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Physicochemical properties of two brands of pregelatinised starch from maize cultivated in Nigeria

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Abstract

The aim of this work was to investigate the physicochemical properties of two brands of pregelatinised starch processed differently from the same starting material. Particle size distribution, microscopy, photomicrography, flow properties, compactibility and purity tests were carried out on the brands [Evansgel® powder (EGP) and Evansgel® flakes (EGF)] processed by a company in Nigeria from locally cultivated maize. A commercially available pregelatinised starch (PS) and a traditional starch (CS) were employed for comparison. 68% each of EGP and PS were retained on sieve size 100 and their particle size ranged between 30 and 130μm. The packing and flow characteristics of EGP and PS such as bulk densities of EGP and PS were the same, being 0.374g/cm^3 while their tapped densities were 0.548 and 0.521g/cm^3 respectively. EGF on the other hand had most of the particles (98%) retained on sieve number 40 and the particle size range was between 50 and 200μm. Compact of PS and EGP had hardness of 3.5 and 5.9N respectively and their friability was 6.57 and 4.55% respectively. EGF had a friability value of 100% and could not form good compacts. It was concluded that processing techniques influenced their physicochemical properties. These differences are likely to play a role in the use to which these excipients can be put in pharmaceutical formulations. EGP and PS showed better similarities in their physicochemical properties than EGF with either of them and consequently EGP may be a good substitute for PS as a tablet excipient.

Keywords: Pregelatinised starch; Physicochemical properties; Tabletting excipients

Introduction

Excipients are increasingly being recognised for the critical role they play in pharmaceutical products. Excipients provide specific and special functionalities in formulations and contribute enormously to the efficacy of a pharmaceutical product. They bind granules together under the stress of direct compression, control the release of active ingredients, help tablets disintegrate and dissolve efficiently and influence absorption. Formulators of finished dosage forms depend entirely on excipient manufacturers to provide substances that are uniform in chemical and physical characteristics, offer processing benefits and meet the highest quality standards. Starch is a natural polymer that has found use as the most common excipients in pharmaceutical solid dosage forms. It is a natural, renewable and abundant excipients ingredient that can meet the needs of formulators better than the

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synthetic alternatives (Heinze, 2003). Starch is highly versatile and allows for manipulation and customisation.

Pregelatinised starches are excipients that have been processed chemically and or/ mechanically. The process ruptures all or part of the starch granules in the presence of water and subsequently dried. Compendial pregelatinised starch is available as a fully or partially pregelatinised starch. Pregelatinised starches offer a number of benefits both in processing and performance. They enhance flow and compressibility and can be used as binders in direct compression as well as in wet granulation. They can easily be processed since they swell in cold water and therefore reduce processing time and cost compared to traditional starch paste preparation. The technology employed in the processing of the pregelatinised starch determines its quality such as level of purification, particle size and size distribution, densities and flow properties, parameters that cannot be ignored by any formulator (Heinze,2003). In this work the physicochemical properties of two brands of pregelatinised maize starch produced by different technologies (Evans Medical PLC, Nigeria) were investigated. Native maize starch and a commercially available maize starch were used for comparison.

Experimental

Materials. The materials used in this work include the following: Maize starch, (Roquette Chemical Industries, Hamburg, Germany); Pregelatinised starch (Repasack, London), two brands of pregelatinised starch - Evansgel® flakes (EGF) and Evansgel® powder (EGP) obtained from Evans Medical PLC, Nigeria as donation.

Methods

Microscopic examination and photo micrograph of samples. A 0.020g quantity of each of EGP, EGF, PS and CS was weighed on an electronic analytical balance (Explorer, Ohaus Corporation, USA) suspended in 0.5mL of distilled water and placed on a microscope slide. This was mixed with a droplet of glycerine and iodine. The resultant suspension was examined under the Light Microscope (M 1000-D, Japan) fitted with a calibrated eye piece. The magnifications employed were x100 and x400. The microscope was then fitted with a camera (Olympus OM-1) and photographs were taken at different positions by adjusting the knob. The film used was from Agfa Company and printing was carried out on Kodak photographic paper. The procedure was repeated for all the samples at the two magnifications.

