RESEARCH ARTICLE

Evaluation of the disintegrant properties of native and modified forms of fonio and sweet potato starches

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The effects of acid modification on the disintegrant properties of two native starches obtained from Digitaria exilis (white fonio) and Ipomea batatas (sweet potato) were evaluated in comparison with official corn starch in paracetamol tablet formulations. The starches were extracted from grains of white fonio and tubers of sweet potato, and modified by acid hydrolysis using 6% w/w hydrochloric acid for 48 h. The native and modified forms of the starches were employed as exo-disintegrants in paracetamol tablet formulations at concentrations of 2.5, 5.0, and 10.0% w/w. The disintegrant properties were assessed using crushing strength (C_S), friability (F_r), disintegration time (D_T), disintegrant efficiency ratio (DER), and the dimensionless quantity DER_c. The results showed that crushing strength and friability of the tablets appeared to depend on the type, concentration, and nature of disintegrant used. Disintegration time generally decreased with increase in disintegrant concentration and the values complied with the pharmacopoeial standard for uncoated tablets (≤15 min). Tablets containing acid modified starches showed longer disintegration times than those containing the native starches although there were no significant differences ($p > 0.05$) in the values. Acid modification generally increased the disintegration efficiency ratio (DER) of the formulations while the values of DER_c indicated that sweet potato starch would be the most efficient disintegrant with greater ability to enhance the balance between the mechanical and disintegration properties of the tablet. Thus, the experimental starches compared well with corn starch as disintegrants and could be useful for commercial tablet formulations.

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1 Introduction

Disintegrants are substances that when added to tablet formulations, ensure that the tablets break up into small particles on contact with fluid in the gastro-intestinal tract to facilitate dissolution. Several mechanisms that have been proposed to rationalize the action of disintegrants are porosity, capillary action, water absorption, swelling, gas release, melting, enzymatic action, heat of wetting, and lysis of physicochemical bonds [1, 2]. Disintegrants are incorporated either intra-granularly (endo-disintegrants), extra-granularly (exo-disintegrants), or a combination of both (endo-exo-disintegrants) [3]. The mode of incorporation of disintegrants in the formulation has been shown to determine their effectiveness [4–6].

Starches are one of the oldest disintegrants used in tablet formulations with corn starch being a traditional disintegrant. Starches obtained from various plant sources such as cocoyam, breadfruit, pigeon pea, plantain, millet, and yam in their native or modified forms, have been used as disintegrants with each behaving differently depending on the botanical source and physicochemical properties of the starches [3, 7–9]. Researchers have continued to explore other sources of starch disintegrants to meet formulation needs.

A recent study has shown the material and compaction properties of native and acid modified forms of fonio starch

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Abbreviations: DER, disintegration efficiency ratio obtained from the grains of *Digitaria exilis* Stapf. (family Poaceae, local name – "*Acha*") and sweet potato starch obtained from the tubers of *Ipomea batatas* Lam. (family Convolvulacae, local name – "*Odunkun*") [10]. The starches were shown to exhibit low levels of protein, fat, and crude fibre (<1 % each) indicating a high level purity (98.6–98.9 % w/w) comparable with official corn starch. The native forms of fonio and sweet potato starches were shown to contain 24 and 28 % amylose, respectively [10]. However, acid modification using hydrochloric acid for 48 h resulted in starches with increased solubility and relative crystallinity but decreased swelling properties. The amylose content also decreased significantly ($p < 0.05$) to 15 and 16 % respectively, for fonio and sweet potato starches, indicating the potential usefulness of the starches as disintegrants in tablet formulations.

Thus in the present study, the disintegrant properties of the native and acid modified forms of fonio and sweet potato starches have been evaluated in paracetamol tablet formulations in comparison to official corn starch. The starches were incorporated extra-granularly into paracetamol tablet formulation and the crushing strength, friability, and disintegration times were evaluated. The disintegrant efficiency ratio, DER, and the dimensionless quantities, T_C and T_N, which have been used to describe the activities and efficiency of different disintegrants in formulation in comparison to the standard/control disintegrant, was used to compare the activity of the disintegrants [11, 12]. These quantities permit direct comparison of trends in tablet behavior with compressional force or any other variable affecting disintegration time [11]. While T_C measures the disintegrant efficiency in comparison to the standard disintegrant, T_N measures the disintegrant efficiency within a batch, *i.e.*, tablets with different relative densities. In addition, T_C gives a clear indication of disintegrant performance with respect to variable (s) being tested. Thus, in the present study, the dimensionless quantity, T_C, redefined as DER_C [12] was used to evaluate the disintegrant efficiency of the experimental starches in comparison to the standard disintegrant at the same concentration and relative density.

