Cellulose nanocrystals and nanofibrils obtained from corn straw by hydrolytic action of four acids: particulate, powder and tablet properties

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ABSTRACT

Nanocellulose derived by the hydrolysis of alpha cellulose of corn straw using different acids has been examined. Its particulate and structural characteristics including morphology (SEM), thermal behavior (DSC) and crystallinity (XRD) showed dependence on the acid type. Packing and flow properties showed similar dependence, while hydration and swelling capacities exhibited direct and inverse correlation to packing characteristics, respectively. Tablet characteristics were satisfactory at the compression force used. Hence, the nanocellulose powder obtained using any of the acid types is a potential pharmaceutical excipient.

Keywords: Cellulose. Nanocrystals. Nanofibrils. Nanocellulose. Agricultural residue. Tablet. Corn straw

1. INTRODUCTION

Cellulose is the major constituent of the cell wall of most plants and therefore provides the backbone structure of plant materials. It is perhaps the most abundant and one of the most useful phytochemical compounds on earth. It makes up about 10 percent of the dry weight of leaves, about 50 percent of the woody structures of plants and over 90 percent of cotton fibres (Hon and Shiraishi, 2001). It is tasteless and is a non-reducing carbohydrate. About 85% of cellulose from wood pulp is insoluble in 17.5% sodium hydroxide solution. This is arbitrarily designated as alpha cellulose and is the material that is commonly used in preparing regenerated cellulose and various cellulose derivatives (Nitz, 1995).

While the research on cellulose and its derivatives have gone on for close to two centuries, nanocellulose (NC) which are products of acid hydrolysis, and enzymatic hydrolysis have only recently gained attention because of their ability to take various forms, such as gels

and films, and for the range of their potential applications, which include drug delivery, electronics and tissue engineering, to mention but a few. They possess unique quintessential physical and chemical properties, such as biocompatibility, biodegradability, non-toxic, and lightweight, and exhibit high strength and stiffness, as well as high strength-to-weight ratio. Additionally, they have low coefficient of thermal expansion, useful optical properties, and are thermally stable, as well as being inherently renewable and sustainable (Chemical & Eng News, 2014).

Nanocellulose presents commonly as two forms, namely, nanocrystals and nanofibrils that are chemically similar, but show somewhat different physical properties. Nanocrystals are needle-like in shape, depending on the source, have diameters in the 5- to 10-nmrange and lengths on the order of 100 to 200 nm. On the other hand, nanofibrils have roughly 5-nm diameters and are spaghetti-like since they are longer, flexible and easily entangled (Chemical & Eng. News, 2014). NC are multifunctional nanomaterials in that they find applications in various industries, including pharmaceutical industry where they have been reported as drug carriers in form of microspheres, microparticles, hydrogels and membrane films – either as single material or as a mixture with other polymers of interest**.** Lin et al. (2014) reported that microspheres fabricated from cellulose nanocrystals and sodium alginate controlled the release of drug from the system.

Cellulose nanocrystals have been shown to function as co-stabilizer in emulsion polymerization – proving to be a suitable excipient (Villariova et al., 2011). Kolakovic et al. (2011) evaluated the usability of spray-dried nanofibers in a tablet formulation and reported that cellulose nanofibers exhibited better packing properties compared to two grades of commercially available microcrystalline cellulose. Additionally, Emara et al. (2016) found nanocrystalline cellulose to improve the solubility and dissolution of Meloxicam, a poorly water-soluble drug, in a solid dispersion preparation, in comparison to microcrystalline cellulose.

Corn (*Zea mays*), an annual plant of the grass family (Gramineae) and believed to have originated in tropical South America, is considered the most important cereal in the Western Hemisphere. It is the largest of the cereals, reaching 3 to 15 feet (1 to 4.5 meters) or more in height. The plant has a solid, jointed stalk or stem and large but narrow, wavy-margined leaves (The Encyclopedia Americana, 2002).

In previous investigations, alpha- and microcrystalline- cellulose, have been obtained from corn straw, as well as degrained corncob (Okhamafe*et al*., 1995; Audu-Peter *et al*., 2004) and they function as disintegrants, diluents and dry binders in tablet formulations. Stalks of some species in the family of Gramineae like wheat *(Triticum spp)*, guinea corn (*Sorghum bicolour),* and sugar cane *(Saccharum officinarum),* have been reported in the literature as sources of cellulose and or its modified form, MCC, (Okhamafe *et al*., 1995; Alfa *et al*., 1999;Sun *et al*., 2004, 2005; Ohwoavworhua and Adelakun, 2010). Work on corn straw/stalk, which exists as a huge waste after harvesting of the corncobs as a source of nanocellulose has not been reported in literature to the best of our knowledge. Thus, in this work, we report the preparation of nanocellulose from the straw of corn by the hydrolytic actions of four different acids, and examined the particulate-, powder- and tablet properties.

2. EXPERIMENTAL

Preparation of alpha cellulose

The method reported previously (Ohwoavworhua and Adelakun, 2010) was used to obtain the α-cellulose. Briefly, a 300 g pulverized corn straw residue was treated with 2% w/v sodium hydroxide (4 L) at 80 ^{0}C for 3 h – to effect the delignification of the lignocellulosic material. The marc was washed and filtered. This was followed by bleaching step using a 1:1 aqueous dilution of sodium hypochlorite at 100 ^{o}C for 30 min. The material having been freed of lignin was washed, filtered and treated with 17.5 % w/v sodium hydroxide at 80 ^{o}C for 60 minutes. To achieve whitening, the resulting α-cellulose was treated with a 1:1 aqueous dilution of sodium hypochlorite at 80 ^{o}C for 5 min. The α-cellulose was washed, and when the filtrate tested neutral to litmus paper, it was pressed and manually reduced to small lumps and dried in a fluidized bed dryer (Copley), at 60 ^{o}C for 60 min.

