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RESEARCH ARTICLE

Formulation and Evaluation of Matrix Tablets of Naproxen for Colon Targeting

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ABSTRACT

The present study is the development of colon targeted matrix tablets of the drug Naproxen, a NSAIDS. Designed to prolong the release for sustained effect. Different formulation (MT1 TO MT3) batches were made with the help of different polymers and their different proportions (Guar Gum, Xanthan Gum) with the help of Wet granulation techniques. The prepared matrix tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, *invitro* drug release. From this study we concluded that the batch MT3 shows good results then the other batches. The batch MT3 shows maximum prolong release up to 12 hrs.

Keywords: Naproxen, Colon, Sustain release, Guar gum, Xanthun gum

1. INTRODUCTION

Colonic delivery refers to targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e., colon). 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 diseases (Crohn's disease and ulcerative colitis), irritable bowel syndrome, and colon cancer. Other potential applications of colonic delivery include chronotherapy, prophylaxis of colon cancer and treatment of nicotine addiction. [1]Targeting of drugs to the colon by the oral route could be achieved by different approaches including matrix and coated systems, for which the drug release is controlled by the gastrointestinal pH, transit times or intestinal flora. The method by which the drug release will be triggered by the colonic flora appears to be more interesting with regard to the selectivity. A number of synthetic azo polymers and natural or modified polysaccharides (chondroitin sulphate, guar gum, xanthan gum, locust gum, inulin, dextrans, starch, amylose,pectins) degraded by the human colonic flora, have thus been investigated as colonic drug delivery carriers. [2] The human colon has over 400 distinct species of bacteria as resident flora, a possible population of up to 1010 bacteria per gram of colonic contents. Among the reactions carried out by these gut flora are azoreduction and enzymatic cleavage i.e. glycosides. These metabolic processes may be responsible for the metabolism of many drugs and may also be applied to colontargeted delivery of peptide based macromolecules such as insulin by oral administration. [3]

2. MATERIAL AND METHOD:

Materials: The drug Naproxen was obtained as a gift sample from RPG LIFESCIENCE, Mumbai. Guar Gum, Xanthan Gum was obtained as gift sample from Remidix Pharmaceutical, Banglore.

Methods:

Preparation of Granules:

Powdered ingredients were weighed, mixed and granulated with the binder solution/paste prepared as above. This mixture was thoroughly blended manually and passed through a sieve no 250. The granules prepared were dried in a tray drier at a temperature 50°C. The dried

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granules were screened, mixed with lubricants and stored for tableting[4].

Preparation of Naproxen Matrix Tablets:

Matrix tablets of Naproxen were prepared by wet granulation technique using 8% starch paste as binder. Lactose was used as diluent and mixture of talc and magnesium stearate at 2:1 ratio was used as lubricant. Naproxen matrix tablets containing Guar gum , Xanthan gum were prepared. The composition of different formulations used in the study containing 150 mg of Naproxen in each case is shown in table Polymers were sieved through a mesh no 250 and mixed with Naproxen and Lactose. The powders were blended and granulated with 8% Starch paste. The wet mass was passed through a mesh no 12 and the wet granules were dried at 50 °C for 2 h. The dried granules were passed through a mesh no 22 and were lubricated with a mixture of talc and magnesium stearate (2:1). The lubricated granules were compressed with a maximum force of compression using 11.5 mm round, flat and plain punches on single station tableting machine. [4,5,6,7]

Formulation of Naproxen Tablets

Sl. no	Ingredients	MT1	MT2	MT3
1	Naproxen	150	150	150
2	Guar Gum	200	200	200
3	Xanthan Gum	150	125	100
4	Lactose	85	110	135
5	Starch	52	52	52
6	Magnesium stearate	5	5	5
7	Talc	8	8	8
	Total weight	**650**	**650**	**650**

EVALUATION STUDIES [8]:

Evaluation of Granules

Determination of bulk density and tapped density

A quantity of 5g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 Sec intervals. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using the following formulas Bulk density = W / V_O,Tapped density = W / V_f Where,

W = weight of the powder

V_O = initial volume

V_F = final volume

Compressibility index

The *Compressibility index* and *Hausner ratio* are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of interparticulate teractions. In a free flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value for poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the *Compressibility Index* and the *Hausner Ratio.* The compressibility index and Hausner ratio may be calculated using measured values for bulk density ***(ρ bulk***) and tapped density ***(ρ tapped***) as follows:

$$\text{compressibility index} = \frac{\rho \text{ tapped} - \rho \text{ bulk}}{\rho \text{ tapped}} \times 100$$

$$\text{Hausner ratio} = \frac{\rho \text{ tapped}}{\rho \text{ Bulk}}$$

Angle of repose

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose.

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

$\tan\theta = h/r$

$\theta = \tan^{-1} h/r$

Where *h* = height of pile

r = radius of the base of the pile

θ = angle of repose

EVALUATION OF TABLET

All the prepared Sustained release tablets were evaluated for following official and unofficial parameters.

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight by more than the percentage shown in Table 1 and none deviate by more than twice the percentage shown.

Average weight of tablet(Xmg)	Percentage deviation
X□ 80 mg	10
80□ X □ 250 mg	7.5
X□ 250 mg	5

Table1: Percentage deviation allowed under weight variation

Thickness

Twenty tablets were randomly selected from each batch and there thickness and diameter was measured by using digital vernier caliper.

