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RESEARCH ARTICLE

Study of Disintegration Properties of Common Reed Cellulose

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Summary

Cellulose, CP, extracted from the dry leaves and hollow stems of common reed, Phrahmites Australis F. Graminaceae was evaluated as a disintegrant in direct compression tablets made from calcium carbonate, CC. Maize starch, MZ, was employed as a reference disintegrant. The result showed that the incorporation of a disintegrant in formulation generally negatively affected the mechanical properties of the produced tablet batches. Tablet crushing load decreased and friability increased, respectively. Tablet thickness increased.

The disintegration rate constant, k_d, was found to fairly linearly correlate to C in the studied tablet batches. A relationship expressed as: $k_d = k^o_{d-} \times C$ where k^o_d stands for the disintegration rate constant of the batches containing no disintegrant and x is the efficiency of the disintegrant in the formulation was found to work. The relative disintegration efficiency could be calculated for CP and was 160 % of that of MZ.

Key Words: *Pulping, tabletting, disintegration, relative disintegration efficiency.*

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Common Reed Cellulose' un dağılma özellikleri üzerine çalışma

Özet

Kalsiyum karbonat, CC, ile doğrudan basım yapılan tabletlerde common reed'in kuru yaprakları ve içi boş köklerinden ektre edilen, Phrahmites Australis F. Graminaceae selülozun (CP) dağıtıcı etkisi incelenmiştir. Mısır nişastası (MZ) referans dağıtıcı olarak kullanılmıştır. Sonuçlarda formülasyona dağıtıcı ilavesinin üretilen tabletlerde mekanik özellikleri negatif yönde etkilediği bulunmuştur. Tabletin kırılma kuvveti azalmış ve ufalanma artmıştır. Tablet kalınlığı artmıştır.

Çalışılan tablet serilerinde tablet dağılma hız sabitinin (k_d), C ile doğrusala yakın bağıntısı bulunmuştur. Bu ilişki şöyle ifade edilmiştir: $k_d = k^o_{d-} \times C$

k^o_d: dağıtıcı içermeyen tablet serilerinin dağılma hız sabiti

×: formülasyonda kullanılan dağıtıcının etkinliği

CP'nin MZ'ye göre dağıtıcı etkinliği %160 olarak hesaplanmıştır.

Anahtar Kelimeler: *Ekstract, tablet hazırlama, dağılma, bağıl dağılma etkinliği*

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INTRODUCTION

Disintegration is the process where the deformation, disaggregation and fragmentation of a solid dosage forms take place under the effect of the disintegration medium. It is considered as the rate limiting step of the *in-vitro* availability of the ingredient from their corresponding dosage forms. Disintegration of solid dosage form is multi-factorial dependent process. It depends on the physico-chemical properties of the formulation excipient (s), their activity with the disintegration medium such as solubility, wetting and hygroscopicity (1-3). The pH and temperature of the disintegration medium are affecting factors (5). In addition, the tensile strength, the porosity, pores volume and pore distribution, the type and concentration of the lubricant, binder and disintegrant contributed to formulation are factors (3, 4) controlling, to a great extent, the disintegration process of tablets.

Disintegrants may induce their action via different mechanisms. The early suggested mechanism assumed that the heat of wetting of ingredients in tablets or capsules causes the entrapped air to expand and deform their structures (6). The second mechanism assumes that disintegration proceeds by increasing the capillary forces due to the rapid up-take of the aqueous fluid (5). Cellulose proved to be powerful disintegrants because of their large capacity to absorb and withdraw liquids within short times. Celluloses, due to their fibrous structure, can absorb 6 to 7 times of their weights aqueous fluid (1). Starches have the ability to swell and absorb up to 3 to 5 times its weight liquid. Disintegration of solid dosage forms is the rate limiting step of liberation of drug (s) for dissolution and absorption and building up the drug (s) in blood stream. Some physic-chemical inter-action such as adsorption that may take place between disintegrant and a drug in a tablet or capsule dosage form may however counteract the physiological availability of drug (4).

Direct compression. DC, the simplest tablet manufacture technique requires proper blending of the drug material with a single or a blend of recommended excipients and lubricating the blend just before compression. The key advantages of DC is the reduction of the capital, labor and energy costs. DC is the technique of choice to manufacture of tablets containing heat and moisture sensitive drug substances such as vitamins and antibiotics. However, the flow, the compaction behavior of the blend being compressed, and drug content uniformity in the blend as well as in the final tablets are the main limitations of DC application (7).

