# Mechanical and Release Properties of Paracetamol Tablets Formulated With Some Natural and Modified Starch Mucilages

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**ABSTRACT**

Mechanical and release properties of paracetamol tablets formulated with mucilages of natural and pregelatinized forms of trifoliate yams, rice and standard corn starch BP have been evaluated. Tensile strength (T) and degree of brittleness (BFI) were employed to assess the mechanical properties of the tablets while disintegration time ($D_t$) and dissolution profiles ($t_i$, $t_{80}$, $k_1$ and $k_2$) were used to study their release properties. Results of the evaluation showed that tablets containing pregelatinized starches had lower T but also lower BFI than those formulated with natural starch binders. Values of disintegration time $D_t$ and $t_{80}$ (the time for 80% paracetamol to be released) were generally higher for formulations containing natural starch binders than those containing pregelatinized binders. The rate of drug release, as expressed by the dissolution rate constants $k_1$ and $k_2$, were higher for formulations containing pregelatinized binders, with $k_2$ being generally higher than $k_1$. Statistically, there were significant differences ($p$<0.05) between the values of these parameters for natural and pregelatinized starch binders. The ranking of T and $t_{80}$ for all the starch binders was corn > yellow T. yam > white T. yam > rice. For BFI, the ranking was yellow T. yam < corn < white T. yam < rice. These results suggest that mucilages of natural and pregelatinized starches from white and yellow trifoliate yams and rice are suitable as binders in paracetamol tablet production and may even perform better than corn starch BP in some formulations.

**KEY WORDS:** Natural starch; Pregelatinized starch; Tensile strength; Brittleness; Disintegration time; Dissolution rate

## INTRODUCTION

Starch is a unique and ubiquitous polysaccharide stored in the plant kingdom – found especially in roots, rhizomes, fruits and seeds – and is used in a variety of food and pharmaceutical industries (Thomas and Atwell, 1999). Worldwide, it constitutes 70-80% of the calories consumed by humans and is generally deposited in the form of minute granules or cells ranging from 1-100µm or more in diameter depending on its botanical source and treatment (Zobel and Stephen, 1995; Whisler and Bemiller, 1997, Buleon *et al*, 1998) Generally, it is tasteless and odourless solid, white, amorphous in nature and is insoluble in cold water (B.P .1998; Evans, 2002). In tablet formulations, starch is a multifunctional excipient, which can be employed as binders, disintegrants, glidants, lubricants or fillers (Garr and Bangudu, 1991; Kottke *et al*, 1992; Alebiowu and Itiola, 2001; Odeku *et al*, 2005) owing to its relative inertness and suitable physicochemical characteristics (Alebiowu and Itiola, 2002).

Consequent to heat-treatment of starch (pregelatinization), various starch properties such as physicochemical properties, rheology and compaction behaviour are expected to be affected. For example, a few minutes of heat treatment has been observed by Jacobs and Delcour (1998) to result in notable changes in physicochemical properties. These changes are expected to have a bearing on the mechanical and release properties of formulations in which these materials are incorporated as excipients.

The flesh of the peeled tubers of trifoliate yam are of three types; white, yellow and pink. The first two are found in Western and Eastern Nigeria while the third type is found in Cameroon. Trifoliate yam starch has about the smallest grains of all starches (about 1-3µm). It also produces a very thin paste of very low viscosity (Ayernor, 1985). Natural rice starch has granule size of about 2-6µm (Ayernor, 1985; Evans 2002). Rice starch amylose and its amylopectin have more branches than those of other starches. Also, rice starches are much more stable overtime (very slow retrogadation), and yield smooth gels. These unique properties had prompted the interest in studying the materials as tablet binders comparatively with corn starch BP. More so that little or no work has been documented on the mechanical and release properties of tablets formulated with these materials as binders especially involving more than one varieties of trifoliate yam starches studied together with rice starch and compared with Corn starch BP. The radial tensile strength of tablets (T) has been employed to assess the mechanical strength of compressed tablets. It is measured by firstly determining the diametrally applied force $F_d$ (MN) required to break a tablet, which is the load required to cause fracture (crushing strength), and then applying the following expression (Fell and Newton, 1970): $T = 2F_d/\pi dt$ (1) Where *d* and *t* are tablet diameter (m) and thickness (m), respectively.

The brittleness or the brittle fracture index (BFI) of a tablet has been defined by Itiola and Pilpel

(1986a) as an inverse measure of the relief by plastic deformation of localized stress within the tablet. It is an important measure of lamination or capping tendency of a tablet (Hiestand *et al*, 1977). It is calculated using the eq: $BFI = 1/2 (T/T_h-1)$ (2)

Where T is the tensile strength of the tablets without a central hole and $T_h$ is the apparent tensile strength of tablet having a hole, both measured at the same relative density. The hole acts as a built- in stress concentrator defect. Since this parameter is an inverse measure of localized stress relief, a low 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 (Hiestand *et al*, 1977).

For a compressed tablet to be worth its value, when exposed to fluid, it must undergo some sequential processes that ultimately lead to the bioavailability of the active component(s). For most conventional tablets, the first main step in the sequence is disintegration, followed by dissolution. Determination of disintegration time usually involves some mechanical agitation. Evaluation of dissolution profiles is commonly by employing Kitazawa's eq:

$$\ln [W_\infty/(W_\infty-W_t)] = k't \quad (3)$$

Multiple regression curves, intersecting at various times t's are usually obtained from the plots of $\ln [W_\infty/(W_\infty-W_t)]$ against t as employed by Kitazawa *et al* (1975) to determine the dissolution rate constant of caffeine tablets. The t's are the time phases of tranformation of the physical state of the dosage form solid granules to fine particles (Kitazawa *et al*, 1975, 1977a; Itiola and Pilpel, 1986b). Usually, the various slopes k' of the regression curves at the various times $t_1$, $t_2$, $t_3$ ...$t_n$ are respectively designated as $k'_1$, $k'_2$, $k'_3$... $k'_n$.

