Evaluation of Physicochemical Properties of Starch from Two Modified Sri Lankan Rice Varieties to Be Used as Excipients in the Pharmaceutical Industry

LMH Piyumini[1], KWDC Lalindra[1], HSAM Premathilake[1], SU Kankanamge[1#] TS Suresh[2], P Danthanarayana[3] and WJABN Jayasuriya[4]

[1]*Department of Pharmacy, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Sri Lanka*
[2]*Department of Biochemistry, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka*
[3]*State Pharmaceutical Manufacturing Corporation of Sri Lanka, Sri Lanka*
[4]*Department of Pharmacy and Pharmaceutical science, Faculty of Allied Health Sciences, University of Sri Jayewardenepura, Sri Lanka*

#supekshi@yahoo.com

Abstracts: Starches are the main excipients used in the formulation of solid oral dosage forms and the majority of the excipients are imported to Sri Lanka for the country's pharmaceutical manufacturing industry. Therefore, research studies need to be done on finding the suitability of the available sources as pharmaceutical excipients which in return would be more beneficial for the country when making it self-reliant and secured in healthcare. Thus, the present study was aimed at evaluation of the physicochemical properties of rice starch isolated from two modified Sri Lankan varieties of rice, in order to facilitate their exploitation as suitable excipients for the local pharmaceutical manufacturing industry. Two Sri Lankan varieties of rice, BW 267/3 and BW 367 were subjected to experiments in the present study. Starches were isolated following the alkali extraction method used by Valgadde *et al.,* 2015. The starches obtained were characterized by their physical and chemical properties. The results showed both the rice varieties have favourable physicochemical characteristics in their starches as pharmaceutical excipients while some modifications in the isolation and storage procedures would rather enhance those characteristics more precisely. This knowledge of starch properties will be helpful in explaining the behaviour of these starches and selecting them as necessary when used as pharmaceutical excipients.

Keywords: Rice varieties, Rice Starch, Physicochemical properties, Pharmaceutical excipient

Introduction:

According to the International Pharmaceutical Excipient Council, "Excipient" is defined as "Any substance other than active drug or prodrug that is included in the manufacturing process or is contained in finished pharmaceutical dosage forms" (Hartesi *et al.*, 2016). In the pharmaceutical industry starch is an important excipient that has been commonly used because of its versatility and cheapness (Muazu *et al.*, 2012).

Rice (*Oryza sativa* L) is the staple food for millions of people in Southeast Asia. The climate and the fertile soil of Sri Lanka are favorable for growing different types of rice crops. Sri Lanka has about 730,000 ha available land for rice cultivation. It is grown under both irrigated and rain fed conditions in the dry, intermediate, and wet zones. Cultivation is done in two main cropping seasons [Maha (October to March) and Yala (April to August)], (Premasiri *et al.*, 2016).

Rice starch has commercial value in different industries because of its smallest particle size among commercial starches, whitest color and neutral state such as in cosmetic and tableting industries (Vithyashini and Wickramasinghe, 2016).

The whole pharmaceutical manufacturing in Sri Lanka imports the total quantity of starches that are required for manufacturing. In general, the manufacturing of tablets and capsules are higher due to its high consumption. The importation cost could be minimized resulting reduction of total manufacturing cost if the manufactures can obtain raw materials such as starch from the most available sources in Sri Lanka. Because some of the crops cultivated in Sri Lanka could be used to extract excipients. Research studies can be carried out to assess the suitability of the extracted starches from such crops as excipients. The priority must be given to those with characteristics such as high availability, cost-effectiveness and high yield of targeted excipient. Rice (*Oryza sativa*) is a commonly grown crop in Sri Lanka and rice starch is already being used as an excipient in the pharmaceutical industry (Rowe,2009). In Sri Lanka, many varieties of rice are being grown and the excipient properties of starches extracted from those need to be studied to confirm the most suitable variety. Therefore, this study would focus on the evaluation of the excipient properties of starch from two modified Sri Lankan varieties of rice (BW 267/3 and BW 367) for oral dosage forms that satisfy the aforesaid characteristics. Thus; focusing on the attempt to make Sri Lanka self-reliant and secure in healthcare.