The thrust of this work was to evaluate the disintegration property of the cellulose, CP, locally processed from the dry leaves and hollow stems of the Common Reed, *Phargmites Australis*, *F. Graminaceae*. The disintegration property of CP was evaluated next to maize starch, MZ, in direct compression calcium carbonate, CC, tablet systems. The effect of incorporation of a given disintegrant on tablet physic-chemical properties was also studied.

MATERIALS AND METHODS

Materials

The plant material (dry leaves and hollow stems of the common reed) was collected at harvest time which lies between March and June, from Sakaka zone. The analytical grade chemicals namely: sulfuric acid 98% ,, Nitric acid 69%, sodium hydroxide pellets, sodium hypochlorite (bleaching powder), Calcium carbonate, CC, the insoluble DC tabletted based material was obtained from Loba Chemie Pvt Ltd., Mumbai 400005 and magnesium stearate, the lubricant used was purchased from Schalau Chemie, SA, La Jota, 86 08016, Barcelona, Spain. All the chemicals used were of analytical grade.

Methods

CP Processing

The alkaline pulping technique used by Al-Muaikel (8) to process the cellulose from the plant material was adopted with slight modified. The plant powder was first soaked overnight in 3L of 3% nitric acid to destroy and oxidize the lignin and other impurities. The mass was filtered and thoroughly washed with water and then boiled in 3L fresh solution of 3% nitric acid for 1 h. to accomplish the oxidation of lignin and other impurities. The filtered mass was washed to get rid of the acid and boiled in 5L of 10 % sodium hydroxide solution for 2 hours to accomplish the

extraction. The washed mass was subjected to acid hydrolysis using 3L 5 % sulfuric acid followed by boiling in 2L 3% acetic acid solution for 1 h to remove the heavy metals. The solid mass was thoroughly washed with water and neutralized with dilute sodium hydroxide solution. The cellulose mass was bleached using 2L 6% sodium hypochlorite solution for 1 h. The yield was washed and digested in 1.0 % sodium meta-bisulfite for 1 h to get rid of excess chlorine. The yield was washed several times with water, neutralized, dried and stored at screw capped brown powder bottles.

CP Characterization

Chemical properties

The solubility of the processed cellulose in water, dilute mineral acid solutions (hydrochloric, sulfuric, and nitric acid), dilute solution of sodium hydroxide, dilute ammonium hydroxide, acetone, alcohol and chloroform was investigated. The degree of polymerization, DP, the pH of CP we were determined as described in BP 2009. CP was chemically characterized

IR Characterization of CP

The IR spectrum for the processed CP was carried out using pellets prepared from 1mg CP mixed with 100 mg of KBr The pellets were prepared using a press at a force of 10,000 pounds. The infrared spectra were run between 650 and 4000/ cm using a Perkin Elmer IR Spectrometer (Spectrum BX, PerKin Elmer, CA, USA) equipped with the Ommic software (Nicolet Corp., Madison, WI, USA). The resolution, interval length, and number of scans employed were 16, 2, and 16/ cm, respectively.

Physical properties of CP powder

Particle shape and size and size distribution

Particle size was characterized using an electron microscope (BM-180, Boeco, Germany) coupled with a digital camera (S8000fd, Fujifilm Corp., Japan). Sieving technique as used employed to determine the mean particle size as used earlier[9]. Densities (apparent, tap and bulk), hydration capacity, HC, swelling index, and water adsorption isotherm of the CP were evaluated adopting the earlier published techniques (8).

Formulation and compression of CC tablets

Direct compression CC tablets containing 0.0, 2.5, 5.0, 7.5 and 10.0% w/w of a disintegrant (CP or MZ starch) were formulated using simple mixing technique. A precisely weighed amount of CC powder passed through a 90 um sieve was thoroughly mixed with the given weight of a disintegrant (previously sieved through the 90um sieve) in a laboratory drum mixer of suitable capacity. A formulated batch was lubricated with 0.5% w/w magnesium stearate, MS, just before compression. A Riva single punch tabletting machine (Riva S.A, FRG) fitted to bi-convex punches was adjusted to compress tablets of 9. mm ±0.05 mm mean diameter, 250 ±5 mg mean weight, 30 N mean crushing load and 0.1% mean friability, F, from the batch containing no disintegrant. The machine settings were kept constant throughout compressing all the formulated batches. Altogether 300 tablet were compressed from each batch. The produced batches were evaluated for the uniformity of weight and thickness, crushing load, friability and disintegration.

