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Effects of Pigeon Pea and Plantain Starches on the Compressional, Mechanical, and Disintegration Properties of Paracetamol Tablets

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ABSTRACT A study has been made of the effects of pigeon pea starch obtained from the plant *Cajanus cajan* (L) Millisp. (family Fabaceae) and plantain starch obtained from the unripe fruit of *Musa paradisiaca* L. (family Musaceae) on the compressional, mechanical, and disintegration properties of paracetamol tablets in comparison with official corn starch BP. Analysis of compressional properties was done by using density measurements, and the Heckel and Kawakita equations, whereas the mechanical properties of the tablets were evaluated by using tensile strength (T—a measure of bond strength) and brittle fracture index (BFI—a measure of lamination tendency). The ranking for the mean yield pressure, P_y , for the formulations containing the different starches was generally corn < pigeon pea < plantain starch while the ranking for P_k , an inverse measure of the amount of plasticity, was pigeon pea < plantain < corn starch, which indicated that formulations containing corn starch generally exhibited the fastest onset of plastic deformation, whereas those formulations containing pigeon pea starch exhibited the highest amount of plastic deformation during tableting. The tensile strength of the tablets increased with increase in concentration of the starches while the Brittle Fracture Index decreased. The ranking for T was pigeon pea > plantain > corn starch while the ranking for BFI was corn > plantain > pigeon pea starch. The bonding capacity of the formulations was in general agreement with the tensile strength results. The disintegration time (DT) of the formulation increased with concentration of plantain and corn starches but decreased with concentration of pigeon pea starch. The general ranking of DT values was plantain < pigeon pea < corn starch. Notably, formulations containing pigeon pea starch exhibited the highest bond strength and lowest brittleness, suggesting the usefulness of pigeon pea starch in producing strong tablets with minimal lamination tendency. Plantain starch, on the other hand, would be more useful where faster disintegration of tablet is desired. The results show that the starches could be useful in various formulations depending on the intended use of the tablets with the implication that the experimental starches can be developed for commercial purposes.

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INTRODUCTION

Starch is one of the most widely used excipients in the manufacture of solid dosage forms probably due to its abundance, relative cheapness, and inertness. In recent times, a lot of efforts have been expended on the development of new starches from different botanical sources as pharmaceutical excipients. These starches have been found to be useful as fillers, binders, and disintegrants in tablet formulations (Esezobo & Ambujam, 1982; Odeku, et al., 1998; Alebiowu & Itiola, 2001; Odeku, et al., 2005).

With the versatility of starches in various solid dosage forms, there is the need to continue to develop new starch excipients with suitable properties to meet the special needs of drug formulators. Pigeon pea starch is obtained from a tropical cereal plant, *Cajanus cajan* (L) Millisp. (family Fabaceae). It is popularly eaten as food or as a source of flour in developing tropical countries (Duke, 1981). Work done by Onah and Bristol (1999) has shown that starch obtained from pigeon pea contains glucose and galactose. The amylose:amylopectin content was found to be in the ratio of 11.08:88.99. Plantain starch, on the other hand, is obtained from the unripe fruit of *Musa paradisiaca* L. (family Musaceae). The fruit contains about 48% starch on dry weight, and the starch contains a ratio 16:84 of amylose:amylopectin (Foulkes, et al., 1987). The starch has been shown to possess binding and disintegrant properties (Alebiowu & Itiola, 2002).

A literature search revealed that so far, no work has been done to evaluate the potentials of pigeon pea starch as an excipient in pharmaceutical tablet formulations. On the other hand, limited work appears to have been done on the effects of plantain starch on tablet properties. Thus, in the present study, the effects of pigeon pea and plantain starches have been investigated on the compressional, mechanical, and disintegration properties of paracetamol tablets in comparison with corn starch BP.

The compressional properties of pharmaceutical materials have been studied by using density measurements and the Heckel and Kawakita equations (Heckel, 1961; Kawakita & Ludde, 1970/71; Odeku & Itiola, 1998),

whereas the mechanical properties of tablets have been assessed by using the tensile strength (T, a measure of bond strength) and brittle fracture index (BFI, a measure of lamination tendency) (Itiola & Pilpel, 1986, 1991; Odeku & Itiola, 1998; Odeku & Itiola, 2003).