Methodology:

Modified rice varieties of BW 267/3 and BW 367 were collected under the authentication of Rice Research and Development Institute, Bombuwala, Sri Lanka. The authentication was also granted from National Herbarium, Peradeniya, Sri Lanka.

The alkali starch extraction method described in Valgadde *et al.,* 2015 was used to isolate the starch from rice grains. Starch identification was done according to the method mentioned in British Pharmacopoeia 2015. The texture, colour, odour and taste of starch powders were examined via sensory evaluations.

The starch yield of rice was calculated according to the following equation.

dry weight of starch

$$\text{Starch yield percentage of rice} = \frac{\text{dry weight of starch}}{\text{weight of rice}} * 100\%$$

pH values of the starches were determined following the method in British Pharmacopoeia, 2015.

Scanning Electron Microscopic images of starches were obtained according to the method described in Sainio (2011) by using a Carl Zeiss EVO 18 Scan Electron Microscope (SEM).

Particle size distribution was estimated by dry sieving method described in British Pharmacopoeia 2015 by allowing the powders to pass through the nest of sieves.

Moisture contents of the dried starches were calculated by using a moisture analyzer. Proximate composition analysis of starch samples was evaluated according to the methods described in AOAC: Official Methods of Analysis, 1990 and the purity of the starches were calculated from the following equation (Vasanthan, 2001

$$\text{Percentage of starch purity} = \frac{\%\text{carbohydrate}}{(100 - \%\text{moisture})} * 100\%$$

The methods used by Tuffor (2013) and Mosisa (2014) were used to find the Amylose contents of the two starch samples. The swelling capacity of the starch powders was determined by the method of Hasan *et al.,* 2015. The solubility of the starches was calculated from the test carried out according to Emenike *et al.,* 2017.

To evaluate the True densities, the fluid displacement method described in the

Standard Test Method for Specific Gravity of Soil Solids by Water Pycnometer, 1997 was performed. Tapped densities and Bulk densities were evaluated using the methods in Obitte and Chukwu (2007).

Angle of Repose, Hausner Ratio and Compressibility Indices of the starches were measured and calculated according to the methods in British Pharmacopoeia, 2015. The method which was described in Emenike *et al.,* 2017 was used to measure the flow rate.

The test results were expressed as Mean ± Standard Deviation using SPSS software version 23 following results gained each test for both varieties, BW 267/3 and BW 367.

Results and Discussion:

Extractions from BW 267/3 and BW 367 were able to satisfy the Pharmacopoeia's specifications for identification of starch by the conversion of orange-red to dark blue colour following the iodine test and disappearing of colour upon heating (British Pharmacopoeia, 2015), confirming the extractions consisted of starch. Both the starch samples were smooth and creamy in texture, white in colour, odourless and neutral in taste which would be advantageous in using these starches in dosage forms as excipients.

The starch yield percentages were 41.36% (w/w) for BW 267/3 and 37.88% (w/w) for BW 367. Meanwhile, the pH value of BW 267/3 was 9.63 and BW 367 was 9.50 which were above the reference range of the pH value of rice starch, 5.00-8.00 as pharmaceutical excipient (Bao, 2019). Modifications in the extraction procedure might be a solution in gaining more starch yield within the preferred pH value range.

The SEM images (see Figure 1 and Figure 2) showed they were diverse in size, and irregular and polygonal in shape due to the damage of the starch during the isolation process (Bhotmange and Reddy, 2013). The mean particle diameter of the starch from BW 267/3 was 5.52 μm and BW 367 was 5.34 μm as observed by the SEM. The average diameter of a rice starch particle is referred to be as 5 μm while all the particles having diameters within the range of 2-20 μm (Rowe *et al.,* 2009). The particle size and shape can influence a large variety of important physical properties, manufacturing processability and quality attribute including dissolution rate, drug release rate for sustained and controlled release dosage formulations (Shekunov *et al.*, 2007).

