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Physical/Chemical modifications of *Oryza glaberrima* and *Digitaria exilis* starches: Effect on packing and compression properties of ibuprofen tablet formulations

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ABSTRACT

Imported grain starches are in high demand but are expensive, and their supply is unreliable. To address the need for innovative formulators, the development and use of native starches or the synthesis of modified starches with predetermined functions from locally sourced underused plants as excipients in pharmaceutical industries is critical. The primary goal of this research is to explore the influence of physical and chemical modification on the compressional and packing features of dual blends of Ibuprofen with *Oryza glaberrima* and *Digitaria exilis* starches in oral tablet formulation. Different ratios of starches and Ibuprofen were used in the direct compression method to prepare the tablets. From the native starch forms, pregelatinized and carboxymethylated starches were produced. The manufactured tablets' compressional features were investigated using the Heckel, Gurham, and Kawakita equations, as well as density measurements. Pregelatinization resulted in a faster onset but a lower amount of plastic deformations than native and carboxymethylated starch formulations. Increasing the particle size of these starches substantially impacts densification, rearrangement of particles, fragmentation propensity, and elastic/plastic deformation. The modified starches would make acceptable excipients because they increased tablet densification compared to the native forms.

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INTRODUCTION

For many decades, several plant starches have been investigated as pharmaceutical excipients[1]. Due to their affordability, inertness, and capacity to serve as a binding, gliding, disintegrating, and filling agent for solid dosage forms, starches are among the most readily available and widely utilized excipients in the drug industry to prepare tablets[2, 3]. Native or untreated starches are weak structurally and have limited functional options when making tablets; their function must be increased through modifications. Modifying or treating native starches through physical, chemical, or enzymatic techniques can be used to obtain desired functionalities or improve their physiochemical properties[3,4].

Understanding powders' packing, cohesive, and compressional characteristics are crucial in developing and manufacturing solid dosage forms like powders, tablets, and capsules of pharmaceutical standards; this is critical when combining powders, filling capsules with powders or granules, and dies in the course of tableting[5]. Several models characterizing powder blends have drawbacks, such as requiring a spherical shape for model validation[6], working only with a small particle size fraction[7], or losing accuracy as an additional powder component is added[8]. As a result, model failure will arise when the particle size distribution is wider or skewed[5].

Various techniques, such as compaction stimulators or instrumented production presses, can be used[9] to evaluate the compaction characteristics of pharmaceutical dosage forms. The compaction equation can demonstrate the link between powder parameters such as volume, porosity, density, void space, and compaction pressure. Constructing a linear plot by fitting the experimental data to an equation is necessary to make comparisons between several data sets easier[10].

The association between volume and compression pressure is used to generate a mathematical model of the compaction process[11]. Thus, increasing the compression force or pressure causes the volume of powders to decrease during powder compression; however, this compression process may be well described by monitoring changes in powder porosity as the compression pressure is increased[12]. The manufactured tablets' compressional features were studied using the Heckel, Gurham, and Kawakita equations and density measurements[13, 14, 15]. Various equations provide a comprehensive picture of the powder com-

paction process and excipient behavior. Tablets should also be strong enough to withstand post-compaction stress during handling and transportation[16].

The Heckel equation depicts the relationship between the powder's relative density (D) and the compaction pressure (P). The equation is expressed as:

$$\ln [1 \div (1 - D)] = KP + A \quad \text{..... [1]}$$

K is the plasticity slope of the compressed powder and the reciprocal of the mean yield pressure (Py). The constant A, commonly known as the equation's intercept, is related to the tableting method, which comprises die filling, powder particle rearrangement, and deformation. Using the equation below, the value of relative density (D_A or D), also known as the overall degree of densification and rearrangement of powder particles, can be derived from constant A[11,17].

$$D_A = 1 - e^{-A} \quad \text{..... [2]}$$

The initial rearrangement phase of densification due to die filling is described by the powder's relative density at the point where the applied pressure equals zero (D_o). The difference between D_A and D_o, known as the relative density D_B, represents the rearrangement when low pressures are applied to the powder bed:

$$D_B = D_A - D_o \quad \text{.....} \qquad [3]$$

Powder compression can be analyzed using the Kawakita equation and the amount of volume decrease (C), which is stated as:

$$C = (V_o - V_P) \div V_o = abP \div (1 + bP) \quad \text{..... [4]}$$

The preceding equation can be rewritten as follows:

$$P \div C = (P \div a) + (1 \div ab) \quad \text{..... [5]}$$

Where V_o is the initial bulk volume of the powder, and V_P is the bulk volume after compression. The constant a represents the material's lowest porosity before compression, while the constant b represents its plasticity. P_k is the pressure necessary to lower the powder bed by half, defined by the reciprocal of b[12,17,18].

The Gurnham equation states that a fractional increase in pressure increases apparent mass density relative to the prior pressure[19]. The association is as follows:

$$\frac{dP}{P} = A\, dD \quad \text{..... [6]}$$

P represents pressure, D represents apparent density based on solid weight and total volume, and A represents a constant.

