

THE ROLE OF ACID TREATED SWEET POTATO STARCH (MICROCRYSTALLINE STARCH) ON DISINTEGRANT PROPERTY OF PARACETAMOL TABLET FORMULATION.

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ABSTRACT

Acid treated sweet potato (*Ipomea batatas*) starch (microcrystalline starch) was evaluated as a disintegrant using paracetamol tablet formulation and compared with similar concentrations of untreated sweet potato starch and maize starch B.P. Concentrations of 2.5, 5, 7.5 and 10%w/w disintegrant were incorporated as intradisintegrants in the study. The sample starch powders used were characterized and the various properties of the starch powders compared. Wet granulation method was adopted for the production granules. The compacts formed (tablets) were subsequently subjected to quality control tests; uniformity of thickness and diameter, uniformity of weight test, crushing strength, friability test, disintegration and dissolution rate tests. The results obtained indicated that acid treated sweet potato starch has a better disintegrant property compared to untreated sweet potato and maize starch B.P. By implication, acid treated sweet potato starch can therefore be used as an alternative disintegrant to maize starch B.P.

Key words: Acid Treated Sweet Potato Starch, Disintegrant, Starch, Paracetamol, Tablet

INTRODUCTION

Starch is an important pharmaceutical raw material found in abundance in many growing plants, it is popularly used in solid pharmaceutical dosage forms as diluents, binders, glidants and disintegrants. Starch is obtained from both cereals and tubers^[1]. Native starches are produced through the separation of naturally occurring starch from either grain or root crops, such as maize, cassava and sweet potato. The raw starches produced still retain their original structure and characteristics and are called "native starches". For those characteristics which are unattainable with native starch, modified starch can be used for other industrial applications through a series of techniques; chemically, physically, and enzymatic modification. Thus, modified starch is a native starch that has been changed in its physical and/or chemical properties^[2].

Sweet potato (*Ipomea batatas*) is a tuberous-rooted perennial plant usually grown annually. It is a tropical and sub tropical plant which can adapt to more temperate climates. It can be cultivated in the 30° and 40° latitudes in both hemispheres^[3].

Disintegrants constitutes one of the six important major excipient categories of tablet bioavailability agent^[4]. A tablet would be useless if after being swallowed does not disintegrate to release the active medicament. The active ingredient must be released from the tablet matrix as efficiently as possible to allow for its rapid absorption. A disintegrant is a

substance, or mixture of substances added to tablet to facilitate its break down or disintegration after administration. Substances or materials used as disintegrants are starches, clays, cellulose, alginates, or gums^[5].

The aim of this study is to evaluate the disintegrant property of acid treated sweet potato starch in paracetamol tablet formulation compared with Maize starch B.P. and Sweet potato starch.

MATERIALS AND METHODS

Sweet potato tubers (Obtained from Monday market, Maiduguri, Borno State was identified by Professor S. S. Sanusi a Taxonomist in the Department of Botany, University of Maiduguri). Paracetamol powder (Royal Ingredients Group B.V., Holland), Magnesium stearate (BDH chemicals, Poole, England), Talc (BDH chemicals, Poole, England), Lactose (India), Maize starch B.P. (BDH chemicals, Poole, England).

Extraction of starch from sweet potato tubers

Two methods of starch extraction from sweet potato were used;

i. Extraction of starch from fresh sweet potato tubers

The method Isah *et al*, 2009^[6] was adopted with some modifications. The fresh sweet potato tubers were washed and peeled using a stainless steel knife and subsequently reduced to small sizes which were weighed using weighing balance (Salter mode, England) before grinding. The grounded sweet potato

tubers were then passed through a sieve of diameter 150 μ m and the slurry allowed to sediment for three hours. The supernatant water was then decanted while the sediment (starch) treated with 0.1N NaOH in order to precipitate the protein content of the starch. The starch was then washed two times with distilled water in order to remove excess sodium hydroxide. The potato starch extracted was air dried on a tray and the starch lumps size reduced using porcelain pestle and mortar, the weight of tubers and the starch obtained were noted and the percentage yield of potato starch was calculated.

ii. Extraction of starch from dried sweet potatoes

Similar method employed in the extraction of starch from fresh sweet potato tubers was used here with some modifications. The modifications being that after the tubers were reduced to small sizes, they were then air dried before grinding. The weight of the grounded powder was then taken and the sweet potato powder mixed with sufficient volume of distilled water. Subsequently, same procedure used in the extraction of starch and yield was noted.

