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Evaluation of *Albizia procera* gum as compression coating material for colonic delivery of budesonide

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ABSTRACT

The purpose of this research was to develop and evaluate *Albizia procera* gum as compression-coating polymer for colonic delivery of budesonide. Tablets were prepared by direct compression method using spray-dried lactose and microcrystalline cellulose as filler binders. The compatibility between the drug and the polymer was studied through TGA and FTIR spectroscopy. In vitro drug release were studied in dissolution media with or without 2% rat cecal contents while in vivo X-ray study was conducted on rabbits. The results indicate that procera gum and the drug were compatible with each other and tablet coated with procera gum was suitable for colonic delivery of drugs.

1. Introduction

Biomacromolecules such as naturally occurring polysaccharides have been widely explored as drug delivery devices due to their inherent biocompatibility and biodegradability [1]. These polymers are high molecular weight compounds found in abundance, inexpensive, safe and available in a variety of structures which can be easily modified chemically and biochemically. In recent years natural polysaccharides have received considerable interest as carrier for specific delivery of drugs to the colon. Many polysaccharides such as amylase [2,3], pectin [4,5], guar gum [6], Chitosan [7] and konjac glucomannan/xanthan gum [8] have been investigated for peroral delivery of drugs to the colon. Due to the distal location of the colon in the GI tract, a colon specific drug delivery system should prevent drug release in the stomach as well as the small intestine. Natural polysaccharides are reported to be capable of preventing this drug release in the upper GI tract while being susceptible to enzymatic degradation by colonic bacterial enzymes thereby releasing the drug for local action or improved absorption. Since the abrupt increase in bacterial population and its associated enzymatic activity in the colon are independent of the pH and GI transit time, these colonic microflora activated systems become most effective and preferable means in terms of target specificity for colonic drug delivery systems [9].

Albizia trees are known to produce gums and have been reported as substitute for arabic gum as natural emulsifier for foods and pharmaceuticals. Structural studies on *Albizia* gums reveal the presence of β-(1-3) D-galactopyranose units with some β-(1-6) D-galactopyranose units and α-(1-3) L-arabinofuranose units [10]. *Albizia procera* (Roxb.) Benth is a fast growing, medium sized tree belonging to Mimosaceae family and is known to exude gums in small transparent tears and vermiform pieces. In our previous studies we investigated the detail physicochemical properties of the gum [11] and have also reported the drug release mechanism of controlled release matrix tablets based on this gum [12]. In the present paper, we develop a two stage/platform drug delivery system based on a compression coated tablets containing budesonide as the core and *A. procera* gum as the coat layer. The main reason for selecting *A. procera* gum, an arabinogalactan was the biodegradation of arabinogalactans in the colon by the colonic microflora as these microorganisms produce a wide range of enzymes such as β-glucuronidase, β-xylosidase, α- arabinosidase, β-galactosidase, nitroreductase, azoreductase, deaminase, urea hydroxylase etc. [13,14]. Budesonide, a novel gluccocorticoid which is highly effective in the treatment of IBD due to its superior topical anti-inflammatory activity than many other gluccocorticoids has been selected as the model drug. Due to its rapid, near complete first-pass hepatic conversion to its metabolites, the systemic effects of budesonide are significantly less than other conventional corticosteroids making it an ideal candidate for specific delivery to the colon for topical treatment of IBDs.

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2. Materials and methods

2.1. Materials

Budesonide (Batch No. B110263) was received as gift sample from Cipla (Baddi, India). Microcrystalline cellulose (Avicel PH 101), spray-dried lactose, magnesium stearate and talc were used as supplied without further purification. *A. procera* gum exudates (Authenticated at the Department of Forestry, School of Earth Sciences, Mizoram University) were collected by hand picking in Mizoram (India) during the month of January–March and purified [11]. Geographically, Mizoram is located between East longitude 92°15′ to 93°29′; North Latitude 21°58′ to 24°35′ with an average altitude of 900 m. All other chemicals and reagents used were of analytical grade.

2.2. Methods

2.2.1. Instrumental analysis

2.2.1.1. FTIR spectroscopy. FTIR spectroscopy was performed to assess the interaction of the drug with the polymer. Budesonide and procera gum were taken in 1:1 ratio and this sample is mixed uniformly in a porcelain dish with 100 times its weight of KBr. About 10 mg of the mixed sample was transferred into sample holder and pressed lightly to make a smooth surface. The % transmittance was recorded between 400 and 4000 cm^{-1} on FTIR spectrophotometer (IR Prestige-21, Shimadzu). FTIR spectrum for budesonide, the dried procera gum and budesonide-gum mixture was recorded and the resultant spectra were carefully analyzed for possible signs of interaction between the gum and budesonide. Disappearance or significant shifts in characteristic peaks were considered as a testimony to the interaction.

