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Research Article

FORMULATION AND CHARACTERIZATION OF COLON TARGETING DRUG DELIVERY

Upasna ,Vivek Patel, Kailash Pathak and Nishi Prakash jain

RKDF College Pharmacy, Bhopal, MadhyaPradesh, India

Abstract

The colon, as a site for drug delivery, offers distinct advantages on account of a near neutral pH, a much longer transit time, relatively low proteolytic enzyme activity, and a much greater responsiveness to absorption enhancers. The formulation for matrix tablets of aceclofenac were prepared by wet granulation technique using starch paste as binder. The optimized batch of tablets were coated using Eudragit polymer. Coating solution was prepared by dissolution of 500 mg of Eudragit polymers in ethanol:acetone (2: 1) to give 10% coating. Coating was continued until there is no drug release in SGF fluid. matrix tablets containing chondrointin sulfate 100 mg with guar gum 60 mg of polymer are considered suitable for colon targeting. This is because the optimum ratio of chondrointin sulfate polymer alone not make proper film. Thus, the matrix formulations containing 30% guar gum are most likely to target Aceclofenac to colon with being released at lower or half the percentage of release in stomach and small intestine.

Keywords: drug delivery, aceclofenac, matrix tablets ect.

Introduction :

The colon, as a site for drug delivery, offers distinct advantages on account of a near neutral pH, a much longer transit time, relatively low proteolytic enzyme activity, and a much greater responsiveness to absorption enhancers. These criteria favour this distal part of the gastrointestinal tract (GIT) as a site for the delivery of various drug molecules, including proteins and peptides. Colon-specific delivery systems should prevent the release of the drug in the upper-part of GIT and require a triggering mechanism to affect an abrupt release on reaching the colon. In the past, various primary approaches for colon specific delivery, such as pro-drugs, pH sensitive polymers, timed release delivery systems, and microbially degraded delivery systems, have achieved limited success. The majority of these systems developed during the past decade, were based on pH and time dependent mechanisms with limited in-vivo evaluation.

Corresponding Author

E.mail: shailgpharma@gmail.com

Minor variation in pH between the small intestine and the colon makes the pH-dependent systems less specific, in terms of targeted release in the colon. Time-dependent formulations predominantly depend on the transit time of the delivery system in the GIT. A major limitation with these systems is that *in vivo* variation of the small intestinal transit time may lead to release of the bioactive in the small intestine or terminal part of the colon. The pathophysiological state of an individual will have a significant impact on the performance of these time-dependent systems. Patients with irritable bowel syndrome and ulcerative colitis exhibited accelerated transit through different regions of the colon.[1-8]

Materials and Methods[6-13]

Procurement of drug and excipients:

Preparation of Tablet

Step-I

The formulation for matrix tablets of aceclofenac is given in Table 1. Matrix tablets of aceclofenac were prepared by wet granulation technique using starch paste as binder. Microcrystalline cellulose was used as diluents and mixture of talc and magnesium stearate was used as lubricant. Firstly all the ingredients were accurately weighed. Aceclofenac was separately passed through mesh (60) then Guar gum; Chondroitin Sulfate and microcrystalline cellulose were sieved through mesh (44) and mixed with drug. Then powders were blended and granulated with starch paste. Then the granules were passed through mesh (22) and then granules were dried at 50° C for 2h. Then dried granules were passed through a mesh (22) and lubricated with a mixture of talc and magnesium stearate. The lubricated granules were compressed using 10 mm flat plain punches on compression machine.

Step-II

The optimized batch of tablets were coated using Eudragit polymer. Coating solution was prepared by dissolution of 500 mg of Eudragit polymers in ethanol:acetone (2: 1) to give 10% coating. Coating was continued until there is no drug release in SGF fluid. After the coating, the tablets were gently fluidized for about 5 min after which they were air dried in an oven for 24 h at 40°C. A 10% w/w increase in the coating level was selected as an optimum coating percentage level. Then the pH dependent polymeric coated tablets were tested for drug release studies

Evaluation of Compression Tablet

General appearance

The tablets should be free from cracks, depression, pinholes etc. the color and polish of the tablets should be uniform on whole surface. The surface of the tablets should be smooth.

Hardness:

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging, and shipping. Tablet hardness has been defined as, the force required to break a tablet in a diametric compression test[81].Tablet hardness of all the formulations was measured using a Monsanto hardness tester.

Thickness

The thickness of tablets was determined using a Digimatic vernier caliper (Mitutoya, Japan). Three tablets from each batch were used, and average values were calculated. The results are shown in Table.

Friability test

The friability of tablets was determined using Roche Friabilator. It is express in percentage (%). Ten tablets were initially weighed and revolved at 25 rpm for 4 min. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated. The % friability was then calculated by,

F = Winitial – Wfiinal x 100 / Winitial

Weight Variation Test

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with average weight for the weight variations. The following percentage deviation in weight variation is allowed. The results are shown in Table.

