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Research Article

ASSAM BORA RICE STARCH AS DIRECTLY COMPRESSIBLE FILLER-BINDER

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ABSTRACT

Introduction: North-east India, including Assam, is recognized as a centre of origin of rice and is endowed with exceptionally rich rice diversity. Assam Bora rice (*Oryza sativa L*, Japonica variety), a group of glutinous rice of Assam has been reported to contain up to 90% starch. With increasing demand and search for natural starches with desirable properties for use in the pharmaceutical industries, the present work evaluates the possible use of Assam Bora rice starch as directly compressible tablet excipient.

Methods: The starch was extracted from the rice and the powder characteristics were evaluated. Various parameters studied, include, particle size, true density, bulk density, tapped density and flow characteristics. Tablets containing Ketotifen Fumarate as a model drug were prepared with Assam Bora rice starch as unique filler-binder.

Results and conclusion: The tablets were evaluated for tensile strength, friability, drug content, disintegration and dissolution profiles. The tablet properties show that Assam Bora rice starch is a useful product for preparation of tablets by direct compression.

Keywords: Assam Bora rice starch, Ketotifen fumarate, Direct compression, *Oryza sativa L.*

INTRODUCTION

Popularity of tablets, coupled with an increased understanding of the physics of compression and manufacturing process variables, has matured the manufacturing of tablets as a ‘‘science’’ in its own right [1]. Until the 1950s, tablets were primarily produced by the wet granulation process. The availability of new excipients, new grades of existing excipients, and manufacturing machinery—such as positive die feeding and precompression stages—has caused a perceptible shift toward direct compression process in the manufacturing of tablets. Nearly 41.5% of pharmaceutical manufacturers prefer direct compression, 41.5% prefer both wet granulation and direct compression, while 17.2% have nonpreference for direct compression as a tabletting method [2].

Since the late 1960’s many excipients have been introduced on the pharmaceutical market as filler-binders for tablets prepared by direct compression. The products are based, among others on starch, cellulose, inorganic calcium salts polyalcohols, lactose and other sugars. Starches from several natural sources and their common derivatives are both well known and safe and have been extensively investigated in tablet formulations for various purposes. In an evaluation of several native starches, rice starch proved to have much better compaction properties than potato, maize and tapioca starch [3]. The overall contribution of excipients in dosage form designing can be better appreciated from the fact that more than 70% of the formulations contain excipients at a concentration higher than the drug [4].

North-east India, including Assam, is recognized as a centre of origin of rice and is endowed with exceptionally rich rice diversity. Among those, Assam Bora rice (*Oryza sativa L*, Japonica variety), a group of glutinous rice of Assam, characterized by high amylopectin content, was introduced to Assam from Thailand or Burma a considerable time ago [5]. The starch is a major constituent of milled rice at about 90% of dry matter [6]. Researches with this starch in tablets of other active ingredients are necessary because of the high percentage of starch content

reported in this plant. The death of primary pharmaceutical industries in some developing economics has led to lack of basic tableting excipients despite the avalanche of unprocessed raw materials. There is the need to bridge this gap. With increasing demand and search for natural starches with desirable properties for use in the pharmaceutical industries, the present work evaluates the possible use of Assam Bora rice starch as directly compressible tablet excipient.

MATERIALS AND METHODS

Materials

Assam Bora rice starch (prepared in our laboratory), Ketotifen fumarate **(**Torrent Pharmaceuticals Ltd. Ahmedabad, India), Magnesium stearate (Vivimed Labs Ltd. Hyderabad, India), Colloidal silica (Vivimed Labs Ltd. Hyderabad, India). The other used materials were of analytical quality.

Extraction of Assam Bora rice starch

Assam Bora rice was collected, washed and sun dried for 7 days. About 8 parts of broken Assam Bora rice were steeped in about 16 parts of a 0.4 % solution of caustic soda. The mass was stirred every six hours and the liquor changed every eighteen to twenty four hours; the process was completed when the grain can be crushed between two fingers. The steeped rice was blended with 2 parts of the dilute soda to each part of the steeped rice and a milky fluid result. The starch suspension was diluted and allowed to settle in vats. The thick suspension was allowed pass through a muslin cloth and the damp starch was transferred to oven at 50-60 ºC [7]. After drying it was passed through 125 μm sieve.

