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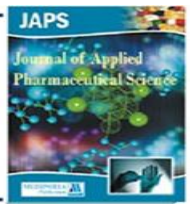

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Effects of Phosphate Modified and Pregelatinized Sweet Potato Starches on Disintegrant Property of Paracetamol Tablet Formulations

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ABSTRACT

Starch is the commonest disintegrant used in tablet formulation. Modified starches, also called starch derivatives, are prepared by physically, enzymatically or chemically treating native starch, thereby changing the properties of the starch. The aim of the study was to investigate the disintegrant property of Pregelatinized and Phosphate modified sweet potato starches in comparison with the native sweet potato starch and maize starch BP in paracetamol tablet formulation.Pregelatinized starch was prepared by drying 8% (w/v) sweet potato starch mucilage whilestarch phosphate was prepared by phosphorylation of sweet potato starch with monosodium phosphate dehydrate solution. The starches were evaluated for moisture content, swelling capacity, hydration capacity and flow properties while the tablet were assessed for disintegration time and dissolution rate using standard methods. Results obtained showed 82.22% yield of Pregelatinized starch and 83.33% of starch phosphate. The modified starches showed hydration capacities of 2.36 and 2.05 and swelling capacities of 6.25 and 4.48 respectively for PGS and SP, values that doubled those produced by unmodified sweet potato starch and maize starch B.P. The tablets formulated using 5.0%w/w concentrations of phosphate starch, pregelatinized starch, unmodified sweet potato starch and maize starch BP as disintegrant, respectively, disintegrated at 0.53min, 0.82min, 1.06min and 1.26min. Phosphate starch and Pregelatinized starch derived from sweet potato displayed superior disintegration properties than the unmodified starch and maize starch B.P.

Keywords: potato, Pregelatinized starch, Starch phosphate, Disintegrant, Paracetamol

INTRODUCTION

Starch is a common name applied to a white, granular or powdery, odourless, tasteless, complex carbohydrate, $(C_6H_{10}O_5)_x$, abundant in the seeds of cereal plants and in bulbs and tubers. Molecules of starch are made of hundreds or thousands of atoms, corresponding to values of *x*, as given in the formula above, that range from about 50 to many thousands. Native starch denotes untreated starch (International Starch Institute, 2009). The commonest starches employed include maize, cassava, yam, potatoes and plantain starches. They have very good tablet excipient properties especially in wet granulation method of massing and screening (Esezobo, 1986). It uses are based mainly on its adhesive, thickening, gelling, swelling and forming properties (Kunle *et. al*, 2003).

Sweet potato (*Ipomoea batatas*) is a dicotyledonous plant that belongs to the family Convolvulaceae. Its large, starchy, sweet-tasting, tuberous roots are important root vegetable. The plant is a herbaceousperennialvine, bearing alternate heart-shaped or palmately lobed leaves and medium-sized sympetalous flowers. The edible tuberous root is long and tapered, with a smooth skin whose color ranges between purple, red, brown, and beige. Its flesh ranges from beige through yellow, orange, and purple. They grow well in many farming conditions. Nigeria is the second world largest grower of sweet potato after China,which produced about 3.3millon tones in the year 2009.

Tubers of sweet potato are potential starch source that are useful in food, textile, and pharmaceutical industries. In tableting, starch is useful as diluent, binder, disintegrant and lubricant due to its physiochemical properties and relative inertness (Odeku and Itiola, 2007).

The use of starch is however limited by it poor functional properties of flow, compressibility and compatibility. Several modifications have been shown to improve these functional properties (Bos *et. al*, 1992). Modified starches, also called starch derivatives, are prepared by physically, enzymatically or chemically treating native starch, thereby changing the properties of the starch. The different types of modifications include heat gelatinization, enzymatic hydrolysis, acid hydrolysis and other various forms of chemical modifications (Okafor *et. al*, 2000).

The aim of this study is to investigate the disintegrant property of Pregelatinized and Phosphate modified sweet potato starches in comparison with the native potato starch and maize starch BP in paracetamol tablet formulations.

