THE CONTRIBUTION OF BIO-POLYMERS TO PHARMACEUTICAL INDUSTRY : EVALUATION OF CELLULOSE PROCESSED FROM THE HOLLOW STEMS AND LEAVES OF COMMON REED, PHARGMETS AUSTRALIS, F. GRAMINACEAE, AS TABLETTING EXCIPIENT

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Abstract

The leaves and the hollow stem of *Phargmets Australis,* a plant growing widely near water sources in Sakaka town, were used as a crude material to extract cellulose [1]. Commercial grade of native cellulose was employed as a reference material for the comparative study. The extracted cellulose, PC, was found to comprise of long, fibrous particles of irregular shape and rough surface which creat resistance to flow. The extracted cellulose powder was not freely flowing. The addition of a glidant was found to reduce the inter-particulate friction and induced a positive effect on the flow rate and repose angle of the powder [2]. Beyond 3.5 % w/w, the fine particles of the added glidant furnish inter-particulate bridging and the powder became co-hesive. Moisture sorbed by an added glidant was found to be the affect its glidant action. Magnesium stearate followed by stearic acid and aerosol 200 were at 2% w/w, respectively were the most effective glidants.

Keywords: Common reed, Cellulose , compression, disintegration

Introduction

A great deal of attention was directed to the agro-residues as available and cheap source of crude materials to process cellulose, the mostly abundant, naturally occurring and renewable bio-polymer on the earth. Cellulose could be processed from cotton linters as well as cellulosic fiber of different origins of plants. Due to the strong intera and inter-molecular hydrogen bonding between the individual molecules chains, cellulose is practically insoluble in water and in other common solvents. Cellulose and cellulose

derivatives have strongly found their way of vast applications in pharmaceutical, cosmeceutical as well as food industries. Due to the crystallinity of its particles , microcrystalline cellulose proved to be a successful direct compression tabletting based material while the non crystalline native cellulose failed to be auto-compressible excipient. Native cellulose is more considered as a powerful disintegrant than being a direct compression excipient. Its disintegration action is proceeding via wicking mechanism. During the test, the disintegration medium is withdrawn into tablet body by wiching to destroy the bonding holding tablet structure.

The present study deals with the evaluation of a brand of native cellulose extracted from the leaves and hollow stems of *Phargmets Australis*, *F. Graminaceae*, as tabletting excipient.

Experimental

Materials

The dry plant was collected from some local areas in Sakaka town. The analytical grade chemicals namely: nitric acid 69%, sodium hydroxide, sodium hypochlorite, native cellulose powder, lactose, starch (maize) and gelatin were obtained from Loba Chemi. Private Ltd., Mumbai, India; sulfuric acid and magnesium stearate were purchased from Scharlau, Chemie. S.A. Spain, respectively. Anhydrous lactose was given by Shiffield union, NJ., USA.

Methods

Processing of cellulose

A sample weighing 1.0 kg of the dry plant was washed thoroughly in boiling water for one hour and dried at 70^{o} C in a Binder convection oven (model ED 115 U). The dried plant fibers was reduced in size using a cutting mill and passed through a 0.400 mm sieve mesh. A precisely weighed 500 g sample was digested in 10 % sodium hydroxide solution at 100^{o}C for 3 h in order to destroy the lignin, hemi-cellulose and other cell contents. The alkali solution was filtered out and the thoroughly washed mass was re-digested in 5% sulfuric acid. to accomplish the oxidation and getting rid of the remaining impurities. The acid digestion was carried out at 80^{o} C for 90 min. The acid and acid soluble materials were filtered out and the mass was washed, bleached with 800 ml 6% sodium hypochlorite solution. The bleached cellulose was neutralized, dried, pulverized and stored in screw capped bottles at room condition till use. The yield of the extracted cellulose reached to 27% w/w of the dried mass i.e. ≈ 67.5% of the cellulose content in the plant.

