INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

CHARACTERIZATION AND EVALUATION OF COLON TARGETED ORAL TABLETS OF NAPROXEN

Biresh Kumar Sarkar*[1], Devananda Jain[1] and Mamta Parwal[2]

[1]Bhagwant University, Dept.of Pharmaceutical Tech and Science, Ajmer, Rajasthan, India.
[2]Chemind Diagnosis & Biosolutions, Jaipur, Rajasthan, India.

***Corresponding Author: bireshsarkar@gmail.com**

ABSTRACT

In the present work, we have formulated the oral tablets of naproxen using guar gum alone and in combination with other polymers. The eight different tablet formulations were prepared by wet granulation method. Guar gum (GG), xanthan gum (XG), ethyl cellulose (EC) and cellulose acetate phthalates (CAP) were included in the formulations containing 100 mg of naproxen; tablets were subjected for the evaluation of hardness, friability, drug content uniformity swelling index, scanning electron microscopy and in vitro drug release in rat caecal contents. Hardness was found to be in the range of 5.5 to 7.5 kg/cm2, the percent friability was in the range of 0.80 to 0.90 % and tablets showed 98.00 % to 99.55 % of the labeled amount of naproxen indicating uniformity in drug content. The tablets containing GG alone released 91.55 % of drug, at the end of 24th hour in rat caecal contents whereas; drug release from tablets containing GG with XG, GG with EC and GG with CAP was 96.88 %, 80.51 % and 85.82 respectively at the end of 24th hour. The drug release followed the diffusion controlled mechanism.

Keywords: colon targeted oral tablets, naproxen and xanthene gum

INTRODUCTION

Delivery of drugs to the colon is useful in the treatment of several colonic diseases (ulcerative colitis and crohn's disease). Corticosteroids have traditionally formed the basis of treating inflammatory bowel disease. However chronic treatment of inflammatory bowel disease with steroids, while often effective, is plagued by a number of serious side-effects (e.g. acne, moonface, hypertension, peptic ulcer, impaired glucose tolerance and mood disturbances. If these undesired side-effects could be overcome or markedly reduced in both sub chronic and chronic dosing regimes. Corticosteroids would have the potential of being ideal therapeutic treatments of inflammatory bowel disease.

A potential matrix material for colonic drug delivery is guar gum. Owing to its high viscosity this polysaccharide may carry certain drugs to the large intestine without appreciable release in the stomach or small intestine. Once in the large intestine, the guar gum matrix will be degraded by specific enzymes produced by the gut microflora (i.e, α-galactosidases and β-mannanase) to initiate drug release[1].

In the present work, we have chosen a non-steroidal anti-inflammatory drug, naproxen as a model drug. The tablets were prepared using guar gum alone and in combination with other

polymers and these tablets were evaluated for their ability to remain intact in stomach and small intestine and release the majority of drug in colon.

MATERIALS AND METHODS

Naproxen was obtained as gift sample from Pharma Impex Lab, Kolkata. Guar gum (GG), ethyl cellulose (EC), cellulose acetate phthalate (CAP), lactose, starch, talc and magnesium stearate were purchased from s.d.fine chemicals, Mumbai and xanthene gum (XG) was purchased from Loba Chemie, Mumbai. All the reagents used in the study are of analytical grade and quality standard.

METHODS

Preparation of tablets

The tablets were prepared by wet granulation method using starch mucilage as a binder. Lactose was used as diluents and mixture of talc and magnesium stearate was used as lubricant. GG, XC, EC and CAP were included in the formulations containing 100 mg of naproxen (see Table 1). GG, XC, EC and CAP were passed though mesh no.250 and mixed with naproxen, which was previously passed through mesh no.250. The powders were mixed and granulated with 8 % starch mucilage and wet mass was passed through a mesh no.12, then granules were dried at 50o C. The dried granules were passed through mesh no. 22 superimposed on mesh no. 44 and these granules were lubricated with the mixture of talc and magnesium stearate (2:1), finally granules were compressed into tablets using rotary tablet press (Cadmach Company). The prepared tablets of each batch were subjected for evaluation of Hardness test, Friability test, Drug content, Swelling index, Scanning electron microscopy and *In vitro* drug release in phosphate buffer pH 1.2, pH 7.4 and in rat caecal contents.