MATERIALS AND METHODS

Paracetamol powder (BDH chemicals Ltd Poole England), Maize starch (BDH chemicals Ltd Poole England),Lactose (BDH chemicals Ltd Poole England), Magnesium stearate Talc (BDH chemicals Ltd Poole England), Talc (BDH chemicals Ltd Poole England) N/50 Iodine (BDH laboratory suppliers, Poole BH151TD England) and sweetpotato tubers(from Baga Market in Maiduguri, Borno State) were all purchased from commercial source.

Sample Collection and Identification

Sweet potato tubers were purchased at Baga station market Maiduguri, Borno State. The sample was identified by Prof. S.Sunusi a Taxonomist from the Department of Biological science University of Maiduguri.

Extraction of starch

The sweet potato tubers were washed, peeled, cut into smaller pieces, weighted and then ground with a local grinding machine. The grounded material was diluted with water and sieved with a muslin. 0.1N NaOH was added to the slurry filtrate (to deproteinize the starch as well as to neutralize the slight acidity) and allowed to stand for about 3hours. Supernatant water was decanted off carefully, and fresh water was added again to wash the starch, the supernatant water was then decanted off after three hours (3hrs). The starch sediment was then air-dried.The weight of the potato tubers and the weight of starches obtained were noted. The percentage yield was calculated;

$$\text{Percentage yield} = \frac{\text{Final weight of starch}}{\text{weight of sweet potato tubers}} \times 100$$

Preparation of PGS

The method of Musa (2005) was adopted; 100ml of water was added to 450g of powdered starch place in stainless steel bowl tarred of 5.625L volume. Hot water (60^0C) was then added with continuous stirring until the tarred mark was reached. The bowl was then put on the heating mantle and heated with continuous stirring of the content until translucent mucilage was formed. The content was air dried on a stainless steel tray,the flakes were milled and passed through 180µm sieve mesh. The final weight was noted and the percentage yield calculated.

$$\text{Percentage yield} = \frac{\text{Final weight of gelatinized starch}}{\text{Total weight of potato starch}} \times 100$$

Preparation of SP

The method of Prasanthi *et. al*(2010) was adopted, 300g weight of sweet potato starch was dispersed into ½ mole of monosodium phosphate dehydrate solution, and stir for about 10minutes.The swollen starch was then filtered and the filter cake residue was air dried.The dried lumps were the heated in a vacuum oven at 135^0C for 3hours. The dried mass was then milled and sieved through 180µm sieve mesh. The final weight was noted and the percentage yield calculated using the above equation.

Solubility Test

The solubility of the starch in cold water and 95% ethanol were determined according to the methods of Muazu *et. al* (2011) and the results recorded.

Iodine Test

The BP (2002) starch identification test was adopted; 1g of starches was boiled with 15mls of water. After cooling to 1ml of the mucilage, 2drops of 0.1N iodine solution was addedand the colour change noted.

Angle of repose

A 30 g sample of the granules was poured into a plugged glass funnel with the tip, 10 cm above the flat surface of the bench. The granules were allowed to flow freely through the orifice of the funnel to form a heap whose height and diameter were determined. The angle of repose was calculated using the equation below:

$\text{Tan } \theta = h/r$

Where h = height and r = radius of circular heap

Bulk Density

A 30g weight of each of the starch to be used as disintegrant was weighted and poured in to a 100ml measuring

cylinder and the volume was recorded. The bulk density was then calculated.

$$\text{Bulk Density (BD)} = M / V$$

Where M is mass and V is volume

Tapped Density

A 30g weight of each of the starch was weighted and poured into a 100ml measuring cylinder and tapped on a hard surface 30 times from about 2cm height and the volume was recorded.

$$\text{Tapped Density (TD)} = M / V$$

Where M is mass and V is volume

Carr's Index

Carr's Index (%) was determined using the following relationship

$$\text{C.I.} = (\text{TD} - \text{BD}/ \text{TD}) \times 100$$

Hausner's ratio

Hausner's ratio was determined using the following relationship

$$\text{H.R} = \text{TD}/\text{BD}$$

Where TD is Tapped density, BD is Bulk density

Hydration Capacity

A 1g weight of starch was in placed 15ml plastic centrifuge tube, 10ml distilled water was added and then closed. The contents were shaken for 2 min then allowed to stand for 10 min and immediately centrifuged at 1000 rpm for 10 min in a bench centrifuge. The supernatant water was decanted and the weight of the wet starch was recorded. The hydration capacity was determined using the equation below:

$$\text{Hydration capacity} = \frac{W_S}{W_D}$$

Where W_S and W_D are the weights of the sediment formed and weight of the dry sample respectively

