Production of Micro Crystalline Cellulose from Corn Husk and Its Evaluation as pharmaceutical Excipient

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***Abstract*: We have extracted cellulose from corn huskusing an eco-friendly multistep procedure involving acid-alkaline treatment andbleaching. This multistep procedure essentially removed lignin and hemicelluloses. The extracted cellulose is highly crystalline as verified by X-ray diffraction, Fourier transform infrared spectroscopy. The aim of this work was to prepare and evaluate micro crystalline cellulose as a potential excipient in the production of pharmaceutical dosage forms due to itslow cost as it is derived byrecycling wastes.**

I. INTRODUCTION

Annually renewable agricultural wastes represent an abundant, inexpensive and readily available source of renewable lignocellulosic biomass. Each year, farming and agricultural processing generate millions of tones of wastes, such as corn cobs and husks, groundnut shells, rice straw, sugarcane bagasse, banana stems, soy hulls and sugar beet pulp. Agricultural wastes could be put into viable use through various recycling methods as a source of energy, sources of major compounds like cellulose, gums, polymers etc and also as a major source of livestock feeds. Cellulose, one of the major component of lignocellulosic biomass, is a polydisperse polymer of high molecular weight and comprising of long chains of D-glucose units joined together by β-1, 4-glucosidic bonds.[1]

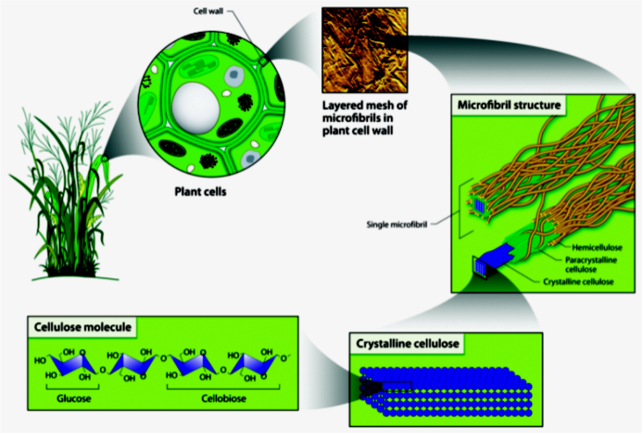

Fig 1 Structure of Cellulose

Cellulose is the backbone of structure of plants and it is the chief constituent of plant cell wall. It is the most widely used organic material in the world.[2]

In spite of its poor solubility characteristics, cellulose enjoys extensive use in the pharmaceutical industry as diluents, lubricants, disintegrants, binders and coatings in the manufacture of tablets and capsule.[3,4]

Among other uses, cellulose is widely employed as a raw material to prepare a number of excipients. Micro-crystalline cellulose is defined as 'purified, partially depolymerized cellulose' prepared by treating alpha cellulose obtained as a pulp from fibrous plant material with mineral acids. Commercially available microcrystalline cellulose is derived from highly costly hard wood and also from purified cotton. The chemical composition and physical structure of microcrystalline cellulose depend significantly on the characteristics of the raw material employed and the manufacturing conditions.[5,6]

As part of the on-going efforts to develop low-cost indigenous raw materials from lignocellulosic materials with desired physicochemical properties for the industrial applications, we have reported some physical properties of microcrystalline cellulose prepared from corn husk and also evaluate their structural and thermal properties with a view ofascertaining its potential as a pharmaceutical excipient. These properties were also compared with a commercial brand Avicel PH 101 (FMC, U.S.A).

II. MATERIALS AND METHOD

MATERIALS

- Corn husk an agricultural waste obtained from local farmer
- Avicel PH 101 - a commercial brand of microcrystalline cellulose obtained from FMC-U.S.A
- Sodium hydroxide (reagent grade, 98%),
- Sulphuric acid (ACS reagent, 98%)
- Distilled water

METHOD

PREPARATION OF MAIZE HUSK POWDER:

A 2.0 kg weight of corn husk was weighed, sliced with a hand knife and dried in hot air oven (Ambassador-Laboratory electric oven) at 60 ^{o}C for 9 hours. The sun dried husk was pulverized in domestic blender to produce powdered corn husk.

