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Research Article

FORMULATION AND EVALUATION OF COLON SPECIFIC NAPROXEN TABLET

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ABSTRACT

The aim of present work was to develop and evaluate colon specific sustained release matrix tablet of naproxen using different concentration of microbially degradable polysaccharides such as olibanum gum and sterculia gum. The colon targeted matrix tablets were prepared by wet granulation technique. All the matrix formulations showed the desired physicochemical properties as per the official limits. All the batches of matrix tablet were subjected for *in vitro* dissolution study in various simulated gastric fluid for suitability for colon specific drug delivery system. Based on drug release study, formulation S5 showed good sustained release dissolution profile.

Keywords: Colon specific, Natural gums, Naproxen, Microbial triggered.MDT.

INTRODUCTION

Colon-specific drug delivery system has been developing as one of the site specific drug delivery system. Along with many applications in local and systemic delivery of drugs the colon delivery would also be advantageous when a delay in absorption is desirable from a therapeutic point of view as for the treatment of diseases that have a peak symptom in the early morning and that exhibit circadian rhythm, such as angina, asthma and rheumatoid arthritis. So by developing the pulsatile device for colonic delivery, plasma peak is obtained at an optimal time, number of doses per day can be reduced. Naproxen is used to treat symptomatic pain and inflammation. It is known to have reduced side-effect, especially related to the gastrointestinal tract (GIT) when ingested as 200 mg single daily or in divided doses.[1-4]

MATERIALS AND METHODS

Naproxen was provided as a gift sample from RPG life science, Bharuch. Sterculia gum and Gum olibanum were purchased from Nutriroma Gum Industries, Hyderabad. All other ingredients were used of analytical grade.

Formulation of colon targeted matrix tablet

Colon specific sustained release tablets were prepared by 3^2 full factorial design using different proportion of sterculia gum and gum olibanum with the help of wet granulation technique. The detailed compositions of matrix tablets are as shown in table no. 1.

EVALUATION

Pre compression parameters[5-8]

Bulk density

The powder sample under test was screened through 18# sieve and the sample equivalent to 10g was weighed, filled in a 50 ml graduated cylinder, the powder was leveled and the unsettled volume (Vo) was noted. The bulk density can be calculated in g/cm^3 by using the following formula,

Bulk density (ρb) = M/Vo

Where, M = mass of powder taken and Vo= apparent unstirred volume

Tapped density

The powder sample under test was screened through sieve # 18 and the weight of sample equivalent to 10g was filled in 50 ml graduated cylinder. The mechanical tapping of the cylinder was carried out using bulk density apparatus at a constant rate for 100 times. Volume was considered as tapped volume (Vf). The tapped density was calculated in g/cm3 by using the following formula

$$\textbf{Tapped density } (\rho t) = M/V_f$$

Where, M = weight of sample powder taken and V_f = tapped volume

Carr's index

Based on the bulk density and tapped density, the percentage compressibility of the granules was computed using the Carr's compressibility index by using the following formula,

$$\textbf{Carr's Index} = \rho t - \rho b/\rho t * 100$$

Where, ρb = bulk density and ρt = tapped density.

Hausner's ratio

Hausner's ratio was calculated by using the following formula.

Hausner's ratio =

Tapped density/Bulk density

Angle of repose

Angle of repose of the granules was measured by the fixed height method. A funnel was fixed to a desired height and granules were filled in it. They were allowed to flow down on a graph paper fixed on a horizontal surface and angle of repose was calculated using the following formula.

$$\textbf{Tan } \theta = h/r$$

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

Where, θ = angle of repose, h = height of pile, r = radius of the base of the pile.

Post compression parameters

Hardness [10-15]

The tablet hardness is defined as the force required breaks a tablet in a diametric compression test. To perform this test, a tablet was placed between two anvils, force is applied to the anvils and the crushing strength that just caused the tablet to break was recorded. The hardness was measured using Monsanto hardness tester. It is expressed in kg/cm^2.

Friability

The friability of the tablets was determined using Roche friabilator. It is expressed in percentage (%). Approximately 4 g (Wo) of dedusted tablets are subjected to 100 free falls of 6 inches in a rotating drum and are then reweighed (W). The friability is given by

$$F = 100 \times (1 - Wo/W)$$

Weight variation test

Weight variation test can be done as per the Indian Pharmacopoeia. 20 tablets were generally taken and were weighed individually and the weight variation was calculated with the use of standard deviation.

Drug Content

Ten Tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 0.1 N HCl and made up to 100ml of 0.1 N HCl. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10ml using 0.1 N HCl. Absorbance was measured by UV spectrophometrically at 272 nm using 0.1 N HCl as a blank. The amount of drug present in one tablet was calculated.