Volume decrease can be expressed as porosity (ε) in pharmaceutical powder compaction, as follows:

$$Porosity = 1 - \frac{(Apparent\ density)}{(True\ density)}$$

$$\varepsilon = 1 - \frac{D}{\rho_t} \quad \text{.....[7]}$$

Where ρ_t denotes the material's particle or actual density.

Previous studies have shown that excipient compressional qualities can be utilized to validate the role of excipients in medication formulations[16, 20, 21]. The Heckel, Kawakita, and Gurnham compressional equations were employed to examine Ibuprofen tablets made by direct compression utilizing native, pregelatinized, and carboxymethylated starches from *Oryza glaberrima* (African/Ofada rice) and *Digitaria exilis* (Fonio/Acha). Ofada rice is the generic name of the indigenous rice species *Oryza glaberrima,* Steud Family Poaceae, which is mainly cultivated in Southwest Nigeria[22]. Rice has high starch content making it a potentially inexpensive source of starch for the pharmaceutical industry[23]. Also, *Digitaria exilis* (Acha), a food grain consumed in many parts of Africa and India, belongs to the same subfamily as maize, sorghum, and pearl millet. The starch from its grains is comparable in structure and physicochemical properties to starch from conventional cereal grains. However, Acha starch shows a higher water binding capacity than wheat, rice or maize starches[24], making it suitable for several pharmaceutical applications.

The principal goal of this study was to establish the packing, flow and cohesive characteristics of Ibuprofen tablet formulations containing untreated and treated versions of these locally sourced starches as filler binders. This study used Ibuprofen as the benchmark drug to determine how starch-based excipients affected tablets made from drugs with poor compaction characteristics[25]. Several studies reported that Ibuprofen bulk powder has poor flow properties, inadequate compaction behavior, and adheres to the surfaces of punch and die, making tablet formulation development difficult [26, 27, 28].

METHODOLOGY

Ibuprofen powder BP, sodium chloride and acetic anhydride were sourced from BDH Chemicals Limited. Magnesium stearate was acquired from Aldrich Chemical Company Inc., USA. Acetone was obtained from Merck Limited,

Germany. All the active and inactive pharmaceutical ingredients used in this study were of pharmaceutical standard and analytical grade.

Production of the native starches

The *Oryza glaberrima* and *Digitaria exilis* grains were acquired locally in Nigeria. The pure starch polymers were generated by aqueous extraction using Odeniyi[29] method with modification. In a nutshell, each sample's grains were soaked in distilled water for 2-3 days. The mixture was blended using an Osterizer Dual range Pulse Matic Milling blender (John Oster Manufacturing Co., Racine, Wisconsin, USA) into a slurry before being strained through a muslin cloth. The filtrate was allowed to settle after being suspended in distilled water. The obtained supernatant was decanted at 12-hour intervals, and the starch slurry was re-suspended in distilled water. After 72 hours, the cake was collected and milled on a local milling machine; then dried for 48 hours in a 50 °C oven (Laboratory oven TT-9083, Techmel and Techmel, TX, USA) before being milled to smaller particles with the Osterizer Dual range Pulse Matic Milling blender. A sieve with a mesh size of 0.315 mm was used to obtain the fine powder. The powder that resulted was then sealed in an airtight container. A sieve with a mesh size 120 was used to sift dry whitish end-products.

Synthesis of the pregelatinized starches

The two native excipients were pregelatinized in the laboratory according to the method by Okunlola and Adewusi[30]. 100 g of dry starch powder was dissolved in 100 mL of distilled water to create an aqueous slurry of each starch, which was then heated at 55 °C while being stirred every 10 minutes. The derived paste was crisp-dried for 48 hours at 60 °C in a hot air laboratory oven (TT-9083, Techmel and Techmel, TX, USA). The dried mass was ground into powder in a laboratory mill (Christy and Norris Ltd., Chelmsford, UK). Before use, all the starches were run through a sieve with a number 120 mesh (125 μm). These modified excipients were kept in airtight amber containers.

Synthesis of the carboxymethylated starches

A 100 g sample of native starch powder was combined with 400 mL of a 7.5 % w/v monochloroacetic acid solution in 1-propanol. The starch suspension was mixed with 10 mL of a 30 % w/v sodium hydroxide solution and heated on a hot plate for 20 minutes at 50 °C with constant stirring (200 revolution per minute). The reaction was then neutralized with glacial acetic acid before filtering through filter paper. The remaining sediment was washed with 80 % methanol, then 100 % methanol. The obtained starch was dried for six hours in an oven at 50 °C. The dehydrated starch fragments recovered were crushed into

a fine powder and sifted utilizing a British standard sieve with a mesh size of 120 mesh (125 μm). The powdered starch was weighed and kept in airtight vessels[31].