The Heckel equation is widely used for relating the relative density, D, of a powder bed during compression to the applied pressure, P. It is written as:

$$\ln [1/(1 - D)] = KP + A \quad (1)$$

The slope of the linear region, K, is the reciprocal of the mean yield pressure, P_y , of the material. From the value of A, the relative density, D_A , can be calculated by using the following equation (Humbert-Droz et al., 1983):

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

D_A represents the relative density of the material during densification at the point at which a coherent or intact tablet is just formed.

The relative density of the material before compression (i.e., when no pressure has been applied, D_0) is used to describe the initial rearrangement phase of densification as a result of die filling only and is the loose initial relative density of the material (Odeku & Itiola, 1998). The relative density D_B describes the phase of densification after application of low pressures due to rearrangement and/or fragmentation of the particles before appreciable deformation of the particles has occurred and is the difference between D_A and D_0 :

$$D_B = D_A - D_0 \quad (3)$$

The Kawakita equation is used to study powder compression using the degree of volume reduction (C) and is written as:

$$C = (V_0 - V_p)/V_0 = a b P/(1 + b P) \quad (4)$$

The equation, in practice can be rearranged to give:

$$P/C = P/a + 1/ab \quad (5)$$

where V_0 is the initial bulk volume of the powder and V_p is the bulk volume after compression. The constant

a is equal to the minimum porosity of the material before compression, whereas the constant b is related to the plasticity of the material. The reciprocal of b gives a pressure term P_k , which is the pressure required to reduce the powder bed by 50% (Shivanand & Sprockel, 1992; Lin & Cham, 1995).

The BFI was devised by Hiestand et al., 1977, and it is obtained by comparing the tensile strength of tablets with a hole at their center, which acts as a built-in stress concentration defect, with the tensile strength of tablets without a hole, both at the same relative density (Hiestand et al., 1977; Odeku & Itiola, 1998).

Paracetamol was chosen for the present work because of its poor compression properties; hence, it needs a binding agent among other excipients to form satisfactory tablets.

MATERIALS AND METHODS

Materials

The materials used were paracetamol BP, lactose BP, corn starch BP, and magnesium stearate (all obtained from Neimeth Pharmaceuticals International Plc., Lagos, Nigeria). Pigeon pea starch was extracted from the dried seed of *Cajanus cajan*, and plantain starch was extracted from the unripe fruit of *Musa paradisiaca* obtained from a local market in Ibadan, Nigeria.

Preparation of Starches

One kilogram of pigeon pea was soaked in distilled water for 1 h to soften the seed coat, which was then peeled off manually. The peeled pea was washed with sodium metabisulphite in distilled water to prevent the pea from becoming dark in color. The softened pea was milled with distilled water into a fine paste with a laboratory mill. The slurry was sieved to remove the chaff and allowed to settle, after which the supernatant was decanted leaving the starch sediment. The sediment was washed continuously for 5 days until the supernatant was colorless and neutral to litmus test. The water was squeezed out by using a muslin cloth, and the wet mass was dried in a hot air oven at 50°C for 18 h. The dried mass was blended by using a laboratory mill and then sieved with a 120- μ m mesh. Plantain starch was prepared by peeling 1 kg of the plantain fruit, which was milled with distilled water

and then processed as described above for pigeon pea starch (Young, 1984; Alebiowu & Itiola, 2001).

The particle size distributions of the starches were determined by optical microscopy on approximately 300 particles for each starch, from which the values of the mean projected particle diameter (d) were calculated. The values of d were 48.3, 23.5, and 17.4 μ m for pigeon pea, plantain, and corn starches, respectively.

Preparation of Granules

Batches (250 g) of a basic formulation of paracetamol (82% w/w), corn starch (10% w/w), and lactose (8% w/w) were dry-mixed for 5 min in an Erweka AR400 planetary mixer and then moistened with 34 mL of distilled water or appropriate amounts of starch mucilages to produce granules containing different concentrations of the starches—pigeon pea, plantain, and corn—as binders. Massing was continued for 5 min, and the wet masses were granulated by passing them manually through a number 12 mesh sieve (1400 μ m), dried in a hot air oven for 18 h at 50°C, and then resieved through a number 16 mesh sieve (1000 μ m). The granules were then stored in airtight containers. Particle densities were determined by the pycnometer method with xylene as the displacement fluid.

