Research Article

EVALUATION OF TAMARIND SEED POLYSACCHARIDE AS A DRUG RELEASE RETARDANT

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ABSTRACT

Plant polysaccharide has been shown to be useful for the drug delivery in recent years. Isolation of xyloglucan the polysaccharide from tamarind kernel powder was carried out by aqueous extraction-non aqueous precipitation method. Various batches of tablets were formulated using NSAID drug ketoprofen using drug: polymer in different ratios with non-aqueous wet granulation technique. The hardness of the tablets was found to be between 4.5-5.5 kg/cm^2 with friability values less than 0.3%. The weight variation and the drug content were within the standard limits. The *in-vitro* dissolution studies of the ketoprofen tablets showed a slow and sustained release over a period of 12 h. The increase in polymer content decreased the drug release from the tablets which may be attributed by the formation of gel layer surrounding the core drug. The IR spectral studies confirmed the good compatibility between the drug and the polymer in the dosage form. Thus isolation of tamarind seed polysaccharide has proven to be an effective drug retardant.

Keywords: Ketoprofen, Tamarind seed polysaccharide, Oral drug delivery, Sustained release, Xyloglucan.

INTRODUCTION

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years. Regular research is going on for the use of natural occurring biocompatible polymeric material in the design of dosage form for oral controlled release administration. Hydrophilic matrices are an interesting option when developing an oral sustained-release formulation[1,2]. Natural gums are biodegradable and non-toxic, which hydrate and swell on contact with aqueous media[3-5] and so these have been used for the preparation of dosage form. Plant polysaccharide has been shown to be useful for the design of specific drug delivery. Tamarind gum xyloglycon (XGL) present in tamarind seed which is hydrophilic polymer had been limited for use as stabilizer, gelling agent, thickener, binder, suspending and emulsifying agents in pharmaceutical industry[6] and has advantages such as nontoxic, biocompatible and biodegradable[7]. The present study was aimed to evaluate the feasibility of using XGL as matrix material for prolonged release of drugs[8]. The tamarind seed polysaccharide constitutes about 65% of the tamarind seed components[9]. 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 forth d-glucopyranosyl unit through an β-d-(1,6) linkage. One d-galatopyranosyl unit is attached to one of the xylopyranosyl units through a β-d-(1, 2) linkage[10].

Ketoprofen is a nonsteroidal anti-inflammatory drug with analgesic and antipyretic properties. Ketoprofen is rapidly and well-absorbed orally, with peak plasma levels occurring within 0.5 to 2 h. So, the present investigation was aimed to formulate the sustained release tablets of ketoprofen using tamarind polysaccharide as a release retardant.

MATERIALS AND METHODS

Ketoprofen was procured from BEC Chemicals Limited, Mumbai. Tamarind seed powder was purchased from the local supplier, Bangalore. All the other chemicals and reagents used were of pharmaceutical or analytical grade.

Isolation of tamarind seed polysaccharide (TSP)

The isolation of tamarind seed polysaccharide was performed in the following manner. 30g of tamarind kernel powder was added to 200 ml of cold distilled water and slurry prepared. The slurry was slowly poured into 800 ml of boiling distilled water and further boiled for 20 min under stirring conditions on a water bath. The resulting mixture was kept overnight and then it was centrifuged at 5000 rpm for 20 min. The supernatant liquid was separated and poured into twice the volume of absolute alcohol by continuous stirring to precipitate the polysaccharide. The precipitate was washed with 200 ml of absolute ethanol and then dried at 50^{0}C for 10 h. The dried polymer was powdered and stored in desiccators until further use[11].

Preparation of tablets of ketoprofen using TSP

The ketoprofen tablets by non-aqueous wet granulation method were prepared using drug with different concentrations of XGL polymer (Table-1). Ketoprofen was mixed with XGL and dicalcium phosphate diluent to which binder PVP solution was added quantity sufficient to form dough mass. The mass obtained was passed through sieve # 12 and the granules obtained were dried at 50^{0}C for 2h. The dried mass were regranulated through sieve # 16 and blended with purified talc and magnesium stearate as glidant and lubricant.