2 Materials and methods

2.1 Materials

The materials used are: paracetamol BP (Neimeith Nig. Plc), polyvinylpyrrolidone (Bond Chemical Nigeria Ltd, Ibadan, Nigeria), grains of white fonio (purchased from a local market in Samaru-Zaria, Nigeria) and tubers of sweet potato (purchased from a local farm in Offa, Nigeria). The extraction of the starches from the relevant plant parts has been described by Akin-Ajani et al [10].

2.2 Method

2.2.1 Acid modification of starches

Acid hydrolysis was done at a steeping time of 48 h without stirring at room temperature using the method described by Akin-Ajani et al [10]. The starch obtained was passed through a 125 μm mesh sieve and stored in an airtight container.

2.2.2 Preparation of granules

Paracetamol granules (250 g) were prepared using 3 % w/w polyvinylpyrrolidone, PVP (MW = 40 000) as binder. The required amount of paracetamol was moistened with the binder solution and the wet mass was screened using a number 12 mesh sieve (1400 μm), dried at 60°C for 6 h in a hot air oven and then screened using a number 16 mesh sieve (1000 μm). The required quantity of starch (2.5, 5.0, and 10.0 % w/w) was then added to a known quantity of granules in a bottle and mixed using a rotomixer (VSF3843C Forster equipment Co. Ltd, Whetstone, Leicester, England) for 10 min.

Quantities of 500 ± 10 mg of granules (500–1000 μm) were compressed using pre-determined pressures to produce tablets which on measurement gave a thickness 4.95 ± 0.3 mm at zero porosity as calculated from particle density values.

2.2.3 Density determination

The true density of the granules was determined by liquid pycnometer method with xylene as the displacement fluid. The bulk density of the granules at zero pressure (loose density) was determined by pouring the granules at an angle of 45° through a funnel into a glass measuring cylinder with a diameter of 12 mm and a volume of 10 mL [13]. The relative density of the tablets at zero pressure, ρ_o, was obtained from the ratio of its loose bulk density to its particle density. Determinations were done in quadruplicate.

2.2.4 Crushing strength test

The crushing strength of the tablets was determined using a hardness tester (Tester Model: EH 01500N, DBK Instruments, Mumbai, India). The tablet was placed between the plates of the tester and the knob screwed until there was enough pressure to cause the tablets to split cleanly into two halves without sign of lamination and the force required to break the tablet was obtained. Determinations were done in quadruplicate.

2.2.5 Friability test

The friability (%) of the tablets was determined using a DBK friabilator (DBK Instruments). Ten tablets were weighed and placed in the friabliator operated at 25 rpm for 4 min. Determinations were done in quadruplicate.

2.2.6 Disintegration time test

The disintegration time test of the tablets was determined in distilled water at 37 ± 0.5°C using a DBK disintegration tester (DBK Instruments). Determinations were done in quadruplicate.

2.2.7 Disintegration efficiency ratio (DER)

The DER, a measure of the balance between mechanical and disintegrant property of tablets, was obtained using the formula

$$\mathrm{DER} = \frac{(C_a/F_r)}{D_T} \quad (1)$$

where C_s is crushing strength, F_r is friability, and D_T is disintegration time.

The dimensionless disintegration quantity, DER_c, was obtained using the formula

$$\mathrm{DER}_c = \frac{\mathrm{DER}_{sample}}{\mathrm{DER}_{control}} \quad (2)$$

where DER_{sample} is the DER of tablet containing the experimental disintegrant (*i.e.*, fonio or sweet potato starch) at a given concentration and relative density; and $\mathrm{DER}_{control}$ is the DER of the tablet containing the standard disintegrant (corn starch) at the same concentration and relative density. Value of $\mathrm{DER}_c > 1$ indicates that the DER of the experimental starch is better than that of the standard disintegrant [12].

2.2.8 Statistical analysis

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). Kruskal–Wallis test was employed to compare the individual differences between the samples. At 95% confidence interval, *p* values greater than 0.05 (that is 5%) were considered not significant.

