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Design and Characterization of Diclofenac sodium tablets containing Tamarind seed polysaccharide as Release retardant

R.Deveswaran*, Sindhu Abraham, S.Bharath, B.V.Basavaraj, Sharon Furtado, V.Madhavan

Department of Pharmaceutics, M.S Ramaiah College of Pharmacy,M.S Ramaiah Nagar, M.S.R.I.T post, Bangalore- 560054,India.

E-mail: devs_mdu@yahoo.com

Abstract : Polysaccharides are the choice of materials among the hydrophilic polymers used as they are nontoxic and most acceptable by the regulating authorities. The tamarind seed polysaccharide (TSP) was isolated from tamarind kernel powder and this polysaccharide was utilized in the formulation of matrix tablets containing Diclofenac Sodium by wet granulation technique and evaluated for its drug release characteristics. Hardness of the tablets was found to be in the range of 4.0-6.0 kg/cm^2. The swelling index increased with the increase in concentration of TSP. Increase in polymer content resulted in a decrease in drug release from the tablets. The tablets showed 96.5-99.1% of the labeled amount of drug, indicating uniformity in drug content. The drug release was extended over a period of 12 h.. The release of the formulations matched with the marketed sustained release tablets with a similarity factor of 83.52. The *in-vitro* release data of the formulations followed zero order kinetics.

Keywords : Polymer matrix tablets, Tamarind seed polysaccharide, Diclofenac Sodium

Introduction:

Hydrophilic matrices are an interesting option when developing an oral sustained release formulation. The drug release from such matrices can be controlled through their physical properties. Polysaccharides are the choice of materials among the hydrophilic polymers used, because they are nontoxic and acceptable by the regulating authorities[1]. The various polysaccharides used in drug delivery application are cellulose ethers[2], xanthan gum[3], locust bean gum[4] and guar gum. Another natural polysaccharide, Tamarind seed polysaccharide (TSP) obtained from the seed kernel of Tamarindus indica, possesses properties like high viscosity, broad pH tolerance, noncarcinogenicity, mucoadhesive nature, and biocompatibility[5]. It is used as stabilizer, thickener, gelling agent, and binder in food and pharmaceutical industries. The tamarind seed polysaccharide constitutes about 65% of the tamarind seed components[6]. 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[7].

The present study was aimed to evaluate the feasibility of using TSP as matrix material for prolonged drug release using a model nonsteroidal anti-inflammatory drug, Diclofenac sodium.

Materials and Methods :

Materials

Tamarind kernel powder was obtained as gift sample from Sri Balaji industries, Bangalore**.** Diclofenac Sodium was obtained as gift sample from Bangalore Pharmaceuticals Research
Laboratory Ltd, Bangalore. 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 A.R grade.

Isolation of TSP

The isolation of TSP was performed by following the method reported earlier[8] . 20 g of tamarind kernel powder was added to 200 ml of cold distilled water to prepare

slurry. The slurry was poured into 800 ml of boiling distilled water. The solution was boiled for 20 min with continuous stirring. The resulting solution was kept overnight and centrifuged at 5000 rpm for 20 min. The supernatant liquid was separated and poured into twice the volume of absolute alcohol with continuous stirring. The precipitate obtained was washed with absolute ethanol and air-dried. The dried polymer was milled, passed through sieve no.60 and stored in a desiccator until further use.

Formulation of Tablets:

The matrix tablets were prepared by wet granulation method using IPA: water (3:1) as binder solvent, lactose as diluent, and mixture of talc and magnesium stearate as glidant and lubricant. TSP was included in the formulations containing 100 mg of Diclofenac Sodium (Table 1). Tamarind seed polysaccharide were passed though mesh no. 85 and mixed with Diclofenac Sodium and lactose which was previously passed through mesh no. 85. The powders were mixed, granulated with IPA: water (3:1) and the wet mass was passed through mesh no. 12. The wet granules obtained were dried at 40°C. The dried granules were subjected to dry screening by passing through mesh no. 16, blended with a mixture of talc and magnesium stearate and compressed into tablets using rotary tablet press (M/s Remek, Ahmedabad, India).

