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European Journal of Pharmaceutics and Biopharmaceutics 70 (2008) 326–334

European Journal of Pharmaceutics and Biopharmaceutics

www.elsevier.com/locate/ejpb

Research paper

The interplay between yam (*Dioscorea* sp.) starch botanical source, micromeritics and functionality in paracetamol granules for reconstitution

Cliff K. Riley [a,*], Sarafadeen A. Adebayo [c], Andrew O. Wheatley [a,b], Helen N. Asemota [a,b]

[a] *University of the West Indies, Jamaica*
[b] *Department of Basic Medical Sciences (Biochemistry), University of the West Indies, Jamaica*
[c] *University of Technology, Jamaica*

Received 29 November 2007; accepted in revised form 3 March 2008

Abstract

A comparative investigation of the interplay between starch botanical source, micromeritics and their functionality in formulated paediatric paracetamol granules for reconstitution was conducted using starches extracted from five local yam (*Dioscorea* spp.) species. Significant differences were observed in the physicochemical properties of the different starches studied ($p < 0.05$). The observed differences in paracetamol dissolution correlated well with the physicochemical properties of the starches. Granules formulated with Chinese yam and Bitter yam starches showed the fastest rate of paracetamol dissolution with T_{80} of 2.2 and 2.6 min, respectively, at 2.5%w/w, and 3.75 and 4.00 min, respectively, at 10% w/w binder concentrations. Those formulated with Round leaf yellow yam starch had the slowest dissolution rate with T_{80} of 4.5 and 8.75 min, respectively, at 2.5% and 10% binder concentrations. The results generally indicate a significant dependence of the rate of paracetamol dissolution from granules on starch surface tension, viscosity, swelling power and water binding capacity, particle size distribution, specific surface and porosity. These, in turn, were found to be starch botanic source-dependent suggesting careful consideration of botanic source when substituting one starch product for another in granule formulation.

Keywords: Yam; Starch; Excipient; Granules for reconstitution; Dissolution; Physiochemical properties; Moisture sorption; Particle size

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1. Introduction

Starch is the major carbohydrate reserve in yam tubers, accounting for about 85% of the dry weight matter [1]. It is normally found as granules, typically consisting of amylose (10–30%) and amylopectin (70–90%) molecules [2]. Despite its high carbohydrate content, mainly in form of starch, yam is not listed among the most common sources of industrial starch which is primarily obtained from corn, potato, wheat, tapioca and rice [3–6].

Starch and its derivatives are ranked among the top ten pharmaceutical excipients [7], usually employed as disintegrant, glidant or lubricant in powdered form or as binders in the mucilaginous (paste) form. Although the use of native starches have declined in favour of modified, semi-synthetic starch products, starch in powder form and as mucilage still constitute important ingredients of tablet formulation [8], especially in the developing countries.

Recent developments in the field of Process Analytical Technology (PAT) have necessitated a deeper understanding of the effects of material properties on ease of processing and product quality. Starch products extracted from various species of yam grown in Jamaica have shown significant variations in their physical and chemical properties [9]. With the plethora of starch botanic sources, accidental

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[*] Corresponding author. Biotechnology Centre, University of the West Indies, Mona Campus, UWI, Mona, Kingston 7, Jamaica. Tel.: +876 9774652; fax: +876 9773331.
E-mail address: cliff.riley@uwimona.edu.jm (C.K. Riley).

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doi:10.1016/j.ejpb.2008.03.001

or deliberate contamination of starch products of one origin with another could occur. If the particulate properties of starch from these sources are strikingly different, they may impact significantly on processing and product quality and these may be a potential source of differences in brand/generic product performance or even in batch-to-batch and lot-to-lot variation in the same product formulated with different starch excipients. In addition, these differences in material properties may impact on the quality of modified starch products and their performance in dosage forms.

In the formulation of granules for tablets and capsules preparation, control of particle size and size distribution in the powder bed is essential if adequate fluidity, mixing, packing and compression characteristics are to be achieved [10,11]. Since these parameters have been reported to affect solid dosage properties in a botanic-source dependent manner [12], it should be possible to correlate the differences in physicochemical properties of yam starch powders with their functional performance in granules and tablets in a way that will enable the selection of the most appropriate source for dosage form design and development work.

Paracetamol, one of the most popular analgesic and antipyretic drugs, is a drug of poor aqueous solubility (1 in 70 parts of water, BP [13]). Hence, its paediatric solution formulations invariably incorporate alcoholic co-solvents. Apart from the limited shelf-stability of aqueous drug products, recent demand by the paediatricians for alcohol-free paracetamol formulation has necessitated consideration of alternative dosage formulation. Presently, no commercial paracetamol granule for reconstitution appears to be on the market, especially in the tropics where extremes of climatic conditions could compromise shelf-stability of liquid preparations.

