

## MATERIAL AND COMPRESSSIONAL PROPERTIES OF TWO-STEP MODIFIED PLANTAIN AND CORN STARCHES

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### ABSTRACT

This study is aimed at evaluating the pharmaceutical properties of pregelatinized, then citric acid modified corn and plantain starches. Citric acid modified pregelatinized corn and plantain starches (CAMPCS and CAMPPS respectively) were evaluated for their properties in comparison with pregelatinized corn and plantain starches (PCS and PPS respectively) using Fourier Transform Infrared (FTIR) spectroscopy, Scanning Electron Microscopy (SEM), Volume reduction equations, density measurements and rheological properties. Quadruplicate determinations were made and results were analyzed using ANOVA ( $p$ -values  $< 0.05$ ). FTIR plots revealed the addition of new functional groups due to modification, while maintaining the basic integrity of the pregelatinized starches. Sphericity, particle size and density were ranked CAMPPS = CAMPCS  $<$  PPS  $<$  PCS. CAMPCS and CAMPPS were more free flowing with higher bulk and tapped densities, higher viscosities, but lower swelling indices than PPS and PCS. Citric acid modification led to improved pharmaceutical functions of the unmodified pregelatinized starches.

**Key words:** Pregelatinized starch, Chemical modification, Compressibility, Citric acid modification

### INTRODUCTION

Pharmaceutical formulations contain active ingredients and excipients, which principally affect the compression, physicochemical and biopharmaceutical properties of the formulation. Also, excipients are included in pharmaceutical formulations to ensure the consistency of doses during administration of the medicament by acting in various capacities such as binders, diluents, disintegrants and lubricants [1].

The wide use of starch as a pharmaceutical excipient is due to the inexpensive and biodegradable nature of the polymer [2]. However, several challenges, including poor flow properties [3], low thermal resistance and poor compressibility [4], among others, limit the use of native starches as excipients in pharmaceutical delivery systems. Hence, starches are often modified to improve on the challenges observed. Restructuring of the starch granules and dispersion of amylopectin polymers within the granules are the goal of starch modification; this ensures that the reactive polymers are available and accessible. The approaches adopted for starch modification also depends on the intended use of the starch as an excipient.

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**Receiving Date** : December 18,2020

**Acceptance Date** :January 23,2021

**Publication Date** : January 25,2021

Pregelatinization of starch has been documented to enhance the degree of bond strength [5] by refining the size and shape of the starch particles [6]. Chemical modification of starch usually follows the pathway of substitution, degradation or cross-linking, and these methods are employed to optimize the structural and nutritional properties for targeted applications.

The usual approaches to chemical modification of starches for pharmaceutical use include hydrolysis, esterification, etherification and oxidation. Chemically modified starches confer enhanced thermoplasticity, increased solubility and increased flow properties [7]. Phosphorylation of starch was shown to enhance the physicochemical properties of starch [8], while silicification of *Sorghum bicolor* starch, when incorporated in ibuprofen tablet formulations, enhanced disintegration properties [9]. Modification of starch in dilute hydrochloric acid also led to increase in crushing strength and decrease in friability when white fonio and sweet potato starches were acidified and incorporated as exo-disintegrants in paracetamol tablet formulations [10]. The aim of this study is to assess the material and compressional properties of plantain and corn starches after the starches have been modified using two steps involving the product of the first step acting as the primary product for the secondary modification. It is expected that the two-step simultaneous modification technique (thermal modification by pregelatinization and subsequent chemical modification with citric acid) will lead to better functional properties in the resulting modified starch particles.

## **MATERIALS**

Citric acid crystalline powder BP (E330/77-92-9; Shanghai Honghao Chemicals Co.,Ltd.) and sodium hydroxide solution BP (No:1091384000, Sigma-Aldrich Chemie GmbH, Germany) were gifts from the Bond Chemical Industries, Aawe, Oyo State, Nigeria. Corn starch BP (Lot 69833 BDH Chemical Limited, Poole UK) was a gift from Bentos Pharmaceutical Products, Podo-Ibadan, Oyo State, Nigeria. Ultrapure water was obtained from the Centre for drug discovery development, and production, University of Ibadan (UI), Nigeria. Officially authenticated native unripe plantain (*Musa sapientum*) was obtained from the Botanical gardens of UI, Nigeria. Other reagents used were of analytical grade.

