

Research Article

Comparative Evaluation of the Disintegrant Properties of Starches from Three Cultivars of *Dioscorea rotundata* (Poir)

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ABSTRACT

Dioscorea rotundata Poir starches from three cultivars (*Lagos*, *Giwa*, and *Sule*) were evaluated as exo-disintegrants (5 and 10%^{w/w}) in paracetamol tablet formulations to determine whether the similarity in their physicochemical and material properties translates to performance in tablet formulation. The tablets were prepared by wet granulation and were evaluated for compressional properties (Heckel equation), mechanical strength (crushing strength and friability), and drug release (disintegration and dissolution times). Plastic deformation occurred in all tablets with rank order for the onset of plastic deformation *Lagos*>*Giwa*>*Sule*. An increase in the concentration of disintegrants in the tablets led to a decrease in mean yield pressure, total relative precompression density, and relative density at low pressure, but an increase in relative density at zero pressure. The crushing strength and disintegration times of the tablets were dependent on the disintegrants' concentration. All tablets passed the disintegration test (≤ 15 min) with tablets containing the *Sule* cultivar producing the fastest disintegration ($p < 0.05$). Tablets containing 10% of the *Sule* cultivar had the fastest release of paracetamol ($t_{80} = 32.1$ min), though it failed the compendial standard for immediate release tablets ($t_{80} \leq 30$ min). Starches from the three cultivars despite their similar physicochemical and material properties exhibited different disintegrant properties and could find different applications as excipients in tablet formulations.

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INTRODUCTION

Starch remains one of the most widely used excipients as fillers, diluents, glidants, binders, and disintegrants in the manufacture of solid dosage forms. Starches obtained from different botanical sources have been shown to possess different functional attributes and physicochemical properties (Odeku, 2013). Among them are starches obtained from *Dioscorea species* Family Dioscoreaceae. The long history of local consumption of yams either cooked or processed among the various communities suggests a good safety profile and a high potential for regulatory acceptance (11TA, 2004; Udoh et al., 2005; Riley et al., 2006; Umar et al., 2006; Timothy and Bassey, 2009; Okunlola and Odeku, 2011; Bassey, 2017).

White yam, *Dioscorea rotundata* (Poir), starch has been shown to have superior disintegrant properties to corn starch when used as an intragranular disintegrant in Chloroquine Phosphate tablets (Okunlola and Odeku, 2008). However, more than twenty cultivars of *D. rotundata* have been identified in Nigeria with different local names depending on the area where they are grown (Odu et al., 2004). Previous studies on three cultivars of the widely cultivated *Dioscorea rotundata* viz; *Lagos*, *Giwa*, and *Sule*, have shown that starches obtained from the three cultivars had similar proximate, physicochemical and material properties, and functional properties suggest that they could be used interchangeably in tablet formulations (Ahmadu et al., 2018). However, the performance of starches from the different cultivars has not been evaluated in tablet formulations. Thus in the present study, the disintegrant properties of the

starches obtained from three cultivars of *D. rotundata* starches namely, *Lagos*, *Giwa*, and *Sule*, have been evaluated to determine whether the similarity in their physicochemical properties would translate to their performance in tablet formulations and if they could be used interchangeably as pharmaceutical excipients in tablet formulations.

MATERIALS AND METHODS

Materials

Paracetamol and polyvinylpyrrolidone (PVP) were gifts from Bond Chemicals Nig. Ltd (Awe, Nigeria), and lactose (DMV Veghel, Netherlands). Yam (*D. rotundata*) tubers from three different cultivars (*Giwa*, *Lagos*, and *Sule*), were harvested fresh from farms in Pmazi village in Bosso, Minna, Niger State, Nigeria. The starches from the three cultivars were extracted, dried, pulverised, screened, and stored away in airtight containers until required (Okunlola and Odeku, 2011; Ahmadu et al., 2018).

