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Design and evaluation of fast dissolving tablets containing diclofenac sodium using fenugreek gum as a natural superdisintegrant

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Comments

The paper is well written and interesting for reading. The topic of the manuscript is quite interesting and results are hesitating. I believe that this manucsrit could contribute to the knowledge in terms of design and evaluation of fast dissolving tablets containing diclofenac sodium in combination with fenugreek gum, as a natural superdisintegrant.
Details on Page S334

ABSTRACT

Objective: To formulate diclofenac sodium as fast dissolving tablets (FDTs) using fenugreek gum as a natural superdisintegrant which also possess anti-inflammatory activity.
Methods: An attempt was made to extract the fenugreek gum and evaluated it for various physicochemical characterizations. The swelling index and viscosity of fenugreek gum was 221% and 293.4 mpa·s respectively. FDTs of diclofenac sodium was formulated by direct compression technique using different concentrations (1%-6%, w/w) of fenugreek gum as a natural superdisintegrant and compared with renowned synthetic superdisintegrants like sodium starch glycolate and croscarmellose sodium. The anti-inflammatory activity of a formulation was evaluated with carrageenan induced experimental rats.
Results: The formulated tablets were evaluated for various physical tests like weight variation, friability, hardness and results complied with the limits. The drug release from all the formulations ascertained first order kinetics. Among all the formulations F3 containing fenugreek gum with the concentration of 6% produced least disintegrating time 21 seconds resulting in higher drug release rate 93.74% at the end of 25 min. Hence, it was considered as optimized formulation. The present study revealed that the fenugreek gum as a natural superdisintegrant showed better disintegrating property than the most widely used synthetic superdisintegrants like sodium starch glycolate and croscarmellose sodium in the formulations of FDTs.
Conclusions: The results suggested that the fenugreek gum act as a good super disintegrating agent and it showed promising additive anti-inflammatory activity with diclofenac sodium.

KEYWORDS

Diclofenac sodium, Fenugreek gum, Superdisintegrant, Anti-inflammatory activity, Sodium starch glycolate, Croscarmellose sodium, Direct compression, Quick pain relief

1. Introduction

Oral route is the most preferable and convenient route of administration as it offers advantages like ease of administration, highly versatile, patient compliance and accurate dosing[1]. The most popular solid dosage forms are being tablets and capsules. One important drawback of these dosage forms for some patients, is the difficulty to swallow and readily access to water for easy swallowing dosage[2]. Difficulty in swallowing (dysphasia) is also a common problem of all age groups, especially the elderly and paediatrics, because of physiological changes associated with these groups[3]. Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology which aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance[4]. The fast dissolving tablet (FDT) has remarkable disintegration properties and it can rapidly disintegrate without water in the mouth within few seconds. When an FDT is placed in the oral cavity, saliva quickly penetrates into the pores causing rapid disintegration[5]. Based on the absolute bioavailability of diclofenac sodium[6], tablet is about 50-60%. The half-life is 2 h and highly protein

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bound (>99%). In the bioavailability classification system, diclofenac is classified as a class II drug, because of its low water solubility and high permeability. The bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Usually, superdisintegrants are added to a drug formulation to facilitate the break-up or disintegration of tablet or capsule content into smaller particles that can dissolve more rapidly than drugs in the absence of disintegrates. Many superdisintegrants like cross povidone, croscarmellose sodium (Ac-di-sol) and sodium starch glycolate (SSG) have been used in the formulations of FDTs. In the present study it was proposed to formulate an oral drug delivery, in the form of FDTs by using direct compression method[7]. The purpose of the present study was to extract the fenugreek gum, evaluate its powder flow properties (bulk density, tapped density, angle of repose, Carr's index and hausner ratio), swelling index and loss on drying and to compare disintegration efficiency of fenugreek gum with widely used synthetic superdisintegrants *i.e.* SSG and croscarmellose sodium in the formulation of FDTs. All the superdisintegrants were used in optimized concentration levels to assess their efficiency. The tablets were evaluated in various physical tests. The formulation of a FDTs, thus containing diclofenac sodium and fenugreek gum, produces additive anti-inflammatory activity resulting in reduction in a dose of diclofenac sodium and thereby its dose related side effects.