Table 1: Composition of TSP matrix tablets

Ingredients (in mg)	**Formulation code**			
	DFS F1	DFS F2	DFS F3	DFS F4
Diclofenac Sodium	100	100	100	100
Tamarind seed Polysaccharide	100	200	300	400
Lactose	293	193	93	-
Talc	5	5	5	5
Magnesium stearate	2	2	2	2

Evaluation Parameters:

a) Weight variation test[9]:

Randomly twenty tablets were selected after compression, weighed individually and average weight was determined.

b) Hardness Test:

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 noted.

c) Friability Test:

The friability of a sample of 20 tablets was measured using a Roche friabilator (Electrolab). 20 previously weighed tablets were rotated at 25 rpm for 4 min[9]. The tablets were dedusted and again weighed. The percentage weight loss was calculated using the following formula,

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

d) Drug content:

Ten tablets were randomly sampled from each formulation, finely powdered and individually estimated for the drug content after suitable dilution with phosphate buffer (pH 7.4) using UV-VIS spectrophotometer (UV-1601, Shimadzu) at 276 nm)

e) Measurement of swelling index:

Six tablets were weighed individually (W1) 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 the petri dishes and excess water was removed using filter paper without pressing[10]. The swollen tablets were re-weighed (W2) and the swelling index of each tablet was calculated using the equation:

$$\textbf{Swelling Index} = \frac{W2 - W1}{W1}$$

f) Disintegration test:

The test was performed using Disintegration test apparatus by placing each tablet in each basket with the disc. The process was carried out using pH 7.4-phosphate buffer maintained at 37°C.

Table 2: Evaluation Parameters

Evaluation Parameters	Formulation Code			
	DFS F1	DFS F2	DFS F3	DFS F4
Hardness (kg/cm^2)	4	5	5	6
% Friability	0.12	0.15	0.16	0.14
Uniformity of weight (mg)	500±2	502±5	504± 4	498±3
% Drug content	96.5	98.3	99.1	98.4
Swelling index	1.12	2.30	2.98	3.56
Disintegration time (mins)	5	7	8	8

g) *Invitro* drug release study:

Drug release study was carried out using USP dissolution rate test apparatus-II (Electrolab, Mumbai, India). The study was conducted at 37°C and 50 rpm for 2 h in 900-ml buffer of pH 1.2 and then the dissolution medium was replaced with 900 ml of pH 7.4-phosphate buffer and studied for drug release up to 12 h. Two ml of sample was withdrawn at different time intervals, filtered and the drug content was estimated at 276 nm after suitable dilution.

Fig.1: I.R.Spectra of Tamarind Seed Polysaccharide(TSP)

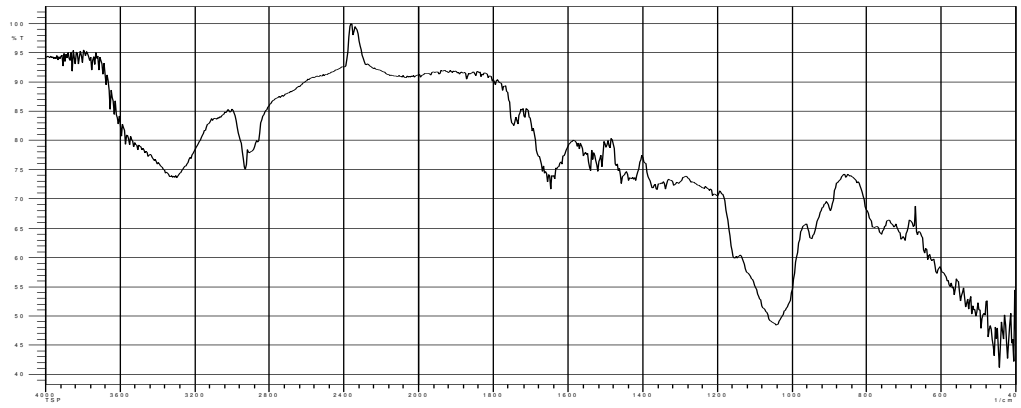


Fig.2: I.R.Spectra of Diclofenac Sodium (DFS)