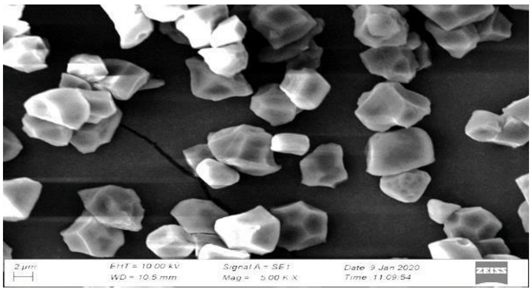

Figure 1: SEM image of starch from BW 267/3

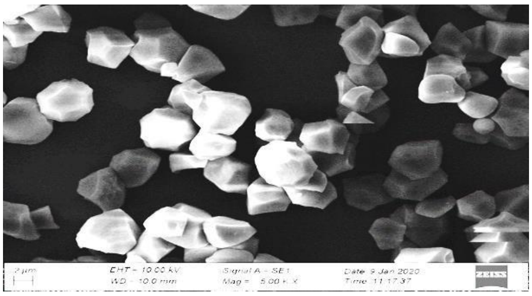

Figure 2: SEM Image of starch from BW 367

Sieve analyses are one of the most widely used methods for the determination of the dispersive composition of the dust and powders (Bayvel and Jones, 1981). The highest particle size distribution of BW 267/3 was observed within the 150-300 μm range while BW 367 was observed within the range 300-850 μm range (see Table 1).

Table 1: Particle size distribution of starches

Starch Variety	**Particle size range (μm)**	**Percentage retained (%)**
BW 26	>850	9.68

	300-850	31.84
	150-300	45.56
	<150	12.92
BW 367	>850	9.82
	300-850	52.20
	150-300	35.32
	<150	2.66

All starches are hygroscopic in nature. They absorb atmospheric moisture to reach equilibrium humidity (Crouter and Briens, 2014). For many powders including starches, moisture is known to modify the flow and mechanical properties (Tester *et al.,* 2004). With compared to the recommended moisture percentage (14%) of rice starch as pharmaceutical excipients (Rowe *et al.,* 2009), moisture content percentages of 15.78% (w/w) and 19.78% (w/w) were obtained respectively for BW 267/3 and BW 367 were higher. The quality of starches is adversely affected by the high amount of moisture content than the recommended level. The high moisture content of starch is favorable for molds to grow resulting in reduced shelf life. The quantity of starch is also reduced and as a result, the market value is also reduced as there is a weight loss on drying. To produce compacts with high tensile strength and low friability, it is essential to have the moisture contents of starches at optimum levels (Staniforth, 1971). Improvements in the starch drying process will help to lower the moisture contents of the starches.

Devoid of other plant components such as fibre, protein and lipid, a good starch material for pharmaceutical application should contain more than 96% (w/w) of starch and as much as possible (Vasanthan, 2001). Along with the results of proximate composition analysis and moisture content, the purities of starches were calculated as 97.73% (w/w) for BW 267/3 and 95.98% (w/w) for BW 367 which indicated that they were good starch materials for pharmaceutical applications.

Amylose content appears to be the major factor controlling almost all physicochemical properties of rice starch such as turbidity, syneresis, freeze-thaw stability, pasting, gelatinization, and retro degradation properties (Wickramasinghe and Noda, 2008). The amylose contents of BW 267/3 and BW 367 were estimated to be 9.5% and 46.0% respectively. The higher the amylose content, the lower is the swelling power and the smaller is the gel strength for the same starch concentration. To a certain extent, however, a smaller swelling power due to high amylose content can be counteracted by a larger granule size and therefore expected to exert stronger disintegrant action (Tuffour, 2013). The swelling capacity of a material is the ability of a material to absorb water and swell up. Materials with high swelling power have good disintegrating properties. Results obtained from BW 267/3 and BW 367 were 27.40% (w/v) and 21.34% (w/v) respectively. The results indicated that the swelling capacity of BW 267/3 was faster than BW 367. Both varieties were insoluble at the cold water, hot water and ethanol (96%). British Pharmacopoeia, 2015 reveals that rice starch is insoluble in cold water and ethanol (96%).

One of the critical importance of powders to be considered in the pharmaceutical dosage forms is the ability of the powder to flow. The flowability of powders is of immense importance in the manufacture of pharmaceutical tablets and capsules with the correct amount of pharmaceutical active ingredients (Staniforth, 1971). The compendial methods available for the measurement of powder flow are flow rate, measurement of angle of repose, bulk density, tapped density, true density, compressibility index and Hausner ratio.

