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Modified tamarind kernel polysaccharide: A novel matrix for control release of aspirin

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ABSTRACT

pH dependent hydrogels of modified tamarind kernel polysaccharide (TKP) were synthesized by grafting with polyacrylamide chains on TKP backbone in presence of microwave irradiation and initiator. The present study is carried out to design oral controlled drug delivery systems for aspirin using synthesized hydrogels as carrier in form of tablets. TKP-g-PAM based hydrogels show significant enhancement for control release of aspirin. Release behavior of aspirin has been evaluated using USP type I apparatus in 900 mL of buffer solutions (pH 1.2, 6.8, 7.4), maintained at 37 °C at 100 rpm. It is observed that with increase in percentage of grafting (% *G*), swelling of matrices increases whereas erosion and rate of drug release decrease. The effect of % *G* onto t_{50} value (time taken for release of 50% drug) has also been discussed. The release characteristics from the matrices under study show non-Fickian diffusion mechanism, suggesting the controlled release of aspirin.

1. Introduction

Oral administration of drugs in form of tablets has long been used, which is the natural, uncomplicated, convenient and safe route [1]. In this route drug will pass through gastrointestinal tract where pH differs widely. Stomach is acidic while lower GI tract is neutral or mildly alkaline in nature [2–8]. Thus it is a challenge of controlled release or delayed release of drug in this route. Controlled drug delivery systems offer numerous advantages compared to other conventional dosages. The advantage of control release is elimination of peaks and troughs resulting from periodic and uneven dosing intervals. In addition, few drugs are required to elicit the same therapeutic effect. It is also required for improved, patient compliance and convenience [9,10].

Use of biodegradable polymeric hydrogels has gained lot of importance during the last decades in drug release research. Many synthetic biodegradable polymers are being used as a matrix for control drug release for its efficacy. In spite of the advent of many synthetic polymers, the use of natural polysaccharides and modified polysaccharides based hydrogels to deliver drug is an active area of research because of their easy availability, biocompatibility, non-toxicity, and hydrophilicity [11–16].

One of the effective ways to modify the structure and properties of natural polysaccharide is grafting. Controlled release systems have been developed and studied to increase the drug pharmacological action and reduce their side effects. The basic concept is based on the fact that the rate of drug absorption may be adjusted through a controlled rate of drug release from the matrix. Various systems have been proposed over last two decades. Out of them, the simplest system is the matrix device, where the drug is dispersed within the polymer network [17]. The present study reflects the application of a novel hydrogel (comprised of tamarind kernel polysaccharide grafted with polyacrylamide in presence of microwave irradiation and initiator) [18] as matrix for control release of aspirin using a diffusion mechanism. The purpose of the present work is to evaluate the effect of % grafting (% *G*) on the controlled release behavior of a model drug aspirin. A higher initial dosage of aspirin produces a high peak in the blood level content with potential toxicity and/or harmful side effects where as control release of aspirin can relief pain for periods of 24 h or even longer and can maintain minimum effective concentration (MEC). The effect of % swelling and rate of erosion on the controlled release of the enclosed drug in the polymer matrix has also been studied, as it is well known that swelling and erosion of polymers may affect the release rate of drugs significantly.

2. Materials and methods

2.1. Materials

Graft copolymers composed of polyacrylamide and tamarind kernel polysaccharide (TKP) were synthesized using microwave

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assisted method [18], have selected for drug release study. The products were dried in a hot air oven at 60 °C for 6 h, pulverized by mortar and pastel to obtain powder samples. Sieve fractions of 125 μm were selected for all graft copolymers as well as polysaccharide (TKP). TKP and various graft copolymers were kept in a desiccator using silica-gel as desiccant to obtain products dried to constant weight.

Aspirin (Spectrochem Pvt. Ltd., Mumbai, India) was selected as model drug, is freely soluble in water. TKP and guar gum were gift samples from Hindustan Gum & Chemicals Ltd., Bhiwani, Haryana, India. All chemicals were used as received, without further modifications.

2.2. Preparation of hydrogel

The graft copolymer based hydrogel was synthesized by grafting synthetic polyacrylamide chains onto the backbone of tamarind kernel polysaccharide using microwave assisted method. By varying the reaction parameters, various graft copolymers were synthesized and optimized the best one with respect to % *G*, intrinsic viscosity and radius of gyration. The details of synthesis procedure and reaction parameters have already been discussed in earlier report [18].

2.3. Preparation of tablets

The polymer matrix under evaluation was finely ground in a blender, with a model drug (aspirin) and binder (guar gum) in 10:1:0.3 ratios [21]. The mixture was wetted with ethanol and mixed further. The paste was dried at 50 °C to a constant weight and ground. Then a mixture of silicon dioxide and magnesium stearate (2:1 ratios) was added as lubricant, in amount not exceeding 3% of the ground powder. After mixing and sieving (20 meshes), tablet of 250 mg was prepared by compression in a standard Carver laboratory press at 2–3 t/cm^2. Eventually, the drug load of each tablet was 22.123 mg.