Synthesis of Microcrystalline starch from sweet potato starch

The procedure of Isah *et al*, 2009^[6] was adopted. A 730g weight of an aqueous suspension of potato starch (36%w/v potato starch) was prepared in an aluminum pot. With the aid of a dropper, 45.4ml of 6N hydrochloric acid (HCl) was added drop wise with continuous stirring. The reaction was then conducted for 24 hours at a temperature that gives the best yield below gelatinizing temperature (below 55°C) using digital thermostat water bath (DK-8A, Shanghai, China). The suspension (starch product + reaction medium) was allowed to cool before the reaction medium was separated with the starch product using vacuum filter (TW-1A model). The starch product was then washed in ratio 1:1 with distilled water and then suspended in 420ml of distilled water. The suspension formed was then brought to pH 6 by the addition of 62ml of 1N NaOH using a pH meter (Mettler Toledo, UK). The starch product was then separated using vacuum filter. The wet starch product was subsequently suspended in 2L of ethanol and stirred for 30 min. The resulting dehydrated starch product was separated by the use of vacuum filter and air dried.

Preparation of paracetamol granules.

The paracetamol granules were prepared by the wet granulation method with batch size of 250 tablets.

Maize starch BP, potato starch, and microcrystalline starch were employed at concentration level of 2.5, 5, 7.5 and 10%w/w as disintegrant. Weighed quantities of paracetamol powder and intra-granular disintegrant were dry mixed in a porcelain pestle and mortar for five minutes. Subsequently, lactose was added separately after 5 minutes of mixing. Sufficient quantity of maize starch B.P. mucilage was then added and mixed until a damp coherent mass was formed.

The coherent mass formed was passed through number 5 stainless steel sieve to form granules. The wet granules were dried and passed through number 8 stainless steel sieve in order to produce uniformly sized granules. Extra- granular excipients (glidant and lubricant) magnesium stearate and talc were then added and mixed thoroughly before the granules were characterized.

Characterization of Starch Powders and Paracetamol Granules

Organoleptic properties

The colour, odour, texture, and taste of the three different starch samples were observed and the observation recorded.

Chemical tests

i. Iodine test

To a 2ml solution of starch in a test tube, 2 drops of iodine was added and shaken. The mixture was then warmed and allowed to cool. The colour change was recorded.

ii. Barfoed's test

Two milliliters of Barfoed's reagent was added into a test tube containing 2ml of aqueous suspension of starch and the colour change was noted after heating for some time in a water bath.

pH

The pH of 20% w/v slurry of each of the sample starch powder was determined using a pH meter and the result recorded.

Moisture content

The moisture content of each sample starch powder and paracetamol granules were determined using a moisture analyzer (Sartorius, Germany). A 3g weight of each sample starch was poured unto the moisture balance and evenly distributed on the tray. The machine was set at 130°C \pm 1°C. The readings were

noted at a temperature when the machine automatically stops.

Angle of repose

The angle of repose of each sample starch powder and paracetamol granules were determined using a glass funnel clamped on a retort stand which is 10cm away from the flat surface of the bench. 50g of each sample starch powder and paracetamol granules were placed into the funnel and allowed to flow freely forming a conical heap. The angle of repose was calculated from the heap of each sample using the equation;

$$\text{Angle of repose, } \tan \theta = \frac{h}{r}$$

Where h = height and r = radius of the circular heap.

Bulk and tapped density

These are carried out measuring the volume occupied by a 50g weight of each sample starch powder and paracetamol granules in a dry measuring cylinder. The bulk density was calculated using the formula;

$$\text{Bulk density} = \frac{\text{Weight of sample}}{\text{Volume of sample}}$$

The measuring cylinder was then tapped 50 times on a wooden table from a height of 2cm and the tapped volume was recorded. The tapped density was calculated as;

$$\text{Tapped density} = \frac{\text{weight of sample}}{\text{Tapped volume of sample}}$$

Determination of Carr's index

Carr's index was calculated from the results obtained from bulk and tapped densities above using the relation;

$$\text{Carr' index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Determination of Hausner's ratio

Hausner's ratio was determined using the results obtained from both bulk and tapped density. It was calculated using the formula;

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Hydration capacity

A 1g weight of each sample starch powder was weighed and poured in to centrifuge tubes. 10ml of distilled water was then added and mixed for 2 minutes. The mixture was then centrifuged for 10 minutes at 1000 rpm. The supernatant obtained was decanted and the sediment weighed. 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 ^[7].