Particle size analysis. The particle size distribution was investigated using a nest of Apex sieves, arranged in decreasing order of aperture size. A 100g quantity of the sample was placed on the topmost sieve (mesh size 40) and the nest was subjected to mechanical shaking for 10minutes. The size distribution of the samples on sieve size 40, 100 and 200 mesh were then determined. The experiment was repeated four times for all the samples under investigation.

Hydration capacity determination. The method described by Shangraw *et al* (1980) was used. A 2.5g sample was placed on a 50ml centrifuge tube, whose weight was previously known. 20ml of distilled water was added and shaken vigorously for 3 minutes. The sample was centrifuged for 10 minutes at 1000rpm (Labofuge Heraeus Christ, Germany). The aqueous supernatant was carefully decanted. The tube and the sediment were re-weighed and the weight of the centrifuge tube subtracted. Three determinations were made for each sample and the average taken. Hydration capacity was determined as the amount of water absorbed by 1g of powder after suspending in 20mL of distilled water and centrifuging (Bertoni *et al.,* 1995).

Bulk density and tapped density determination. A 20.00g quantity of sample was weighed on an electronic balance. The powder was gently transferred into a 100ml measuring cylinder. The volume occupied by the powder was taken and the bulk density was calculated from the expression:-

Bulk density (gm^{-3}) = mass of the powder / volume occupied .....(1)

Tapped density was similarly obtained from the above expression after gently tapping the powder in the cylinder on a flat table lined with thin foam. The tapping was done by raising the cylinder to a height of 6.00cm and allowing it to fall on the flat surface. The tapping continued for 300 times when no observable decrease in volume of the powder occurred. The volume was noted. Four determinations were made from which the average volume was used.

Moisture content determination. The electronic moisture content balance (Ohaus, USA) was used at 4watts heat intensity rating. A 20g quantity of Sample was placed in the sample chamber and the temperature set at 105^0C. The moisture content value was displayed after the set time.

Determination of angle of repose. An open ended plastic cylinder (internal diameter of 4.92cm, outer diameter of 5.60cm and the height of 10.7cm) was used. The cylinder was placed on a graph paper on a flat base and filled with a sample of the powder. On slowly raising the cylindrical tube, the powder mass flowed out to form a conical heap on the base. The height, h, of the cone formed and the radius, r, of the base of the cone were measured. The experiment was repeated four times and the average value was obtained for each sample. The angle of repose,θ, was calculated from the expression

$$\theta = \tan^{-1} h/r \quad \text{.....(2)}$$

Flow properties. Hausner's quotient (Hausner, 1967) and Carr's compressibility (Carr, 1970) are useful for predicting the flow characteristics of materials. Hausner Quotient of a powdered material is the ratio of the tapped density (ρ_t) to the bulk density (ρ_b) of the material.

$$\text{Hausner's equation} = \rho_t / \rho_b \quad \text{.....(3)}$$

While the Carr compressibility is obtained also from the bulk and tapped densities using the expression

$$\text{Carr's Compressibility (\% compressible)} = \rho_t - \rho_b / \rho_b \times 100 \quad \text{.....(4)}$$

The flow rates of the samples were determined by the funnel method (Okafor, 1990). A 25.00g sample of the material was allowed to flow under gravity from a funnel of 1cm diameter and the time taken for the powder to flow through the funnel was noted. The test was repeated four times and the average of the results taken and used for the determinations.

Determination of protein and nitrogen content. The protein content was determined using micro Kjeldahl nitrogen method of the Association of Analytical Chemists (AOAC 1980). The protein content was calculated using the formula:

$$\% \text{ protein} = \{(a-b) \times \upsilon \times 14 \times c \times 100 \times 6.25\} / (d \times e) \quad \text{.....(5)}$$

(where a = titre value for the digested sample, b = the titre value for the blank, c = volume to which the digest is made up with water, d = aliquot distilled, e = weight of the sample, while 6.25 is the conversion factor from percent nitrogen, υ = volume of 0.1N HCl used).