## **METHODOLOGY**

### **Extraction of Starch**

The method developed by Adebowale *et al* [11] was adopted in the extraction of plantain starch. The plantain was peeled and cut into small pieces. Sufficient quantity of 2% sodium metabisulphite was added and allowed to soak for 30 min before it was homogenized using a laboratory blender. The homogenized mixture was filtered using muslin cloth and soaked in distilled water for 12 h after which the water was decanted. The process of adding distilled water and decanting after 12 h was done for a further 7 days to obtain a slurry of the plantain starch. The slurry was centrifuged and sufficient quantity of 1 %w/v sodium chloride solution in ultrapure water was added to wash the slurry in three cycles. The slurry was then dried in a hot air oven set at 50 °C until a constant weight was obtained. Pulverization of the dried starch was achieved using a laboratory blender and the dried mass obtained was sieved through a sieve of mesh size 0.125 mm. The plantain starch obtained was weighed and stored in an air-tight container.

### **Pregelatinization of Starch**

The method described in the British Pharmaceutical Codex 1979 was adopted for the pregelatinization of the starches with slight modification. Exactly 40 g of plantain starch was dissolved in 100 mL of ultrapure water and boiled on a water bath with constant stirring till a paste was formed. The paste was spread thinly over a white tile placed in hot air oven at 50 °C to dry for 24 h. The starch was milled using a laboratory blender to obtain dried pregelatinized plantain starch (PPS), which was stored in an air-tight container. Pregelatinized corn starch (PCS) was also obtained using the same procedure. The PPS and PCS were tested for the presence of starch using N/50 iodine solution.

### Chemical Modification of Pregelatinized Starch

Exactly 10 g of PPS was soaked in 20 %v/v citric acid solution (pH 3.5) in ultrapure water at  $27 \pm 2$  °C for 18 h. Slurry of this mixture was made by heating on water bath with constant stirring till a paste was formed. The resulting paste was spread thinly on a white tile and dried in hot air oven at 50 °C until a mass with a constant weight was achieved. The dried mass was pulverized using a laboratory blender to obtain citric acid modified pregelatinized plantain starch (CAMPPS). Citric acid modified pregelatinized corn starch (CAMPCS) was obtained using the same procedure. The CAMPPS and CAMPCS obtained were tested for the presence of starch using N/50 iodine solution

### CHARACTERIZATION OF SAMPLES

#### Fourier Transform Infrared (FTIR) Spectroscopy

Spectra were obtained for the samples (PPS, PCS, CAMPPS and CAMPCS) using Magna-IR, 560 spectrometer (Perkin Elmer, USA). Exactly 5mg of each of the completely dried powdered samples was weighed and then dispersed in 200 mg potassium bromide (pellet procedure). Signal averages were obtained at a resolution of  $4\text{cm}^{-1}$  [12].

#### Scanning Electron Microscopy (SEM)

The SEM of the samples (PPS, PCS, CAMPPS and CAMPCS) was done using VEGA3 TESCAN (Germany) electron microscope. A small portion of the sample were placed on aluminum stubs using a double-sided tape and the sample was slightly coated with a layer of carbon in order to aid proper surface and cross-section visualization and also prevent excess charging of the sample. All samples were examined at accelerated voltage.

#### Density (particle,bulk and tapped) Determinations and Carr's Compressibility Indices

The particle densities of the samples (PPS, PCS, CAMPPS and CAMPCS) were determined by the liquid pycnometer method using xylene as the displacement fluid. For the determination of the bulk densities, 10 g of each sample was poured into a 50 mL glass cylinder and the bulk volume was determined. The British standard 1460 of 38 taps/min at a height of 2.54 cm was adopted in evaluating the tapped densities of the samples. The samples were subjected to 100 taps of the cylinder from a height of 2.54 cm within approximately 2 sec between taps. Thereafter, the tapped densities were determined. The percentage of sample porosity ( $P\%$ ) was calculated from the equation:

$$P\% = (1 - P_f) \times 100 \quad (1)$$

Where  $P_f$  (Packing fraction) is the ratio of the bulk density of each sample to its particle density  
Carr's compressibility index (CI) for each sample was calculated using equation:

$$CI = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100 \quad (2)$$

#### Determination of Volume Reduction

The reduction in volume of the samples was evaluated using Kawakita[13] and Gurnham [14] equations. The relationship between the degree of volume reduction (C) and applied pressure (P) is represented by the Kawakita equations below:

$$C = (V_0 - V_p) = abP / (1 + bP) \quad (3)$$

$$N/C = 1/a \times N + 1/ab \quad (4)$$

Where a is the minimum porosity of each sample prior to compression, b is each sample's plasticity and N is the number of taps,  $V_0$  and  $V_p$  represent the maximum bulk volume reduction and the volume after the application of pressure based on number of taps. Gurnham's equation was adapted to describe the relationship between each sample's porosity ( $\epsilon$ ) and compaction using the equation 5 and the plot of N/C versus ln N:

$$\epsilon = 1 - [\text{Bulk density } (\rho_b) / \text{Particle density } (\rho)] \quad (5)$$

### Determination of Angle of Repose

About 10 g of each was poured through a funnel clamped on a retort stand to a flat surface under the funnel. The hypotenuse of the resultant cone that was formed and its diameter was measured. The radius of the cone was then calculated and the angle of repose was determined using the equation;

$$\text{Angle of repose } (\theta) = \tan^{-1} (H/R) \quad (6)$$

Where H and R are the hypotenuse of the cone formed and radius of the circular base respectively.

### Determination of Rheological Properties

The swelling index of each sample was calculated as the ratio of the volume occupied by a 5 %w/v slurry of the sample to the initial volume of the dry sample (5 g) after storage for 24 h in a 100 mL cylinder [15]. The Brookfield viscometer (Model – DV – 11 + pro, Brookfield Engineering laboratory Middlebro, MA, USA) was used to determine the viscosity of each sample at a speed of 50 rpm with spindle no 2.

### Statistical Analysis

Determinations were carried out in quadruplicates and the results obtained were analyzed using one-way ANOVA at a significance level of p-values < 0.05.

## RESULTS AND DISCUSSION

### Confirmation of Starch

The presence of starch was confirmed in the samples (PPS, PCS, CAMPPS and CAMPCS) as a deep blue colouration was obtained after the N/50 iodine solution was added to each sample. This is necessary to ensure that the samples still retain their content of amylose, an important component of starches. [16]

### FTIR Spectra

Fourier Transform Infrared (FTIR) spectroscopy is used in monitoring various stages of matter based on harmonic oscillations associated with the bending and stretching of bonds. FTIR spectroscopy has been applied to analyze the secondary and tertiary structures of compounds [17]. Significant changes in a sample can be detected from changes in the stretching and bending of bonds due to the intimate mixing of sample with other components. From the results obtained (Figures I-IV), there was an addition of new functional groups due to the introduction of citric acid (C-O bonding associated with OH groups) , stretching vibrations at  $\sim 1080\text{cm}^{-1}$ . Basic structural integrities of the pregelatinized starches were not altered due to the significant peaks in the fingerprint region of the FTIR spectra that were retained in the spectra of the citric acid modified starches.

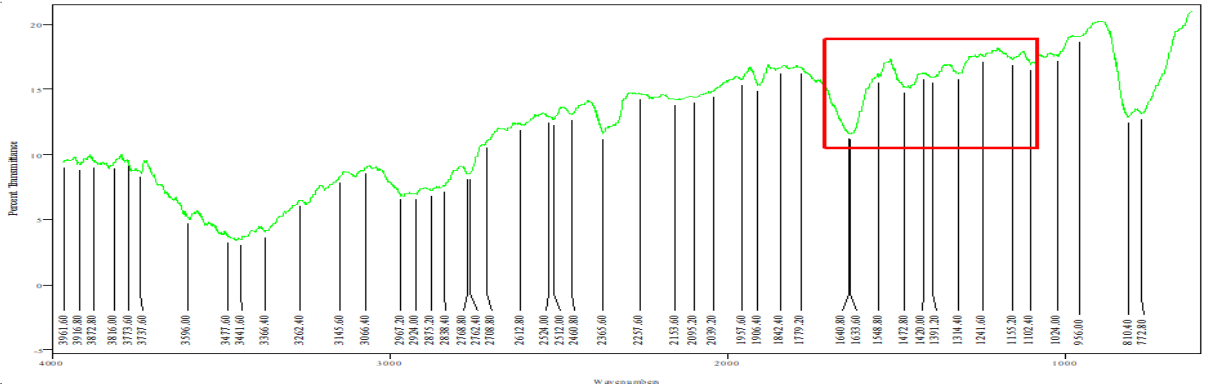


Figure 1 : FTIR spectrum for pregelatinized corn starch showing definitive functional groups in the finger print region retained