Swelling capacity

The swelling capacity was determined by weighing 5g of each sample starch powder into a measuring cylinder and then tapped 50 times on a wooden bench from the height of about 2cm and the tapped volume recorded. The starch was then dispersed in 100ml of distilled water and allowed to stand for 18 hours. The volume of the sediment formed was noted. The swelling capacity was calculated by the relation;

$$Q = \frac{V_S}{V_T}$$

Where V_S and V_T are the volume of sediment and tapped volume respectively.

Ash value

A 2g weight of each starch powder sample was poured into a nickel Crucible which was initially heated at 105°C to a constant weight and allowed to cool. The crucible with its content was then gently heated until it was moisture free and completely charred. Subsequently, the heat was increased gradually until most of the carbon vapourised. The sample was finally heated strongly until the residue is free from carbon (i.e. almost white). The crucible with its content was allowed to cool and weighed. The heating and cooling step was then repeated until the residue (ash) was constant.

The weight of the ash was then determined and the percentage ash value calculated using the relation below;

$$\text{Percentage Ash value} = \frac{W_A}{W_{SP}} \times 100$$

Where W_A and W_{SP} are weight of ash formed and initial weight of starch powder respectively.

Compression of granules

Prior to compression of the granules, the granules were mixed thoroughly with extra granular recipients (glidants and lubricants). The granules were then compressed in a single punch tableting machine (Manesty type F₃, England) at a compression pressure of 7.5 metric tones. The tablets were kept in air tight container for 24 hours prior to quality control tests. This is to allow for recovery^[8].

Quality Control Tests on the Tablets Produced

Uniformity of thickness and diameter.

The vernier caliper was used to measure the thickness and diameter of the tablets. The mean value of five determinations was recorded in each case.

Uniformity of weight test

Ten tablets were randomly selected from each batch and weighed individually. The mean weight of the tablets was then calculated and the standard deviation determined.

Crushing strength

The Monsanto hardness tester (Gupta Agencies, India) was used in measuring the crushing strength of the tablets. Six (6) tablets were randomly selected from each batch and placed individually between the anvil and the spindle of the Monsanto hardness tester and subjected to increasing pressure by turning the knurled knob until the tablet was crushed. The mean of the six determinations was taken for each batch.

Friability test

Ten (10) tablets were randomly picked from each batch and weighed accurately. They were then placed inside the drum of Erweka friabilator (D-63150, Germany) and operated for four (4) minutes at a speed of 25 rpm. Thereafter, the intact tablets were removed from the drum, dusted and weighed. The percentage loss of weight was calculated and recorded as friability value for that batch.

Disintegration test

The British Pharmacopoeia, 2009^[9] method was used. Six tablets were randomly selected from each batch and placed individually in the six tubes of the rack. The rack was then raised and lowered at constant rate in distilled water contained in a glass jar suspended in a water bath whose temperature was thermostatically maintained at 37°C±1°C the time taken for the last tablet or its fragment to pass

through the 2mm mesh into the disintegrating medium (distilled water) was recorded for each batch.

Dissolution Time Test

Calibration curve

The calibration curve was constructed using standard paracetamol powder and phosphate buffer pH 5.8 as dissolving medium. 27.89mg of the standard paracetamol powder was weighed and serially diluted to obtain a stock solution of 0.0446mg/ml (44.62µg/ml). 0.5, 1.0, 1.5, 2.0, 2.5ml of the stock was then re-diluted in 10ml volumetric flask to give 2.2, 4.4, 6.6, 8.9 and 11µg/ml concentrations respectively. The absorbance's of the different concentrations was spectrophotometrically determined at 257nm wavelength and a graph of absorbance against concentration was plotted.

Procedure for dissolution rate test

The Erweka dissolution test apparatus (model DT 6R, Germany) was used to determine the dissolution rate of the paracetamol tablets from the different batches using the procedure as stated by the British Pharmacopoeia^[9].

The dissolution medium used was 900ml phosphate buffer pH 5.8 thermostatically maintained at 37±0.5°C. The paddle which was adjusted 25mm away from the base of the glass jar was set to rotate at 50 rpm. One tablet was placed into each glass jar. Samples of the dissolution medium (5ml) was then withdrawn at specified time interval of 5, 15, 30, 45, and 60 minutes respectively and spectrophotometrically analysed for paracetamol at 257nm. After each withdrawal of the sample, same volume of the dissolution medium was replaced.

