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STUDIES ON A HYDROPHILIC CELLULOSE MATRIX DERIVED FROM *IPOMOEA BATATAS* TUBERS I: PROCESSING AND PHYSICOCHEMICAL PROPERTIES

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ABSTRACT

This work was designed to develop a hydrophilic cellulose matrix from the fibre contained in the tubers of *Ipomoea batatas* and to evaluate its excipient functionality. Starch was filtered from the slurry of milled tubers to obtain the fibre which was dried at 60 ^{o} C and pulverised. A 500 g of fibre was submerged in 3.50 % w/v of sodium hypochlorite and blended for 10 min. This was washed with distilled water to a neutral pH, then slurried in 96 % ethanol for 5 min, dried at 60 ^{o} C and reduced to 250 µm. The product was coded as *I-hydrocel*. Its organoleptic, pH, densities, flows, elemental content, moisture studies, differential scanning calorimetry (DSC), scanning electron microscopy (SEM) and ash properties were evaluated. *I-hydrocel* was a tasteless, off-white, smooth, odourless powder, mean particle size, 10.65 ± 4.27 µm and insoluble in organic solvents but disperses and swells in water yielding a pH of 6.45± 0.12. Swelling, hydration and moisture adsorption capacities were high. Heavy metals like mercury, lead or vanadium was not detectable. The ash contents and extractives were within standard limits. Powder flow was fair and DSC thermogram shows a melting range of 80-85 ^{o} C. The SEM micrograph suggests a cellulosic morphology. Its ability to swell and hydrate fast in water indicates that it is a hydrophilic cellulose matrix that could serve as an alternative filler-disintegrant in solid dosage drug delivery.

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INTRODUCTION

There has been a tremendous growth in the development of newer excipients needed for drug formulations in the pharmaceutical industries. The increase is inevitable due to the growing need for more complex excipients and/or new uses for conventional ones. The need has further escalated due to the following reasons. There is need to ease the development of novel drug delivery systems and biotechnology-derived drugs. Up to 40 % of available drugs in current use fall into the low solubility category. This trend is seen increasing close to 80 % and for this reason, the market demand may be tending towards novel excipients that would enhance drug solubility. In trying to create new excipients that would solve the problem of poor drug solubility, other needs that cause the need for newer excipients are the growth in the demand for new excipients in drug manufacturing techniques, high-tech progress in drug delivery systems and the appearance of state-of-the-art drugs for the management or mitigation of lingering diseases [1-3]. Pharmaceutical excipients are substances that are used alongside the pharmacologically active drug commonly known as the active pharmaceutical ingredient (API). This inclusion is necessary to ease the administration of medicinal products to the target patient population(s) through the intended route, to enhance dosing compliance by the patient, maintain consistency and control of drug bioavailability as well as obtain a better-quality API stability such as safeguarding it from degradation, etc. Thousands of different excipients are used in medicines and on the average, constitute about 90% of each product [4, 5].

Most pharmaceutical excipients are sourced naturally, basically, plant-based. They may be processed either chemically or by other means. Some of the excipients obtained naturally include starch, guar gum, gelatin, pectin, acacia, tragacanth, cellulose, etc. They are useful in the firms that produce medicinal products binding or granulating agents, disintegrants, sustained drug release agents, etc. [6]. The gains in their application are as follows: low cost, fairly free from side effects, biocompatible, of a renewable source, environmental friendliness in processing, locally available, etc. [7]. The specific application of natural polysaccharide polymers in pharmaceutical formulations include to aid in the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety, effectiveness or delivery of the drug during storage or use [8].

Some excipients can be synthesized chemically or semi-synthetically or by co-processing of existing excipients. Such excipients include microcrystalline cellulose, sodium starch glycolate, croscarmellose sodium, polyvinyl pyrrolidone (PVP), hydroxypropylmethylcellulose (HPMC)), etc. [5, 9]. Irrespective of the source of excipient, they are classified based on their role in the drug formulation, their interactions and influence on drug delivery as well as their chemical or physicochemical characteristics [10].

Since most of the excipients are plant based [7], the agro-biomass is composed mainly of cellulose, hemicellulose and lignin. Cellulose is the most abundant polysaccharide on earth and is a highly ordered polymer of cellobiose. Renewable resource based biopolymers like starch and other biodegradable polymeric products account for up to 85% of the total production capacity. The lesser percent constitute the synthetic biopolymers [11].

