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Application of the Gurnham Equation in Characterizing the Compressibility of Fonio and Sweet Potato Starches and their Paracetamol Tablet Formulations

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: A number of empirical relationships have been proposed to describe the compaction of pharmaceutical materials, among them are the Heckel, Kawakita and Gurnham equations.

Objective: To characterize the compressibility of fonio, sweet potato and corn starches and their paracetamol formulations using the Gurnham and Kawakita equations, and to determine the complementarity of these equations.

Materials and Methods: Starches were extracted from fonio (*Digitaria exilis)* grains *and* sweet potato (*Ipomea batatas)* tubers and modified by acid hydrolysis for 96 h. Paracetamol formulations containing 2.5–10.0 $\%^{w}/_{w}$ starch binders were prepared by wet granulation. Packing and compaction properties of native and modified starches and their formulations were determined using tapping procedures. The data obtained was analyzed using the Gurnham and Kawakita equations.

Results: The ranking for Gurnham compressibility, *c*, for the starches was sweet potato>corn>fonio, which was inversely related to the ranking for Kawakita maximum volume reduction, *a* and angle of internal flow, θ. There was no clear-cut pattern in the Gurnham compressibility of paracetamol formulation probably due to its multicomponent nature. There was correlation between *c, a* and θ for all the starches with the modified starches exhibiting higher compressibility than native starches. There appeared to be no correlation between *c* and Kawakita compressibility index, *b*.

Conclusion: The Gurnham equation appeared useful in characterising compressibility in single component systems and could be used along with Kawakita functions, to gain a better understanding of the deformation of powdered materials under pressure.

Keywords: Compressibility, Gurnham equation, Kawakita function, Fonio starch, sweet potato starch

INTRODUCTION

Compression, a phenomenon of compaction of pharmaceutical powders, is the reduction in bulk volume due to a decrease in the gaseous phase as a result of the application of pressure and deformation of the solid matter (Gurnham and Masson, 1946; Odeku, 2007; Mohan, 2012). The application of pressure to a powder bed causes a reduction in volume as a result of an initial closer packing of the powder particles and subsequent rearrangement of particles (Odeku, 2007). Deformation of solid matter could either be elastic or plastic along with the viscous flow of particles as a result of particles being pressed into the voids/interstices or even microsquashing as in the case of smaller particles (Gurnham and Masson, 1946; Odeku, 2007). The principles that govern the compression of a material largely depend on the nature of the material and some factors such as true density, nature of the solid i.e. crystalline/amorphous, size and shape of particles, brittleness/friability of solid and resistance to slipping/lubricating effect of particles (Gurnham and Masson, 1946; Mohan, 2012).

A number of empirical relationships have been proposed to describe the compaction of pharmaceutical materials; among them are the Kawakita, Heckel and Adams equations which may be expressed in terms of stress-strain, pressure-volume or pressure-density (Heckel, 1961; Kawakita and Ludde, 1970/71; Adams and McKeown, 1996; Odeku, 2007).

The Gurnham equation was first introduced in Chemical Engineering to study the expression of liquids from fibrous material by Gurnham and Masson (1946). They proposed that an increase in pressure expressed as a fractional increase over the existing pressure, results in a proportional increase in the apparent density of the mass.

$$\frac{(\Delta P)}{P} = A(\Delta\rho) \qquad (1)$$

where P is pressure, ρ is apparent density based on solid weight and total volume and A is a constant.

The volume reduction of fibrous materials described by Gurnham and Masson (1946) is similar to the events taking place during tablet compression. Thus, equation 1 has been integrated by Zhao et al, (2006) to describe compressibility

$$\rho = a \ln(P) + b \qquad (2)$$

where *a* and *b* are constants. Replacing density with porosity, ϵ (a measure of void spaces in a material) in Equation (2),

$$\epsilon = 1 - \rho_b/\rho_t \qquad (3)$$

To linearize the relationship between ln P and porosity for powder compression Equation 4 was obtained.

$$\epsilon = -c\ln(P) + q \qquad (4)$$

Where *c* and *q* are constants.

Expressing the equation in its differential form gave:

$$d\epsilon = 1 - \rho_b/\rho_t = \frac{-cdP}{P} \qquad (5)$$

The constant, *c*, indicates the effect of a change in pressure on compact porosity. Materials with large values of *c* indicate high volume reduction ability.

