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The effects of starches on mechanical properties of paracetamol tablet formulations. I. Pregelatinization of starch binders

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A study has been made of the effects of pregelatinization of native sorghum and plantain starches on the mechanical properties of a paracetamol tablet formulation in comparison with corn starch BP. The mechanical properties tested, *viz*. tensile strength (*T*) and brittle fracture index (*BFI*) of the paracetamol tablets were affected by pregelatinization of the starch. The results suggest that pregelatinized starches may be useful as binders when a particular degree of bond strength and brittleness is desired.

Keywords: starch, sorghum, plantain, pregelatinization, tensile strength, brittle fracture index

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Native starch has been recognized as one of the most commonly used excipients in the manufacture of tablets which can be used as fillers, disintegrants or as binders (1). In recent years pharmaceutical scientists have been paying increasing attention to the extraction, development and use of starches in the formulation of dosage forms (2). However, due to the limitations of native starches such as poor compressibility and flow properties, some special starch products, like pregelatinized starch (3, 4), were introduced.

Sorghum and plantain starches obtained from *Sorghum bicolor (Poaceae)* and *Musa paradisiaca (Musaceae)*, respectively, have been investigated as binders and disintegrants in tablet formulations (2, 5). This study was aimed at ascertaining the effects that pregelatinized forms of these starches, as binders, would have on the mechanical properties of tablet formulations in comparison with corn starch BP as a reference standard.

Paracetamol was chosen because it possesses poor compression properties and therefore requires a binder to form good quality tablets.

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Bond strength and lamination tendencies are two important mechanical properties of tablets that are measurable by tensile strengths (*T*) and the brittle fracture index value (*BFI*) (6). The *BFI* is obtained by comparing the tensile strengths of tablets with a hole at their center (which acts a built-in stress concentrator defect) with the tensile strengths of the tablets without a hole (7). The *BFI* is defined as.

$$BFI = [0.5\ (T/T_0) - 1] \qquad (1)$$

where T is the tensile strength of the tablet without a hole and T_0 is the apparent tensile strength of the tablet when a hole is present, both at the same relative density. The *BFI* is a measure of localized stress relief within the tablet (at the edge of the hole) by plastic deformation. A low *BFI* value indicates the ability of the material to relieve localized stresses, while a value approaching unity indicates a tendency of the material to laminate or cap.

EXPERIMENTAL

Materials

Paracetamol BP was obtained from Nigerian German Chemical Co. (Nigeria), corn starch BP from BDH Chemicals (UK), lactose from AB Knight and Co. (UK). The native sorghum and plantain starches were prepared in our laboratory using an established method of starch extraction (8), while the pregelatinized starches were prepared according to the literature (9–11).

Methods

Preparation of granules. – Batches (300 g) of a basic formulation of paracetamol (85%, *m/m*), corn starch (7%, *m/m*) and lactose (8%, *m/m*) were dry-mixed for 5 minutes in a Hobart planetary mixer (Hobart Manufacturing Co., UK) and then moistened with either 35 mL of distilled water or an appropriate amount of starch mucilages to produce samples containing different concentrations of the starch binder. Massing was continued for 5 minutes and the wet masses were granulated by passing them manually through a sieve, size 1400 μm. The granules were dried in a hot air oven for 24 h at 60 °C and then resieved through a sieve, size 1000 μm. Particle density of the granules was determined using a pycnometer with benzene as the displacement fluid.

Preparation of tablets. – Granules (550 mg) of 500–1000 μm size fractions were compressed for 1 minute at predetermined loads (96.0–159.9 MN m^{-2}) using a Carver hydraulic hand press (Model C, Carver, USA). Before each compression, the die (12.5 mm diameter) and the flat faced punches were lubricated with a 2% dispersion of magnesium stearate in benzene. After ejection, the tablets were stored over silica gel for 24 h to allow elastic recovery and hardening and prevent falsely low yield values. Their masses, m, and dimensions were then determined to within ± 1 mg and 0.01 mm, respectively, and their relative densities, D, were calculated using the equation:

$$D = m/V_t \rho_s \qquad (2)$$

where V_t is the volume (cm^3) of the tablet and ρ_s is the particle density (1.325–1.334 g cm^{-3}) of the solid material. All determinations were done in triplicate and the mean values were used.

