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Isolation, characterization and investigation of *Plantago ovata* husk polysaccharide as superdisintegrant

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ABSTRACT

Psyllium husk (*Plantago ovata*, Family: Plantaginaceae) contains a high proportion of hemicellulose, composed of a xylan backbone linked with arabinose, rhamnose, and galacturonic acid units (arabinoxylans). Polysaccharide was isolated from Psyllium husk using solvent precipitation method. The isolated polysaccharide was evaluated for various physicochemical parameters. The rheological behavior of polysaccharide (1% w/v in water) was studied using Brookfield viscometer. Polysaccharide derived from the husk of *P. ovata* was investigated as superdisintegrant in the fast dissolving tablets. Valsartan, an antihypertensive drug, was selected as a model drug. The tablets of Valsartan were prepared separately using different concentrations (1, 2.5, 5, 7.5% w/w) of isolated *Plantago ovata* (*P. ovata*) husk polysaccharide (Natural) and crospovidone as a synthetic superdisintegrant by direct compression method. The prepared tablets were evaluated for various pre-compression and post-compression parameters. The drug excipient interactions were characterized by FTIR studies. The formulation F4 containing7.5% polysaccharide showed rapid wetting time and disintegration time as compared to formulation prepared using synthetic superdisintegrant at the same concentration level. Hence batch F4 was considered as optimized formulation. The stability studies were performed on formulation F4. The disintegration time and *in vitro* drug release of the optimized formulation was compared with the marketed formulation (Conventional tablets).

1. Introduction

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. Tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Fast dissolving tablet (FDT) is the fast growing and highly accepted drug delivery system with better patient compliance. FDT are not only indicated for people who have swallowing difficulties, but also are ideal for active people [1–3].

FDT disintegrate in patient's mouth within a few seconds without the need of water, or chewing, providing best remedy for the patient suffering from dysphasia [4,5]. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down the stomach. In such cases the bioavailability is greater than those observed for conventional dosage form. The advantages of mouth dissolving dosage form are increasingly being recognized in both industry and academia [6]. FDT are commonly known as orally disintegrating tablets, mouth dissolving tablets, Fast dissolving tablets or Rapid melt tablets.

Excipients are the additives used to convert active pharmaceutical ingredients into pharmaceutical dosage form suitable for administration to patients [7]. Plant products serve as an alternative to synthetic products because of local accessibility, environment friendly nature and lower prices compared to imported synthetic products. Herbs are non-polluting renewable resources for sustainable supplies of cheaper pharmaceutical products. Today, we have a number of plant-based pharmaceutical excipients. A number of researchers have explored the utility of plant-based materials as pharmaceutical excipients [8–15].

Fast disintegrating tablets are prepared mainly using superdisintegrants by direct compression method. Disintegrants are the substances or mixture of substances added to the drug formulation that facilitates breakup or disintegration of tablet content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Examples of superdisintegrants are croscarmelose, crospovidone, sodium starch glycolate which represent example of crosslinked cellulose, crosslinked polymer and a crosslinked starch respectively [16–18]. These are the commonly used synthetic origin superdisintegrants. Various natural origin substances like karaya,

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modified starch and agar have been used in the formulations of ODTs. The natural origin substances are comparatively cheaper with desired properties like abundantly available, non-irritating and non-toxic in nature [19].

Psyllium husk (*Plantago ovata*, Family: Plantaginaceae) contains a high proportion of hemicellulose, composed of a xylan backbone linked with arabinose, rhamnose, and galacturonic acid units (arabinoxylans). The seed consists of 35-per-cent soluble and 65-percent insoluble polysaccharides (cellulose, hemicellulose, and lignin).

In the present study, polysaccharide derived from the husk of *P. ovata* (Family: Plantaginaceae) was investigated as superdisintegrant in Fast dissolving tablets. The model drug used for the study was Valsartan, which is an antihypertensive drug belongs to the category of Angiotensin II receptor antagonist. The molecular weight of Valsartan is 435.5, its half-life is 4–6 h, with poor oral bioavailability ranging from 10 to 35 because of poor solubility, dissolution, 95% of the drug undergoes protein binding and most importantly extensive first pass hepatic metabolism [20,21]. The present research work was aimed at the development and evaluation fast dissolving tablets of Valsartan to produce rapid onset of action and patient compliance.