The Heckel and Kawakita equations have been used to characterise the compression properties of native and acid modified starches of fonio (*Digitaria exilis)* and sweet potato (*Ipomea batatas)* (Akin-Ajani *et al.*, 2014). However, the Heckel equation has been shown to be limited in its application because it is based on the assumptions that the yield stress (which is most likely pressure dependent) is constant and that the compact in the die is isotropic (Denny, 2002; Comoglu, 2007). Therefore, the aim of the present study was to characterize the compressibility of fonio, sweet potato and corn starches and their paracetamol formulations by the application of the Gurnham and Kawakita equations in order to gain a better understanding of the deformation of the materials under pressure and determine the complementarity of the equations.

Material and Methods

Materials

The materials used were paracetamol BP (Neimeith Nig. Plc, Lagos, Nigeria), corn starch (BDH, Poole, UK), grains of white fonio (*Digitaria exilis* Stapf. purchased from a local market in Samaru-Zaria, Kaduna State Nigeria) and tubers of sweet potato (*Ipomea batatas* Lam. purchased from a local farm in Offa, Kwara State, Nigeria). Fonio and sweet potato were authenticated at FRIN (Forestry Research Institute of Nigeria, Ibadan, Nigeria).

Method

Extraction and modification of starches

The starches were extracted from the relevant plant parts according to established procedures with little modification to suit each material (Young, 1984). The natural starch (500 g) was hydrolyzed in 1000 mL of 6 $\%^{w}/_{v}$ aqueous HCl acid at room temperature for 96 h without stirring. After hydrolysis, the reaction was terminated by neutralizing the suspension with 0.2 M sodium hydroxide solution, on attaining a pH of 7 (pH meter, Mettler Delta 340, Mettler Toledo Ltd, Halstead, England). The starch slurry was washed three times with distilled water and the water was decanted. The acid-modified starch was dried in a hot air oven at 60 °C for 18 h and then powdered using a laboratory mill. The starch was passed through a 125 µm mesh sieve and stored in an airtight container (Punchongkavarin *et al*, 2003; Akin-Ajani *et al*, 2014).

Preparation of paracetamol tablets

Batches (250 g) of paracetamol formulation (paracetamol 82%, corn starch 10% and lactose 8%)

with different concentrations (2.5 %, 5 %, 7.5 % or 10 %$^w/_w$) of starch (fonio, sweet potato or corn) as binder were prepared by wet granulation method (Akin-Ajani et al, 2005). The starch binders were used as mucilage. The masses were wet screened using a number 12 mesh sieve (1400 µm), dried at 60 °C for 6 h in a hot air oven and then dry-screened using a number 16 mesh sieve (1000 µm). Granules (500 – 1000 µm) were compressed into tablets (500 mg ± 10 mg) using pre-determined pressures. The tablet thickness of 4.88 mm ± 0.5 mm at zero porosity was calculated from particle density values.

Density measurements

Starch powder or formulation granules (20 g) was weighed and transferred into a dry measuring cylinder with known diameter. The height of the powder was measured and used to calculate the initial volume of the powder using the equation:

$$\text{Volume} = \pi r^2 h \qquad (6)$$

Where π is a constant, r is the radius of the cylinder (mm) and h is the height of the powder (mm).

The powders were subjected to increasing number of taps (signifying pressure) in the cylinder according to British Standard 1460 (38 taps per minute). The bulk volume (V_N) was determined at intervals of 25 taps until no further reduction in volume was observed.

The particle density of the starches was determined by the liquid pycnometer method with xylene as the displacement fluid. The bulk density was calculated and the relative density was obtained from the ratio of the bulk density to the particle density (Korhonen *et al.*, 2002; Itiola and Odeku, 2005).

Packing and cohesive property determination

Gurnham plots of % porosity, Є (Equation 3) against ln N (N being number of taps and taps being a form of pressure) for the starches; and against ln P (pressure applied) for paracetamol formulations were obtained. The values of Gurnham compressibility, *c* were derived from the slope (Equation 4).