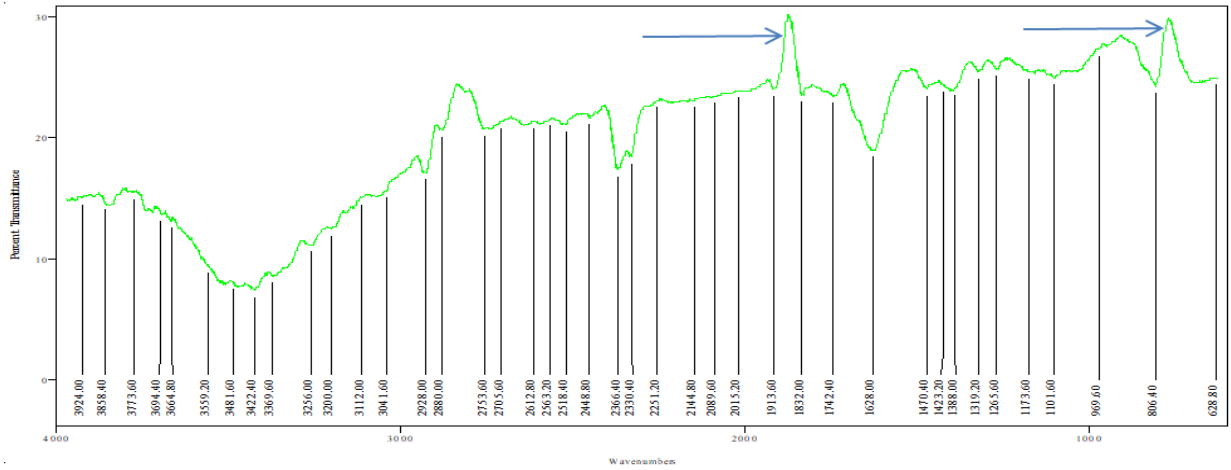


Figure 2 : FTIR spectrum for citric acid modified pregelatinized corn starch showing functional groups that were incorporated due to the modification

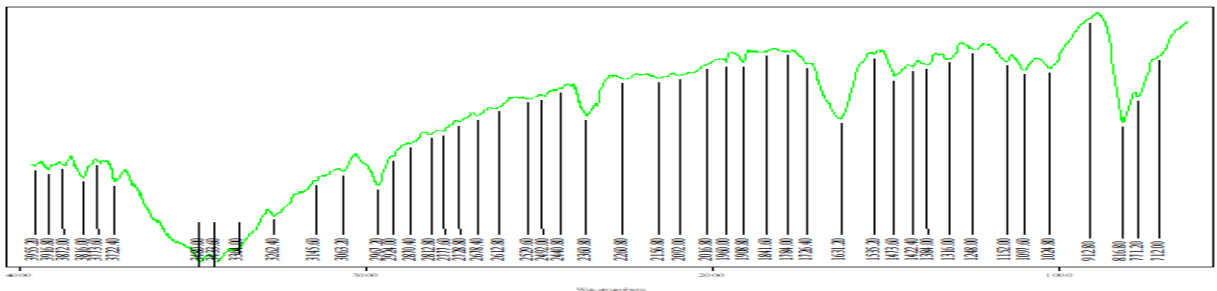
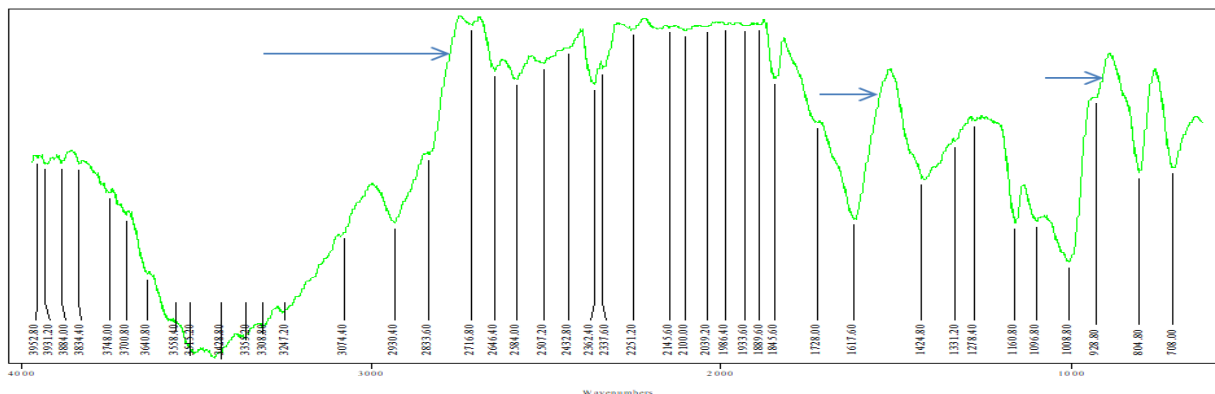