Swelling capacity

The tapped volume occupied by 10g of each starch (*Vd*)in a 100ml measuring cylinder was noted. The powder was then dispersed in 85ml of distilled water and the volume made up to 100ml with more water. After 18hours of standing, the volume of the sediment, (*Vw)* was estimated and the swelling capacity was computed as;

$$\text{Swelling capacity} = Vw - Vd$$

Moisture Content

A 3g weight of each starch was heated at 135^0C using moisture analyzer (Sartorius, Germany); andthe reading was recorded.

PREPARATION OF GRANULES

Using the wet granulation method, the active ingredient was dry mixed with the diluent and the disintegrant for 5 minutes.

The disintegrants were added intragranularly at four different concentrations of 2.5, 5.0, 7.5 and 10 % w/w to form the 4 batches each. A 5% w/v mucilage of the binder was made and added into the dry mixed powder which was massed for 5 minutes. The damp mass of the different batches was then force through a 1.7mm sieve and allowed to dry. The granules were then passed through a 1.6mm sieve and dried

COMPACTION OF GRANULES INTO TABLETS

The granules were then mixed with the Extragranular excipients(0.2%w/w magnesium stearate and 2%w/w Talc). The granules were compressed using 12.5mm punch and die set at compression pressure of 6-metric tonne using single punch tablet press (Manesty Ltd, England)

EVALUATION OF TABLETS

Crushing strength

Crushing strength (KgF) of five (5) tablets randomly selected from each batch was determined using Hardness tester (TBH 100 Erweka, Germany). The result was recorded.

Friability Test

Ten tablets from each batch were weighted and then put into the friabilator (JM0004-MG-001 Erweka, Germany) and then rotated at 25rpm for 4minutes. The tables were then collected dusted and re-weighted. The percentage lost in weight of the original tablet was calculated for each batch and recorded.

Disintegration Test

Disintegration times of six tablets randomly selected from each batch were individually determined in B.P. specified disintegration apparatus (Erweka type ZT3, Germany) containing purified water maintained at 37 ± 1^0C.The time that took the tablets to pass though the wire mesh of the disintegration apparatus was taken as the disintegration time of the tablets.

Dissolution Test

Using dissolution test apparatus(DT 700 Erweka, Germany), 900ml phosphate buffers (pH 5.8) maintained at 37± 0.5°C as dissolution medium, with the paddle was caused to rotate at 50rpm, a tablet from each batch was placed into the dissolution medium and sample appropriately collected at time interval.

The withdrawn sample was diluted with and the analyzed using U.V spectrophotometer (Beckman CoulterDU520, Germany) at wavelength of 257nm. The absorbance was recorded and the amount of drug dissolved was calculated using standard paracetamol calibration curve.

RESULTSAND DICUSSION

The percentage yield of sweet potato tubers was 20.47% which is within the range as specified by the international starch institute (Isah *et. al,* 2010). The percentage yield for the PGS and SP were 82.22% and 83.33% which were all high. The high yield could have been occasioned by the production of mucilage from

starch to rapture some crystalline-like, microscopic granule which was neither an addition nor reduction to the final weight (Musa, 2005)

Table. 1: Percentage Yield of Starches.

Starch	Yield(%)
SPS	20.47
PGS	82.22
SP	83.33

All the starch powders where practically insoluble in water and 95% alcohol at room temperature. The powders also turn blue black on addition of iodine solution which confirmed the presence of starch.

An angle of repose 18.19^0,36.03^0,37.57^0,and 38.97^0 were obtained for SP, PGS, SPS and MS respectively which all fall with the required range for pharmaceutical powders which is $25\text{-}45^0$(Musa *et. al*, 2004), except that of the phosphate starch which is lower and indicates a better flow property. Angle of repose has been used to characterized the flow properties of powders, it also related to inter-particulatefriction or resistance to movement between particles (shiihii *et. al*, 2011).