Determination of mechanical properties. – The tensile strengths, T, of the normal tablets and apparent tensile strengths T_0 of those containing a hole were determined at room temperature by diametral compression (12) using a Monsanto hardness tester (Monsanto Chemical Co., USA) and by applying the equation:

$$T = 2F/\pi\, d\, t \tag{3}$$

where T (or T_0) is the tensile strength of the tablet (MN m^{-2}), F is the load (MN) needed to cause fracture, d is the tablet diameter (m), and t is the tablet thickness (m). Statistical ana-

Table I. Tensile strength and brittle fracture index for paracetamol tablets at a relative density of 0.90

Starch binder	Binder concentration (%, *m/m*)	Mechanical property					
		Native starch			Pregelatinized starch		
		T (MN m^{-2})[a]	T_0 (MN m^{-2})[a]	*BFI*	T (MN m^{-2})[a]	T_0 (MN m^{-2})[a]	*BFI*
None	–	0.264 ± 0.027	0.163 ± 0.018	0.310	0.264 ± 0.027	0.163 ± 0.018	0.310
Sorghum	0.5	0.462 ± 0.012	0.361 ± 0.019	0.140	0.426 ± 0.014	0.337 ± 0.011	0.132
	1.0	0.508 ± 0.024	0.413 ± 0.020	0.115	0.451 ± 0.022	0.367 ± 0.008	0.114
	2.0	0.564 ± 0.031	0.492 ± 0.019	0.073	0.465 ± 0.018	0.392 ± 0.017	0.093
	3.0	0.609 ± 0.033	0.563 ± 0.026	0.041	0.499 ± 0.24	0.451 ± 0.019	0.053
	4.0	0.617 ± 0.039	0.587 ± 0.022	0.025	0.567 ± 0.020	0.517 ± 0.016	0.048
Plantain	0.5	0.651 ± 0.033	0.475 ± 0.020	0.185	0.352 ± 0.019	0.298 ± 0.017	0.091
	1.0	0.655 ± 0.016	0.511 ± 0.021	0.141	0.483 ± 0.016	0.403 ± 0.021	0.074
	2.0	0.666 ± 0.029	0.533 ± 0.019	0.125	0.543 ± 0.025	0.506 ± 0.019	0.036
	3.0	0.731 ± 0.025	0.617 ± 0.021	0.092	0.588 ± 0.020	0.562 ± 0.023	0.023
	4.0	0.831 ± 0.019	0.765 ± 0.026	0.043	0.590 ± 0.027	0.577 ± 0.024	0.011
Corn	0.5	0.421 ± 0.015	0.330 ± 0.011	0.138	0.360 ± 0.014	0.292 ± 0.015	0.116
	1.0	0.494 ± 0.024	0.401 ± 0.020	0.116	0.398 ± 0.013	0.331 ± 0.011	0.101
	2.0	0.520 ± 0.019	0.440 ± 0.016	0.091	0.516 ± 0.018	0.448 ± 0.022	0.076
	3.0	0.724 ± 0.019	0.658 ± 0.024	0.050	0.572 ± 0.015	0.516 ± 0.021	0.054
	4.0	0.786 ± 0.027	0.723 ± 0.022	0.043	0.593 ± 0.021	0.558 ± 0.558	0.031

[a] Mean ± SEM, n = 3.
T – tensile strength of tablets without a hole
T_0 – tensile strength of tablets with a hole
BFI – brittle fracture index

lysis of the results in Table I revealed that the variability within the tablets was at a minimum level. Results were taken only from tablets which split clearly into two halves without any sign of lamination. All measurements were made in triplicate or more and the results given are the mean value. The *BFI* of the tablet was calculated using equation *(1)*.

RESULTS AND DISCUSSION

Results of the tensile strength tests on the paracetamol tablets were found to fit the general equation:

$$\log T \text{ (or } T_0) = \mathrm{AD} + \mathrm{B} \qquad (4)$$

with a correlation coefficient higher than 0.963. A and B are constants that depend on the form and concentration of the starch binder present in the formulation and on whether the tablet has a hole in it or not, and *D* is the relative density of the tablets. Representative plots for tablets made from formulations containing 2% (*m*/*m*) of starch binder are presented in Fig. 1.

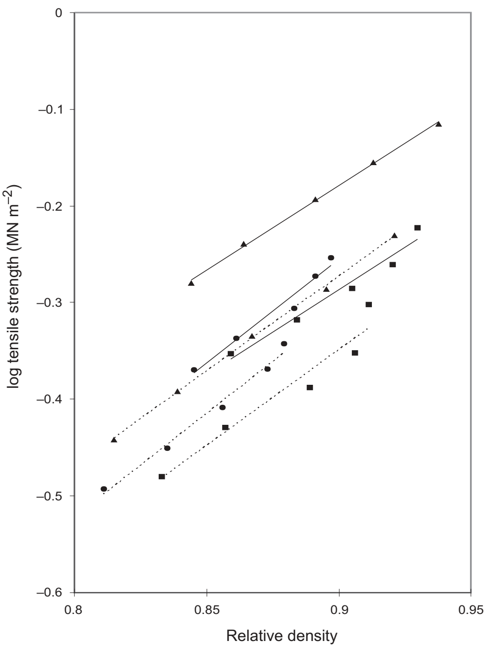

Fig. 1. Effect of relative density on log tensile strength for paracetamol tablets containing 2% (*m*/*m*) of native starch binders: ● sorghum, ▲ plantain, ■ corn; __ without a hole; …. with a hole.

