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Effects of Native and Pregelatinised Fonio starches on compression, mechanical and release properties of paracetamol tablet formulations

J. MUAZU*[1], H. MUSA[2] AND P.G. BHATIA[2].

[1]*Department of Pharmaceutical Services, University of Maiduguri Teaching Hospital, PMB 1414, Borno State, Nigeria.*

[2]*Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University, Zaria, Nigeria.*

Native and modified (pregelatinised) Fonio starches were evaluated as binding agents in comparison with maize starch B.P. in paracetamol tablet formulations. Compressional properties of the formulations were analyzed using density measurements and assessed by the compression equation of Heckel. The mechanical properties of the formulations were assessed using crushing strength and friability while drug release properties were assessed using disintegration and dissolution times. Tablet formulations containing pregelatinised Fonio starch exhibited low onset of plastic deformation, while that of native Fonio starch were similar to that of maize starch BP. The crushing strength, disintegration and dissolution times increased with increase in binder concentrations while the friability value decreased. The results show that Fonio starch would be a good alternative to maize starch in producing uncoated tablets.

Keywords: Fonio starch, pregelatinised starch, binder, compression, Heckel equation.

INTRODUCTION

The plant Fonio (*Digitaria exilis*, DE, family Poaceae) originated from West Africa. It is called *findi* by fulanis, *acha* in Hausa and Fonio or Hungry rice in English. Many starches obtained from food crops have shown great potential as excipients in tablet formulations [1]. However, no work has been reported on the effect of Fonio starch and pregelatinised Fonio starch (PGS) on compression, mechanical and release properties of paracetamol tablet formulations.

Many researchers have carried out studies on compression characteristics of pharmaceutical powders with many equations and expressions reported [2-4]. The Heckel equation is one of the most widely used equations for describing the compression properties of powders [5-8], it relates the relative density (D) of a powder bed during compression to the applied pressure (P) which provides information on the mechanism of powder consolidation during compact formation by the equation

$$1n(1/1-D) = kP + A \quad \ldots(1)$$

Where k and A are constants.
The slope of the straight line portion, k, is the reciprocal of the mean yield pressure, Py, of the material. The intercept of the extrapolated linear portion (A) is a function of the original compact volume. From the value of A, the relative Density, DA can be calculated using the following equation.

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

The relative density of the powder bed at the point when the applied pressure equals zero (D0) is used to describe the initial rearrangement phase of densification as a result of die filling and this is obtained from the ratio of the loose density to the particle density [9]. The relative density DB, describes the phase of

* Author to whom correspondence may be addressed

rearrangement of particles during the initial stages of compression. The extent of the rearrangement phase depends on the theoretical point of densification at which deformation of particles begins (Equation 3)

DB = DA - D0 …… (3)

In the present study, the compression properties of Fonio starch and PGS were evaluated using the compression equation of Heckel. The mechanical properties were assessed by crushing strength and tablet friability while the release property was assessed by disintegration and dissolution times. Paracetamol was used as the model drug for the study because of its poor compression properties [6].

EXPERIMENTAL

Materials and Reagents

Paracetamol powder and maize starch B.P. were from May and Baker LTD (Essex, UK). Magnesium stearate was from BDH Chemicals (Poole, England) while lactose was from East Anglia Chemicals (Suffolk, England) and Fonio grains were from Samaru market, Zaria, Nigeria.

Extraction and pregelatinisation of Fonio starch

The extraction of Fonio starch from the grain was carried out as described previously [11] and the pregelatinisation was performed using the method described by Musa *et al.* [11].

Preparation of granules

Dried powdered Fonio starch or PGS equivalent to 0, 2.5, 5.0, 7.5, 10.0 and 12.5% w/w or 7.5% w/w maize starch B.P. respectively, were mixed with paracetamol powder (70% w/w) and made up to 100% with lactose. The powders were dry-mixed for 5 minutes in a tumbler mixer and moistened with distilled water. Massing was continued for 5 minutes and the wet masses were granulated by passing them manually through a wire mesh (1.7 mm) and dried in a hot air oven for 18 hours at 50°C. The dried granules were sieved through a wire mesh (1.0 mm) and then stored in airtight containers.

