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Effects of starches on the mechanical properties of paracetamol tablet formulations. II. Sorghum and plantain starches as disintegrants

GBENGA ALEBIOWU[1]*
OLUDELE ADELANWA ITIOLA[2]

[1] *Department of Pharmaceutics*
Faculty of Pharmacy
Obafemi Awolowo University
Ile-Ife, Nigeria

[2] *Department of Pharmaceutics*
and Industrial Pharmacy
Faculty of Pharmacy
University of Ibadan, Ibadan, Nigeria

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This study evaluates the disintegrant properties – tablet disintegration time (*DT*) and crushing strength – friability/disintegration time (*CSFR/DT*) ratio of a paracetamol tablet formulation prepared with sorghum and plantain starches in comparison with corn starch BP. The effects of disintegrant concentration, relative density of tablets and the mode of disintegrants addition were studied. The study revealed that the rank order of effectiveness of the starches as disintegrants was corn > plantain > sorghum. The mode of addition of disintegrants, disintegrant concentration and relative density had a significant impact on the disintegrant properties. The tested starches, namely, sorghum and plantain, showed promising results.

Keywords: sorghum starch, plantain starch, pregelatinization, crushing strength, friablility, disintegration time

Disintegrants are a category of excipients that are incorporated into conventional tablets. A common example is starch (*e.g.*, corn starch). It may be incorporated into the powder mixture before granulation (internal disintegrant), or it may be added as a dry powder to the already prepared granules (external disintegrant), or it may be added both internally and externally. Many tablet formulations contain both internal and external starch. Pilpel *et al.* (1) proposed that tablets containing both internal and external starch followed an intermediate pattern, initially disintegrating into granules, which then deaggregated into fine particles.

Various research has been carried out on the use of starches as disintegrants in tableting (2, 3). *Sorghum bicolor* L. (*Poaceae*) and *Musa paradisiaca* L. (*Musaceae*) Only preliminary studies were carried out on starches from (4, 5)

This paper reports a detailed study of the effects of relative density and disintegrant concentration on the disintegrant properties of paracetamol tablets prepared with sorghum and plantain starches added as internal, external or internal-external disintegrants. Corn starch BP was used as a standard.

* Correspondence, e-mail: galebiowu@yahoo.co.uk

EXPERIMENTAL

Materials

Sorghum and plantain starches were extracted from seeds of *Sorghum bicolor* Linn (*Poaceae*) and mature unripe fruits of *Musa paradisiaca* Linn (*Musaceae*), respectively, using established methods (6). Corn starch BP (7) (BDH, UK), paracetamol BP (Nigerian-German Chemical Company, Nigeria) and gelatin BP (Hopkin and Williams, UK), were used.

Methods

Swelling and water retention capacity. – The method described by Bowen and Vadino (8) was used for swelling capacity determination. Ring's method (9) was used for water retention capacity determination. Both determinations were done in triplicate. Swelling capacity and water retention capacity values are shown in Table I.

Table I. Swelling and water retention capacities of starche

Starch	Swelling capacity (V_2/V_1)[a]	Water retention capacity (m_1/m_2)[a]
Sorghum	1.48 ± 0.08	3.28 ± 0.11
Plantain	1.53 ± 0.05	3.43 ± 0.09
Corn BP	1.57 ± 0.01	3.06 ± 0.09

[a] Mean ± SEM, $n = 3$.
V_1, V_2 = initial, final volume (after swelling) of starch powder.
m_1, m_2 – mass of a residue before (after) drying at 70 °C

Preparation of granules. – Paracetamol granules containing different concentrations of starch disintegrants (2.5, 5.0, 7.5 and 10.0% *m/m*), added either as internal (type A), external (type B) or 50% external plus 50% internal (type C) disintegrants, were prepared by wet granulation in a Hobart planetary mixer (Hobart Manufacturing, UK) using gelatin BP binder solution to produce samples containing 4% *m/m* gelatin in the final dried granules.

