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FORMULATION AND EVALUATION OF ACECLOFENAC MATRIX TABLETS FOR COLON DRUG DELIVERY

T. Ratnakumari*, C. Madhusudhana Chetty, P. Dwarakasnadha Reddy,P.Ramyakrishna

Department of Pharmaceutics, Annamacharya College of Pharmacy, New Boyanapalli, Rajampet-516126, A.P, India.

Corresponding author E-mail: Ratnatkumari@gmail.com

ABSTRACT

In the present study the formulations were prepared by using different proportions of polymer. Aceclofenac Matrix tablets were prepared by wet granulation method. The weighed quantities of active ingredient, lactose, polymers are mixed thoroughly then add starch paste (10%) made it in to a cohesive mass. After forming the mass, it was passed through the sieve no. 22. The obtained granules were dried. The dried granules were again passed through sieve no. 16 for the purpose of uniformity. Finally, Talc and Magnesium Stearate substances were mixed to the prepared granules to increase the flow property and to reduce the friction between the granules. Dried granules were compressed into tablets using rotary tablet punching. The prepared formulations were evaluated for different physicochemical characteristics like thickness and diameter, drug content, weight variation, hardness and friability. The release characteristics of formulation were studied *in-vitro* condition.

KEY WORDS： 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.

In addition to local therapy, the colon can also be utilized as a portal for the entry of drugs into the systemic circulation. The site-specific delivery of drugs to lower parts of the GI tract is advantageous for localized treatment of several colonic diseases, mainly inflammatory bowel disease (Crohn's disease and ulcerative colitis) [1,] Irritable bowel syndrome, and colon cancer. Other potential applications of colonic delivery include chronotherapy. Colon targeted drug delivery (2) of drugs has recently gained importance in addressing specific needs in the therapy of colon based diseases. The design of novel colon targeted drug delivery systems by the utilization of natural biodegradable polymers .Successful delivery through this colon also requires the drug to be in solution form before it reaches in to the colon or alternatively, it should dissolve in the luminal fluids of the colon, but this can be a limiting factor for poorly soluble drugs as the fluid volume in the colon is much lower and more viscous than in the upper part of the gastrointestinal tract. Aceclofenac is an orally administered phenyl acetic acid derivatives with effects on a variety of inflammatory mediators. Aceclofenac contains not less than 99.0% and not more than the equivalent of 101.0 percent of 2-[[2-[2-[(2, 6-dichlorophenyl) amino] phenyl] acetyl] oxy] acetic acid. Aceclofenac is a white or almost white crystalline powder. Practically insoluble in water, freely soluble in acetone, soluble in alcohol. Aceclofenac is an orally administered non-steroidal analgesic and anti-inflammatory agent with a good gastrointestinal tolerability profile. It is official in B.P. Aceclofenac is used in the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and scapulohumeral periarthritis. It is also indicated for pains of various etiologies, such as musculoskeletal pain, dental pain or post surgical pain.

MATERIALS AND INSTRUMENTS:

Aceclofenac, Guar gum, Pectin, Starch, Magnesium stearate, Talc were obtained as gift sample from Indian drugs, Hyderabad. Potassium dihydrogenphosphate, Di sodium hydrogen phosphate, Lactose were obtained as gift sample from SD Fine Chem.Ltd. Mumbai.

Instruments:

UV-Visible spectrophotometer (labomed), Digital balance and Dhona electronic balance, Rotary tablet punching machine (chamunda), Dissolution apparatus USP XXI Paddle (Electro lab), Monsanto tablet hardness tester, Thickness tester, Roche friabilator.

FORMULATION OF FABRICATED MATRIX TABLETS:

Wet granulation Method [3]:

The weighed quantities of active ingredient, lactose, polymers are mixed thoroughly then add starch paste (10%) made it in to a cohesive mass.After forming the mass, it was passed through the sieve no. 22. The obtained granules were dried in a conventional hot air oven. The dried granules were again passed through sieve no. 16 for the purpose of uniformity. Finally, Talc and Magnesium Stearate substances were mixed to the prepared granules to increase the flow property and to reduce the friction between the granules. Dried granules were compressed into tablets using rotary tablet punching.

TABLE 1: DATA FOR MICROMERITIC PROPERITES OF ACECLOFENAC GRANULES:

S.NO	FORMULATIONS	ANGLE OF REPOSE	BULK DENSITY	TAPPED DENSITY	CARR'S INDEX	HAUSNER'S RATIO
1	**F-I**	23.98±2.07	0.268±0.007	0.323±0.006	14.42±0.48	1.19±0.02
2	**F-II**	21.02±1.23	0.266±0.005	0.298±0.01	9.39±0.5	1.10±0.01
3	**F-III**	19.44±3.75	0.251±0.017	0.28±0.005	10.7±0.37	1.12±0.05
4	**F-IV**	22.19±2.60	0.233±0.013	0.287±0.007	14.3±0.22	1.16±0.01

EVALUATION:

Hardness: The hardness of the tablet was determined by using a Monsanto hardness tester.

Thickness and diameter: The thickness and diameter of the tablets were measured by Vernier Calipers.

Weight Variation: 20 tablets were selected at random and average weights were determined. Then individual tablets weighed and the individual weight was compared with the average.

Friability:

This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated according to Percentage friability.