Solubility determination

A 2% w/w dispersion of starch was prepared in a 50 ml volumetric flask. The dispersion was shaken frequently for some time and allowed to stand for about 8 hrs. It was then filtered with a filter paper and 30 ml of the clear filtrate evaporated to dryness in a pre-weighed dry crucible.

The weight of starch residue obtained was determined by difference. Solubility was calculated in g/dm^3 and mg % [8]. This was repeated five times and average solubility recorded.

Particle size distribution

The particle size distribution was estimated by the microscopic method [9].

True density

Liquid displacement method using glass pycnometer was used to determine the true density. In this determination benzene was used as intrusion fluid. This was repeated five times and average true density was recorded.

Bulk and tapped densities

Exactly 50 g of starch was weighed on chemical balance and transferred into a 100 ml measuring cylinder. The volume occupied by the starch recorded as the bulk volume. The cylinder was dropped on a wooden platform from a height of 2.5 cm three times at 2 seconds intervals until the volume occupied by the starch remained constant [10]. This was repeated five times and average bulk and tapped volumes recorded. The data generated were used in computing the compressibility index and Hausner's quotient for the starch.

Angle of repose

Angle of repose was determined by fixed funnel method. The accurately weighed starch was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the starch. The starch was allowed to flow through the funnel freely onto the surface. The height and diameter of the starch cone was measured and angle of repose was calculated [11]. This was repeated five times and average angle of repose was recorded.

Tablet preparation

Tablets containing 1 mg Ketotifen fumarate were prepared. The batch contained Assam Bora rice starch in concentration of 98.3% w/w with 1% magnesium stearate as lubricant and 0.2%

colloidal silica as glidant were compacted in Tablet Punching Machine using 9.0 mm circular standard flat punch.

Evaluation of compressed tablets

Tensile strength

This was carried out using hardness tester, Pfizer type (Elite Scientific Corp., Mumbai). The lower plunger is placed in contact with the tablet, and a zero reading is taken. The upper plunger is then forced against a spring until the tablet fractures. It was expressed in Kg/cm^2.

Friability

The friability of the tablets was determined by using friabilator (Roche, USA). Ten tablets were weighed from each batch and placed in the friabilator and operated for 4 min. at 25 rpm. The tablets were then made free from dust and reweighed. The percentage friability was calculated for the batch of tablets.

Drug content

The tablets were crushed in a mortar. A mass of powder equivalent with the average weight of one tablet was transferred into a 100 ml volumetric flask and 50 ml of methanol was added. The flask was then shaken automatically for 20 min., the resulting solution made up to the mark with methanol, and mixed thoroughly. A 20 ml aliquot was centrifuged at 4000 rpm. The absorbance of the clear supernatant was measured at 296 nm against methanol. A reference solution of Ketotifen hydrogen fumarate 2.5-Hydrate was prepared, and absorbance measured at 300 nm against methanol. From the absorbance obtained the Ketotifen content in one tablet was calculated out. Mean drug content was calculated for each batch and thus their standard deviations.

Disintegration time

The method specified in the USP/NF (2003) was used. The machine was Tablet Disintegration Test Machine IP/BP/USP Std. (Tab-Machines, Mumbai). Disintegration medium used was 0.1 N HCl. Five tablets selected at random from each batch and the time taken for each

tablet to break up into small particles and pass out through the mesh was recorded. Mean disintegration time was calculated for the batch.

Dissolution study

The *in vitro* dissolution study was carried out using USP Type II dissolution apparatus. The dissolution study was carried out in 900 ml of 0.1 N HCl. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37 ± 0.5˚C. The concentration of Ketotifen was measured spectrophotometrically at 300 nm (Hitachi, U-2001, Japan).