Analysis of particle size

The light microscope with batch number BH-2 BHS and manufactured by Olympus, Tokyo, Japan, was used for determining the particle size, with approximately 200 particles per sample being viewed. Each starch form's mean diameter, d, was ascertained by plotting the cumulative number of percent oversize versus particle size.

Determination of moisture content

Using an Ohaus infrared moisture content analyzer (Ohaus Scale Corporation, New Jersey), the percentage moisture content of 10 mg of each starch form was determined and recorded.

Densities measurements and compressibility characteristics

Using xylene as the displacement fluid, the particle density of each starch form was determined using the pycnometer method by Ayorinde et al[32]. Each starch powder's bulk density was ascertained using established procedures from the previous study[31]. Tapped density was determined by applying 100 taps at a standardized rate of 38 taps per minute to 30 g of each starch sample in a graduated cylinder. The calculations were carried out in triplicate. Each starch powder's relative density, D_o, was calculated by dividing its bulk density by its particle density. Previous research on these specific starches forms generated Hausner's ratio and Carr's index values[31].

The preparation of tablets

Binary blends of drug and excipients were made for direct compression, as illustrated in Table 1.

Each formulation containing the appropriate amounts of starch and Ibuprofen was well combined. The powder combinations (total of 400 mg per tablet) were compacted by utilizing a Carver Hydraulic Hand Press (Model C, Fred S. Carver Inc., Menomonee Falls, Wisconsin, USA) equipped with a calibrated pressure gauge. The flat-faced punch and 12.5 mm die were lubricated with a 2 % w/v magnesium stearate in acetone before each compression to prevent the tablet from sticking to the surface of the punch and die. The compressional pressures used were from 0.25 to 1.5 metric tonnes, with a dwell period of sixty seconds. After being carefully removed from the assembly, the pills were stored in sealed containers atop silica gel for 24 hours for elastic recovery before determining their properties.

Table 1. Drug and excipient composition in tablet forms

Formulation	Ibuprofen	Excipient
	%	%
F_1	90.0	10.0
F_2	75.0	25.0
F_3	50.0	50.0
F_4	25.0	75.0
F_5	00.0	100.0

Establishment of Heckel relationships for the native and modified starches

The ln 1/1-D was plotted versus applied pressure P for the different types of starches, also at different amounts of starch in the formulations. The extended linear plots' slope and intercept on the y-axis were K and A. Equation 2 was used to calculate total pre-compression density D_A at zero and low pressures, whereas mean pressure P_y was derived as a reciprocal of K. D_B (relative density at low pressures) was calculated by subtracting D_A from D_o, the powder bed's relative density at zero pressure (Equation 3)[16,20].

$D_A = 1 - e^{-A}$ ..... [2]

$D_B = D_A - D_o$ ..... [3]

Determination of Kawakita relationships for the different starches

The constant C, which signifies the level of volume reduction, was estimated utilizing Equation 4. P/C was plotted versus applied pressure P for the native and modified starches in the preparations at the varied starch concentrations. The constants a and ab were calculated using the slope and intercept of the straight line from Equation 5. Regression plots with Equation 6 were used to calculate P_k, the pressure needed to drop the powder bed volume half, and D_i, the packed beginning relative density[16,20].

$C = (V_o - V_p) \div V_o = abP \div (1 + bP)$ ..... [4]

$P \div C = (P \div a) + (1 \div ab)$ ..... [5]

$\frac{dP}{P} = A\, dD$ ..... [6]

Establishment of Gurnham relationships for the native and modified starches

Percent porosity (% ε) was plotted against lnP (natural logarithm of applied pressure) for different starches in the formulation at various concentrations. As previously stated, the slope of the regression line derived from each plot was used to calculate the value of c, a term for compressibility that signifies the influence of change in pressure on porosity, and d, which corresponded to the enhanced compressibility features[16, 20].

Statistical analysis

The data derived from the formulations were statistically analyzed using the Students' t-test and ANOVA, with $P < 0.05$ regarded as the importance level (GraphPad Software Inc., San Diego, USA)

RESULTS and DISCUSSION

Physical properties of the untreated and treated starches

Particle sizes of the starches had almost doubled following modifications (Table 2). Particle size study revealed that the native form had the smallest diameter, *d*, for the two different starches used in this study. Native African rice starch granules (7.24 μm) proved to be of a smaller size than pregelatinized (15.37 μm) and carboxymethylated (13.13 μm) granules. Native Fonio starch granules (3.16 μm) were also smaller than those that had been pregelatinized (4.98 μm) and carboxymethylated (7.69 μm). The mean diameter of native African rice and Fonio starch increased considerably after modification. The swelling of the starch granules brought on by gelatinization and the subsequent amylose leaching could be the source of the pregelatinized starches' larger particle size. The loss of amylose content after gelatinization results in enhanced amylopectin activity, improving starch swelling capacity. Several investigations have found that swelling power is closely related to amylose and its characteristics. Therefore, it was suggested that the degree of amylose lipid complexation, the amount of amylose that has been leached, and the phosphate content all substantially impact swelling power. Amylose lipid complexes limit swelling power, but the presence of phosphate groups in starch improves starch's water binding ability and, therefore, its swelling power[16,31,33]. These events are likely responsible for the high solubility, swelling power, and water absorption indices observed in pregelatinized starches[31]. Previous research has confirmed that pregelatinized starch has more excellent water absorption, swelling capacity, and solubility than native starch due to hydrogen bond breakdown and amylose leaching caused by gelatinization[34,35]. The highest value for anticipated

particle diameter was found in pregelatinized African rice. Larger particle sizes improve powder flow, which should improve compressibility[36,37].

