

APPLICATION OF ASSAM BORA RICE STARCH AS A BINDER IN FORMULATION OF PARACETAMOL TABLETS

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ABSTRACT

Objective: Evaluation of binding properties of the Assam Bora rice starch powder in comparison to the official gelatin powder in formulation of paracetamol tablets.

Methods: The starch was extracted from the rice and evaluated for relevant properties and used as a binder in paracetamol tablets at concentrations of 2.0, 4.0...8.0% w/w. The tablets were evaluated for hardness, friability, uniformity in weight, disintegration and dissolution profiles. Paracetamol tablets containing equal concentrations of gelatin as standard binder were also produced and comparative study was done.

Results: Results obtained indicated that Assam Bora rice starch performed as good as gelatin as binder in paracetamol tablets.

Conclusion: Assam Bora rice (*Oryza sativa L*, Japonica variety), a group of glutinous rice of Assam has showed promising result of its use as an effective binder in formulation of paracetamol tablets in comparison to gelatin.

Keywords: Assam Bora rice starch, Paracetamol.

INTRODUCTION

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 [1]. The starch is a major constituent of milled rice at about 90% of dry matter [2]. Researches with this starch in tablets of other active ingredients are necessary because of the high percentage of starch content reported in this rice. It is reported that Assam Bora rice starch could compete favorably with pregelatinized starch as direct compressible table excipient [3]. Additionally Assam Bora rice starch showed effectiveness as directly compressible tablet excipient to Ketotifen tablets [4]. 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 tablet excipient.

Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets. They impart cohesiveness to the tablet formulation, which ensures that the tablet remains intact after compression as well as improving the free flowing quality [5]. Binders have been used as solutions and in dry form depending on the other ingredients in the formulations and the method of preparation. The choice of a particular binding agent depends on the binding force required to form granules and its compatibility with the other ingredients particularly the active drug [6]. Starches from different sources have been evaluated and used as excellent binders in either mucilage or the dry powdered form [7, 8, 9]. Maize and potato starches have been in common use and recently cassava starch appeared in the British Pharmacopoeia as an official starch for use as binder [10]. Their use has increased in the tropics where previously recognized starches are unavailable. Apart from starches, other natural gums, gelatin, sugar solutions, modified natural and synthetic polymers have been employed with considerable success as binders. In all evaluations, the type and binder concentrations have direct effect on the crushing strength, friability, disintegration time and tablet dissolution.

MATERIALS AND METHODS

Materials

Assam Bora rice starch (prepared in our laboratory), Paracetamol (Torrent Pharmaceuticals Ltd. Ahmedabad, India), Lactose, Maize starch, Gelatin, Magnesium stearate (Vivimed Labs Ltd. Hyderabad, India), Hydrochloric acid 37% (May and Baker).

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 °C. 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/dm³ and mg %. This was repeated five times and average solubility recorded. The same procedure was repeated for gelatin powder.

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. 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. The same procedure was repeated for gelatin powder.

Formulation of paracetamol tablets

Two batches of the tablet containing 400 mg paracetamol were prepared. The batches contained Assam Bora rice starch and gelatin as binder at the same concentrations of 2, 4, 6, and 8% w/w. Maize starch at 5% w/w acted as the disintegrant with 1% magnesium stearate as lubricant in both cases. Wet granulation method was employed in the formulation of the tablet batches.

Granulation and compression

Wet granulation method was used for all tablet production. Calculation was made for 50 tablets in each batch. In each case, accurately weighed quantities of paracetamol, lactose and disintegrant were mixed in a mortar and the binder solution (gelatin) or mucilage (Assam Bora rice starch) added to obtain a damp coherent mass. The damp mass was sieved with 1.7 mm sieve and dried at 50°C in oven for 1 h. The dried granular mass was passed through a 1.0 mm sieve to obtain uniform sized granules. The different batches of the granules were then mixed with calculated equal quantities of magnesium stearate, and then compressed into tablets under constant pressure with a tablet punching machine (Shakti Pharmatech Pvt. Ltd. Ahmedabad). The punch size and volume of fill were carefully adjusted to give the required tablet size and weight.

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/cm².

Uniformity of weight

Twenty tablets from each batch were selected randomly and weighed individually using a highly sensitive electronic balance (Salter, Karl Kolb, Germany). Their mean weights were calculated; deviations and coefficients of variation for each batch were calculated.

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.

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 2 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 paracetamol was measured spectrophotometrically at 245 nm (Hitachi, U-2001, Japan).