Evaluation of the processed PC

Physico-chemical properties

The PC and NC powders were subjected to some pharmacopoeial tests. The degree of polymerization, pH, % sulfated ash, and heavy metals content were determined using the methods mentioned in BP 2010.

Shape and size and size distribution of PC particles

The shape of particles of the celluloses under study were described and characterized using an electronic microscope (BM-180, Boeco, Germany) coupled with a digital camera (S8000fd, Fujifilm Corp., Japan). Sieving technique was used to determine the size distribution of the processed cellulose as follows: A precisely weighed 50 g sample was placed on the top sieve of a set of sieves arranged in descending order and shaken using a magnetic shaker for 20 min. The remaining powder fraction on the top of each sieve was accurately weighed. The arithmatic mean diameters was calculated and the geometric mean diameter was graphically determined from the log probability plot of size distribution.

Density and recovery modulus measurements

The apparent density of PC and NC powders were determined using a pycnometer calibrated at room temperature and water as a displacement liquid. The mean of such 5 determinations was taken as the apparent particle density of the extracted cellulose.

Loose , ρ_L, and tap, ρ_T , densities of PC and NC powders were determined as follows: a 50 g sample of a given powder sample was placed into a 100 ml measuring cylinder. The volume, v_o, was precisely recorded. The powder was tapped till no change in volume was attained. The volume recorded was denoted as v_t and the loose and tape densities were calculated as reported earlier. The mean of such 5 determinations in each case was taken as the mean of the loose or tap density of the powder. Hausner ratio and Carr's index were accordingly determined for the cellulose powders under evaluation. The values of recovery modulus, RM, of PC and NC were measured using the reported method and the applied apparatus as shown earlier.

Flow rate and repose angle

Funnel technique was employed to determine the flow rate and repose angle of PC and NC samples using a cathometer as mentioned earlier. For the test, a 50 g sample of a given cellulose was poured into a funnel attached vertically at a distance of 10 mm from the horizontal plan where there is a sheet of paper to receive the fallen powder. The height, *H*, of the powder heap is measured by the cathometer and the redius, *r*, of the base of the heap is measured from the area of the paper sheet. Tan repose angle, ϑ, was calculated from the relation: $\tan \vartheta = H/r$.

Water vapor adsorption isotherm

Langmuir water vapor adsorption isotherm characteristics exhibited by PC and NC and their corresponding tablets were studied as shown earlier. For the test, prcisely weighed 5 g powder sample was placed onto a small glass plate and stored at varying conditions of temperatures, *T*, and relative humidity, *RH*, achieved by using different concentrations of salts. The % w/w moisture adsorbed by the sample being investigated was calculated at a pre-determined time intervail.

Swelling index and hydration capacity of celluloses

The swelling index, I_s, for the cellulose powders under study was determined as follows: The tap volume, v_t, of a precisely weighed 1g powder sample was determined using a 10 ml measuring cylinder as mentioned early in the text. The powder sample received 6 ml distilled water and shaken well and then the volume was completed by distilled water and left to equilibrate for 24 h. The powder volume, v_s, was re-determined after 24 h. I_s was calculated from :

$$I_s = v_s - v_t / v_t \times 100 \quad \text{(Eq.1)}$$

The hydration capacity, H_c, of a given cellulose sample was determined as follows:: A precisely weighed 2 g powder sample was suspended in 20 ml distilled water for 1 h. The suspended powder was centrifuged for 5 min at 25000 r/min and the water was drained off. The powder was then precisely re-weighed and the weigt, was denoted as w_c. H_c as calculated from:

$$H_c = (wc - 2) / 2 \times 100 \quad \text{(Eq.2)}$$

Compression and evaluation of tablets

The NC and PC samples were each lubricated with 2% w/w magnesium stearate. A single punch tabletting machine (Riva GMbH) fixed to flat faced punches of 9.5 mm was adjusted to compress tablets of 250 mg mean weight and of 5 kp mean crushing strength and 0.5% w/w mean friability from the the batches formulated with NC. The machine settings were kept constant to compress tablets formulated with PC. Altogether 1000 tablets were compressed from each batch batch.