Preparation of paracetamol Tablets

Paracetamol granules (composed of paracetamol 70 %, lactose 20, 25 or 30 % based on batch, see Table 1) containing 0.0, 5.0, and 10.0 %^{w/w} of the starches as exo-disintegrants were prepared by wet granulation. Appropriate quantities of paracetamol and lactose were weighed, sieved and dry-mixed for 5 min in an Erweka AR400 planetary mixer and then moistened with granulating fluid (PVP- M.Wt. 30,000 solution, to produce 2 %^{w/w} of the binder in the final granulation). Massing continued for 5 min and the wet mass was granulated by passing it through a number 12 mesh sieve (1400 μm) manually. The granules were then dried in a hot air oven (Laboratory oven TT-9083, Techmel and Techmel, TX, USA) for 6 h at 50 °C and were then re-sieved through a number 16 mesh sieve (1000 μm).

The starches were then added to the granules before compression by mixing in a cubic mixer for 5 min. Granules (500 mg) were compressed into tablets using a Carver hydraulic hand press (Model C, Carver Inc, Menomonee Falls, Wisconsin, USA) fitted with a pressure gauge reading up to 2.5 metric tons. Compression was carried out using predetermined pressures and a dwell time of 30 s after lubricating the die (10.5 mm) and flat-faced punches with a 2 %^{w/v} dispersion of magnesium stearate in the ether: ethanol (1:1) before each compression. After ejection, to allow for elastic recovery and hardening the tablets were kept over silica gel for 24 hours.

Table 1. Composition of Tablet Formulations

Starch	Concentration (%)	Paracetamol (%)	Lactose (%)
	0	70	30
Lagos	5	70	25
	10	70	20
Giwa	5	70	25
	10	70	20
Sule	5	70	25
	10	70	20

Compressional properties

The compression properties of the paracetamol tablet formulations were analysed using the Heckel equation [$\ln(1/1 - \rho d)$] widely used in relating the relative density, ρd (Equation 1) of a powder bed during compression to the applied pressure, P (Odeku and Itiola, 1998).

$$\rho d = \frac{\text{Bulk density}}{\text{particle density}} \quad (1)$$

Values of A and K were obtained from the intercept and slope respectively. The mean yield pressure, P_y was obtained from the reciprocal of K , and the total precompression density ρa was obtained by applying the equation:

$$\rho a = 1 - e^{-A} \quad (2)$$

Values of relative density at low pressures, ρb were obtained by applying Equation 3:

$$\rho b = \rho a - \rho o \quad (3)$$

Where: ρo is the relative density at zero pressure measured using a liquid pycnometer (Odeku et al., 2005).

Crushing Strength

The crushing strength of the tablets was determined on 10 tablets per batch using a hardness tester (Model: EH 01500N, DBK Instruments, Mumbai, India).

Friability

The friability (%) of the tablets was determined on 20 tablets per batch using a DBK friabilator (DBK Instruments, Mumbai, India) operated at 25 rpm for 4 min.

Disintegration Time Test

The disintegration time, DT , of the tablets was determined on 6 tablets per batch in distilled water at 37 ± 0.5 °C using a Veego disintegration tester (Veego scientific devices, Mumbai, Maharashtra, India).

Disintegration Efficiency Ratio (DER)

The DER was obtained from the equation below:

$$\left(\frac{\text{Crushing strength/Friability}}{\text{Disintegration time}} \right) \quad (4)$$

Dissolution Test

The dissolution times of the tablets were determined on 3 tablets of equivalent weight per batch at 37 ± 0.5 °C in 900 mL of simulated gastric fluid (0.1 N hydrochloric acid, pH 1.2) at 100 rpm using an Erweka dissolution rate apparatus (Erweka GmbH, Langen, Germany). The tablets were placed in a rotating basket, and 5 mL of the samples were withdrawn at 2, 5, 10, 15, 20, 30, and 40 min, and replaced with equal amounts of fresh medium. The sample was diluted and the amounts of paracetamol released were determined using a UV spectrophotometer (UV spectrophotometer, Pye Unicam, UK) at the wavelength of 249 nm.

