PRELIMINARY INVESTIGATIONS INTO THE PHYSICOCHEMICAL AND COMPACtion CHARACTERISTICS OF MODIFIED STARCH OF DISCOREA ALATA USING DICLOFENAC SODIUM TABLET

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ABSTRACT

Objective: This work focused on evaluating the micromeritic and compressional properties of pregelatinized African water yam (Discorea alata) starch and its modified forms with comparison to pregelatinized corn starch and microcrystalline cellulose.

Methods: Two modifications of the water yam starch were prepared; acetone dehydrated pregelatinized form (DSA) and an admixture of DSA and pregelatinized corn starch (CDSA). A third form of starch is the acetone dehydrated pregelatinized corn starch (CSA). These were used to form batches compacted as tablets using diclofenac sodium as the active moiety. Physicochemical and flow characteristics of the starch powders were elucidated, and the drug starch compatibility studies done using the Fourier transform Infra-red (FTIR) technique. Compaction studies were investigated on tablets formed at different compression pressures and Heckel plots were prepared.

Results: The slope of the straight line (K) of 0.8959 was greatest for F1 while yield pressure (Py) value of 10.965 was highest for F3. These values from the Heckel plot suggest that while the tablets of control batch of microcrystalline cellulose (F-1) and a batch of pregelatinized corn starch (F-2) formed harder compacts, less likely deformed plastically, the Discorea alata batch (F-1) and the admixed batch (F-2) were likely to deform plastically. Also, the binding efficiency of the compact was significantly high (47.81%Kgscm⁻¹) for F4 at 56.5Kpas compaction pressure, higher than that obtainable for any of the other formulations at the compaction pressures under consideration. All starches formed had similar moisture content (of 10%) despite the different sources but the interaction between the water molecule and pregelatinized water yam starch improved as revealed by viscoity(7.18mPas), hydration capacity(3.27%) and swelling index(250%) of CDSA.

Conclusion: It could be concluded that pregelatinized water yam starch could be used as a substitute for corn starch or micro-crystalline cellulose as a pharmaceutical excipient (binder/filler) in tablets formulation.

Keywords: Pregelatinization, Compaction, Discorea alata, Heckel plots

INTRODUCTION

Research questions prompting innovative thinking are constantly on the minds of researchers and manufacturers of excipients. Such questions as; what is likely the next ideal excipient with greater degree of functionality to go for? Will the approval of such adjuvant by the relevant regulatory authorities be a very tall order? How can an existing excipient be improved upon to achieve better dosage forms? No doubt, the search for excipients having improved properties is in no way meagre since the desires and convenience of patients are intended to be achieved in dosage form design, while not compromising therapeutic efficacy.

Starch is widely used as drug excipients, owing to its properties, avalanche and availability. Starches obtained from different sources vary in their respective constitution. Using equations such as Kawakita’s and Heckel’s and their interpretations, pharmaceutical excipients could be studied and differentiated into plastic or brittle materials. Specifically, the yield pressure in Heckel plot is used as the determining factor [1]. Such knowledge is essential to achieve compacts having the good tensile strength and binding efficiency. Native starch has desirable disintegration properties but its crystalline characteristics give it its poor water solubility [2].

Excipient modification has reportedly knocked off certain undesirable properties inherent in some polymers while introducing newer improved ones [3]. Synthetic, semi-synthetic and natural products have been modified, with derivatives having better flow properties, improved binding properties, emulsification features and even hydrophilic characteristics. Starch, gums, and mucilage have been reportedly modified; chemically by acetylation, carboxymethylation, oxidation; thermally by pregelatinization and even physically by admixture of excipients with different properties [2, 4, 5].

Diclofenac sodium, a Non-Steroidal Anti-inflammatory Drug (NSAID) is employed clinically for the management of several pain and inflammatory-related conditions such as osteo- and rheumatic arthritis, dysmenorrhea, and lower back pain.