Drug content

Ten tablets were finely powdered and the powder equivalent to 100 mg of naproxen was weighed and transferred to 100 ml volumetric flask. Initially, about 50 ml of phosphate buffer (pH 7.4) was added and the flask was shaken thoroughly and kept for 12 hrs, warmed and then volume was made upto 100 ml using phosphate buffer (pH 7.4). Drug content was estimated using UV-spectrophotometer (Shimadzu, UV-1601) at 241nm with suitable dilutions.

Measurement of swelling index

The tablets were weighed individually (W1) and placed separately in petri dishes containing 10 ml of phosphate buffer pH 7.4. At regular intervals (0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 10, 12 and 24 hr) the tablets were carefully removed from Petri dishes and excess water was removed using filter paper. The swollen tablets were reweighed (W2) and the swelling index of each tablet was calculated using the following equation,

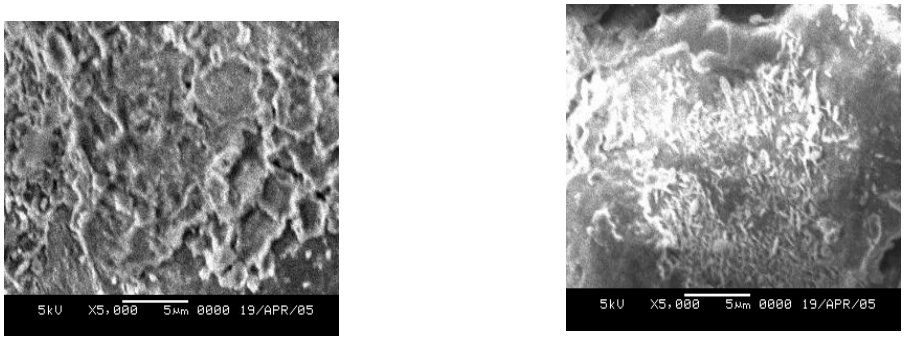
$$\text{Swelling index} = \frac{W_2 - W_1}{W_1}$$

Table 1: Composition in Naproxen Tablets with Guar Gum and other Polymers

Ingredients (mg)	Fn-1	Fn-2	Fn-3	Fn-4	Fn-5	Fn-6	Fn-7	Fn-8
Naproxen	100	100	100	100	100	100	100	100
Guar gum	300	300	300	300	300	300	300	300
Xanthan gum	-	180	-	-	90	-	90	60
Ethyl cellulose	-	-	180	-	90	90	-	60
Cellulose acetate phthalate	-	-	-	180	-	90	90	60
Lactose	190	10	10	10	10	10	10	10
Magnesium stearate	05	05	05	05	05	05	05	05
Talc	05	05	05	05	05	05	05	05

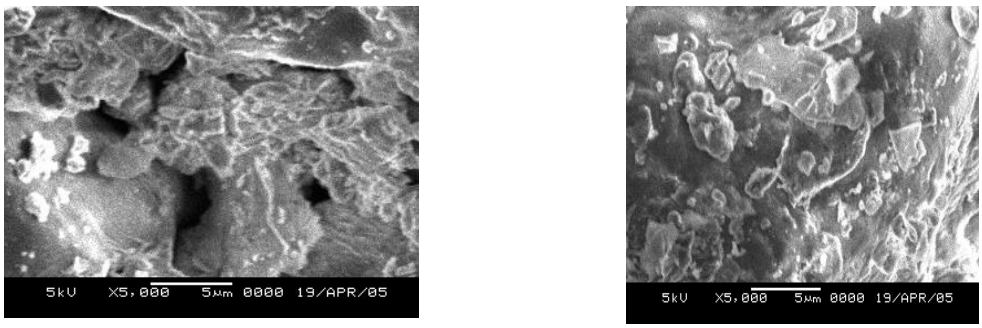
Table 2: Data Obtained from Evaluation of Tablets