Content uniformity:

Five tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powder was dissolved and made up to volume with 6.8pHphoshate buffer. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and analyzed for drug content by UV spectrophotometer.

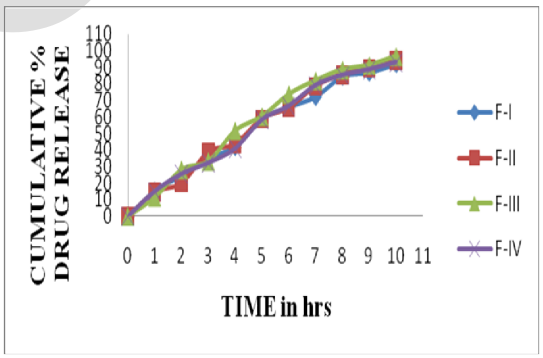
INVITRO DISSOLUTION STUDIES: [4-9]

In-vitro and *in vivo* methods are used to evaluate different carrier systems for their ability to deliver drugs specifically to the colon. The ability of the coats or carriers to remain intact in stomach and small intestine is generally assessed by conducting drug release studies in 0.1N hydrochloric acid for 2 hours followed by phosphate buffer (pH - 7.4) for 3 hrs by using dissolution apparatus. The drug release studies may also be performed by using rat cecal contents.

Dissolution apparatus United States Pharmacopeia Dissolution Testing Apparatus 2 -paddle type was carry out in vitro drug release studies on prepared bathes of matrix tablets using pH 6.8 phosphate buffer, at 37 ± 0.5°C and 50 rpm. The *in vitro* drug releases of the formulations were determined up to 10 hrs by using UV visible spectroscopy. F-III has shown 96.4% drug release. The data were shown in table-2

TABLE 2: IN VITRO DISSOLUTION DATA FOR FI-FIV

TIME in hrs	CUMULATIVE % DRUG RELEASE			
	F-I	F-II	F-III	F-IV
1	15.3	14.7	11.6	15.2
2	24.5	20.1	28.2	25.7
3	35.0	38.9	33.3	32.4
4	41.9	43.7	51.7	41.0
5	58.7	59.0	60.4	58.4
6	65.9	65.4	73.7	66.7
7	72.0	78.6	82.0	79.2
8	84.2	85.7	88.6	85.3
9	86.6	89.6	91.3	88.7
10	91.7	94.5	96.7	93.1



Graphs:1

INVITRO CUMULATIVE DRUG RELEASE OF FI-FIV:

Another *in-vitro* method involves incubation of the drug delivery system in a fermentor with commonly found colonic bacteria. *In vivo* methods offer various animal models. Guinea pigs 50 were used to evaluate colon- specific drug delivery from a glucoside prodrug of dexamethasone. *In vivo* gamma scintigraphic studies were carried out on the guar gum matrix tablets, using technetium 99 m- DTPA as a tracer. Scintigraphs taken at regular intervals have shown that some amount of tracer present on the surface of the tablets was released in stomach and small intestine. Radiotelemetry, Roentenograpgy are the other *in vivo* evaluation methods for colon-specific drug delivery systems.

DRUG RELEASE KINETICS:

The data obtained in the in-vitro dissolution studies of best formulation F-III were grouped according to modes of data treatment as follows:

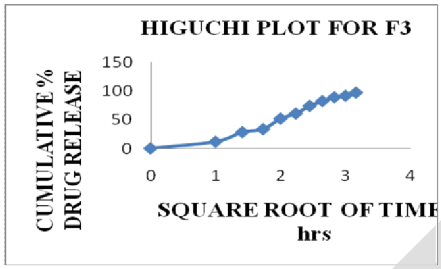
-Cumulative percent drug release V/s. Time (Zero-order).

-Cumulative percent drug retained V/s Square root of Time (Higuchi Matrix Model)

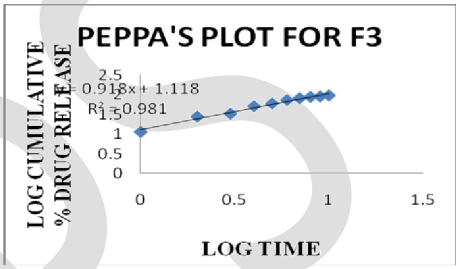
-Cumulative percent drug release in (mg) V/s. Time (Krosmeyer- Peppas Model). Calculated regression co-efficient for formulation F-III. Based on the regression values (r), the best –fit model was observed. All the prepared tablets follow zero order release model by the 'R' values which are obtained from graphs. The Peppas model is widely used when the release mechanism is not well known or when more than one type of release phenomenon could be involved. The 'n' value could be used to characterize different release mechanis

The mechanism of drug release can be predicted by 'n' value:

If 'n' values which is less than 0.45, the drug release mechanism would be Fickian diffusion mechanism, If 'n' value is more than 0.45 and less than 1, the release mechanism would be non - Fickian diffusion, If 'n' value is equal to 1, the drug release mechanism would be case II transport (Zero order release),If 'n' value is more than 1, The release mechanism would be super case II transport, If 'n' value is equal to 0.918, The 'n' value of formulations F-III is equal to 0.918 and it followed non-Fickian drug release. The graphs for F-III as follows.



Graphs: 2



Graphs: 3

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