Type A granules were prepared by dry mixing the required quantity of paracetamol and each starch for 5 min in a Hobart planetary mixer and then moistening them with gelatin binder solution. The resulting wet masses were granulated by passing them manually through a sieve size 1400 μm, dried at 60 °C for 6 hours and then resieved through a sieve size 1000 μm. Type B granules were prepared by mixing the required amount of paracetamol with the binder solution. The resulting wet masses were then granulated as for type A granules. The required amount of starch was then added as external starch. Type C granules were prepared by dry mixing the required amount of paracetamol and 50% of starch disintegrant for 5 minutes and then moistening them with binder solution. The resulting wet masses were granulated as before, and the remaining

50% of disintegrant was added as external starch. Particle density was determined by the pycnometer method with benzene as displacement fluid. Sieve size fractions of 500–1000 μm were separated to be used for the remaining studies and stored in screw-capped jars until required.

Preparation of tablets. – Each batch of 550 mg granules was compressed for 1 min into tablets with predetermined loads (95.95–159.92 MN m^{-2}) on a Carver hydraulic hand press (Carver, USA) using a 12.5-mm die and flat-faced punches lubricated with a 2% (*m/m*) dispersion of magnesium stearate in benzene before each compression. After ejection, the tablets were stored over silica gel for 24 hours to allow for elastic recovery and hardening, and to 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 density (*RD*) was calculated using the equation:

$$RD = m/V_t \rho_s$$

where V_t is the volume (cm^3) of the tablet and ρ_s is the particle density (1.280–1.304 g cm^{-3}) of solid material. The volume reduction, which increased with successive increase in compressional pressure, led to variable of relative density.

Disintegration test. – Tablet disintegration time (*DT*) was determined in distilled water at 37 ± 0.5 °C in a BP Manesty (Manesty Machines, UK) disintegration test unit. Six tablets were tested at each relative density and the results were expressed as an average of three determinations.

Determination of tablet crushing strength and friability. – A Monsanto hardness tester (Monsanto Chemical, USA) was used at room temperature to determine the load required to diametrically break the tablets (crushing strength) into two equal halves. Tablets with signs of lamination or capping were not used.

The percent friability of the tablets was determined using a Roche friabilator (Erweka Apparatebau, Germany) operated at 25 rev min^{-1} for 4 minutes. Ten tablets were used at each relative density. The average of three determinations was taken for the crushing strength and friability values. Statistical analysis (standard error of the mean at a confidence level of 0.95) of the results in Tables I to III revealed the low variability between the tables.

RESULTS AND DISCUSSION

The crushing strength of 5% (*m/m*) disintegrant concentration for tablets of relative density of 0.90 is presented in Table II. The rank order of crushing strength for the three modes of addition of starch disintegrant is: external > internal – external > internal, for all starches. This could be due to the fact that in the case of external disintegrant, there were more particle-particle contact points, particularly with the particles of the starch which help create more solid bonds; hence, higher crushing strength values were obtained. It was equally observed that as the relative density increased, the crushing strength of the tablets increased (Fig. 1). This could be due to the decrease in porosity and subse-

Table II. Values of crushing strength (CS) disintegration time (DT), friability (FR) and crushing strength-friability/disintegration time ratio (CSFR/DT) of paracetamol tablets[a] disintegrant concentration and relative density 0.90

Disintegrant	Mode of addition	*CS* (N)[b]	*DT* (min)[b]	*FR* (%)[b]	*CSFR/DT*[b]
None	–	70.84 ± 0.47*	40.35 ± 0.17	0.86 ± 0.07	2.04
Sorghum starch	Internal	59.34 ± 0.18	18.40 ± 0.33	1.26 ± 0.07	2.56
	External	62.11 ± 0.11	9.67 ± 0.26	1.24 ± 0.06	5.18
	Internal-external	59.74 ± 0.25	9.26 ± 0.06	1.06 ± 0.009	6.09
Plantain starch	Internal	63.44 ± 0.22	14.19 ± 0.04	1.20 ± 0.06	3.72
	External	68.12 ± 0.31	10.27 ± 0.04	1.18 ± 0.05	5.62
	Internal-external	66.70 ± 0.18	12.48 ± 0.02	1.13 ± 0.08	4.73
Corn starch	Internal	66.36 ± 0.15	10.84 ± 0.11	1.10 ± 0.07	5.56
	External	67.57 ± 0.29	9.57 ± 0.07	1.03 ± 0.09	6.85
	Internal-external	66.36 ± 0.21	9.23 ± 0.10	0.88 ± 0.04	8.20

* Standard error of the mean *n*, number of independent analysis = 3
[a] 5.0 % (*m/m*)
[b] Mean ± SEM, *n* = 3.