Cellulose is an organic compound that is found in the cell wall of plants, some bacteria, and algae which combine with lignin to provide the mechanical strength for the cell wall of plants. It is found in several parts of many plants within our environment such as stem and bark of trees, leaves, fibrous roots, tubers, etc. Cotton linters and fast growing plants are reported to be the highest sources of cellulose. Several pharmaceutical excipients with multiple applications such as microcrystalline cellulose, methylcellulose, carboxymethylcellulose, hydroxypropyl cellulose, etc. have been derived from cellulose.

Ipomoea batatas, of the family, Convolvulaceae, is an important arable vegetable and food crop cultivated in the tropics, subtropics and warm temperate areas of the world because of its edible tubers that have an abundance of starch, cellulose, etc. Among the tuber crops that thrive in the hot climate, sweet potato comes after cassava [12]. It is now cultivated in 117 countries in all the tropical and sub-tropical regions of the world and it ranks fifth among the most staple food crops in over 50 countries with Asia being the world's major producing region, with about 107 million tonnes of annual production, followed by Africa and the Americas, with approximately 15 and 30 million tonnes respectively [13]. About 80-90 % dry matter of the sweet potato constitute carbohydrates and are mainly starch, cellulose, hemicellulose, sugars and pectin. These make up the dietary fibre fraction of the sweet potato roots [14, 15].

The purpose of this work is to derive a hydrophilic cellulose matrix from the fibre contained in the tubers of *Ipomoea batatas* and to evaluate its physicochemical properties as a pharmaceutical excipient.

EXPERIMENTAL

Materials

The following materials were used as procured and include sodium hypochlorite (3.5%) (Multipro, Nigeria), gelatin (Fisher, USA), corn starch, magnesium stearate (BDH, England), lactose (Surechem UK), n-hexane (JHD, China), hydrochloric acid (Loba Chemie, India), Paracetamol (Cipla, India).

Methods

A sample of *Ipomoea batatas* tubers which were obtained from the oil mill market, Elelenwo, Port Harcourt, Nigeria was identified in the University of Port Harcourt herbarium and deposited with a specimen voucher no: UPH/V/1263.

Processing of sample

The method developed by Ugoeze *et al* in the production of a novel hydrophilic biopolymer from *Ipomoea batatas* tubers was partially adopted [16]. The tubers of the *Ipomoea batatas* were washed, sliced and milled. The starch was separated to obtain the fibre which was washed further, dried at 60 ^{o}C and pulverised. A 500 g of this was plunged in an abundant amount of a 3.50 % w/v of sodium hypochlorite and blended for 10 min. The blend was washed with distilled water to arrive at a neutral pH. It was got rid of water and then flooded with enough of 96 % ethanol and stirred for 5 min, drained and dried at 60 ^{o}C. The dry material was classified with a 250 µm stainless sieve (Retch, Germany) and the hydrophilic cellulose matrix obtained was coded as the *I-hydrocel*.

Evaluation of some properties of *I-hydrocel*

Solubility and organoleptic properties

The solubility and the organoleptic properties were verified.

Determination of the ash and extractive values

The parameters that were evaluated included the total ash, acid insoluble ash, water soluble ash, ethanol and water extractive values using the USP (2017) [17] and The WHO (1998) quality control methods for herbal materials [18].

Determination of pH

A 2 % w/v aqueous dispersion of the *I-hydrocel* was prepared and its pH was checked using a pH meter (Corning, model 10, England).

Hydration capacity

To determine this parameter, 1g of *I-hydrocel*, designated as *y* was placed in a 15 ml plastic centrifuge tube and submerged with 10 ml of water and shaking the tubes occasionally for 2 h and left to stand for 30 min. It was centrifuged for 10 min at 3000 rpm and the resulting supernatant was poured out. The new weight of the sample, *x*, due to the uptake of water was noted [19]. The test was repeated three times. The hydration capacity was calculated using the equation below.

$$Hydration\ capacity = x/y \quad \text{..... (1)}$$

where: *x* is the weight of the moist sample after centrifugation and *y* is the weight of the dry sample of *I-hydrocel*.