Determination of Precompression Density

The bulk density of each formulation at zero pressure (loose density) was determined by pouring 20 g of the granules at an angle of 45° through a funnel into a glass measuring cylinder with a diameter of 24 mm and a volume of 50 mL (Paronen & Juslin, 1983; Itiola, 1991). Determinations were done in triplicate. The relative density D_o of each formulation was obtained from the ratio of its loose density to its particle density. This determination represented a simulation of the filling of particles in a cylindrical die before the application of any pressures (Paronen & Juslin, 1983; Itiola, 1991; Odeku & Itiola, 1998;).

Preparation of Tablets

Tablets (500 \pm 10 mg) were prepared from the 500 to 1000- μ m size fraction of granules by compressing them for 30 sec with predetermined loads on a Carver

hydraulic hand press (Model C, Carver Inc., Menomonee Falls, WI, USA). Before each compression, the 10.5-mm die and flat-faced punches were lubricated with a 2% w/v dispersion of magnesium stearate in ether:ethanol (1:1). Tablets with a hole (1.59-mm diameter) at their center were made by using an upper punch with a hole through the center and a lower punch fitted with a pin (Itiola & Pilpel, 1986; Itiola, 1991). After ejection, the tablets were stored over silica gel for 24 h to allow for elastic recovery and hardening and to prevent falsely low yield values. The weights (w) of the tablets were determined to within ± 1 mg with use of a Mettler balance PC 440, and the thickness of the tablets was measured to within ± 0.01 mm with a micrometer screw gauge (Moore & Wright, Sheffield, UK). Their relative densities (D_r) were calculated by using the equation:

$$D_r = w/V_t \cdot \rho_s \quad (6)$$

where V_t is the volume (cm^3) of the cylindrical tablet (including the hole when present) and ρ_s is the particle density (gcm^{-3}) of the solid material.

Testing

The tensile strengths of the normal tablets (T) and apparent tensile strengths of those containing a hole (T_h), were determined at room temperature by diametral compression (Fell & Newton, 1970) using a Kanara hardness tester (Kanara Industries Cooperation, Bombay, India) and by applying the equation:

$$T \text{ (or } T_h) = 2 F/\pi dt \quad (7)$$

where T (or T_h) is the tensile strength of the tablet (MNm^{-2}), F is the load (MN) needed to cause fracture, d is the tablet diameter (m), and t is the tablet thickness (m). Results were taken only from tablets, which split cleanly into two halves without any sign of lamination. All measurements were made in quadruplicate.

The BFI of the tablets was calculated by using the equation:

$$\text{BFI} = [(T/T_h) - 1] \quad (8)$$

where T is the tensile strength of the tablets without a hole, and T_h is the apparent tensile strength of the tablets when a hole is present.

An estimation of the bonding capacity, k , of the formulations was obtained from the Ryshkewitch-Duckworth relation (Duckworth, 1953), which states an inverse relationship between tensile strength and porosity (1-relative density, D_r) of the tablet and is written as (Maarschalk, et al., 1997; Tye, et al., 2005):

$$T = T_o \cdot e^{-k \cdot E} \quad (9)$$

where T_o is the tensile strength at zero porosity and E is the porosity of the tablet. Determinations were done at $E = 0.10$ (i.e., relative density = 0.90).

Disintegration Tests

The disintegration times, DT , of the tablets were determined in distilled water at $37 \pm 0.5^\circ\text{C}$ by using a Veego disintegration tester (Model VTD-3D, Veego Scientific Devices, Maharashtra, India). All measurements were made in quadruplicate.

Statistical Analysis

Statistical analysis to compare the effects of the various starches on the mechanical and disintegration properties of the tablets was done by using the analysis of variance (ANOVA) on a computer software GraphPad Prism[®] 4 (GraphPad Software Inc. San Diego, CA, USA). Tukey-Kramer multiple comparison tests was used to compare the individual differences between the starches. At 95% confidence interval, probability, P values less than or equal to 0.05 were considered significant.