![Fig. 1: Chemical structure of diclofenac sodium](image)
properties and compaction potentials of the acetone dehydrated pregelatinized forms of the starch (DSSA) with that of similarly modified corn starch (CSA), and when the two are admixed (CDSA) using powder of diclofenac sodium as the active pharmaceutical ingredient (API). Microcrystalline cellulose was used as a reference.

**MATERIALS AND METHODS**

**Materials**

Acetone (BDH Chemicals, UK), cornstarch, water yam starch (obtained from *Discorea alata* sourced in Uyo metropolis, Nigeria), distilled water, all other chemicals being of analytical grade.

**Methods**

**Preparation of acetone treated pregelatinized starch**

To a 3.3L of distilled water at room temperature, 500g of water yam starch was suspended to form a slurry which was then heated to 90 °C forming a mucilage. The mucilage was precipitated with acetone 5 L. The precipitated rubber-like products were cut into small lumps and allowed to cool and dried. The dried products were diminished using the laboratory blender (Sonic, Japan) and sieved to obtain powder size fraction of ≤1.0 mm which was used for determination of powder characteristics. Cornstarch sample was also subjected to similar treatment to obtain its pregelatinized form.

**Physical characterization**

**True density**

The true density of powder sample was carried out using the liquid displacement method. Xylene was used as the inert displacement liquid as reported in literature [8]. The numerical value of the parameter was calculated from the equation

\[ D_t = \frac{w}{(\rho_x \cdot v)} \times \rho_g \]  

Where \( D_t \) is true density, \( w \) is the weight of powder sample, \( \rho_g \) is the specific gravity of the xylene, \( a \) is the weight of the density bottle+xylene, and \( b \) is the weight of bottle+solvent+powder sample. This was done in triplicates.

**Bulk and tapped density**

A quantity of 10g of powder was placed in a 25 ml clean dry measuring cylinder and the volume, \( V_b \), occupied by each of the samples without tapping was obtained. After 100 taps at regular intervals, the volume, \( V_{t0} \) was also determined. The bulk (\( D_b \)) and tapped (\( D_{tp} \)) densities were then computed as the ratio of the mass of powder to the volume (\( V_b \) and \( V_{t0} \) respectively.

**Carr’s index and hauser’s ratio**

These were calculated to assess the propensity of the powder samples to be compressed. Carr’s index was derived from the formula

\[ CI = \frac{D_{tp}-D_b}{D_b} \times 100 \]  

Where \( CI \) is the Carr’s index as a percentage, \( D_{tp} \) is the Tapped density and \( D_b \) is the Bulk density.

For Hausner’s ratio, this was calculated as the ratio of the tapped density to the bulk density of the powder samples i.e. tapped density/bulk density

**Angle of repose**

The angle of repose was measured using the fixed funnel and free-standing cone method [9]. The tangent of the angle of the powder heap was calculated from the equation

\[ \tan \theta = \frac{2h}{D} \]  

Where \( D \) and \( D \) are the bulk and true densities respectively

**Moisture sorption profiles**

Specifically 2g of the powder sample was accurately weighed and evenly distributed over the surface of a 70 mm petri dish. The samples were then placed in a large desiccator containing distilled water in its reservoir (100%) at room temperature and the weight gained by the exposed samples over a seven-day period was recorded and amount of water absorbed calculated from the weight difference [10].

**Loss on drying**

A 5g quantity of the powder sample was transferred each to a petri dish and then dried in an oven at 105 °C until a constant weight was obtained. The percentage (%i) moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as percentage [11]

\[ LOD = \frac{w_i-w_f}{w_i} \times 100 \]  

Where \( LOD \) = Loss on drying, \( Wi \) is the initial weight of the sample and \( Wf \) is the final weight.