This study was therefore designed to investigate the effect of physicochemical properties of starches extracted from five yam (*Dioscorea*) species on their effectiveness as binders in paracetamol granules using granulate physical and dissolution properties as assessment parameter.

2. Materials and methods

2.1. Materials

Tubers of *Dioscorea cayenensis,* cultivar (cv), Round leaf yellow yam (RY), *Dioscorea polygonoides* cv. Bitter yam (BY), *Dioscorea alata* cv. Sweet yam (SY), *Dioscorea rotundata* cv. Negro yam (NY) and *Dioscorea esculenta* cv. Chinese yam (CY) were collected from a local farmer in St. Ann, Jamaica. Samples of tubers and aerial parts of the plants were submitted for identification by botanist at the University of the West Indies, Mona Campus, Kingston, Jamaica and confirmed with herbarium specimens. Paracetamol, Corn starch (CS) and sucrose were products of BDH Chemicals, Poole, U.K. All other reagents were products of Sigma-Aldrich and were used without further modification.

2.2. Methods

2.2.1. Starch isolation

Starch was extracted by the method of Moorthy and Nair [14] with some modifications. Freshly harvested yam tubers (100.0 g) were peeled and homogenized in 1% NaCl solution (900 mL) using a Waring commercial blender. The mixture was filtered through triple layered cheesecloth (≈125 μm) and washed through with 1% NaCl solution. Starch granules in the combined washings were allowed to settle overnight (12 h) at room temperature, the supernatant was decanted and the slurry centrifuged (Beckman centrifuge) at 3000*g* for 10 min. A rusty brown top layer was scraped off and the starch was re-suspended in 1% NaCl solution and de-ionized water, respectively, and centrifuged after each washing. The pasty mass obtained was dried at 60 °C for 12 h in a Gravity Compression oven (Precision Scientific, GCA Corporation, USA), pulverized and stored in a tightly closed glass bottle.

2.2.2. Measurement of the starch particle diameter

Starch samples for Scanning Electron Microscopy were sieved using a number 60 mesh (250 μm) Fisher Scientific Sieve, mounted and coated with gold (1 nm) using a Polaron sputter coater and analyzed using a Philips 505 Scanning Electron Microscope (Phillips, Holland) at a magnification of 3.26×10^2 for RY, NY, SY and BY starches. CY starch was viewed at a magnification of 1.32×10^3 due to the smaller size of the granules.

Starch for particle size determination was suspended in liquid paraffin. A slide of the dispersion was examined on a Leica DMRME light microscope (Leica, Germany). Particle size and size distribution of starches were studied using an eyepiece graticule previously calibrated with a stage micrometer [15,16]. At least 500 granules were measured from each sample.

2.2.3. Calculation of equivalent diameters

Using the projected diameters, the surface and volume parameters of the starch particles were calculated by application of the Edmundson [17] equation:

$$d_{\text{mean}} = \left(\frac{\sum nd^{p+f}}{\sum nd^{f}}\right)^{\frac{1}{p}} \tag{1}$$

where n = number of particles in each size range, d = diameter of particles in a given size range, f = frequency factor (or index), p = an index of size, with values of 1, 2 and 3 ($p = 1$ gives particle length, $p = 2$ gives particle surface area and $p = 3$ gives particle volume). The Surface – no. mean (d_{sn}) was calculated with the equation:

$$d_{\text{sn}} = \left(\frac{\sum nd^{2}}{\sum n}\right)^{\frac{1}{2}} \tag{2}$$

Volume-surface mean (d_{vs}) was calculated using the equation:

$$d_{vs} = \left(\frac{\sum nd^3}{\sum nd^2}\right) \tag{3}$$

2.2.4. Calculation of the geometric mean diameter and geometric standard deviation

Geometric mean diameter was determined from a plot of the log of particle size against cumulative frequency% on a probability scale (log probability plot). The geometric mean diameter (dg) was calculated as the log of the particle size equivalent to 50% on the probability scales i.e. 50% size [17]. The geometric standard deviation (σ_g) was calculated from the slope of the line using the equation:

$$\sigma_g = \frac{84\%\ \text{undersize}}{50\%\text{size}} \tag{4}$$

2.2.5. Specific surface area

The specific surface area of starch granules was calculated using the equation for a spherical particle:

$$S_w = \frac{6}{\rho d_{vs}} \tag{5}$$

where ρ is the density of the granule, 6 is a constant for spherical particles and d_{vs} the surface-volume diameter.

2.2.6. Derived properties of the powders

Starch granular density was determined by the fluid displacement method [15] using petroleum ether as the immersion fluid. The loose and tapped bulk densities of the granules were determined as outlined by Adebayo and Itiola [18]. Thirty grams of starch powder was poured at an angle of 45° through a glass funnel into a measuring cylinder of 28 mm internal diameter and volume capacity of 100 ml. The cylinder was carefully set upright and the height of the powder bed was measured and bulk density calculated. The powder bed was subjected to 100 taps at a height of 2.54 cm and the taped bulk density was determined. The percentage porosity was calculated as (1 − relative density) × 100.