Evaluation of CC tablets

The produced CC tablets were evaluated for the uniformity of weight and thickness. A randomly collected 20 tablets were precisely individually weighed and the corresponding thickness was measure. The mean weight and thickness and the % C.V.s for the weight and thickness variation were calculated. The mean of three such determinations was taken as the mean weight and the mean thickness of the corresponding thickness. The mean crushing load, H, was determined as follows: randomly selected 10 tablets were individually tested for H using a digital automated hardness tester (PTB 11E, Pharma test apprarabeau AG, Siemens strasse, D-63512 Haniburg, FRG). The friability, F, of CC tablets was determined using Erweka friabilator. For the test, a randomly collected 20 tablets sample was brushed and precisely weight. The tablets were fed into the friabilator which was monitored at 25 rpm for 5 min. At the end of the test, the tablets were re-brushed and precisely weighed. F was calculated as: $\% F = (W_1 - W_2) \times 100 / W_1$. The mean of five such determinations was calculated as F of the tested tablets.

Moisture sorption isotherm of CC tablets

Moisture sorption isotherm exhibited by the tablets containing 10% w/w a disintegrant was studied at 40° ±2°C–80% RH using a humidity oven (Gallenkamp Humidity Oven, Weiss Technik UK, Ltd., UK). The 80% RH was achieved by using a saturated solution of a salt. For the test, the weight, W_1, and the mean dimensions (diameter and thickness) of 10 tablets randomly selected from the a given batch were precisely determined and recorded. The tablets were placed in a small flat plastic dish of 8.5 cm diameter. The dish was kept inside the oven exposing the tablets to the oven atmosphere. At a predetermined time interval, the weight of the tablets was determine as W_2. The percent of the water adsorbed by the tablets was calculated as: % sorbed moist. = (W_2 – W_1) / W_1 x 100. The effects of sorbed moisture on the tablet diameter and thickness were examined.

Disintegration time determination for CC tablets

An auto tablet disintegration test apparatus (PTZ Pharma test apprarabeau AG, Siemens strasse, D-63512 Haniburg, FRG) was employed to determine disintegration time of CC tablets. For the test, a randomly collected 6 tablets were individually weighed. Each tablet was put on the screen of the disintegration cup. The disintegration medium used was 0.1N HCl maintained at 37 ±1°C. The time recorded when the all tablet fragments passed through the screen. The men of the disintegration time was recorded. This experiment was carried out in triplicate and the mean was taken as the disintegration time of the tested tablet batch.

RESULTS

Chemical properties of CP powder

IR spectrum

Figure 1 shows IR spectrum of the extracted powder. All the vibration peaks characterizing cellulose molecule are clearly seen in this chart. The vibration peaks at 3440.29/cm and 2898.02/cm characterize the intra-molecular OH stretching including hydrogen bonds and CH and CH_2 stretching, respectively. The peak at 1653.2/cm corresponds to OH of absorbed moisture and the peak at 1470/cm characterizing CH_2 symmetric bending. Vibration peaks at 1375.87/