It can be seen that at all relative densities the tensile strength of a tablet with a hole was less than that of the same tablet without a hole, the hole acting as a stress concentrator (7). Furthermore, the effect of pregelatinization on T is seen in Fig. 2 with plots of the tablet made using 2% (m/m) of plantain starch as binder (native or pregelatinized). The tablets made using native starches as binder had higher T than those made using pregelatinized starches. This result is in agreement with a previous report (3) and our earlier work (13) that native forms of starches have a higher T than their pregelatinized forms. This higher T could be due to the higher amount of total plastic deformation occurring in native starches during the compression process than in pregelatinized starches (13, 14).

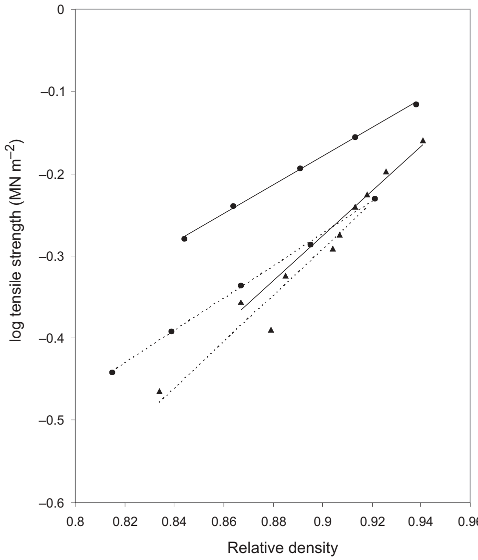

Fig. 2. Effect of relative density on log tensile strength for paracetamol tablets containing 2% (m/m) plantain starch binder: ● native starch, ▲ pregelatinized starch; ___ without a hole; …. with a hole.

The value of T (T_0) for all formulations at D = 0.90, which is representative of commercial paracetamol tablets, is presented in Table I. The values of T (T_0) are seen to generally increase with an increase in binder concentration. This effect is consistent with previous work on starch and other binders (5, 15) and is assumed to result from the heat produced during compression that could cause melting of the asperities and of the binding agents. On cooling, these asperities would solidify to form strong solid bonds between the particles (16). The degree of binding depends on the amount of the binding agent present (15) and on the compression force. Being soft and plasto elastic, binders undergo plastic and elastic deformation under high compression pressure and are forced into the interparticulate spaces. This increases the area of contact between particles due to further densification and formation of more solid bonds (17).

The *BFI* values at a relative density of 0.90 (Table I) indicate that as the concentration of binder increases, the *BFI* values decrease. This implies that the presence of a binder at interparticulate junctions facilitates plastic deformation for the relief of localized stresses (5, 18). Generally, tablets containing pregelatinized starches had lower *BFI* values than the native starches.

In general, tablets containing native plantain starch exhibited the highest values for both *T* and *BFI*, while those containing native sorghum starches had the lowest values. Tablets containing pregelatinized starch, either plantain or corn starch, had approximately the same *T* value, higher than that of tablets containing pregelatinized sorghum starch. The results of this investigation also suggest that the activity of plantain starch is closer to that of corn starch BP than that of sorghum starch, and could be hold as a substituents of corn starch BP when the need arises.

CONCLUSIONS

The results of this investigation show that pregelatinization of starch binders has significant effects on the mechanical properties of tablets. The results for native starches indicate that sorghum starch produces tablets with the lowest bond strength but also with the lowest brittleness; thus, it could be more useful as a binder than native plantain and corn starch when problems of lamination and capping are of more concern than bond strength. Furthermore, pregelatinized plantain starch exhibited the highest bond strength and the lowest *BFI* among pregelatinized starches. This suggests applicability of pregelatinized plantain starch in particular situations where a high bond strength is required with minimal lamination and capping problems. The results also suggest that the tested starches have comparable activity to that of corn starch BP and could be substituted for it when the need arises.

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S A Ž E T A K

Učinak vrste škroba na mehanička svojstva tableta paracetamola. I. Pregelatinizacija škrobnog veziva

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Istraživan je učinak pregelatinizacije na nativni škrob sorga i pisanga na mehanička svojstva tableta paracetamola i uspoređivan s kukuruznim škrobom BP. Pregelatinizacija škroba utječe na čvrstoću (*T*) i indeks rastrošljivosti (*BFI*) tableta. Rezultati ukazuju da se ispitivani pregelatinizirani škrobovi mogu upotrijebiti kao vezivo ako je potrebno pripraviti tablete određene čvrstoće i rastrošljivosti.

Ključne riječi: škrob, sorgo, pisang, pregelatinizacija, čvrstoća, indeks rastrošljivosti

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