The Carr's index (C_I) of the starch material was calculated as:

$$C_I = \frac{\rho_T - \rho_B}{\rho_T} x 100\% \tag{6}$$

where C_I is the Carr's index, ρ_T the tapped density and ρ_B the loose bulk density.

2.2.7. Starch water binding capacity

The starch water binding capacity was determined as outlined by Adebayo and Itiola [8]. Approximately 500 mg of starch previously sifted through 250 µm was weighed in a centrifuge tube and mixed with 15 mL of de-ionized water at room temperature. The suspension was agitated in a Fisher Shaker (Fisher, USA) at 100 rpm for 30 min. After centrifugation at 10,000 rpm for 15 min in a Fisher Scientific Centrifuge, the sediment was weighed and its water content determined by drying at 70 °C to constant weight. Water absorption capacity was determined as the difference in the mass of the moist and dried sediment, expressed as % w/w.

2.2.8. Starch swelling power

Starch swelling power was determined by the method of Schoch [19]. Briefly, 500 mg sample of the starch material was dispersed in 15 mL distilled water followed by heating at 60 °C and 95 °C for 30 min in a Labconco water bath (Labconco Corporation, USA). The suspensions were then cooled and centrifuged at 5000 rpm for 15 min. Water was decanted and the residue weighed. Swelling power was determined using the equation;

$$\text{Swelling\%} = \left(\frac{w_2 - w_1}{w_0}\right) \times 100\% \tag{7}$$

where w_2 is the weight of the tube with the wet residue, w_1 is the weight of tube with the dry starch and w_0 is the weight of starch used.

2.2.9. Moisture sorption studies

The moisture sensitivity of the yam starches was studied as a function of time at 11%, 33% and 93% relative humidity (RH) over a period of 480 h. One gram of starch sample previously dried to constant weight at 60 °C was placed in a calibrated cup with an internal diameter of 2.4 cm. Samples were then placed in hygrostats prepared using saturated salts solutions [8] and percentage moisture sorbed was determined from the weight gained at specified time intervals, up to 480 h. The data was treated to the Freundlich adsorption equation:

$$\frac{x}{m} = kP^{\frac{1}{n}} \tag{8}$$

where x is the mass of moisture adsorbed, m the mass of starch powder used, k the adsorption rate constant (Freundlich isotherm), p the vapour pressure (created by the relative humidity of the salt solution) and $\frac{1}{n}$ is the rate order of moisture adsorption.

2.2.10. Viscosity determination

The viscosity of a 0.5% starch solution in 0.5 M KOH and of reconstituted paracetamol granules, respectively, was determined with a Technico size B Ostwald capillary viscometer [9]. The viscosity was calculated using the equation;

$$\eta_2 = \frac{\eta_1 \rho_2 t_2}{\rho_1 t_1} \tag{9}$$

where ρ_1 is the density of the reference fluid (0.5 M KOH), ρ_2 is the density of the starch or paracetamol suspension of known concentration (g/cm^3), t_1 and t_2 are the efflux times of KOH and starch solutions, respectively, and η_1 and η_2 are the viscosities of KOH and test solution, respectively. The intrinsic viscosity η_i (dl/g) was computed by the equation;

$$\eta_i = \ln\left(\frac{\eta_r}{0.5}\right) \qquad (10)$$

where η_r is the relative viscosity (ratio of reference viscosity to the viscosity of the test liquid formulation) of the test solutions.

2.2.11. Starch mucilage surface tension

A 1% (w/v) starch suspension was made up in water and placed in a water bath at 80 °C for 1 h. The solution formed was then cooled in a water bath at 25 °C for a further 30 min and surface tension (mN/m) of the solution was determined by means of a Fisher surface tensiometer (Fisher Scientific, USA).

2.2.12. Preparation of paracetamol granules for reconstitution

The batch formulation comprised of paracetamol (2.5% w/w), starch (2.5% and 10% w/w) and sucrose (20% w/w). Each batch of paracetamol granules (240 g) was prepared using the wet-massing technique. Starch powders as specified in the batch formulation were suspended in distilled water. Sucrose and paracetamol powders were dry-mixed in a porcelain mortar with pestle; the starch mucilage (paste) was added in small aliquots and wet-massed for five minutes. The wet mass was passed through a Fisher number 14 (1400 µm) mesh sieve. The resulting granules were tray dried at 60 °C for 12 h in a cabinet oven (Labconco Corportaion, USA) and the dried granules were screened through a Fisher number 20 (850 µm) mesh sieve. The granules were stored in air tight bottles at 25 °C until used in dissolution testing. The degree of mixing of the drug in the granules was assessed by the British Pharmacopoeia [13] assay for paracetamol at 257 nm. The degree of mixing was calculated using the equation.

