

Effects of Natural and Pregelatinized Sorghum, Plantain, and Corn Starch Binders on the Compressional Characteristics of a Paracetamol Tablet Formulation

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A study of the comparative effects of natural and pregelatinized sorghum, plantain, and corn starch binders on the compressional characteristics of a paracetamol tablet formulation was made using density measurements and the Heckel and Kawakita plots for analysis. Results suggest that the use of pregelatinized starches would improve the plastic deformation in the tablet formulations during compression when compared with the use of natural starches.

Starch is a multipurpose excipient in tablet formulations. It can be used as a binder, disintegrant, and filler. Natural starches also have been pregelatinized to increase their cold-water swellability and increase their flowability (1). Pregelatinization can be carried out by thermal methods (2). Although some research has been carried out on the compressional characteristics of natural starches (3,4), little or no research appears to have been conducted on the effect of pregelatinization on the compressional characteristics of starches in relation to their usefulness in tablet formulations.

Sorghum and plantain starches obtained from *Sorghum bicolor* L. (poaceae) and *Musa paradisiaca* L. (musaceae), respectively, have been investigated as binders and disintegrants in tablet formulations (5,6). However, it appears that no attempt has been made to study the effects of these starches in either natural or pregelatinized forms on the compressional characteristics of tablet formulations.

In the present work, a study has been made of the effects of natural and pregelatinized sorghum and plantain starch binders

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on the compressional characteristics of a paracetamol tablet formulation in comparison with official corn starch BP using density measurements and the Heckel and Kawakita equations for the analysis of the compression data (7,8).

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

$$\ln\left(\frac{1}{1-D}\right) = KP + A \quad [1]$$

The slope of the straight line portion, K , is the reciprocal of the mean yield pressure, P_y , of the material. From the value of the intercept, A , the relative density, D_a , can be calculated using the following equation (9):

$$D_a = 1 - e^{-A} \quad [2]$$

The relative density of the powder bed at the point when the applied pressure equals zero, D_o is used to describe the initial rearrangement phase of densification as a result of die filling. The relative density, D_b , describes the phase of rearrangement at low pressures and is the difference between D_a and D_o :

$$D_b = D_a - D_o \quad [3]$$

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

$$C = \frac{V_o - V_p}{V_o} = \frac{abP}{1 + bp} \quad [4]$$

The equation, in practice, can be rearranged to give

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \quad [5]$$

in which V_o is the initial bulk volume for granular materials and V_p is the bulk volume after compression. The constant a is equal to the minimum porosity of the material before compression; the constant b , which is termed the coefficient of compression, is related to the plasticity of the material. The reciprocal of b is related to the pressure term P_k , which is the pressure required to reduce the powder bed by 50% (10,11).

Both the Heckel and the Kawakita plots have their limitations and are believed generally to exhibit linearity for many materials at high and low pressures, respectively (12). Therefore, the combined use of the two plots should provide more accurate information about the effects of the starch binders on the compressional characteristics of the paracetamol formulations.

Paracetamol was chosen for the present work because it possesses poor compression properties and therefore requires a binder, among other excipients, to form satisfactorily strong tablets.

Materials and methods

Materials. The materials used were paracetamol BP and corn starch BP (BDH Chemicals Ltd., Poole, UK), lactose BP (AB

Knight and Co., London, UK), and sorghum (*Sorghum bicolor* L.) and plantain (*Musa paradisiaca* L.) starches prepared in our laboratory. The pregelatinized forms of the three starches also were prepared in our laboratory.

Preparation of natural and pregelatinized starches. Sorghum and plantain starches were prepared according to established procedure (13). The fully pregelatinized forms of the two starches and of the official cornstarch BP were prepared as described in the British *Pharmaceutical Codex* (14) and by Herman et al. (2). An aqueous slurry of each starch was made with 100 g of starch powder in 100 mL of deionized water and then heated at 55 °C, with stirring, for 10 min. The resultant paste was crisp-dried (i.e., dry and brittle) in a hot-air oven (Gallenkamp, model OV-335, Vindon Scientific Ltd., Oldham, UK) at 60 °C for 48 h. The dried mass was powdered in a laboratory mill (Christy and Norris Ltd., Chemsford, UK). All the starches were passed through a number 120 mesh sieve (125 μm) before use.