The particle diameter of the two starches was also increased by carboxymethylation, which disrupts the starch granule structure and increases amylose leaching, resulting in starch granule enlargement. Adding the carboxymethyl group makes these starches more hydrophilic and aids in water holding, expanding the particle dimension of the chemically modified starches[16,38].

Table 2. Physical properties of the pure and modified starches (n =3, mean ± s.d)

Starch Source	Starch form	Mean Diameter, d (μm)	Particle density (gcm^{-3})	Hausner's Ratio	Carr's index	Moisture Content (%)
African Rice	Native	7.24±3.78	1.56±0.002	1.23±0.05	19.35±4.80	11.00
	Pregelatinized	15.37±13.17	1.47±0.01	1.18±0.02	14.62±4.66	10.44
	Carboxymethylated	13.13±7.15	1.53±0.02	1.21±0.05	17.50±4.97	9.48
Fonio	Native	3.16±1.85	1.48±0.002	1.25±0.06	19.90±6.04	10.12
	Pregelatinized	4.98±3.02	1.47±0.001	1.19±0.04	16.26±4.00	9.93
	Carboxymethylated	7.69±3.99	1.52±0.003	1.33±0.02	23.55±1.42	10.23

Table 2 also shows the different starches' physical properties, their respective particle densities, Hausner's ratios, and Carr's indices. The particle density of Ibuprofen was 1.062 gcm^{-3}, while its mean particle diameter was 44.15 μm.

The particle density of Ibuprofen powder was very low (1.063 gcm^{-1}), and the mean particle diameter was exceptionally high (44.15 μm). Ibuprofen's weak flow properties and elevated cohesion explain its poor compression qualities and, thus, the necessity for acceptable excipients with good flow and compression capabilities[16]. Ibuprofen demonstrates poor flow, compaction (tableting), and dissolution profile because of its hydrophobic structure and high cohesive, adhesive, and viscoelastic characteristics; therefore, it should be combined with excipients with superior physicochemical properties to enhance its compression and dissolution behavior[39]. Except for the carboxymethylated fonio, pure starch forms from the starches used in this study showed lesser particle density values than the treated forms. During powder mixing, the powder density had an impact, and segregation could occur due to size and shape. The behavior of the starch during packing affects unit operations like die, capsule filling, and compression[40].

Flowability test using the Hausner ratio and Carr's index (compressibility index) revealed lower values for the pregelatinized and carboxymethylated forms of African rice starch compared to their native form (Table 2), suggesting superior flow characteristics to their untreated form[35]. Pregelatinized Fonio flowed better than its native form, whereas carboxymethylated Fonio exhibited poor flow properties (Table 2). The Hausner and Carr's indices for starches were ranked in the following order: African rice; pregelatinized < carboxymethylated < native and Fonio; pregelatinized < native < carboxymethylated. The flowability of botanical starches was generally ranked in the order of African rice > Fonio. From the previous study on these native and modified forms of these starches by Omoteso et al.[31], the larger particle size of these modified starch granules may be attributed to the improved flow of pregelatinized and carboxymethylated starches. Larger particles flow better due to superior density and gravitational influences, but finer particles are more cohesive as a result of surface effects[35].

The native and the modified starches exhibited Hausner ratios more prominent than 1.11 and Carr's indices greater than 10. Values below 15 on Carr's index denote good flowability, while values above 25 denote poor flowability. Additionally, Hausner ratio values higher than 1.25 indicate poor flowability. The values of these indices will help the formulator in the judicious selection of excipients to prevent impeding the movement of powder into the die cavities through the hopper, which could affect the weight uniformity of the produced tablets[20,31,41,42]. Pregelatinized starches exhibiting lower Hausner's ratio values than native starch indicate improved flowability[20,35,40]. Therefore, starch modification, particularly pregelatinization, increases the flowability of native starch. Carboxymethylated starch also demonstrated outstanding flow properties. The most common pharmaceutical-modified starch is pregelatinized starch. Based on earlier research on pregelatinized starch, this treatment enhances starch flowability, disintegration, and hardness[43]. Generally, there was a direct relationship between the particle density, Carr's index, and Hausner ratio values between the native and modified starches (Table 2).