$$M = \frac{1 - \delta}{\sqrt{y - (1 - y)}} \qquad (11)$$

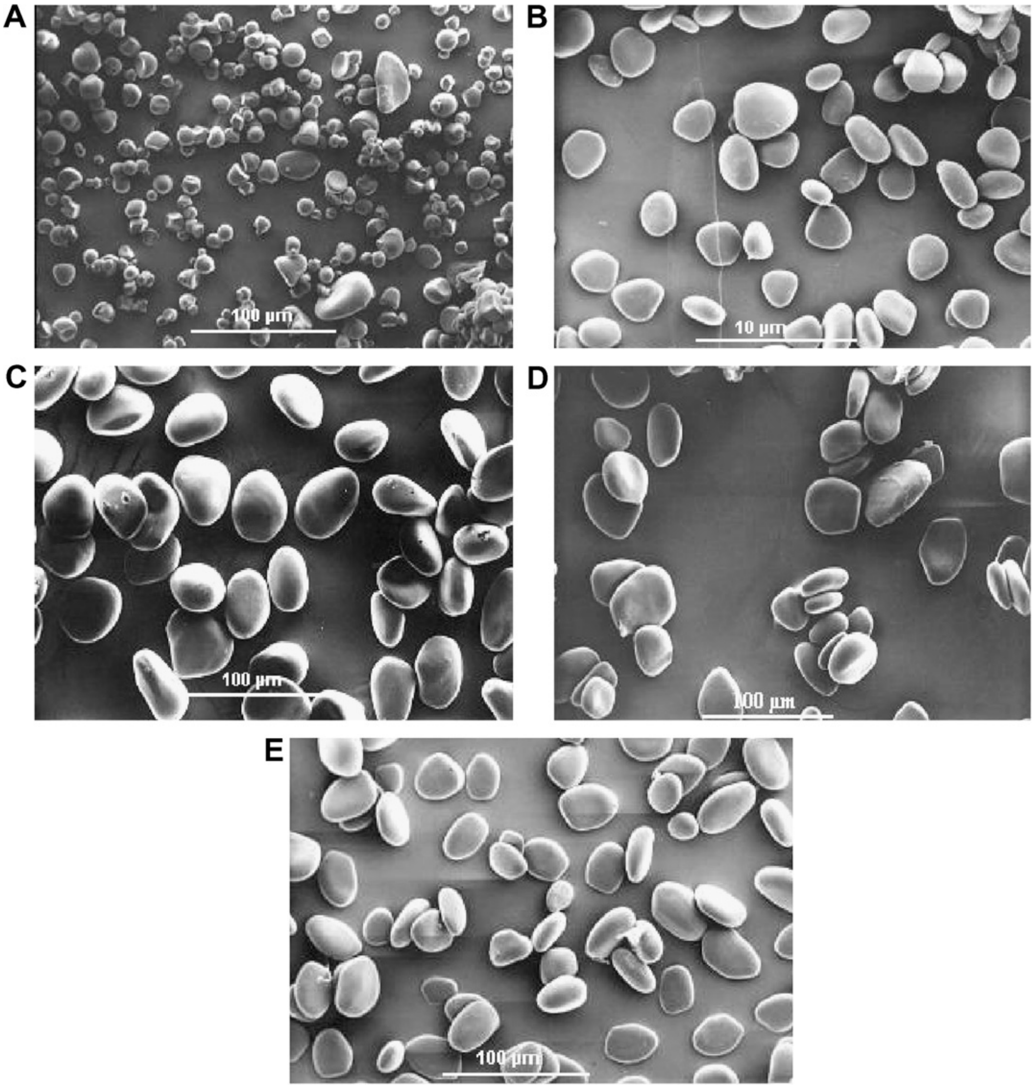

Fig. 1. Scanning electron micrographs of (A) Bitter yam, (B) Chinese yam, (C) Round leaf yellow yam, (D) Sweet yam and (E) Negro yam.

In which δ is the standard deviation of the analyzed sample and y is the proportion of paracetamol in the mixture [20]. Batches for which M was consistently higher than 95% were used for further studies.

2.2.13. Determination of the rate of paracetamol dissolution from granules

The rate of dissolution of paracetamol from the granules was studied as outlined by Adebayo [12]. Paracetamol granules (500 mg) formulated with the different starch mucilage were weighed and transferred to 900 mL phosphate buffer (pH 5.8) maintained at 37 ± 0.05 °C in an Ewreka DTZ disintegration/dissolution test apparatus II (Erweka, Germany). Machine rotation speed was set at 50 rpm. Samples (5 mL) were withdrawn at 5 min interval and immediately replaced with 5 mL of fresh buffer solution maintained at the same temperature. The samples were filtered through a 0.45 μm syringe filter and the absorbance reading was taken at 257 nm on an Ultraspec UV/visible spectrophotometer (Pharmacia Biotech, Tokyo, Japan). Mass of paracetamol released at different time interval was calculated using a previously prepared, standard calibration curve.