Swelling index

A 5 g of *I-hydrocel* introduced into a glass measuring cylinder was tapped and its volume, *Vx* was noted. It was then dispersed in 85ml of water and made up to 100 ml with water. This was left for 24 h and the volume of the sediment, *Vv* was recorded [20]. This was carried out in triplicate and the swelling index was calculated as follows:

$$Swelling\ index = Vv/Vx \quad \text{..... (2)}$$

where *Vv* is the volume of sediment and *Vx* is the tapped volume occupied by 5 g of *I-hydrocel*.

Elemental analysis

This was carried out using an Atomic Absorption Spectrophotometer (AAS), Model AA-7000, ROM version 1.01, S/N A30664700709 (Shimadzu, Japan).

Moisture content (loss on drying, LOD)

A digital moisture balance (Citizen, MB-50, China) was used. A 2 g of *I-hydrocel* was placed in the equipment and operated at 105 ^{o}C. The equipment automatically switches off when an optimal moisture contained in the sample was up taken by heat. The equipment automatically displays digitally the value of the moisture content in percent.

Moisture sorption capacity

To establish the moisture sorption ability of *I-hydrocel*, 1.0 g of it was stored in respective air-tight desiccators containing saturated aqueous solution of potassium sulphate, potassium chloride, sodium chloride and magnesium nitrate for 7 days at an ambient temperature of about 30 ^{o}C to sustain a relative humidity of 96, 84, 75 and 52 % respectively [21]. The rise in weight of the sample was calculated as percentage moisture gain as follows:

$$\%\ Moisture\ gain = (Moisture\ gain)/(Original\ weight)) x\ 100 \quad \text{..... (3)}$$

Differential Scanning Calorimetry (DSC) of *I-hydrocel*

The DSC was carried out using a DSC equipment (Mettler Toledo; Model DSC 822, USA).

Scanning Electron Microscopy (SEM)

The SEM of the *I-hydrocel* was carried using a scanning electron microscope, (Phenom Prox, Phenom-World, Netherlands).

Evaluation of the bulk, tapped and particle densities

The bulk and tapped density of 15.0 g of *I-hydrocel* were determined using Stampfvolumeter (STAV 2003JEF, Germany). The particle density was established by the displacement method with a 25 ml pycnometer using *n*-hexane as a non-solvent [22]. The weight of the pycnometer (w) was determined. It was filled with *n*-hexane and reweighed (w_1). The weight of *n*-hexane (w_2) was obtained by subtracting w from w_1. A 0.5 g (w_3) of *I-hydrocel* was introduced into the pycnometer containing *n*-hexane and weighed (w_4). The respective densities were calculated from the following equations after triplicate determinations of each parameter:

$$\text{Bulk density} = \text{Weight of Powder}/\text{Bulk volume of powder} \quad \text{..... ..(4)}$$

$$\text{Tapped Density} = \text{Weight of Powder}/\text{Tapped volume of powder} \quad \text{..... (5)}$$

$$\text{Particle Density}, \ \rho t = w2 \times w3/v(w3 - w4 + w2 + w) \quad \text{..... (6)}$$

where: v is the volume of pycnometer, 25 ml.

Study of the flow properties of *I-hydrocel* powder

The flow rate was studied using the funnel method [23]. The time for the complete out flow of 15.0 g of the sample placed in the funnel was recorded. To study the angle of repose, 50 g of it was poured into a tubular paper cylinder kept on to a flat base of known diameter and is the same as the internal diameter of the cylinder. The tubular paper cylinder was slowly pulled vertically so as to discharge the powder which formed a cone of powder on the base. The height of the cone was estimated. This is a modification of the method of Jones and Pilpel [24]. The angle of repose, θ was calculated after three replicate determinations from the equation:

$$\theta = \tan^{-1}\frac{2h}{d} \quad \text{..... (7)}$$

where h = the height of the heap, d = base diameter of the heap.

Other derived properties of the *I-hydrocel* were calculated from the following equations below:

Hausner's ratio (HR) [25] was calculated:

$$HR = \text{Tapped density}/\text{Bulk density} \quad \text{..... (8)}$$

Compressibility Index (CI) [26] was calculated from the formula:

$$CI = (1 - HR) \times 100 \quad \text{..... (9)}$$

Porosity (ρ) was calculated from the expression:

$$\rho = \left(1 - \frac{\text{Bulk density}}{\text{Tapped density}}\right) \times 100 \quad \text{..... (10).}$$

Particle size determination

The sample was mounted on the slide using a 10 % v/v glycerol. The micromeritic analysis was carried out on a biological binocular microscope (Model XSZ-107BN, Zenithlabo, USA) using a Phenix Micro Image Analysis Software (PHMIAS 2006 Ver. 2.0).