The moisture level of the samples that were examined ranged from 9.48 % to 11.00 % (Table 2). Except for carboxymethylated Fonio starch, which has a slightly greater % moisture content than native Fonio starch, native starches were shown to have higher moisture contents than their modified counterparts. The moisture content of native African rice was the highest (11.00 %), while carboxymethylated African rice had the lowest moisture content (9.48 %). Because starch is typically absorptive, the minor increase in carboxym-

ethylated Fonio's moisture content from 10.12 % to 10.23 % may be the result. However, all experimental starch samples' moisture content ranges were within the normal ranges anticipated at 50 % relative humidity[38,44].

The Heckel relationships of the pure and treated starches of African rice and Acha

Heckel relationships in Table 3 and Figure 1 yielded the following conclusions. The type A Heckel relationship was achieved due to the plot of ln (1/1-D) against applied pressure for pure starches (100 % starch) being linear and nearly parallel. Plastically deformed materials do this[45]. All formulations with experimental starch excipients produced linear plots with correlation coefficients over 0.970.

The slope and intercept of the extrapolated linear plots determine K and A, respectively. P_y, the pressure needed to distort particles, was computed as a reciprocal of K and measured plasticity. Low P_y values suggest higher and faster initiation of plastic deformation, whereas high P_y values indicate the opposite. P_y values were found to be usually lower in formulations comprising pregelatinized starch. Also, untreated starch formulations had lower P_y values than carboxymethylated ones but higher than the pregelatinized ones; this implies that pregelatinized starches stimulated faster commencement of plastic flow than other forms of starches[16], with pregelatinized < carboxymathylated< native for African rice starch and pregelatinized < native < carboxymethylated for Fonio. P_y values in African rice formulations primarily increased as the amount of starch excipients rose; however, there were differences in the values obtained for Fonio formulations. Table 3 demonstrates that the plasticity of the formulations appears to decrease as the amount of starch in the preparations increases. The order of P_y values by the source was mainly Fonio > African rice. Low P_y values suggest higher and faster initiation of plastic deformation, whereas high P_y values indicate the opposite.

The constant A is related to the particle rearrangement and filling of the die prior to the deformation and bonding of the particle. D_o is the powder bed's relative density when no pressure is exerted. It describes the early rearrangement stage of densification and is calculated from the relationship between loose bulk density and particle or true density. The entire degree of densification accomplished at zero and low pressures following rearrangement processes before any significant amount of inter particulate bonding is the relative density D_A of the material during densification at which a cohesive unbroken tablet has just been generated. The phase of densification is the powder's relative density

under low-pressure D_B, which occurs after using low pressures because of particle rearrangement or fragmentation before significant particle deformation occurs[16]. Tablet formulations containing pregelatinized starch had the highest D_A and D_o values[20] and the lowest D_B values.

In contrast, carboxymethylated starch formulations had intermediate D_o and D_B values and the lowest D_A values. Tablets containing natural starch exhibited moderate D_A values, the highest D_B values, and the lowest D_o values. The D_o values for the various tablet preparations declined as the amount of starch increased.

The values for D_o, D_A, and D_B for two botanical sources decrease with increasing the amount of starch in the formulations with minor variances. Greater values of these factors indicate a higher level of early packing in the die, a higher overall densification, and higher particle rearrangement during the initial stages of compression, respectively. The perceived drop in D_B values showed that powder particle rearrangement in the initial stages of compression declined at these starch amounts for formulations with increasing starch contents.

The decreasing D_o values as the quantity of starch adjuvants in the preparations grew suggested that as the starch content increased, the initial packing of the powder particles in the preparations because of die-filling decreased. D_o values rose in formulations, including modified starches, with the highest levels in formulations utilizing pregelatinized starch. Pregelatinized and carboxymethylated starches with larger powder particles were expected to have greater D_o values in their formulations. Previous researches have described this pattern[16,46]. As a result, pregelatinization of these two starches generated the optimum early packing of the formulation particles in the die, followed by carboxymethylated particles.

In native and carboxymethylated Fonio and native African rice starch and Ibuprofen tablet formulations, D_B values were higher than D_o values, representing the particle rearrangement stage at the preliminary step of compression; this might be ascribed to powder particle fragmentation caused by the use of low pressures, resulting in the stuffing of inter particulate void spaces that were primarily in existence at zero pressure; this promotes compaction[16, 47].

Table 3. Parameters calculated from Density measurements and Heckel plots for drug-native and modified starch blends