Determination of fat content. A 5g quantity of sample was suspended in 20ml of distilled water and heated to boiling. A 60 ml aliquot of boiling 4N hydrochloric acid was added and boiling was continued for 5minutes. The reaction was cooled to 25^0 to allow for complete precipitation of fatty acids. The precipitate formed was filtered through Whatman No.1 filter paper. The residue was washed with distilled water and dried at 40^0 in

an oven for 12 hours. This was extracted with 20ml of petroleum ether for 1 hour in an extraction unit. The solvent was evaporated and the residue dried and weighed. The lipid content of all the samples was determined.

pH determination. This was determined on a 2%w/v suspension of the samples using a pH meter (Jenway, USA)

Redispersion time. The modified method of Oyegunju (1991) was used. The time taken for the sediment to re disperse on shaking was taken as the re-dispersion time. Average of four determinations was taken for each sample as the re-dispersion time.

True density determination. The liquid displacement method was used. A 25ml pycnometer (Raytheon, UK) was used to measure the true density. A 5.0g sample was introduced into the pycnometer that was half filled with acetone. The pycnometer with its content was placed in a desciccator fitted with vacuum pump to allow for de-aeration for 10 minutes. The pycnometer was then filled with acetone completely. The excess acetone was wiped off using cotton wool. The true density of the sample was calculated from the equation:

$$\rho s = \rho e\,(w2-w1) / V\rho e-(w3-w2) \quad ....(6)$$

(Where ρs = true density; ρe = specific gravity of acetone; w1 = weight of pycnometer; w2 = weight of pycnometer and the powder; w3 = weight of pycnometer + powder and acetone; V = volume of pycnometer).

Preparation of tablet compacts. Compacts of the samples were made in a Manesty-16 station tabletting machine at an average weight of 600mg.A 12.7mm (½'') punch tip diameter was used and the compression pressure was about 60N. The samples were compacted as obtained. Compact of Avicel was also made.

Results and Discussion

Particle size distribution. The particle size and particle size distribution are represented in Table 1. The size distribution of EGP and PS were similar to each other (majority of particles, 68% were retained on mesh size 100) but different from those of either EGF or CS. Larger percentage of the particles of EGF were retained on the 40 mesh. Significant particle size and particle size distribution of powders produce variations in the flow rate, angle of repose, bulk properties and hardness as well as dissolution of compacts. Particle size distribution is particularly important in direct compression process as they influence the flow and quality of compacts. It seems from the particle size of EGF that further milling and size reduction may be necessary to be useful as an excipient in direct tablet compression. The order of decreasing particle size of the samples was EGF>EGP= PS> CS Plates 1 to 4 showed the photomicrographs of EGF, EGP, PS and CS.

The EGP, EGF and PS did not assume any definite regular shape (plates 1 to 3). Some were big and flake–like while others were small. It appeared that the starches in plates 1-3 lost their original shape and size during modification and processing and now assumed different shapes. The sizes of EGF were bigger than those of EGP and PS. Both EGP and PS showed some similarities in their shapes and sizes. The CS granules had not lost their regular shapes and size as can be seen in plate 4. None of the regular shapes and sizes observed in plate 4 was seen in plates 1-3 and this may indicate that EGF, EGP and PS were completely hydrolysed.

Physicochemical characteristics. Proteins and fats found in starch above certain limit can affect their effectiveness. It is therefore necessary to control the content of these items during the manufacture of starch and its derivatives. Table 2 shows the values of protein in the samples to be in the range of 0.35 to 1.08%. The highest value of 1.08%

protein content was obtained with CS while EGF had the lowest value of 0.35%. The corresponding values of EGP and PS were 0.41 and 0.66 % respectively. The ranking of the protein content value was of the order CS>PS>EGP >EGF.

The fat content values showed that the highest value of 5.79% was obtained in EGF while the lowest value of 4.35 was obtained in PS. The corresponding values for CS and EGP were 4.78 and 5.62 respectively. This is an indication of the level of purification of the starches with respect to fats, which if present in high quantity can affect the quality of the sample. There was no significant difference in the values obtained as to adversely affect the quality of the powders as tablet excipients.

Moisture content plays a significant role in the stability of a pharmaceutical product. High moisture content tends to encourage bacterial growth and chemical degradation. Excipients that are to be used in direct compression or in the final stage of dry blending for tabletting are thus expected to have low moisture content. Table 2 also shows the values of the moisture content of the samples. EGF had the highest moisture content while EGP and PS had the lowest values of 7.21 and 7.88% respectively.