The compressibility of the starches was determined using a modification of the Kawakita function (Equation 7) as described by Itiola and Odeku (2005) and later Adeoye and Alebiowu (2014)

$$\frac{N}{C} = \frac{1}{a} + \frac{1}{ab} \quad \text{when powders are used}$$

Or $\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} = \frac{abP}{(1+bP)}$ when compacts/ tablets are involved (7)

$$C = \frac{(V_o - V_N)}{V_o} \qquad (8)$$

$$a = \frac{(V_o - V_\infty)}{V_o} \qquad (9)$$

Where *a* (maximum volume reduction due to tapping) and *b* (coefficient of compression) are constants characterizing the material, N is the number of taps, P is pressure applied, C represents the degree of volume reduction achieved after N taps or P applied, V_o is the maximum bulk volume of the powder, V_N is the bulk volume of the powder after N taps, and V_∞ is the volume at zero porosity. V_∞ cannot be achieved in practice, thus the constant *a* was obtained from the slope of the linear plot of N/C versus N (Itiola and Odeku, 2005).

Determination of Angle of internal flow

The angle of internal flow, θ, which is a measure of interparticle friction that affects flowability of powder systems, was determined from plots of the decreasing porosity of the materials also known as porosity factor, K = ($Є^2 N/[1 - Є]$) against number of taps, N which leads to consolidation (Itiola and Odeku, 2005; Ogunjimi and Alebiowu, 2013).

$$K = GN + K_o \qquad (10)$$

Where G and K_o are constants (Itiola and Odeku, 2005).

Plotting K - K_o against N, gave a linear relationship from which the slope, tan θ was determined and where θ was the angle of internal flow (Ogunjimi and Alebiowu, 2013).

Statistical analysis

The statistical analysis was done using ANOVA, with the Origin® 6.1 software (OriginLab Corporation Northampton, MA, USA). The level of significance was set at 0.05.

Results and Discussion

Gurnham parameters of starches and paracetamol formulations

Gurnham plots for the starches are presented in Figure 1 while the representative Gurnham plots for formulations containing 7.5 % $^{w}/_{w}$ native and acid-modified starch binding agents are presented in Figure 2. The compressibility, *c*, obtained from the Gurnham equation for the starches and the paracetamol formulations are shown in Tables 1 and 2, respectively. The ranking of compressibility, *c*, was sweet potato > corn > fonio for the native starches and sweet potato > fonio > corn for the modified starches. The modified starches had higher values of *c* compared to the native starches indicating that they had better compressibility and higher volume reduction ability under pressure. Acid hydrolysis has been shown to result in starches with higher degree of packing and better compressibility compared to natural starches (Akin-Ajani *et al.*, 2014).

