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DEVELOPEMENT OF COLON SPECIFIC DRUG DELIVERY OF ACECLOFENAC BY USING EFFECTIVE BINDER SYSTEM OF ETHYL CELLULOSE

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ABSTRACT

Colon targeted drug delivery system by using dextrin, polysaccharide, as a carrier for Aceclofenac is the objective of the present study. Very common wet granulation technique is used for preparation of matrix tablet. Different binder like ethyl cellulose, sodium CMC and sucrose were used during preparation of matrix tablets containing dextrin and various excipients. Evaluation was done by different IPQC tests, content uniformity and in vitro drug release study. Drug release profile was evaluated in simulated gastric, intestinal fluid and simulated colonic fluid. Drug release profile in simulated gastric, intestinal fluid and colonic fluid decide the best formulation. The matrix tablet containing binder system of ethyl cellulose and dextrin as a carrier was found to be suitable for targeting the colon as compare to other matrix tablets containing different binders because of fewer amounts (8-10%) of drug release in the simulated gastric and intestinal fluid. Matrix tablets containing dextrin releases 82.43 % of Aceclofenac in simulated colonic fluid with 4 % human fecal matter solution. No change was found in physical appearance and dissolution profile upon storage at 40^0C / 75 % relative humidity for six months with the tablets containing dextrin polysaccharide as a carrier. Ethyl cellulose as binder was most suitable binder to deliver the drug specifically in colonic region as compare to matrix tablets of dextrin with other binder systems.

KEY WORDS

Aceclofenac, colon specific drug delivery, polysaccharide, Ethyl Cellulose

INTRODUCTION

Colon is being extensively investigated as a drug delivery site. Oral colon-specific drug delivery system (CDDS) has been developed by means of combination of one or more controlled release mechanisms, hardly releases drug in the upper part of the gastrointestinal (GI) tract, but rapidly releases drug in the colon following oral administration [1- 4]. CDDS is convenient for treating localized colonic diseases, i.e. ulcerative colitis, Crohn's disease and constipation *etc.*, CDDS, also selectively deliver drug to the colon, but not to the upper GI tract[2]. Colon is referred to as the optimal absorption site for protein and polypeptide after oral administration, because of the existence of relatively low proteolytic enzyme

activities and quite long transit time in the colon[4,5]. CDDS would be advantageous when a delay in absorption is desirable from a therapeutically point of view, as for the treatment of diseases that have peak symptoms in the early morning and that exhibit circadian rhythms, such as nocturnal asthma, angina and rheumatoid arthritis [1,5,6] . A large number of polysaccharides such as pectin, amylose, guar gum, chitosan, inulin, cyclodextrins, chondroitin sulphate, dextrans, dextrin and locust bean gum have been investigated for their use in colon targeted drug delivery systems.[6] Aceclofenac is a novel NSAID known to exhibit multifactor mechanism of action. Aceclofenac was developed in order to provide a highly effective pain relieving therapy with a reduced side effect profile, especially colon events that are frequently experienced with NSAID therapy[6]. The finding of the present study conclusively state that dextrin tablets are promising to colon targeting of Aceclofenac to synchronize the effective treatment of rheumatoid arthritis.

MATERIALS AND METH ODS

Materials

Aceclofenac, Wochkardt Pvt. Ltd. Aurangabad (MS) as gift sample. Ethyl Cellulose, MCC, Dextrin, Sucrose, Sodium CMC, Magnesium Stearate LOBA chem., Lobachem Private Limited, P. box No.6139, Mumbai 400005, India. All other chemicals used were of analytical grade.

Preparation of Granules [7, 8, 9]

Granules were prepared by using wet granulation method by using different binder systems. Details of granulation are given in following table1.

Table .I

Composition of different dextrin matrix tablets of Aceclofenac.

Sr. No.	Name Of The Ingredient	Quantity/tablet (mg/tablet)								
		Formulation Codes								
1	Aceclofenac	100	100	100	100	100	100	100	100	100
2	Dextrin	050	075	100	050	075	100	050	075	100
3	Microcrystalline cellulose	340	310	280	340	310	280	340	310	280
4	Sodium CMC(10%aq. Solution)	005	010	015						
5	Sucrose (70% aq. solution)				005	010	015			
6	Ethyl Cellulose							005	010	015
7	Magnesium stearate	005	005	005	005	005	005	005	005	005
	Total Weight of Tablet (mg)	500	500	500	500	500	500	500	500	500

Preparation of Tablets[8,9]

Initially granules were treated with lubricants like talc and magnesium stearate. Tablets were prepared by compressing the lubricated granules on rotary tablet compression machine by using 10mm SC (Shallow concave) die and punch set. Details of compression parameters are given in following table I.

Study of In-Process Quality Control Parameters of Tablets[8,9]

Tablets were evaluated during compression for different IPQC parameters like Weight, Hardness, Thickness, Diameter, and Friability. Thickness and diameter of the tablet were measured using caliper scale. Hardness was evaluated manually by using Monsanto hardness tester. Friability test was performed at speed of

25 rpm with tablets dropping from height of six inches with each revolution. After the test, the tablets were dedusted and reweighed. Results are shown in table II.