Statistical analysis

All statistical analysis of data was carried out using the IBM SPSS Statistics 20 software.

RESULTS AND DISCUSSION

Table 1 shows some of the physicochemical properties of *I-hydrocel* that were investigated. The material of *I-hydrocel* was an off-white smooth, odourless, non-irritating, non-pungent and tasteless powder with a pH of 6.45 ± 0.12, particle size range (4.70 – 10.65 – 20.30) µm and a mean particle size of 10.65 ± 4.27 µm (Fig.1). Its processing yield was 60.50% and it was insoluble in organic solvents but disperses and swells quickly in water. Such heavy metals as mercury, lead or vanadium (Table 2) was not detectable. When excipient of the herbal source is processed, consideration for its ash values is very important to aid in the evaluation of the degree of handling to guarantee its quality and purity. To this concern, total ash, acid insoluble and water soluble ashes are regarded as the ash remaining after its combustion at various stages. They become substantial parameters for the quantitative assessment of processed herbal substances. The total ash may include carbonates, phosphates, silicates, silica, etc. A high value of this shows possible adulteration and implies that the sample was not properly processed. Acid insoluble ash portrays the level of such substances as silica, earth or sand while water soluble ash represents an aspect of the total ash that is soluble in water. It shows the water soluble salts existing in the sample [18, 27-28]. However, the total, acid- insoluble and water-soluble ashes and the extractives of water and ethanol obtained for *I-hydrocel* were lower than the standard limits [18, 29] and shows that it *was* well processed.

The results of the flow parameters such as flow rate, the angle of repose, Carr's index and the Hausner's ratio as well as the bulk and tapped densities and porosity does not indicate good flowability and compressibility for *I-hydrocel* [25, 26, 30]. However, it is promising as a hydrophilic cellulosic matrix considering its high swelling index and hydration capacity which could be confirmed from the moisture content and increasing moisture adsorption with increasing relative humidity (Table 3). This trend of hydrophilicity presents it as a good material for possible use as a disintegrant in solid dosage forms drug deliveries. The DSC thermogram for *I-hydrocel* shows a melting range of 80 - 85 ^{o}C (Fig. 2). The SEM micrograph of *I-hydrocel* portrays cellulosic morphology (Fig. 3).

Table 1: Physicochemical properties of *I-hydrocel.*

Parameters	Value
Colour	Off-white
Odour	Odourless, non-irritating, non-pungent
Texture	Smooth
Taste	Tasteless
Yield (%)	60.50
pH of 2% w/v	6.45 ± 0.12
Mean particle size (µm)	10.65 ± 4.27
Solubility	Insoluble in water and most organic solvents
Total ash (%)	2.30±0.10
Water soluble ash (%)	0.10±0.10
Acid insoluble ash (%)	0.50±0.10
Sulphated ash (%)	2.35±0.10
Ethanol extractive yield (%)	0.50±0.10
Water extractive yield (%)	4.89±0.10
Flow rate (g/s)	No free flow
Angle of repose (deg.)	34.66±0.03
Bulk density (g/ml)	0.45±0.02
Tapped density (g/ml)	0.67±0.08
True density (g/ml)	1.47±0.08
Porosity (%)	32.84±0.09
Hausner's ratio	1.11±0.01
Carr's Index (%)	15.42±0.72
Moisture content (LOD) %	9.73±0.12
Swelling index (%)	242.00±0.14
Hydration capacity (%)	165.00±0.04

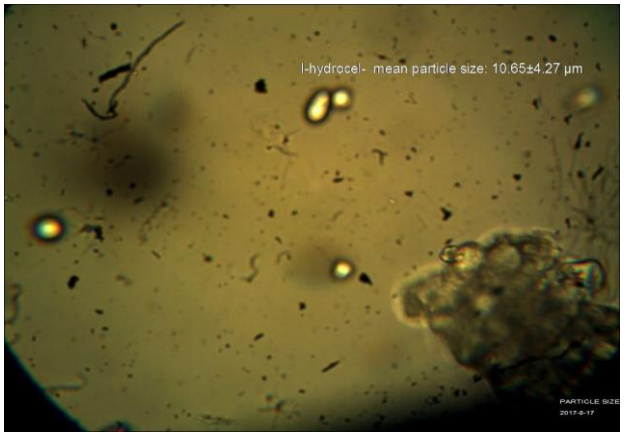

Fig. 1: Photomicrograph of I-hydrocel particle.

