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DEVELOPEMENT OF COLON SPECIFIC DRUG DELIVERY OF ACECLOFENAC

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ABSTRACT

The objective of the present study is to develop a colon targeted drug delivery systems for Aceclofenac using Gaur gum and Pectin as a carrier. Very common wet granulation technique is used for preparation of matrix tablet. Binder like ethyl cellulose was used during preparation of matrix tablets containing 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 pectin as a carrier was found to be suitable for targeting the colon as compare to other matrix tablets. Matrix tablets containing pectin (20%) releases 69.24% of Aceclofenac in simulated colonic fluid within 12 hours. This study confirms that pectin 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.

Keywords: Aceclofenac, Guar gum, Pectin, Colonic Specific delivery.

INTRODUCTION

Colonic delivery is a targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e. colon). Targeted drug delivery to the colon would therefore ensure direct treatment at the disease site, lower dosing and fewer systemic side effects. It has been proved effective in treating colonic diseases such as inflammatory bowel diseases and colon cancer or improving absorption of protein or polypeptide drugs. A colonic drug delivery system is expected to protect the drug during the transit time in the gastro intestine and to allow its release only in the colon. Conventional oral dosage forms are ineffective in delivering drugs to the colon due to absorption and /or degradation of the active ingredient in the upper part of the gastrointestinal tract. Therefore, colon-specific drug delivery systems, which can deliver drugs in an appropriate concentration in the colon without releasing them in the upper part of GI tract, can be expected to decrease the side-effects of the drug and improve the quality of life for the patients suffering from colon-specific diseases [1-3].

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 [4].

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 [5].

The finding of the present study conclusively state that pectin tablets are promising to colon targeting of Aceclofenac to synchronize the effective treatment of rheumatoid arthritis.

MATERIALS AND METHODS

Materials

Aceclofenac was obtained as a gift sample from Blue Cross Pvt. Ltd., Mumbai. Pectin, Gaur gum,

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Microcrystalline cellulose, Sodium CMC, Ethyl Cellulose, Magnesium stearate were purchased from Research-Lab Fine Chem Industries, Mumbai. All other chemicals and reagents used were of analytical grade.

Methods

Preparation of Granules

Granules were prepared by using wet granulation method by using different binder systems. Details of granulation are given in following table 1 [6-8].

Preparation of Tablets

Initially granules were treated with lubricants like 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 [9].

Evaluation of the Tablets

The prepared tablets were evaluated for weight variation, hardness, friability, drug content and *In- vitro* dissolution time as per the official methods.

i) Weight variation

Randomly, twenty tablets were selected after compression and the mean weight was determined using an electronic digital weighing balance. None of the tablets deviated from the average weight by more than ±5%

ii) Hardness

The crushing strength of the tablets was measured using a Pfizer hardness tester (Erweka hardness tester). Three tablets from each formulation batch were tested randomly and the average reading noted.

iii) Friability

Ten tablets were weighed and placed in a Roche friabilator (Electrolab friability tester-USP), and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

$$\text{Percentage friability} = \frac{\text{Initial weight-Final weight}}{\text{Initial weight}} \times 100$$

iv) Drug content

Three tablets were powdered and weigh accurately equivalent to 100 mg of Aceclofenac and transferred into a 100 ml volumetric flask. Initially, 10 ml of methanol was added and shaken for 10 minutes. Then, the volume was made up to 100 ml with methanol. Subsequently, the solution in the volumetric flask was filtered, and 1 ml of the filtrate was suitably diluted and analyzed for drug content at 273 nm using UV-spectrophotometers.

v) *In vitro* release study

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 37.5^0C. One tablet was placed in the dissolution medium and apparatus was run. At intervals of every 1 hour, 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 273 nm.

Drug Excipients Compatibility Study

The drug-excipients interaction study was carried out by using FTIR spectroscopy [10-12].

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 diameter were found to be in the range of 4.2 to 6.0 kg/cm^2, 0.54% to 0.78 %, 1 cm respectively. Tablets showed 98.99 % to 100.34% of the labeled amount of Aceclofenac indicating uniformity in drug content (90-110%).

All formulations were complying with the I.P. specifications. 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. As shown in table 3, Drug release studies shows that F3 shows good release behavior in colon and restricts release in stomach and intestine as compare to F1 – F6. This study confirms that pectin 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.

Figure 2 to 4 shows that the IR spectra of pure Aceclofenac and its physical mixtures revealed no considerable changes in the IR peaks of Aceclofenac when mixed with polymer and it conformed absence of any chemical interactions between the drug and polymer.