EXTRACTION OF CELLULOSE FROM CORN HUSK:

The corn husk was sun dried forseven days.(average temperature was 33˚C, the relative humidity was(67 %) The sun dried husk was then size reduced using a mill. A 200g of the powdered corn husk was treated with 100 ml of a 1 N of sodium hydroxide to delignify the plant material for thirty minutes. The resulting slurry was filtered using cotton cloth and the residue on the cotton cloth was further treated with 500 ml of 1 N Sulphuric acid to digest the powdered materials at 80°C for 1 h. The resulting slurry was filtered and the residue was thoroughly washed with distilled water, further treated with 3.2%w/v of sodium hypochlorite for 20 min at 80 °C to bleach it. This was further washed with distilled water until the residue was neutral to litmus paper. The cellulose material was filtered using cotton cloth and the water was manually squeezed out to obtain small lumps, which were dried at 60°C for 6 hr. The yield of cellulose was calculated.

III. PHYSICOCHEMICAL CHARACTERIZATION OF CELLULOSE

INFRARED SPECTROSCOPY [7]

Fourier transform infrared (FT-IR) spectra were recorded using KBr discs on a Perkin-Elmer FT-IR spectrometer. KBr pellets containing 1% of the samples were prepared. The scanned range was 4,000 to 400 cm^{-1}

POWDER X-RAY DIFFRACTION [8]

X-ray diffraction patterns of the cellulose samples were obtained using an X-ray diffractometer (Philips Xpert MPD). Samples for analysis were prepared by pressing the powder into the cavity of a sample holder and smoothen with a glass slide. The crystallinity index (CI) was calculated using Equation 1.

$CI = (I_{002} – I_{am}) / I_{002} *100$ ……1

Where 1_{002} is the maximum intensity of the principal peak (002) lattice diffraction, and 1_{am} is the intensity of diffraction attributed to amorphous cellulose.

THERMAL ANALYSIS[9]

The thermal properties of the cellulose samples were investigated by DSC on a simultaneous thermal analyzer (Perkin Elmer Pyris1 DSC). Samples weighing between 6 and 10 mg were used. Each sample was heated from room temperature from 45 to 400°C at a rate of 10°C/min under nitrogen.

VISCOSITY[10]

Viscosity is a measure of the resistance of a fluid to deformation under shear stress. It describes a fluid’s internal resistance to flow and is a measure of fluid friction

$\eta1 = \{(P1 / P2)*(t1/t2)\} * \eta2$

MOLECULAR WEIGHT AND DEGREE OF POLYMERIZATION[10]

Molecular weight = n/k

Where $k = 2.5*10^{-5}$

Degree of polymerization= Molecular weight of mean molecule/molecular weight of monomer

Where molecular weight of monomer= 162

ASH CONTENT[11]

2 gram of sample was taken and was burnt in silica crucible on burner and was ignited at 450 ^{0} C to constant temperature.

IV. CHARACTERIZATION OF MICRO CRYSTALLINE CELLULOSE AS PHARMACEUTICAL EXCIPIENT

BULK AND TAPPED DENSITY[12]

For the determination of the bulk and tapped densities, 2.5 g of the cellulose powder was accurately weighed and poured into a 100-mL graduated cylinder. The cylinder was stoppered and the bulk volume (v_b) was recorded. For tapped density, the cylinder was tapped from a height of 2.5 cm on a hard surface to a constant volume. The final volume (v_t) was noted to be the tapped volume. The bulk density, D_{bulk}, and tapped density, D_{tap}, were determined using Equations 2 and 3

$D_{bulk} = w/v_b$ ……2

$D_{tap} = w/v_t$ …….3

POWDER POROSITY[13]

The porosity (P_b) of MCC powders was evaluated using following Equation 4

$P_b = \{(V_b – V_P) / V_b\} * 100$ …….4

Where $V_b$is bulk volume

V_P is porous volume

ANGLE OF REPOSE[12]