## MATERIALS AND METHODS

The four natural starches used were corn starch BP (BDH Chemicals, Ltd, Poole, UK) and the starches of white trifoliate yam (white T. yam), yellow trifoliate yam (Yellow T. yam) and rice prepared in the laboratory of the Department of Pharmaceutics and Industrial Pharmacy, University of Ibadan, Nigeria. Other materials used included paracetamol B.P. (BDH Chemicals Ltd, Poole, UK), Lactose B.P. (Aldrich Chemical Co. Ltd, Gillingham, Dorset, UK) and Polyvinylpyrrolidone, PVP (molecular weight 40,000; Aldrich Chemical Co. Ltd, Gillingham, Dorset, UK).

Tubers of white and yellow varieties of trifoliate yam (*Dioscorea dumetorum* Pax) were purchased from a local farm near Oyo town, Nigeria. The specimen tubers and shoots of the plants were authenticated in the herbarium department of the Forestry Research Institute of Nigeria, Ibadan, Nigeria. Grains of unmilled upland rice (*Oryza sativa,* Linn; ITA 150) were obtained from the International Institute for Tropical Agriculture, Ibadan, Nigeria.

**Preparation of natural and pregelatinized starches**

Isolation and purification of the natural starches of white T. yam, yellow T. yam and rice were carried out using established procedures (Nkala et al 1999, Adedokun and Itiola, 2010). The yields (% w/w) of the isolated natural starches were found to be 14.81, 15.60 and 83.20, respectively. All the four starches were fully pregelatinized using the method described by some workers and in The Pharmaceutical Codex (The Pharmaceutical Codex, 1979; Adedokun and Itiola, 2010). A quantity (100g) of each of the natural starches was dispersed in 100ml of distilled water and then heated at $55^0$C with constant stirring for 10 minutes to form a paste which was crisp-dried in an oven at $60^0$C for 48 hours. The resultant mass was pulverized in a laboratory mill (Christy and Norris Ltd., UK). Each sample was passed through a number 120 mesh sieve (125μm) and then stored in air-tight amber-coloured bottles.

**Granulation**

280g quantity of a basic formulation containing paracetamol (84%w/w); corn starch (7%w/w) and lactose (9%w/w) were prepared to evaluate the effects of the starch binders on mechanical and release properties of the tablets. The powders were dry-mixed in a Kenwood planetary mixer for 5minutes, and then moistened with either 37ml of distilled water (0% starch binder) or appropriate quantities of hot mucilages of each starch sample to produce granules containing different concentrations (1- 4%) of each starch binder. Massing was continued for 5 minutes and then wet-screened using a number 12 mesh sieve (1400μm), dried at $60^0$C for 6 hours in a hot air oven and then dry-screened using a number 16 mesh sieve (1000μm).

**Preparation of tablets**

Samples of 500mg $\pm$ 2mg of each starch sample were compressed for 1minute into tablets with predetermined loads on a Carver hydraulic press (Model C, Carver Inc. Wisconsin, USA), using a 10.5mm die and flat faced punches lubricated with a 2% w/v dispersion of magnesium stearate in diethylether- ethanol (1:1) prior to each compression. Tablets of 3.68$\pm$ 0.22mm thickness at zero porosity as calculated from particle density values were obtained. Tablets with a central hole (1.59mm diameter) were made using an upper punch with a hole through its centre and a lower punch fitted with a pin (Alebiowu and Itiola, 2002). The tablets were then stored over silica gel for 24h to allow for elastic recovery and prevent falsely low yield values. The weights (w) and dimensions of the tablets were then measured to within $\pm$1mg and $\pm$0.01mm, respectively, and their relative density, R was calculated using the eq:

$$R = w/V_t\rho_p \qquad (4)$$

Where $V_t$ is the volume of the tablets ($cm^3$) including the hole when present.

**Determination of Tensile strength and Brittle fracture index**

The load, F (MN) required to break each starch tablet diametrically into two halves

(crushing strength) was measured using a Monsanto hardness tester (Fell and Newton, 1970). The values were used to calculate the tensile strength T and $T_h$ for the tablets without and with a central hole at different relative densities, respectively (Eq 1). Brittle fracture index, BFI values of the tablets was also calculated using Eq 2. All determinations were made in quadruplicate.

**Disintegration time test**

The disintegration time of the tablets was determined in distilled water at 37 $\pm$ $0.5^0$C using a B.P. Manesty disintegration test unit (Manesty Machines Ltd; Poole, UK). A tablet each was placed on the wire mesh just above the surface of the distilled water in the test tubes and the unit was switched on simultaneously with a stop clock. The time taken for the tablets to disintegrate and all particles to pass through the wire mesh was recorded as the disintegration time. Determinations were made in quadruplicate.

**Dissolution rate test**

The dissolution rates for the tablets at different relative densities were determined at 37+$0.5^0$C in 1 litre of phosphate buffer (Potassium dihydrogen orthophosphate buffer, pH of 7.4) using an Erweka dissolution rate apparatus (Erweka Apparatebau, G.M.B.H Hensenstamm Kr Offenbach/main, Germany). The stirring rate used was 50rpm (USP 2000). The tablets were placed in a rotating basket, and with the aid of a pipette, 5ml of the medium was taken at preselected time intervals.

The same quantity of the medium was added at the same temperature immediately after each sampling to keep the volume of the dissolution medium constant. With the aid of a Unicam 8620UV/Visible spectrophotometer (UV spectrometer, Pye, Unicam, UK), the proportion of paracetamol that had dissolved in the medium at each sampling time was determined. All determinations were made in quadruplicate.