3. Results and discussion

The scanning electron micrograph of starch products of different botanic origin is shown in Fig. 1. The crystalline structure of the starch granules classifies them into types A (BY and CS), type B (RY, SY and NY) and type C (CY) [11]. The projected mean diameter, granule volume and specific surface area of the powders are shown Table 1. CY starch has the smallest mean granule diameter and the largest specific surface area while RY starch has the largest granule diameter and lowest specific surface, respectively (Table 1). Generally, the rank order of projected diameter is RY $\geqslant$ NY $\geqslant$ SY $\geqslant$ BY $\geqslant$ CY $\geqslant$ CS. Granule diameter and effective surface area are important parameters controlling particle–particle interaction, mixing and homogeneity of product particularly in powder, capsule and tablet formulations where large surface area would enhance drug-additive contact [10]. These parameters will also impact significantly on the processing of pharmaceutical formulations in which they are used. Finer particles tend to have greater number of particles per unit weight, indicating higher potential for achieving homogeneity when mixing the substance with the active pharmaceutical and other powder ingredients [21]. The higher specific surface area of CY and BY starches may facilitate their mixing with other ingredients of formulation to a greater extent than when other starch powders are used. It may also impact on their effectiveness as adsorbents for liquid ingredients in formulations. Apart from the physical quality of products, particle size and specific surface can influence the bioavailability potential of drugs from dosage forms. Although no definitive report on the effect of particle size of excipients on drug release appears to have been reported in the literature, Finholt and Solvang [22] reported an increase in the rate of dissolution of tablets with decrease in size of the granules used for their preparation.

The density of the starch powder differed significantly ($p < 0.05$) among botanic sources. RY starch has the highest density while BY starch has the lowest (Table 2). Particle density of powders is known to influence mixing and segregation potential while particle shape, size and size distribution would, in addition, influence the packing down behavior of materials during the various unit operations of capsule/die filling and compression [23]. Moreover, the

Table 1
Micromeritics of starch powder from different botanical sources

Starch Source	Projected mean diameter (μm)	Surface – no. mean (μm^2)	Granule-volume (μm^3)	Volume-surface mean (μm)	Specific surface area (m^2/Kg)
SY	25.60^{d}	26.00^{d}	26.83^{d}	28.57^{e}	151.09^{d}
NY	25.70^{d}	26.05^{d}	26.45^{d}	27.28^{d}	154.34^{d}
RY	34.50^{c}	34.80^{c}	35.12^{c}	35.88^{c}	117.40^{c}
BY	15.30^{b}	15.71^{b}	16.11^{b}	16.95^{b}	258.76^{b}
CY	5.40^{a}	5.67^{a}	6.00^{a}	6.74^{a}	626.91^{a}
Corn	12.30^{e}	4.24^{e}	4.66^{e}	5.06^{f}	232.00^{e}

Mean ± SEM ($n = 6$). Figures in columns sharing the same superscript are not significantly different ($p < 0.05$).

Table 2
Particle density, bulk density, tap density, Carr index and porosity of starches from different botanical sources

Starch source	Particle density (g/cm^3)	Bulk density (g/cm^3)	Tap density (g/cm^3)	Carr index (%)	Porosity (%)
SY	1.39 ± 0.01^{b}	0.53 ± 0.01^{e}	0.82 ± 0.03^{e}	35.16 ± 0.01^{e}	61.63 ± 0.12^{e}
NY	1.43 ± 0.01^{d}	0.59 ± 0.03^{d}	0.85 ± 0.03^{d}	30.91 ± 0.01^{d}	58.70 ± 0.23^{d}
RY	1.53 ± 0.01^{c}	0.62 ± 0.02^{c}	0.90 ± 0.02^{c}	31.29 ± 0.12^{c}	56.73 ± 0.13^{c}
BY	1.37 ± 0.01^{b}	0.44 ± 0.01^{b}	0.63 ± 0.01^{b}	33.07 ± 0.02^{b}	68.07 ± 0.03^{b}
CY	1.42 ± 0.01^{a}	0.31 ± 0.01^{a}	0.58 ± 0.01^{a}	34.80 ± 0.03^{a}	78.07 ± 0.03^{a}
Corn	1.48 ± 0.01^{e}	0.46 ± 0.02^{b}	0.64 ± 0.01^{b}	29.03 ± 0.10^{f}	68.92 ± 0.03^{c}

Mean ± SEM ($n = 6$). Figures in columns sharing the same superscript are not significantly different ($p < 0.05$).

