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SOME PHYSICOCHEMICAL PROPERTIES AND APPLICATION OF A-CELLULOSE FROM PENNISETUM PURPUREUM AS A DISINTEGRANT IN TABLET FORMULATION

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ABSTRACT

This study was undertaken to process a locally available tablet disintegrant from Pennisetum purpureum inorder to reduce importation of such pharmaceutical excipients into the country. Some physicochemical and flow properties of the processed α-cellulose were studied. The α-cellulose was also employed as disintegrant in some tablet formulations. Some of the physicochemical and flow properties evaluated were, moisture content, bulk density, packed density, Carrs compressibility, angle of repose and Hausner quotient. The tablet properties studied were, disintegration time, hardness, friability and dissolution rate. The prepared α-cellulose had poor flow properties since it recorded high values of angle of repose, Carr's compressibility and Hausner's quotient. All the batches of tablets passed the weight uniformity test. Tablets formulated with the α-cellulose showed lower disintegration and dissolution times than the tablets containing maize starch as disintegrant. Hence the processed α- cellulose could be employed as a locally available substitute to maize starch as a tablet disintegrant.

KEYWORDS:

INTRODUCTION

Many of the early researches in the area of tablet disintegrants were primarily with materials that were known to swell or expand when wetted with water. The idea was that these agents would swell when exposed to the gastric fluids and exert sufficient mechanical pressure from within the tablet to cause it to break apart into small fragments and thus hasten the vital act of absorption by increasing the surface area of particles (List and Muazzam, 1979). The disintegration of solid dosage forms is a vital process since it is considered the rate limiting step of drug dissolution which contributes to drug absorption and excretion (Wagner, 1961). Disintegration takes place when the magnitude of the static pressure generated into the tablet as a result of accumulating disintegration medium exceeds the magnitude of the bonds between particles and granules, which hold the tablet structure (Lowental, 1972). An ideal disintegrant should be tasteless, able to oppose the effect of binders, able to initiate the rupture of the tablet, physiologically inert, penetrable by water and fluids into tablet core and compatible with all types of active ingredients. The mechanisms whereby tablet disintegrants induce their effects have been studied extensively (Gissinger and Stamm, 1980; Guyot-Hermann and Ringard, 1981; Shangraw and Mitreveg, 1980). Over the years starches, celluloses and their derivatives have been widely employed as disintegrants. In this study, an attempt was made to evaluate the α-cellulose produced from Pennisetum purpureum as a disintegrant in sodium salicylate tablets using maize starch as a standard disintegrant for comparison.

EXPERIMENTAL MATERIALS

The following chemicals were used as supplied by their manufacturers: sodium chloride, concentrated hydrochloric acid (36 %) (M & B, England); chloroform, methanol (Vickers), concentrated sulphuric acid (Merck); iodine solution, Millon's reagent, Fehling's reagent, sodium hypochlorite, lead subacetate (BDH, England).

METHODS

Collection of the plant material

The aerial parts of the plant Pennisetum purpureum were collected from farms in Nsukka, Enugu State of Nigeria. The plant was identified and authenticated by Mr. K. K. Agwu of the Department of Pharmacognosy, University of Nigeria, Nsukka.

The plant parts were cut into small pieces of about 2 cm and sun dried in a hot air oven at 50 °C for 12 h.

Preliminary phytochemical Tests

The tests were carried out to qualitatively detect the constituents of the plant using the phytochemical methods of Harborne (1981).

Preparation of α-cellulose from Pennisetum purpureum (Schum)

Since the natural fibre contain a reasonable quantity of lignin β- and α-cellulose, these have to be removed to obtain a high quality of α-cellulose from the plant fibres.

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De-lignification of the fibre

Small dried pieces (about 2 cm) of the aerials parts of the plant were heated to 60 °C for 8 h, with 10 % solution of NaOH in a round bottom flask to remove the lignin. The alkali was completely removed from the mass by several washings with water. The material was heated with 0.1 N HCl and heated to 50 °C for 3 h. It was then washed with water until neutral to litmus paper.