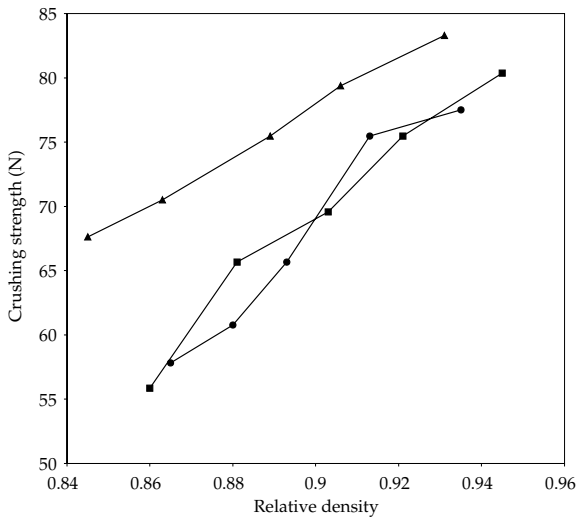

Fig. 1. Effect of relative density on crushing strength for paracetamol tablets containing 7.5% (*m/m*) of externally added starch disintegrant: ● - sorghum starch, ▲ - plantain starch, ■ - corn starch BP. Each point is the mean of three measurements.

quent increase in the number of contact points, which would lead to an increase in the degree of bonding between the particles (10, 11). It is well known that friability tends to decrease with an increase in the crushing strength and relative density of tablets, as shown in Fig. 2 for the external mode of addition of starch disintegrant at a concentration of 7.5 % (*m/m*).

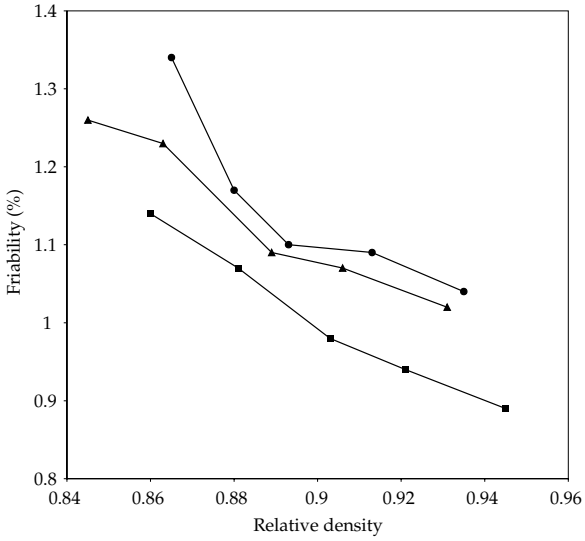

Fig. 2. Effect of relative density on friability of paracetamol tablets containing 7.5% (*m/m*) of externally added starch disintegrant: ● - sorghum starch, ▲ - plantain starch, ■ - corn starch BP. Each point is the mean of three measurements.

The rank order of disintegration rate for the mode of addition was observed to be external < internal – external < internal. This order could be due to the initial amount of starch disintegrant exposed to the disintegrating medium (deionized water). For external disintegrants, a larger amount of starch disintegrant was initially exposed to the disintegrating fluid, which led to the absorption of large quantities of water and subsequent generation of higher swelling force. This force activated the active mechanism of disintegration at a faster rate than for internal-external and internal modes of disintegrant addition (12).