Starch Source	Conc. (%w/w)	Native				Pregelatinized				Carboxymethylated			
		P_y (MNm^{-2})	D_0	D_A	D_B	P_y	D_0	D_A	D_B	P_y (MNm^{-2})	D_0	D_A	D_B
Fonio starch (Digitaria exilis)	10	357.14	0.326	0.904	0.578	70.42	0.618	0.906	0.288	833.33	0.361	0.878	0.517
	25	588.24	0.309	0.850	0.541	555.56	0.587	0.913	0.326	126.58	0.340	0.706	0.366
	50	555.56	0.284	0.850	0.566	476.19	0.542	0.887	0.345	714.29	0.310	0.734	0.424
	75	416.67	0.262	0.733	0.471	263.16	0.503	0.773	0.270	588.24	0.285	0.763	0.478
	100	500.00	0.244	0.713	0.469	434.78	0.470	0.766	0.296	666.67	0.264	0.780	0.516
African rice (Oryza glaberrima)	10	294.12	0.387	0.814	0.427	204.08	0.648	0.951	0.303	166.67	0.562	0.870	0.308
	25	344.83	0.362	0.868	0.506	222.22	0.607	0.865	0.258	200.00	0.532	0.840	0.308
	50	454.55	0.328	0.707	0.379	322.58	0.549	0.830	0.281	666.67	0.489	0.803	0.314
	75	588.24	0.300	0.732	0.432	238.10	0.502	0.869	0.367	285.71	0.452	0.674	0.222
	100	625.00	0.276	0.642	0.366	250.00	0.462	0.720	0.258	312.50	0.421	0.760	0.339

P_y, Mean yield pressure/ mean pressure; D_o, Relative density at zero pressure; D_A, Overall degree of densification and rearrangement of powder particles or total pre-compression density at zero and low pressures; D_B, Relative density at low pressure.

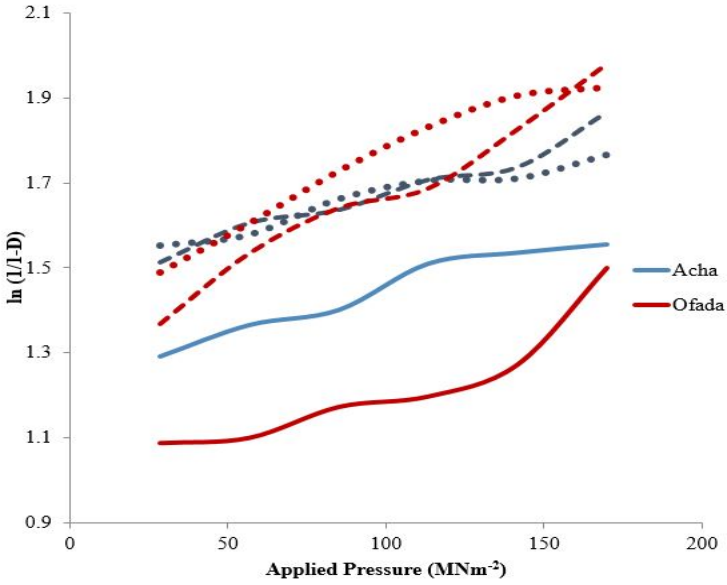

Figure 1. Overlays of Heckel plots for tablet preparations comprising Native (-), Pregelatinized (- - - - -), and Carbokxymethylated (. . . . .) starches of African rice (Ofada) and Fonio (Acha): 100%

Kawakita relationships for the untreated and treated starches of African rice and Fonio

Since no single expression has been proven to be perfect for describing powder compatibility, the Kawakita expression is frequently employed in examining the compressibility of pharmaceutical powders. Figure 2 showed linear relationships for all formulations and applied pressures, with a correlation value greater than 0.999. Thus, the densification mechanisms of the formulation of Ibuprofen tablets can be explained by equation[23].

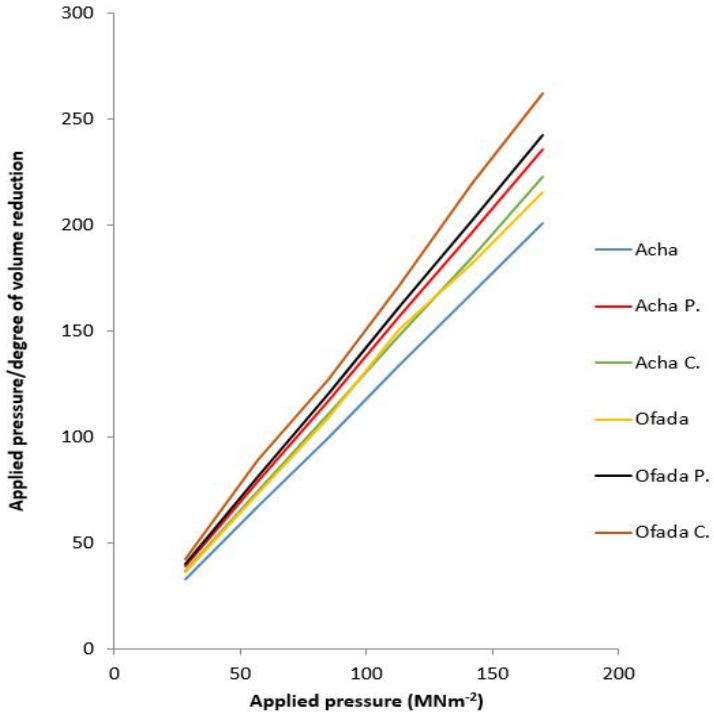

Figure 2. Overlay of Kawakita plots for Ibuprofen tablet preparations containing pure and treated starches (Pregelatinized and Carboxymethylated) of African rice (Ofada) and Fonio (Acha) at 10% w/w

The Heckel equation parameter P_y differs from the Kawakita parameter P_k in that the latter (Heckel) seems to correspond to the overall amount of plastic deformation happening in the course of compression, whilst the previous (Kawakita) is related to the commencement of plastic deformation in the course of compression[47]. Since P_k measures the inverse plastic deformation during compression, a reduced P_k value indicates enhanced or greater overall plastic deformation [47]. In the untreated and treated starch forms and different quantities of starch in the preparations, the level of P_k values by botanical starch origin varied.