Preparation of nanocellulose

This was carried out by hydrolyzing α-cellulose, at boiling temperature, in the selected acid for 30 min. A concentration of 2.5 N of the acids were used. (The acids include hydrochloric, sulfuric, phosphoric and acetic acids).At the end 30 min, the hot mixture of acid-cellulose was poured into excess water and allowed to stand overnight before filtration. The nanocellulose was then dried in a fluidized bed drier at 60 ^{o}C for 60 min. The particulate and powder characteristics of the nanocellulose are examined; also, using the nanocellose as filler-disintegrant tablets were prepared and the properties determined.

Determination of particulate and structural properties

Scanning electron microscopy (SEM)

Scanning electron micrograph of the nanocellulose powders were obtained using a Joel 6310 (Joel Instrument, Tokyo, Japan) system

running at 10 KeV. The samples were prepared by fixing the powders unto two-sided carbon adhesive tape and sputtered with platinum for 25 s using Agar sputter device (Agar Scientific Ltd., Stansted, UK) and the photomicrographs taken and used for morphological characterization and particle size estimation.

X-ray powder diffractometer (XRD) studies

Diffraction patterns were obtained using Phillips X-ray diffractometer. To record the diffraction patterns, Cu-Kα radiation at 40 kV and 25 Ma were used. The powder samples were compacted into pellets (2.50 cm in diameter) at a pressure of 50 MPa. The crystallinity index (CrI) of the samples calculated as in Eq. 1 (Segal et al., 1959):

$$CrI = [(I_{200} - I_{am})] / I_{200} \quad (1)$$

Where I_{002} being the intensity peak at about 2θ = 22° and I_{am} the intensity peak at about 2θ =16°.

Differential scanning calorimetry (DSC)

The DSC scans of the nanocellulose powder samples were acquired using a DSC 204 F1 (Netzsch Geratebau, GmbH, Selb, Germany). This instrument, a heat-influx DSC, was equipped with Netzsch Thermokinetic Analysis Software. The scan was done by heating the samples in a sealed aluminum pan, with the lid perforated, from 26 to 500 °C at a heating rate of 10 °C, under an inert nitrogen dynamic atmosphere (70 ml/min),with an empty pan as the reference. The parameters evaluated were: (a) temperatures of NC water loss (T_d), melting point (T_M) and (b) heats of melting (ΔH_{NC}).

Powder Properties

Moisture content

The moisture balance (Sartorius MA 100, UK) was used for this assessment. A 1.0 g of each of the samples was heated, at 105 °C, until constant weight, and the calculated weight loss equals the moisture content.

True density

This determination was carried out using xylene as the displacement liquid, and the value computed as in Eq. 2:

$$D_t = w/[(a + w)-b] \times SG \quad (2)$$

where *w* is the weight of powder, SG is the specific gravity of xylene, *a* is the weight of bottle + solvent and *b* is the weight of bottle + solvent + powder.

Bulk and tapped density

The Stampfvolumeter (Model STAV 2003 JEF, Germany) was used for these determinations. The powder sample (30g) was weighed into the measuring cylinder (250 mL) and the volume, V_o, occupied, without tapping, was recorded. After 500 taps, the volume, V_{500} was also noted. Bulk and tapped densities were computed from these volumes (V_0 and V_{500}), respectively using Eq. 3:

$$\text{Density} = \text{Weight}/\text{Volume} \quad (3)$$

Powder porosity

This was derived from the values of true and bulk densities when fitted into the equation:

$$e = 1 - \text{Density}_{bulk}/\text{Density}_{true} \times 100 \quad (4)$$

where *e* is the porosity.

Flow properties

The battery of tests described by Carr was performed to determine flowability indices for the NC powders (Carr, 1965a & b). These tests include, angle of repose, compressibility and Hausner ratio.

(a) Angle of repose: The static angle of repose, *a,* was measured using a long cylindrical tube open at both ends. The tube was placed on a graph paper and filled with nanocellulose powder. The tube was gradually lifted vertically away from the graph paper to form a cone. The height, *h*, and mean diameter, *D,* of the base of the cone were determined and the tangent of the angle of repose calculated using Eq. 5:

$$\text{Tan } a = 2h/D \quad (5)$$

(b) Compressibility: This was calculated as in Eq 6:

$$\% \text{ Compressibility} = [\text{Tap density} - \text{bulk density})/\text{Tap density}] \times 100\% \quad (6)$$

The values obtained for these 3 parameters were converted into index numbers using Carr's table (Baruah et al., 2000).

(c) Hausner ratio: This was computed using the formula in Eq. 7:

$$\text{Hausner ratio} = \text{Tap density}/\text{bulk density} \quad (7)$$

Hydration capacity

The method of Kornblum and Stoopak (1973) was used. A 1.5 g of nanocellulose powder was placed in each of four 15 ml glass centrifuge tubes and 10 mL distilled water was added and then stoppered. Using the vortex mixer (Vortex-Gennie Scientific Industry, USA) the content was mixed for 2 min. Using the Gallenkamp bench centrifuge (Gallenkamp, England) the mixture was centrifuged at 1500 rpm for 10 min, the supernatant decanted and the sediment weighed. The hydration capacity was computed as the ratio of the weight of the sediment to the dry sample weight.

Swelling capacity

This was determined concurrently as the hydration capacity and calculated as:

$$S = 100 \times (V_2 - V_1) / V_1 \quad (8)$$

Where S is swelling capacity (%), V_2 is the volume of the hydrated or swollen material and V_1 is the tapped volume of the material before hydration (Okhamafe and Azubuike, 1994).

Moisture sorption capacity

Each of the nanocellulose materials (2 g)was evenly distributed in a tarred *Petri* dish. The weight gained by the samples after 5 days of exposure at room temperature to relative humidity of 100%, simulated in a large desiccator using distilled water, were recorded. The amount of water taken up was calculated from the weight difference (Ohwoavworhua et al., 2007).

Tablet Preparation and Properties

Tablet preparation using NC as a disintegrant

Acetylsalicylic acid (ASA, 75%) was used as a model drug and NC (25%) as a disintegrant and batch size was two hundred tablets. NC was weighed and dry-mixed with ASA, which has previously been screened through a 200-mesh sieve, in a planetary mixer (Kenwood, UK) for 10 min. A 400 mg portion of the mixture was compressed at a fixed compression force of 27.5 KN using a single punch-tableting machine.