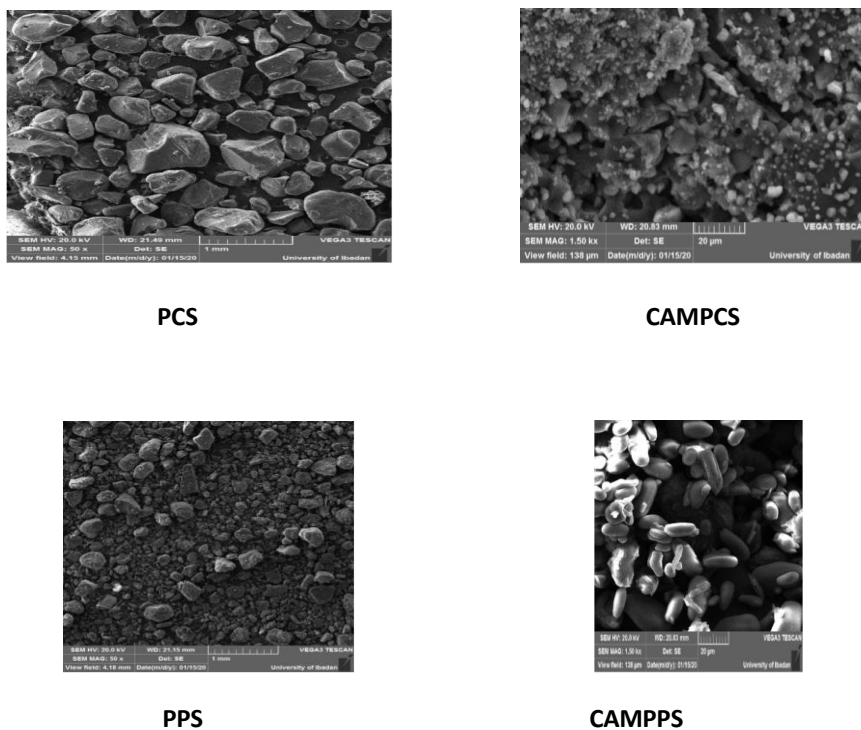
Figure 3 : FTIR spectrum for pregelatinized plantain starch



**Figure 4 : FTIR spectrum for citric acid modified pregelatinized plantain starch showing functional groups that were incorporated due to the modification**

### Morphological Properties

Scanning electron microscopes produce images of a sample by scanning the surface with a focused beam of electrons. The electrons interact with atoms in the sample, producing various signals that contain information about the surface topography and shape of the samples. Particle shape and size have been documented to have significant behavior of ingredients during the processes involved in manufacturing of dosage forms, with spherically shaped particles having better tendency to flow than irregular shaped particles [18]. The electron micrographs for the samples are shown in Figures V. It was observed that citric acid modification of the pregelatinized starches led to more spherically shaped particles, with the CAMPPS particles having the highest sphericity. Also, the modification led to a reduction in the size of the particles, but not significant to lead to cohesion that may cause flow problems. Fine particles with very high surface to mass ratios are more cohesive than coarser particles (influenced more by gravitational forces). Generally, particles greater than 250  $\mu\text{m}$  are relatively free flowing, but as the size falls below 120  $\mu\text{m}$ , powders become cohesive and flow problems are likely to occur [19].