The discrepancies in P_k values reported between starch formulations and Ibuprofen tablet preparations can be related to variations in characteristics throughout the preparation process, as Ibuprofen formulations, unlike starch, are several-component systems. In a one-component system, specifically native starch, deformation capacity is free from other components; however, plastic deformation starts whenever any component's yield point is surpassed in a several-component system, like Ibuprofen tablet formulations. The defor-

mation of any component after its yield value in the latter system may activate the deformation of other components in the system. Since the type of the speed and amount of plastic deformation are more complex for several components than for a single component, it may be hard to forecast the deformation parameter of multiple component systems and identify its characteristics from those of its single components[48]. However, the presence of Ibuprofen in the formulation is responsible for the changes observed in the binary formulation established in this work.

The pure form of the starch increased the P_k values. Pregelatinization reduced overall plastic deformation in the formulation of two botanical sources. Also, pregelatinized starches had the highest P_k values (Table 4). At 10 % starch concentration, pregelatinized Fonio and African rice starch showed extremely high P_k values. The carboxymethylated P_k value was also high at 10 % starch content of Fonio starch. P_k values for pure starches were in the order African rice > Fonio by botanical origin at 10 % starch concentration. The P_k values for pregelatinized and carboxymethylated starch tablets were Fonio > African rice in that order at 10 % starch concentration. A higher P_k number indicated lesser overall plasticity, whereas a lower value indicated increased total plasticity.

D_i (packed initial relative density) values varied with the rise in starch quantity in the Ibuprofen formulations, including the different starches, except native and pregelatinized Fonio starch, where D_i values increased with increasing starch concentration. D_i levels were often more significant in treated than in pure starch preparations. The formulations comprising pregelatinized starch had lower values than those including carboxymethylated starches. Thus, carboxymethylation and pregelatinization increased initial particle packing in Ibuprofen preparation. Furthermore, modification of starches at greater concentrations of starch resulted in higher packed initial relative density values of the Ibuprofen preparations compared to lower packed initial relative density values at smaller concentrations of starch content in the preparations.

D_i and D_o (loose initial relative density) values from the Kawakita and Heckel parameters (Tables 3 and 4) showed no clear trend or pattern in identifying the higher value. Although D_i had the most significant and lowest numbers, D_o's values were in the middle. D_i values represent the packed primary relative density of formulations when modest pressure or tapping is applied, whereas D_o values represent the loose initial relative density caused only by die filling. In the corresponding formulations, the Heckel parameter D_B, which pertains to densification at low pressures, had both greater and lower values than D_i. Particle size, morphology, and packing geometry of powder affect the two parameters.

Table 4. Features calculated from Kawakita plots for the drug-native and modified starch blends

Starch Source	Starch Conc. (%w/w)	Native		Pregelatinized		Carboxymethylated	
		P_k (MNm^{-2})	D_i	P_k (MNm^{-2})	D_i	P_k (MNm^{-2})	D_i
Fonio *(Digitaria exilis)*	10	3.578	0.186	29.281	0.388	15.594	0.308
	25	7.016	0.198	2.955	0.407	0.505	0.354
	50	4.923	0.199	1.455	0453	6.290	0.374
	75	2.846	0.227	0.793	0.454	0.729	0.339
	100	16.163	0.232	0.500	0.466	6.966	0.345
African rice *(Oryza glaberrima)*	10	0.871	0.274	26.632	0.428	1.385	0.546
	25	7.118	0.269	0.569	0.500	4.014	0.544
	50	0.799	0.306	1.299	0.508	2.508	0.632
	75	11.899	0.323	0.939	0.475	0.405	0.809
	100	1.002	0.347	0.668	0.525	0.441	0.679

P_k, Pressure necessary to lower the powder bed by 50%; D_i, Packed initial relative density.

Gurnham relationships of the untreated and treated starches of African rice and Acha

The Gurnham equation is another way to determine the compressibility of bulk powders. A rise in pressure causes a proportionate elevation in the apparent density of a substance[16,49]. The apparent density D and the natural logarithm of applied pressure, ln P, can thus have a linear relationship. Porosity ε is commonly used to express volume reduction. Then, porosity and ln P are linearly related. The slope and intercept are represented by the inferred linear plot's constants c and d, respectively. The slope constant c is a metric of excipient compressibility, describing the influence of pressure variation on compact porosity.