The measurement of the angle of repose was carried out using a long cylindrical tube open at both ends as shown in [12]. The tube was perpendicularly placed on a clean cardboard paper and filled flat with the cellulose powder. The tube was then gradually lifted away, vertically, from the cardboard. The height, h, and radius, r, of the conical heap formed were measured and then the angle of repose, θ, was calculated from Equation 5

$\Theta = \tan^{-1}(h/r)$ ……..5

CARR’S INDEX AND HAUSNERS RATIO[13,14]

Carr's index and Hausners ratiofor cellulose were calculated from bulk and tapped densities using Equations 6 and 7

Carr's index=$\{(D_{tap}–D_{bulk})/D_{tap}\}*100$ …..6
Hausners ratio=D_{tap}/D_{bulk} …..7

MOISTURE CONTENT[15]

The moisture content (MC) of the cellulose powders was found out as shown in[15].

MC={(Wet Wt.–Dry Wt.)/Wet Wt}* 100 ….8

ELEMENTAL ANALYSIS[16]

The analytical method is based on the complete and instantaneous oxidation of the sample by "flash combustion", which converts all organic and inorganic substances into combustion products. The resulting combustion gases pass through a reduction furnace and are swept into the chromatographic column by the carrier gas (helium), where they are separated and detected by a thermal conductivity detector (TCD), which gives an output signal proportional to the concentration of the individual components of the mixture.

TEST FOR HEAVY METALS[17]

Amount of inorganic impurities during unit operation, are mostly ionic matters which are water soluble cations & anions. Cations are iron (Fe2+/Fe3+), arsenic (As3+/As5+), lead (Pb2+) and anions are chloride (Cl-), sulfate (SO42-). All heavy metal impurities are cumulative poison which has affinity to bind with lipid layer to produce health hazards. The test is generally performed by turbidity comparison test between test sample and standard sample. If the intensity of turbidity of test sample is equal to or less than standard sample then the sample passes the limit test, if the intensity of turbidity of test sample is greater than standard sample then the sample fails to pass the limit test.

PARTICLE SIZE ANALYSIS[18]

Particle size influences many properties of particulate materials and is a valuable indicator of quality and performance in tableting. The size and shape of powders influences flow and compaction properties. The most obvious example is milling (or size reduction by another technology) where the goal of the operation is to reduce particle size to a desired specification. In the pharmaceutical industry the size of active ingredients influences critical characteristics including content uniformity, dissolution and absorption rates.

V. RESULTS AND DISCUSSION

FT-IR SPECTROSCOPY

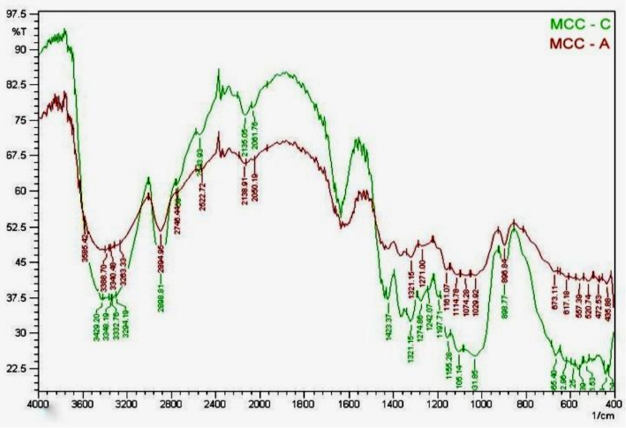

Fig 2 FT-IR spectra of a) MCC-C, b) MCC-A

FT-IR spectroscopy has the ability to predict structural differences not seen by other physicochemical analyses.The polymers are having both crystalline and amorphous nature, their proportionality is important for processibility, optical, mechanical and chemical properties. In spite of minor differences among them, the FT-IR spectra of the MCC samples (Figure 2) show the general characteristic spectrum of cellulose. For example, absorption bands are clearly observed at 896 cm−1 (corresponding to β-glycosidic linkages), 1,072 cm−1 (ring vibration and C-OH bending), 2,893 and 2,898 cm−1 (C-H asymmetric and symmetric tensile vibration) and the broad peak at 3,100 to 3,400 cm−1 (OH stretching, hydrogen bonds). the peaks at 1429, 1365, and 1321 are associated with intermolecular hydrogen bonds at the C group and the O—H in plane bending vibration, respectively.[19] The other characteristics IR peaks of cellulose are at and 1269 cm-1 (C-O-C aryl-alkyl), 1029 cm-1 is C-O stretching [20].