Tablets	Hardness (kg/cm2)	Friability (%)	Drug content (%)	Swelling index	% drug released at 24th hr. in the presence of rat caecal contents.	Correlation coefficient (Higuchi) (r2)
Fn-1	5.5	0.80	98.00	2.7829	91.55	0.9189
Fn-2	5.5	0.80	98.55	3.3101	96.88	0.9269
Fn-3	7.0	0.90	99.55	1.6967	90.51	0.9223
Fn-4	6.5	0.85	98.98	2.0431	95.82	0.9190
Fn-5	7.5	0.90	99.12	-	83.12	0.9162
Fn-6	7.0	0.90	98.55	-	88.81	0.9191
Fn-7	6.5	0.85	98.50	-	67.63	0.9182
Fn-8	7.0	0.90	99.00	-	76.82	0.9162



Fn -1 **Fn -2**

Fig. 3: SEM Photomicrographs of formulations Fn-1 and Fn-2.



Fn -3 **Fn -4**

Fig.4: SEM Photomicrographs of formulations Fn-3 and Fn-4.

Fn-3 and Fn-4 was 2.7829, 3.3101, 1.6967 and 2.0431respectively (Table 2 & Fig. 2). The maximum swelling has been observed for the tablets prepared by GG with XG compared to

other tablets. The tablets containing GG with CAP have shown lesser swelling index, which may be due to lesser uptake of buffer (water) by the polymer. The tablets of Fn-1, Fn-2, Fn-3 and Fn-4 were subjected for SEM to examine the surface topography and morphology of fractured surfaces. It is evidence from the SEM photomicrographs that all tablets have smooth and plane surfaces, the Fn-2 formulation has shown lesser fractured surface compared to others (Fig. 3 & 4). Figure 1 shows the drug release profile from tablets. The tablet containing GG alone released 91.55 % of drug at the end of 24th hour of dissolution study in presence of rat caecal contents. Drug release from all the tablet formulations followed diffusion controlled mechanism with r2 values nearer to one (see table 1). Since the formulation Fn-2, contains both GG and XG, the water uptake capacity of this is more compared to Fn-1, which contains GG alone and we observed proportionality in swelling capacity and drug release pattern. The formulations of GG in combination with EC and CAP have demonstrated lesser swelling capacity and similarly showed delayed and lesser drug release.

In conclusion it can be said that; the tablet containing GG with XG (Fn-2) has shown maximum drug release of 96.88 % at the end of 24th hour of dissolution study in rat caecal contents, hence this formulation can be useful for the colonic targeted delivery of naproxen.

REFERENCES

1. Bussemer T, Otto I and Bodmeier R. Crit. Rev. Ther. Drug Carrier Syst. 2001;18:433.
2. Friend DR. Adv Drug Deliv Rev. 1991;7:149.
3. Watts P and Illum L. Drug Dev Ind Pharm. 1997;23: 893.
4. Yang L, Chu J and Fix J. Int J Pharm. 2002;235:1
5. Van den Mooter G and Kinglet R. Drug Delivery. 1995; 2:81
6. Rama Prasad YV, Krishnaiah YSR and Satyanarayana S. Indian Drugs. 1996;33:1.
7. Ashford MJT. J. Control. Rel. 1993;26:213.
8. Rama Prasad YV, Krishnaiah YSR, Satyanarayana S. J Control Rel. 1998;51:281.
9. Rubinstein A, Nakar D, Sintov A. Int J Pharm. 1992; 84: 141.
10. Rubinstein A, Nakar D and Sintov A. Pharm Res. 1992;9: 276.