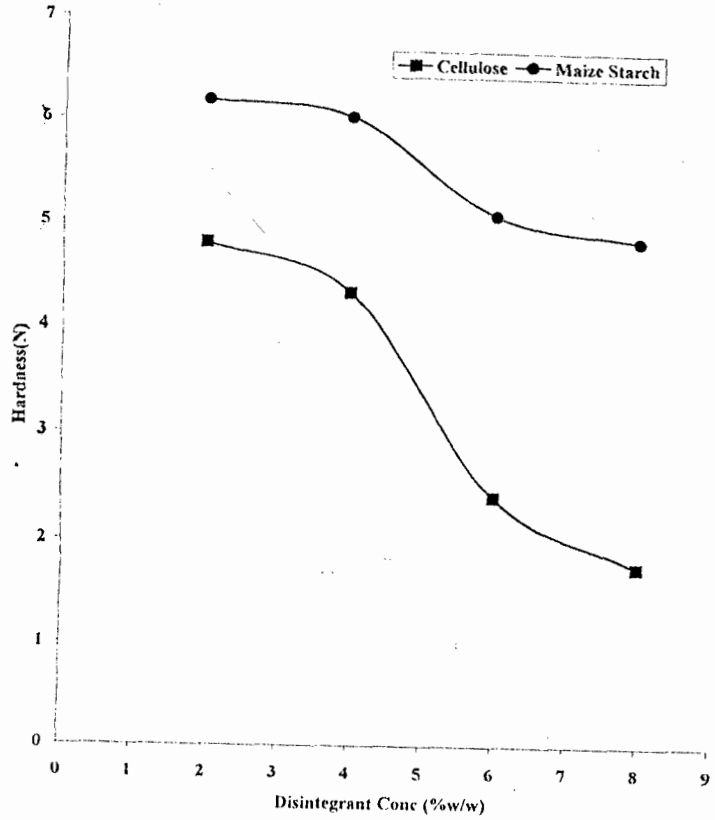

Fig.1. Effect of disintegrant onthe hardness of sodium salicylate tablets

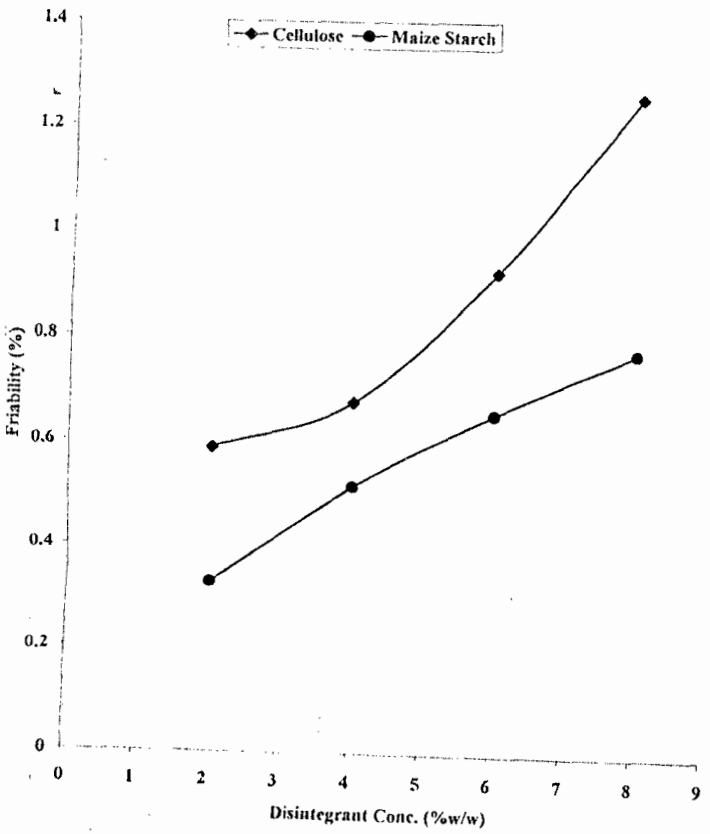

Fig.2. Effect of disintegrant on the friability of sodium salicylate tablets.