The test results for True density, Bulk density and Tapped density are in the Table. When the powder is free flowing the ratio of bulk density over tapped density is small in value and when the powder is poor in the flowability that value is also greater. This due to the inter-particular interactions of the powder particles (United States Pharmacopoeia, 2016).

Table 2: Flow properties of starches

Flow property	**Results**	
	BW 267/3	**BW 367**
Bulk density (g/mL)	0.46±0.01	0.44±0.00
Tapped density (g/mL)	0.58±0.01	0.58±0.01
True density (g/mL)	1.69±0.42	1.54±0.46
Flow rate (g/s)	2.26±0.12	2.83±0.16
Angle of Repose (º)	42.07±1.76	43.64±1.89
Hausner Ratio	1.26±0.01	1.32±0.06
Compressibility Index	20.57±0.33	24.09±0.37

The flow rate of powder is an essential parameter of powder in determining the ability of powder as a direct compression excipient. Flow rate is the time taken by a powder mass to pass through an orifice (United States Pharmacopoeia, 2016). The flow rate of powder is good if it is below 5 g/s (Rowe *et al.,* 2009) where for BW 267/3 and BW 367 the powder flow rates (see Table 2) were good.

The angle of repose of powder is an indicator that shows how easily particles in a powder roll over one another (Edde, 2016). The Hausner ratio indicates the degree of densification which could occur during tableting and with higher values better the densification and flowability (Gbenga *et al.,* 2014). The compressibility of a powder can be described as the ability of a powder to reduce its volume (Klevan, 2011). According to the general scales of flowability for Angle of Repose, Hausner Ratio and Compressibility Index (British Pharmacopoeia, 2015) the results (see Table 2) obtained by both the starches show passable flow properties. The flow properties of these starches can be further improved with the use of glidants, lowered moisture content and precise particle sizes.

Conclusion:

The study showed that starches from the two modified Sri Lankan Rice varieties BW 267/3 and BW 367, have favourable physicochemical properties to be used as pharmaceutical excipients. Suitable modifications in the isolation and storage procedures would rather enhance some of these properties more precisely. Furthermore, it is recommended to study the properties of the above starches incorporated into pharmaceutical dosage forms together with active pharmaceutical ingredients and other excipients.

References:

ASTM International (2014): Standard Test Methods for Specific Gravity of Soil Solids by Water Pycnometer, available from: https://www.astm.org/Standards/D854 [Accessed on 16.09.2019].

Bao, J (Ed.). (2019): Rice: Chemistry and Technology. In Fourth edition, USA, AACC International Press. pp. 55–108.

Bayvel, L P and Jones, A R (1981): Methods of Measuring Particle Size Distribution, Electromagnetic Scattering and its Applications, pp. 132–162.

Bhotmange, M G and Reddy, D K (2013): Isolation of Starch from Rice (Oryza Sativa L.) and its Morphological Study using Scanning Electron Microscopy, International Journal of Agriculture and Food Science Technology 4 (1), pp. 859–866.

British Pharmacopoeia (2015): Eight edition, London, Council of Europe. (5), pp. 501-530.

Crouter, A and Briens, L (2014): The effect of moisture on the flowability of pharmaceutical excipients, AAPS PharmSciTech 15 (1), pp. 65–74.

Emenike, I V, Yusuf, I I, Timothy, S Y, Adamu, O J, Oduola, A R and Musa, H (2017):

Evaluation of the physicochemical properties of native and modified starch obtained from Manihot esculentus as pharmaceutical excipient, Asian Journal of Pharmaceutical Science & Technology 7 (1), pp. 34–39.

Gbenga, B L, Olakunle, O and Adedayo, A M (2014): Influence of pregelatinization on the physicochemical and compressional characteristics of starches obtained from two local varieties of Dioscorea rotundata, IOSR Journal of Pharmacy (IOSR-PHR) 4 (6), pp. 24–32.

Hartesi, B, Sriwidodo, Abdassah, M and Chaerunisaa, A Y (2016): Starch as pharmaceutical excipient, International Journal of Pharmaceutical Sciences Review and Research 41 (2), pp. 59–64.