Preparation and evaluation of compacts

A 12.5mm diameter die set was lubricated with 1% w/v dispersion of magnesium stearate in chloroform. Compacts equivalent to 500 mg paracetamol were produced by compressing the granules for 60 s with predetermined loads using an Erweka AR 400 (Erweka, Heusenstamm, Germany) single punch tablet press. Fifty tablets were compressed at each pressure level. After ejection, the tablets were stored over silica gel in a dessicator for 24 h to allow for elastic recovery and hardening in order to prevent falsely low yield values [12]. Their masses (m) and dimensions were then determined. Their relative densities, R were calculated using the equation:

$R = m / V_t.\rho_s$ ……..(4)

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

Crushing strength and friability tests

The crushing strengths of the tablets were determined using a TBH 100 Erweka hardness tester (Erweka, , Heusenstamm, Germany) while the percentage friability of the tablets was determined using an Erweka fribiliator operated at 25 rpm for 4 min.

Disintegration and dissolution tests

Disintegration times of the tablets were determined in distilled water maintained at 37 ± 0.5 °C using a ZT 71 disintegration tester (Erweka, Heusenstamm, Germany).

The dissolution test was carried out on the tablets using the USP [13] basket method on an Erweka dissolution Type DT 700 tester, (Erweka, Heusenstamm, Germany) rotated at 50 rpm in 900 ml of 0.1 M HCl, maintained at 37 ± 0.5°C. Samples (15 ml) were withdrawn at different time intervals and replaced with equal amounts of fresh medium. The sample was appropriately diluted and the amount of paracetamol released was determined using a

DU 520 series UV spectrophotometer (Beckman Coulter, Burkinghamshire, UK) at 243 nm.

Statistical analysis

The i-stat software (Instat, GraphPad Software Inc., CA, USA) was used to compare the effects of Fonio starch, PGS and maize starch B.P. on the tablet properties. At 95% confidence interval, the p value of 0.05 was considered the limit of significance.

RESULTS AND DISCUSSIONS

Fig. 1 shows representative Heckel plots for paracetamol formulations containing 7.5% w/w binder.

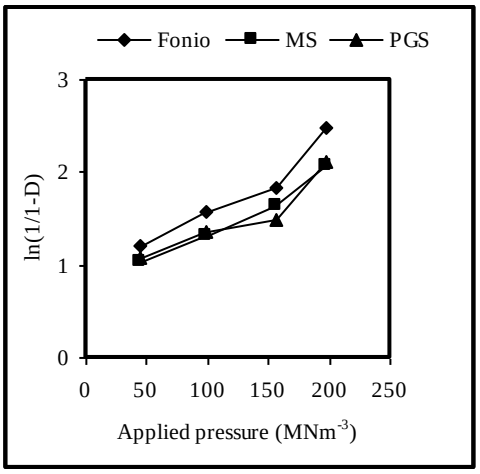

Figure 1. Heckel plots for paracetamol tablet formulations containing 7.5% w/w binder

The mean yield pressure, Py, was calculated from regions of the plots showing linearity. The intercept (A) which represents the point at which an intact tablet was just formed during compression, was determined from the extrapolation of the region used for the determination of Py. The DA and DB values were calculated using equations 2 and 3 respectively. The values of D0, Py, DA and DB for the formulations are presented in Table 1

The degree of initial packing in the die as a result of die filling (D0) for all formulation increased as the binder concentration was increased. This shows that initial packing of the granules as a result of die filling increased with increase in binder concentration which is in agreement with earlier reports [5, 14]. The formulation containing MS has the lowest D0 value. The order of D0 found was MS<DE<PGS

Table 1. Parameters obtained from Heckel plots for paracetamol tablet formulations

Starch	Sample conc. %w/w	D0	Py (MNm^{-2})	DA	DB
	0	0.216	101.52	0.728	0.512
Fonio	2.5	0.227	148.97	0.825	0.598
	5	0.241	186.36	0.823	0.582
	7.5	0.255	176.03	0.820	0.565
	10	0.262	158.71	0.818	0.556
	12.5	0.269	162.08	0.815	0.546
PGS	2.5	0.231	142.87	0.837	0.606
	5	0.249	125.16	0.833	0.584
	7.5	0.252	121.56	0.830	0.578
	10	0.265	132.03	0.826	0.561
	12.5	0.271	110.32	0.821	0.550
MS	7.5	0.247	121.02	0.798	0.551

PGS- Pregelatinised Fonio starch MS- maize starch

The DB value represents the particles rearrangement phase in the early compression stages and indicates the extents of particles or granules fragmentation, although fragmentation can occur concurrently with plastic or elastic deformation of constituent particles [14]. The DB value generally decreased with increase in the binder concentration. The order of DB value was PGS>DE>MS. This indicates that granule fragmentation decreased with an increase in starch concentration.