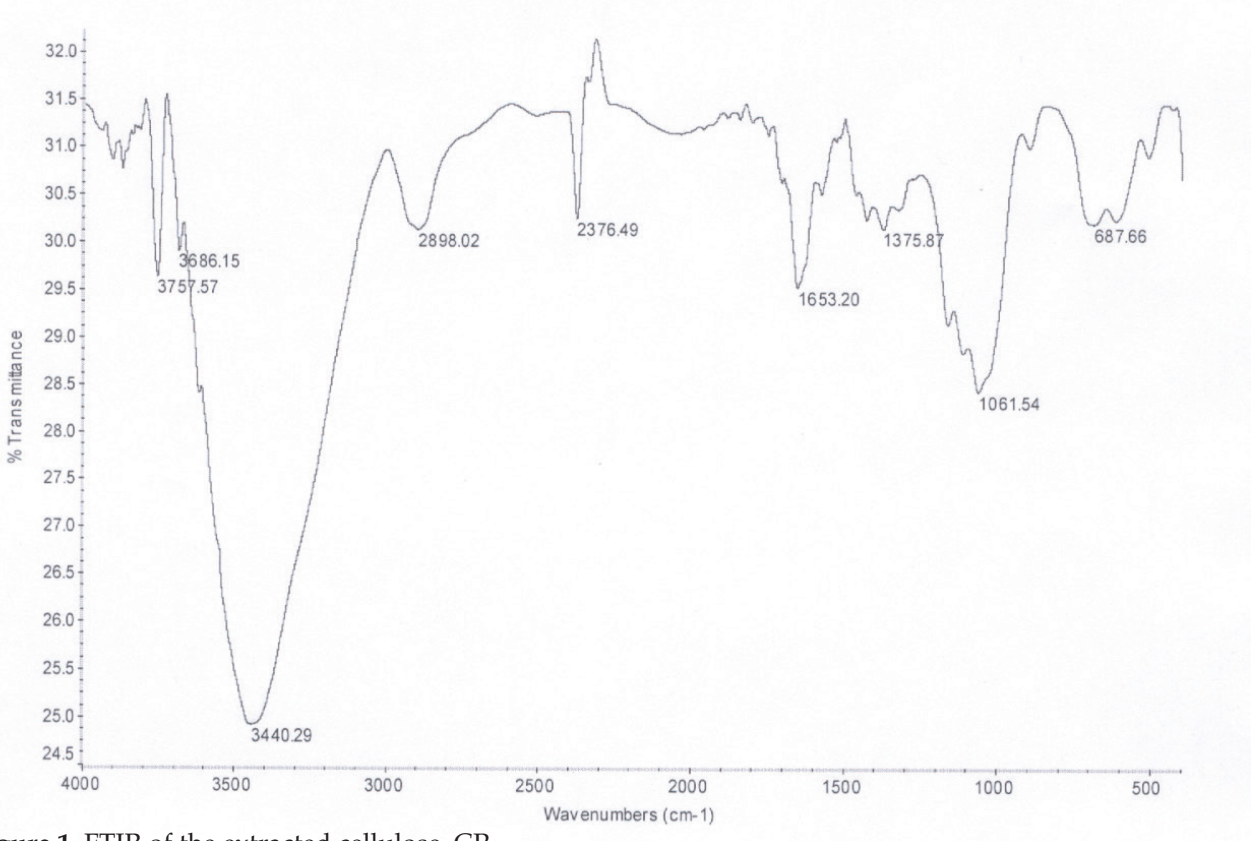

Figure 1. FTIR of the extracted cellulose, CP.

cm and at 1340/cm are due to CH bending; and OH in-plane bending, respectively. Peaks at 1165/cm and 1061.54/cm indicate the C-O-C asymmetric stretching (β-glucosidic linkage) and C-O/C-C stretching, respectively. The asymmetric C-1 (β-glycosidic linkage) out-of-plane stretching is characterized by vibrations peak at 895.8/cm.

Solubility and degree of polymerization

The extracted powder was insoluble in water, dilute acids, alkalis, alcohol, acetone and chloroform. The degree of polymerization, DP, determined using the BP 2009 test was found to be 278.

CP physical properties

Particle shape, size and size distribution

Figure. 2. Shows that CP particles were long and fibrous. The data given in Table 1 show that CP powder was a poorly flowing powder comparative to CC and MZ respectively. Its flow rate was ≤0.3 g/sec and the repose angle was 50°. On the other hand, CC and MZ possessed adequate flow rates. Drying the powders at 60° C for 2 h did not exert any effect on the flow rates and repose angles. CP powder possessed high swelling and high hydration capacity indexes,

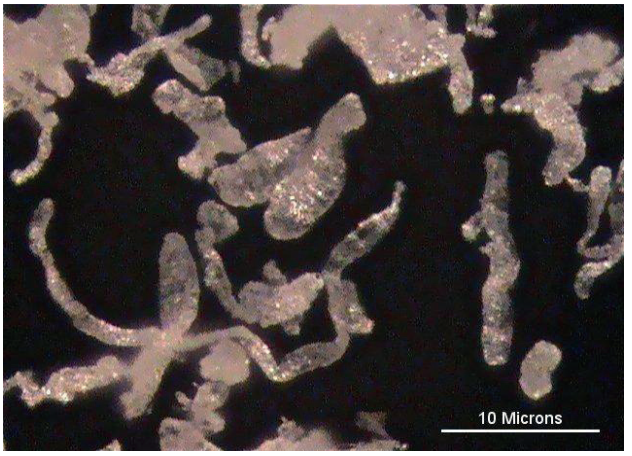

Figure 2. Micro-image of the elongated CP particles

Evaluation of CC tablets

Weight and Uniformity

Table 2 show that the compressed tablets were generally uniform in weight and thickness. Generally, the weight and thickness of tablets increased as the C of the disintegrant incorporated in formulation increased. MZ generated marked effect.