Bleaching

The pulp cellulose was placed in a round bottom flask with 4 L of 0.4 % sodium hypochlorite. This was maintained at 60 °C for 30 min. The partially bleached pulp was washed several times until neutral.

Removal of Beta and Gamma cellulose

The pulped material was boiled in a 17.5 % NaOH solutions for 1 h. This solubilized the Beta and gamma cellulose. The alpha cellulose that remained was washed several times with water until neutral to litmus.

The alpha cellulose was further bleached by placing it in a solution of 0.4 % sodium hypochlorite and heating at 50 °C for 30 min. The cotton like cellulose was washed several times with water until neutral to litmus to remove traces of the bleaching agent. The cellulose was dried using hot air oven at 50 °C for 1 h. The dried cellulose was milled using an attrition mill (Retch ski, Germany). The dried powder obtained was passed through a 250-mm aperture sieve. The yield of the product was calculated from the following formular:

$$\frac{\text{Weight of product}}{\text{Original weight of material}} \times \frac{100}{1}$$

Solubility of the prepared α-cellulose

The cellulose (1.5 g) was introduced in a beaker and 10 ml of cold water added and stirred. The procedure was repeated using hot water, dilute NaOH, dilute HCl and chloroform. The solubilities were observed.

The cellulose (3 g) was also introduced in a beaker containing 10 ml of 17.5 % NaOH. The mixture was stirred and the solubility observed.

Moisture content of the prepared cellulose

The cellulose (4 g) was introduced into a previously weighed evaporating dish. It was placed in an oven at 105 °C and dried to constant weight. The moisture content was then calculated.

Determination of Bulk Density, packed Density and % compressibility

Ten- (10) g of the cellulose was introduced into a 100 ml measuring cylinder. The bulk volume was noted. The cylinder was then tapped until a constant volume was obtained (packed volume). The bulk density packed density and % compressibility were then calculated.

Tablet Formulation

The required quantities of sodium salicylate powder, lactose and disintegrant were weighed and mixed properly to form a homogenous powder mix. A mucilage of acacia was made by dissolving 20 g of acacia powder in 100 ml of water. Adequate quantity of the binder solution was added to the powder mix (the

volume of the mucilage was noted), until a damp mass was formed. The damp mass was passed through a sieve No. 10 and then dried in the oven at 50 °C for about 1 h. The dried granules were further passed through sieve No. 20. The percentage of fines produced was determined using sieve No. 52. The fines were mixed with the lubricant (weighed magnesium stearate) and incorporated into the coarse granules and mixed for 5 min. The granules were compressed into tablets using an f_3 tabletting machine (Manesty Machines, Liverpool) set at 50 kgf. The formula for the tablet formulation is shown in Table 1.

Evaluation of Tablets

Disintegration Time

The B.P 2001(Anonymous) method was employed using the Erweka disintegration unit (Erweka, Germany). The medium for the disintegration was 100 ml of 0.1 N HCl. The temperature was maintained at 37 ± 1 °C throughout the test. Five tablets from each batch were placed in turn in the five baskets (No. 90 mesh) and the unit switched on. The time taken for the tablets to disintegrate was recorded for each batch and the mean taken as the disintegration time of the batch.

Hardness test

The Monsanto hardness tester was used. The tablet was placed between the spindle and anvil of the tester. The knurled knob was turned gradually and gently until the tablet was held slightly in position by the spindle and anvil. The reading pointer was adjusted to zero on the scale. Pressure was applied by turning the knob until the required pressure was read in terms of kilogram force (kgf) on the scale. The average of twenty determinations on each batch was recorded.