Preparation of granules. We dry-mixed 300-g batches of a basic formulation of paracetamol (85% w/w), corn starch (7% w/w), and lactose (8% w/w) for 5 min in a Hobart planetary mixer (Hobart Canada Inc., Don Mills, ON). The batches were then moistened with either 35 mL of distilled water or appropriate amounts of starch mucilages to produce samples containing various concentrations of the starch binders. Massing was continued for 5 min, and the wet masses were granulated by passing them manually through a number 12 mesh sieve (1400 μm). The granules were dried in a hot-air oven for 24 h at 60 °C and then resieved through a number 16 mesh (1000 μm). The degree of mixing of the granules then was determined by spectrophotometric assay of paracetamol at 249 nm and was found to be >0.95. The moisture content of the formulation as determined with an Ohaus moisture balance (Ohaus Scale Corp., Pine Brook, NJ) was between 1.0 and 2.0% w/w. Particle densities were determined by the pycnometer method with benzene as the displacement fluid.

Preparation of starch mucilage. Starch mucilages were prepared by weighing amounts of starch powder that will produce various concentrations: 1% w/w, 2% w/w, 3% w/w, and 4% w/w of the starch binders in the formulation. Each weighed quantity then was suspended in the required amount of deionized water in a beaker and heated with continuous stirring until a mucilage was formed. The mucilage was used while still hot for more effective binding.

Determination of precompression density. The bulk density of each formulation at zero pressure (loose density) was determined by pouring the 500–1000 μm-size fractions of granules at an angle of 45° through a funnel into a glass measuring cylinder with a diameter of 22 mm and a volume of 50 mL (4). Determinations were conducted in triplicate. The relative density, D_o , of each formulation was obtained from the ratio of its loose density to its particle density.

Preparation of tablets. Five hundred fifty-mg quantities of 500–1000 μm-size fractions of the granule formulations, giving a tablet thickness of 3.37 ± 0.01 mm at zero porosity as calculated from particle density values, were compressed for 1 min into tablets with predetermined loads using a Carver hydraulic hand press (Model C, Carver Inc., Menomonee Falls, WI). Be-

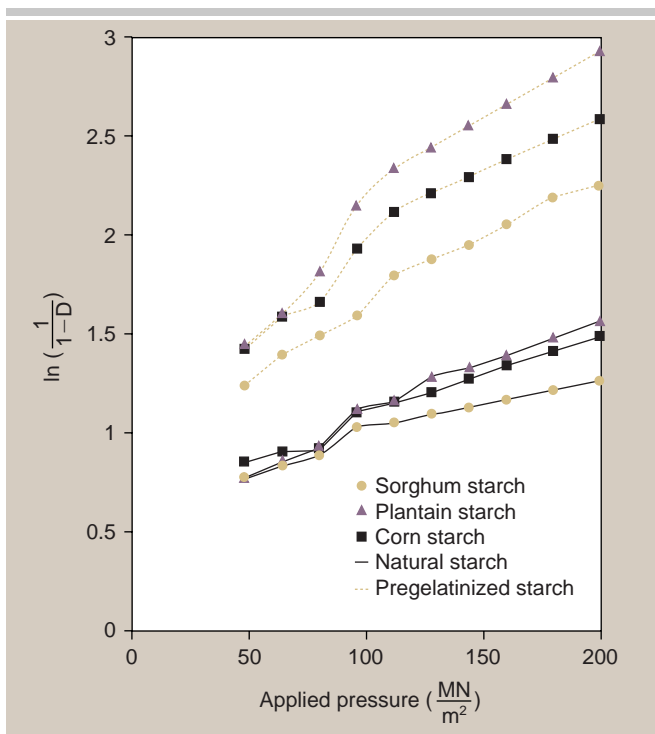


Figure 1: Heckel plots for paracetamol formulations containing 2% w/w of binders.