The machine settings were re-adjusted to compress directly lactose tablets containing 10% w/w NC as disintegrant and each of 0.250 g mean weight and 10 kp mean crushing strength. The batches were lubricated with 2% w/w magnesium stearate. The settings were kept costant to compress the analoge tablet set containing 10% PC as disintegrant. Altogether 300 tablets were compressed from each batch batch The produced tablets tablets were evaluated for the uniformity of weight and thickness, crushing load, friability and disintegration rate.

Results

Physico-chemical properties of PC

Table 1 shows that the data obtained on DP, pH, % sulfated ash and heavy metals for PC were satisfactory. The produced PC powder complies with BP 2010 specifications

Shape and size distribution of PC powder

Fig. 1 shows the electron micrograph of PC particles. The particles are long, fibrous, and of irregular shape. Such particles tend to intermesh and therefore a resistance against the flow of the whole powder bed is created by such intermeshed particles. The log probability plot for cumulative weight % frequency under-size distribution of PC particles is shown in Fig. 2. The geometric mean particle diameter, d_g, calculated from the plot was 121 μm and the standard deviation is 0.88.

Flow rate and repose angle of PC powder

The data given in Table 1 shows that the flow rates measured for the investigated cellulose powders did not exceed 0.3 gs^{-1} (tapping was effected to pursue the powder to flow). The repose angles determined for the powder under investigation were over 50^o. The cellulose powders were cohesive and their particles seemed to be intermeshed.

Water vapor adsorption

Fig.3 shows water vapor adsorption exhibited by the celluloses under investigation.

The processed PC powder adsorb more water than NC powder i.e. it has a larger capacity adsorb moisture. This may be attributed to the larg surface of PC particles to accomodate larger quantity of adsorbed moisture.

Mechanical properties of PC powder

Hausner and Carr's indexes were calculated for the cellulose under the test and the data are given in Table 1. The two cellulose powders almost have the same values of Hausner and Carr's indexes. These values reveals that PC and NC possess poor compression behavior. This is confirmed by the data obtained on the recovery modulus, RM, which are high values. For directly compressible powders such as micro-crystalline cellulose the modulus value does not exceed 5%.

Evaluation of cellulose tablets

Evaluation of tablets

Celluloses could not be compressed into tablets even at high pressures. The powders became compressible after boiling in 0.5% sulfuric. It seems that boiling the cellulose particle in 0.5% sulfuric acid may have changed the particles surface initiating the sites of bonding available on that surface to bond upon compression. In addition, particle grafting by the acid may create bonding sites on particle surface and thus the particles became compressible. It is also possible that boiling cellulose in the acid increased the brittleness of its particles and the chance of generating new surfaces for bonding becomes greater and

therefore hard tablets were produced. However, the crushing loads of the produced tablets were low. It did not reach 4 kp. Table 2 also shows that tablets generally disintegrated within very short times. Direct compression cellulose tablets disintegrated after a relative longer times. Cellulose tablets disintegrated within longer times. It seems that the effect of lubricant on tablet disintegration is more pronounced in case of the tablets prepared with direct compression

Conclusion

Cellulose could be extracted from the hollow stems and leaves of common reed, *Phargmets Australis, F. Graminaceae* The extracted cellulose was found to compare favorably with standard grade of native cellulose. The extracted cellulose was found to be useful as a disintegrant.

Table 1 Some physic-chemical properties of PC determined according BP 2010

Paramter	PC	NC	Acid treated PC
Degree of polym., DP,	630	510	-
pH	6.81	6.97	-
% sulphated Ash	0.26	0.15	-
Heavy Metals (µg/g)	9	3	
Mean diameter , µm			
Arithmatic	188	70	
Geometric	121	90	-
Flow rate, g s^{-1} **	< 0.3		0.3
Repose angle, degree**	> 50.0		50.0
Density, g cc^{-1}*			
App.	1.52	1.50	-
Tap	0.42	0.30	0.33
Loose	0.29	0.32	0.30
Carr's index %	6.45	19.23	8.21
Hausner ratio	1.07	1.24	1.03
% RM	7.00	5.00	6.09
% w/w Moist. Content* (dry wt. basis)	3.50	4.10	-