**RESULTS**

Representative plots of log tensile strength versus relative density for tablets formulated with 3%$^w/_w$ natural starch binders are presented in Fig. 1. At all relative density values, tablets without a central hole had higher tensile strength values than those with a hole. The results were found to fit the general linear eq:

$$\text{Log } T \text{ (or } T_h) = mR + c \qquad (5)$$

with correlation coefficient, $r > 0.966$. Also, for all the formulations, the higher the concentration of binding agent, the higher was the value of T or $T_h$. At the same relative density, tensile strength values for tablets formulated with natural starch binders were higher than those for tablets formulated with

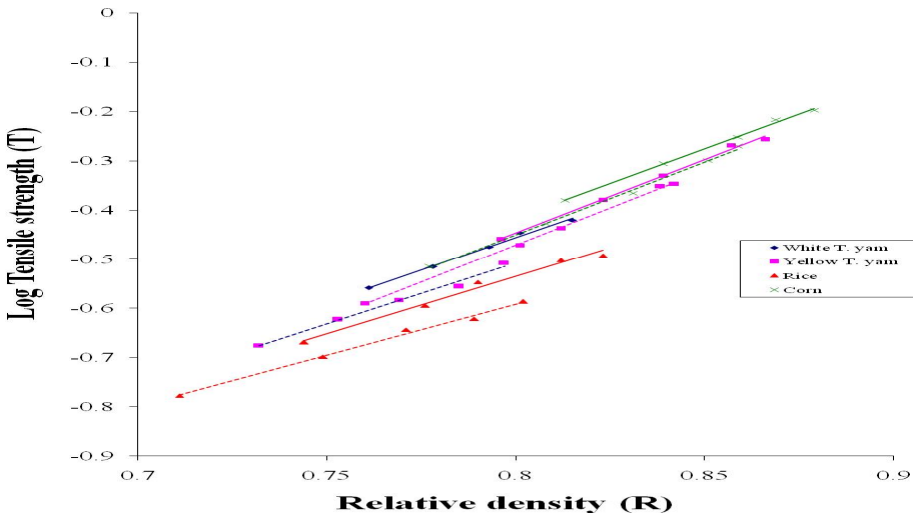


Fig. 1: Plots of log tensile strength against relative density for paracetamol tablets formulated with 3% w/w natural starch binders with ( --- ) and without ( ___ ) a central hole.

pregelatinized starch binders. The rankings of T for tablets containing natural and pregelatinized starch binders are; corn > yellow T. yam > white T. yam > rice, and, yellow T. yam > corn > white T. yam > rice, respectively. BFI values for the paracetamol tablets at different relative densities were calculated using Eq 2. Representative plots of BFI versus relative density for tablets containing 3%$^{w}/_{w}$ starch binders and of BFI against concentration of starch binder are presented in Figs. 2 and 3, respectively. These values show that BFI varies with the nature, form and concentration of starch binder and with relative density of the tablets. (Values of T and BFI at relative density of 0.90 are presented in Table 1). While T values increased with binder concentration, the BFI values decreased. Tablets formulated with pregelatinized starch binders had lower BFI values than those formulated with natural starches. For both natural and pregelatinized starch binders, tablets formulated with yellow T. yam starch produced the least BFI values while those formulated with rice starch had the highest. In both forms of starch, corn starch also exhibited very low BFI values. The ranking of BFI for tablets containing natural and pregelatinized starch binders was; yellow T. yam < corn < white T. yam < rice.

The values of disintegration time, $D_t$, at various relative densities, R, for paracetamol tablets formulated with starch binders were obtained. The results show that $D_t$ values

increased as R increased. Representative plots of $D_t$ values against R for tablets formulated with 3%$^w/_w$ natural and pregelatinized starch binders are shown in Figs. 4 and 5, respectively. Values of $D_t$ at relative density of 0.90 are included in Table 2. From the Table, it can be seen that $D_t$ values increased as binder concentration increased. Generally, for both natural and pregelatinized starch binders, tablets formulated with rice starch exhibited the least $D_t$ values while those formulated with corn starch had the highest values. Tablets formulated with pregelatinized starch binders had lower $D_t$ values than those formulated with natural starch binders. This could be due to the higher swelling ability of the former than the latter. The ranking of $D_t$ values for both natural and pregelatinized starch binders was; corn > yellow T. yam > white T. yam > rice.

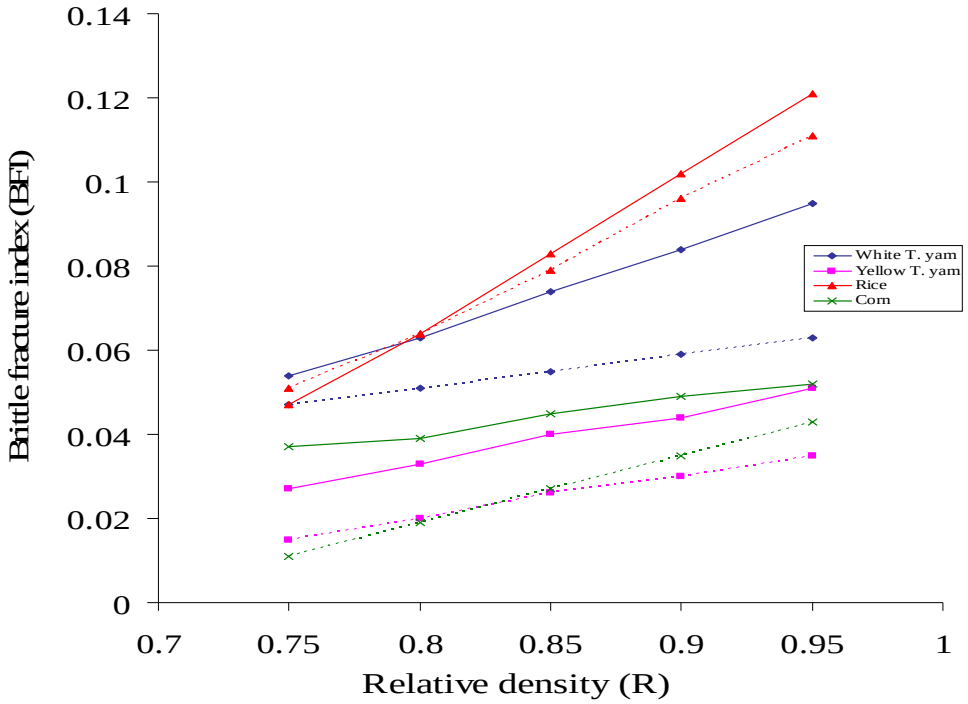


Fig. 2: Plots of brittle fracture index against relative density for Paracetamol tablets containing 3% w/w of natural ( __ ) and pregelatinized (----- ) starch binders

Representative plots were made of percentage paracetamol released against time for tablets formulated with 3%w/w natural and pregelatinized starch binders at various relative densities (Figs. 6 and 7). The values of $t_{50}$ and $t_{80}$, that is, the time required for 50% and 80%

paracetamol to be released respectively, were obtained from the plots for all the formulations. Kitazawa plots of $\ln\{C_s/(C_s-C_t)\}$ against time were also made and, generally, two regression lines of slopes $k_1$ and $k_2$,intersecting at time $t_1$, were obtained for all the formulations.