***In Vitro* drug release studies**

In Vitro drug release studies were performed using USP dissolution test apparatus (Type 1). The dissolution studies were performed in 900ml of dissolution medium which was stirred at 50 rpm at 37±0.5°C following a pH progression method[16]. i.e. 1.2 pH for first 2hrs, 6.8 pH for next 4hrs and 7.4 pH in the presence of rat caecal material[17] for rest of studies. Aliquots were withdrawn periodically and replaced with fresh medium and analyzed by UV spectrophotometrically at 272 nm.

RESULTS AND DISCUSSION

Pre compression studies

All the formulations were evaluated and it was found that all the results are in acceptable limit. The results of flow properties are as shown in Table no. 2.

Post compression studies

All the formulations were evaluated for their physical properties. All the results of physical tests are in acceptable limit. The results of hardness, friability, weight variation and drug content are as shown in Table no. 3.

***In vitro* dissolution study**

All the formulations were subjected for their dissolution studies. The results of the dissolution are as shown in Figure 1 to 3.

SUMMARY AND DISCUSSION

- Over the time there has been a growing appreciation on the importance of colon drug delivery on GIT physiology and on disease states, together with the realization of the significance of time-of-day of drug administration on resultant pharmacodynamic and pharmacokinetics parameters.
- In the present study, an attempt was made to design and characterize colon drug delivery tablet of microflora approach.
- Formulations were initially characterized by precompression studies. The formulations were found to possess good flow characteristics as well as satisfactory compressibility.
- The tablets were passed in different physical evaluation test and in vitro drug release study.
- S5 batch containing 30% Sterculia gum and 30% Olibanum gum showed the highest % CDR at 12th hr of 99.69 %.

Table 1: Formulation of colon tablet of Naproxen

Batch	Bulk Density (g/cm^3) n=3	Tapped Density (g/cm^3) n=3	Hausner's ratio n=3	Angle of repose (Θ) n=3	Compressibility index (%) n=3
S1	0.59±0.031	0.69±0.041	1.12±0.045	19.53±0.035	12.47±0.052
S2	0.45±0.027	0.57±0.026	1.21±0.029	30.21±0.039	21.38±0.055
S3	0.53±0.025	0.56±0.024	1.12±0.051	27.41±0.039	13.05±0.035
S4	0.51±0.059	0.55±0.032	1.17±0.041	28.37±0.043	11.82±0.032
S5	0.48±0.030	0.54±0.039	1.17±0.046	26.31±0.039	13.41±0.056
S6	0.48±0.058	0.53±0.036	1.13±0.051	22.36±0.069	16.27±0.041
S7	0.45±0.033	0.64±0.061	1.16±0.029	28.52±0.040	17.41±0.023
S8	0.58±0.044	0.63±0.045	1.12±0.043	28.33±0.047	19.62±0.075
S9	0.62±0.066	0.68±0.055	1.10±0.037	24.36±0.052	15.35±0.018

Table 2: Pre compression parameters of batches S1 to S9

Batch	Hardness (kg cm^2 ± %S.D) (n=6)	Friability (%)	Weight variation Avg weight (mg) (%S.D < 10%)	% Drug Content (n=3)
S1	6.75± 0.35	0.36	349.7±1.31	97.55± 0.61
S2	6.34±0.36	0.49	348.6±1.26	99.27± 0.35
S3	7.42± 0.43	0.59	349.8±1.25	96.29± 0.31
S4	7.53± 0.31	0.61	349.7±1.28	98.56± 0.69
S5	7.53± 0.37	0.53	348.5±1.32	99.65 ±0.19
S6	7.29±0.41	0.69	349.3±1.19	98.81± 0.68
S7	6.56±0.40	0.62	350.1±1.81	97.45± 0.41
S8	7.58±0.29	0.65	348.7±1.27	99.71± 0.31
S9	7.59±0.35	0.67	348.9±1.24	95.36± 0.61

Table 3: Post compression parameters of batches S1 to S9

Ingredients (mg)	S1	S2	S3	S4	S5	S6	S7	S8	S9
Naproxen	150	150	150	150	150	150	150	150	150
Sterculia gum	25 %	25 %	25 %	30 %	30 %	30 %	35 %	35 %	35 %
Olibanum gum	25 %	30 %	35 %	25 %	30 %	35 %	25 %	30 %	35 %
MCC	122	117	112	117	112	107	112	107	102
Talc	6	6	6	6	6	6	6	6	6
Mg. Stearate	4	4	4	4	4	4	4	4	4
PVP K 30	5%	5%	5%	5%	5%	5%	5%	5%	5%
TOTAL (mg)	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**