Friability Test

The Gallenkamp mechanical shaker was used. Ten tablets from each batch were randomly selected and weighed (Sautorius, England). The tablets were placed in a sample bottle and fixed on the shaker. The tablets were subjected to shaking for 5 min, and then removed, de-dusted and weighed. The loss in weight was calculated.

Dissolution Rate

The beaker method was employed using 500 ml of 0.1 N HCl as the dissolution medium. The temperature of the dissolution medium was maintained at 37 ± 1 °C. At predetermined intervals, 5 ml aliquot was diluted to 100 ml. Colour development was accomplished by adding 3 drops of $FeCl_3$ to the solution. The absorbance was read at 540 nm using an Sp6-spectrophotometer (Pye-Unicam, England).

Calibration Curve for Sodium Salicylate

A 1 mg/ml stock solution of sodium salicylate was prepared by dissolving 100 mg of sodium salicylate in 100 ml of 0.1 N HCl. Serial dilution was performed to yield a concentration range of 0.1 – 1.0 mg %. Colour development was achieved using 3 drops of freshly prepared $FeCl_3$ solution. The absorbances of the solutions were determined in a Sp6-spectrophotometer at 540 nm.

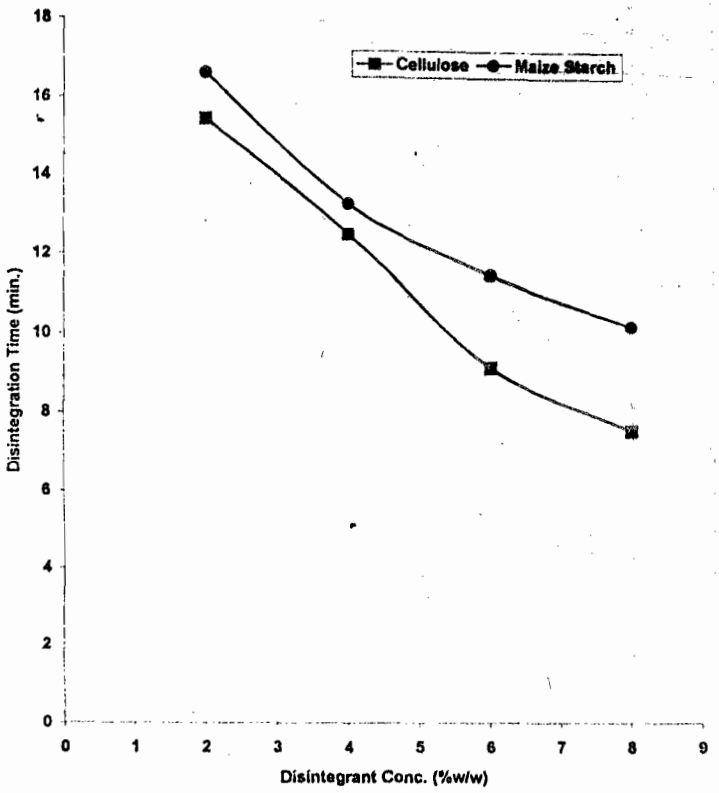

Fig.3. Effect of disintegrant on the disintegration time of sodium salicylate tablets.