Table 2: Result of elemental analysis for *I-hydrocel.*

Metal	Value (%)
Mercury (Hg)	BDL
Zinc (Zn)	7.79×10^{-6}
Manganese (Mn)	9.72×10^{-6}
Potassium (K)	1.34×10^{-3}
Iron (Fe)	1.47×10^{-4}
Arsenic (As)	9.03×10^{-5}
Calcium (Ca)	20.00
Sodium (Na)	6.55×10^{-4}
Copper (Cu)	1.62×10^{-5}
Lead (Pb)	BDL
Nickel (Ni)	4.10×10^{-5}
Vanadium (V)	BDL

BDL = below detectable limit.

Table 3: Moisture adsorption capacity of *I-hydrocel.*

Relative Humidity (%)	Moisture adsorption (%)
52	12.37±0.01
75	13.46±0.01
84	14.55±0.001
96	15.31±0.001

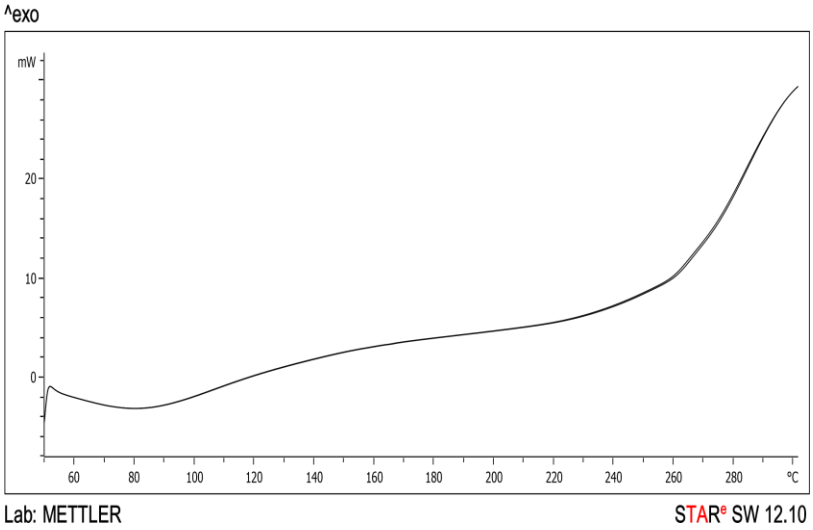

Fig. 2: DSC thermogram of *I-hydrocel.*

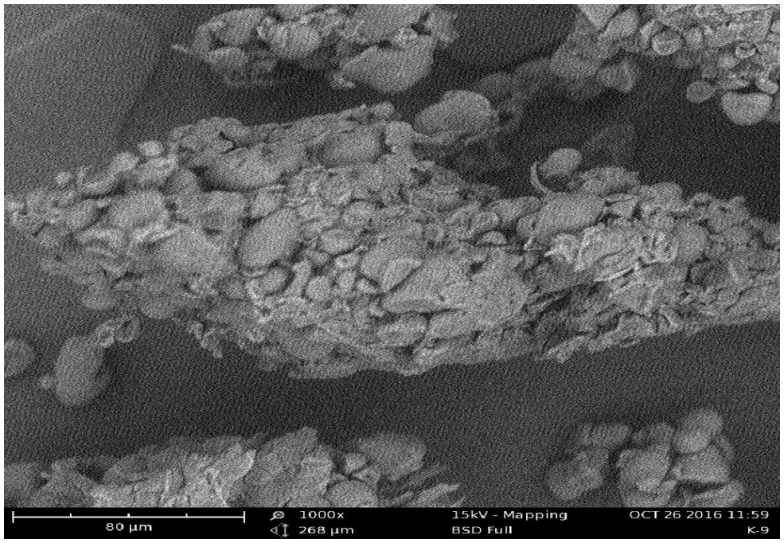

Fig. 3: SEM micrograph of *I-hydrocel.*

CONCLUSION

The ability of *I-hydrocel* to swell and hydrate fast in water indicates that it is a hydrophilic cellulose matrix that could serve as an alternative filler-disintegrant in solid dosage drug deliveries.

Conflict of interest

We, the authors, declare that there is no conflict of interest regarding this research and its publication.

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