RESULTS AND DISCUSSION

Figure 1 shows representative Heckel plots for paracetamol formulations containing 7.5% w/w of the starches. The mean yield pressure, P_y , was calculated from the regions of the plots showing the highest correlation coefficient for linearity of ≥ 0.990 for all the formulations (generally between 56.62 and 141.54 MPa). The intercept A was determined from the extrapolation of the region used for the determination of P_y . The intercept represented the point at which a coherent or

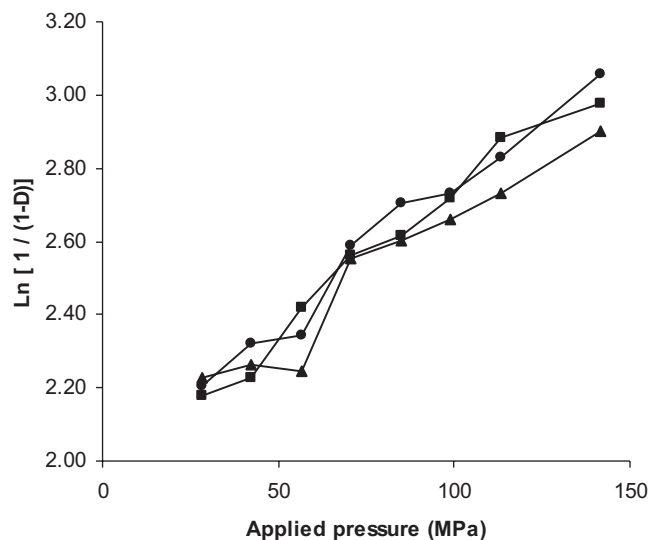


FIGURE 1 Heckel plots for paracetamol tablet formulations containing 7.50% w/w of the starches. ▲, pigeon pea; ■, plantain; ●, corn.

TABLE 1 Parameters Derived From Density Measurements and From Heckel and Kawakita Plots

Starch	Concentration of starch (%w/w)	D_o	Heckel plots			Kawakita plots	
			P_y	D_A	D_B	P_K	D_I
Pigeon pea	0.00	0.262	200.03	0.833	0.571	2.960	0.271
	2.50	0.275	163.93	0.863	0.588	2.176	0.306
	5.00	0.290	149.25	0.861	0.571	1.452	0.333
	7.50	0.299	133.33	0.860	0.561	1.339	0.355
	10.00	0.312	128.21	0.853	0.541	1.011	0.363
Plantain starch	2.50	0.271	217.39	0.879	0.608	2.250	0.276
	5.00	0.279	188.68	0.877	0.598	1.625	0.286
	7.50	0.292	151.52	0.871	0.579	1.444	0.301
	10.00	0.349	128.21	0.863	0.514	1.162	0.375
Corn	2.50	0.263	181.82	0.863	0.600	2.560	0.273
	5.00	0.294	136.99	0.862	0.568	1.795	0.299
	7.50	0.319	128.46	0.861	0.542	1.571	0.328
	10.00	0.335	123.46	0.859	0.524	1.240	0.353

intact tablet was just formed during compression. The values of P_y , D_o , D_A , and D_B for the formulations are presented in Table 1. The value of D_o , which represents the degree of initial packing in the die as a result of die filling for the formulations increased with increase in the concentration of the starches.

The values of the relative densities, which represent the total degree of densification achieved at zero, and low pressures (D_A) and the rearrangement of particles in the early stages of compression (D_B) are seen to decrease with increase in the concentration of the starches. There were no clear-cut patterns to the variations in the values of the relative densities from starch to starch.

The mean yield pressure, P_y , is inversely related to the ability of the formulations to deform plastically under pressure. The values of P_y decreased with increase in concentration of the starches. The ranking of P_y at the lowest concentration of starches was pigeon pea < corn < plantain starch but was corn < pigeon pea < plantain starch at higher concentrations of starch. The results indicate that formulations containing corn starch as binder generally exhibited the fastest onset of plastic deformation during compression, whereas formulations containing plantain starch exhibited the slowest.