RESULT AND DISCUSSION

Table 1 shows the various properties of the Assam Bora rice starch. The cold water solubility of starches is related to their amylose/amylopectin constituents. The higher the water soluble amylopectin constituent the higher the cold water solubility of the candidate starch [8]. The low bulk and tapped densities of Assam Bora rice starch indicate that the material is not highly porous and is a poor flowing powder. The low bulk density results when the void spaces created by larger powder particles are not filled by smaller particles in distribution leading to consolidation of powder particles. The confirmation of the non-free flowing nature of Assam Bora rice starch was derived from the fact that their Hausner's quotient of 1.47 is greater than 1.2 which indicate low inter particulate friction in powder [12]. However, Assam Bora rice starch possessed better flow properties with Carr's compressibility index of 31.93%. This index as a one point measurement does not always show the ease of consolidation of powders. Angle of repose showed Assam Bora rice starch having fair flow properties with values 40.31˚ [11]. The *in vitro* tablet properties are shown in Table 2. The tablet tensile strength was found satisfactory with the Assam Bora rice starch. The same trend was found with the friability for the tablets with values 0.65%, which is below 1.0% friability. The drug content in the batch was found within the limits of 97.8 to 101.8% with value 99.70. In dissolution study it was found that the $t_{50\%}$ and $t_{90\%}$ of that the batch

containing Assam Bora rice starch with values 13 and 28min. respectively. The percentage dissolved in 30 min. for the batch is found to be 95.05%.

Table 1: Properties of Assam Bora rice starch.

Properties	**Assam Bora rice starch**
Cold Water Solubility (g/dm^3) ± SD [a]	1.01 ± 0.08
Average Particle Size d_{sn} (μm) ± SD	21.75 ± 12.65
True density (g/cm^3) ± SD	1.74 ± 0.03
Bulk density (g/cm^3) ± SD	0.31 ± 0.06
Tapped density (g/cm^3) ± SD	0.46 ± 0.01
Carr's Compressibility Index (**%**) ± SD	31.93 ± 2.88
Hausner Ratio ± SD	1.47 ± 0.06
Angle of Repose (˚) ± SD	40.31 ± 1.52

[a] SD = Standard Deviation

Table 2: In- vitro tablet properties with Assam Bora rice starch as filler-binder.

Properties	**Assam Bora rice starch as filler-binder**
Tensile Strength (Kg/cm^2) ± SD [a]	11.63 ± 0.44
Friability (%) ± SD	0.65 ± 0.08
Drug Content (%) ± SD	99.70 ± 0.06
Disintegration Time (sec.) ± SD	330 ± 7.91
$t_{50\%}$ (min.)	13
$t_{90\%}$ (min.)	28
% dissolved in 30 min.	95.05

[a] SD = Standard Deviation.