**Figure 5 : Scanning electron micrographs of the starches**

### **Density Measurements, Flow and Compressibility Properties**

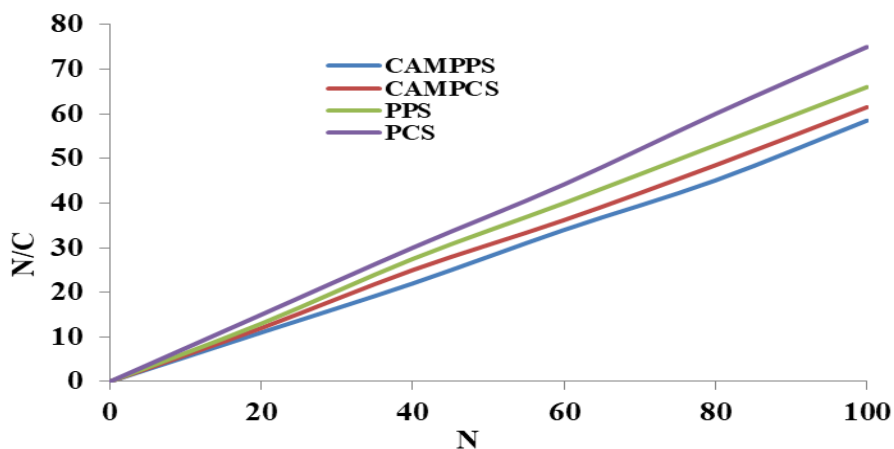
Table 1 shows the density measurements and compressibility properties of the starch samples. The chemically modified starches had higher bulk and tapped densities in the ranking order: CAMPCS > CAMPPS > PPS > PCS. Bulk density depends majorly on particle shape, particle size distribution and the particle's tendency to adhere to one another within the bed. The packing behavior of powders during operations such as mixing, die filling, granulation and compression are also affected by the bulk density of powders. The chemically modified pregelatinized starches are more density packed than the unmodified pregelatinized starches, thus indicating that the modification led to smaller particles sifting between the larger particles. Various aspects of powder processing such as flow from hoppers, milling, blending and packing into shells (for capsules) are affected by the ability of powders to flow; the lower the angle of repose, the more the tendency of the powder to flow [20]. Powder flow also affects blending and segregation potential as a reduction in powder flow leads to increased segregation, which could be a consequence of the plastic or dilatant nature of the starch powder. Flowability of the starches was positively affected by chemical modification as indicated by the angle of repose with the rank order: CAMPPS < CAMPCS < PPS < PCS. This same order was obtained for the Carr's indices of the samples. There was volume reduction as observed by the tapped density values, which followed the same trend as the bulk density values. The high tapped density observed due to the chemical modification could be an indication of good packing behavior due to reduction in die fill volume during tableting<sup>20</sup>. Particle density is the density of the powder when voids and inter-particle pores are eliminated<sup>21</sup>. The results obtained indicates that there was a reduction in particle density of the pregelatinized starches after chemical modification, thus processes such as the initial phase of tablet compression, which are affected by particle density<sup>22</sup>, will produce better results with CAMPCS and CAMPPS.

**Table 1: Powder properties of starch samples (n= 4 ± SD)**

Powder Properties	PCS	PPS	CAMPCS	CAMPPS
Particle density (g/cm <sup>3</sup> )	1.53 ± 0.08	1.71 ± 0.12	1.47 ± 0.03	1.48 ± 0.08
Bulk density (g/cm <sup>3</sup> )	0.42 ± 0.03	0.71 ± 0.03	0.83 ± 0.11	0.96 ± 0.06
Tapped density (g/cm <sup>3</sup> )	0.56 ± 0.03	0.88 ± 0.07	1.00 ± 0.04	1.01 ± 0.17
Carr's Index	25.00 ± 0.03	19.32 ± 0.03	17.00 ± 0.03	4.95 ± 0.03
Porosity (ε)	0.725 ± 0.12	0.585 ± 0.01	0.435 ± 0.02	0.351 ± 0.18
Angle of repose (degrees)	39.23 ± 0.07	42.51 ± 0.18	27.18 ± 1.02	19.22 ± 0.93
Volume reduction (a)	1.341 ± 0.01	1.513 ± 0.00	1.635 ± 0.01	1.724 ± 0.02
Viscosity (Cp) at 27 ± 1°C	4.13 ± 0.11	4.17 ± 0.02	8.09 ± 0.12	8.12 ± 0.00
Swelling Index (%)	2.67 ± 0.71	1.86 ± 0.01	0.71 ± 0.01	0.50 ± 0.13