Drug Content

Two tablets were weighed individually and powdered. The powder equivalent to 100mg of Aceclofenac was weighed and dissolved in 100mL of Saline Phosphate buffer (pH 6.8). The solution was then filtered and from this solution 1 mL was taken and makes up with Saline Phosphate buffer (pH 6.8) in 100 mL standard volumetric flask. The amount of drug present in each tablet was determined spectrophotometrically at 268 nm using UV– spectrophotometer. The percentage content was determined using standard graph**.**

In-vitro drug release studies

The invitro release of aceclofenac was carried out by using USP apparatus I (Paddle) method.300mg of tablets (f1 – f4) were placed separately in to the paddle and introduced in to the vessels of the dissolution test (Lab India, Disso 8000). The continuous dissolution method was used for simulating pH conditions of the GI tract (Huyghebaert et al., 2005). Initially, tablets were added in 700ml of 0.1N HCL (pH 1.2) for 2 h. At the end of 2h, 200ml of 0.2M tribasic sodium phosphate solution was added to all the dissolution vessels and the pH was adjusted to 7.4 by using 2M NaOH. At the end of 5h, 2M HCL was added to all the dissolution vessels and the pH was adjusted to 6.8. 5ml samples withdrawn every hour and analysed in a UV spectrophotometer at 266.5nm for first two hours samples for acid buffer, after 2 hours analysed at 274nm and the remaining hour samples were analysed at 268nm. The percent drug released was recorded

and graph was constructed by plotting % drug release versus time.

Results and Discussion

Evaluation of Formulated fast dissolving Tablet:

Bulk density

The term bulk density refers to a measure used to describe a packing of particles. It is (gm/ml) and was determine using a balance and measuring cylinder. The results were given on the table.

Tapped density

Tapped density is determined by placing a graduated cylinder containing same mass of powder used for B.D. on a mechanical tapper apparatus which is operated for a fixed number of taps until powder bed volume has reached a minimum. The results were given on the table

Carr's Index (CI):

Tapped and bulk density measurements can be used to estimate the carr's index of a material. The results were given on the table.

Hausner's ratio (HR):

The results are given in the table

Angle of repose (Tan θ):

Angle of repose is the tan inverse of angle between height (h) of pile of powder and the radius (r) of the base of conical pile. Powder is carefully poured through funnel until the apex of conical pile just touches the tip of funnel. The results were given on the table.

Hardness:

Tablet hardness has been defined as, the force required to break a tablet in a diametric compression test[81].Tablet hardness of all the formulations was measured using a Monsanto hardness tester. The results were given on the table.

Thickness

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Friability test

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Weight Variation Test:

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with

average weight for the weight variations. The results were given on the table.

Drug Content:

Two tablets were weighed individually and powdered. . The amount of drug present in each tablet was determined spectrophotometrically at 268 nm using UV– spectrophotometer. The results were given on the table.

In-vitro Drug release studies of Core Tablets:

The In-vitro release of aceclofenac was carried out by using USP apparatus I (Paddle) method. The results were given on the table.

Conclusion

Matrix tablets containing chondrointin sulfate 100 mg with guar gum 60 mg of polymer are considered suitable for colon targeting. This is because the optimum ratio of chondrointin sulfate polymer alone not make proper film. Thus, the matrix formulations containing 30% guar gum are most likely to target Aceclofenac to colon with being released at lower or half the percentage of release in stomach and small intestine. **In-vitro Drug release of Coated Tablets:**

Based on Invitro release of core tablet the formulations of F3 and F5 were selected for a coating a core tablet**.** The release of coated tablet was showed on table.

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Table.1: Preparation of aceclofenac with Guar Gum

Sl.no.	Ingredients	Quantity (mg) present in each tablet				
		F1	**F 2**	**F 3**	**F4**	**F5**
1.	Aceclofenac	100	100	100	100	100
2.	Chondroitin Sulfate	100	100	100	100	100
3.	Guar Gum	-	30	60	70	80
4.	Micro Crystalline Cellulose	98	68	38	28	18
5.	Magnesium Stearate	1	1	1	1	1
6.	Talc	1	1	1	1	1

TABLE.2: Bulk Density (F1-F4)

	BULK DENSITY			AVERAGE	STD DEV	MEAN DEVIATION
	T 1	T2	T3			
F1	0.58	0.49	0.55	0.54	0.046	0.54 ± 0.046
F2	0.5	0.47	0.52	0.50	0.025	0.50 ± 0.025
F3	0.6	0.57	0.59	0.59	0.015	0.59 ± 0.015
F4	0.5	0.45	0.48	0.48	0.025	0.48 ± 0.025
F5	0.51	0.48	0.47	0.47	0.026	0.48 ± 0.023

Table.3: Tapped density (F1-F4)