fore each compression, the die (12.5-mm diameter) and the flat-faced punches were lubricated with a 2% w/w dispersion of magnesium stearate in benzene. 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. Their weights, w , and dimensions then were determined to within ± 1 mg and 0.01 mm, respectively, and their relative densities, D , were calculated using the equation

$$D = \frac{w}{V_t \rho_s} \quad [6]$$

in which V_t is the volume (cm^3) of tablet and ρ_s is the particle density (gcm^{-3}) of the solid material.

Results and discussion

Figure 1 shows representative Heckel plots for paracetamol formulations containing 2% w/w natural or pregelatinized starch binders, with those formulations containing the pregelatinized starches showing more compressibility. Two phases of compression are discernible in the plots, with the second phase commencing generally at approximately 100 MNm^{-2} and showing a higher correlation coefficient for linearity of >0.970 for all the formulations containing natural starches and >0.990 for all the formulations containing pregelatinized starches. Values for the mean yield pressure, P_y , of the formulations were calculated from the second compression region, and the intercept, A , was determined from the extrapolation of the region. The values of D_a and D_b were calculated from Equations 2 and 3, respectively. The values of P_y , D_0 , D_a , and D_b for all the formulations are presented in Table I.

The values of D_0 for the various formulations increased with the increase in binder concentration, implying that the initial packing of the formulation as a result of die filling increased with the increase in binder content. This could be a result of the increase in granular size of granulation with an increase in binder concentration (see Table II). A similar trend was observed for the starches in which pregelatinized starches with bigger particle sizes had higher D_0 values (see Table III). It also can be observed that the D_0 values for the formulations containing pregelatinized starch binders were higher than those for the formulations containing natural starch binders, showing that the pregelatinized starch binders facilitated the initial packing of the granule formulations in the die.

The phase of rearrangement of particles at low pressure is represented by D_b . It can be observed that the D_b values for the formulations containing pregelatinized starches were higher than those for the formulations containing natural starches. This suggests more fragmentation of granules containing pregelatinized starch binders at low pressures. The values of D_b also can be observed to decrease with an increase in binder concentration. These values also are much higher than the values of D_0 , probably as a result of fragmentation of granules at low pressures.

The values of D_a representing the total degree of packing achieved at zero and low pressures

Table I: Parameters obtained from density measurements and from Heckel plots for paracetamol tablet formulations.

Starch Binder	Concentration of Binder (% w/w)	Formulations Containing Natural Starch				Formulations Containing Pregelatinized Starch			
		D_0	P_y	D_a	D_b	D_0	P_y	D_a	D_b
Sorghum	0.0	0.145	340.2	0.505	0.360	0.145	340.2	0.505	0.360
	1.0	0.227	585.8	0.558	0.331	0.233	272.0	0.725	0.492
	2.0	0.230	410.1	0.544	0.314	0.245	192.3	0.698	0.459
	3.0	0.240	319.8	0.540	0.300	0.249	152.3	0.693	0.444
	4.0	0.247	246.8	0.515	0.268	0.259	116.1	0.677	0.424
Plantain	1.0	0.205	358.6	0.558	0.353	0.216	212.4	0.803	0.587
	2.0	0.208	235.5	0.516	0.308	0.220	147.3	0.795	0.575
	3.0	0.213	185.7	0.498	0.285	0.227	115.3	0.794	0.567
	4.0	0.219	154.5	0.468	0.249	0.232	85.8	0.777	0.545
Corn	1.0	0.232	363.4	0.527	0.295	0.252	234.0	0.791	0.539
	2.0	0.238	257.5	0.514	0.276	0.256	187.8	0.788	0.529
	3.0	0.242	205.0	0.511	0.269	0.259	141.2	0.786	0.527
	4.0	0.247	149.5	0.480	0.233	0.261	109.6	0.753	0.492

(as implicit in Equation 3) are higher for the formulations containing pregelatinized starches than for those containing natural starches. These values also decrease with an increase in binder concentration.