Figure 2 shows representative Kawakita plots for paracetamol formulations containing 7.50% w/w of

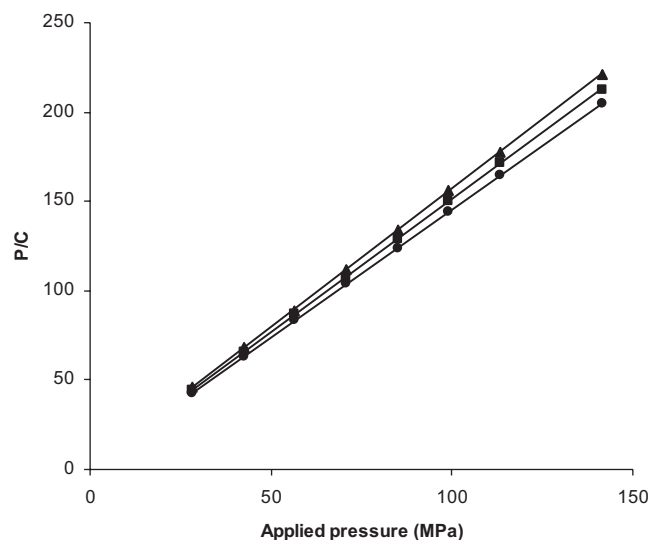


FIGURE 2 Kawakita plots for paracetamol tablet formulations containing 7.50% w/w of the starches. ▲, pigeon pea; ■, plantain; ●, corn.

the starches. A linear relationship was obtained at all compression pressures used with correlation coefficient of 0.999 for all the starches. Values of a and ab were obtained from the slope and intercept of the plots respectively. Values of $1-a$ give the initial relative density of the starches, D_I , whereas P_K values were obtained from the reciprocal of the values of b . The values of D_I and P_k are included in Table 1.

The values of D_I , which is a measure of the packed initial relative density of the formulations with the application of small pressure or what may be referred to as tapping of the formulations (Podczek & Sharma, 1996; Odeku & Itiola, 1998), are seen to generally increase with increase in concentration of the starches. These values are also seen to be generally higher than the corresponding values of the loose initial relative density, D_o . This is in agreement with previous findings (Odeku & Itiola, 1998; Alebiowu & Itiola, 2002).

The values of P_k , which is an inverse measure of the total amount of plastic deformation occurring during the compression process (Odeku & Itiola, 1998), were also found to decrease with increase in the concentration of the starches. It has been established that the lower the P_k value, the more the total plastic deformation occurring during compression (Odeku & Itiola, 1998; Alebiowu & Itiola, 2002). The ranking of P_k for the formulations was pigeon pea < plantain < corn starch.

The results of the tensile tests on the paracetamol tablets fit the general equation:

$$\text{Log } T \text{ (or } T_h) = AD + B \quad (10)$$

with a correlation coefficient > 0.985. A and B were constants for each formulation and depended on whether the tablet had a hole in it. Figure 3 shows representative plots of log tensile strength vs. relative density for formulations containing 7.5% w/w of the starches. The tensile strength of tablet with a hole is lower than that of the same without a hole, because the hole acts as a stress concentrator (Hiestand et al., 1977). Values of T and BFI for the starches at relative density of 0.90, which is representative of commercial paracetamol tablets, are presented in Table 2. The values of T for the paracetamol tablets increased with increase in concentration of the starches, whereas the BFI decreased. The ranking of T for the formulations containing the different starches was pigeon pea > plantain > corn starch. The ranking for BFI was corn > plantain > pigeon pea. Statistical analysis showed that there was generally significant difference ($P < 0.001$) in the tensile strength and BFI values for tablets containing the various starches. Obviously, a low value of BFI is desirable for the minimization of