Table .II

I.P.Q.C. Parameters of different dextrin matrix tablets of Aceclofenac

Sr. No.	Formulation code	Average weight (mg)	Average Diameter(cm)	Average Hardness (kg/cm^2)	Friability (%)	Average Thickness (%)	Drug Content (%)
1	Acec1	497	01	4.8	0.21	3.0	96.67
2	Acec2	502	01	5.3	0.32	3.2	99.34
3	Acec3	503	01	5.3	0.26	3.4	98.99
4	Acec4	504	01	5.2	0.21	3.2	99.12
5	Acec5	500	01	5.3	0.28	3.2	98.67
6	Acec6	501	01	5.6	0.24	3.3	100.34
7	Acec7	503	01	5.3	0.21	3.2	103.23
8	Acec8	500	01	5.2	0.23	3.2	99.89
9	Acec9	500	01	5.3	0.24	3.3	99.45

Drug Content Uniformity Test for Tablets[9]

Aceclofenac tablets were analyzed by United State Pharmacopoeia. Three tablets of each type of formulation were weighed and crushed in mortar and was dissolved in 100ml methanol. This was the stock solution from which l ml sample was withdrawn and diluted to 100 ml with 6.8 phosphate buffer. The absorbance was measured at wavelength 275 nm using double beam UV-Visible spectrophotometer.

In-Vitro Drug Release Study[9]

Test was carried out using USP apparatus II (paddle) and the medium was Simulated gastric fluid, Simulated intestinal fluid and simulated colonic fluid. Quantity of each dissolution medium was 900 mL. The speed of paddle was 50 rpm and temperature of dissolution medium was 37.50C. One tablet was placed in the dissolution medium and apparatus was run. At intervals of 2, 5, 8, 12, 16, 20 and 24 hours, 5 mL aliquots were withdrawn and replacement was made each time with 5 mL of fresh dissolution medium. Each 5 mL sample was filtered through whatman filter paper no. 41 and diluted up to 50 ml with respective dissolution medium. Then absorbance was measured at 249 nm.

Table .III

Dissolution behavior of dextrin matrix tablets of Aceclofenac

Dissolution Media	Time (Hrs)	Cumulative % Drug Release									
		Acec1	Acec2	Acec3	Acec4	Acec5	Acec6	Acec7	Acec8	Acec9	Acec9S

Simulated Gastric Fluid	02	22.67	19.46	18.36	22.36	20.92	18.73	16.78	13.87	10.23	10.12
Simulated Intestinal Fluid	05	34.89	32.67	29.89	36.89	33.23	31.56	21.78	19.78	16.67	15.98
Simulated Colonic Fluid	08	89.88	86.38	87.32	77.76	75.76	74.79	69.56	66.78	61.45	61.67
	12	93.23	92.00	92.76	89.97	87.87	86.56	79.48	78.03	70.77	68.80
	16	97.45	96.02	95.98	97.09	94.67	95.36	89.31	92.56	83.23	80.12
	20	99.78	98.56	98.18	98.23	96.98	97.22	93.01	94.78	96.67	94.87
	24	99.91	99.12	99.02	99.38	99.09	99.11	96.09	98.59	98.43	95.23

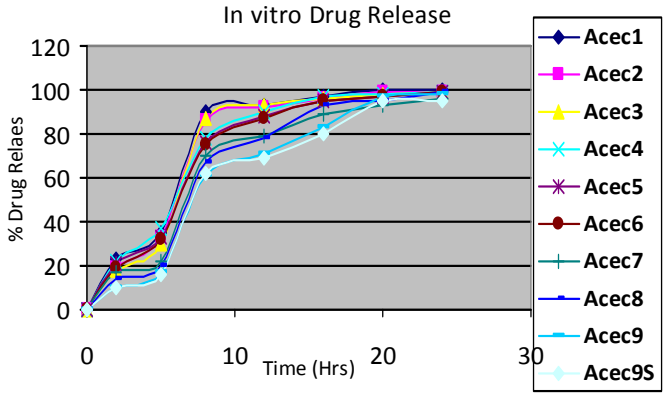

Figure: % Drug release pattern of different dextrin matrix tablets of Aceclofenac

Stability Study

Best formulation (F9) was exposed to three months stability study at 40 °C/75 % RH. These samples then again evaluated for drug release study.[10,11.]

RESULTS AND DISCUSSION

Granules were prepared successfully by using wet granulation method and tablets were prepared by compressing the lubricated granules on rotary tablet compression machine. Tablets were evaluated as per I.P. 96 guidelines. As shown in table 2, hardness, percent friability and average thickness were found to be in the range of 4.8 to 5.6 kg/cm2, 0.21% to 0.32 %, 3.0 to 3.4 mm respectively. Tablets showed 96.67 % to 103.23% of the labeled amount of Aceclofenac indicating uniformity in drug content (90-110%). All formulations were complying with the I.P. specifications[9]. Resulted tablets were evaluated for drug release by using USP dissolution apparatus II. Assay of tablet shows that tablets are of required purity and matches the IP specification. Drug release studies shows that Acec9 shows good release behavior in colon and restricts release in stomach and intestine as compare to Acec1 – Acec8. This study confirms that dextrin can act as good carrier in the form of matrix tablet for Aceclofenac to deliver it in colon specifically by using ethyl cellulose as

binder[12].Stability study of formulation Acec9 confirms that tablets are stable and there was no significant change in Hardness, Friability, Drug content and Dissolution profile of Acec9.

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