Evaluation of tablet properties

The compressed tablets were evaluated for their dimensions, friability, crushing strength, disintegration time, and dissolution rate of the medicament. These tests were carried out after storage of tablets for one week, in silica gel desiccators.

Tablet dimensions

Tablet thickness and diameter were measured with thickness gauge (ID type, Mitutoyo, Japan) from a random selection of twenty

tablets per batch.

Friability

A sample of twenty tablets was selected from each batch and de-dusted by directing a stream of air unto the tablets. The tablets were weighed and placed in the drum of a Roche fribilator programmed to revolve for 4 min at 25 r.p.m, after which the tablets were freed of dust and weighed again. The weight, before and after the test, were used to calculate friability as in Eq. 9:

$$\text{Friability} = W_L/W_O \times 100 \quad (9)$$

where W_L is weight loss and W_O is original weight.

Crushing strength

The crushing strength of six tablets obtained at the fixed compression force setting was determined using a tablet crushing strength tester (Karl Kolb, West Germany). The mean crushing strength was determined in each case for the nanocellulose types.

Disintegration time

The B.P. (2008) method was adopted anda disintegration apparatus (DT 2, Ereweka) was used. The disintegration medium consisted of 0.1N hydrochloric acid that was maintained at 37°C. A tablet was placed in each of the six glass tubes carrying a 10 mesh-sieve. Using a stopwatch the time it took for each tablet to disintegrate was determined. Six replicate determinations were made and the mean and standard deviation calculated for each batch.

Dissolution time

Dissolution rate test was performed in a dissolution test unit (Erweka Dissolution Rate Testing Unit, Type DT). The paddle method was used. For acetylsalicylic acid tablets, 900 ml of 0.05 M acetate buffer of pH 4.5 was used as the dissolution medium. The temperature of the bath for all determination was kept constant at 37° ± 0.5°C and the paddle rotation speed was 50 r.p.m. 5 ml samples were withdrawn at regular intervals from the dissolution medium with the aid of a syringe fitted with cotton wool for filtration. The sample withdrawn was replaced with equal volume of the medium in each case to maintain sink conditions.

The concentration of drug in the withdrawn samples was determined spectrophotometrically (Millonspectronic 1001) using an aliquot suitably diluted (1:1) with 0.05 M acetate buffer. The measurement wavelength was 263 nm for acetylsalicylic acid. Calibration curve (or Beer's plot) for the active drug reference standard was prepared. The concentration of each sample was calculated from the calibration curve. Drug dissolution was ploted against time and the result is shown in Fig 5.

Statistical analysis

The data obtained were expressed as means of five determinations, except otherwise stated. The percent yields of nanocellulose from acid hydrolysis however, were calculated using three determinations. Standard deviations, expressed as ±, were computed using Microsoft Excel.

3. RESULTS AND DISCUSSION

Percent yield of nanocellulose

All four acids achieved the depolymerizations of α-cellulose to cellulose nanocrystals and nanofibrils. However, the depolymerization was more with hydrochloric acid at the fixed 2.5 N concentrations, as evidenced by the obtained percent yields. The yields of nanocellulose were 49.8 ± 0.85%, 65.5 ± 1.1%, 67.5 ± 1.4%, and 70.3 ± 1.7%. It is observed that the only organic acid, acetic acid, had the highest yield. This might be because of its low power to depolymerize the α-cellulose compared to the rest of the inorganic acids.

Particulate and structural characteristics

Scanning electron microscopy (SEM)

Figure 1 compares the SEM photographs of NCs prepared by hydrolysis of corn stalk α-cellulose using different acids. The photomicrographs show that NCs prepared with acetic, phosphoric and sulphuric acids predominantly consist of nanofibrils that are spaghetti-like in appearance, and these NCs could be said to be highly fibrous. In contrast, the NC prepared with HCl consisted of only short rod-like shaped particles, which are nanocrystals. Thus, the differences seen in the morphology of the NCs may be attributed to the different hydrolytic powers of the acids. As it seems, the hydrolytic power is highest with hydrochloric acid since the resulting

particles are free of strands of fibrils. The nanofibrils (Fig 1B-D) would be excellent materials for bio-nanocomposites applications, where they may be needed to reinforced-polymer manufacturing, and even in nanocellulose membranes production.