Table 1: Composition of ketoprofen tablets

INGREDIENTS (mg)	F1	F2	F3	F4
Ketoprofen	200	200	200	200
Tamarind seed polysaccharide (TSP)	50	100	150	175
PVP in alcohol 5 % w/v	q.s	q.s	q.s	q.s
Magnesium stearate	8	8	8	8
Purified talc	12	12	12	12
Dicalcium phosphate (q.s)	400	400	400	400

EVALUATION STUDIES

Drug-polymer compatibility studies

The IR spectra of ketoprofen, TSP and physical mixture of (1:1) drug-polymer were carried out using FTIR model-1601 (shimadzu corporation, Tokyo). Samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was between 500 to 4000 cm^{-1}.

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading was noted (Table-2).

Friability

The friability of a sample of 20 tablets was measured using a Roche friabilator (Electrolab, Mumbai). 20 previously weighed dedusted tablets were rotated at 25 rpm for 4 min. The tablets were again dedusted and weighed. The weight loss was calculated using the following formula.

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight variation

Twenty tablets were selected randomly from each formulation after compression, weighed using a digital balance and average weight was determined. The individual weights were compared with the average weight for the weight variation[12].

Drug content

Ten tablets were randomly taken from each formulation batch, finely powdered using mortar and pestle, powder triturate equivalent to 200mg of ketoprofen was weighed accurately, estimated for the drug content after suitable dilution with phosphate buffer pH 7.4, using UV-VIS spectrophotometer (UV-1601, Shimadzu) at 260 nm.

In-vitro drug release studies

Drug release studies were carried out according to USP XXIII paddle method. The dissolution media used was phosphate buffer, pH 7.4 maintained at 37^0C and the media was stirred at 50 rpm. Aliquots were withdrawn at different time intervals, filtered and analyzed spectrophotometrically at 260 nm for cumulative drug release.

Drug release kinetics study

The *in-vitro* drug release profile values were used to predict the drug release mechanism of the formulations using the soft ware PCP Disso v2.08.

RESULTS AND DISCUSSION

The matrix tablets of ketoprofen using TSP were prepared by non-aqueous wet granulation method and evaluated for sustained drug release from the dosage form. IR spectral studies showed similar peaks in drug-polymer blend when compared to drug and polymer (Fig.1-3) indicating good compatibility between drug and polysaccharide. The tablets of different formulations were subjected to various evaluation parameters and the results obtained were found to be within the range (Table-2). The hardness of all the tablets was in the range 4.5 to 6.5 kg/cm^2 and the loss of total weight in friability test was in the range 0.24 to 0.27 % which showed good mechanical strength to the tablets (Table-2). The uniformity of drug content for all the formulations were between 99.6 to 102.4 %. The matrix tablets (F1) containing 50 mg polysaccharide released 95.75 % of drug at the end of 3h study, where as the drug release from tablets F2, F3, F4 containing 100, 150 and 175 mg of polysaccharide were 90.13, 85.83 and 75.68 % respectively, at the end of 12^{th} h. An inverse relationship was observed between the concentration of polymer and release rate of ketoprofen from the formulated tablets. The highest correlation coefficient values recorded for the drug release mechanism studies using the software revealed formulation F1 as the first order and formulations F2-F4 with the matrix type as the best fit model.

Table 2: Post compression studies of the ketoprofen tablets.

CODE	HARDNESS (kg/cm^2)	WEIGHT VARIATION (mg±S.D.)	FRIABILITY (%)	DRUG CONTENT (%)
F1	4.5±0.2	402±6	0.24	102.4±1.6
F2	4.5±0.4	404±8	0.25	99.6±2.8
F3	5.5±0.3	401±4	0.27	101.3±1.7
F4	6.5±0.6	398±8	0.24	100.7±3.1

Table 3: Drug Release kinetics of the formulations.