Table 1. Composition of Different Tablets of Aceclofenac

Sr. No.	Name of the Ingredients	Quantity/ Tablet (mg/tablet) Formulation Codes					
		F_1	F_2	F_3	F_4	F_5	F_6
1	Aceclofenac	100	100	100	100	100	100
2	Pectin	50	75	100	-	-	-
3	Gaur Gum	-	-	-	50	75	100
4	Microcrystalline Cellulose	340	310	280	340	310	280
5	Ethyl Cellulose	5	10	15	5	10	15
6	Magnesium Stearate	5	5	5	5	5	5
Total Weight of Tablet (mg)		500	500	500	500	500	500

Table 2. Evaluation parameters of tablets of Aceclofenac

Sr. No.	Formulation code	Average Weight (mg)	Average Diameter (cm)	Average Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
1	F_1	510	01	4.2	0.72	99.55
2	F_2	499	01	4.8	0.78	100.03
3	F_3	516	01	5.0	0.54	100.34
4	F_4	500	01	5.4	0.62	99.43
5	F_5	513	01	6.0	0.73	98.99
6	F_6	502	01	5.2	0.58	99.12

Table 3. Dissolution behavior of tablets of Aceclofenac

Dissolution Media	Time (Hrs)	Cumulative % Drug Release					
		F_1	F_2	F_3	F_4	F_5	F_6
Simulated Gastric Fluid	1	3.78	2.394	1.584	9.77	8.32	8.18
	2	7.76	6.97	4.55	15.86	13.87	11.94
Simulated Intestinal Fluid	3	17.78	13.87	10.20	32.88	27.34	18.76
	4	22.63	18.73	14.33	37.65	31.99	23.08
	5	29.37	22.36	19.78	48.83	42.12	32.21
Simulated Colonic Fluid	6	35.32	31.56	27.56	54.79	46.67	38.78
	7	42.65	33.23	32.59	60.78	54.34	45.32
	8	51.76	46.89	41.11	66.11	63.23	55.34
	9	58.20	49.89	47.09	71.31	68.89	59.90
	10	67.11	59.67	52.02	78.65	79.45	69.22
	11	76.95	68.80	63.45	87.20	82.32	73.11
	12	79.48	74.79	69.24	92.76	89.97	80.12