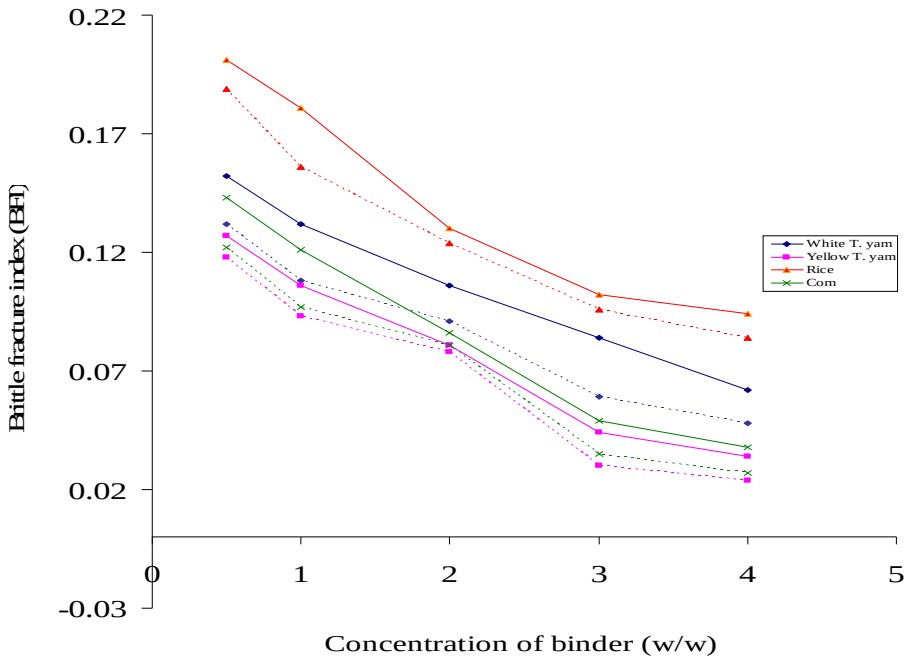


Fig. 3: Plots of brittle fracture index against concentration of natural ( __ ) and pregelatinized ( --- ) starch binders

**Table 1: Values of tensile strength and brittle fracture index at relative density of 0.90 for paracetamol tablets formulated with starch binding agents**

| Nature of Starch Binders | Conc. % w/w | Natural | | Pregelatinized | |
|---|---|---|---|---|---|
| | | Tensile strength, T | BFI | Tensile strength, T | BFI |
| None | 0.0 | 0.331 | 0.344 | – | – |
| White T. yam | 0.5 | 0.411 | 0.152 | 0.364 | 0.132 |
| | 1.0 | 0.461 | 0.132 | 0.405 | 0.108 |
| | 2.0 | 0.537 | 0.106 | 0.459 | 0.091 |
| | 3.0 | 0.644 | 0.084 | 0.515 | 0.059 |
| | 4.0 | 0.690 | 0.062 | 0.543 | 0.048 |
| Yellow T. yam | 0.5 | 0.415 | 0.127 | 0.403 | 0.118 |
| | 1.0 | 0.515 | 0.106 | 0.447 | 0.093 |
| | 2.0 | 0.588 | 0.081 | 0.541 | 0.078 |
| | 3.0 | 0.711 | 0.044 | 0.566 | 0.030 |
| | 4.0 | 0.775 | 0.034 | 0.613 | 0.024 |
| Rice | 0.5 | 0.404 | 0.201 | 0.343 | 0.189 |
| | 1.0 | 0.451 | 0.181 | 0.379 | 0.156 |
| | 2.0 | 0.489 | 0.130 | 0.398 | 0.124 |
| | 3.0 | 0.495 | 0.102 | 0.424 | 0.096 |
| | 4.0 | 0.504 | 0.094 | 0.433 | 0.084 |
| Corn | 0.5 | 0.481 | 0.143 | 0.392 | 0.122 |
| | 1.0 | 0.534 | 0.121 | 0.436 | 0.097 |
| | 2.0 | 0.624 | 0.086 | 0.471 | 0.081 |
| | 3.0 | 0.734 | 0.049 | 0.517 | 0.035 |
| | 4.0 | 0.821 | 0.038 | 0.692 | 0.027 |

**Table 2: Values of disintegration time ($D_t$) and dissolution parameters for paracetamol tablets containing different starch binders at relative density of 0.90**