granular density of the starch powders would influence the compressibility since hard and dense granules are known to undergo poor compression and give compacts of high porosity. The bulkiness of the starch powders has significant implication on packaging: light, fluffy magnesium carbonate requires about five times the volume of container used for the heavy, denser form [24]. The fluidity of starch materials (expressed as Carr Index, CI) is shown in Table 2. The Carr index provides an indirect measure of material fluidity and the higher its value, the more cohesive the substance. Generally, materials with CI up to 16% indicate good flow behavior while those above 28% indicate cohesive or poor powder flow [9]. SY was found to be the most cohesive and corn starch (CS) the least (Table 2). All the yam starches studied had CI value above 30% thus indicating high cohesiveness and are not likely to improve the rheological properties of a poor flowing API. The density of the various starches showed no direct influence on the rate of paracetamol dissolution in this study; however, it gave an indication of the starch granule porosity. CY starch was the most porous while RY was the least porous. Porosity has been shown to have a direct effect on the rate of drug dissolution. Regression of dissolution rate (T_{80}) on porosity (%) showed a good correlation at both 2.5% and 10% w/w starch mucilage binders (Table 5).

The water binding capacity and swelling power of starches varied significantly among yam varieties studied (Table 3). CY starch powder showed the highest water binding capacity while RY and corn starch had the lowest. The differences in the hydration property may be due to difference in starch molecule polarity, normally a function of the inter-molecular forces including H-bonding, dipole-dipole and van der Waals forces [25]. At 95 °C CY starch had the highest swelling power while corn and BY starches had the least, however at lower temperatures SY had the highest and RY the least (Table 3). The low swelling power demonstrated by some of the starches is ascribable to their extensive and strongly bonded micellular structure. Highly associated starches with extensive and strongly bonded micellular structure are relatively resistant to swelling [26]. The observed lower swelling in starches with high amylose content is due to the amylose reinforcement of the internal network within the granules thus restricting swelling. High amylose starches are therefore poorer disintegrants because, following a wicking process of water into the microstructure, they do not swell enough to inactivate the interparticulate bonds in granules/tablets [27]. Rudnic et al. [28] opined that disintegrants work by wicking water into granule/tablet microstructure and by swelling, with optimal disintegration/de-aggregation being achieved by the combination of both actions. As a result, starches with higher swelling powers and water binding capacity, such as that from CY, would produce more rapid disintegration/de-aggregation and, hence, produce a faster dissolution of component drugs.

The moisture sorption profiles for the different starches at different equilibrium vapour pressures (Fig. 2) appear to follow the Freundlich model of monolayer adsorption [17]. Moisture adsorption increased generally with increase in vapour pressure (Table 4). Percent moisture sorbed ranged from 2.5% (at 11% RH) to over 50% (at 93% RH). The parameters of the power regression of x/m on% RH according to the Freundlich equation (Eq. (8)) are shown in Table 4. SY and NY had the fastest rate of moisture sorption ($K = 0.89\%^{-1}$ and $0.84\%^{-1}$, respectively), while RY ($K \approx 0.45\%^{-1}$) and CS ($K \approx 0.31\%^{-1}$) had the lowest (Table 4). For the starches studied, values of $\frac{1}{n}$ in the

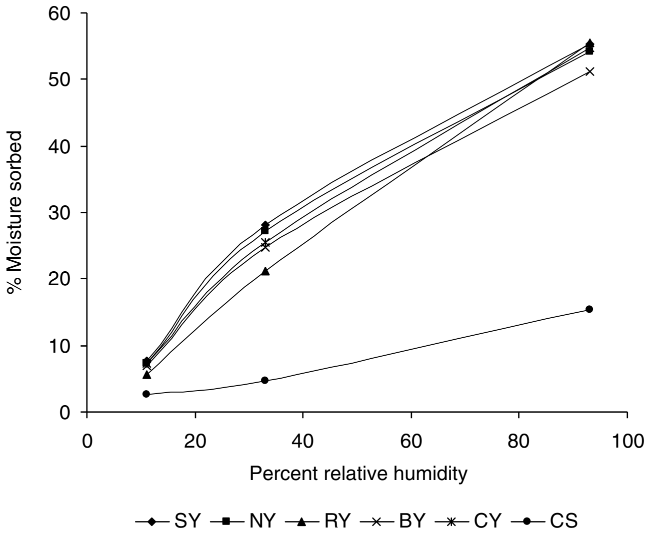

Fig. 2. Moisture sorption profile of yam and corn starch at 11%, 33% and 93% relative humidity.

Table 3
Swelling power and water binding capacity of starches from different botanical sources

Botanical Source	Water binding capacity (g)	Swelling power (%)		
		30 °C	60 °C	95 °C
SY	1.21 ± 0.01^{d}	141.51 ± 0.71^{d}	157.05 ± 0.65^{d}	840.05 ± 2.65^{c}
NY	1.10 ± 0.02^{d}	90.23 ± 0.51^{c}	101.10 ± 3.20^{c}	874.71 ± 1.40^{d}
RY	0.89 ± 0.01^{c}	89.90 ± 0.52^{c}	100.10 ± 1.30^{c}	831.31 ± 3.10^{c}
BY	1.49 ± 0.02^{b}	109.99 ± 2.01^{b}	113.95 ± 1.95^{b}	650.20 ± 5.90^{b}
CY	4.61 ± 0.03^{a}	125.11 ± 0.55^{a}	135.62 ± 2.62^{a}	1359.11 ± 8.51^{a}
Corn	0.87 ± 0.01^{e}	105.10 ± 1.32^{e}	115.23 ± 1.52^{b}	730.20 ± 2.53^{e}

Mean ± SEM ($n = 6$). Figures in columns sharing the same superscripts are not significantly different ($p < 0.05$).