X-RAY DIFFRACTION SPECTRA

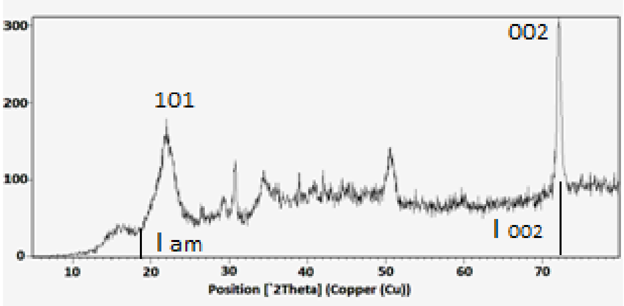

Fig 3 XRD of MCC-C

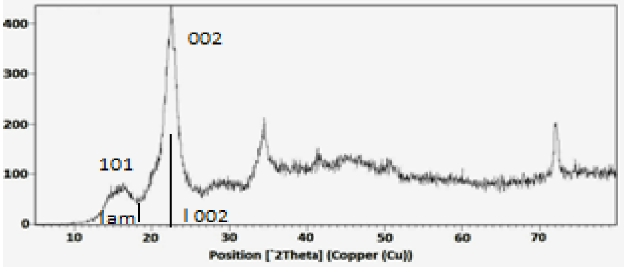

Fig 4 XRD of MCC-A

	MCC-C		MCC- A	
No.	Pos. [°2Th.]	Height [cps]	Pos. [°2Th.]	Height [cps]
1	15.9351	11.58	14.3276	13.53
2	21.928	83.29	22.5016	301.82
3	26.5545	11.96	34.5463	77.48
4	29.3105	28.02	41.6146	16.94
5	30.7423	71.68	50.6362	17.68
6	34.336	35.23	72.0578	101.8
7	38.9738	19.8		
8	40.9002	15.66		
9	42.0656	18.98		
10	47.3471	7.39		
11	50.52	61.78		
12	72.0891	222.42		
CI	81.83		86.55	

Table 1 XRD peak Height

The crystallinity of the cellulose samples was observed by X-ray diffraction. The powder X-ray diffraction spectra of all four cellulose samples are shown in Figure 3 and 4. The diffractograms of the microcrystalline cellulose samples exhibit diffraction pattern typical of cellulose I, with diffraction peaks of the 2θ angles at 15.93°, and 14.32°, which can be assigned to the 101 [21]. The method of Segal [7] is still the most widely used to calculate the crystallinity index of cellulose and is being cited in several works [22-24]. It is a simple method that does not need background subtraction and it uses the peak heights. Through Segal's method, the crystallinity index is calculated by the equation 1(Physico chemical characterization)

I002 is the 002 peak, the highest peak, which represents both crystalline and amorphous material. The lowest height between 002 peak and 101 peak is Iam and represents only the amorphous part. Figure 4 and 5 shows the X-ray diffraction pattern of MCC-C and MCC-A as well as the values of the crystallinity index (calculated by using Eq. 1). The value of the crystallinity index of our MCC-C is 81.83 which is very close to that found for commercial MCC-A is 86.55 % and are as similar to those reported in other studies for MCC [25-28,]. High crystallinity indicates an ordered compact molecular structure, which translates to dense particles, whereas lower crystallinity implies a more disordered structure, resulting in a more amorphous powder. These results mean that the overall multistep procedure employed is adequate to obtain highly crystalline cellulose.