| Nature of starch binders | Form of starch binders | Conc. (% w/w) | $D_t$ (min) | $t_{50}$ | $t_{80}$ | $t_1$ | $k_1$ | $k_2$ |
|---|---|---|---|---|---|---|---|---|
| None | – | 0.00 | 1.08 | 8.01 | 12.08 | 8.27 | 0.082 | 0.224 |
| White T. yam | Natural | 0.50 | 1.93 | 10.87 | 16.70 | 10.55 | 0.047 | 0.120 |
| | | 1.00 | 1.99 | 12.99 | 18.88 | 12.97 | 0.041 | 0.116 |
| | | 2.00 | 2.22 | 14.37 | 20.01 | 14.44 | 0.037 | 0.113 |
| | | 3.00 | 2.36 | 15.40 | 22.19 | 15.43 | 0.030 | 0.111 |
| | | 4.00 | 2.63 | 17.95 | 25.04 | 18.40 | 0.026 | 0.106 |
| | Pregelatinized | 0.50 | 1.66 | 10.90 | 15.74 | 10.44 | 0.049 | 0.144 |
| | | 1.00 | 1.78 | 12.50 | 17.53 | 12.35 | 0.045 | 0.141 |
| | | 2.00 | 1.90 | 14.20 | 19.60 | 14.10 | 0.040 | 0.138 |
| | | 3.00 | 2.00 | 15.22 | 21.05 | 14.56 | 0.036 | 0.134 |
| | | 4.00 | 2.18 | 18.64 | 24.97 | 17.79 | 0.029 | 0.127 |
| Yellow T. yam | Natural | 0.50 | 2.00 | 12.70 | 18.68 | 12.98 | 0.042 | 0.118 |
| | | 1.00 | 2.22 | 14.37 | 20.93 | 15.14 | 0.037 | 0.115 |
| | | 2.00 | 2.66 | 15.27 | 22.17 | 16.22 | 0.035 | 0.112 |
| | | 3.00 | 2.98 | 16.47 | 23.55 | 17.18 | 0.029 | 0.109 |
| | | 4.00 | 3.37 | 18.31 | 26.08 | 19.59 | 0.023 | 0.103 |
| | Pregelatinized | 0.50 | 1.75 | 12.55 | 17.52 | 12.04 | 0.040 | 0.139 |
| | | 1.00 | 1.88 | 13.93 | 19.56 | 13.70 | 0.038 | 0.136 |
| | | 2.00 | 2.05 | 14.94 | 21.00 | 14.58 | 0.036 | 0.130 |
| | | 3.00 | 2.21 | 16.34 | 22.81 | 16.16 | 0.032 | 0.127 |
| | | 4.00 | 2.28 | 18.06 | 23.77 | 17.14 | 0.028 | 0.124 |
| Rice | Natural | 0.50 | 1.75 | 10.78 | 15.16 | 10.36 | 0.051 | 0.139 |
| | | 1.00 | 1.89 | 11.39 | 17.11 | 12.00 | 0.048 | 0.128 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 2.00 | 2.05 | 12.45 | 18.92 | 13.62 | 0.041 | 0.121 |
| | | 3.00 | 2.18 | 14.74 | 20.62 | 14.02 | 0.033 | 0.117 |
| | | 4.00 | 2.29 | 16.91 | 24.45 | 18.08 | 0.029 | 0.112 |
| | Pregelatinized | 0.50 | 1.56 | 9.79 | 13.17 | 10.02 | 0.048 | 0.156 |
| | | 1.00 | 1.69 | 10.83 | 14.92 | 11.15 | 0.047 | 0.152 |
| | | 2.00 | 1.84 | 11.75 | 16.27 | 12.00 | 0.043 | 0.146 |
| | | 3.00 | 1.92 | 13.46 | 18.68 | 13.36 | 0.038 | 0.141 |
| | | 4.00 | 2.06 | 15.32 | 20.86 | 15.14 | 0.034 | 0.138 |
| Corn | Natural | 0.50 | 2.01 | 13.33 | 19.57 | 14.12 | 0.037 | 0.114 |
| | | 1.00 | 2.34 | 15.12 | 21.46 | 16.23 | 0.034 | 0.110 |
| | | 2.00 | 3.12 | 18.61 | 23.97 | 17.33 | 0.030 | 0.104 |
| | | 3.00 | 3.44 | 19.35 | 25.41 | 18.28 | 0.025 | 0.099 |
| | | 4.00 | 4.01 | 20.46 | 28.33 | 20.53 | 0.021 | 0.074 |
| | Pregelatinized | 0.50 | 1.83 | 13.23 | 18.65 | 12.35 | 0.039 | 0.130 |
| | | 1.00 | 1.96 | 14.94 | 20.70 | 14.16 | 0.036 | 0.125 |
| | | 2.00 | 2.10 | 18.28 | 23.85 | 17.25 | 0.028 | 0.117 |
| | | 3.00 | 2.36 | 19.00 | 25.21 | 17.83 | 0.027 | 0.117 |
| | | 4.00 | 2.49 | 20.43 | 27.01 | 19.13 | 0.025 | 0.112 |

Representative Kitazawa plots for tablets formulated with 3%$^{w}/_{w}$ starch binders are presented in Figs. 8 and 9. The amount of paracetamol released (%) at designated time intervals were obtained for all formulations. Values of $t_{50}$, $t_{80}$, $t_1$, $k_1$ and $k_2$ for all formulations at relative density of 0.90 are included in Table 2. Dissolution times $t_{50}$, $t_{80}$ and $t_1$ were generally higher for formulations containing natural starch binders. The rate of drug release, as expressed by the dissolution rate constants $k_1$ and $k_2$, were higher for

formulations containing pregelatinized binders. The values of $k_2$ were higher than $k_1$ values. In all cases, $D_t$ values were lower than the corresponding $t_1$ values. The ranking of the values of $D_t$, $t_{50}$, $t_{80}$ and $t_1$ for all the starch binders was corn > yellow T. yam > white T. yam > rice and the reverse was the case for $k_1$ and $k_2$. Results of Regression analysis of relationship between $D_t$, $t_{50}$, $t_{80}$, $t_1$, $k_1$ and $k_2$, for natural and pregelatinized starch binders are presented in Table 3

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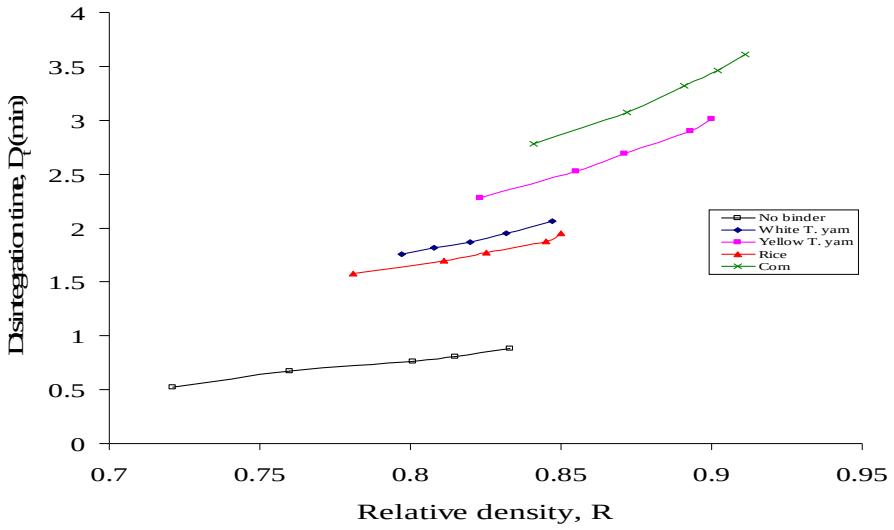


Fig. 4: Plots of disintegration time against relative density for paracetamol tablets formulated with 0% and 3% w/w natural starch binding agents