Table 4
Parameters of the Power Regression of the mass of moisture per unit mass of powder (x/m) on % RH according to the Freundlich equation $\frac{x}{m} = kP^{\frac{1}{n}}$ (Eq. (8))

Starch source	*Freundlich (kinetic order, $\frac{1}{n}$)	*Moisture sorption rate constant, k ($\%^{-1}$ RH)	R^2
SY	0.932^b	0.893^e	0.972^d
NY	0.942^a	0.837^d	0.974^d
RY	1.072^c	0.452^c	0.995^c
BY	0.940^a	0.785^b	0.981^b
CY	0.944^a	0.818^a	0.985^a
Corn	0.841^d	0.305^f	0.959^e

Figures in columns sharing different superscript are significantly different at $p < 0.05$.

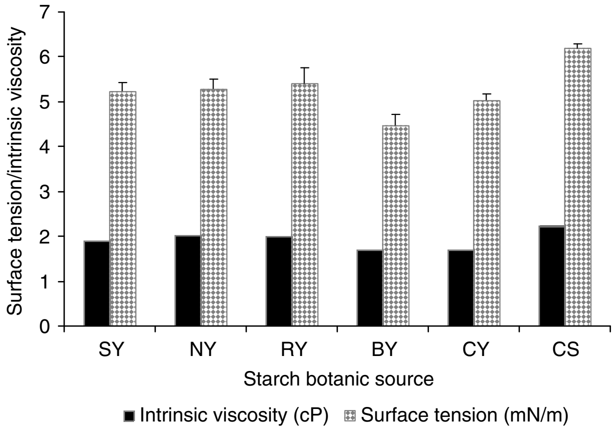

Fig. 3. Intrinsic viscosity and surface tension (10×) of yam starch and corn starch.

Freundlich equation (Eq. (8)), ranged from 0.84 for CS to 1.07 for RY starch. This indicates that the mechanism of moisture sorption fall generally in the anomalous transport model (exponent = 0.5 – 1.0), except for RY which falls into Super Case II diffusion (exponent ⩾ 1) [29]. Thus, the mechanism of moisture adsorption is a complex form dependent partly on residual porosity, vapour pressure and starch hydrophilicity. Generally, literature values of $\frac{1}{n}$ range from 0.3 to 0.5 ($n > 1$) [17]. Moisture sorption has been correlated with the dissolution of the Active Pharmaceutical Ingredient (API) from granule and tablet formulations [30]. Although other factors such as compact density (packing fraction) and nature and amount of lubricant would affect moisture permeability of tablets/granules, SY, NY and CY produced faster disintegration/de-aggregation of paracetamol granules than RY and CS starch due to their more hydrophilic nature.

The surface tension and viscosity of the yam starch mucilages (pastes) also varied significantly among the different starches studied (Fig. 3). Both the surface tension and viscosities of CS are significantly higher than those of the different yam starches. The rank order of starch mucilage viscosities is CS > NY > RY > SY > CY ⩾ BY while that of the surface tension is CS > RY > NY > SY > CY > BY. Previous report has shown that starch mucilage with high viscosity and surface tension produced slower rate of drug release relative to those with lower viscosity and surface tension values [10]. The surface tension and viscosity of a polymer are believed to be directly related to its molecular weight as the molecular weight (Mw) of a polymer approaches 2000–3000, the surface tension reaches within 1 dyne/cm (1 mN/m) at an infinite molecular weight and this can have significant effects on the rate of penetration of dissolution media [31]. Hence, the type of binder used would significantly influence the rate of paracetamol dissolution.

The correlation between key physical properties of starch powder or mucilage and the time for 80% paracetamol dissolution from formulated granules are shown in Table 5. As shown, the swelling power, specific surface area, powder porosity and water binding capacity of starches are negatively correlated with T_{80} with the relative strength of the correlation (R) being of the rank order porosity > specific surface area > water binding capacity > swelling power. On the other hand, mean particle diameter, intrinsic viscosity and surface tension of mucilage are positively correlated with T_{80}, with the strength of association in the rank order of mean diameter > intrinsic viscosity > mucilage surface tension. Thus, the higher the value of any parameter that is negatively correlated with T_{80}, the shorter the time for 80% dissolution and the faster the drug release from the granules. However higher values of the parameters which are positively correlated with T_{80} would result in a longer time for 80% dissolution and slower drug release from the granules. In this study gran-