Formulation	Release Kinetics	Correlation Coefficient (R)	T-test value	Best fit model
F1	Zero order	0.8863	3.315	First order
	First order	-0.9946	16.634	
	Matrix	0.9824	9.101	
	Peppas-Korsmeyer	0.9899	12.099	
	Hixson-Crowell	-0.9706	8.124	
F2	Zero order	0.9725	10.225	Matrix
	First order	-0.8769	4.469	
	Matrix	0.9911	18.261	
	Peppas-Korsmeyer	0.9897	16.893	
	Hixson-Crowell	-0.9633	8.785	
F3	Zero order	0.9846	13.801	Matrix
	First order	-0.9625	8.688	
	Matrix	0.9919	19.174	
	Peppas-Korsmeyer	0.9851	14.048	
	Hixson-Crowell	-0.9913	18.488	
F4	Zero order	0.9881	15.760	Matrix
	First order	-0.9931	20.775	
	Matrix	-0.9994	71.651	
	Peppas-Korsmeyer	0.9940	22.189	
	Hixson-Crowell	0.9821	12.757	

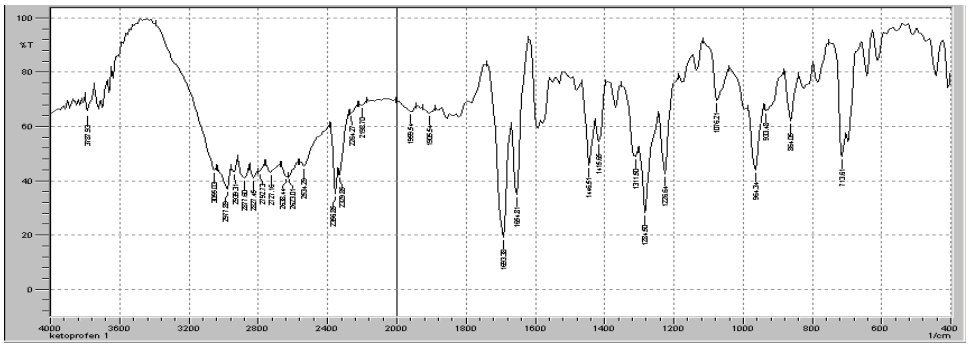

Figure 1: I.R spectrum of ketoprofen.

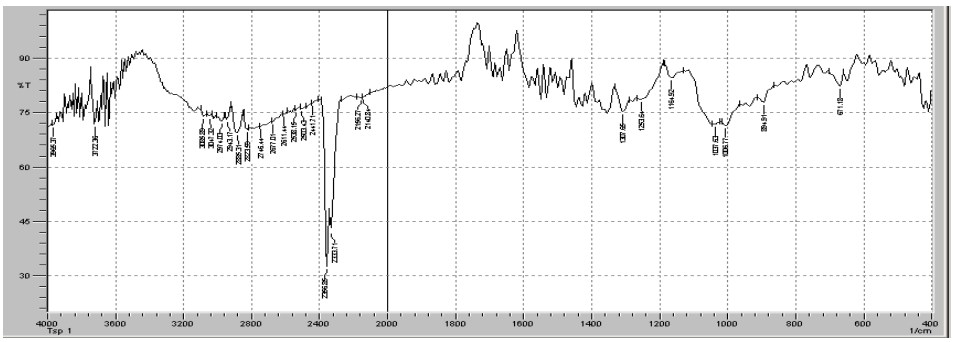

Figure 2: I.R spectrum of TSP.

