RESEARCH ARTICLE

Development and evaluation of xyloglucan matrix tablets containing naproxen

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The xyloglucan (XGL) matrix tablets containing naproxen were prepared by conventional wet granulation technique and evaluated for its drug release characteristics. Hardness of the tablets was found to be in the range of 5.0-7.0 kg/cm^2. The tablets showed 98.23-99.12% of the labeled amount of drug, indicating uniformity in drug content. The swelling index increased with the increase in concentration of XGL and with the addition of hydroxypropylmethyl cellulose (HPMC) in the matrices, whereas swelling index decreased with the addition of cellulose acetate phthalate (CAP) and ethyl cellulose (EC). The compaction pressure had no significant effect on the drug release. Increase in polymer content and increased initial drug loading resulted in decreased drug release from the tablets. Addition of HPMC, CAP, and EC to XGL tablets decreased the drug release, and release was extended over a period of 8 h. The mechanism of release from all the tablets deviated from Fickian mode.

Key words: *Drug release, matrix tablets, naproxen, xyloglucan*

INTRODUCTION

The last two decades have witnessed a mammoth growth in the development of drug delivery systems using natural polysaccharide matrices. The drug release from such matrices can be controlled through their physical properties.[1,2] Polysaccharides are the choice of materials among the hydrophilic polymers used, because they are nontoxic and acceptable by the regulating authorities.[3] The various polysaccharides used in drug delivery application are cellulose ethers,[4] xanthan gum,[5] scleroglucan,[6] locust bean gum[7], and gaur gum[8] etc. Another natural polysaccharide, obtained from the seed kernel of *Tamarindus indica*, possesses properties like high viscosity, broad pH tolerance,[9] noncarcinogenic,[10] mucoadhesive, and biocompatible.[11] It is used as stabilizer, thickener, gelling agent, and binder in food and pharmaceutical industries. The tamarind seed polysaccharide, obtained from kernels of tamarind tree, is indigenous to India and South East Asia, constituting about 65% of the seed components.[12,13] It is a branched polysaccharide with a main chain of β-D-(1,4)-linked glucopyranosyl units, and that a side chain consisting of single D-xylopyranosyl unit attached to every second, third, and fourth D-glucopyrnosyl unit through an α-D-(1,6) linkage. One D-galatopyranosyl unit is attached to one of the xylopyranosyl units through a β-D-(1,2) linkage.[14,15]

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The present study was aimed to evaluate the feasibility of using XGL as matrix material for prolonged release of drugs. The XGL alone and in combination with hydroxypropylmethyl cellulose (HPMC), cellulose acetate phthalate (CAP), and ethyl cellulose (EC) has been used to prepare matrix tablets. Naproxen, a nonsteroidal anti-inflammatory drug, has been used as a model drug.

MATERIALS AND METHODS

Tamarind seed powder and naproxen were kindly obtained as gift samples, respectively, from Dabur India Limited and Natco Pharm Ltd., Hyderabad, India. Ethyl cellulose, HPMC, CAP, lactose monohydrate, talc, magnesium stearate, and absolute ethanol were purchased from s.d. Fine Chemicals Pvt. Ltd., Mumbai, India. All the chemicals used were of analytical grade.

Isolation of xyloglucan

The isolation of xyloglucan (XGL) was performed by following the method reported earlier.[12] The 20 g of tamarind kernel powder was added to 200 ml of cold distilled water to prepare a slurry. The slurry was poured into 800 ml of boiling distilled water. The solution was boiled for 20 min under stirring condition in a water bath. The resulting thin clear solution was kept overnight, then the solution was centrifuged at 5000 rpm for 20 min. The supernatant liquid was separated and poured into excess absolute alcohol with continuous stirring. The precipitate was washed with 200 ml of absolute ethanol and then dried at 50°C

for 10 h. The dried polymer was powdered and stored in desiccator until further use.

Preparation of matrix tablets

The matrix tablets were prepared by wet granulation method using starch mucilage as binder, lactose as diluent, and mixture of talc and magnesium stearates as lubricants. Xyloglucan, HPMC, CAP, and EC were included in the formulations containing 100 mg of naproxen [Table 1]. Xyloglucan, HPMC, CAP, and EC 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 starch mucilage (5% w/v) and the wet mass was passed through a mesh no. 10. The obtained wet granules were dried at 45°C. The dried granules were subjected to dry screening by passing through mesh no. 22 superimposed on mesh no. 44 and the granules were lubricated with the mixture of talc and magnesium stearate, finally these granules were compressed into tablets using rotary tablet press (M/s Remek, Ahmedabad, India).

The formulation variables studied were (1) effect of drug-polymer ratio, (2) effect of addition of hydrophilic and hydrophobic polymers, (3) effect of drug loading, and (4) effect of compaction pressure.

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 24 h, warmed, and then volume was made up to 100 ml using phosphate buffer (pH 7.4). Drug content was estimated using UV-spectrophotometer (UV-1601, Shimadzu) at 241 nm with suitable dilutions.