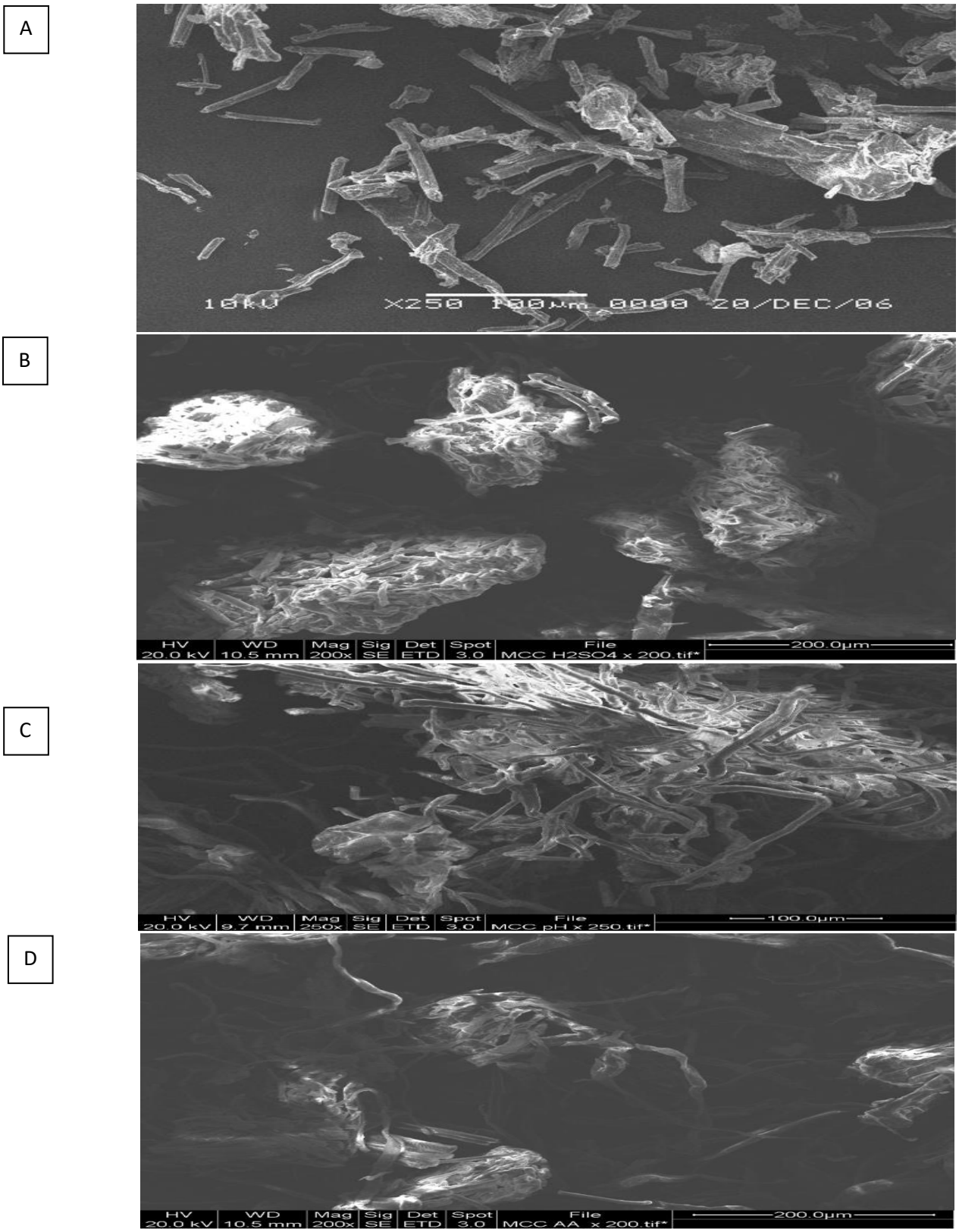


Fig.1 SEM of nanocellulose produced using: A hydrochloric acid; B sulphuric acid; C phosphoric acid; and D acetic acid; showing 'A' as nanocrystals and 'B-D' are nanofibrils.

Differential scanning calorimetry (DSC)

The DSC is a technique use to study what happens to polymers when they are heated, that is in terms of the thermal transitions that takes place in the polymer. Figure 2 shows the thermograms of NCs and α-cellulose derived from corn stalk. Each of the NC thermograms indicates that depolymerization and decrystallization of α-cellulose to produce NC was achieved by all the acid types, at the concentration of 2.5 N, used in the hydrolysis reactions. This is evident from the appearance of a second endothermal peak in the thermograms of the NCs after the one that correspond to desolvation. The absence of this second endothermal peak in α-cellulose thermogram is due to its amorphous nature. It could be explained that the amorphous portion in the α-cellulose somewhat occluded the crystallite portion, hence the sharp melting point (Tm) peaks, which are characteristics of the NCs are not observed in the α-cellulose thermogram.

The second endothermal peak, which corresponds to the melting of the polymer, is a transition that occurs in crystalline polymers, which indicates that the polymer chains in the crystal structures has become disorderly. It is a first order transition that involves both a change in heat capacity, and a latent heat (Polymer Science Learning Center, 2007). The peak temperature, T_m for this event varied among the NCs (Figure 2). In all the NCs thermograms except $NC_{sulphuric}$, the second endothermal peaks were sharp, while for $NC_{sulphuric}$ the peak is broad and asymmetric, as well as having the lowest melting point.

Revol et al., (1992) reported that using H_2SO_4 in the preparation of MCC results in the formation of sulphate groups onto the cellulose chain, that is, esterification of cellulose. Splitting of the sulphate groups during NC thermal degradation may be the reason for the broad and asymmetric nature of this peak. The different melting points of the NCs could be due to the structural changes that occured during their preparation. To produce NC, the cellulose fibres undergo controlled hydrolysis in strong acid solution. This process preferentially reduces the molecular weight of the amorphous regions to a degree of depolymerization of ~100 - 200 (Doelker et al., 1987). This depolymerization of the amorphous regions increases the number of end groups in these amorphous regions, which is associated with an increase in free volume. Thus, we believe the lowering of molecular weight, perhaps to varying degrees, via acid hydrolysis may be responsible for the different melting points.

In addition to differences in molecular weight, there may also be differences in chemical structure. For example, carboxyl groups from processing can be found in MCC (Edelson and Hermans, 1963). Also, it is very likely that aldehyde groups are formed during processing with acid (Picker and Hoag, 2007). These workers stated that the carboxyl and aldehyde groups are not only located in the amorphous regions of NCs that are most susceptible to acid hydrolysis, but are unevenly distributed throughout the amorphous regions and hence the heterogeneous regions could result in each with its own melting point. This explanation is supported by the observed two different melting points obtained fortwo batches of $NC_{sulphuric}$ samples under the same DSC experimental conditions (see Fig. 2 *e* and *f*).

Additionally, native and processed cellulose fibres are known to compose of highly oriented fibres called micro-/nanofibrils (Gilbert and Kadla, 1998). These micro/nanofibrilsre arranged to varying degrees in response to thermal treatment. Thus, the non-uniform response of the micro/nanofibrils could, also, have accounted for the observed melting point variation among the NCs.