Hasan, M M, Rana, M S, Uddin, N, Rahman, K J and Chowdhury, S S (2015): Comparative Evaluation of Solanum tuberosum L. and Manihot esculenta Starch as Pharmaceutical Excipients: Assessment by Preformulation Studies, Bangladesh Pharmaceutical Journal 17 (2), pp. 128–134.

Helrich K (Ed.). (1990): Official Methods of Analysis: Association of Official Analytical Chemists. In Fifteenth edition, USA, Association of Analytical Chemists, Inc. pp. 380-384, 788,789.

Klevan, I (2011): Compression Analysis of Pharmaceutical Powders: Assessment of Mechanical Properties and Tablet Manufacturability Prediction, PhD Thesis, University of Tromso, Norway.

Mosisa, B (2014): Isolation, Physicochemical Characterization and Evaluation of Triticum Decocum Starch as Binder and Disintegrant in Paracetamol Tablets, Master's Thesis, School of pharmacy, Department of Pharmaceutics and Social Pharmacy, Addis Ababa University, Addis Ababa, Ethiopia.

Muazu, J, Girbo, A, Usman, A and Mohammed, G T (2012): Preliminary studies on Hausa potato starch I: The disintegrant properties, Journal of Pharmaceutical Science and Technology 4 (3), pp. 883–891.

Obitte, N and Chukwu, A (2007): Preliminary Studies on Tacca Involucrata (Schum & Thonn) Starch. FAM: Taccaceae, West African Journal of Pharmacy, pp. 2–3.

Premasiri, R, Weerasinghe, A, Fernando, P and Gunarathna, P (2016): Use of high accuracy GPS for soil geochemical mapping in paddy fields; A case study in Kalutara, Sri Lanka. 37th Asian Conference on Remote Sensing 2016, 1 May 2017. pp. 384–392.

Rowe, R C, Sheskey, P J and Quinn, M E (Eds.). (2009): Handbook of Pharmaceutical Excipients. In Sixth edition, UK, RPS publishing, Pharmaceutical Press. pp. 685-690.

Sainio, J A (2011): Characterization and Evaluation of Melibiose as Novel Excipient in Tablet Compaction, Master's Thesis, Division of Pharmaceutical Technology, Faculty of pharmacy, University of Helsinki, Finland.

Shekunov, B Y, Chattopadhyay P, Tong H H Y and Chow A H L (2007): Particle size analysis in pharmaceutics: Principles, methods and applications, Pharmaceutical Research 24 (2), pp. 203–227.

Staniforth J (1971): Powder flow. In Aulton, M E (Ed.), Pharmaceutics: The Science of Dosage Form Design. Second edition, USA, Churchill Livingstone. pp. 197-210.

Tester, R F, Karkalas, J and Qi, X (2004): Starch-composition, fine structure and architecture, Journal of Cereal Science 39 (2), pp. 151–165.

Tuffour, E (2013): Evaluation of starch from ghanaian sweet potato varieties as excipients for solid oral dosage forms, MPhil Thesis, Department of Pharmaceutics, Kwame Nkrumah University of Science and Technology, Ghana.

United States Pharmacopoeia (2016): Powder Flow. Stage 6 Harmonization. 30 (60) (6), pp. 7.

Valgadde, P S, Wankhade, V and Sahoo D A K (2015): Isolation of Starch from the Brokens of Sona Masuri Rice (Oryza Sativa L.), International Journal of Engineering Research and Technology 4 (9), pp. 467–469.

Vasanthan, T (2001): Overview of Laboratory Isolation of Starch from Plant Materials. Current Protocols in Food Analytical Chemistry 0(1), pp. E2.1.1-E2.1.1.6.

Vithyashini, L and Wickramasinghe, H A M (2016): Genetic diversity of seed storage proteins of rice (Oryza sativa L.) varieties in Sri Lanka, Tropical Agricultural Research 27 (1), pp. 49.

Wickramasinghe, H A M and Noda, T (2008): Physicochemical Properties of Starches from Sri

Lankan Rice Varieties, Food Science and Technology Research 14 (1), pp. 49-54.