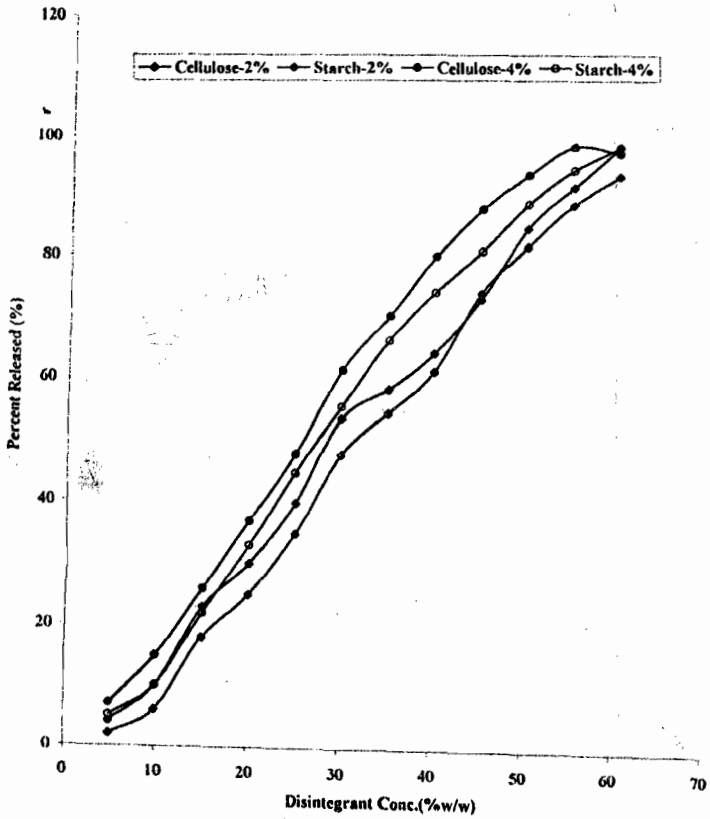

Fig.4. Dissolution profiles of sodium salicylate tablets formulated with 2%w/w and 4%w/w disintegrant.

Table 1

Some physicochemical properties of the prepared cellulose

Physicochemical Property	Remarks
Colour	Cream
Odour	Odourless
Texture	Fibrous
Flow rate	No flow
Angle of repose	48.99 °
Yield	32.8 %
Solubility	
Cold water	Insoluble
Hot water	Insoluble
Dilute NaOH	Insoluble
Dilute HCl	Insoluble
Chloroform	Insoluble
Moisture content	5.75 %
Density	
Bulk density	0.1155
Tapped density	0.1971
% Compressibility	41.34 %
Hausner quotient	1.71
Phytochemical analysis	
Tannins	Absent (-)
Proteins	Absent (-)
Starch	Present (++)
Carbohydrates	Present (++)
Oils	Absent (-)

RESULTS AND DISCUSSION

Physicochemical properties

Table 1 shows some of the physicochemical properties of the cellulose from P. purpureum. The phytochemical tests revealed the presence of starch and carbohydrate. Since the yield of cellulose from the plant was on the high side, the production of cellulose from P. purpureum should be encouraged since the raw material is cheap and available locally. The α-cellulose proved to be insoluble in both hot and cold water and in all other organic and inorganic solvents investigated.

The prepared cellulose powder showed very poor flow characteristics since it blocked the funnel orifice completely. This blocking of funnel orifice could be attributed to the small size of the cellulose particles. It has been reported that frictional and vanderwaal forces predominate at particle sizes of less than 150-μm (Martin et al, 1969). The high values of angle of repose, Carr's compressibility and Hausner's quotient further supports the poor flow properties of the cellulose powder. Hence the prepared cellulose powder might be said to be cohesive.

Usually for good flow, angle of repose, Carr's compressibility and Hausner's quotient values should not be more than 20^0, 28% and 1.20 respectively (Hausner, 1967). The increase in tapped density is advantageous since it indicates better packing behaviour. The cellulose passed the official test on moisture content since the Martindale extra Pharmacopoeia (Anonymous) specified not more than 7 % loss on drying for powdered cellulose at 105 °C.

Weight Uniformity

All the tablets passed the B.P 2001 weight uniformity test because none of the batches showed deviation greater than ± 5 % for tablets weighing more than 250 mg. The coefficient of variation were low varying from 1.02 – 1.32 for all the tablet batches.

Hardness

Tablet hardness decreased as disintegrant concentration increased as shown in Fig. 1. This decrease was more pronounced with tablets formulated with cellulose. The poor compressibility and flow of the cellulose may be responsible for this observation. Hardness is a function of cohesiveness between the granules, which is increased during compression as a result of melting and subsequent solidification of the binder. Disintegrants reduce this cohesion by preventing intragranular contact during compression. At equal concentrations tablets containing maize starch were harder than that of cellulose indicating that maize starch may be more compressible than the cellulose. Maize starch could also have acted as an auxiliary binder since it normally gels on swelling in the presence of water (Lowental and Burrus, 1971).