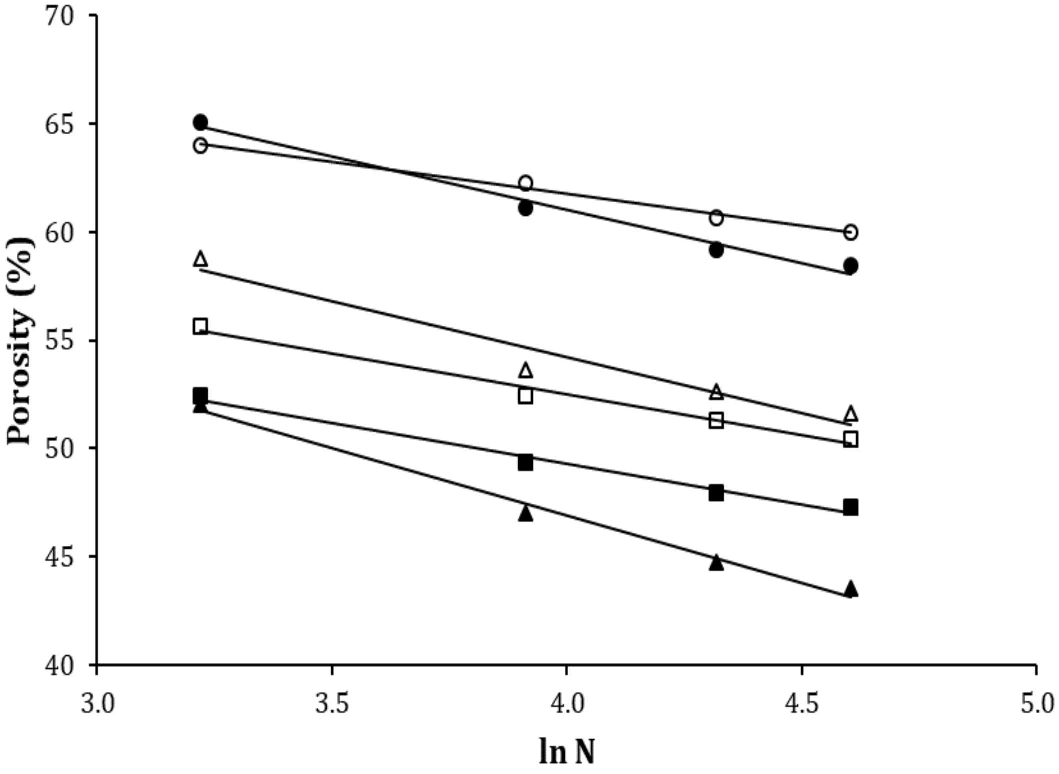

Figure 1. Gurnham plots of the native (open) and modified (closed) starches (● fonio, ▲ sweet potato, ■ corn)

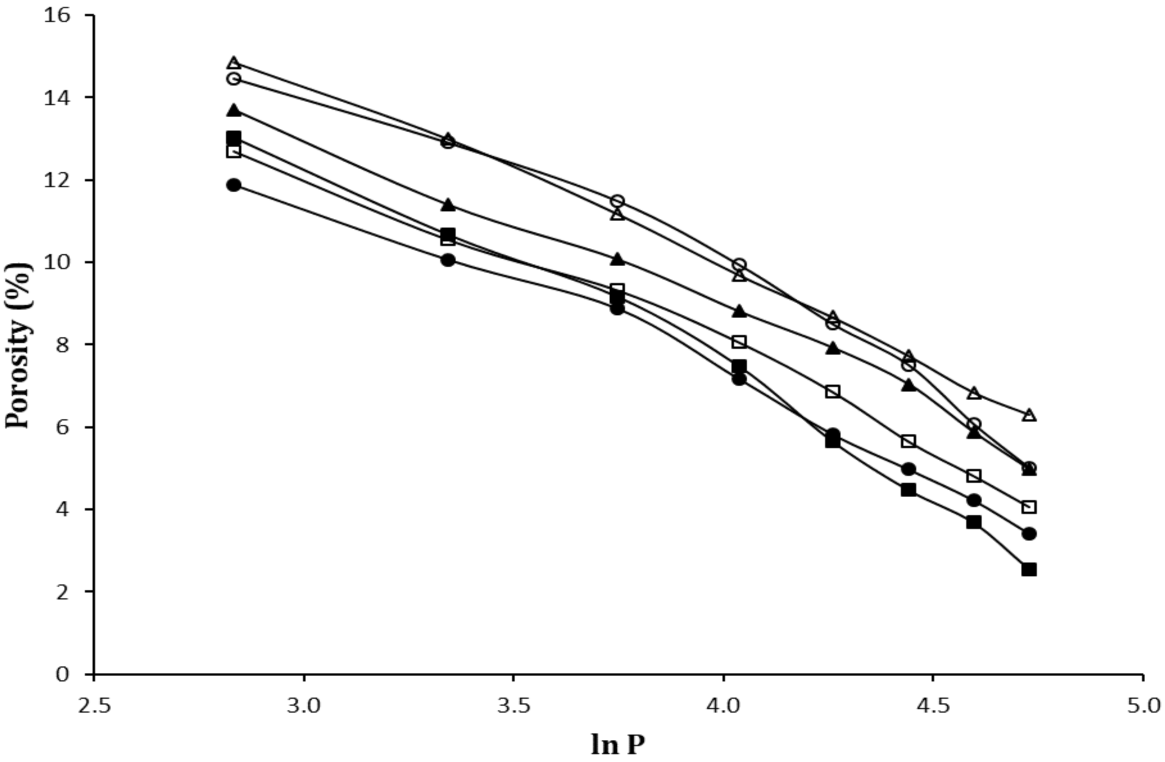

Figure 2. Representative Gurnham plots for paracetamol tablets containing 7.5 % $^{w}/_{w}$ native (open) and modified (closed) starch binding agents (● fonio, ▲ sweet potato, ■ corn)

There was no clear trend in compressibility of paracetamol formulations containing different concentrations of starch binding agents as neither nature of starch nor modification of the starches resulted in any major difference. This was probably due to the multi-component nature of the formulation. In a multi-component system, plastic deformation begins once the yield point for any of the components is exceeded during compression, which can then initiate the deformation of other components in the system, making it difficult to predict the deformational properties of the system (Zhao et al, 2006). The fragmentation of the granules in the formulation during compression may also add more complicating dimensions to predicting deformation.