Figure 1. % Drug Release pattern of Aceclofenac Tablet

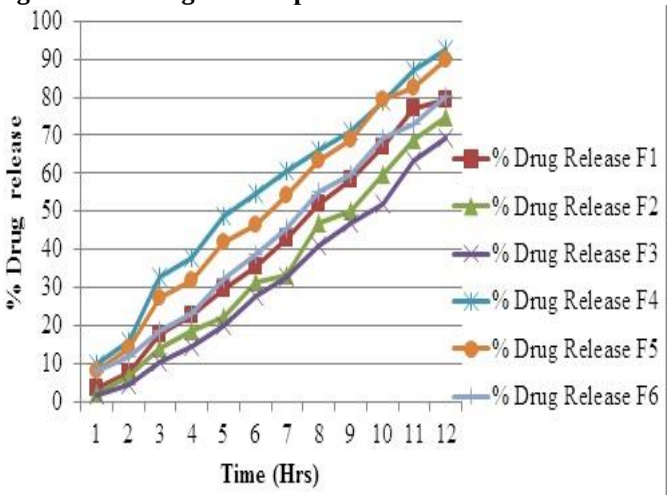


Figure 2. IR spectra of the pure drug Aceclofenac

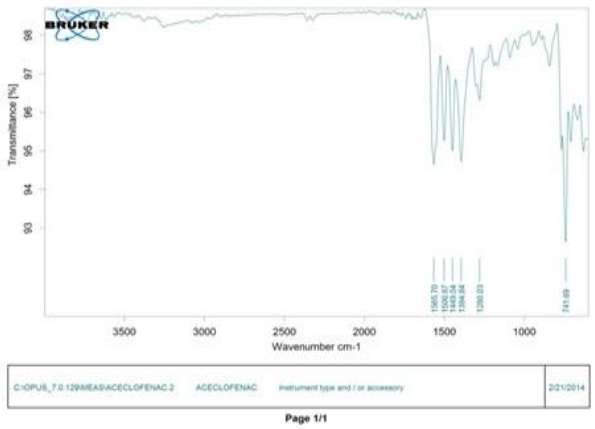


Figure 3. IR spectra of the pure drug Aceclofenac with gaur gum formulation

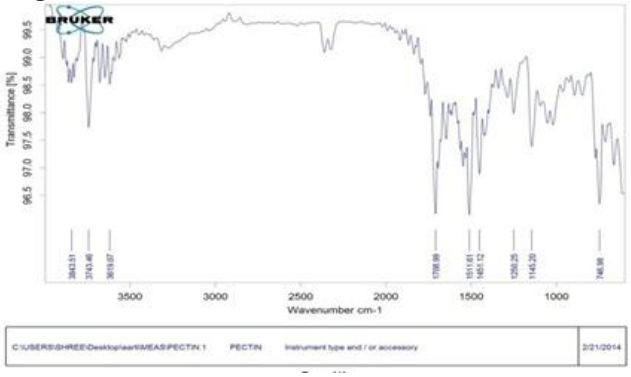
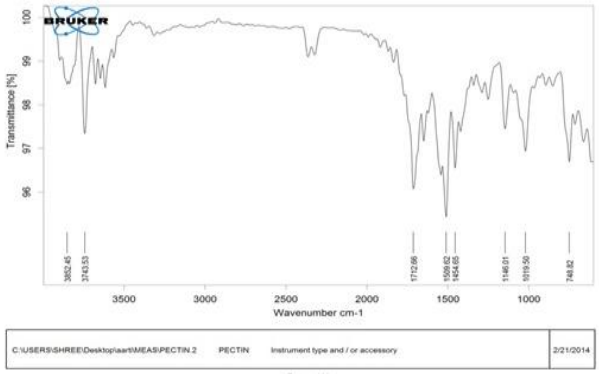


Figure 4. IR spectra of the pure drug Aceclofenac with pectin formulation



CONCLUSION

The study was undertaken with an aim to formulate and evaluate Aceclofenac matrix tablets to deliver the drug in the colon. The *in vitro* dissolution studies shows that Guar gum and pectin in the form of matrix tablets is capable of protecting Aceclofenac from being released in the upper region of GI system, i.e. stomach and small intestine. The in vitro drug release studies indicated that formulation F3 was a promising system to provide targeting of Aceclofenac to the colon. FT-IR spectral studies showed that there is no interaction between the drug and excipients. This study confirms that pectin 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.

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REFERENCES

1. Hemant H.Gangurde, Mayur A, Chordiya, Tamizharasi S, and Sivakumar T, A review on Diseases, approaches and evaluation parameterrs for colon specific drug delivery. *International Journal of Drug Research and Technology*, 2(3), 2012, 239-262
2. Tarak Jayraj Mehta,A.D.patel,Mukesh R.Patel,N.M.patel. Need Of Colon Specific Drug Delivery System,A Review on primary and novel Approaches. *International Journal of Pharma Research & Development*, 3(1), 2011, 134-153.
3. Shailendra wasnik, poonam parmar. The design of colon-specific drug delivery system and different approaches to treat colon disease. *International journal of pharmaceutical sciences review and research*, 6(2), 2011, 167-177.
4. Mohit Khandelwal, Ankit Ahlawat and Ram Singh. Polysaccharides and Natural Gums for Colon Drug Delivery. *The Pharma Innovation*, 1(1), 2012, 9-13
5. Hindustan Abdul Ahad. Formulation and evaluation of Once-daily sustained release Aceclofenac Prosopis Cumanensis Gum Matrix Tablets. *Journal of Innovative Trends in Pharmaceutical Sciences*, 1(1), 2010, 53–63.
6. Lachman L, Herbert A, Liberman J. The Theory and Practice of Industrial Pharmacy, 3rd Edn, Varghese publishing House, Hind Rajasthan Building Dadar Mumbai-400001, 318.
7. "Indian Pharmacopoeia" Government of India Ministry of Health and Family Welfare, published by Controller of publication, Delhi, 1996, 736,
8. "The United States pharmacopoeia"-XXIV, US Pharmacopoeial Convention Inc. Rockville, MD 2085, 2302, 2303-2306, 2621-2622, 2396.
9. Thiruganesh Ramasamy, Uma Devi Subbaih Kandhasami, Himabindhu Ruttala, Suresh Shanmugam. Formulation and evaluation of xanthan gum based aceclofenac tablets for colon targeted drug delivery. *Brazilian Journal of Pharmaceutical Sciences*, 47(2), 2011, 300-311.
10. Nirav V. Patel, Jayvadan K. Patel, Shreeraj H. Shah, Jagruti J Patel. Design, development and in vitro evaluation of Mesalamine tablets containing Pectin and Chitosan for colon-specific drug delivery. *Int J Res Pharm Sci*, 2010, 194-102.
11. Rajesh kumar R, Ramasamy P, Vengadesh Prabu K. Formulation and Evaluation of Guar gum compressed tablets for colon targeted drug delivery. *Journal of Pharmacy Research*, 3(7), 2010, 1538-1540.
12. Krishnaiah YSR, Satyanarayana S, Ramaprasad YV, NarasimhaRao S. Evaluation of Guargum as a Compression coat for drug targeting to colon. *International Journal of Pharmaceutics*, 171, 1998, 137-146.