained drug delivery system.

In this study, we have prepared and evaluated sustained drug delivery system of aceclofenac tablets with HPMC K100 M and EC. The physical characteristics like weight variation, hardness, friability, drug content and dissolution rate were investigated.

EXPERIMENTAL

Materials and methods

Materials

Aceclofenac was a gift sample received from Caplin Point Laboratories Ltd., Pondy. Hydroxypropylmethylcellulose (HPMC) K100 M, ethylcellulose (EC) and isopropyl alcohol (IPA) were gift samples received from Medopharm, Chennai. Lactose, microcrystalline cellulose (MCC), polyvinyl pyrrolidone K 30 (PVP), propylparaben sodium, talc, magnesium stearate were procured from Axon Drugs Pvt Ltd., Chennai. All other reagents used were of analytical grade.

Preparation of tablets

The aceclofenac sustained release tablets were prepared by wet granulation technique[3,4] with various ratios of HPMC and EC as per the formula given in Table 1.

Table 1. Composition of aceclofenac sustained release tablets

Ingredients mg / tablet	Formulation No.									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Aceclofenac	200	200	200	200	200	200	200	200	200	200
Hydroxypropyl methylcellulose K100 M	25	50	75	100	125	-	-	-	-	-
Ethylcellulose	-	-	-	-	-	25	50	75	100	125
Lactose	40	40	40	40	40	40	40	40	40	40
Microcrystalline cellulose	50	50	50	50	50	50	50	50	50	50

Ingredients mg / tablet	Formulation No.									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Polyvinylpyrrolidore K30	10	10	10	10	10	10	10	10	10	10
Propylparaben sodium	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26
Isoprophyl alcohol	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
Talc	8	8	8	8	8	8	8	8	8	8
Magnesium stearate	8	8	8	8	8	8	8	8	8	8

The drug aceclofenac was passed through sieve # 40. The release retarding polymer like HPMC, EC and additives like microcrystalline cellulose, lactose, propyl paraben sodium, talc and magnesium stearate were passed through sieve # 60. They were mixed well. Sustained release granules of aceclofenac were prepared by wet granulation method. Polyvinyl pyrrolidone in isopropyl alcohol was used as granulating agent. The wet granules were dried at room temperature. Then the dried granules were passed through sieve # 14, lubricated with talc and magnesium stearate and compressed into tablets. The granules were evaluated[4] for angle of repose, bulk density and compressibility index. The prepared tablets were evaluated[4] for hardness, friability, weight variation, drug content[5] and dissolution studies.

RESULTS AND DISCUSSION

The granules of different formulation were evaluated for angle of repose, loose bulk density, tapped bulk density and compressibility index. The results of angle of repose and compressibility index (%) ranged from 18.38 to 23.16 and 8.72 to 19.21, respectively. The results of loose bulk density and tapped bulk density ranged from 0.348 to 0.466 and 0.399 to 0.539, respectively.

The present study was undertaken to design and evaluate the sustained release tablets of aceclofenac with HPMC and EC. The tablets were preliminarily evaluated for various physical parameters like weight variation, hardness, friability and drug content. The hardness of all the tablets were maintained in the range of 4 to 6.8 kg/cm^2. The loss in

total weight of tablets due to friability was in the range of 0.443 to 0.732 %. The drug content in different formulations was highly uniform and in the range of 98.36 to 100.43%.

in vitro dissolution study was carried out for all the formulations. From these studies, it was observed that formulation F3 showed better sustained release rate of aceclofenac from tablet. The formulation F3 released 5.12 % and 94.63 % of drug at the end of 2^{nd} and 12^{th} h of dissolution study. From the results, F3 formulation showed better release than other formulations. The release of drug from formulation F3 was compared with two marketed formulations.

in vitro release from the formulation F3 with the hardness of 6.8 kg/cm^2 was found to be within predicted release profile for longer time than the other formulations. All other tested parameters of formulation F3 were in acceptable limits. Formulation F3 was found to be a better formulation than other 9 batch of formulations.

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