The mean yield pressure is related inversely to the ability of a material to deform plastically under pressure. The values of P_y for the formulations containing pregelatinized starches were much lower than for those containing natural starches. This implies that the onset of plastic deformation in the formulations containing pregelatinized starch binders occurred at much lower pressures. The values of P_y also decrease with an increase in the concentration of starch binder. It also is notable that the formulations containing plantain starch generally exhibited the lowest P_y values, whereas those containing sorghum starch generally exhibited the highest P_y values. However, the indication of the rate of plastic deformation (i.e., P_y) appears to be more complicated for multicomponent formulations, probably because of the different deformational properties of the various components. This is reflected in the P_y values of the base granulation (340.2 MNm^{-2}), which is rather high compared with

Table II: Values of mean granule size (G) for the various formulations.

Binder	Concentration (% w/w)	Mean granule size (G) (μm)	
		Natural Starch	Pregelatinized Starch
Sorghum starch	0.00	437	437
	1.00	575	571
	2.00	610	590
	3.00	632	617
Plantain starch	4.00	680	661
	1.00	655	571
	2.00	690	609
	3.00	708	633
Corn starch	4.00	725	664
	1.00	650	523
	2.00	660	571
	3.00	675	587
	4.00	725	625x

Table III: Physical properties of experimental materials.

Powder	Mean* Particle Size (μm)	Particle** Density, D (gcm^{-3})	Loose Bulk Density (gcm^{-3})	Relative Density, D_0	Moisture Content (%)
Paracetamol	51.50	1.286	—	—	—
Lactose	28.50	1.548	—	—	—
Natural sorghum starch	16.70	1.493	0.515	0.345	7.1
Pregelatinized sorghum starch	17.90	1.531	0.580	0.379	6.5
Natural plantain starch	23.20	1.424	0.424	0.298	7.8
Pregelatinized plantain starch	24.90	1.515	0.480	0.317	6.9
Natural corn starch	15.20	1.471	0.498	0.338	6.8
Pregelatinized corn starch	18.10	1.521	0.537	0.353	6.1

* Determination by microscopic method

**Determination by liquid pycnometric method

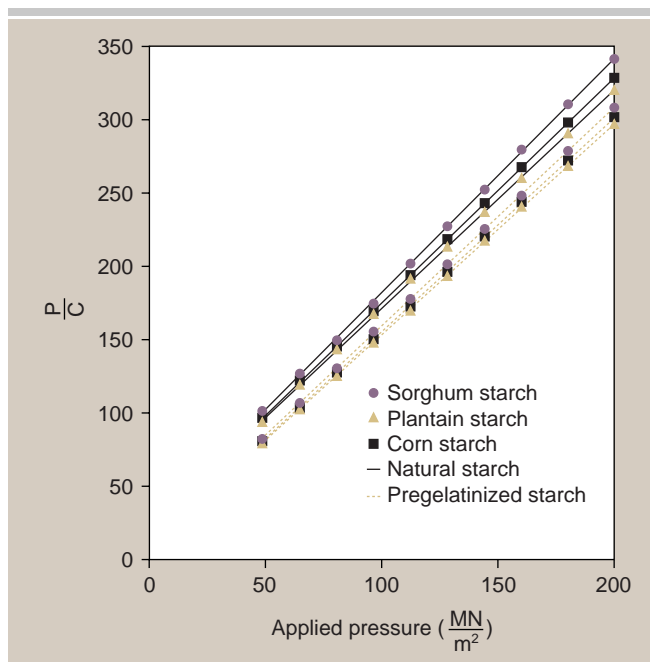


Figure 2: Kawakita plots for paracetamol formulations containing 2% w/w of binders.

what could be expected from an 85% formulation of paracetamol — P_y of pure paracetamol reported by other authors to be 96.9 and 110 MNm^{-2} (15,16).