2. Materials and method

2.1. Materials

Valsartan was obtained as gift samples from Unichem Laboratories Ltd., Mumbai. Microcrystalline Cellulose (MCC PH 102), crospovidone (CP), Magnesium Stearate (Mg-stearate), Talc, Aspartame and Vanilla flavor were procured from Colorcon Asia Pvt. Ltd. Mumbai. *P. ovata* husk were purchased from Local market, Thane (Maharashtra, India). All the chemicals and reagents were of analytical grade.

2.2. Isolation and characterization of polysaccharide

2.2.1. Isolation of polysaccharide from Plantago ovata husk

The husk of *Plantago ovata* were soaked in distilled water for 48 h and then boiled for few minutes for complete release of mucilage into water. The material was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate so as to precipitate the polysaccharide. The separated polysaccharide was dried in oven at temperature less than 60 °C, powdered, sieved (no. 80) and stored in a desiccators until use [22].

2.2.2. Physicochemical characterization of isolated polysaccharide

The isolated polysaccharide was evaluated for various physicochemical properties such as solubility, pH (1% w/w in water), swelling factor, loss on drying, ash value, bulk and tapped density, Compressibility index, Hausners ratio and angle of repose as per reported method [23,24].

2.2.3. Particle size analysis

The particle size analysis of isolated polysaccharide was performed using Nanophox (NX0073) particle size analyzer.

2.2.4. Rheological study of isolated polysaccharide

One gram of dried and finely powdered mucilage was suspended in 75 mL of distilled water for 24 h. Distilled water added up to 100 mL to produce the concentration of 1% w/v. The mixture was homogenized by mechanical stirrer for 2 h and its viscosity determined using a Brookfield viscometer. The viscosity values were determined at 5, 10, 20, 50, 100 rpm at 25° C using spindle no.5.

2.2.5. Estimation of total polysaccharide content

The total polysaccharide content was determined according to the procedure of Dubois et al. [25]. About 10 mg of isolated polysaccharide was dissolved in 100 mL distilled water. One milliliter of 5% phenol solution was added to 1 mL gum solution in acid-washed test tube. Five milliliter concentrated $H_2SO_4$was directly and rapidly added to the test tubes. The solution was allowed to stand for 10 min and was shaken. Absorbance of the solution was read at 490 nm using a UV–vis spectrophotometer.

Standard calibration curve was prepared using solutions ranging from 50 to 100 mcg/mL. Solutions were prepared in triplicates from 1000 mcg/mL stock glucose solution.

2.2.6. Total microbial count

The total microbial count of the isolated polysaccharide was determined by Plate count method as per Indian Pharmacopoeia [26].

Pretreatment of sample:

10 g isolated polysaccharide was dissolved in buffered NaCl-peptone solution (pH 7). The volume was then adjusted to 100 mL with the same medium.

Plate count method:

i) For bacteria:
   1 mL pretreated sample preparation was added to 15 mL of liquefied Casein Soyabean digest agar at 45 °C. This mixture was then transferred to petri dish and allowed it to solidify. Two such petri dishes were prepared using same dilution and incubated at 30 °C to 35 °C for 5 days. At the end of this period the numbers of colonies were counted.
ii) For fungi:
   Proceeded as described in the test for bacteria, but used Sabourauds dextrose agar with Chloramphenicol (5 mg/100 mL) in place of Casein Soyabean Digest agar and plates were incubated at 20–25 °C for 5 days. At the end of this period the numbers of colonies were counted.

2.3. Formulation of fast dissolving tablets

FDTs of Valsartan were prepared by the direct compression method using isolated polysaccharide and synthetic superdisintegrant at concentration of 1, 2.5, 5, 7.5% w/w. All the ingredients were passed through 60 mesh sieve. Required quantity of each ingredient was taken for particular formulation and the blend was mixed and compressed into tablets of 200 mg using 9 mm round flat punches on single rotary tablet machine (Royal artist). The composition of each formulation is given in Table 1.

2.4. Evaluation of powder blend (pre compression parameter)

The powder blend was evaluated for various flow properties such as angle of repose, bulk and tapped density, Hausners ratio and Carr's index.

2.4.1. Angle of repose

The angle of repose of powder was determined by the fixed funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The