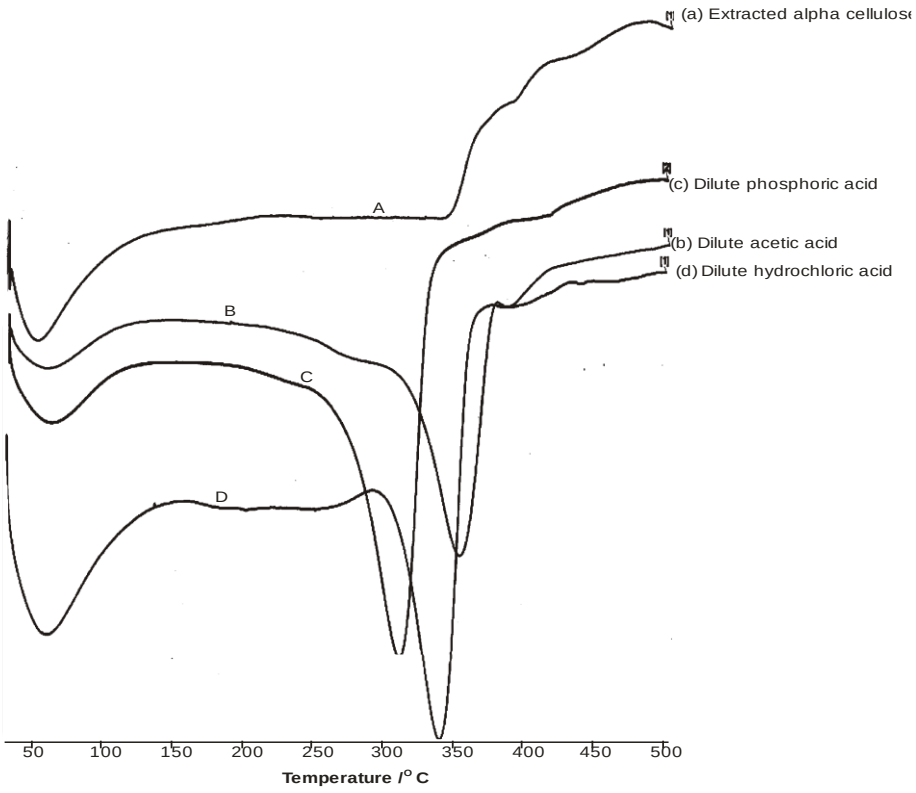
Because crystalline polymers usually have some amorphous portion, they have both glass transition-and melting temperatures. The glass transition is a phenomenon that occurs in amorphous polymers, that is, a polymer whose chains are not arranged in ordered crystals, though they are in the solid state. Glass transition involves change in heat capacity but it does not involve latent heat, and hence, it is a second order transition (Polymer Science Learning Center, 2007). The glass transition temperature, T_g, is the critical temperature at which the material properties of a polymer dramatically change from hard and brittle to soft and pliable form, and it is the characteristic temperature for amorphous and semicrystalline materials such as NCs and microcrystalline cellulose (Hancock et al., 1995; Hancock and Zografi, 1997). Therefore, knowledge of T_g may be important in characterizing NC.

In this work however, T_g (at a the heating rate of 10 ˚C per minute) was not detected in the NC thermograms. Stubberud *et al*., (1996) reported a similar difficulty in determining the T_g of microcrystalline cellulose by DSC at standard heating rates. Picker and Hoag (2007) explained that in conventional DSC, a reversing event like glass transition may be hidden by a non-reversing event, such as enthalpic relaxation.

X-ray diffractometer (XRD)

X-ray diffraction patterns of the NCs – prepared using different acids are shown in Fig. 3. The diffractograms are similar, with the diffraction peaks appearing at about ~15.5 and ~22˚C 2θ due to 110 and 200 crystallographic planes (Costa et al., 2015), respectively, and so the patterns are characteristic of cellulose I (Nelson and O'Connor, 1964). The calculated crystallinity indices using the instrument's computer programme are 50.6, 50.9, 56.7, and 58.0 % for $NC_{phosphoric}$, NC_{acetic}, $NC_{sulphuric}$ and $NC_{hydrochloric}$, respectively.

The value for $NC_{hydrochloric}$ is within the crystallinity index range of 58 – 69% reported for commercial brands of crystalline cellulose (Rowe *et al*., 1994).



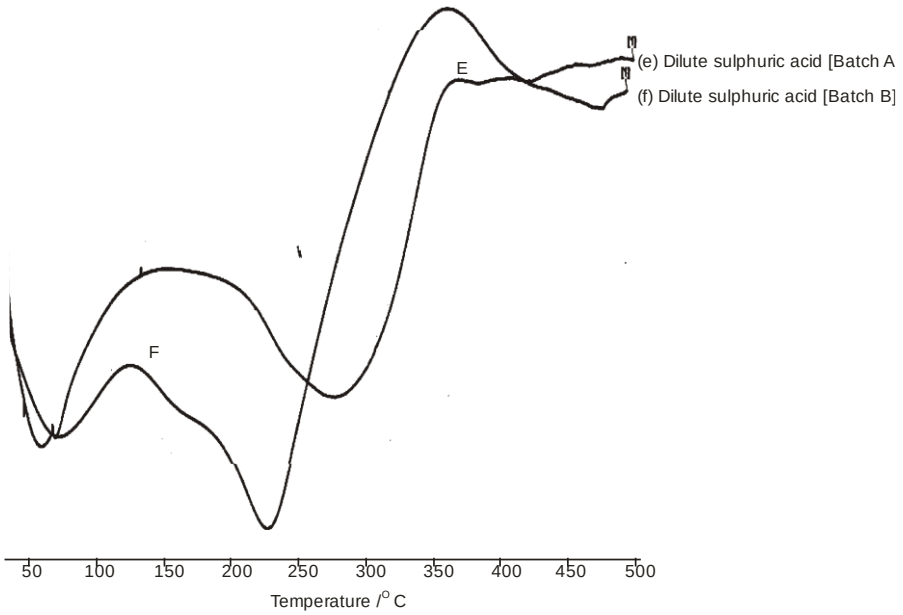


Fig. 2 Diffraction scanning calorimetry thermograms of corn stalk α-cellulose and NCs prepared by different acids hydrolysis

The values for $NC_{phosphoric}$ and NC_{acetic} are relatively low but similar to the value (50.42%) reported for low crystalline powdered cellulose obtained by phosphoric acid (85% w/w) hydrolysis of cotton linters at an agitation rate of 700 rpm (Kumar *et al.,* 2001). Thus,

the crystallinity of NC is dependent on the acid used. This observation is not in agreement with the findings of El-Sakhawy and Hassan (2006), who reported that the kind of the acid used in hydrolysis had no effect on crystallinity and crystallite size of microcrystalline cellulose.