Table. 2: Physicochemical Properties of Starch Powder.

Properties	Phosphate starch	Pregelatinized starch	Sweet potato starch	Maize starchBP
Iodine test	Positive	Positive	Positive	Positive
Solubility	Insoluble	Insoluble	Insoluble	Insoluble
Angle of repose(^{0})	18.19	36.03	37.57	38.97
Bulk density (g/ml)	0.55	0.60	0.50	0.46
Tab density (g/ml)	0.64	0.68	0.59	0.56
Carr's index (%)	14.06	11.76	15.24	17.86
Hausner's ratio	1.18	1.13	1.18	1.00
Moisture	4.05	11.53	12.94	11.03
content(%)	2.05	2.36	1.19	1.75
Hydration capacity	4.48	6.25	3.75	0.96
Swelling capacity				

The Hausner's ratio and Carr's index give a preview on the degree of densification, which could occur during tableting, the lower the Hausner ratio, the lesser the tendency for densification to occur. As the values of these indices increase, the flow of the powder decreases (Staniforth, 1996) and more likelihood of producing tablets with more weight variation(Olayemi *et. al*, 2008).

The hydration capacity of the starch indicated 2.36, 2.05, 1.91 and 1.75 respectively for the PGS, SP, SPS and MS with the PGS having the highest. The common feature of all the theories of disintegration is that penetration of water (or liquid medium) must precede disintegration and this can be assumed by the hydration capacity and porosity (Caramella, 1991).The swelling capacity of PGS and SP were also the highest which indicates good disintegration properties. The higher swelling ability (Table 2) could lead to the absorption of large quantities of water into the tablet mass and the subsequent generation of a higher swelling force (Guyot-Hermann, 1992), which would initiate the active mechanism of disintegration at a faster rate than for natural starch disintegrants.

The lower moisture content of the modified SP indicate it less prone to microbial attack, less ability to interact with drugs that are moisture sensitive and high ability to absorb water to facilitate disintegration, although the moisture content of modified starches were within official limit 4% to 12% (Olayemi, 2008). High moisture may lead to activation of enzymes and proliferation of micro-organisms.

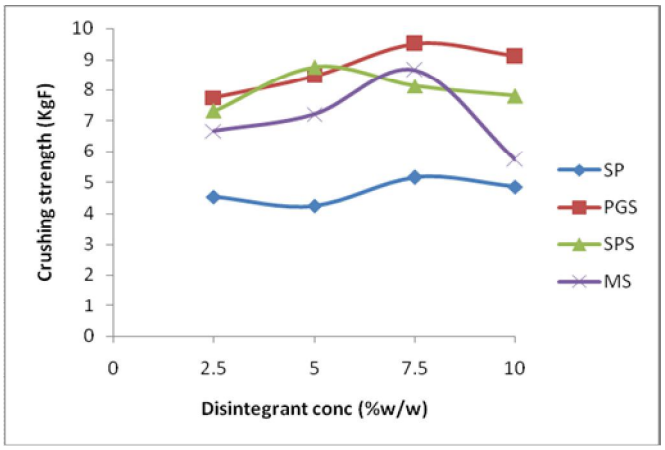

Fig. 1: Effect of disintegrant concentration on the crushing strength of the paracetamol tablets formulated.

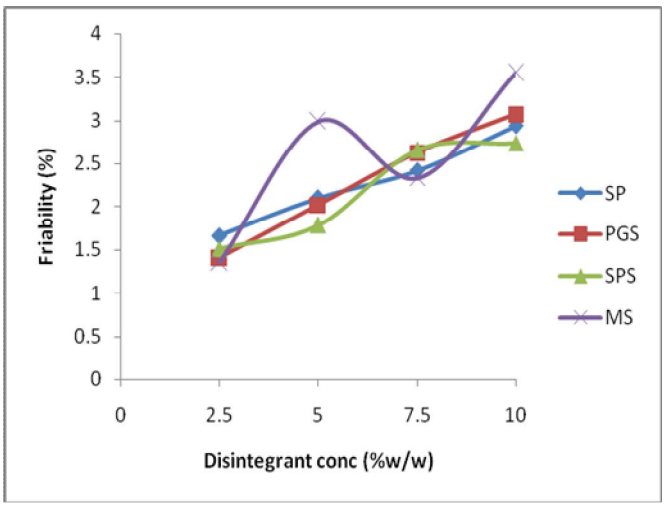

Fig. 2: Effects of Varying Disintegrant on Disintegration Time.