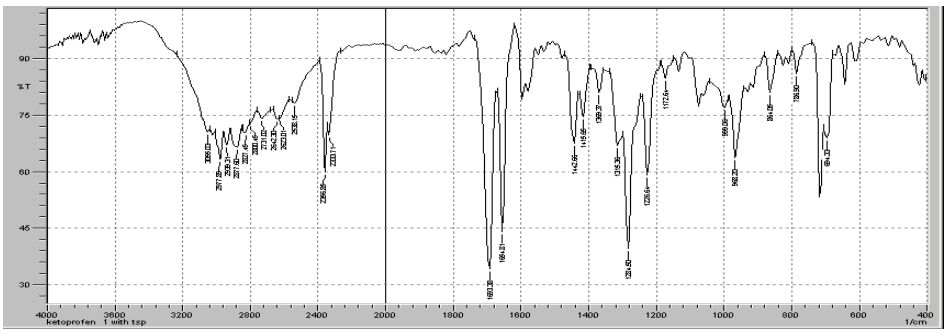

Figure 3: I.R spectrum of ketoprofen with TSP.

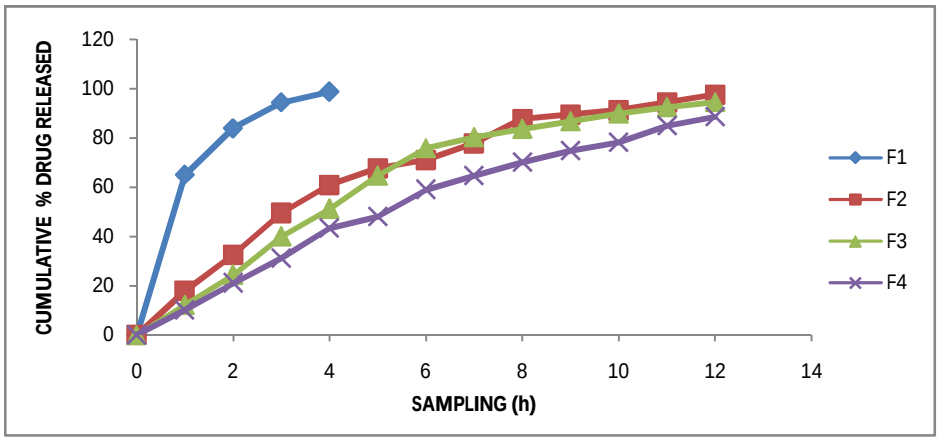

Figure 4: Comparative *in-vitro* release studies of ketoprofen from tablet formulations.

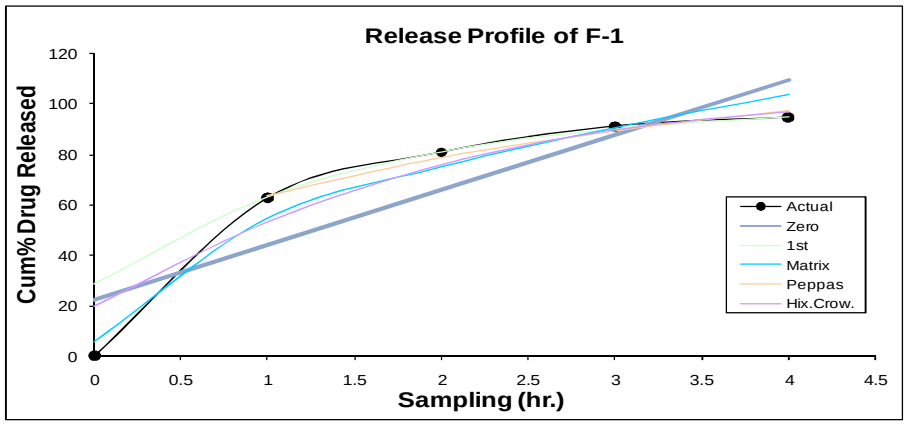

Figure 5: *In-vitro* drug release kinetics of formulation F1.