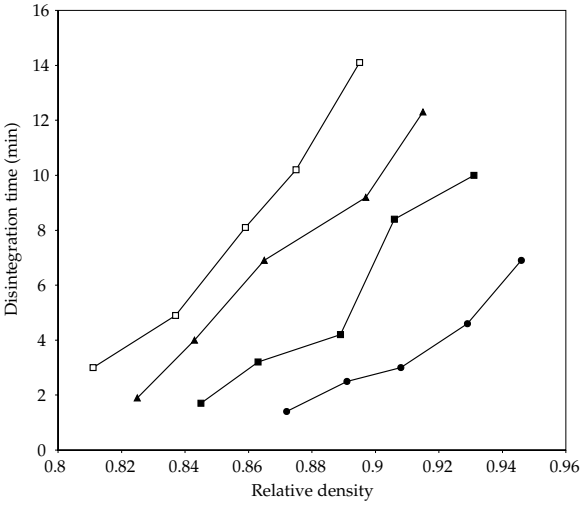

Fig. 3. Effect of relative density on disintegration time for paracetamol tablets containing different concentrations of externally added plantain starch disintegrant: □ - 2.5% (*m/m*), ▲ - 5% (*m/m*), ■ - 7.5% (*m/m*), ● - 10% (*m/m*). Each point is the mean of three measurements.

The effect of the concentration of starch disintegrant on the disintegration time is shown in Table III. Increase in concentration led to a decrease in the disintegration time (Fig. 3). This could be due to the increase in swelling, which is associated with the increase in starch concentration (13, 11). The increase in relative density led to an increase in the disintegration time; similar observations have been already reported (1, 14). With the increase in relative density, there was a decrease in porosity (15); consequently, water penetration into the tablets would slowdown, swelling would be reduced and development of the active mechanism of disintegration was reduced. When porosity decreased, more solid bridges were formed, which made the annihilation of interparticle force more difficult (10). Plots of disintegration time, *DT*, *vs.* relative density for 5.0% (*m/m*) externally applied starch disintegrant are shown in Fig. 4.

Table III. Values of crushing strength (CS), disintegration time (DT), friability (FR) and crushing strength-friability/disintegration time ratio (CSFR/DT) of paracetamol tablets with external disintegrants

Disintegrant	Starch concentration. (%, *m/m*)	*CS* (N)[b]	*DT* (min)[b]	*FR* (%)[b]	*CSFR/DT*[b]
None	–	70.84 ± 0.47	40.35 ± 0.62	0.86 ± 0.07	2.04
Sorghum starch	2.5	58.90 ± 0.21	17.66 ± 0.04	1.26 ± 0.06	2.65
	5.0	62.11 ± 0.11	9.67 ± 0.26	1.24 ± 0.06	5.18
	7.5	67.14 ± 0.27	5.89 ± 0.02	1.14 ± 0.02	9.99
	10.0	70.93 ± 0.19	3.00 ± 0.04	1.11 ± 0.05	21.30
Plantain starch	2.5	62.02 ± 0.24	14.56 ± 0.03	1.20 ± 0.10	3.55
	5.0	68.12 ± 0.031	10.27 ± 0.04	1.18 ± 0.05	5.62
	7.5	77.73 ± 0.36	6.97 ± 0.07	1.09 ± 0.09	10.23
	10.0	80.58 ± 0.21	3.03 ± 0.08	1.00 ± 0.08	26.59
Corn starch	2.5	67.18 ± 0.28	11.64 ± 0.10	1.06 ± 0.05	5.44
	5.0	67.57 ± 0.29	9.57 ± 0.07	1.03 ± 0.09	6.85
	7.5	68.82 ± 0.24	3.67 ± 0.04	1.01 ± 0.01	18.57
	10.0	69.40 ± 0.28	2.19 ± 0.04	0.99 ± 0.04	32.01

* Standard error of the mean n, number of independent analysis = 3
[a] Relative density of 0.90.
[b] Mean ± SEM, $n = 3$.