The dissolution profiles of the paracetamol tablets containing the different disintegrants were then subjected to measures of Difference, f_1 , and similarity, f_2 .

Statistical analysis

Determinations were carried out in triplicate (except friability and disintegration tests) and statistical analysis was done to evaluate the disintegrant activity of the starches using two-way Analysis of Variance (ANOVA) on a computer software GraphPad Prism® 5 (GraphPad Software Inc., San Diego, USA). The individual differences between the samples were compared using the Kruskal–Wallis test. At 95% confidence interval, p values ≤ 0.05 (that is 5%) were considered significant.

RESULTS AND DISCUSSION

Compression properties of the tablets

The Heckel plots of the paracetamol tablets prepared with *D. rotundata* starches from the different cultivars as disintegrants are shown in Figure 1 while the parameters derived from the Heckel plots are presented in Table 2. The plots were linear with $r \geq 0.998$, which is indicative of plastic deformation. The mean yield pressure, P_y , an inverse relation of the ability of a material to deform plastically under pressure (Odeku and Itiola, 1998; Akin-Ajani et al., 2014), was in the rank order of *Sule* > *Giwa* > *Lagos* at all concentrations of the disintegrants.

This indicates that starch from the *Lagos* cultivar exhibited the fastest onset of plastic deformation while the *Sule* cultivar had the slowest onset. Lower P_y values indicate a faster onset of plasticity at lower pressures. Tablets containing 10 % w/w disintegrants exhibited a faster onset of plastic deformation than those containing 5% w/w disintegrants and are likely to deform more readily at low pressures on a high-speed tablet machine (Odeku and Itiola, 1998). An increase in the concentration of disintegrants in the

paracetamol tablets also led to a decrease in values of total relative precompression density, ρ_a , and relative density at low pressure, ρ_b , but an increase in values of relative density at zero pressure, ρ_0 . Higher values of ρ_a and ρ_b indicate a greater degree of packing at zero and low pressures respectively. Thus, paracetamol tablets with 5 % w/w disintegrants would have a greater degree of packing at zero and low pressures than those containing 10 % w/w disintegrants.

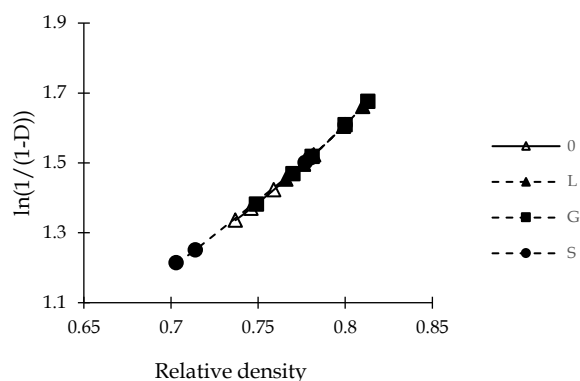


Fig. 1. Heckel plots of paracetamol formulation containing 0 and 5 %w/w of the yam starch (*Lagos*, *L*; *Giwa*, *G* & *Sule*, *S*) disintegrants.

Mechanical properties of the tablets

The plots of crushing strength and friability versus relative density of the paracetamol tablets are shown in Figures 2 and 3, respectively, while the parameters at the relative density of 0.85 are presented in Table 3. The crushing strength of the tablets increased with an increase in relative density while the friability decreased with tablets without disintegrants exhibiting higher crushing strengths and lower friability than those with disintegrants at lower relative densities. The rank order of the crushing strength of the tablets with 5 % w/w disintegrants was *Lagos* > *Giwa* > *Sule* while those with 10 % w/w disintegrants were inverse. The crushing strength of the tablets was concentration-dependent, although there was no significant ($p > 0.05$) difference between the values.