Crushing load and friability

The incorporation of CP or MZ in formulation brought about a negative effect on H, of the tablets. Two

Table 1. Some physico-chemical properties of CC, CP and MZ

Parameter	Material		
	CC CP	MZ	
Degree of polym., DP,		630	–
pH		6.81	–
% sulphated ash		0.26	–
Heavy Metals (µg/g)		9 3.00	–
Mean diameter, µm			
Arithmatic		188.70	–
Geometric		121.90	–
Flow rate, g s^{-1}**	2.1	< 0.30	1.3
Repose angle, degree**	32.0	> 50.00	33.0
Density, g cc^{-1}*			
App.	2.12	1.53	1.60
Tap	0.62	0.30	0.38
Loose	0.29	0.32	0.30
% w/w Moist. Content*			
(dry wt. basis)	2.50	4.10	8.50
Hydration capacity index		2.30	2.40
Swelling index 1.50		1.30	

**Mean of 10 determinations * Mean of 5

Table 2. Physical properties of CC direct compression containing increasing concentrations of the named disintegrants

Disintegrant		weight (g)		Thick. (cm)		Friab. Loss% w/w		Disint. Rate $K_d \times 10^{-3}$
Name	Conc %	mean	CV%	mean	CV%	mean	CV%	
CP	0.0	0.251	12.5	0.241	12.9	0.21	11.1	3.15
	2.5	0.249	8.9	0.244	14.1	0.22	7.3	7.50
	5.0	0.256	6.7	0.248	7.5	0.28	5.6	14.32
	7.5	0.258	5.2	0.251	11.4	0.33	4.8	22.23
	10.0	0.266	2.5	0.259	6.1	0.42	3.4	27.97
MZ	0.0	0.254	13.5	0.241	12.9	0.23	21.1	3.15
	2.5	0.258	8.3	0.246	14.1	0.25	8.3	7.50
	5.0	0.265	4.7	0.252	7.5	0.28	9.6	14.32
	7.5	0.269	4.2	0.269	11.4	0.37	6.2	22.23
	10.0	0.277	1.5	0.272	6.1	0.57	4.1	27.97

distinct phases for the drop in H were recognized as seen in Figure 3. This Figure shows the incorporation of MZ at a concentration at 2.5% w/w caused a slight drop in H of the tablets. Beyond 2.5% w/w, MZ caused dramatic drop in H of the tablets. These observations are recorded for the batches containing. higher concentrations of CP. In other words, a. slight drop in H was seen at 5% of CP and beyond this concentration the dramatic drops took place.

Friability, F, of a given tablets batch increased as the concentration of the disintegrant incorporated in formulation increased. It seems that MZ and CP had no binding effect.

Disintegration time

The positive effect of CP and MZ on the disintegration rate constant of the tested tablet batches is seen in Figure. 4. This plot reveals that the relationship expressed as:

$$k_d = k^o_d \cdot x\, C \qquad \text{Eq.1}$$

where the intercept, k^o_d, and the slope, x, stand for the disintegration rate constant of the control tablets (containing no disintegrant) and the efficiency of

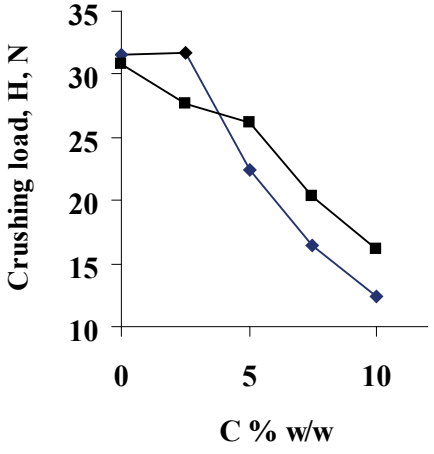

Figure 3. The effect of increasing concentrations, C, of ■, CP and ◆, MZ on the crushing load of CC tablets