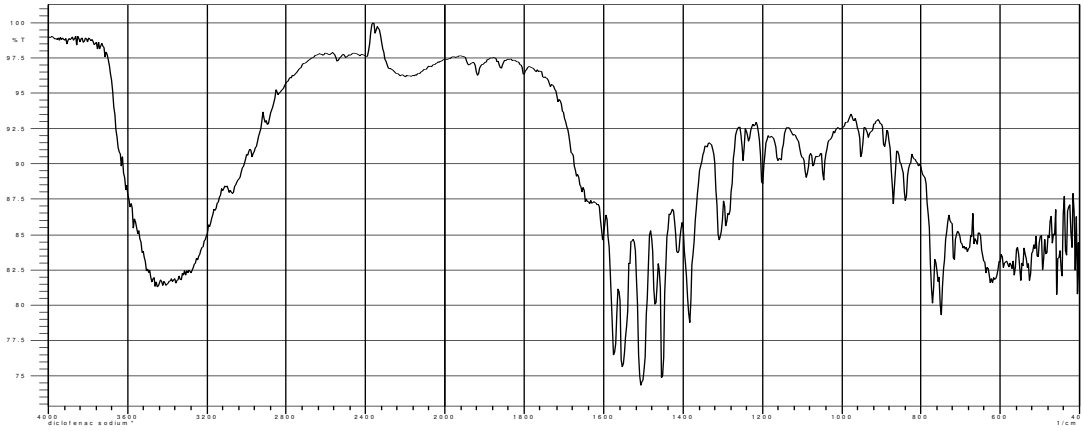
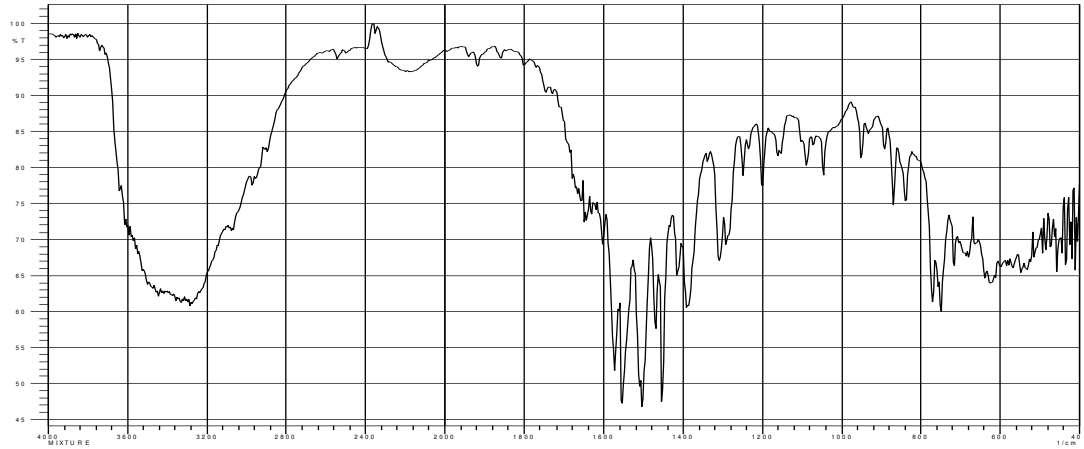


Fig.3: I.R.Spectra of a physical mixture of DFS & TSP



h) Similarity Factor (f_2) analysis:

In-vitro release profile of Diclofenac Sodium from selected TSP matrix tablet formulation and the marketed sustained release tablets were performed under similar conditions. The similarity factor between the two formulations was determined using the data obtained from the drug release study. The data was analyzed by the formula:

$f_2 = 50\log \{[1 + (1/N) \Sigma(Ri - Ti)^2]^{-0.5} \times 100\}$
where N = number of time points, Ri & Ti = dissolution of reference and test products at time 'i'.
If f_2 is greater than 50 it is considered that 2 products share similar drug release behaviors.

i) Model used for drug release kinetics:

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

$Mt / M\infty = k\, t^n$

Where t is the fractional drug release into the dissolution medium, k is the 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 non fickian or anomalous release.