2.2.1.2. Thermogravimetric analysis (TG analysis). TG analysis was also performed on TGA (Pyris TGA, PerkinElmer) between 40 °C and 855 °C to study the possible interaction between budesonide and procera gum and the thermal stability of the product. The heating rate and nitrogen purging were maintained at 10 °C/min and 20 ml/min respectively. For each analysis, about 6 mg of the sample was taken into the aluminium sample pan and sealed. Empty aluminium pan was used as a reference and the thermogram was then recorded for budesonide, procera gum and budesonide-gum mixture (1:1).

2.2.2. Preparation of budesonide core tablets

Budesonide core tablets were prepared by direct compression method. Each core tablet consists of 3 mg budesonide and spray-dried lactose was used as direct compression vehicle. Talc at 2% and magnesium stearate at 1% was used as lubricant. Tablets with total weight of 100 mg each containing 3 mg budesonide were compressed on a 12-station rotary tablet press (MiniPress II MT, Karnavati Engg.) at 4000 kg using 6 mm, round and concave punches. Standard tablet quality control tests such as weight variation, crushing strength, content uniformity and friability were performed on the core tablets.

2.2.3. Compression coating of tablets

Budesonide core tablets were compression coated with different coat formulations as given in Table 1 using microcrystalline cellulose (Avicel PH101) as a filler binder. Firstly, about 50% of the coat formulation was placed in the die cavity (diameter of the die was 10 mm) and budesonide core tablets were carefully positioned in the centre of the die cavity. The remainder of the tablet coat formulation was then used to fill up the die and then the whole system was compressed at an applied force of 5000 kg using 10 mm concave punches to make a tablet with total weight of 400 mg.

Table 1
Compression coat formula.

Ingredients (mg)	Formulation codes			
	F1	F2	F3	F4
Core tablet (containing 3 mg budesonide)	100	100	100	100
Procera gum	150	200	250	291
Microcrystalline cellulose	141	91	41	0
Talc	6	6	6	6
Magnesium stearate	3	3	3	3
Total	400	400	400	400

2.2.4. Characterization of compression-coated tablets

For uniformity of weight, 20 tablets from each batch were selected and weighed individually and their mean weights were calculated. The crushing strength of the tablets was determined using Digital Tablet Hardness Tester (EH-01, Electrolab) taking 5 tablets from each batch and the average was taken. Friability test was performed on dual drum unit Friability Tester (EF-2, Electrolab). For each test, 20 tablets were taken and the drum was maintained at 25 rpm for 4 min and all the determinations were done in triplicate.

2.2.5. In vitro release study

The in vitro release of budesonide from the compression-coated tablets was performed on USP Dissolution Tester using Apparatus I (Rotating basket, USP Dissolution Test Apparatus, ACMAS Technocrat, India) at a rotation speed of 50 rpm and the dissolution media was maintained at 37.0 ± 0.5 °C. The release study was performed in 250 ml 0.1 N HCl for the first 2 h, followed by 250 ml pH 6.8 phosphate buffer for another 3 h and finally 250 ml pH 7.4 phosphate buffer till 24 h to simulate the gastro-intestinal pH condition. 2 ml of dissolution medium was withdrawn at predetermined time intervals and analyzed for the drug using Waters HPLC system with UV/Visible detector (2489, Waters). Budesonide determination was modified from the method developed by Naikwade and Bajaj [15] and validated accordingly. Briefly, the analysis was carried out using Symmetry C18 Column (dimension = 150 × 4.6 mm and particle size 5 μm, Waters) at a wavelength of 244 nm. 20 μl of the suitably diluted and filtered sample was injected and the mobile phase used was methanol–water (80:20) maintaining a flow rate of 0.8 ml/min. Data acquisition and processing were performed by using Empower 2 software (Waters).

2.2.6. In vitro release study in presence of rat cecal content

Rat cecal content was prepared by the method reported by Paharia et al. [16]. Dissolution medium containing 2% rat cecal content were prepared on pH 7.4 phosphate buffer which was previously bubbled with N_2 to make an anaerobic condition. Drug release behavior of the compression coated tablets in the physiological environment of colon was assessed by performing drug release studies in rat cecal content medium. Budesonide tablet was placed in 250 ml of dissolution medium which was maintained at 37 ± 0.5 °C. Dissolution study was performed in 0.1 N HCl for the first two (2) hours followed by pH 6.8 phosphate buffer for the next three (3) hours. Finally, pH 7.4 phosphate buffer containing 2% rat cecal content was taken and the study was continued up to 24 h. At different time intervals, 2 ml of the dissolution medium was withdrawn, suitably diluted and filtered and analyzed using Waters HPLC system at 244 nm with UV/Visible detector (2489, Waters) following the validated method previously described.