The ranking for the friability of the tablets with 5 % w/w disintegrant was *Lagos* < *Sule* < *Giwa* while 10 % w/w disintegrant was *Giwa* < *Lagos* < *Sule*, with tablets containing 10 % w/w disintegrants showing lower values except for tablets containing *Giwa*. However, the tablets generally failed the friability test as most had values > 1 % (USP, 2016). This is in line with previous studies that have shown starch disintegrants to weaken the tablet structure at relatively high concentrations (Odeku and Alabi, 2007; Akin-Ajani et al., 2016).

Table 2. Parameters derived from Heckel plots of paracetamol tablets containing *Dioscorea* starches as disintegrant

Starch	Concentration (%)	ρ_0	P_y	ρ_a	ρ_b
Lagos	5.0	0.312	246.10	0.896	0.584
	10.0	0.321	169.67	0.872	0.551
Giwa	5.0	0.320	277.78	0.892	0.572
	10.0	0.328	185.29	0.891	0.563
Sule	5.0	0.356	350.70	0.922	0.566
	10.0	0.379	243.82	0.890	0.511

Table 3. Mechanical and release properties of the paracetamol tablets containing yam starch disintegrants at a relative density of 0.85

Starch	Concentration (%)	Crushing strength (N)	Friability (%)	Disintegration time (min)	DER [(Cs/Fr)/DT]	t_{50} (min)	t_{80} (min)
Lagos	0.0	400.0	0.00	1.28	312.5	15.2	33.4
	5.0	314.0	1.60	2.76	71.1	18.1	36.5
	10.0	119.0	1.01	1.46	80.7	16.1	34.0
Giwa	5.0	258.0	0.95	1.66	163.6	16.5	33.4
	10.0	183.0	1.10	1.55	107.3	16.3	35.1
Sule	5.0	232.0	1.33	0.94	185.6	16.8	35.3
	10.0	235.0	0.49	1.33	360.6	15.5	32.1

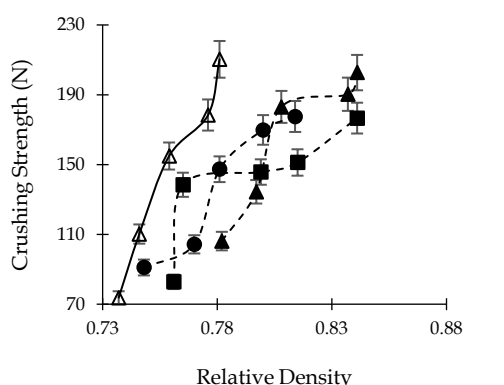


Fig. 2. The plots of crushing strength versus relative density of paracetamol tablets containing 0 and 10 %w/w of the yam starch (Lagos, L; Giwa, G, and Sule, S) disintegrants.

Drug Release properties of the tablets

The disintegration time of the tablets generally increased with an increase in relative density as shown in Figure 4, but generally decreased with an increase in disintegrant concentration (Table 3). All the tablets passed the disintegration time test for uncoated tablets with values all lower than the stipulated ≤ 15 min (USP, 2016). The disintegration times of the tablets decreased with an increase in the concentration of starch disintegrant except for the *Sule* cultivar where the 5 % w/w disintegrant produced faster disintegration than the 10 % w/w although there was no significant difference between the disintegration times. However, only tablets

containing the *Sule* cultivar exhibited improved disintegrant activity as none of the other tablets exhibited lower disintegration times than the tablet without disintegrant. Paracetamol tablets containing the 5% *Sule* cultivar exhibited the fastest disintegration time ($p < 0.05$). Swelling, wicking, strain recovery, interruption of particle-particle bonds, and the heat of interaction are some of the mechanisms of disintegration (Desai et al., 2016) with swelling cited as the basis for disintegrant effects of most starches (Guyot-Hermann and Ringard, 1981).