THERMAL PROPERTIES

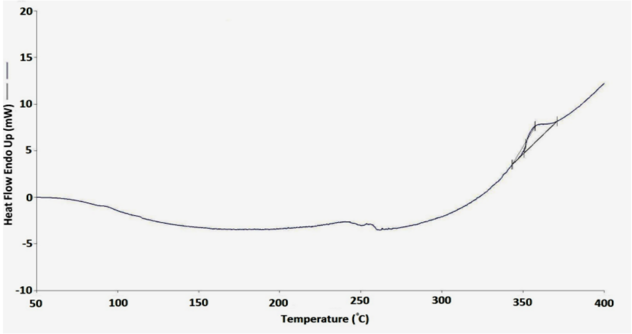

Fig 5 DSC thermograms of the MCC- C

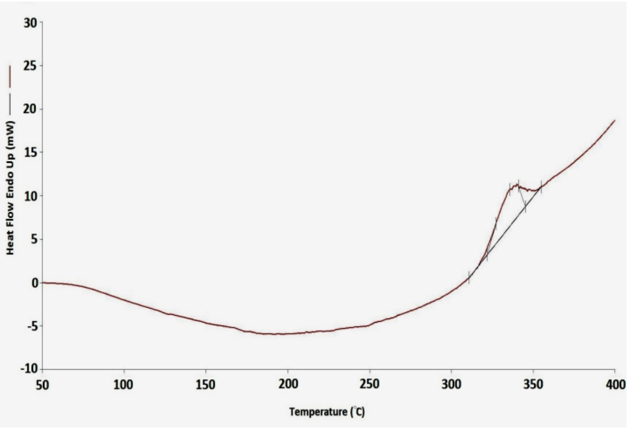

Fig 6 DSC thermograms of the MCC-A

DSC thermograms of MCC-C and MCC-A are shown in Figure 6 and 7. It was found that MCC-C has higher glass transition temperature (*Tg*) (350.69°C) as compared to MCC-A (321.92°C). The onset temperatures of the decomposition as well as the midpoint and inflection point temperature data for all the microcrystalline cellulose samples are similar and are presented in Table 2.This can probably be due to the more intense interpolymer chains interaction occurring in MCC-C. Theoretically, the presence of extensive hydrogen bonding between cellulose hydroxyl group creates stronger interaction between polymer and it should enhance the thermal stability.[29] The higher onset temperatures are associated with higher thermal stability. This behavior could be attributed to the high degree of crystallinity of the microcrystalline celluloses. A more notable difference among the microcrystalline cellulose samples is observed at inflection slope temperatures. [9].

Temp (^{0}C)	**MCC- C**	**MCC-A**
Onset	350.69	321.92
Peak	357.24	335.55
End	383.38	345.24

Table 2 DSC Temperature of MCC-C, MCC-A

PHYSICO CHEMICAL PROPERTY

Property Microcrystalline cellulose powder		
	MCC-A	**MCC-C**
Bulk density (g cm−3)	0.40	0.36
Tap density (g cm−3)	0.45	0.42
Carr's index	11.11	14.28
Hausners ratio	1.12	1.16
Powder porosity	11.29	14.49
Angle of repose (°)	31.76	33.42
Moisture content (%)	3.06	4.2
Viscosity	1.07	1.25
Molecular Weight	37120	42400
Degree of Polymerization	229.13	261.72
Ash content	0.03%	0.02%

Table3 Physicochemical property of the cellulose samples

Bulk density gives an estimate of the ability of a material to flow from a hopper into the die cavity of a rotary tablet compression machine, while tap density is a measure of how well a powder can be packed in a confined space on repeated tapping. In general, the higher the bulk and tapped densities, the better the potential for a material to flow and to re-arrange under compression. This suggests that all microcrystalline cellulose samples might have good flow properties[13].

The Carr's compressibility index gives an idea of how much a powder can be compressed, while Hausner index measures/estimates cohesion between particles; the values for both varies inversely with particle flow[11].