Measurement of swelling index

The five tablets were weighed individually (W_1) and placed separately in petri dishes containing 25 ml of phosphate buffer pH 7.4. At regular intervals of 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, and 8 h, the tablets were removed carefully from petri dishes and excess water was removed using filter paper without pressing. The swollen tablets were re-weighed (W_2) and the swelling index of each tablet was calculated using the equation:

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

In vitro drug release study

Drug release study was carried out using USP dissolution rate test apparatus-I (Electrolab, Mumbai, India). The study was conducted at 37°C and 100 rpm for 2 h in 900-ml buffer of pH 1.2, then the dissolution medium was replaced with 900 ml of pH 7.4 phosphate buffer and tested for drug release up to 12 h. Five milliliters of sample was withdrawn at different time intervals, centrifuged, and estimated the drug content using UV-spectrophotometer at 241 nm by suitable dilutions.

Scanning electron microscopy (SEM)

The matrix surfaces were examined with the SEM (JOEL JSM-T330A, Japan) after the dissolution testing. After dissolution, the matrices were air-dried, mounted with silver paint on aluminum stub, sputter coated with platinum, and finally observed and photographed under SEM.

Model used for drug release analysis

The drug release kinetics was analyzed by plotting the log fraction released versus log time and data fitted to the following simple exponential model:

$$\frac{M_t}{M_\infty} = kt^n$$

where, M_t/M_∞ is the fractional drug release into the dissolution medium, k is a constant related to the properties of the drug delivery system, and n is related to release mechanism; its value ranges from 0.5 (Fickian release) to 1.0 (case II transport), whereas n values between 0.5 and 1.0 are indicative of nonFickian/anomalous release.

RESULTS AND DISCUSSION

The matrix tablets of XGL were prepared by wet granulation method and evaluated. Table 2 shows the data obtained from the evaluation of tablets. The hardness was found to be in the range of 5.0-7.0 kg/cm^2; the tablets showed 98.23-99.12% of the labeled amount of drug, indicating uniformity in drug content.

Table 1: Composition of xyloglucan matrix tablets

Ingredients (mg)	XGL1	XGL2	XGL3	XGL4	XGL5	XGL6
Naproxen	100	100	100	100	100	150
Xyloglucan	100	150	150	150	150	150
Hydroxypropylmethyl cellulose	-	-	100	-	-	-
Cellulose acetate phthalate	-	-	-	100	-	-
Ethyl cellulose	-	-	-	-	100	100
Lactose	180	130	30	30	30	30
Magnesium stearate	8	8	8	8	8	8
Talc	12	12	12	12	12	12

The swelling index increased with the increase in concentration of XGL and with the addition of HPMC in the matrices, whereas the tablets containing CAP and EC showed lower swelling indices; this may attributed to the hydrophobic nature of the polymers in which the water uptake is low [Table 2].

Figure 1 shows the effect of XGL, HPMC, CAP, and EC on the release of naproxen. The drug release decreased as the concentration of XGL in the matrix increased. Further, the addition of HPMC, CAP, and EC in the matrix also decreased the drug release and extended over a period of 8 h. The release of naproxen has been examined at constant polymer content. As the initial drug-loading was increased, the drug release from the matrix was decreased. The drug release mechanism was shifted from Fickian to nonFickian diffusion with the addition of CAP and EC to XGL matrix.

Table 2: Data obtained from evaluation of xyloglucan matrix tablets

Tablets	Hardness (kg/cm²)	Drug content (%)	Swelling index	*n*-values
XGL1	5.0	98.23	2.78	0.452
XGL2	5.5	98.65	3.31	0.487
XGL3	6.0	99.01	4.29	0.508
XGL4	5.5	98.98	2.04	0.658
XGL5	7.0	99.12	1.76	0.693
XGL6	6.5	98.13	1.65	0.661