Sule cultivar, which exhibited the smallest particle size and lowest amylose content (Ahmadu et al., 2018), showed better disintegrant properties than *Giwa* and *Lagos*. The disintegration mechanism that played out in tablets with the *Sule* cultivar, therefore, appears to be a result of granule diameter and fluid penetration. Fluid penetration could be through wicking; or as a result of the creation of repulsive forces, i.e. simple destruction of hydrogen bonds or the destruction of capillary cohesive forces; or a combination of both including swelling (Desai et al., 2016; Okekunle et al., 2020). Studies have shown that no single mechanism is responsible for the action of most disintegrants and tablet porosity plays a more important role than swelling as tablets having disintegrants that do not swell performed similarly to tablets having disintegrants that swell (Guyot-Hermann and Ringard, 1981; Okekunle et al., 2020).

Table 4. Measures of difference, f_1 , and similarity, f_2 of the dissolution profiles of the paracetamol tablets.

Tablet with	Tablets compared with	f_1	f_2
Lagos	5.0	0.0	13.77
	10.0	0.0	3.63
Giwa	5.0	0.0	7.29
	10.0	0.0	3.92
Sule	5.0	0.0	5.29
	10.0	0.0	3.90
Lagos	10.0	Lagos 5.0	12.33
Giwa	5.0	Lagos 5.0	13.71
	10.0	Lagos 5.0	11.99
Sule	5.0	Lagos 5.0	12.60
	10.0	Lagos 5.0	19.67
Giwa	5.0	Lagos 10.0	4.72
	10.0	Lagos 10.0	3.40
Sule	5.0	Lagos 10.0	5.46
	10.0	Lagos 10.0	7.08
Giwa	10.0	Giwa 5.0	4.95
Sule	5.0	Giwa 5.0	6.40
	10.0	Giwa 5.0	8.89
Sule	5.0	Giwa 10.0	2.40
	10.0	Giwa 10.0	6.86
Sule	10.0	Sule 5.0	6.28
			72.88

The disintegrant efficiency ratio (DER) generally increased as the concentration of disintegrants increased with the rank order of *Sule* > *Giwa* > *Lagos*. This indicated that paracetamol tablets containing *Sule* as disintegrant had a better balance of mechanical to disintegrant properties than the other cultivars.

The plots of % paracetamol released over time are shown in Figure 5 and the dissolution times (t_{50} and t_{80} , i.e. time taken to release 50 and 80% of the drug respectively) are presented in Table 2. The results showed that none of the tablets released greater than 80% of paracetamol in 30 min. The tablets containing 10 % w/w of the *Sule* cultivar as disintegrants had the highest release (t_{80} = 32.1 min) of paracetamol while tablets containing 5 % w/w of the *Lagos* cultivar as disintegrant had the slowest release.

The dissolution profiles of the paracetamol tablets containing the different disintegrants were subjected to measures of difference, f_1 , and similarity, f_2 (Table 4). The factor, f_1 , is the average percentage (%) difference over all time points in the amount dissolved by the test brand as compared to the reference brand. The f_1 value is zero when the test and the reference profiles are identical and increase proportionally with the dissimilarity between the two profiles (Kassaye and Genete, 2013).

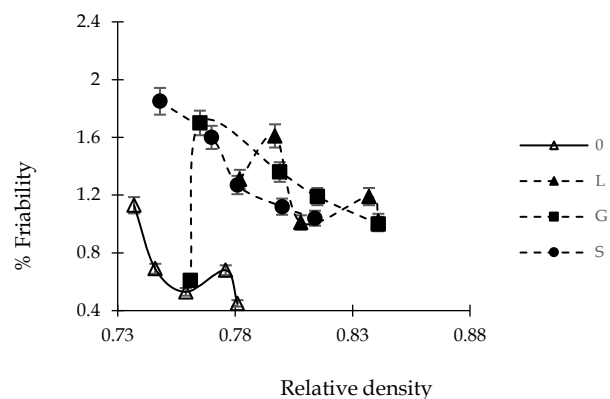


Fig. 3. The plots of % friability versus relative density of paracetamol tablets containing 0 and 10 % w/w of the yam starch (*Lagos*, L; *Giwa*, G & *Sule*, S) disintegrants.