### Volume Reduction

The representative plots of N/C versus N (Kawakita plots) and N/C versus ln N (Gurnham plots) for the starches are shown in Figures VI and VII respectively. The high correlation coefficients of the Kawakita plots (0.995 – 0.999) is an indication of a linear relationship among the starches. The values of the reciprocal of the slope (a), which represents volume reduction obtained from the Kawakita plots (Figure VI) are shown in Table 1. The values were ranked in the order: CAMPPS > CAMPCS > PPS > PCS (p < 0.05). The indication of this result is that the chemically modified starches had the closest repacking of the particles after application of tapping pressure. This result is also supported by the values of porosity where the most densely packed starch sample (CAMPPS) also had the lowest porosity. This is probably due to the spherical shape of the particles as seen in the morphological studies where sphericity of the particles was enhanced as a result of chemical modification.

**Figure 6 : Representative Kawakita plots for the starches**



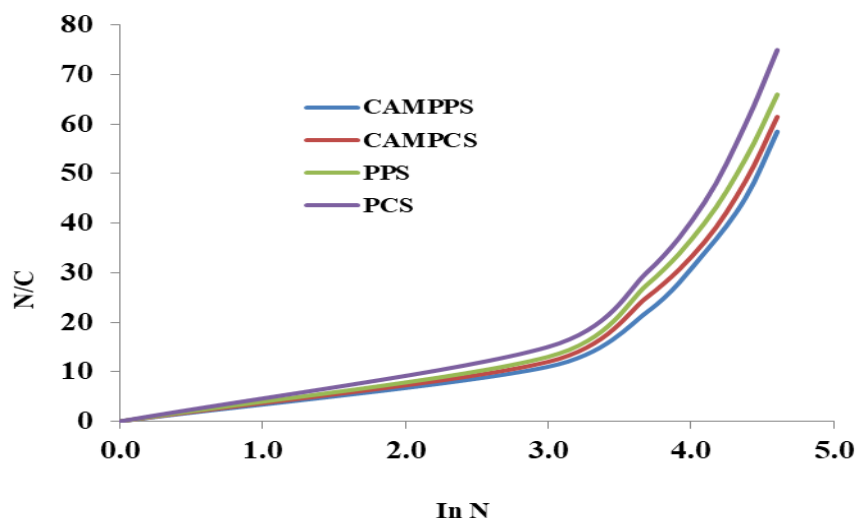


Figure 7 : Gurnham plots for the starches

### Rheological Properties

The choice of processing equipment during manufacturing processes can be influenced by the rheologic properties of the formulation ingredients. The ability of starches to absorb water, which may be attributed to the divergent intensity of the molecular association forces inside the particles, can be assessed using the swelling index [23]. Citric acid modification of the pregelatinized starches led to a decrease in the swelling index (Table 1). Odeniyi *et al* [24] documented the increased swelling capacity of acetylated banana starch when compared with the native starch. This may suggest that it is necessary to carefully choose the media for chemical modification of starches. Viscosity (resistance to physical flow under applied stress) could be a fundamental parameter in the use of excipients in the formulation of semi-solid dosage forms such as pastes. The citric acid modified pregelatinized starches had higher viscosities than the unmodified pregelatinized starches.

### CONCLUSION

The study provides an understanding of the material and compressional properties of two simultaneous modifications, pregelatinization and citric acid modification, of corn and plantain starches. The results clearly indicates that acid modification of pregelatinized corn and plantain starches led to enhanced pharmaceutical functions, which can be exploited when the starches are used as excipients in the pharmaceutical industry.

### CONFLICT OF INTEREST

The authors declare no conflict of interest

### ACKNOWLEDGEMENT

The authors acknowledge Bond Chemical Industries, Aawe, and Bentos Pharmaceutical Products, Podo-Ibadan, both in Oyo State, Nigeria and Centre for Drug Discovery, Development And Production, University of Ibadan, Nigeria for the gifts of materials as described in the manuscript.

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