Table 1. Gurnham Parameter of Compressibility of the Starches

Starch	**Form**	***c***
Fonio	Native	2.962
	Modified	4.907
Sweet potato	Native	5.153
	Modified	6.224
Corn	Native	3.752
	Modified	3.796

Table 2. Gurnham parameter for paracetamol formulations containing starch binders

Binder Concentration (%$^{w}/_{w}$)	Form	Compressibility, c		
		Fonio	Sweet Potato	Corn
2.5	Native	4.637	5.165	4.814
	Modified	3.902	4.384	4.675
5.0	Native	4.260	4. 314	4.025
	Modified	4.694	4.380	4.963
7.5	Native	4.978	4.613	4.510
	Modified	4.532	4.422	5.537
10.0	Native	4.683	4.492	4.898
	Modified	5.884	5.074	4.847

The results of the regression analysis of Gurnham parameters for paracetamol formulations containing starch binders presented in Table 3 indicate that there was a correlation between the compressibility index of paracetamol formulations containing the native and acid modified starches except for corn starch. On the other hand, there was no significant difference in compressibility with increase in the binder concentrations from 2.5 – 10.0 %.

Table 3. Values of multiple regression of the paracetamol formulations containing native versus modified starches as binders

	Fonio	Sweet potato	Corn
Correlation coefficient, r^2	0.752	0.781	0.019
p-value	0.497	0.468	0.990

Packing and cohesive properties of the starches

The packing and cohesive properties of starches have been shown to affect their compaction behaviour and their effects on other materials included in tablet formulation (Odeku and Itiola, 2005). Since there was no observable trend in compressibility using the Gurnham parameters, no further characterisation of the paracetamol formulations was carried out. Kawakita plots of the starches are presented in Figure 3 while the parameters obtained from the plots are presented in Table 4. The plots were linear with correlation coefficient, r > 0.996. The ranking of *a* for the native and modified starches was fonio > corn > sweet potato. This indicates that fonio starch exhibited the largest maximum volume reduction due to packing while sweet potato exhibited the least values. The process of volume reduction of powders is dependent on particle properties such as shape, size and the degree of interparticulate friction (Podczeck and Sharman, 1996). It is, however, not readily possible to quantify the relative contributions of each of these parameters to the volume reduction ability of the starches as no general rule exists concerning the influence of particle size and shape on packing and cohesive properties of powders even though both factors appear to interact (Itiola and Odeku, 2005).

Moreover, the applied tapping pressure would overcome to a large extent the electrostatic forces of attraction between the particles of the starches (Itiola, 1991). It has been shown that the polygonal shape but smaller particle size of fonio starch promoted closer packing of particles than the polyhedral shape and larger particle sizes of corn and sweet potato starches (Akin-Ajani *et al.*, 2014). The maximum volume reduction of the modified starches was however lower than the native starches although there was no significant (p>0.05) difference between the volumes.