**Swelling index**

The swelling index of the powder was carried out is described as follows: A quantity (1g) of the powder sample was placed in 15 ml calibrated centrifuge tubes and the volume occupied was noted as \( V_1 \). Specifically 10 ml of distilled water was added and stoppered. The contents were mixed on a vortex mixer (XH-Stuart, UK) for 2 min. The mixture was allowed to stand for 10 min and centrifuged immediately at 1000 revolutions per minute (rpm) for 10 min on a bench top centrifuge (Model 80-2). The supernatant was carefully decanted and the volume of sediment recorded as \( V_2 \) [10]. The swelling index was computed using equation 6 below;

\[ S = \frac{V_2-V_1}{V_1} \times 100 \]  

Where \( S \) is the swelling capacity, \( V_1 \) is the volume of the hydrated powder, and \( V_2 \) is the volume of powder before hydration.

**Hydration capacity**

The method for determination of the hydration capacity was patterned after that used by Kornblum and Stoopak and described by Owohaanworhua [5]. It was carried out during the same time the swelling capacity was done but instead of the volume of sediment, the weight was determined. The hydration capacity was calculated as the ratio of the weight of sediment to the dry sample weight as shown in the equation below:

\[ HC = \frac{W_i-W_f}{W_i} \times 100 \]  

Where \( HC \) is the Hydration capacity, \( W_i \) is the sediment weight and \( W_f \), the sample weight.

**Fourier-transform infrared spectra**

The surface of the starch (*Discorea alata*) sample was characterized using Perkin Elmer spectrum 100 Fourier transform Infrared spectrophotometer. Each starch sample was scanned at a wavelength of between 4000 cm\(^{-1}\) and 400 cm\(^{-1}\). The diclofenac sodium powder was equally scanned using the same device. An admixture of the each starch sample with diclofenac sodium powder was prepared and equally scanned respectively.

**Compaction properties**

**Preparation and analysis of tablets**

Tablets weighing 400 mg each made up of diclofenac sodium and pregelatinized water yam starch was produced using a single punch Carver Hydraulic press (Model C, USA) at compression pressures from 0.25 to 1.25 tonnes corresponding to the compression pressures 27.3KPa–163.5KPa respectively. Fifteen tablets were compacted at each pressure and retention time being 30s. Prior to compression, the die and the flat-faced punches were lubricated with 1% magnesium stearate in acetone. The tablets were stored in air-tight container for
24 h (to allow for elastic recovery) before evaluation. Parameters of the tablets such as thickness (t), diameter (D), and weight uniformity of the tablets were determined. Also, the crushing strength (Cs) was ascertained using the Monsanto hardness tester (MHT-20, UK). The relative density D was calculated as the ratio of the density of the tablet to the true density of the starch samples, from which Heckel plots were carried out over a compression range of 136.2KPa and the parameters from Heckel plots calculated. The density of the tablet is a ratio of the weight of tablet to its volume. The area under the Heckel curve was calculated by the Trapezoidal method and used to express the extent of volume reduction that the material had undergone during the entire compression pressure range.

$$D = \frac{W}{VtDt} \quad (7)$$

Where Vt is the volume of the tablet in ml, and Dt is the true density, g/ml, of the starch powder.

The compaction potential of the powders was studied using the Heckel equation

$$ln\left(\frac{1}{D}\right) = K.P + A \quad \ldots \ldots \ldots \ldots \ldots \ldots (8)$$

D is the relative density of the compact with reference to the material being compacted, P is the applied pressure, and K (the slope of the straight line portion) is the reciprocal of the yield pressure, Py, of the starch material. The yield pressure is inversely related to the ability of the material to deform plastically under pressure and A is a function of the material undergone during the entire compression pressure range.

$$D_0 = 1 - e^{-A} \quad \ldots \ldots \ldots \ldots \ldots \ldots (9)$$

The relative density becomes D0 when the applied pressure is equal to zero (D0 = loose density/true density), is used for the description of initial particle rearrangement and densification due to die filling. A high value would indicate very dense packing.