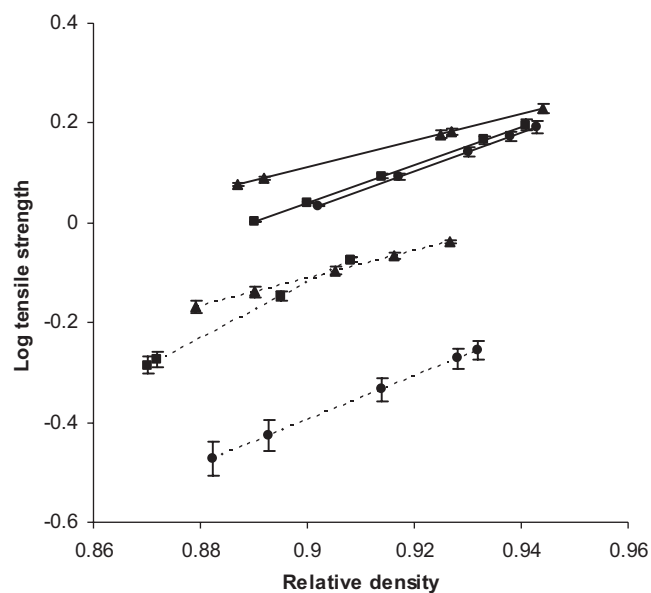


FIGURE 3 Log tensile strength vs. relative density for paracetamol tablet formulations containing 7.50% w/w of the starches with (----) and without (—) a hole at their centre. ▲, pigeon pea; ■, plantain; ●, corn.

TABLE 2 Values of Tensile Strength (T), Brittle Fracture Index (BFI), and Disintegration Time (DT) at Relative Density of 0.90 for Paracetamol Tablets (mean \pm SD, n = 4)

Binder	Concentration of starch (%w/w)	T (MPa)	BFI	DT
Pigeon pea starch	0.00	0.695 \pm 0.061	0.400 \pm 0.029	0.587 \pm 0.060
	2.50	0.933 \pm 0.069	0.291 \pm 0.021	0.520 \pm 0.005
	5.00	1.019 \pm 0.078	0.235 \pm 0.032	0.400 \pm 0.010
	7.50	1.289 \pm 0.020	0.226 \pm 0.048	0.340 \pm 0.002
	10.00	1.464 \pm 0.088	0.200 \pm 0.033	0.310 \pm 0.003
Plantain starch	2.50	0.904 \pm 0.022	0.464 \pm 0.009	0.250 \pm 0.008
	5.00	0.982 \pm 0.021	0.424 \pm 0.012	0.280 \pm 0.011
	7.50	1.251 \pm 0.019	0.335 \pm 0.018	0.290 \pm 0.004
	10.00	1.279 \pm 0.031	0.315 \pm 0.023	0.350 \pm 0.004
Corn starch	2.50	0.755 \pm 0.012	0.572 \pm 0.029	0.403 \pm 0.003
	5.00	0.890 \pm 0.092	0.446 \pm 0.023	0.440 \pm 0.004
	7.50	1.098 \pm 0.067	0.417 \pm 0.021	0.530 \pm 0.001
	10.00	1.228 \pm 0.068	0.318 \pm 0.055	0.577 \pm 0.002

lamination and capping during tablet production. On the other hand, the desirable effect on tensile strength largely depends on the intended use of tablets (Itiola & Pilpel, 1991).

It is notable that the results of T are inversely related to the values of P_k of the various formulations. This supports the assertion that P_k provides a measure of the total amount of plastic deformation occurring during compression as has been previously established by Odeku and Itiola (1998). Higher total plastic deformation would lead to more contact points for interparticulate bonding to produce stronger tablets. It is also notable that pigeon pea starch produced tablets with the highest bond strength and lowest lamination tendency, suggesting that it can be useful for producing strong tablets with minimal lamination tendency.

Plots of the bonding capacity, k , of the formulations vs. concentration of starch are presented in Fig. 4. It can be seen that there is a similar pattern to the values of k for the three different starches, with k generally increasing with increase in the concentration of starch. Thus, the starches generally served to increase the bonding of the formulations during tableting. Furthermore, it can be seen from the plots that formulations containing corn starch exhibited the lowest bonding capacity, whereas formulations containing pigeon pea exhibited the highest bonding capacity. Therefore, it may be concluded that the bonding capacity result generally correlated with tensile strength values for the tablets.