At the moment there are no studies known to us that provide useful explanatory theory for the polysaccharides hydration. Wenzel and Kala (1980) studied the effects of hydration of excipients on the energy distance diagram and on tablets characteristics. The pharmaceutical application of hydration substance may be linked to disintegration ability. The hydration capacity of the starch samples are presented in table 2. EGF, PS EGP and CS have values of 15.37, 4.25, 3.34 and 1.69 respectively.

Packing and flow characteristics. The bulk and tapped densities of the starch samples are presented in Table 3. The bulk density of EGP and PS was 0.374g/cm^3 while those of EGF and CS were 0.061 and 0.472 g/cm^3 respectively. The order of decreasing tapped density of the samples was CS >EGP> PS >EGF.

The Hausner's quotient and Carr compressibility index which were derived from the bulk and tapped densities of the materials are also presented in Table 3. The Hausner quotient values obtained for the samples were between 1.39 and 1.8 for the samples. The Carr's Compressibility Index values were 28.21, 30.38, 31.75 and 44.55% respectively for PS, CS, EGP and EGF. Hauser's quotient and Carr's compressibility are used to predict the flow of granules and powders. Nyqvist and Nicklasson (1985) predicted that values of Hausner' quotient and Carr's compressibility above 1.2 or 23% respectively do not indicate good flow behaviour. Based on the above parameters the starches did not possess good flow properties.

Vesalsco *et al.* (1995) reported that angle of repose values above 50^0 is an indication of a poor flow characteristic of a powder but no relationship has been established between angle of repose and the flow properties of powder. The angle of repose values when ranked in decreasing order were $36.5 > 29.1 > 28.72 > 28.07^0$ for EGF, PS, CS and EGP respectively.

Table 3 also shows the flow rate of the various starch samples. PS had the highest flow rate of 12.2g/sec. The flow rate of EGP was almost half of that of PS while CS had a value of 1.3g/sec. EGF could not flow through the orifice. The large particle size of EGF is the likely explanation for its inability to pass through the orifice. The flow rate of the samples can be ranked in the decreasing order PS >EGP >CS.

Characteristics of sample compacts. The profile of the sample compacts are as shown in Table 4. It was difficult to obtain compacts of target weight of 310mg for CS and EGF while it was possible for PS and EGP. Avicel is a known excipient in direct compression

and was also compressed. The hardness of the compacts were highest with Avicel PH 101 assuming a value of 7.2kgf while the values of 1.5, 3.5 and 5.9kgf were obtained for CS, EGP and PS respectively. The results also show that the compacts of EGF, EGP and PS did not disintegrate within the observation period of 48 hours. These materials rather absorbed water and swelled to about 300 times the original thickness while the weight increased by about 700 times during the period. This behaviour was probably due to the amylopectin content that tends to be activated in the presence of water even for the loosely compressed EGF. The gain in weight was probably due to the water up-take capacity. Chaplin (2002) had described this type of water as the loosely bound water which can be removed by centrifuging.

Table 1. Particle size analysis of the samples (particle size distribution

Fraction in:	EGF	EGP	PS	CS
40 mesh	80	8	7	0
100 mesh	12	68	68	2
200 mesh	8	24	25	98
Particle size (μm)	50-200	30-130	30-130	2-28

Table 2. Some properties of the samples

	EGF	EGP	PS	CS
Protein content %	0.35	0.41	0.66	1.08
Nitrogen content	0.06	0.066	0.106	0.173
Fat content %	5.79	5.62	4.35	4.78
pH of 5% susp. (25°c)	4.86	6.26	7.02	4.78
Moisture content (%)	10.68	7.21	7.88	8.840
Hydration capacity	15.372	3.34	4.25	1.69
True density g/cm3	1.23	1.34	1.34	1.38

Table3. Flow and packing characteristics of samples

Sample	Density (g/cm^3)		% Compressibility	H. quotient	Flow rate (g/s)	ø
	Bulk	Tapped				
EGF	0.061(0.006)	0.11(0.003)	44.55(0.74)	1.8(0.68)	No flow	36.5 (2.65)
EGP	0.374(0.004)	0.548(0.005)	31.75(0.33)	1.47(0.56)	6.5(1.33)	28.07(3.02)
PS	0.374(0.005)	0.521(0.003)	28.21(0.40)	1.39(0.49)	12.2(2.54)	29.0(3.27)
CS	0.472(0.008)	0.678(0.006)	30.38(0.60)	1.44(0.76)	1.3(0.97)	28.73(2.78)

Values in parentheses are standard deviations, ø = angle of repose

Table 4 Characteristics of compacts.