Friability

Twenty tablets were weighed and placed in the Electrolab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

$$\% F = \{1-(Wt/W)\} \times 100$$

Where, % F = friability in percentage
W = Initial weight of tablet
Wt = weight of tablets after revolution

Tablet hardness

The crushing strength Kg/cm2 of prepared tablets was determined for 10 tablets of each batch by using Monsanto tablet hardness tester. The average hardness and standard deviation was determined.[6] The results are shown in Table.

Uniformity of Weight

Twenty tablets were individually weighed and the average weight was calculated. From the average weight of the prepared tablets, the standard deviation was determined. The results are shown inTable

In vitro Dissolution studies

In Vitro dissolution study was carried out using USP II apparatus in 900 ml of 0.1 N HCl (pH 1.2) for 2 hour & pH7.4 for 24 hours. The temperature of the dissolution medium was kept at 37± 0.5°C and the basket was set at 50 rpm. 5 ml of sample solution was withdrawn at specified interval of time and filtered through Whatman filter paper. The absorbance of the withdrawn samples was measured at λmax 332 nm using UV visible spectrophotometer. The concentration was determined from the standard curve of Naproxen prepared in 0.1N HCl (pH 1.2) & ph 7.4 at λ max 332 nm. The pharmacokinetic parameters of Naproxen were used to calculate a theoretical drug release profile for 24 hr oral dosage form.

3. RESULTS AND DISCUSSION

In the present study Narpoxen matrix tablets were prepared with the help of different polymers by wet granulation method**.** After preparation of the matrix tablets Evaluation studies were done with different parameters and the results were shown below

Parameter Batch	Bulk density	Tapped density	Carr's index	Hauser ratio	Angle of repose(degree)
MT1	0.385	0.461	16.33	1.12	0.6352±0.04
MT2	0.375	0.446	15.76	1.19	0.6524±0.02
MT3	0.353	0.420	16.08	1.19	0.5303±0.01

Table2.1: Physico-chemical evaluation of matrix tablets:

Parameter Batch	Thickness	Hardness	Friability	Weight variation
MT1	3.1	5.5	0.046	650.1
MT2	3.1	6	0.054	650.1
MT3	3.1	6	0.061	651.1

Table2.2: Physico-chemical evaluation of matrix tablets:

Formulation code	Sample absorbance	Standard absorbance	% Content uniformity
MT1	0.409	0.411	99.42±0.248
MT2	0.408	0.411	99.37±0.248
MT3	0.410	0.411	99.71±0.519

Table3: Drug Content Uniformity

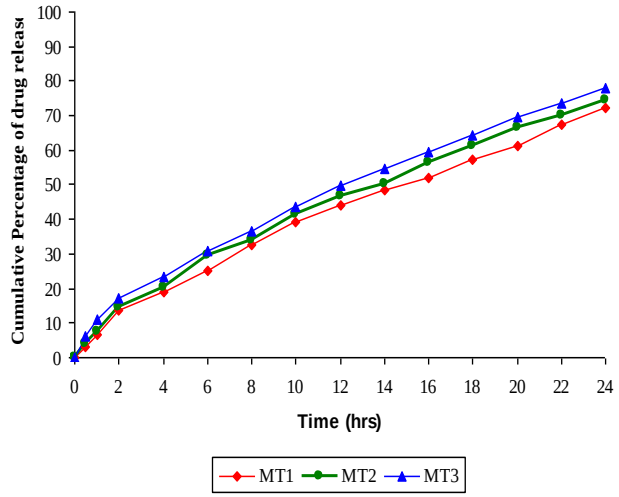

Fig 1: Graph showing dissolution profile for matrix tablets of naproxen

Time (hrs)	Cumulative Percentage of drug release		
	MT1	MT2	MT3
0	0.00	0.00	0.00
0.5	03.28 ± 0.37	04.12 ± 0.38	06.31 ± 0.34
1	06.81 ± 0.54	07.65 ± 0.44	11.23 ± 0.39
2	13.52 ± 0.54	14.41 ± 0.14	17.39 ± 0.24
4	19.14 ± 0.26	20.19 ± 0.39	23.14 ±0 .44
6	25.08 ± 0.42	29.47 ± 0.40	30.68 ± 0.35
8	32.50 ± 0.43	33.78 ± 0.35	36.41 ± 0.38
10	39.07 ± 0.45	41.36 ± 0.37	43.44 ± 0.35
12	43.87 ± 0.50	46.74 ± 0.53	49.63 ± 0.32
14	48.32 ± 0.33	50.05 ± 0.44	54.47 ± 0.30
16	52.03 ± 0.49	56.29 ± 0.40	59.36 ± 0.28
18	57.48 ± 0.37	61.33 ± 0.39	64.44 ± 0.44
20	61.12 ± 0.50	66.48 ± 0.41	69.81 ± 0.30
22	67.37 ± 0.40	70.14 ± 0.34	73.49 ± 0.46
24	72.36 ± 0.53	74.64 ± 0.50	77.99 ± 0.29

*All values are expressed as mean ± S.D, n = 3.

Table 4: dissolution profile for matrix tablets of naproxen

4. CONCLUSION

From this study we concluded that Naproxen matrix tablets with the help Natural polymers prove to be a better drug delivery for colon targeting drug delivery.

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Conflict of Interest: None Declared