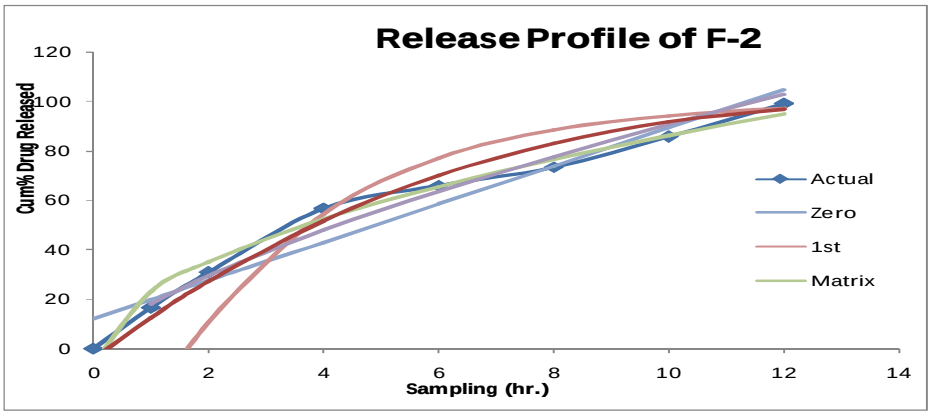

Figure 6: *In-vitro* drug release kinetics of formulation F2.

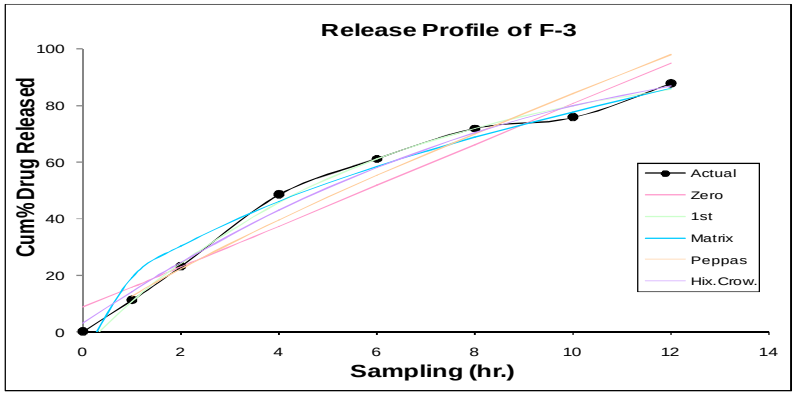

Figure 7: *In-vitro* drug release kinetics of formulation F3.

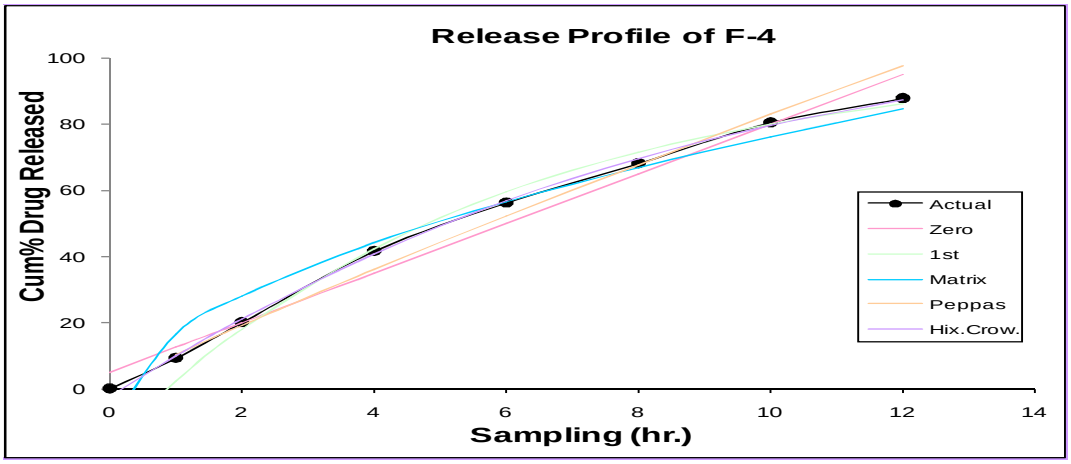

Figure 8: *In-vitro* drug release kinetics of formulation F4.

CONCLUSION

The isolated natural polymer TSP when used as a release retardant exhibited sustained activity of the drug release from the ketoprofen tablet formulations. Hence in the present investigation the search for a new effective natural polymer that can be used as a drug release retardant was explored.

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