2.4. FTIR spectroscopy

The FTIR spectra of matrix (TKP-g-PAM), drug (aspirin), and tablet were recorded in solid state using KBr pellets with a FTIR spectrophotometer (Model IR-Prestige 21; Shimadzu Corporation, Japan) between 500 and 4000 cm^{-1}.

2.5. Scanning electron microscope (SEM)

Surface morphology of matrix (TKP-g-PAM), drug (aspirin) and tablet were analyzed in scanning electron microscopy (SEM) in powdered form (Model: JSM-6390LV; Jeol, Japan). The samples were deposited on brass hold and sputtered with a thin of gold under vacuum. Acceleration voltage used was 20 kV with the secondary electron as a detector.

2.6. Swelling and erosion test

The equilibrium swelling behavior of tablets was measured at 37 °C temperature in buffer solutions similar to that of gastric and intestinal fluids. A small pre-weighed piece of tablet made by polymer matrix is immersed in 200 mL of buffer solutions having pH 1.2, 6.8, 7.4 at 37 °C for 24 h. Then the swollen piece was blotted with filter paper and weight again. The ratio between the swollen and dry weights is defined as the extent of swelling (P_s), which was calculated as follows:

$$P_s = \frac{\text{weight of swollen gel} - \text{weight of dried gel}}{\text{weight of dried gel}} \times 100 \qquad (1)$$

Table 1
Details of graft copolymer based hydrogels, their % grafting, swelling and erosion results.

Polymer	% Grafting	% Swelling			% Erosion		
		pH 1.2	pH 6.8	pH 7.4	pH 1.2	pH 6.8	pH 7.4
TKP	0	395	256	288	87.03	78.95	60.38
TKP-g-PAM 1	42	425	460	420	69.75	69.00	59.18
TKP-g-PAM 2	52	490	510	495	62.29	65.32	58.25
TKP-g-PAM 3	49	445	480	460	66.69	67.12	58.72
TKP-g-PAM 4	64	570	540	590	51.24	64.32	57.28
TKP-g-PAM 5	59	530	508	540	54.61	61.56	57.65
TKP-g-PAM 6	87	613	588	644	42.78	55.6	55.8
TKP-g-PAM 7	79	585	541	621	48.12	58.23	57.01

During drug release, some tablets disintegrated partially. The degree of erosion (D) was calculated by the following equation based on the difference between the initial dry weight of the tablet (W_i) and the dry weight of the tablet (W_d) at time t, considering drug release at time t (M_t/M_α),

$$D(t) = \frac{W_\mathrm{i} - W_\mathrm{d}(t) - W_\mathrm{drug}(1-(M_t/M_\alpha)}{W_\mathrm{i}} \qquad (2)$$

where M_t is the amount of drug release at time t; M_α is the total amount of drug released after infinite time and W_drug is the initial weight of drug.

2.7. In vitro study of drug release

The in vitro release of entrapped drug (aspirin) was determined in various buffer solutions (pH 1.2, simulating gastric fluid, pH 6.8 and 7.4, simulating intestinal fluid at 37 °C). The tests were conducted using standard USP type I (basket) drug dissolution rate test apparatus (M/s SECOR, India), in 900 mL of buffer solution maintained at the physiological temperature (37 °C; using isothermal bath). The spindle rotation was maintained at 100 rpm. At definite time intervals, an aliquot was withdrawn and its absorbance was (at 294 nm, 274 nm and 268 nm in pH 1.2, pH 6.8 and pH 7.4, respectively) measured. The withdrawn sample was replaced with an equal volume of fresh buffer, to keep the volume of release media constant. The drug content assayed spectrophotometrically and is graphically expressed as drug release profile (plot of % cumulative drug release vs. time).

3. Results and discussion

3.1. Hydrogel synthesis

TKP was grafted with polyacrylamide in presence of microwave irradiation as well as ceric ammonium nitrate as initiator. The mechanism of graft copolymerization is based on the fact that microwave energy is being adsorbed by the polysaccharide and forms free radicals. The microwave energy absorbed by the water molecules is quickly transferred to the acrylamide molecules, causing 'dielectric heating' which results in severing of double bonds, producing another set of free radicals. The free radicals recombine with each other through initiation, propagation and termination steps to produce the graft copolymer as explained earlier [18,19]. The various graft copolymers along with their corresponding % *G* have been reported in Table 1.

During the synthesis of graft copolymer based hydrogel, some homopolymer (i.e. polyacrylamide) may produce. If any occluded homopolymer formed, was removed from the grafted polymers by solvent extraction using a mixture of formamide and acetic acid (1:1 by volume).