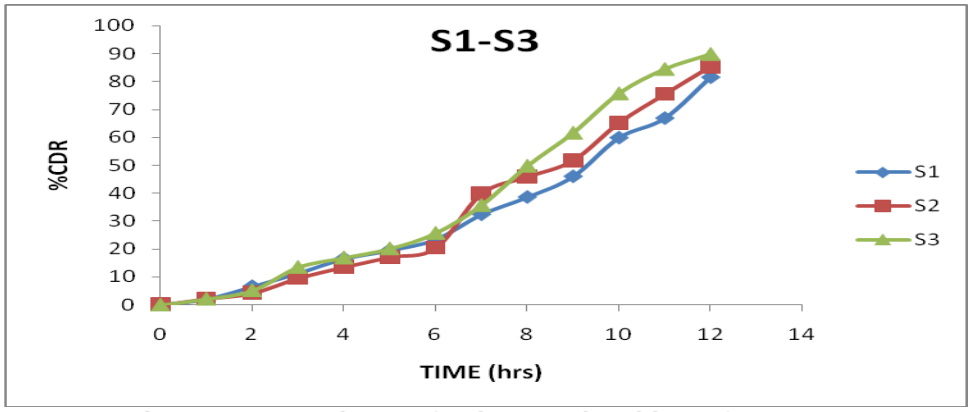

Fig. 1: % Drug release of colon matrix tablets of S1 to S3

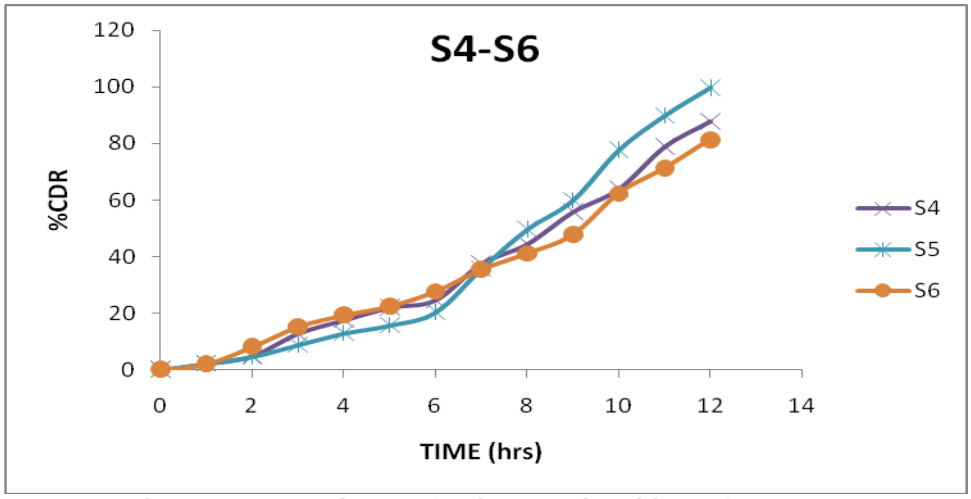

Fig. 2: % Drug release of colon matrix tablets of S4 to S6

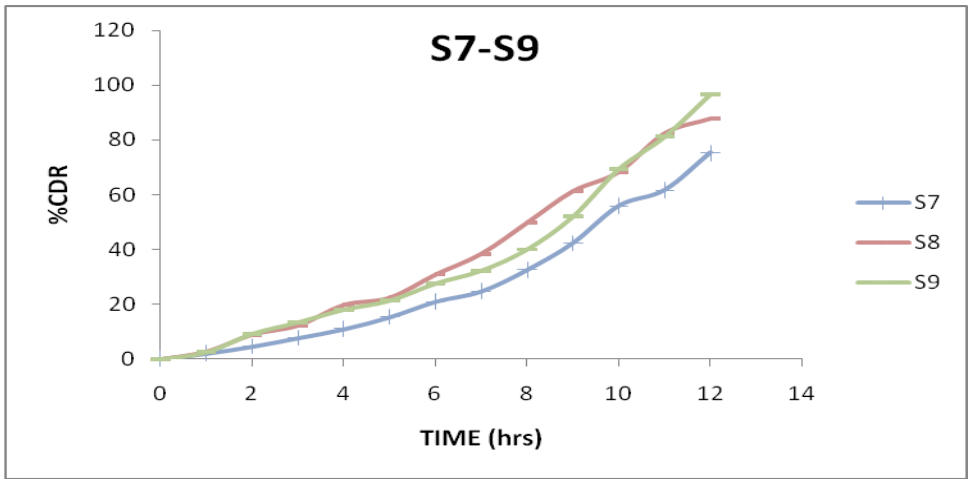

Fig. 3: % Drug release of colon matrix tablets of S7 to S9

Table 4: Design summary

Formulations	Sterculia gum (%) (X_1)	Olibanum gum (%) (X_2)	Response % CDR at 12th hr (hours)
S1	15	5	81.4
S2	15	10	85.34
S3	15	15	89.76
S4	20	5	87.69
S5	20	10	99.69
S6	20	15	81.46
S7	25	5	75.34
S8	25	10	87.67