3 Results and discussion

The plots of crushing strength (C_s) and friability (F_r) versus relative density, ρ_d, are shown in Figs 1 and 2 respectively, while the C_s, and F_r values of paracetamol tablets at relative density of 0.90, which is representative for commercial tablets, are presented in Table 1. The results showed that crushing strength and friability of the tablet did not show a clear-cut pattern. The values appeared to depend on the type and concentration of starch disintegrant used. Starch disintegrants have been shown to weaken the tablet structure at relatively high concentrations [8]. The crushing strength of the tablets containing acid modified starches was generally higher than those containing the native starches except sweet potato which had lower values. Acid modified starches have been shown to be more crystalline in nature. Acid hydrolysis has been shown to result in the erosion of the amorphous regions of the starch granules and a closer packing of the crystalline regions [10, 14]. This results in increased intermolecular forces leading to more ordered arrangement of the starch granules [15]. The concentration of disintegrant

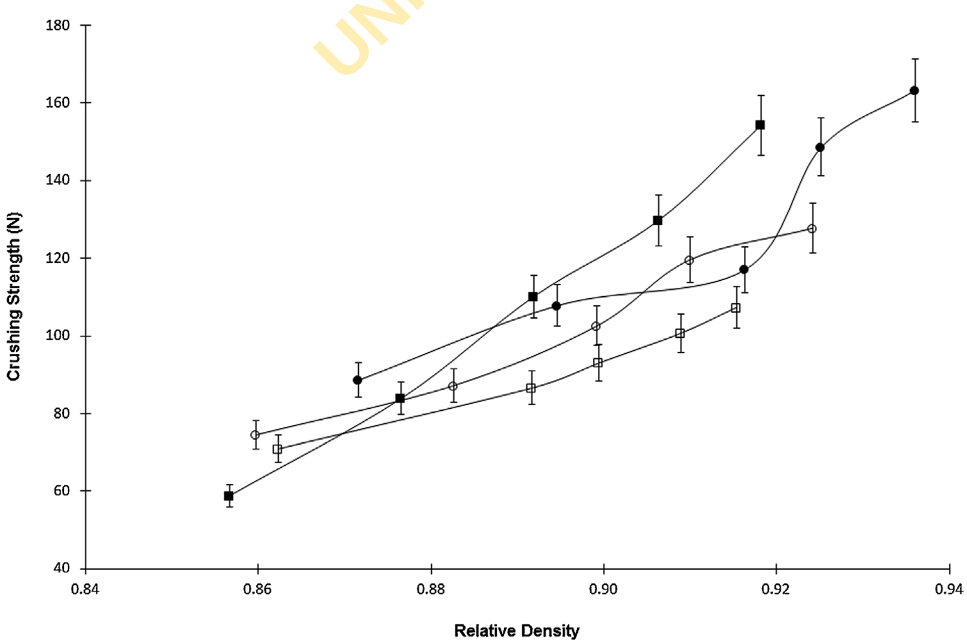

Figure 1. Representative Plots of crushing strength versus relative density for paracetamol tablets formulated with 2.5% w/w native (open) and acid-modified (closed). ●, corn; ■, fonio starches.

