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Short communication

Synthesis, characterization and *in vitro* release behavior of carboxymethyl xanthan

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ABSTRACT

Carboxymethylation of xanthan gum was carried out by reacting xanthan gum with monochloroacetic acid in alkaline condition. FTIR spectroscopy confirmed the formation of carboxymethyl xanthan. DSC and XRD study revealed the crystalline nature of carboxymethyl xanthan. SEM images showed that carboxymethyl xanthan particles are globular in shape and smaller in size. Viscosity measurements also showed that the carboxymethyl xanthan is less viscous as compared to xanthan gum. Diclofenac sodium matrix tablets prepared using carboxymethyl xanthan revealed faster release of drug as compared with xanthan gum matrix.

1. Introduction

Xanthan gum is a high molecular weight natural gum which has been used widely in cosmetic and pharmaceutical industry as suspending, stabilizing, thickening and emulsifying agent [1]. Xanthan gum is soluble in hot and cold water but its dissolution is very slow and requires intense agitation to prevent the formation of lumps on dispersing in water. Xanthan gum particles hydrate and swell with the formation of partially hydrated gelatinous layer on the outside of the gum [2,3]. This gelatinous layer prevents penetration and complete hydration of the particle, and thus slows down the dissolution of the gum. Xanthan gum has earlier been employed to prepare sustained-release matrix tablets due to its slow dissolution properties [4,5]. To tailor the release rate of drug from the natural matrix, several approaches like chemical modification [6], microwave treatment [7] and combination of various hydrophilic and hydrophobic polymers have been employed [8–11].

Carboxymethylation of chitosan [12], cellulose [13], guar [14,15], dextran [16], and gellan gum [17] have earlier modified their properties and enhanced the solubility of these polymers in water. In the present approach, we have prepared the carboxymethyl derivative of xanthan gum to modify its release rate. The matrix tablets of diclofenac sodium were prepared using carboxymethyl xanthan gum as the matrix and compared with the tablets prepared using xanthan gum as matrix.

2. Materials and methods

2.1. Materials

Xanthan gum (XANTURAL-75, C.P. Kelco, UK) was gifted by Burzin Leons Agenturen Pvt. Ltd. (Mumbai, India). Diclofenac sodium (purity 98.58%) was obtained as gift sample from Dabur Research Foundation (Ghaziabad, India). Sodium hydroxide, methanol and glacial acetic acid were procured from Sisco Research Laboratory (Mumbai, India). Monochloroacetic acid was purchased from Hi-Media Lab. Pvt. Ltd. (Mumbai, India). All other chemicals used were of reagent grade, and were used as received.

2.2. Preparation of carboxymethyl xanthan

Carboxymethylation of xanthan gum was performed employing monochloroacetic acid as reported earlier for gellan gum [17]. Xanthan gum (1 g) was dispersed in NaOH solution (45%, w/w) with the aid of stirring for 30 min. To this 10 ml of monochloroacetic acid solution (75%, w/v) was added under constant stirring. The reaction mixture was then heated to 70 °C under constant stirring for 30 min. The reaction mixture was then cooled and suspended in to an 80% (v/v) methanol. The precipitate so obtained was then filtered and washed. The reaction mixture was then neutralized (pH-7) by adding glacial acetic acid. The product so obtained, was washed three times with 60 ml of 80% (v/v) methanol, filtered and dried.

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Table 1
Composition of tablets.

Ingredients	Quantity/tablet (mg)	
	X	CMX
Xanthan gum	75	–
Carboxymethyl xanthan gum	–	75
Diclofenac Sodium	75	75
Magnesium Stearate	1.5	1.5
Total	151.5	151.5

2.3. Characterization of carboxymethyl xanthan

The carboxymethyl xanthan gum so synthesized, was characterized by FT-IR spectroscopy, differential scanning calorimetry, X-Ray diffractometry and viscosity measurements.

2.3.1. FT-IR spectroscopy

The samples were subjected to FTIR spectroscopy in a Fourier-transform infrared spectrophotometer (Perkin Elmer, USA) in range of (4000–500 cm^{-1}) as KBr pellet.

2.3.2. Differential scanning calorimetry

Differential scanning calorimetric thermogram of xanthan gum, and carboxymethyl xanthan gum was recorded using differential scanning calorimeter (Q10, TA Systems, USA) in the temperature range of (40–300 °C) at a heating rate of 10 °C per min in nitrogen atmosphere.