Friability

Fig. 2 shows an increase in tablet friability with increased concentration of disintegrant in the tablet formulation. The increase in disintegrant concentration reduced the breaking strength of the tablets formulated. Since friability is a function of tablet hardness, softer tablets will be more friable than the harder ones. Tablets formulated with the prepared cellulose were more friable than that of maize starch at the same

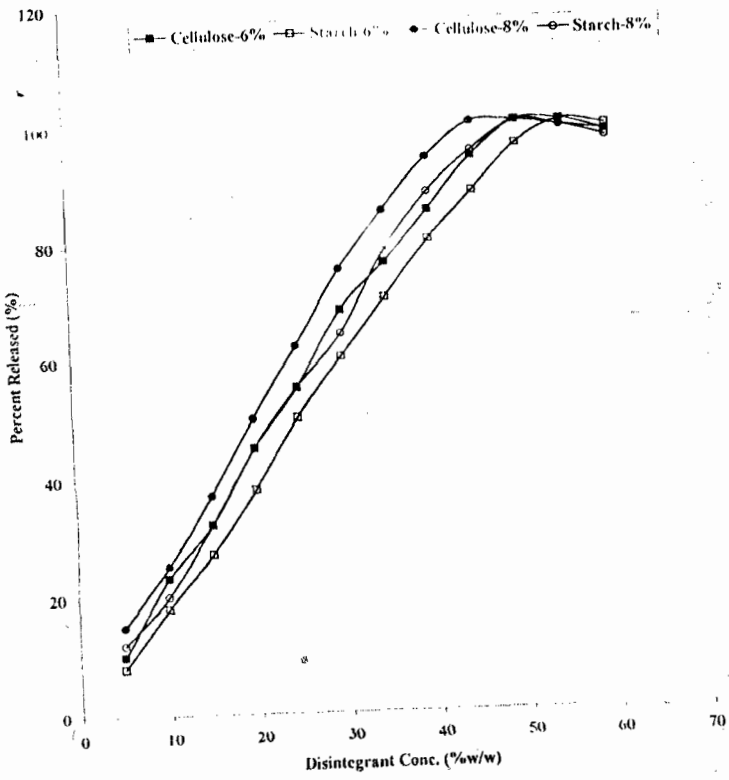

Fig.5. Dissolution profiles of sodium salicylate tablets formulated with 6%w/w and 8%w/w disintegrant.

concentration. This may be attributed to the poor compressibility of the cellulose. Based on the widely acceptable range of 0.8 – 1.0 % (Esezobo and Pilpel,1961), tablets formulated with 8 % cellulose failed the friability test. On the other hand, all the tablets formulated with maize starch at all the given concentrations passed the friability test.

Disintegration Time

Fig. 3 shows that the disintegration time decreased with increase in disintegrant concentration. Also tablets formulated with cellulose gave lower disintegration times. The low disintegration time of the cellulose might be attributed to the fibrillar nature of the cellulose, which is highly hydrophilic. This could speed up water penetration by suction causing swelling of the disintegrant particles and rupture of the entire tablet (Guyot-Harmann,1992).

Dissolution Rate

The dissolution profiles of the tablets are presented in Figs. 4 and 5. In general, dissolution rate increased as disintegrant concentration increased. Tablets containing cellulose had higher dissolution rate than the tablets formulated with maize starch at the same concentrations. This is further illustrated with the T_{50} % and T_{70} % values (Table 2), which showed higher dissolution rates with tablets formulated with cellulose as disintegrant.

CONCLUSION

Since the tablets formulated with the cellulose had lower disintegration time and shorter dissolution rate than that of maize starch, it could be used as locally available substitute to maize starch as a tablet disintegrant.

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