Table 5
Parameters of the linear regression of dissolution rate ($T_{80\%}$) on various physical properties of starch powder and mucilage

Botanic Source-dependent physical properties	Regression of time for 80% paracetamol dissolution (T_{80}) on starch/mucilage properties					
	Granules formulated with 2.5% w/w mucilage binders			Granules formulated with 10% w/w mucilage binders		
	Slope	Intercept	Correlation coefficient (R)	Slope	Intercept	Correlation coefficient (R)
Mean diameter (μm)	0.066	1.570	0.868	0.165	2.153	0.943
Powder porosity (%)	−0.076	7.925	−0.748	−0.197	18.416	−0.846
Water binding Capacity (%)	−0.342	3.637	−0.604	−0.842	7.266	−0.650
Specific surface	−0.003	3.694	−0.638	−0.007	7.483	−0.715
Swelling power	−0.023	5.584	−0.590	−0.044	10.541	−0.484
Surface Tension	0.134	−3.778	0.561	0.411	−15.117	0.754
Intrinsic viscosity	3.645	−3.810	0.681	10.404	−13.735	0.851

Table 6
Dissolution time (T_{80}) for paracetamol granules formulated with 2.5% and 10% starch as binder

Starch source	Dissolution time ($T_{80\%}$) (min)	
	2.5% w/w	10% w/w
SY	2.80 ± 0.12^{f}	6.00 ± 0.12^{e}
NY	2.90 ± 0.10^{e}	6.00 ± 0.10^{e}
RY	4.50 ± 0.10^{d}	8.75 ± 0.11^{d}
BY	2.60 ± 0.08^{c}	4.00 ± 0.09^{c}
CY	2.20 ± 0.08^{b}	3.75 ± 0.09^{b}
Corn	4.55 ± 0.11^{a}	5.25 ± 0.10^{a}

Mean ± SEM ($n = 6$). Figures in columns sharing the same superscript are not significantly different ($p < 0.05$).

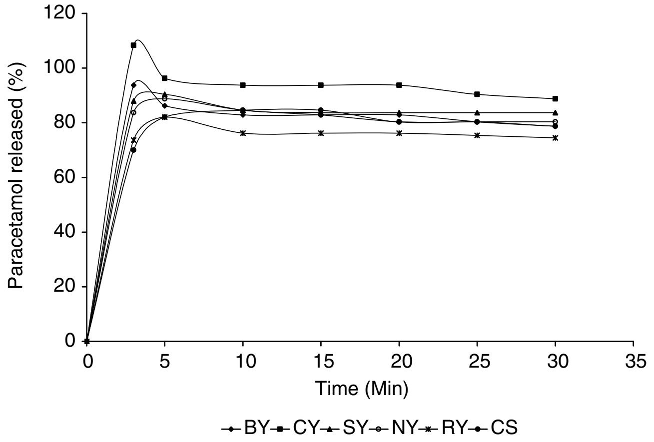

Fig. 4. Dissolution profiles of paracetamol granules formulated with 2.5% yam and corn starch as binders.

ules formulated with CY as binder had the shortest dissolution times while those formulated with RY took the longest time (Table 6; Fig. 4). The rate of paracetamol dissolution was also found to be directly dependent on the binder concentration, as granules formulated with 2.5% starch as binder had a shorter T_{80} than that with 10% starch mucilage binder. Generally, the literature reports that dissolution rate tends to decrease with increase in binder concentration [10,32,33]. At 2.5% binder concentration, all formulations with yam starch binders produced faster dissolution rates than granules formulated with official corn starch. However, at 10% w/w binder, RY, SY and NY, respectively, took longer time than CS to produce 80% dissolution (Table 6).

4. Conclusions

The physicochemical properties of yam starches have been found to be botanic source dependent. Apart from the potential effects of these properties on processability, homogeneity of content and physical characteristics of prepared granules, reasonable correlations have been established between these properties and a dissolution parameter: the time for 80% of drug in granules to go into solution (T_{80},). Generally, average powder diameter, mucilage surface tension and intrinsic viscosity are positively correlated with T_{80} with the strength of association being mean diameter > intrinsic viscosity > surface tension. At low concentration (2.5% w/w), effect of type of the binder on paracetamol dissolution was of the rank order CY > BY > SY > NY > RY > CS, respectively. However, the pattern was slightly different at high starch binder concentration (10% w/w): CY > BY > CS > SY ⩾ NY > RY, respectively. Hence, careful consideration of starch botanic source in starch binder selection is essential in order to obtain the required rapidity of dissolution while preserving other desirable physical properties of the granules. Generally, paracetamol dissolution was quite rapid from all the starch-based formulations ($T_{80} < 5$ min at 2.5% w/w binder and <9 min at 10% w/w binder).

Acknowledgements

The authors are grateful to the School of Graduate Studies and Research and the Biotechnology Centre, University of the West Indies (Mona Campus) for funding this research.

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