Packing Properties

Table 1 shows the packing properties of NCs prepared from corn stalk α-cellulose using the various acids. Generally, the packing properties varied with acid type. Pharmaceutical powders are term as ''light'' and ''heavy'' powders on the basis of bulk density (Sinko, 2017). The term ''light'' powder means low bulk density or large bulk volume, whereas ''heavy'' signifies a powder of high bulk density or small volume. On the basis of this classification, $NC_{hydrochloric}$ is a ''heavy'' powder while the NCs prepared using the other acids are ''light'' powders. The bulk density is important because as it relates to *bulkiness,* which is the reciprocal of bulkdensity – an important consideration in the packaging of powders. Thus, if these NC powders were to be packaged, $NC_{hydrochloric}$ would require a smaller container than the other NCs.

Furthermore, the bulk density of a powder is primarily a function of particle size distribution, particle shape and tendency of the particle to adhere to one another (Sinko, 2017). The low bulk density of NC prepared with acetic, phosphoric and sulphuric acids may be attributed to loose packing of the particles as a result of large gaps between the surfaces of the nanofibrils.

The true density of nanocellulose powders, as determined by a displacement procedure in a non-swelling medium, depends on the proportion of crystalline region in the cellulose (Browning, 1967). Because crystalline regions have a higher density than the amorphous regions, the measurement of density allows ranking of a series of celluloses according to the relative proportions of crystalline and amorphous regions, and such rankings are found to be in the same order as those based on x-ray measurements (Browning, 1967). Consequently, based on true density values, the order of crystallinity would be: $NC_{phosphoric} > NC_{sulphuric} > NC_{hydrochloric} > NC_{acetic}$. However, this does not align with the order of crystallinity as determined by the x-ray diffraction measurements, which was: $NC_{hydrochloric} > NC_{sulphuric} > NC_{acetic} > NC_{phosphoric}$.

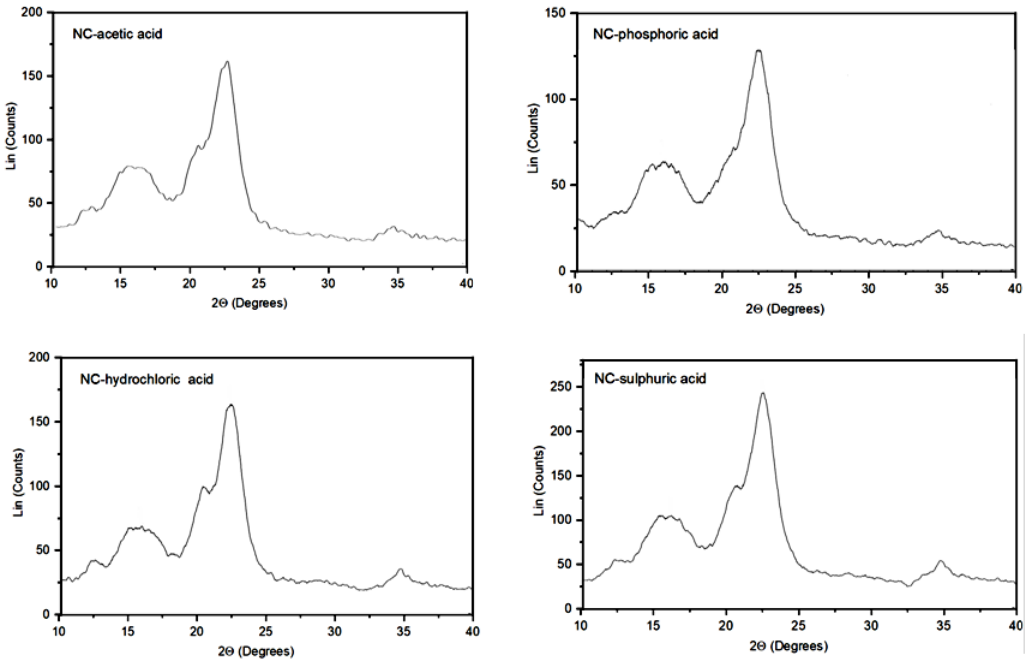


Fig. 3 X-ray powder diffractograms of nanocellulose prepared by different acids hydrolysis of corn strawα-cellulose

Table 1: Packing properties of NCs prepared from corn stalk α-cellulose using different acids (± standard deviation)

NC type	Bulk density (g/ml)	Tapped density (g/ml)	True density (g/ml)	Porosity (%)
NC_{acetic}	0.17±0.08	0.22 ± 0.02	1.34 ± 0.16	87.22
$NC_{hydrochloric}$	0.53 ± 0.05	0.79 ± 0.00	1.36 ± 0.21	60.94
$NC_{sulphuric}$	0.26 ± 0.07	0. 35 ± 0.04	1.45 ± 0.15	82.22
$NC_{phosphoric}$	0.18 ± 0.04	0.21 ± 0.08	1.58 ± 0.32	88.83

Flow Properties

Table 2 shows the flow properties of NC prepared using different acids. It should be noted that the suitability of a material as a direct compression excipient is determined, mainly, by the flow properties of that material. Staniforth (1996) reported indirect metrics for powder flowability that include the angle of repose, Hausner index and Carr's percent compressibility. While Hausner index is a measure of interparticlefriction in a powder bed, Carr's index is indicatives of the tendency of a material to diminish in volume (Rubinstein, 1996). The higher the value of these indices, the lower the flow of the powder. In general, Carr's index below 16% shows good flowability, and values greater than 35% show cohesiveness and hence poor flow, while Hausner ratio greater than 1.25 indicates poor flow. On the basis of these two parameters, the powder flow potential of the NCs powders was ranked as: $NC_{phosphoric} > NC_{acetic} > NC_{sulphuric} > NC_{hydrochloric}$.

Angles of repose greater than 50˚ have very poor flow and minimum angles close to 25˚ suggest very good flow properties (Staniforth, 1996). Thus, on the basis of this parameter, all the NCs could be said to have poor to very poor flow potential. Consequently, glidants will be needed when they are used in solid dosage formulation.