****Mean of 10 determinations * Mean of 5 determinations**

Table 2 Some physical properties of cellulose and lactose tablets prepared by direct compression and wet granulation, respectively

Parameter	Cellulose tablets		Lactose tablets containing (10% w/wextra-granular disint.)			
	PC	NC	PC*	NC*	PC**	NC**
Weight, g	0.24	0.240	0.275	0.270	0.275	0.279
Thickness, cm	0.25	0.241	0.265	0.265	0.276	0.279
Crushing strength, Kp,	3.40	3.60	3.60	9.10	8.90	9.90
Friability, F,(loss%w/w)	0.98	0.49	0.72	0.15	0.21	0.11

*Directly compressed tablets ** tablets made by wet granulation

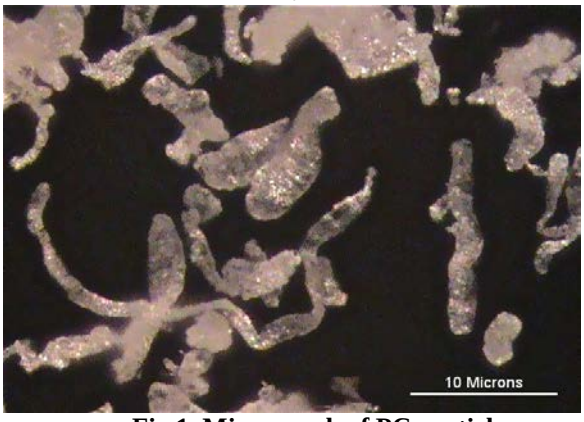

Fig.1 Micrograph of PC particles

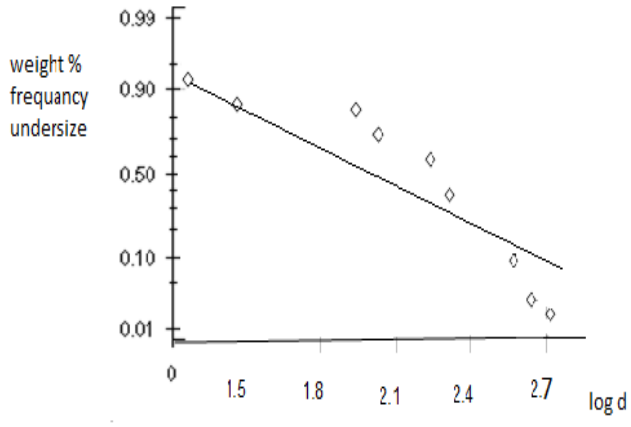

Fig.2 log –probability plot for cumulative weight % 'frequancy' undersize for PC particles

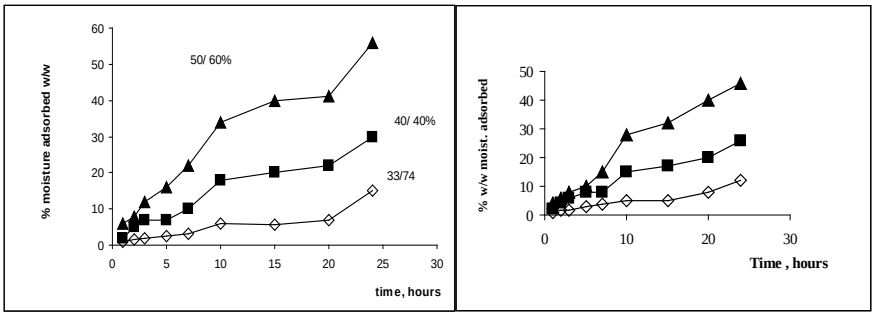

Fig. 3 water adsorption isotherm for PC and NC powder samples stored at varying conditions of temperature, T and relative humidity.

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