Parameters	Samples				
	EGF	EGP	PS	CS	MCC
Mean weight (mg)	400 (23.1)	610 (3.55)	609 (2.38)	568(2.7)	605(2.77)
Hardness (kgf)	Nil	3.5	5.9	1.5	7.5
DT (minute)	None	None	None	1	2
Friability (%)	100	6.57	4.5	93.86	1.89
Tensile strength (N/m^2)	Nil	0.756	0.1279	0.0324	0.1557

The numbers in parentheses are standard deviations

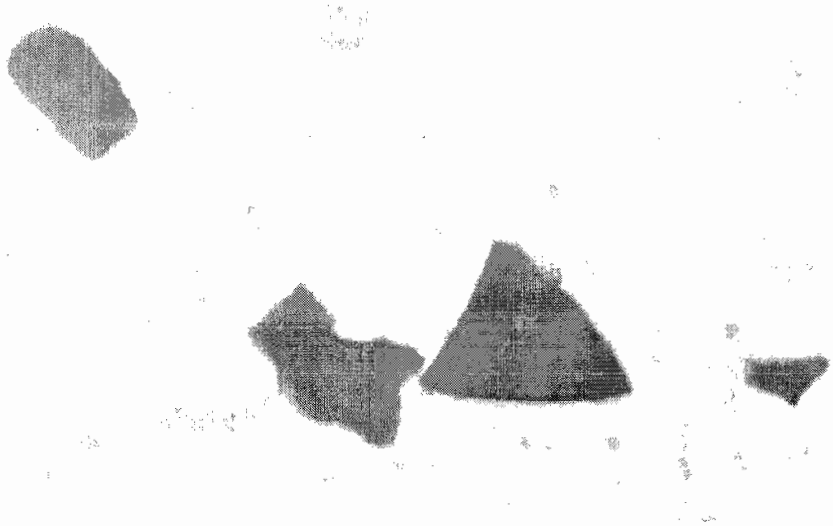

Plate 1. Photomicrograph of Evansgel flakes. Magnification X400

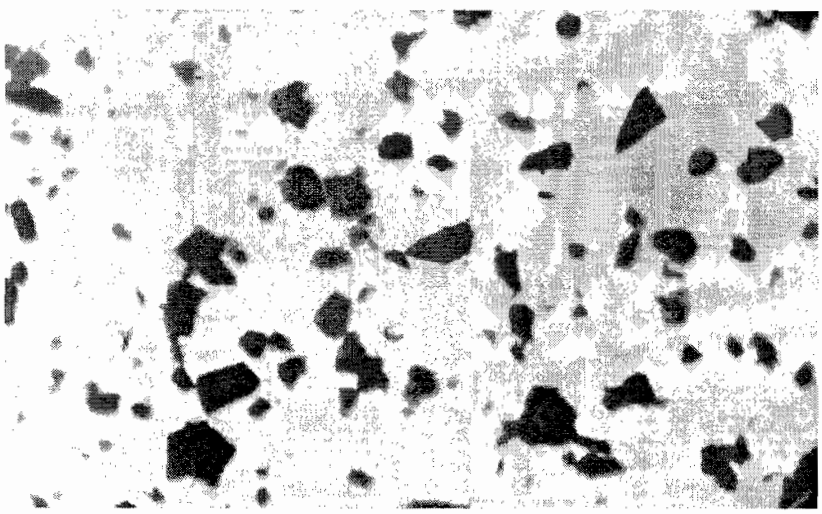

Plate2 . Photomicrograph of Evansgel powder. Magnification X400

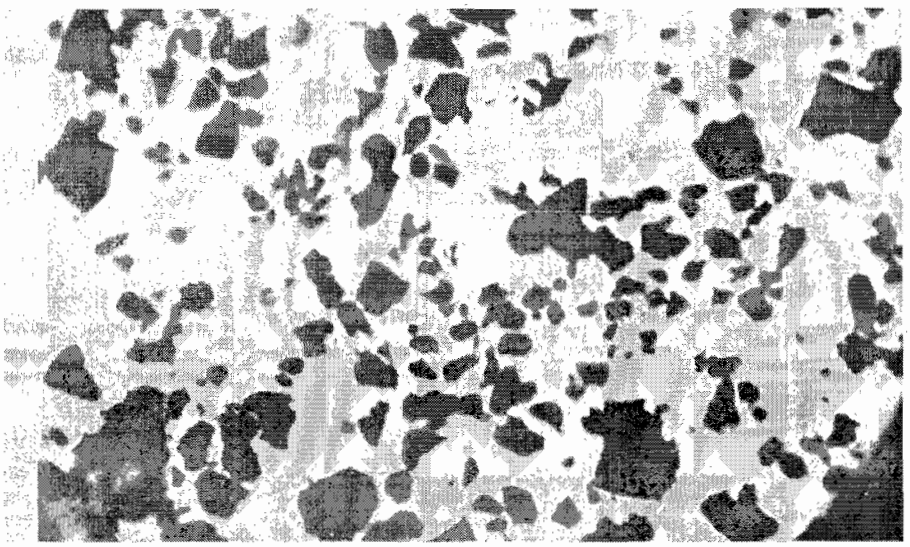

Plate3 . Photomicrograph of pregelatinised starch powder. Magnification X400

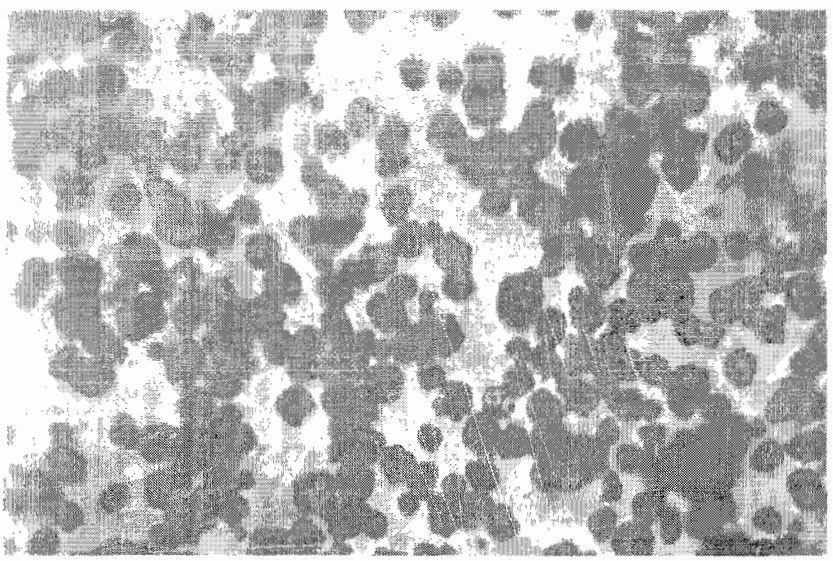

Plate 4. Photomicrograph of corn starch. Magnification X400

Conclusion

It can be concluded that the two brands of pregelatinised starch, EGF and EGP showed some differences in their physicochemical properties. EGP and PS showed more similarities in their physicochemical properties than with either EGF or CS. The photomicrographs suggest absolute gelatinisation of the modified starch samples as they have lost the shape and structure that can be seen in the native corn starch (CS). EGF did not have good flow characteristics and may not be found suitable in direct compression where flow is a very important consideration. EGP and PS exhibited similarities in most of the properties

and thus EGP may find use as tablet excipient where PS is used. EGF may find use as tablet excipient, preferably as a binder in wet granulation technique and as a suspending agent. Work is on going to investigate the properties of granules and tablets made with EGF and EGP as binder in some tablet formulations using the various granulation methods.

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