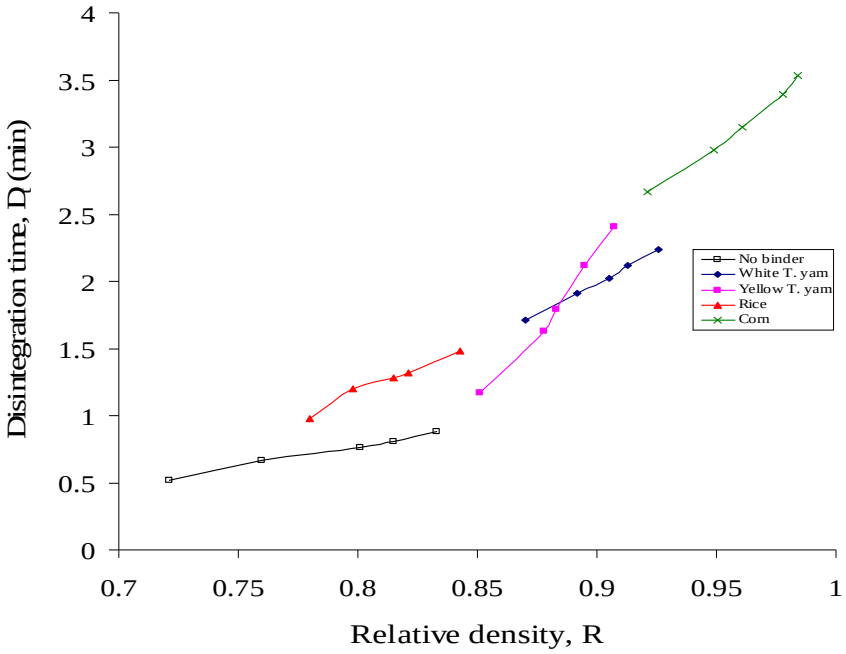


Fig. 5: Plots of disintegration time against relative density for paracetamol tablets formulated with 0% and 3% w/w pregelatinized starch binding agents

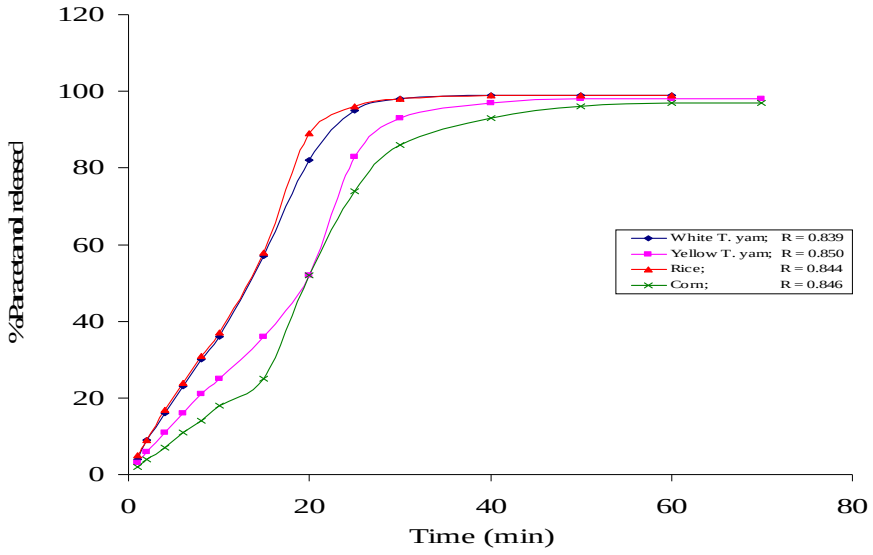


Fig. 6: Plots of percentage paracetamol released against time for tablets formulated

with 3%w/w natural starch binding agents at specified relative densities, R

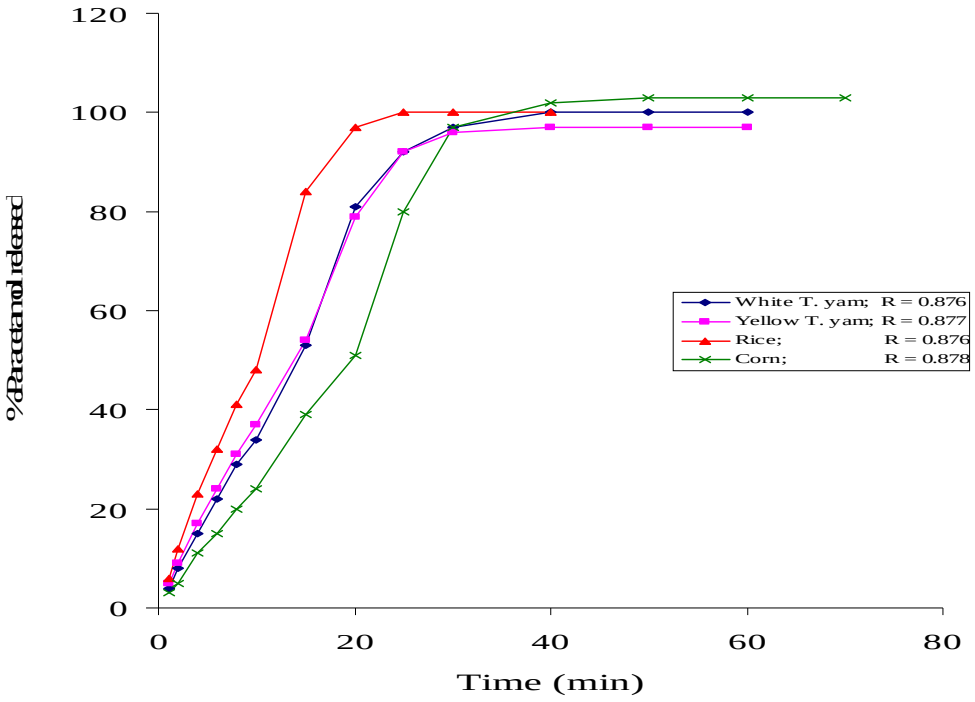


Fig. 7: Plots of percentage paracetamol released against time for tablets formulated with