	TAPPED DENSITY			AVERAGE	STD DEV	MEAN DEVIATION
	T 1	T2	T3			
F1	0.58	0.51	0.62	0.57	0.056	0.57 ± 0.056
F2	0.57	0.47	0.52	0.52	0.050	0.52 ± 0.050
F3	0.71	0.57	0.59	0.62	0.076	0.62 ± 0.076
F4	0.56	0.45	0.48	0.50	0.057	0.50 ± 0.057
F5	0.5	0.46	0.46	0.47	0.023	0.47 ± 0.023

Table.4: Carr's Index (F1-F5)

	CARR'S INDEX			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	12.41	11.57	12.21	12.06	0.439	12.06% ± 0.439
F2	12.28	12.67	11.87	12.27	0.400	12.27% ± 0.400
F3	15.59	14.73	15.12	15.15	0.431	15.15% ± 0.431
F4	11.66	12.98	12.32	12.32	0.660	12.32% ± 0.660
F5	13.3	13.02	12.65	12.99	0.326	12.99% ± 0.326

Table.5: Hausner's ratio (F1-F5)

	HAUSNER'S RATIO			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	1.14	1.19	1.11	1.15	0.040	1.15 ± 0.040
F2	1.14	1.13	1.12	1.13	0.010	1.13 ± 0.010
F3	1.18	1.16	1.19	1.18	0.015	1.18 ± 0.015
F4	1.13	1.12	1.16	1.14	0.021	1.14 ± 0.021
F5	1.15	1.14	1.17	1.15	0.015	1.15 ± 0.015

Table.6: Angle of repose (F1-F5)

	ANGLE OF REPOSE (Θ)			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	29.28	30.14	29.28	29.57	0.497	29°57' ± 0.497
F2	31.04	30.14	31.04	30.74	0.520	30°74' ± 0.520
F3	29.28	28.07	28.07	28.47	0.699	28°47' ± 0.699
F4	28.37	28.37	29.13	28.62	0.439	28°62' ± 0.439
F5	29.05	28.17	29.05	28.76	0.508	28°76' ± 0.508

Table.7: Hardness (F_1-F_5)

	Hardness			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	2.5	2	2.5	2.33	0.289	2.33 ± 0.289
F2	2	2.5	2.5	2.33	0.289	2.33 ± 0.289
F3	2.5	2.5	2	2.33	0.289	2.33 ± 0.289
F4	2	2	2.5	2.17	0.289	2.17 ± 0.289
F5	2	2.5	2	2.17	0.289	2.17 ± 0.289

Table.8: Thickness (F_1-F_5)

	THICKNESS			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	3.64	3.63	3.65	3.64	0.010	3.64 ± 0.010
F2	3.64	3.65	3.66	3.65	0.010	3.65 ± 0.010
F3	3.73	3.75	3.74	3.74	0.010	3.74 ± 0.010
F4	3.73	3.74	3.73	3.73	0.006	3.73 ± 0.006
F5	3.63	3.64	3.63	3.63	0.006	3.63 ± 0.006

Table.9: Friability test (F_1-F5)

	FRIABILITY			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	0.56	0.82	0.91	0.76	0.182	0.76 % ± 0.182
F2	0.67	0.49	0.77	0.64	0.142	0.64% ± 0.142
F3	0.96	0.87	0.65	0.83	0.159	0.83 % ± 0.159
F4	0.78	0.69	0.93	0.80	0.121	0.80 % ± 0.121
F5	0.54	0.83	0.62	0.66	0.150	0.66% ± 0.150

Table 10-Weight Variation Test (F1-F5)

	WEIGHT VARIATION			AVERAGE
	T1	T2	T3	
F1	292.8	292.1	293.1	292.67
F2	296.5	297.1	295.9	296.50
F3	296.2	295.7	296.6	296.17
F4	295.7	296.1	295.3	295.70
F5	299.05	299.2	298.9	299.05

Table.11: Drug Content (F_1-F_5)

	DRUG CONTENT			AVERAGE	STD DEV	MEAN DEVIATION
	T1	T2	T3			
F1	96.78	94.87	96.38	96.01	1.007	96.01 ± 1.007
F2	94.53	96.55	98.37	96.48	1.921	96.48 ± 1.921
F3	98.36	96.56	99.53	98.15	1.496	98.15 ± 1.496
F4	97.52	98.46	95.27	97.08	1.639	97.08 ± 1.639
F5	96.66	97.78	94.67	96.37	1.575	96.37 ± 1.575

Table.12: Invitro Drug release of Core Tablets (F_1-F_5)

TIME	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	40.48	3.12	0.9	3.48	3.5
2	56.98	4.12	2.7	4.56	4.49
3	67.08	16.9	34.6	18.54	17.5
4	87.04	32.6	40.21	28.32	25.87
5	99.48	37.6	45.12	31.02	30.43
6	-	41.4	52.03	36.42	37.63
8	-	49.2	57.32	40.31	45.54
10	-	54.5	61.12	51.54	54.64
12	-	63.1	77.32	60.95	60.63