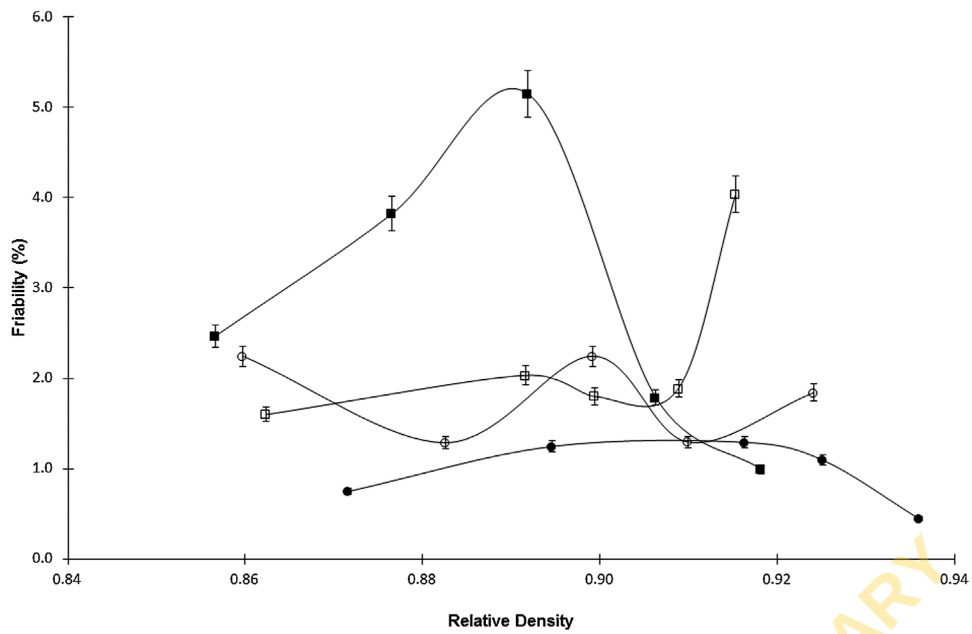

Figure 2. Representative plots of friability versus relative density for paracetamol tablets formulated with 2.5% w/w native (open) and acid-modified (closed). ●, corn; ■, fonio starches.

appeared to have little or no effect on friability although tablets containing modified starches generally had lower friability ($p < 0.05$) than those containing native starches except for fonio starch which had higher values. The rankings for crushing strength was corn > sweet potato > fonio for native starch and corn > fonio > sweet potato for modified starch, while the ranking for friability was fonio > corn > sweet potato for both native and modified starches. Thus, the mechanical properties of the tablets appear to depend on the type and nature of the disintegrant.

The plots of disintegration time, D_T, versus relative density, ρ_d, of paracetamol tablet formulations are shown in Fig. 3 while the D_T and disintegration efficiency ratio, DER, of the starches at relative density of 0.90 are presented in Table 1. The result showed that the disintegration time generally decreased with increase in the concentration of the

Table 1. Values of crushing strength (C_s), friability (F_r), disintegration time (DT), and DER [(C_s/F_r)/DT ratio] for paracetamol tablets containing starch disintegrants at relative density 0.90

Nature of disintegrant	Form	Starch concentration (% w/w)	C_s (N)	F_r (%)	DT (min)	DER
		0.0	114.1	14.46	58.24	0.27
Fonio	Native	2.5	94.8	2.41	4.93	14.97
		5.0	105.7	1.88	1.12	60.12
		10.0	106.0	1.89	0.82	100.71
	Modified	2.5	122.9	2.56	8.84	5.43
		5.0	100.3	4.85	4.02	11.83
		10.0	101.9	1.56	1.21	54.98
Sweet potato	Native	2.5	130.5	0.84	1.98	104.41
		5.0	139.1	1.05	0.72	214.96
		10.0	121.8	1.00	0.88	154.17
	Modified	2.5	102.5	0.60	5.14	44.65
		5.0	134.5	0.73	2.59	310.96
		10.0	81.3	0.66	0.69	179.44
Corn	Native	2.5	106.6	1.76	5.91	14.94
		5.0	126.2	1.23	1.09	96.55
		10.0	124.3	1.89	0.86	91.28
	Modified	2.5	115.3	0.98	12.40	14.45
		5.0	122.2	0.70	1.26	300.41
		10.0	146.5	0.65	0.97	230.90