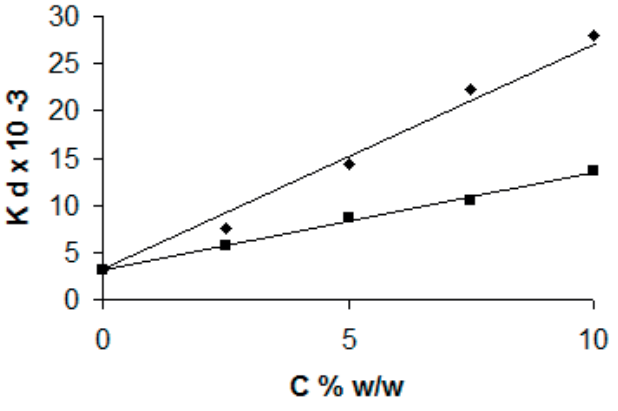

Figure 4. Disintegration rate constant, K_d, as a function of C for CC tablets tested as in Figure 3

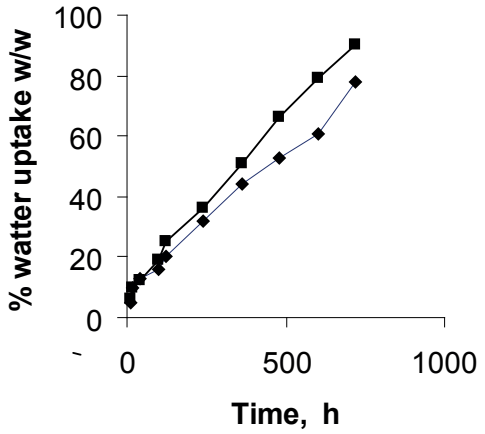

Figure 5. Water adsorption Isotherm exhibited by cc tablets stored in at 40° ±2° 80%RH. Key as in Figure 3.

the incorporated disintegrant is valid. The relative disintegration efficiency calculated for CP was 160%.

Effect of moisture adsorption isotherm on cc tablets

Tablets containing 10% of CP and MZ adsorbed moisture more than the batches containing CP as shown in Figure 5. Table 3 shows the increase in tablet volume due to moisture adsorption was larger in case of CP.

Discussion

The IR spectrum given in Figure 1 shows the stretching peaks characterizing the cellulose molecule. CP powder was insoluble in the common solvents and its degree of polymerization was 630 i.e. complied with pharamcopoeal limit.

It seen in Figure 2 that the particles of the extracted cellulose were elongated and of rough surface. Such particles tend to intermesh and create friction against particles slipping. This explains why CP powder is sluggish powder and had poor flow rate (< 0.3 g/s) and a high repose angle (≥50°).

The compressed CC tablets were uniform in weight and thickness. This may be attributed to the good flow properties of calcium carbonate. This material was admitted as an excellent tabletted based material for manufacturing tablets pellets and lozenges applying compression technique (9).

The two distinct regions seen in the curve of H vs C plot for studied tablets may be due to the isolation effect of the disintegrant on bonding of CC particles. MZ particles had the pronounced isolation. It seems that the incorporation of MZ negatively affected the percolation of the compressed powder. This resulted in a drop in H of the tablets. MZ effect started at 2.5% while that of CP started at 7.5%.

The effects of CP and MZ and friability, F, of the studied tablet batches were in parallel to their effects on H of the tablets.

Tablets containing MZ exhibited more moisture adsorption than that exhibited by the batches containing CP. This may be due to the hygroscopicity of the starch.

It seemed that the high swelling capacity of the CP and MZ was the main factor governing the disintegration process. The disintegration rate constant k_d of the a studied tablet batch was a function of C of the disintegrant in the batch. CP possessed more disintegration power than that of MZ. The % relative disintegration efficiency, % RDE, of CP calculated from the slope of the straight line curves seen in Figure 4. as: % RDE = x [CP] / x [MZ] X (100) was found to be 160%.

Table 3. Physical properties of CC tablets containing 10% of the named disintegrant and stored at 40° ±2°C–80% RH for 10 days.

Disintegrant	% w/w mois.	% increase vol.	vol. % drop in	
			Dt	H
CP	37.6	26	17	20
MZ	36.2	22	13	23

Conclusion

Cellulose extracted from the dried leaves and hollow stems of the common reed has proved to be a powerful disintegrant. It possessed a high hydration capacity and high swelling index. CP induced its disintegration action proceeded via swelling. Processing excipients meeting pharamacopoeal standards from the locally available crude materials is a national aim in developing countries like Egypt. It is a step towards establishing self dependant industry which may create a revenue supporting the economy.

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