The angle of repose of a powder gives a qualitative assessment of its internal and cohesive frictions. In our case, no significant differences were observed among the angles of repose of the microcrystalline celluloses. The angle of repose of the microcrystalline cellulose samples lie around 35° (good flow)[30].

The moisture contents measured for all celluloses in this work fall within the acceptable limits of between 5% and 7%[15]. Furthermore, powder flowability is known to decrease with increasing moisture content[13]. Overall, the good flow properties for the microcrystalline cellulose are likely to be the result of variations in the particle shape, size and surface area of the powders[14] directly related to the process of partial hydrolysis of the original cellulose in an acid. The total porosity of a porous powder is made up of voids between the particles as well as pores within the particles. The results obtained for all the celluloses are similar and indicating poly sized particles and easily compressible powder during tableting.

ELEMENTAL ANALYSIS

Elements	MCC- C	MCC-A
Carbon	42.36%	42.38%
Hydrogen	6.59%	6.47%
Nitrogen	Not Detected	Not Detected

Table 4 Elements in MCC-C,MCC-A

Evident from above table, elemental analysis of MCC-C and MCC-A indicate presence of Carbon and Hydrogen while Nitrogen is absent.

TEST FOR HEAVY METALS

For Cl$^-$, SO$_4^{2-}$, Pb^{+3} and As^{+3} turbidity of the sample is less than standard solution, implying all samples would pass the limit test of all heavy metals.[17]

PARTICLE SIZE ANALYSIS

Larger, more spherical particles will typically flow more easily than smaller or high aspect ratio particles. Smaller particles dissolve more quickly and lead to higher suspension viscosities than larger ones. Smaller droplet sizes and higher surface charge (zeta potential) will typically improve suspension and emulsion stability.

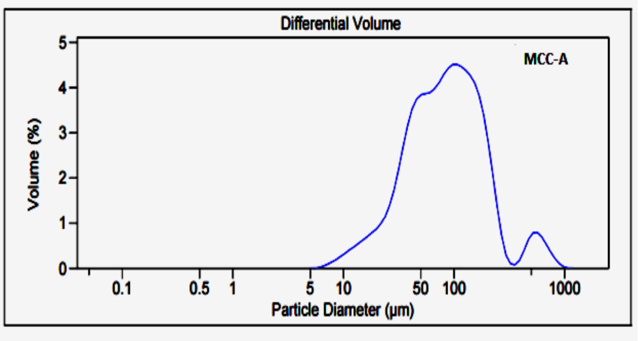

Fig 7 Particle size analysis of MCC-A

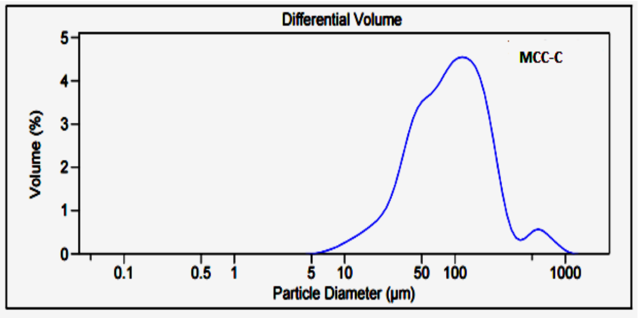

Fig 8 particle size analysis of MCC-C

The particle size analysis is shown in table 5 and figure 7 and 8

Diameter	MCC-C	MCC-A
d10	30.69 µm	28.91 µm
d50	91.58 µm	83.93 µm
d90	228.8 µm	209.0 µm

Table 5 diameter of of MCC-C and MCC-A

VI. CONCLUSIONS

The microcrystalline cellulose powders obtained from the corn husk (MCC-C) compared favorably with the Avicel PH 101 (MCC-A),The results indicated that the production of Pharmaceutical grade cellulose from corn husk waste is technically feasible.The MCC-C, obtained from corn husk possesses the desired physico-technical and tableting properties such asdiluents, binder, disintegrating agent.Indian farmers generate corn husk substantially in the form of waste, MCC can be produced from it indigenously on a large scale with economic consideration in our country.

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