3%w/w pregelatinized starch binding agents at specified relative densities, R

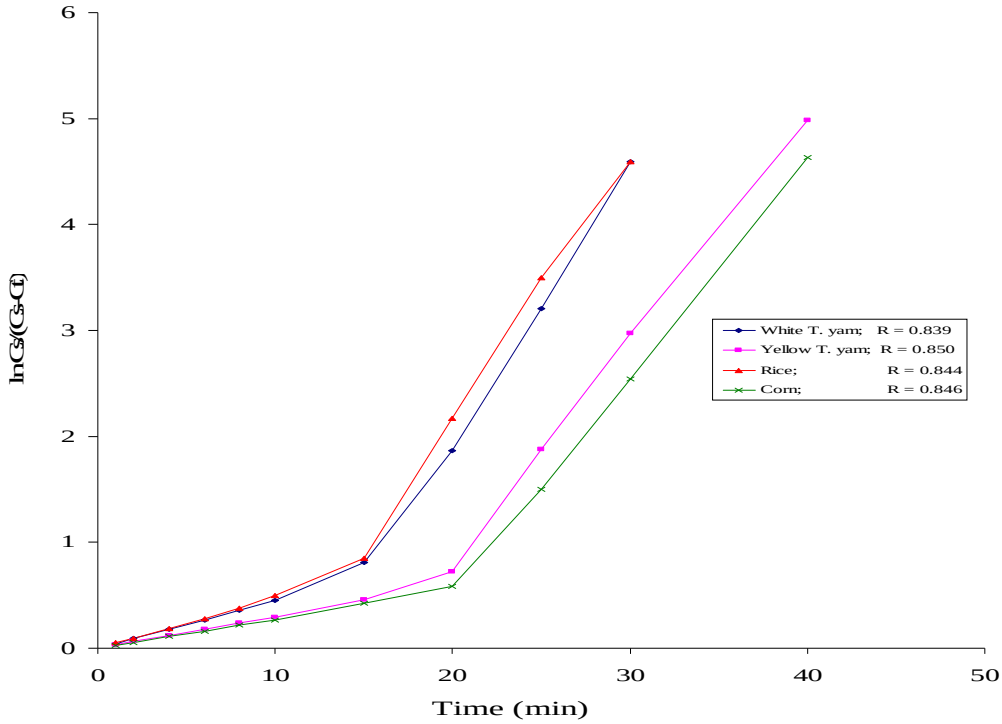


Fig. 8: Kitazawa plots for paracetamol tablets formulated with 3%w/w natural starch binding agents at specified relative densities, R

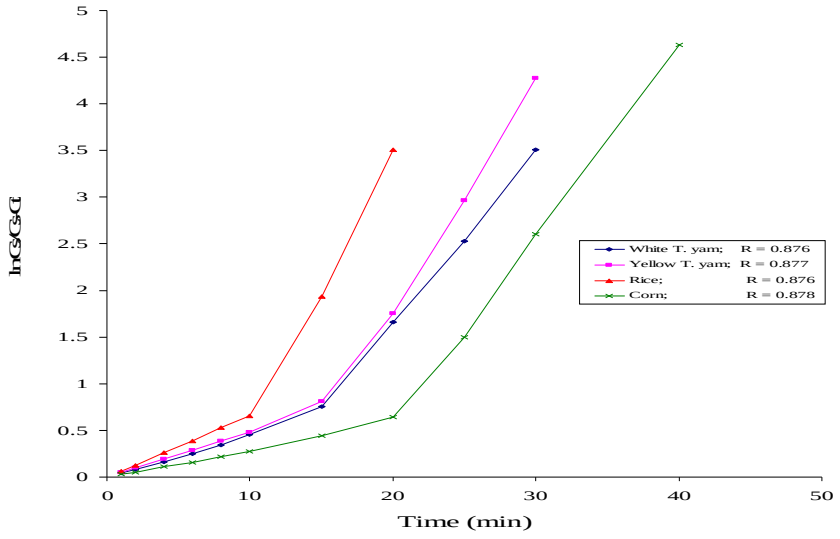


Fig. 9: Kitazawa plots for paracetamol tablets formulated with 3%w/w pregelatinized starch binding agents at specified relative densities, R

**Table 3: Correlations between various disintegration and dissolution parameters of paracetamol tablets formulated with starch binders.**

| Nature of starch binder | Form of starch binder | Ordinate | Abscissa | Equation for line of best fit | Corr. coeff. (r) | Level of sig. (p) |
|---|---|---|---|---|---|---|
| White T yam | Natural | $t_{50}$ | $D_t$ | $t_{50}= 6.592D_t+ 0.926$ | 0.989 | <0.05 |
| | Pregel | | | $t_{50}= 8.677D_t+2.471$ | 0.980 | <0.005 |
| Yellow T yam | Natural | | | $t_{50}= 1.600D_t -0.007$ | 0.986 | <0.001 |
| | Pregel | | | $t_{50}= 4.203D_t+1.229$ | 0.959 | <0.05 |
| Rice | Natural | | | $t_{50}= 3.366D_t -0.828$ | 0.948 | <0.05 |
| | Pregel | | | $t_{50}= 6.068D_t+4.297$ | 0.971 | <0.005 |
| Corn | Natural | | | $t_{50}=10.011D_t+5.202$ | 0.983 | <0.005 |
| | Pregel | | | $t_{50}= 2.888D_t +2.017$ | 0.979 | <0.005 |
| White T yam | Natural | $t_{80}$ | $D_t$ | $t_{80}= 10.222D_t+6.116$ | 0.977 | <0.05 |
| | Pregel | | | $t_{80}= 6.189D_t-0.983$ | 0.981 | <0.005 |
| YellowT yam | Natural | | | $t_{80}= 9.628D_t-0.767$ | 0.971 | <0.005 |
| | Pregel | | | $t_{80}= 7.117D_t-11.216$ | 0.988 | <0.005 |
| Rice | Natural | | | $t_{80}=13.120D_t+3.802$ | 0.981 | <0.0005 |
| | Pregel | | | $t_{80}= 8.366D_t+0.911$ | 0.958 | <0.05 |
| Corn | Natural | | | $t_{80}= 11.006D_t-0.821$ | 0.968 | <0.005 |
| | Pregel | | | $t_{80}= 12.146D_t-2.222$ | 0.989 | <0.001 |

**DISCUSSION**

Constants *m* and *c* in Eq 5 depended on the nature, form and concentration of starch binder present in the formulation and on the presence or absence of a central hole in the tablet. This is in agreement with the observations of other workers (Odeku and Itiola, 1998). Several forces are responsible for the magnitude of the value of tensile strength. The amount of effective surface area of contact between particles is directly proportional to the degree of bonding, which, in turn, is directly proportional to the tensile strength (Luangtana-Anan and Fell, 1990).