Table 2: Flow properties of NC derived from corn stalk α-cellulose prepared using different acids

NCtype	Angle of repose (˚)	Carr's index (%)	Hausner's ratio
NC_{acetic}	43.31	22.79	1.30
$NC_{hydrochloric}$	35.90	32.51	1.48
$NC_{sulphuric}$	47.89	27.09	1.37
$NC_{phosphoric}$	54.35	17.28	1.21

Hydration and Swelling Capacities

The hydration capacity values (see Table 3) indicate that the capacity of the NCs to retain water was a function of their packing properties. NCs prepared by acetic, phosphoric and sulphuric acids (and had low bulk densities as shown in Table 1) retained more water. Probably due to loose packing in these celluloses with the result that water is trapped in the interparticulate spaces. The order of hydration capacity was: $NC_{phosphoric} > NC_{acetic} > NC_{sulphuric} > NC_{hydrochloric}$. Swelling capacity, however, was inversely related to packing properties (see also Table 1). Swellability, which reflects increase in volume of cellulose particles following water adsorption, was highest (66.7%) for $NC_{hydrochloric}$. This is an indication that a lot of the water was absorbed and actually penetrated the individual cellulose particles and aggregates causing them to swell. Thus, if each of these NC were to be incorporated in a tablet formulation as a disintegrant it would produce tablet disintegration by possibly two mechanisms: capillary or wicking (due to interparticulate water) and swelling.

Table 3: Moisture content, hydration and swelling properties of corn stalk NC prepared using different acids

NC type	Moisture content (%)	Hydration capacity	Swelling capacity (%)
NC_{acetic}	10.8 ± 0.78	4.63 ± 0.05	25.70 ± 1.25
$NC_{hydrochloric}$	13.2 ± 0.93	1.74 ± 0.09	66.67 ± 3.42
$NC_{phosphoric}$	16.2 ± 1.92	4.79 ± 0.12	17.33 ± 0.97
$NC_{sulphuric}$	11.6 ± 0.96	3.72 ± 0.23	28.00 ± 2.32

Moisture Sorption Profile

Figure 4 shows the moisture sorption profile for the NCs. Thus, the order of moisture sorption is: $NC_{sulphuric} > NC_{acetic} > NC_{phosphoric} > NC_{hydrochloric}$. Stamm (1964) reported that the crystallite portion of cellulose does not take up moisture and that the extent of moisture taken up by cellulose should hence be proportional to the amount of the amorphous cellulose present in the material. Also, study of moisture sorption is of importance because it reflects the relative physical stability of tablets made with NC when stored under humid conditions. Thus, $NC_{sulphuric}$ containing tablets would be most liable to deterioration when incorporated into tablets/granules/powders along with drugs that subject to hydrolytic decomposition, e.g aspirin, since $NC_{sulphuric}$ exhibited the highest moisture adsorption.

Tablet properties

The acetylsalicylic acid (ASA) on its own has direct compression property. Table 4 shows the tablet characteristics of ASA formulation containing NCs (as disintegrants) that were prepared by different acids.

Thickness:

The prepared tablets showed varying thickness with nanocellulose types. This however was expected, since the powders packing characteristics in terms of bulk-, tapped-, and true densities, as well as porosity (see Table 2) varied somewhat widely. The observed thickness could not be correlated in any particular order, whether directly or inversely, to any of the individual packing properties.

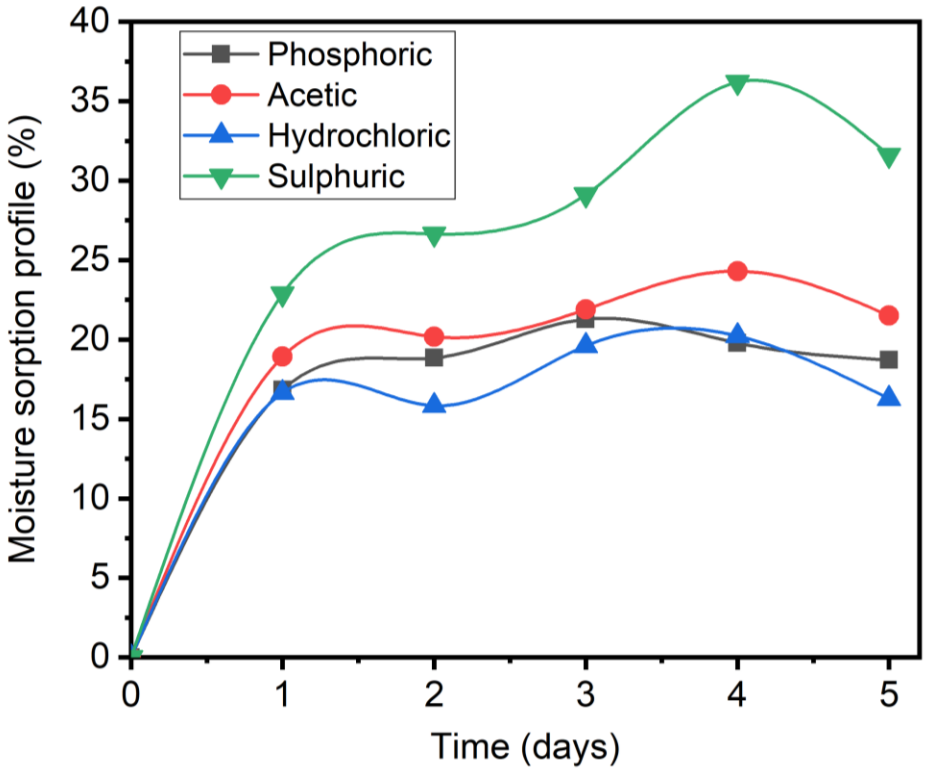


Fig 4: Moisture sorption profile of corn straw nanocellulose obtained using different acids

Crushing strength:

The crushing strengths of the tablets were within 4-7 kgf acceptable limits (BP, 2008). The $NC_{hydrochloric}$ had the highest crushing strength, due probably to strong bonding resulting from the particle-particle interactions between the discrete, rod-shaped nanocrystals (see Fig. 1).