### RESULTS

#### Table 1: Micromeritic properties of the starch powders

| Starch powders | Bulk density (g/l) | Tapped density (g/ml) | True density (g/ml) | Angle of repose(°) | Hausner’s ratio | Compressibility Index (%) | Porosity (%) |
|----------------|-------------------|----------------------|---------------------|-------------------|-----------------|--------------------------|-------------|
| CSA            | 0.42±0.01         | 0.67±0.05            | 1.67±0.09           | 25.20±0.10       | 1.59±0.1        | 37.12±3.12               | 75±2.90     |
| DSA            | 0.41±0.02         | 0.56±0.01            | 1.64±0.13           | 36.25±0.41       | 1.36±0.04       | 26.74±4.72               | 74±1.82     |
| CDSA           | 0.44±0.03         | 0.63±0.12            | 1.65±0.22           | 12.53±0.35       | 1.45±0.05       | 30.90±2.13               | 73±2.16     |

Key: CSA, Pregelatinized Corn Starch; DSA, Pregelatinized Water yam starch; CDSA, a mixture of pregelatinized corn starch and water yam starch. Values are presented as mean±standard deviation (SD). Where the number of the experiment (n) is 3.

#### Table 2: Physicochemical properties of the starch

| Starch powders | pH     | Moisture Content (%) | Viscosity (mPas) | Hydration capacity (%) | Swelling capacity (%) | Loss on drying (%) |
|----------------|--------|----------------------|------------------|------------------------|-----------------------|------------------|
| CSA            | 6.28±0.07 | 10±1.73              | 8.56±0.52        | 3.47±0.14              | 330±14                | 2.0±0.00         |
| DSA            | 5.64±0.38 | 10±1.00              | 6.28±0.22        | 3.04±0.15              | 210±14                | 2.0±0.01         |
| CDSA           | 6.13±0.69 | 10±1.73              | 7.18±0.45        | 3.27±0.23              | 250±14                | 2.0±0.01         |

Key: values are presented as mean±standard deviation and number of the experiment (n) is 3.

#### Table 3: Composition of the diclofenac compact

| Ingredients* | F1 | F2 | F3 | F4(control) |
|--------------|----|----|----|-------------|
| Diclofenac   | 200| -  | 200| 200         |
| DSA          | -  | 136| -  | -           |
| CSA          | -  | 136| -  | -           |
| CDSA         | -  | -  | 136| -           |
| MCC          | 64 | 64 | 64 | 200         |
| Total weight (mg) | 400| 400| 400| 400         |

*Lubricant used was magnesium stearate in 1% acetone during compression.
Fig. 2: Heckel plots of compacts of the different powder samples

Table 4: Values from heckel plot

| Batch code | $R^2$ | AUHC(Kpas) | K   | A    | Py(KPas) |
|------------|-------|------------|-----|------|----------|
| F1         | 0.9498| 238.025    | 0.8959 | 0.4123 | 1.1162   |
| F2         | 0.999 | 166.775    | 0.3603 | 0.6315 | 2.7755   |
| F3         | 0.3557| 129.55     | 0.0912 | 0.8472 | 10.965   |
| F4         | 0.75  | 188.75     | 0.3332 | 0.7421 | 3.0012   |

Key: linearity of the curve was taken at 3 points between 25 and 80KPas of the compaction pressure

Fig. 3: Plot showing binding efficiency of compacts at different compaction pressures, three tablets were randomly selected and used for the determination for each batch at the respective pressure
Fig. 4: Tensile strength–compressional pressure relationship, 3 tablets were used for the determination at the respective pressures.

Fig. 5: Sorption profile of pregelatinized Starches, a sample size of 2g each was used and experiment done in triplicate for each sample.