The DB values were also observed to be higher than D0 value. This can be attributed to granule fragmentation and the subsequent filling of void spaces between particles which occurs extensively at low pressure [14]. Further, the loose packing of the large granules at zero pressure tended to yield low Do value [9].

The Py value (mean yield pressure) is inversely related to ability of material to deform plastically when compressed [9]. The value of Py decreased with increase in binder concentration for all the starches, implying that the onset of plastic deformation in the formulation occurred at lower pressure [7].

Maize starch had a lower Py value, indicating less force was required to deform them. The relative higher Py value observed in 2.5% w/v PGS & Fonio starches indicate that the granules were softer and more plastic and hence could be deformed readily. The crushing strength values increased while friability decreased with an increase in binder concentration.

Table 2. Crushing strength, Friability and Crushing Strength- Friability Ratio (CSFR) for paracetamol tablet formulations.

Starch	Binder concentration (%w/w)	Crushing strength (KgF)	Friability (%)	CSFR
	0	1.01±1.13	100±0.00	0.01
Fonio	2.5	8.88±2.01	0.64±0.02	13.88
	5	11.13±1.18	0.62±0.03	17.95
	7.5	11.17±2.14	0.52±0.04	21.48
	10	13.41±1.62	0.43±0.03	31.19
	12.5	14.01±1.63	0.39±0.01	35.92
PGS	2.5	4.79±1.78	1.08±0.02	4.44
	5	10.18±1.24	0.62±0.05	16.42
	7.5	10.46±1.21	0.58±0.03	18.03
	10	12.98±2.34	0.51±0.01	25.45
	12.5	11.08±1.97	0.41±0.03	27.02
MS	7.5	12.00±2.09	0.46±0.02	26.09

PGS- Pregelatinised Fonio starch MS- Maize starch

It is known that a high concentration of a plasto-elastic binding agent leads to an increase in plastic deformation of the formulation and consequently to the formation of more solid bonds which causes increased tablet strength and resistance to fracture and abrasion [5-6]. Maize starch has higher crushing strength than PGS, but there was no significant difference between MS and Fonio starch ($p>0.05$).

The crushing strength-friability ratio (CSFR) can also be used as a measure of the mechanical strength of tablets. The values of CSFR for the tablets are shown on Table 2. There was an increase in CSFR values as a result of increased binder concentration. The values decreased in the order MS>Fonio>PGS.

The release of paracetamol from tablets was assessed by the disintegration and dissolution tests as shown in Table 3.

Table 3. Disintegration and Dissolution characteristics of paracetamol tablet formulations.

Starch	Binder concentration (%w/w)	Disintegration time (min)	Dissolution time (min)	
			t50	t70
	0	0.32±2.13	5.00±0.24	11.9±4.17
Fonio	2.5	0.48±1.74	8.40±2.07	20.5±3.12
	5	0.77±1.18	11.50±2.19	24.5±4.83
	7.5	0.98±2.15	12.40±1.87	29.4±2.89
	10	1.27±1.89	14.50±2.06	42.3±3.74
	12.5	1.47±2.38	16.10±1.18	51.0±4.80
PGS	2.5	0.37±1.71	5.90±1.07	5.9±3.91
	5	0.86±1.30	11.90±1.96	11.9±1.96
	7.5	1.21±1.47	11.64±2.03	30.1±3.07
	10	1.14±2.01	16.40±1.74	39.7±2.31
	12.5	1.02±1.32	13.60±2.05	42.3±2.74
MS	7.5	1.07±1.61	13.10±1.68	31.4±3.11

MS - Maize starch, PGS - Pregelatinised Fonio starch

Both the disintegration and dissolution times increased with increase in binder concentration for all the starches. However tablets containing PGS showed significantly lower disintegration and dissolution times ($p < 0.05$). This might be as a result of disorganization of the starch by process of pregelatinisation [11]. All the tablets conformed to the British Pharmacopoeia requirement [15] for uncoated tablets on disintegration.

CONCLUSION

The present study shows that paracetomol tablet formulations containing Fonio starch as a binder show similar onset of plastic deformation under applied compression pressure, similar mechanical and release properties with the standard substance (Maize starch B.P.). However the pregelatinized Fonio starch (PGS) exhibits lower plastic deformation, mechanical and release properties. The results show that Fonio starch can be used in place of maize starch B.P. as a binder.

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