The crushing strength of the tablets was shown in figure 1. They all fall within the required specified range, with the tablets produce from the PGS having a relative high crushing strength. The ranking was PGS>SPS>MS>SP. There was slight increase in the crushing strength of the tablets as a result of increase in disintegrant concentration. This might be due to the disintegrant partaking in formation of bonds as a result of wet binder (Musa, 2005). The results of friability test are shown on figure 2. Increase in disintegrant concentration lead to increase in friability for all the starches.

The disintegration time of the batches of tablets are represented in figure 3, tablets produce from the modified starches (i.e. SP and PGS) show a relative lower disintegration time compared to that of the unmodified or maize starchBP. Action of this modified starches are rapid and extensive swelling. They are

highly efficient at low concentration because of their greater swelling capacity. Thus, this reflects a good disintegration profile of both SP and PGS.The ranking of disintegration might be as a result of higher swelling power (table 2) observed for modified starches.

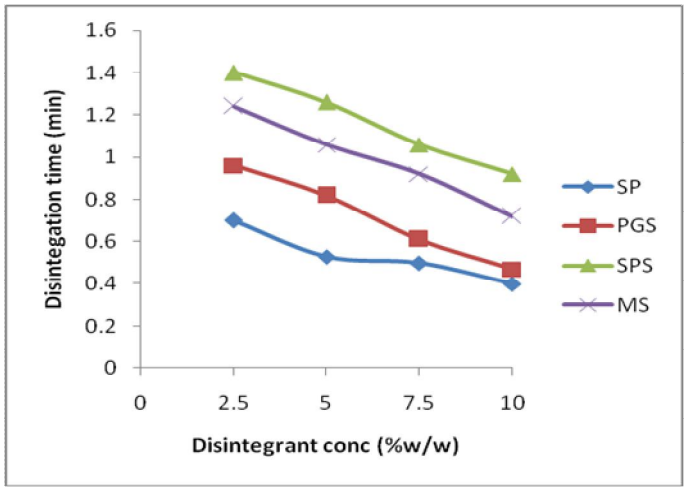

Fig. 3: Effect of disintegrant concentration on disintegration time.

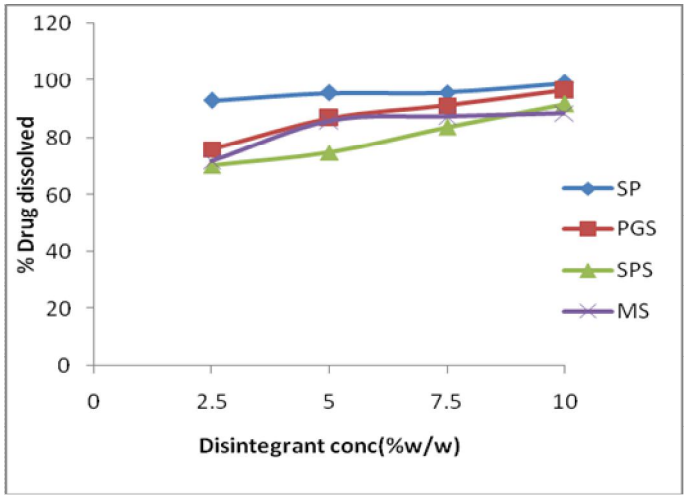

Fig. 4: Effect of varying disintegrant concentration on percentage drug dissolved at 30 minutes.

All the batches of tablets shows good dissolution profile, the ranking is SP>PGS> MS>SPS which can be attributed to their relative higher swelling and hydration capacity. At all concentration, they all release 10% or more of their active ingredient.

CONCLUSION

The study showed that the modified Sweet Potato starch (i.e.SP and PGS) have a better disintegrant property than the unmodified SPS and MS. due to their relative high swelling and hydration capacities. Therefore the modified sweet potato starches can be as an alternative disintegrant in tablet formulation. They can be used when faster disintegration is desired.

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