Fig. 6: FTIR for pregelatinized Discorea alata (DSA)
Fig. 7: FTIR for pregelatinized corn starch (CSA)

Fig. 8: FTIR for admixed pregelatinized starches (CDSA)

Fig. 9: FTIR for pure Diclofenac sodium
Fig. 10: FTIR for Discorea pregelatinized *Discorea alata*+Diclofenac

Fig. 11: FTIR for pregelatinized corn starch (CSA)+diclofenac

Fig. 12: FTIR for admixed pregelatinized starches (CDSA) and diclofenac
so distant from unity

Table 5: Main peaks observable in the FTIR spectra of the modified starches and diclofenac

| S. No. | Wave numbers (cm⁻¹) | Possible functional groups present |
|--------|---------------------|----------------------------------|
| 1      | 3426-3457 broad smooth | -OH of the starches |
| 2      | 2928 Sharp peaks | CH2-CH2 |
| 3      | 1692 | C=O stretch of an aldehyde group in the starches |
| 4      | 3452 peak | -OH of Carboxylic group |
| 5      | 757, 680 peaks | -Cl atoms of diclofenac |
| 6      | 1562, 1505 | C=C stretch in aniline of diclofenac |

DISCUSSION

The ease and proper filling of the die cavity of the tabletting machine during direct compression is related to the flow property of the powdered material [12]. Powders with Hausner’s ratio (HR) of value<1.2 show good flow. Those with values in the range 1.25-1.5 require the use of glidants to improve the flow while those with values>1.5 as seen in powders with flakes indicate poor flow. Values of Carr’s index of range 1-10% indicate powders with the excellent flow; 11-15% describes a good flow and higher values such as 16-20% means flow that is fair while powders with extremely poor flow have greater than 40% Carr’s index [9]. The indirect indicators of flowability (angle of repose, Carr’s index and Hausner’s ratio) from table 2 show the powders have poor flow with the pregelatinized corn starch exhibiting lowest values. Hausner’s ratios for all the powders were greater than 1.25 and the values for Carr’s index are higher than 20% which reflect poor flowability. The order is as follows DSA>CDSA>CSA. Admixed powder (CDSA) showed only slightly improved flow over the pregelatinized corn starch (CSA). One possible reason for this observation could be that the particles of the DSA are well interspersed between those of the CSA thus enhancing the flow property slightly.

The FTIR was employed for determining the compatibility of the pregelatinized starches with the diclofenac sodium powder as well as the functional groups present in the pregelatinized starches. The broad smooth intense peak found at 3426 cm⁻¹ (for water yam) and 3452 cm⁻¹ (for corn starch) are attributable to the diagnostic-OH groups whereas the sharp peaks attached laterally to the OH peaks found at 2928 cm⁻¹ for both spectra characteristic for water yam and cornstarch represents the C=H-CH2 chains of the starch [13, 14]. Peak seen at 1692 cm⁻¹ on all the pregelatinized starch spectra is attributable to C=O stretch of an aldehyde. It is no surprise as starches are aldehyde compounds. The functional groups present in the pregelatinized starch are similar to that in the native starch as reported in literature[1]. It could be inferred then that pregelatinization did not introduce any new functional group nor knock off any pre-existing one, hence it is not a chemical modification method but only affected the rearrangement of the powder particle. The key peaks of the pure diclofenac reveal the presence of-CH₂ group of the carboxylic functional group (3452 cm⁻¹ peak), the-Cl groups (757 cm⁻¹, 680 cm⁻¹) and the aromatic C=C stretch in the aniline rings (1562 cm⁻¹,1505 cm⁻¹) present [14]. The admixed diclofenac sodium powder with the respective starches did not shift or cancel out the prominent diagnostic peaks of the starches or that of the diclofenac. This implies that the pregelatinized starch was compatible with the diclofenac.

The Heckel plot (fig. 2) graphically represents how the powders behave in the presence of compressional force applied to form compact. It is developed on the assumption that powder consolidation of the molecules of F₂ and F₃ is faster than that of F₁. This is explained by the sharp peaks attached laterally to the OH peaks as the functional groups present in the pregelatinized starches. The functional groups (1562 cm⁻¹,1505 cm⁻¹) present [14]. The admixed powder (CDSA) showed only slightly improved flow over the pregelatinized corn starch (CSA). One possible reason for this observation could be that the particles of the DSA are well interspersed between those of the CSA thus enhancing the flow property slightly.