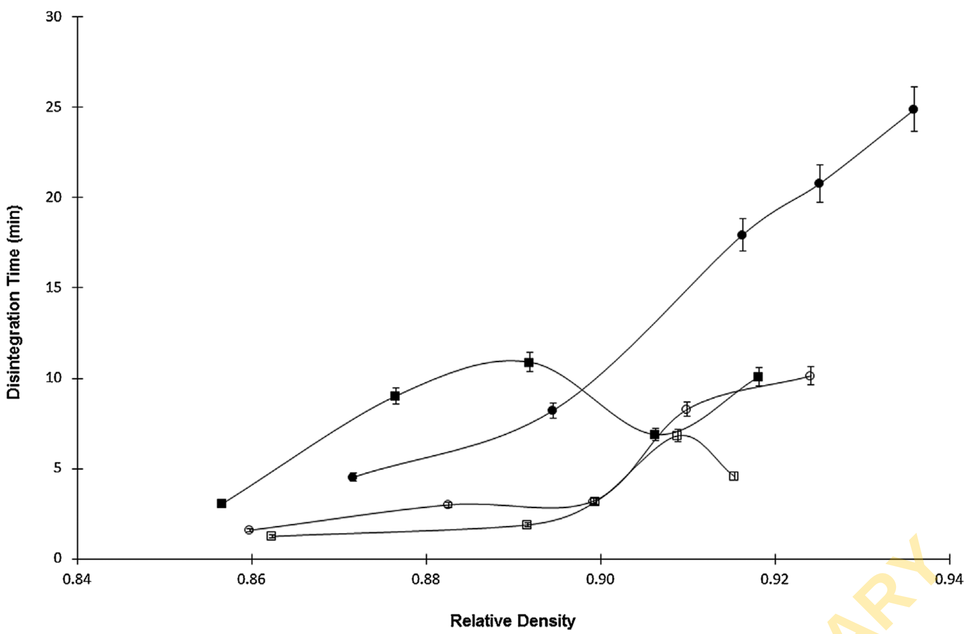

Figure 3. Representative plots of disintegration time versus relative density for paracetamol tablets formulated with 2.5% w/w native (open) and acid-modified (closed). ●, corn; ■, fonio starches.

starch disintegrant with tablets containing the acid modified starches showing higher values although there were no significant differences ($p > 0.05$) in the values. This could be due to the lower swelling and lower amylose content of the acid modified starches [10]. Amylose has been shown to have disintegrant activity [1], and since acid hydrolysis reduced the amylose content, the modified starch showed higher disintegration time. However, all tablets complied with the British Pharmacopoeia (BP) requirement on disintegration of uncoated tablets ($D_T \leq 15$ min) at all starch concentrations. Furthermore, as the concentration of starch disintegrant increased from 2.5 to 10.0% w/w, D_T of the tablets decreased, which is in consonance with previous results [9, 14]. The ranking for D_T was sweet potato < fonio < corn, suggesting that the two experimental starches could be better disintegrants than official corn starch.

Table 2. DERc for paracetamol tablets containing starch disintegrants at relative density of 0.90

Nature of disintegrant	Form	Concentration (%)	DER_c
Fonio	Native	2.5	1.003
		5.0	0.623
		10.0	1.103
	Modified	2.5	0.376
		5.0	0.039
		10.0	0.238
Sweet potato	Native	2.5	6.989
		5.0	2.226
		10.0	1.689
	Modified	2.5	3.090
		5.0	1.035
		10.0	0.777

The result also showed that DER generally increased with disintegrant concentration indicating that the balance between mechanical and disintegrant properties improved as disintegrant concentration increased. The ranking for DER was sweet potato > corn > fonio. Fonio had the lowest DER suggesting that increasing the concentration of fonio starch disintegrant resulted in weaker tablet and less balance between the strength and disintegration time of the tablets. Acid modification generally increased the disintegration efficiency ratio (DER) with the tablets containing modified starches having higher DER values than those containing the native starches except for fonio starch.

The values of the dimensionless quantity, DER_c, are presented in Table 2. DER_c generally decreased with increase in disintegrant concentration indicating that the disintegrants were more efficient at lower concentrations. Tablets containing the native starches had higher DER_c than those containing the modified starches suggesting the native starches are better disintegrants. The DER_c values indicate that the most efficient disintegrant showing the best balance between mechanical and disintegrant properties was sweet potato starch at concentration of 2.5% w/w with DER_c values 6.989 and 3.090 for native and modified forms, respectively. This implies that native sweet potato starch disintegrant was about seven times more efficient than corn starch and the modified form about three times more efficient than corn starch. Conversely, the DER_c for tablets containing 2.5% w/w fonio starch was 1.003 and 0.376 for native and modified forms, respectively. This implies that native fonio starch disintegrant had the same disintegrant activity as corn starch but the modified form had only 37.6 % activity of corn starch.

4 Conclusion

The results showed that tablets containing acid modified starches generally had higher crushing strength and disintegration time but lower friability (F_r) than tablets containing the native starches. The disintegration time of the tablets generally decreased with increase in concentration of disintegrant. Tablets containing acid modified starches had longer disintegration times than tablets containing native starches. Acid modification generally increased the disintegration efficiency ratio (DER) of the formulations thus improving the balance between the mechanical and disintegration properties. The DER_c indicated that sweet potato starch would be the most efficient disintegrant with greater ability to enhance the balance between the mechanical and disintegration properties of the tablet than fonio starch which exhibited similar property with corn starch. Thus, the experimental starches compared well with corn starch as disintegrants and could be useful for commercial tablet formulations.

The authors have declared no conflict of interest.

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