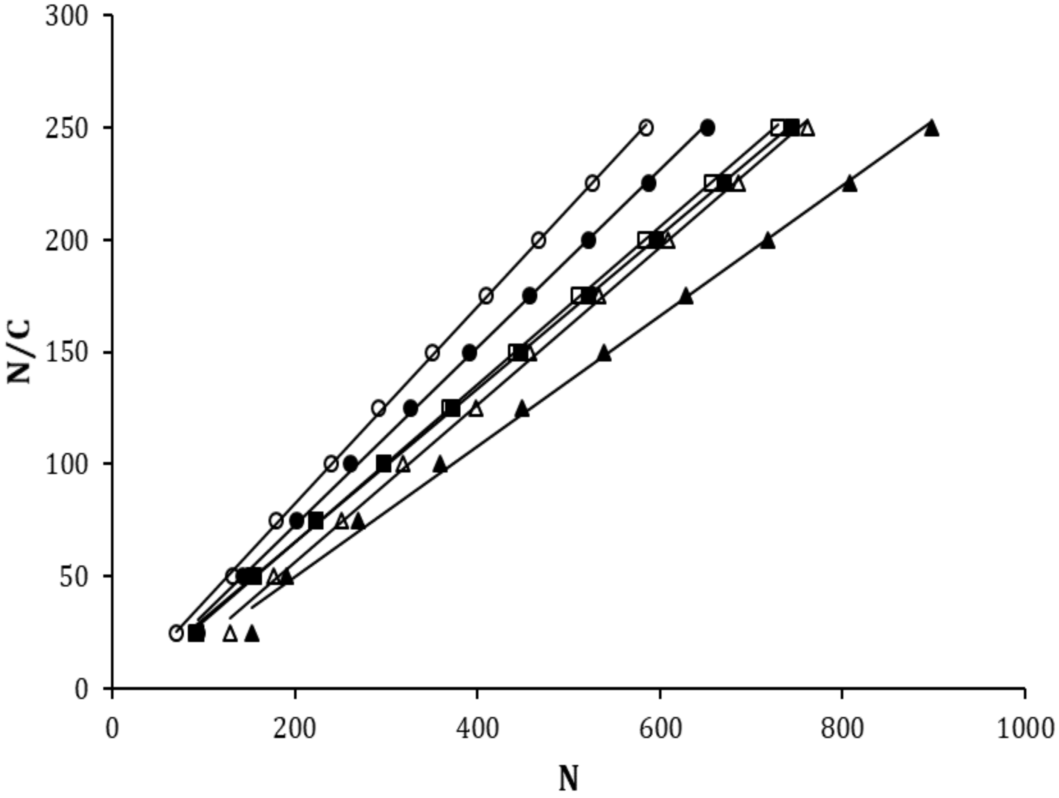

Figure 3. Plots of N/C vs N for native (open) and modified (closed) starches (● fonio, ▲ sweet potato, ■ corn)

Table 4. Values of parameters of compressibility using Kawakita function and flow for the starches

Starch	**Form**	***a***	**Correlation Coefficient r**	***b***	**θ**
Fonio	Native	56.94	0.999	0.185	39.60
	Modified	54.18	0.999	0.149	38.26
Sweet potato	Native	37.66	0.998	0.070	25.64
	Modified	34.19	0.996	0.119	19.18
Corn	Native	41.12	0.999	0.212	26.94
	Modified	40.25	0.999	0.324	24.32

The ranking of the Kawakita coefficient of compression, *b*, was corn > fonio > sweet potato. This implies that corn starch exhibited the highest compressibility while sweet potato exhibited the least. Values of *b* in the modified starches were higher than their natives except for fonio starch.

Values of angle of internal flow, θ, derived from the Kawakita equation are presented in Table 4. The ranking of θ for the native and modified starches was fonio > corn > sweet potato. The higher the angle of internal flow, θ, the higher the cohesiveness of the material and the poorer the flow properties, since cohesiveness of a powder is a measure of the difficulty with which particles can flow past each other when tapped or compressed (Varthalis and Pilpel, 1976). This indicates that sweet potato starch would be expected to have the best flow while fonio starch would have the least. Modified starches had lower values of θ than the natural starches thus supporting their lower cohesiveness. This indicates that modified starches would exhibit better flow properties.

A comparison of the data obtained from Gurnham equation, Kawakita function and angle of internal flow for the starches indicated that there appeared to be a correlation between Gurnham compressibility, *c*, Kawakita maximum volume reduction, *a* and angle of internal flow, θ for the starches. The values of *a*, and θ, were inversely related to the values of *c* with a general ranking of fonio > corn > sweet potato. Values of *a* and θ for the modified starches were lower than those of the native starches.

The results indicate that the lower the maximum volume reduction, the lower the cohesiveness i.e. the easier for particles to slip past each other, and the greater the compressibility. This relationship may be expressed mathematically by replacing P (change in pressure on compact porosity due to compressibility) in equation 5 with P (change in pressure on compact porosity due to maximum volume reduction) from equation 7. Thus, equation 5 can be expressed as:

$$d\epsilon = \frac{-dPa}{P+1} \qquad (11)$$

It appears that the Gurnham compressibility, *c*, and Kawakita volume reduction, *a*, measure change in porosity as a result of the application of pressure.

However, there appeared to be no correlation between the Kawakita coefficient of compression, *b*, and the Gurnham compressibility index, *c* (Tables 1 and 4). Odeku (2007) has shown that the coefficient of compression, *b*, was related to the plasticity of the material. Thus, the two parameters (*c* and *b*) measure different aspects of the compression cycle.

Conclusion

The present study revealed that compressibility was better assessed for single component systems such as the starches using Gurnham equation than the multicomponent systems - paracetamol formulations. The use of Gurnham equation along with Kawakita function and angle of internal flow, θ, improved the characterization of compressibility of the starches.

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