As shown in fig. 4, the increase in compression pressure, the greater the tensile strength for all the four compacts. F₁ measured similarly as F₂ and F₃ at the same compression pressure. From compressional force of 0-100KPas, F₁ showed the highest tensile strength but F₃ was lowest. Above the 100KPas where the F₁ became the lowest and tensile strength for F₃ became highest at increased compression pressure. How compacted a tablet is has been linked to the amount of loading pressure which brings about close proximity of the particles being tableted so that they are held together by cold welding or fusion bonding [20]. Generally higher tensile strength reflects strong interparticulate bond formation, harder compacts and is proportional to the compression force [9]. Thus to form harder tablets of F₃, compression pressure will be optimized at above 100KPas.

Although having the same moisture content and loss on drying, the different pre-gelatinized starches possess separate interactions with water molecules as revealed by the viscosity, hydration capacity and the swelling index. Similar moisture content implies that the class of drugs that pregelatinized corn starch (CSA) has been used for as a pharmaceutical aid can also be used with pregelatinized water yam starch (DSA) with no fears of consequent incompatibility occurring from drug-excipient interaction possibly due to hydrolysis. CSA has the highest interaction with water whereas DSA possess the lowest. As expected, an admixture of the two gave an intermediary value. High moisture content is no far distant from that reported in literature that pregelatinized starch undergoes starch granule de-
structuralisation’ which in turn allows for good water penetration and retention [5]. That a tablet will readily disintegrate could be seen in its index of swelling. The physicochemical properties of hydration capacity and swelling capacity are inter-related and are good indicators reflecting the swelling of the tablets and thus its subsequent ease of disintegration [21]. Each of those indicators describes the different relationships of water molecules with the pharmaceutical aid. For example the swelling index reflects the increase in volume of sample, after water absorption, while the hydration capacity is the amount of water molecule that can be absorbed and held in the excipient after exposure to water. Table 3 shows that for the powders, the swelling index and the hydration capacities follow the same trend, CSA having the highest value while CDSA had improved properties. Such modification mainly could be due to ‘proximal intermolecular association’ of particles of the different powders. It goes with reason that such association ‘opens up’ the molecules of DSA for improved water penetration; a good property looked for in disintegrants.

However, it is noteworthy that although all powders had a same moisture content, moisture sorption profile reveals that the CSA possessed higher sensitivity to atmospheric moisture over the DSA and its admixture (fig. 5). Unlike the relative improvement of the admixed powders in other moisture-related indicators, (swelling index and hydration capacities), the ‘proximal interparticle association’ reduced the effective surface area of the CSA thereby reducing its effective attraction of water moisture. Higher moisture content in a pharmaceutical powder can influence its flow properties, containers for storage and affect negatively any incorporated drug that can hydrolyse in the presence of moisture.

CONCLUSION

Pregelatinized water yam starch would be a good pharmaceutical excipient as a binder/filler for immediate release or delayed tablet just like the standard is known as cornstarch and microcrystalline cellulose. However physical admixture of the two improved the physicochemical and compaction properties of the former and would provide an alternative to employing only corn starch as a pharmaceutical aid. For example the swelling index reflects the increase in volume of sample, after water absorption, while the hydration capacity is the amount of water molecule that can be absorbed and held in the excipient after exposure to water. Table 3 shows that for the powders, the swelling index and the hydration capacities follow the same trend, CSA having the highest value while CDSA had improved properties. Such modification mainly could be due to ‘proximal intermolecular association’ of particles of the different powders. It goes with reason that such association ‘opens up’ the molecules of DSA for improved water penetration; a good property looked for in disintegrants.

CONFLICT OF INTERESTS

We declare no conflict of interests

AUTHORS CONTRIBUTIONS

Timma O and Jacob G designed the work, collected assembled the data. Daniel E wrote the manuscript and analysed the data. All the authors critically revised and approved the final manuscript.

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