Fig.4: In vitro release profile of Diclofenac sodium from DFS F1 (-♦-), DFS F2 (-■-), DFS F3 (-▲-), DFS F4 (-×-) and marketed sample (-●-).

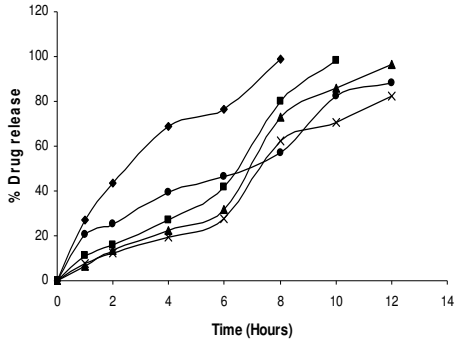
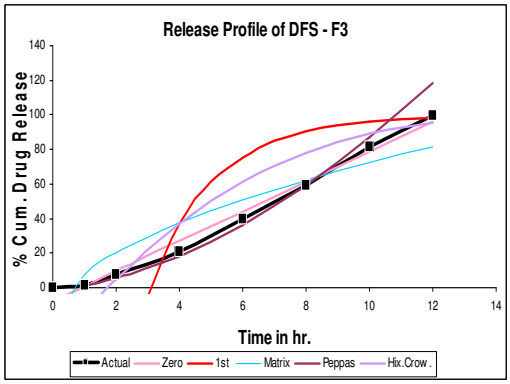


Fig.5: Model for Drug Release Profile



Results and Discussion:

The compatibility between the drug and the isolated polysaccharide (TSP) was found to be good by the I.R studies (Fig.1, 2 &3). The matrix tablets of Diclofenac Sodium using the TSP were prepared by wet granulation method. Table 2 shows the data obtained from the evaluation of tablets. The hardness of the tablets was found to be in the range of 4.0-6.0 kg/cm^2.The tablets showed 96.5-99.1% of the labeled amount of drug, indicating uniformity in drug content. The individual weight variation was found to be within ±7.5% of the average tablet weight. The friability values were found to be in the range of 0.12-0.16% and the disintegration time was found to be in the range of 5-8 min. for all the formulations. The swelling index increased with the increase in concentration of TSP. The drug release decreased as the concentration of TSP in the matrix increased.

The *in-vitro* drug release profile of Diclofenac Sodium from all the formulations and the marketed product is shown in Fig.4.The results indicated retardant release of drug from all the formulations with increase in the polymer concentration. The Formulation DFS F3 showed a slow and complete drug release of 98% over a period of 12 hr.

Based on the mathematical models, the values of the release exponent "n" for DFS F3 and marketed product was 0.7050 and 0.8585 which indicated a case II relaxational release transport, non-Fickian, zero order release. Further the correlation (R^2) values 0.9928 and 0.9934 for the same with the best fit model curve (Fig.5) derived using the PCP-Dissolv software confirmed the above results. Similarity factor analysis between the formulations DFS F3 and marketed product for the drug release showed an f_2 factor of 83.52, which is greater than 50, which confirmed that the release of the drug from the prepared matrix tablets is similar to that of the marketed tablet.

Conclusion:

The result of the present study demonstrated the isolated TSP can be used as a drug release retardant, which was evident, from the results. The drug release was extended over a period of 12 hours and the mechanism of drug release was observed to be following zero order release. Thus the polymer could serve as a new effective drug release retardant with better patient compliance.

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