All the values are average of three determinations

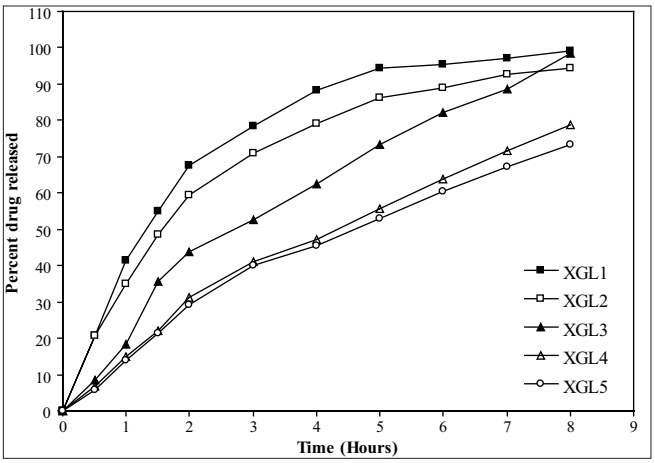

Figure 1: Naproxen release profile from the XGL matrix tablets

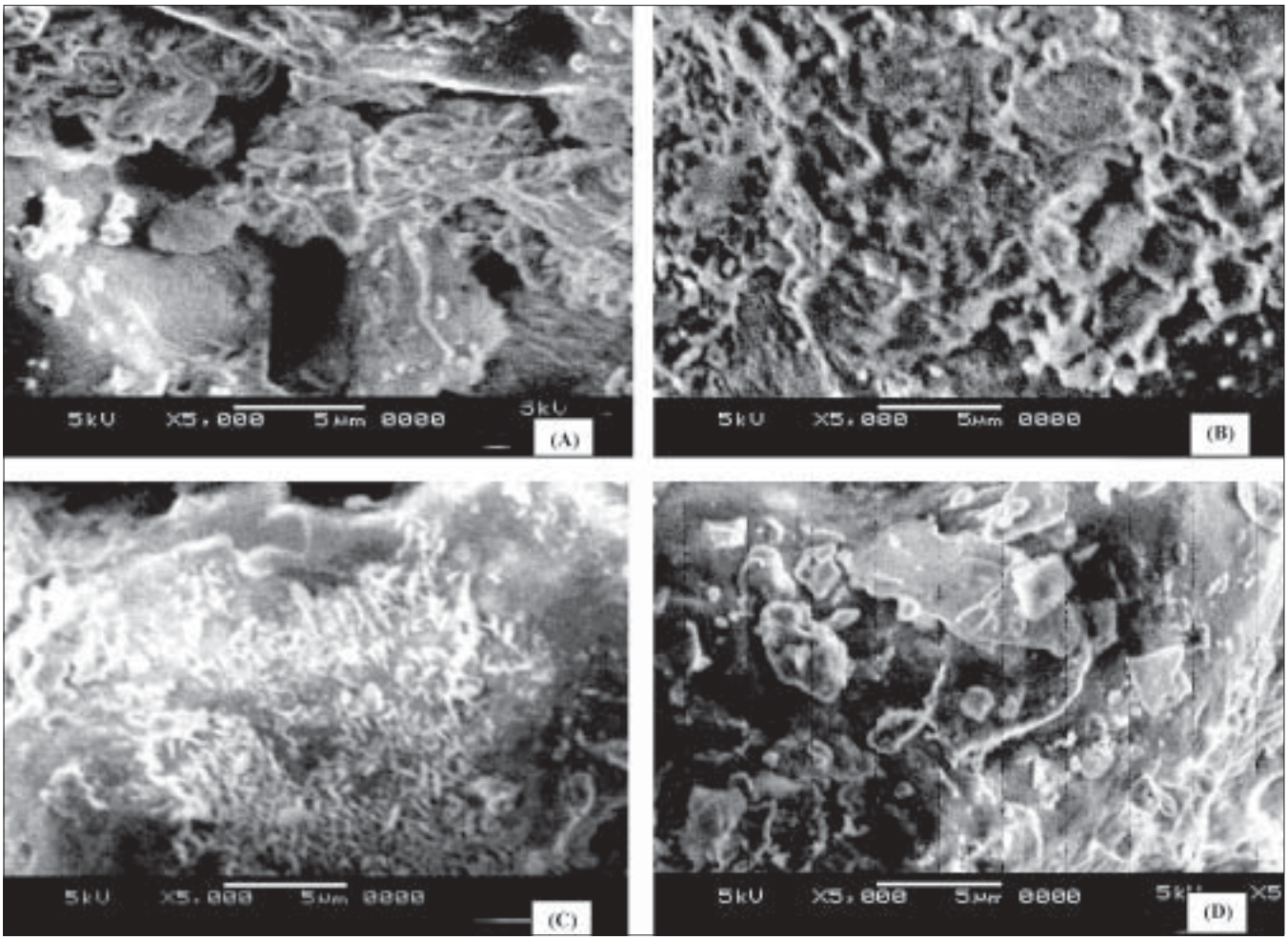

Figure 2: SEM photomicrographs of matrix tablets XGL2 (A), XGL3 (B), XGL4 (C), and XGL5 (D) after dissolution testing

The SEM photographs, taken at the same magnification, show the different pore sizes and the structural differences between the matrices after the dissolution testing [Figure 2]. The tablets containing XGL alone and XGL with HPMC have shown few openings of pores, indicating a diffusional release through 'water-filled pores' and not across the matrix. Whereas, the tablets containing XGL along with CAP and EC have not shown the pore structures on their surfaces, suggesting that the drug release takes place by diffusion across the matrix and not by diffusional release through 'water-filled pores'. This may be the reason why drug release is quicker in case of tablets containing XGL and HPMC.

The diffusion of drug from XGL matrix was found to be dependent on the gel concentration. The release of drug was decreased with the increase in XGL concentration and with the addition of HPMC, CAP, and EC. In conclusion, it can be said that the tablets containing XGL in combination with CAP has released 98.08% drug and release was extended over a period of 10 h of dissolution study, hence, it is a good combination for the controlled release of drugs.

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