2. Materials and methods

2.1. Materials

Fenugreek seeds, diclofenac sodium (Harman Finochem Ltd, Mumbai), microcrystalline cellulose (SD Fine Chemicals), SSG (SD Fine Chemicals), croscarmellose sodium (Arrow Chem. Product., Mumbai), hexane (SD Fine Chemicals) and all other ingredients used throughout the study were of analytical grades.

2.2. Methods

2.2.1. Extraction and purification of fenugreek gum

Fenugreek seed (100 g) were ground to 100 mesh using a laboratory mill. The fine powder was extracted with boiling hexane in Soxhlet apparatus for 80 min. The obtained extract was treated with 95% ethanol (maintaining its boiling point) for 130 min in a conical flask to remove the unwanted saponin. Further enzyme deactivated was initiated by refluxing the extract with 70% ethanol for 180 min. The resulting mixture was repeatedly treated with ethanol to remove undissolved traces if necessary. The residue was filtered through sintered glass at room temperature. The filtered residue was subjected to mechanical stirring at 700 r/min with addition of water for 8 h. The obtained mixture was centrifuged at 5 000 r/min for 12 min at 10 °C. The supernatant contained crude fenugreek gum, which was decanted and precipitated by adding of ethanol (70%). Thus the gum precipitate was washed with acetone, diethyl ether and water. The pure fenugreek gum was oven dried[8].

2.2.2. Physicochemical characterization of gum

The purified and dried extracted gum powder was evaluated for its micromeritic properties, viscosity, solubility studies, swelling index and loss on drying.

2.2.2.1. Swelling index

The study was carried out by using a 100 mL stoppered graduated cylinder. The initial bulk volume of 1 g of fenugreek gum was noted. Water was added in sufficient quantity to ensure 25 mL of uniform dispersion by vigorously shaking every 10 min for 1 h and then allowed to stand for 24 h. The dispersion was stored at room temperature and the sediment volume of the swollen mass was measured after 24 h[9].

Swelling index=$100\times(V_2-V_1/V_1)$

Where, V_1=Initial volume of material before hydration; V_2=Volume of hydrated material.

2.2.2.2. Viscosity

One gram of fenugreek gum powder was suspended in 75 mL of distilled water for 4 h. Distilled water was added up to 100 mL to produce the concentration of 1%. The mixture was homogenized by mechanical stirrer for 2 h and its viscosity was determined by using Brookfield viscometer, spindle SC4-18 (Brookfield Viscometer, DV-2+LV) at 5 r/min[10].

2.2.2.3. Loss on drying

Loss on drying technique is used to determine high levels of moisture or solvents present in the sample. The material sample was weighed (W_1) and heated in an oven for 2 h. It was cooled in the dry atmosphere of desiccators and then finally weighed (W_2).

% Loss on drying=$[(W_1-W_2)/W_1]\times100$

Where, W_1=Initial weight of the powder; W_2=Final weight of the powder.

2.2.3. Characterization of drug and excipients

2.2.3.1. Drug-excipient compatibility studies

The physicochemical compatibility between diclofenac sodium and fenugreek gum used in the research were assessed by subjecting to infrared spectral studies. The samples were scanned under diffuse reflectance mold and the graph was plotted by KBr pellet method. Its spectra were recorded in the wavelength region between 4 000 cm^{-1} to 400 cm^{-1}. The spectra of diclofenac sodium, fenugreek gum and physical mixtures of diclofenac sodium and fenugreek gum were compared.

2.2.4. Formulation of FDTs

FDTs containing 50 mg diclofenac sodium were prepared by direct compression method and the formulae used in