RESULTS AND DISCUSSION

Table 1 shows the various properties of the Assam Bora rice starch powder in comparison to the official gelatin powder. The Assam Bora rice starch exhibited a comparatively higher solubility than gelatin powder in cold water with values of 14.67 and 11.32 g/dm³ respectively. The cold water solubility of starches is related to their amylose/amylopectin contents. Higher the water soluble amylopectin content, the higher the cold water solubility of the candidate starch, whereas higher the content of cold water insoluble amylose, the reverse becomes the case. The solubility result shows that both the excipients are comparable. Interestingly there is positive correlation between starch solubility and their binding/disintegrating efficiency in tablets. The low bulk and tapped densities of both gelatin and Assam Bora rice starch indicate that both the materials are not sufficiently porous and are poor flowing powders. The low bulk density results when the void spaces created by bigger 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 gelatin and Assam Bora rice starch were obtained from the fact that their Hausner's quotient of 1.51 and 1.42 respectively are greater than 1.2 which indicate low inter particulate friction in powder [11]. However, Assam Bora rice starch possessed better flow properties than gelatin with Carr's compressibility index of 29.64 and 33.72% respectively. This index as a one-point measurement does not always show the ease of consolidation of powder granules [12]. The *in vitro* tablet properties are shown in Table 2. The hardness of the tablet batches was within acceptable range of 4 - 7 kg/cm². It is observed that the hardness increased with increasing binder concentration. This is in agreement with previous studies on starches used as binders in comparison to other binders [8]. The tablet hardness were generally higher with the Assam Bora rice starch than gelatin at all the concentrations used, which indicated that lower concentration of Assam Bora rice starch than gelatin could be used to achieve the same level of binding. The same trend was observed with the friability recorded for the two binders. Gelatin and Assam Bora rice starch showed below 1.0% friability at concentration levels of 6.0 and 8.0%. It should be noted that paracetamol tablets are generally prone to capping when starch binder concentration is less than 7.0% [8]. As expected, variations in weight uniformity were less in the tablets prepared using Assam Bora rice starch as binder. The uniformity of weight also indicated the uniformity of drug content. Thus, Assam Bora rice starch produced better flow of the granules. Similarly, the disintegration time increases with increasing concentration of binder as evident from the table 2. It has been reported that starch mucilage used as binder forms a thin film around the particles with increasing the thickness as the quantity of mucilage increases and this retards disintegration [8]. The longer disintegration time for tablets prepared with Assam Bora rice starch is therefore understandable. (The comparative dissolution profiles of the paracetamol tablets prepared with Assam Bora rice starch and gelatin as binder is shown in Figures 1 and 2 respectively). In general, the amount of drug released decreased as the binder concentration increased. At all the binder concentrations, gelatin showed an initial faster release, which progressed more slowly than that of the Assam Bora rice starch of equal concentrations. The t_{50} and t_{70} of all the batches are similar, indicating there comparable nature of drug release.

Table 1: Properties of Assam Bora rice starch and gelatin powders

Properties	Assam Bora rice starch	Gelatin powder
Cold Water Solubility (g/dm ³)	14.67	11.32
Bulk Density (g/ml)	0.6900	0.5370
Tapped Density (g/ml)	0.9807	0.8102
Hausner's Quotient	1.42	1.51
Carr's Compressibility index (%)	29.64	33.72

Table 2: *In-vitro* tablet properties with Assam Bora rice starch and gelatin as binders.

Properties	Assam Bora rice starch				Gelatin powder			
	2.0	4.0	6.0	8.0	2.0	4.0	6.0	8.0
Binder Concentration (%)	2.0	4.0	6.0	8.0	2.0	4.0	6.0	8.0
Mean Table Hardness (kg/cm ²)	3.9	4.4	5.5	6.3	3.6	3.8	4.5	5.1
Friability (%)	1.87	1.64	1.34	0.65	2.64	1.35	0.85	0.72
Weight uniformity* (mg)	498.67 (11.49)	519.43 (12.21)	538.02 (14.58)	564.32 (12.70)	502.46 (10.36)	524.32 (09.41)	541.67 (11.18)	571.82 (08.35)
Mean Disintegration Time (min)	19.50	21.10	26.40	37.20	15.30	19.20	23.40	32.30
t ₅₀ (%)	35.50	32.00	38.00	44.00	24.50	26.00	34.50	42.00
t ₇₀ (%)	48.50	48.50	55.00	62.00	35.00	38.00	55.00	66.50

*Values shown in bracket represent standard deviation.

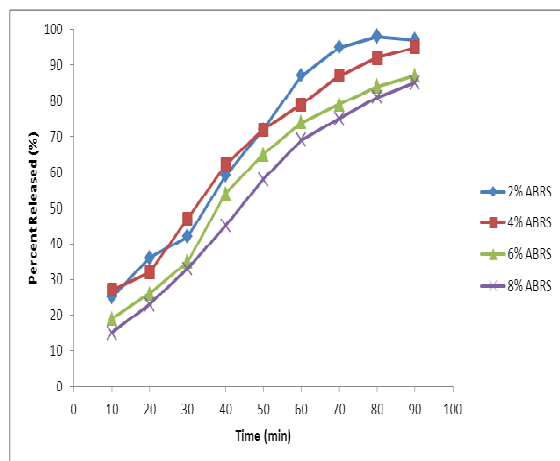


Fig. 1: Dissolution profiles of the paracetamol tablets prepared with Assam Bora rice starch as binder

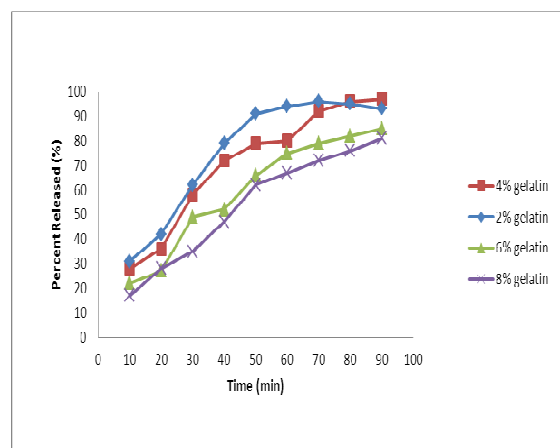


Fig. 2: Dissolution profiles of the paracetamol tablets prepared with gelatine as binder

CONCLUSION

It could be said that the gelatin and Assam Bora rice starch showed comparative effectiveness as binders in paracetamol tablets. In conclusion, Assam Bora rice starch could be used as better binder in tablet formulations comparable to the gelatin powder.

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