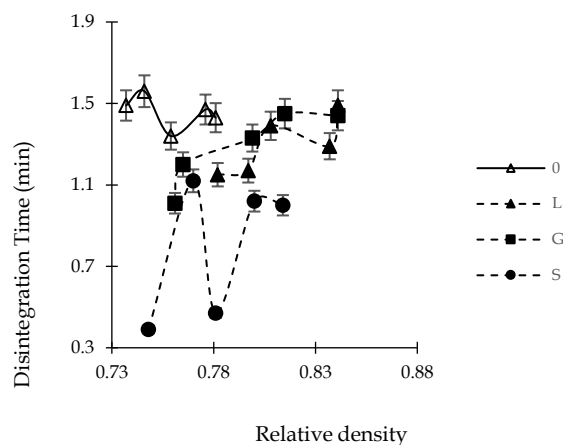


Fig 4. The plots of disintegration time versus relative density of paracetamol tablets containing 0 and 10 % w/w of the yam starch (*Lagos*, L; *Giwa*, G & *Sule*, S) disintegrants.

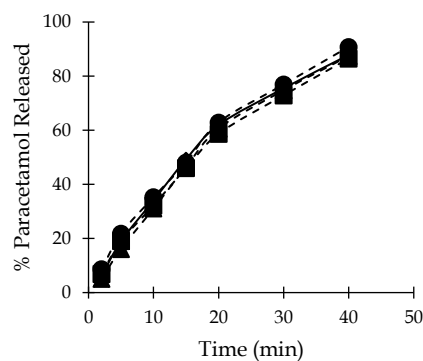


Fig 5. The plots of % paracetamol released versus time of paracetamol tablets containing 0 and 10 % w/w of the yam starch (*Lagos*, L; *Giwa*, G & *Sule*, S) disintegrants.

Acceptable f_1 values are between 0 and 15, and f_1 value over 15 indicates significant dissimilarity (Santos Júnior et al., 2014). The similarity factor (f_2) is a measurement of the similarity in the percentage (%) dissolution between two curves. Values of f_2 > 50 i.e. 50 - 100 indicate similarity or equivalence of the two dissolution profiles and values of 100 indicate

identical profiles (Moore and Flanner, 1996; Akin-Ajani et al., 2020). All tablet formulations showed the similarity of dissolution profiles with the tablet formulations of *Lagos* 5 % w/w and tablets with 10 % w/w *Sule* showed the least similarity while tablets with 10 % w/w *Giwa* and tablets with 5 % w/w *Sule* showed the highest similarity.

Though the three *D. rotundata* cultivars exhibited similar physicochemical and material properties (Ahmadu et al., 2018), this similarity did not translate to similar performance as disintegrants in the tablet formulations.

CONCLUSIONS

The starches of the three *Dioscorea rotundata* cultivars performed differently in tablet formulation despite the similarity in their physicochemical and material properties. Plastic deformation occurred similarly for all the tablets. However, the onset of plastic deformation was faster in tablets with 10 % w/w *Lagos* cultivar. Tablets with the 5 % w/w *Lagos* cultivar had the highest crushing strength, while the least friable were tablets with 10 % w/w *Sule* disintegrant. All the tablets passed the disintegration time test for uncoated tablets with tablets containing the *Sule* cultivar exhibiting the fastest disintegration and the highest DER. The highest release of paracetamol was from tablets with 10 % w/w *Sule* cultivar with all tablet formulations showing similarity in dissolution profiles. Thus, starches from the different cultivars of *D. rotundata* could find different applications as pharmaceutical excipients in tablet formulations.

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