2.3.3. X-ray diffractometry

X-ray diffractogram of xanthan gum, and carboxymethyl xanthan gum samples were recorded employing X-ray diffractometer (XpertPRO, Panalytical, Germany) using copper Kα-radiation generated at 40 kV and 35 mA in the differential angle range of 3–40° (2θ) using an X-ray diffractometer.

2.3.4. Scanning electron microscopy

Scanning electron micrograph of xanthan gum, carboxymethyl xanthan gum particles were taken using a SEM (268 D, Fei-Philips Morgagni). These were coated with gold and mounted in a sample holder. The photomicrograph of sample was taken at an accelerating voltage at 15 kV at different magnifications.

2.3.5. Viscosity

Viscosity of xanthan gum and carboxymethyl xanthan gum solutions was determined using Brookfield viscometer (Model RVDVE 230, Brookfield Engineering Laboratories, Middleboro, USA) using spindle number 3 at different rpm.

2.4. Preparation of matrix tablets of diclofenac sodium

Matrix tablets of diclofenac sodium were prepared employing xanthan gum or carboxymethyl xanthan as per the formula given in the Table 1. The required quantity of diclofenac sodium was mixed with xanthan gum or carboxymethyl xanthan gum and the magnesium stearate (1%, w/w) as lubricant. The powder blend so obtained, was directly compressed using 8 mm biconvex punches and dies in a single station, hand-operated, tableting machine (R and D model, Konark Instruments, Ambala, India).

2.5. Evaluation of tablets

The matrix tablets of diclofenac sodium were evaluated for thickness, diameter, weight variation, hardness, friability, content uniformity, and *in vitro* release.

2.5.1. Thickness and diameter

Thickness and diameter of randomly selected twenty tablets was determined using Vernier caliper (Aerospace, China). Values are reported as mean ± S.D.

2.5.2. Weight variation

The weight of twenty tablets of each batch was measured individually using electronic balance (AND, Japan) and standard deviation was calculated.

2.5.3. Hardness

The hardness of six tablets of each batch was measured using Monsanto hardness tester (Macro Scientific, New Delhi).

2.5.4. Friability

To determine the friability, six tablets of each batch were weighed and placed in a friabilator (Campbell Electronics, Mumbai, India). The tablets were rotated for 4 min at 25 rpm. The tablets were then dedusted and collected, and reweighed. The friability was calculated as the percentage weight loss.

2.5.5. Uniformity of content

The content uniformity of the prepared tablets was determined by powdering the tablet in a pestle mortar and extracting the powder equivalent to 100 mg of diclofenac sodium with 100 ml of phosphate buffer (pH 6.8) by sonication (for 10 min). The aqueous suspension so obtained, was filtered employing 0.45 μ syringe filter and content of diclofenac sodium in the solution was determined by measuring absorbance at 276 nm after suitable dilution.

2.5.6. In vitro release study

The *in vitro* release study of diclofenac sodium from the prepared tablet was conducted using USP type II dissolution apparatus (TDT-08L, Electrolab, India), dissolution media comprised of 900 ml phosphate buffer (pH 6.8) till 16 h, maintained at 37.0 ± 0.5 °C and 50 rpm. An aliquot of 5 ml sample was withdrawn and replaced with another 5 ml of fresh dissolution medium at various time intervals. The contents of diclofenac sodium in sample were determined by measuring the absorbance at 276 nm in UV–visible spectrophotometer (Carry 5000, Varian Australia).

2.5.7. Modeling and release kinetics

To determine the order and mechanism of diclofenac sodium release from matrix tablets, the release rate data was fitted to zero-order, first-order and Higuchi square-root equation [18]. The value of k (the release rate constant) for different models was determined. However, these equations fail to explain the drug release mechanism from matrices that undergo swelling and/or erosion during dissolution. Therefore, the dissolution data was fitted to the Koresmeyer–Peppas equation, which is often used to describe the drug release mechanism from polymeric system.

$$\log\left(\frac{M_t}{M_f}\right) = \log k + n \log t \quad (1)$$

where M_t is the fraction of drug release at time t, M_f is the amount of drug release after infinite time, and k is the release rate constant incorporating structural and geometric characteristics of the tablets and n is the diffusion exponent indicative of the mechanism of the release mechanism. To determine the release exponent, n for different batches of matrix tablets, the log value of percentage drug dissolved was plotted against log time for each batch, according to Eq. (1). For determination of exponent n, only the initial portion of release curve ($M_t/M_f < 0.6$) was used. A value of $n = 0.45$ indicates Fickian (case I) release; the rate of drug release is much less than