Table 5. Features calculated from Gurnham plots for drug-native and modified starch blends

Starch Source	Starch Conc. (%w/w)	Native		Pregelatinized		Carboxymethylated	
		c	d	c	d	c	d
Fonio *(Digitaria exilis)*	10	3.77	40.48	2.59	14.58	0.94	15.00
	25	3.81	38.10	1.02	11.88	7.74	48.85
	50	1.91	23.32	3.81	27.28	2.41	33.87
	75	1.54	19.53	4.49	35.72	2.71	32.04
	100	3.68	22.43	3.27	33.34	2.28	29.17
African rice *(Oryza glaberrima)*	10	3.13	27.33	1.34	9.06	3.43	22.75
	25	2.13	19.48	3.95	26.55	4.12	28.32
	50	4.40	43.26	3.07	26.22	1.73	24.74
	75	3.40	37.90	2.75	21.13	6.58	52.54
	100	3.84	47.57	6.09	46.17	4.74	38.69

c, Slope; d, Intercept.

Table 5 and Figure 3 demonstrate Gurnham correlations for formulations with 75 % starch excipients. There was a decrease in porosity with the increased applied pressure and starch concentration in the starch-Ibuprofen formulation. As pressure increases due to the powder's densification, pores close and porosity decreases. This result is corroborated by previous research[50]. Porosity ε plots vs ln P revealed a linear association with negative correlation coefficients $r > 0.920$, indicating a reverse link amid porosity and applied pressure. More significant slope (c) values were frequently reported for African rice starch formulations than for Fonio starch preparations, signifying that African rice starch formulations had more significant densification than acha starch. The slope values of the two starch sources' untreated, pregelatinized, and carboxymethylated preparations differed significantly ($p < 0.05$).

The intercept (d) was most significant in carboxymethylated starch preparations, smallest in pregelatinized, and intermediate in native. It has been proposed that increased compressibility properties correspond to the influence of d on material compressibility[20].

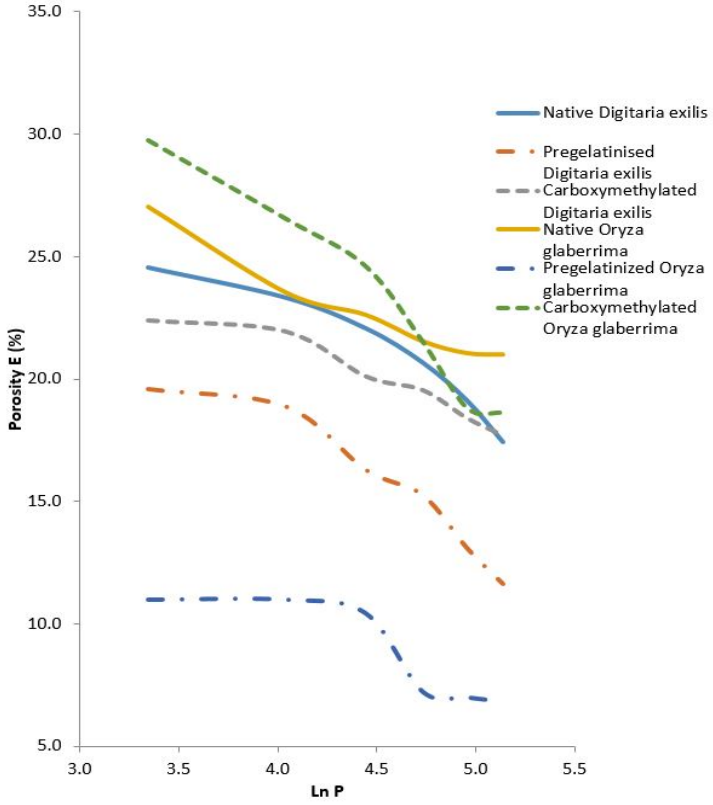

Figure 3. Overlay of Gurnham plots for Ibuprofen preparations comprising Native (-), Pregelatinized (- -) and Carboxymethylated (. . .) starches of Ofada rice and Acha: 75 % w/w

In conclusion, Pregelatinized and carboxymethylated African rice and Fonio starches were successfully synthesized from their native starch forms. Pregelatinization induced faster commencement of plastic deformations but lowered the overall quantity of plastic deformations in formulations. Modified starch forms, particularly pregelatinized ones, would make effective excipients because they increased tablet densification. The amount of pregelatinized starch used in tablet production is less than that of regular starch. Ibuprofen tablets with African rice starch had stronger densification than those utilizing Fonio starch.

STATEMENT OF ETHICS

This study did not include any human or animal subjects.

CONFLICT OF INTEREST STATEMENT

Not Applicable

AUTHOR CONTRIBUTIONS

OAO (Omobolanle Ayoyinka Omoteso) conducted experiments, interpreted the results and wrote the draft of the manuscript and formatted the manuscript to Journal specifications. MAO (Michael Ayodele Odeniyi) designed the research concept, provided some of the materials for the experiments, supervised the conduct of all experiments and reviewed the manuscript. All authors read and approved the final manuscript.

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