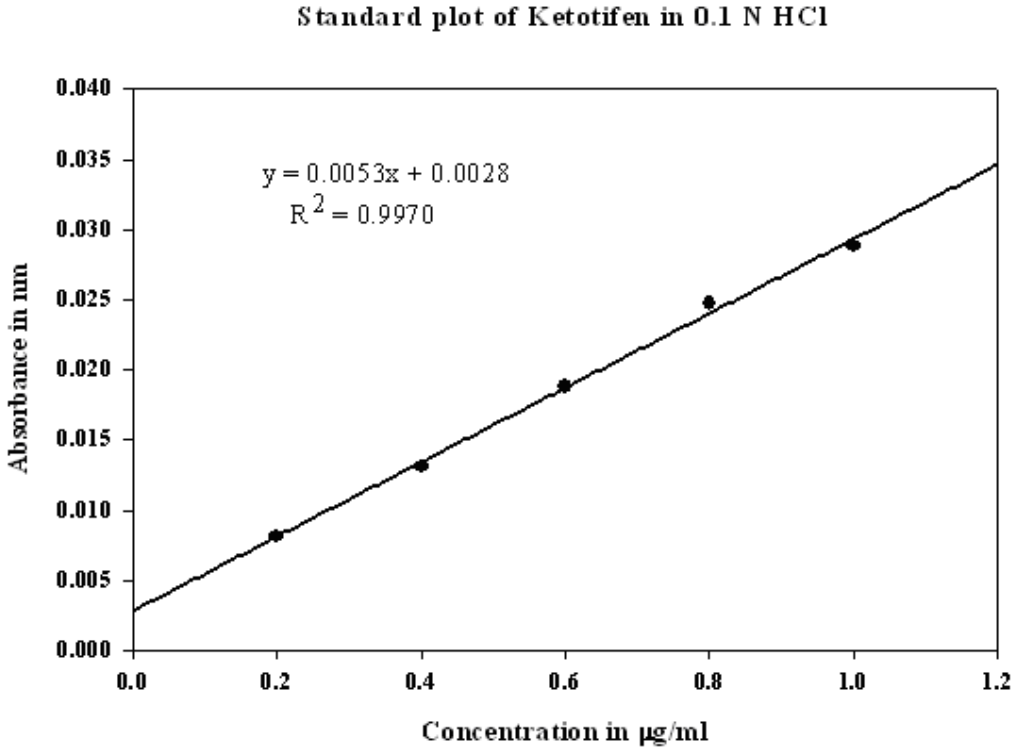

Figure 1: Standard curve of Ketotifen in 0.1 N HCl.

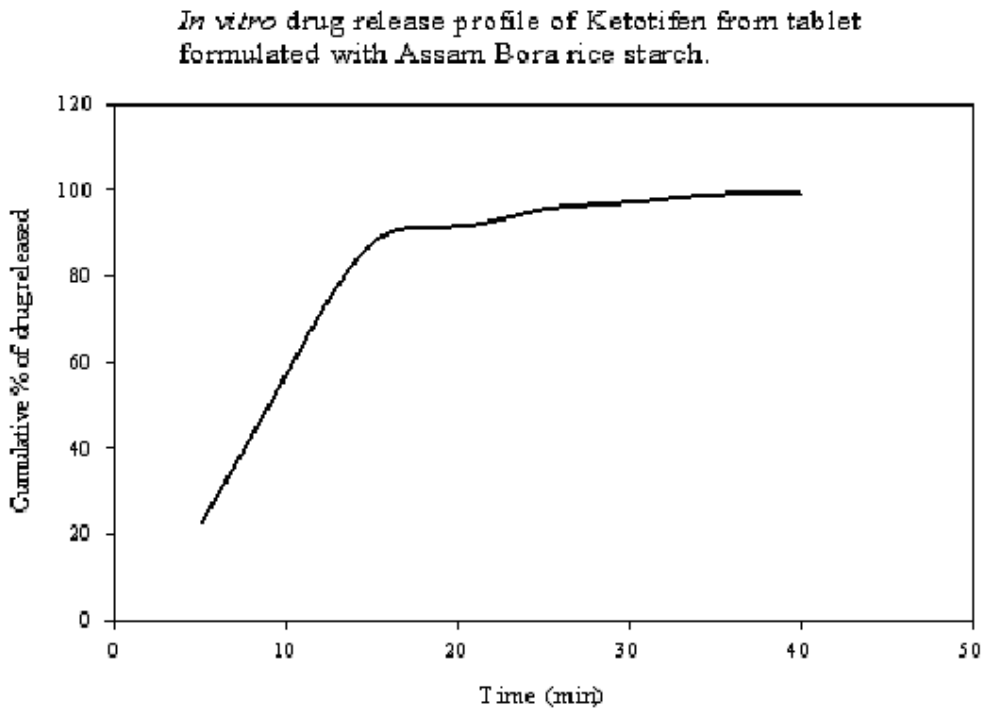

Figure 2: *In vitro* drug release profile of Ketotifen from tablets formulated with Assam Bora rice starch.

CONCLUSION

The tablets prepared by direct compression method were found to be within the in house or official limits with respect to tensile strength, drug content and disintegration time. It could be said that the Assam Bora rice starch showed effectiveness as directly compressible tablet excipient to Ketotifen tablets. Chemical modification of the Assam Bora rice Starch may be undertaken to further improve its properties and hydro stability.

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