Figure 2 shows representative Kawakita plots for paracetamol formulations containing 2% w/w binders. A linear relationship was obtained at all compression pressures used with a correlation coefficient of 0.999 for all formulations, and hence the equation may be used to predict the densification mechanisms of the paracetamol formulations. 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 formulations D_f whereas P_k values were obtained from the reciprocal of values of b .

The values of D_i and P_k are presented in Table IV. The D_i values decreased with the increase in starch binders, with D_i values for the formulations containing pregelatinized starch binders

being lower than those for the formulations containing natural starch binders. The D_i values also are higher than the D_0 values (compare Tables I and IV). Thus, the results suggest that although the D_0 values describe the loose initial relative density of the formulations because of die filling, D_i provides a measure of the packed initial relative density of the formulations with the application of small pressure as has been explained by Odeku and Itiola (17).

Low values of P_k indicate materials that are soft and that read-

ily deform plastically under pressure. Table IV shows that the values of P_k for the formulations decreased with the increase in concentration of the starch binder and that the formulations containing pregelatinized starches exhibited lower P_k values than the formulations containing natural starches. This indicates that the pregelatinized starches increased the softness of the formulation and its ability to deform plastically under pressure more than did the natural starches. The influence of the nature of the starches on P_k values does not appear to be clear-cut, but the formulations containing pregelatinized plantain starch generally exhibited the lowest P_k values.

Odeku and Itiola have shown that P_y is different from P_k in that whereas the P_y values relate essentially to the onset of plastic deformation during compression, the P_k values appear to relate to the total amount of plastic deformation occurring during the compression process (17). Thus, the present results suggest that the use of pregelatinized starches would facilitate the onset of plastic flow and improve the total amount of plastic flow in para-cetamol granule formulation when compared with the use of natural starches.

Conclusions

This article shows that pregelatinization of the starch binders

- produces starches having larger particle size, higher particle density, higher bulk density, higher relative density, and lower moisture content
- enhances the plasticity of the granulations as shown in the values of P_y onset of plastic deformation during compression and P_k total amount of plastic deformation occurring during compression, which were lower for granulations containing pregelatinized starches than for those containing natural starches
- increases both the loose relative density (i.e., D_p) and packed relative densities (i.e., D_i and D_a) of the granulations in the die as reflected in the D_p , D_i , and D_a values of the granulations as reflected in the values obtained for granulations containing natural and pregelatinized starches.

It also can be concluded that the increase in binder concentration enhanced the plasticity of the granulations as shown by P_y and P_k but reduced the packed relative densities of the granulations upon application of pressure, (i.e., D_p , D_i , and D_a) while increasing D_p i.e., loose initial relative density.

Finally, from the results obtained, sorghum and plantain starches along with their pregelatinized forms compared favorably with the standard corn starch BP and its pregelatinized form.

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We are grateful to Nigerian-German Chemical Company Ltd. ([formerly Hoechst Nig. Ltd.], Sango-Otta, Ogun State, Nigeria) for the gift of corn starch BP grade and paracetamol powder.

Table IV: Parameters obtained from Kawakita plots for paracetamol tablet formulations.

Starch Binder	Concentration of Binder (% w/w)	Formulations Containing Natural Starch		Formulations Containing Pregelatinized Starch	
		$D_i(1-a)$	P_k	$D_i(1-a)$	P_k
Sorghum	0.0	0.337	25.953	0.337	25.953
	1.0	0.384	16.960	0.336	9.740
	2.0	0.373	16.863	0.327	9.616
	3.0	0.367	13.911	0.324	8.456
	4.0	0.356	13.084	0.312	8.454
Plantain	1.0	0.346	17.864	0.314	8.696
	2.0	0.329	17.513	0.306	8.650
	3.0	0.312	17.260	0.301	8.275
	4.0	0.304	16.135	0.295	7.761
Corn	1.0	0.358	18.981	0.317	8.759
	2.0	0.345	16.615	0.314	8.375
	3.0	0.319	15.640	0.310	7.893
	4.0	0.312	14.405	0.305	7.872

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