Friability:

The friability values for tablets formulated from the different nanocellulose types however did not fall within the acceptable limit of 1% for conventional tablets (BP 2008).Because of this observation, it is suggested that for powders of this nanocellulose types to be used in tablet formulation, they might require the incorporation of granulating agents to further impact cohesiveness to the particles.

Disintegration time:

Although, their disintegration times varied, they were within the acceptable limit of 15 minutes for conventional tablets (BP, 2008). The disintegration time of tablet types showed a kind of linear relationship with the crushing strengths. Tablets with high crushing strength had long disintegration time. Difference in disintegration time in tablet formulations containing cellulose material as a disintegrant has been attributed to differences in the liquid penetration (Reier and Shangraw, 1966; Lerk et al., 1979). Stamm (1964) has reported that the degree of crystallinity affects the rate of water uptake – a phenomenon that precedes eventual break up of compacts to granules and then to primary particles. The test NCs had the different degrees of crystallinity of between 50.6 and 58, which are low, we could somewhat correlate the observed higher disintegration time of the test $NC_{sulphuric}$ and $NC_{hydrochloric}$ to their high degree of crystallinity. For instance, the order of tablet disintegration time was: $NC_{hydrochloric}$>$NC_{sulphuric}$>NCacetic>$NC_{phosphoric}$, while the order of crystallinity of nanocellulose types was: $NC_{hydrochloric}$ 58%>$NC_{sulphuric}$ 56.7% >NC_{acetic} 50.9% ~ $NC_{phosphoric}$ 50.6%.

Dissolution studies:

Tablet types with crushing strength and disintegration time characteristics shown in Table 4 were used for the dissolution studies. The *in vitro* release profiles of the ASA tablets containing NC as disintegrant are shown in Fig. 5. Generally, the release profiles of all the tablets are largely similar. Although all tablet types disintegrated within 15 min, the dissolution profile showed that at 15 min only about 45 – 59% of the drug was released; and at 30 min only 85 -95 % of the drug was released. This observation could be, in part, due to the nano-dimensions of the powders, which could have formed a fine coating layer around the drug particles, thereby prevented the immediate availability of the drug in the dissolution medium. Also, because the crystallinity of the nanocellulose powders range from 50 -58 %, which means these powders also have large proportions of amorphous portions, the drug particles could have been adsorbed strongly to the amorphous portions. This might explains why $NC_{hydrochoric}$, with highest crystallinity (58%), appears to have released more drugs within the first 15 min of the dissolution studies. Additionally, the discrete rod-shaped nanocrystals of $NC_{hydrochloric}$ could have contributed to the high release profile, in contrast to the nanofibril-networks that characterized the other nanocellulose types (Figure 1).

Table 5: Tablet properties of acetylsalicylic acid formulations containing corn stalk NCs (as disintegrant) prepared using different acids

NCtype	Thickness (mm)	Crushing strength (kgf)	Friability (%)	Distinteg. time (min)
NC_{acetic}	3.4 ± 0.2	4.66 ± 1.21	3.85	6.27 ± 0.5
$NC_{phosphoric}$	3.3 ± 0.3	5.26 ± 0.77	3.90	6.13 ± 0.8
$NC_{sulphuric}$	3.0 ± 0.2	6.24 ± 0.83	1.95	11.0 ± 0.6
$NC_{hydrochloric}$	2.6 ± 0.1	7.48 ± 0.81	1.23	15.2 ± 0.5

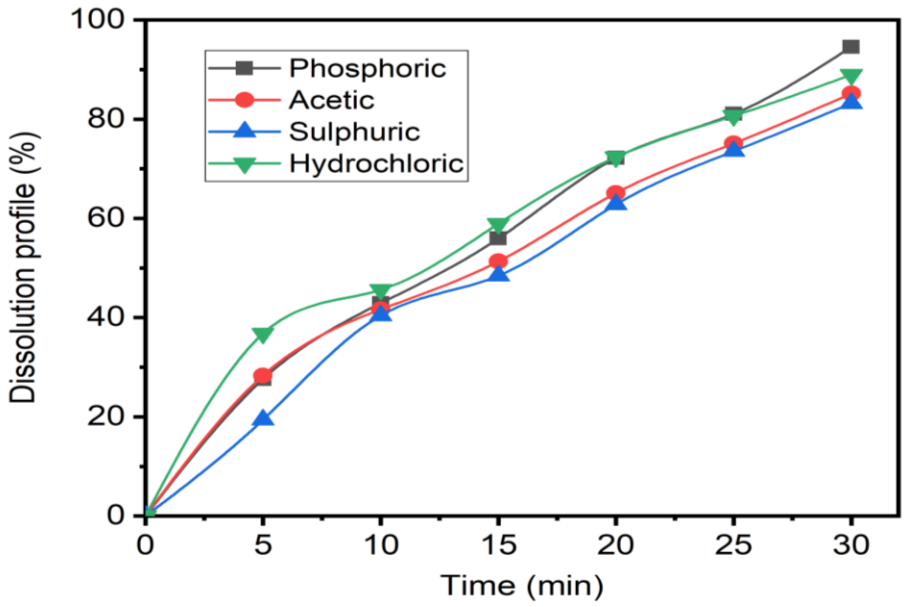


Fig. 5 Dissolution profile of acetylsalicylic acid tablets containing corn straw nanocellulose types

4. CONCLUSION

In this work, we have demonstrated the feasibility of obtaining nanocellulose from alpha cellulose of corn straw using different acids, and presented the comparative analysis of the nanocellulose types in terms of particulate, structural and powder characteristics, as well as tablet properties. We found that these characteristics are dependent on the type of acid used. Also, tablet properties (crushing strength, friability, disintegration time and dissolution) of acetylsalicylic acid tablet formulation incorporating the NC types were, however, comparable. Based on these results, it was concluded that corn straws, which are abundant and renewable, could serve as alternative raw material feedstock to cultivated forest wood in the production of nanocellulose for pharmaceutical and other diverse applications.

Peer-review

External peer-review was done through double-blind method.

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Conflict of Interest
The authors declare that there are no conflicts of interests.

Data and materials availability
All data associated with this study are present in the paper.

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