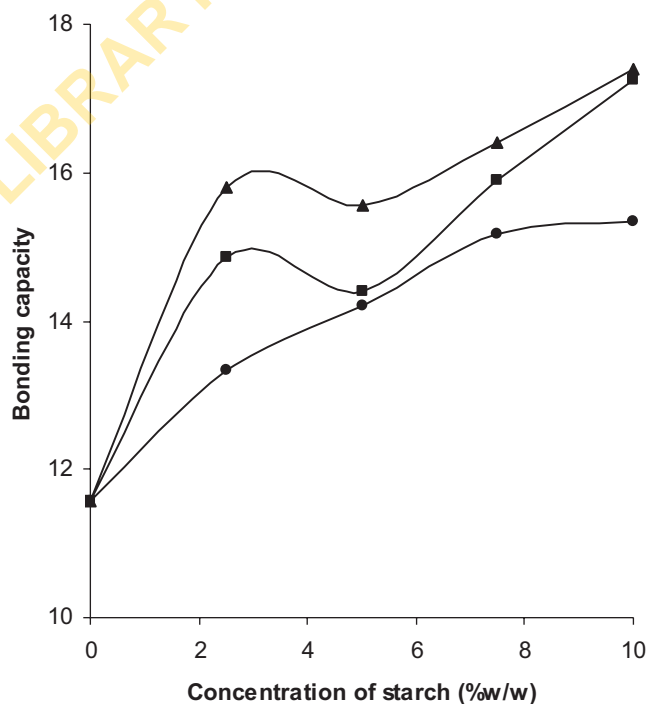


FIGURE 4 Bonding capacity vs. concentration of starch for paracetamol tablet formulations. ▲, pigeon pea; ■, plantain; ●, corn.

Figure 5 shows representative plots of disintegration time vs. relative density for formulations containing 7.5% w/w of the starches. The disintegration times (DT) of the tablet at relative density 0.90 are presented in Table 2. Statistical analysis showed that there were significant ($P < 0.001$) differences in the disintegration time for tablets containing the various starches. It is notable that although the DT for tablets

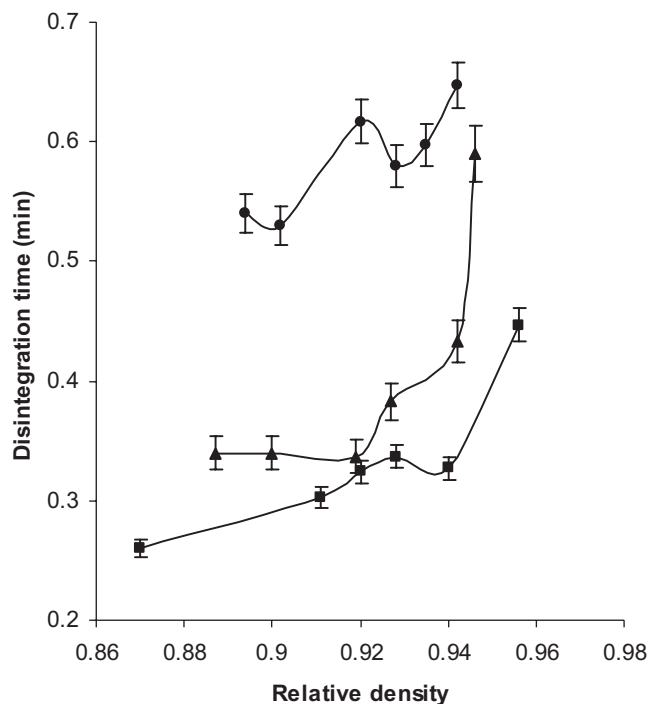


FIGURE 5 Disintegration time (min) vs. relative density for paracetamol tablet formulations containing 7.50% w/w of the starches. ▲, pigeon pea; ■, plantain; ●, corn.

containing corn and plantain starches increased with starch concentration, the values of DT for those tablets containing pigeon pea starch decreased. This made it difficult to rank the starches, but generally, formulations containing plantain starch exhibited the lowest DT values, and those containing corn starches exhibited the highest values. This type of observation can be useful in selecting a binder for particular purposes, especially with the kind of result obtained for pigeon pea starch, for which the disintegration time decreased with increase in concentration of the starch. Formulations containing high concentration of this starch should produce high bond strength with accompanying fast disintegration of tablets.

CONCLUSIONS

The results of the present work show that all the three starches could be useful in various formulations depending on the intended use of the tablets. Formulations containing pigeon pea starch exhibited the highest bond strength and lowest brittleness, showing that it can be useful for producing strong tablets with minimal lamination tendency. Plantain starch, on the other hand, would

be more useful for tablets where faster disintegration is desired. The results suggest that the experimental starches can be developed for commercial purposes.

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