For the starches, the rank order of causing disintegration of paracetamol tablets is corn > plantain > sorghum. This could be due to the swelling and water retention capacities of the starches (Table I). Swelling mechanism has been widely reported to influence the disintegration of tablets (16, 12). The tested starches (*i.e.*, sorghum and plantain) had a lower swelling capacity than corn starch. Furthermore, the water retention capacity value of the tested starches was higher than that of corn starch.

The *CSFR/DT* ratio has been suggested as a better index of measuring tablet quality than the crushing strength-friability ratio (*CSFR*) because in addition to measuring tablet strength (crushing) and weakness (friability), it simultaneously evaluates all negative effects of these parameters on disintegration time (17). In general, higher values of the

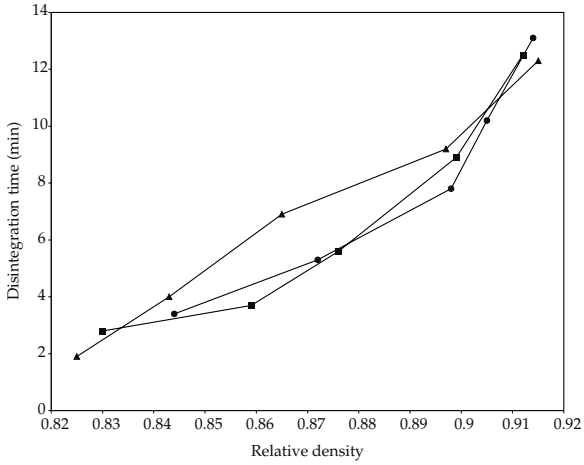

Fig. 4. Effect of relative density on disintegration time for paracetamol tablets containing 5.0% (*m/m*) of externally added starch disintegrant: ● - sorghum starch, ▲ - plantain starch, ■ - corn starch BP. Each point is the mean of three measurements

CSFR/DT ratio indicate a better balance between binding and disintegration properties. From the values shown in Table III it is seen that there was a general increase in the *CSFR/DT* ratio for paracetamol tablets with increasing disintegrant concentration at relative density of 0.90. Considering the *CSFR/DT* ratio the rank order of effectiveness of starches as disintegrants is corn > plantain > sorghum, and it is external > internal > external – internal for the mode of addition. The *CSFR/DT* was equally affected by the relative density of tablets, with the increase in relative density leading to a low value of *CSFR/DT*. This could be due to formation of more solid bonds and reduced porosity leading to higher crushing strength and longer disintegration times.

CONCLUSIONS

Use of the *CSFR/DT* ratio for the assessment of the disintegrant activity of paracetamol tablets indicates that corn starch has the best overall disintegrant property for the three modes of disintegrant addition employed. It also showed that the external mode of disintegrant addition resulted in the balance between binding and disintegration properties. This work has revealed that, from the value of the *CSFR/DT* ratio, the two tested starches (plantain and sorghum) in the paracetamol tablet formulations studied could be useful as alternative disintegrants for tablet formulations.

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S A Ž E T A K

Utjecaj vrste škroba na mehanička svojstva tableta paracetamola II. Škrobovi iz sorga i pisanga kao sredstvo za raspadanje

GBENGA ALEBIOWU i OLUDELE ADELANWA ITIOLA

U okviru ovog rada proučavana su svojstva tableta paracetamola priređenih sa škrobom sorga i pisanga i uspoređivani s kukuruznim škrobom BP: raspadljivost (*DT*) i čvrstoća – odnos rastrošljivosti i raspadljivosti (*CSFR/DT*). Proučavan je utjecaj koncentracije, načina dodavanja sredstva za raspadanje i relativne gustoće tableta. Utvrđeno je da je redoslijed učinkovitosti škroba kao sredstva za raspadanje bio kukuruzni škrob > škrob iz pisanga > škrob iz sorga. Način dodavanja sredstva za raspadanje, njegova koncentracija i relativna gustoća tableta imaju značajni utjecaj na raspadljivost. Ispitivani škrob sorga i pisanga pokazuju obećavajuće rezultate.

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

Department of Pharmaceutics, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Nigeria

Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, University of Ibadan, Ibadan, Nigeria