S9	25	15	96.76

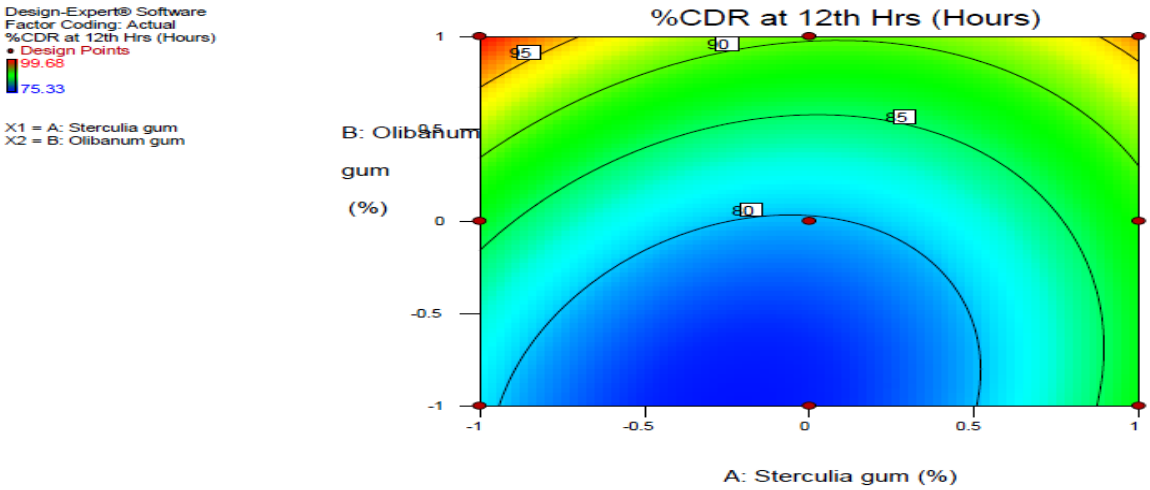

Fig. 4: Contour plot showing the effect of Sterculia gum and Olibanum Gum

As seen from the, contour plot of the revealed that there was corresponding increase in Release time with increase in the concentration of Sterculia gum (A). Moreover, it was revealed that increase in concentration of Olibanum gum (B)

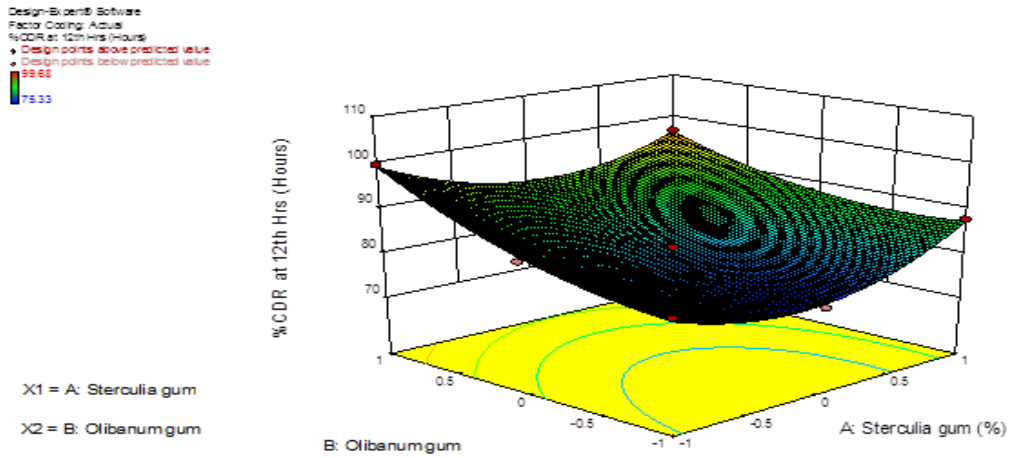

Fig. 5: Response surface plot (3D) showing the effect of Sterculia gum and Olibanum gum

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