From the results, the higher the concentration of binding agent, the higher was the value of T or $T_h$. This occurred because the heat generated in the course of compression cause the asperities and the binding agents to melt and on cooling, solidified to form strong solid interparticulate bonds and as the binder concentration in creases, the amount of bonds formed also increased (Kurup and Pilpel, 1979; Itiola and Pilpel, 1986a). Because of their soft and plasto-elastic nature, binding agents would undergo plastoelasticity upon application of high compressional pressure and would be forced into interparticulate void spaces, thus, increasing interpaticulate contact area and, consequently more solid bonds would be formed. Values of BFI presented in Table 1, show that this parameter varies with the nature, form and concentration of starch binder and with the relative density of the tablets. While T values increased with binder conc, the BFI values decreased. This implies that the presence of a binder at interparticulate junctions facilitates plastic deformation for the relief of localized stresses (Odeku and Itiola, 2002). In both natural and pregelatinized starch forms, corn starches also exhibited very low BFI. For natural starches, corn starch yielded tablets with highest bond strength but also with very low brittleness. Therefore, corn as well as yellow T. yam starch binders could be more useful as binding agents than other starches when high bond strength with minimal capping and lamination are desired. Lower BFI values exhibited by tablets formulated with pregelatinized starch binders than those formulated with natural starches indicated that the former had higher ability to relieve localized stresses in tablets than the latter.

The values of $D_t$ at various relative density, R show that, in agreement with the results obtained by Esezobo *et al* (1989) and Upradashta *et al* (1992), the $D_t$ values increased as R increased. This is probably because the presence of a binder in a formulation leads to formation of solid interparticulate bonds which increases in strength as R increases. An increase in disintegration time thus indicates a measure of difficulty in breaking those bonds. At relative density of 0.90, $D_t$ values increased as binder concentration increased in line with observations made by various workers (Pilpel *et al*, 1978; Upradashta *et al*, 1992; Alebiowu and

Itiola, 2002). Upradashta *et al* (1992) in their studies on chitosan, used as binder in chlorpheniramine maleate tablets, inferred that at higher binder concentrations, porosity and capillary pore size are reduced. Thus, wicking of water into the tablet is markedly reduced, and consequently disintegration is slowed down. However, disintegration of tablets is not only as a result of capillarity and swelling of powder bed (Caramella et al, 1984; Ek et al, 1995). Disintegration time as a function of binder concentration could also be due to the formation of thin film of the starch mucilage around the granules, which, in the presence of water, is converted to a mucillagenous viscous barrier between the granules and the water, thereby slowing down the disintegration of the granules. The thickness of this barrier depends on the quantity of the starch mucilage employed (Pilpel et al, 1978). Another contributory factor could be that, while drying the granules, the binder would migrate to the surface to form solid films (Rubinstein and Ridgeway, 1974; Itiola and Pilpel, 1986b) which, during compression, would readily undergo plastic deformation and would be forced into the intragranular spaces to form a binder matrix. Disintegration of the tablets would be due to softening and dissolution of the binder matrix, and whether or not the granules have been fragmented during compression would not have much effect on the disintegration time (Ferrari et al, 1996). Tablets formulated with pregelatinized starch binders exhibited lower Dt values than those formulated with natural starch binders. This is probably because, during pregelatinization, the starch grains were disrupted causing the release of amylopectin which is partially responsible for the swelling of starch. Pregelatinized starches therefore, with higher amylopectin content (lower amylose content) than the natural starches (Adedokun and Itiola, 2010) would exhibit higher swelling ability. Thus, tablets formulated with pregelatinized starch binders will be expected to have lower values of Dt. The rate of drug release, as expressed by the dissolution rate constants k1 and k2, were higher for formulations containing pregelatinized starch binders. The values of k2 were generally higher than k1 values, indicating that the dissolution rate was faster after time t1. Dissolution times t50, t80 and t1 generally increased as the relative density increased and also as binder concentration increased. The dissolution times were lower for tablets formulated with pregelatinized binders probably due to their higher swelling capacity and, consequently higher rate of water penetration into the tablets, resulting in faster fragmentation and, hence an increase in the surface area of tablet particles exposed to the dissolution medium. The highest correlations were recorded between Dt and t1 ($r>0.989$). This could be because in a similar manner to disintegration, the change from k1 to k2 at time t1 could be attributed to rapid increase in surface area of particles exposed to dissolution medium as a result of break-up of tablets into fragments (Kitazawa et al, 1975). In all cases, Dt values were lower than the corresponding t1 values and this can probably be attributed to the

greater agitation employed in the disintegration test than in the dissolution test (Itiola and Pilpel, 1986b). Statistical analysis, using two-way ANOVA showed that there were significant differences ($p < 0.05$) between the values of Dt, t50, t80, t1, k1 and k2, for natural and pregelatinized starch binders. Regression analyses between Dt and other release parameters, including their levels of linearity, are presented in Table 3. Interrelationships between all the parameters showed differentlevels of significance ($p < 0.05$), except the relationships between k2 and other parameters which were generally insignificant ($p > 0.05$ in many cases). This could be due to the fact that, k2 represents essentially the point in time during dissolution, when the tablet has completely fragmented. Natural starches yielded paracetamol tablets with lower dissolution rate than pregelatinized form, but with higher level of significance in relationship ($p < 0.001$) as opposed to pregelatinized starches ($p < 0.01$).

## CONCLUSION

Natural starches generally show higher binding properties with respect to tensile strength and release profiles, but tablets containing pregelatinized starches were less brittle. All the experimental starch binders produced tablets with faster dissolution rate than the tablets containing official corn starch binder with rice starch exhibiting the highest release rate.

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