DISCUSSION

The percentage yield of starch from fresh sweet potato tubers as well as dried potato was shown in table 1. The percentage appears to be slightly less

Table 1: Percentage yield of sweet potato and microcrystalline starch

Starch	Percentage yield (%)
Sweet potato starch	13.92
Sweet potato starch*	38.36
Micro-crystalline starch	93.36

Sweet potato starch*: Starch extracted from dried Sweet potato tubers.

than the average percentage yield of sweet potato starch for all the varieties of sweet potato tubers which is 16.2%. This might be as a result of marked variation in chemical compositions of the different varieties of sweet potatoes and the environmental conditions of cultivations such as temperature, which is believed to have a marked effect on the starch content of sweet potato. Conversely, starch extracted from the dried sweet potato tubers fell within the range of 30.8%-41.8% in line with the findings of Tewe *et al*, 2003^[10]. The percentage yield of microcrystalline starch was higher than the range of 65%-85% given for the synthesis of microcrystalline starch from starch samples extracted from cassava tubers^[6].

Table 2 shows the result of the chemical tests for the three different starch powders. Iodine test is a

Table 2: Chemical tests for the different starch powders

Starch	Iodine test	Barfoed's test
Maize starch B.P.	+	-
Sweet potato starch	+	-
Micro-crystalline starch	+	-

Key: + = Positive - = Negative

general test for starch and all the three starch powders gave a positive result as dark blue colouration was observed on the addition of 2 drops of iodine to 2ml suspension of starch which disappeared on heating and reappeared when it was allowed to cool. Barfoed's test is a general test for monosaccharides. A negative result was obtained as all the three starch samples did not form a red precipitate on heating. This result indicates that the microcrystalline starch synthesized from sweet potato had undergone a partial hydrolysis because monosaccharides are produced when a starch sample is subjected to complete hydrolysis^[6].

The results of physicochemical properties of various starches are presented in Table 3. Maize starch B.P. and sweet potato starch had a pH which complied with the specification of the British Pharmacopoeia, 2009^[9], while the pH of microcrystalline starch is approximately equivalent to the pH it was initially adjusted to during synthesis. The ranking of the moisture content of the sample starch powders is as follows; MCS<MS<SPS. Therefore, microcrystalline starch is less liable to microbial contamination because it has the lowest moisture content.

Angle of repose indicates the measure of the flow properties of powders (i.e. the ease with which powders are able to flow over others). According to Okhamefe *et al*, 1991^[4] values of angle of repose between 54°-59° have very poor flow properties. Also, Stanforth and Aulton, 2007^[11] stated that powders with angles of repose greater than 50° have unsatisfactory flow properties, whereas minimum angles close to 25° correspond to very good flow properties. The starch powders evaluated have relatively low values of angle of repose and are therefore considered to have good flow properties with microcrystalline starch having the best flow (angle of repose of 18.43°).

It is difficult to judge the flow property with one parameter^[2]. Carr's index is a simple index that can be determined with small quantities of powders. It is used to indicate the measure of flow property of

Table 3: Properties of the different starch powders

S. NO.	Parameters	Maize starch B.P.	Sweet potato starch	Micro-crystalline starch
1.	pH	5.92	5.14	5.82
2.	Moisture content (%)	9.74	16.65	6.83
3.	Angle of repose (°)	29.24	30.71	18.43
4.	Bulk density(g/ml)	0.49	0.59	0.61
5.	Tapped density (g/ml)	0.55	0.81	0.78
6.	Carr's index (%)	10.9	27.16	21.79
7.	Hausner's ratio	1.12	1.37	1.27
8.	Hydration capacity	1.75	1.90	1.96
9.	Swelling capacity	0.96	1.14	1.26
10.	Ash value (%)	0.10	0.47	0.32

powders. Maize starch B.P. has a Carr's index of 10.9% which can be interpreted as excellent flow. Microcrystalline starch has a Carr's index value of 21.79% which implies that it has a fair to passable flow property which may be improved by the addition of glidant. Sweet potato starch has a value of 27.16% indicating that the flow is poor but may however be improved by the addition of a glidant. The above

interpretation was based on Carr's index as an indication of powder flow as stated in Wells and Aulton, 2007^[12]. A similar index has been defined by Hausner which is known as Hausner's ration. The

Table 4 showed that the tablets have uniform diameter and thickness since the values of their standard deviation is low, indicating that the values for uniformity of diameter and thickness are close. The

Table 4: Properties of tablets formulated with different disintegrants.

Starch conc. Parameter	MS I	MS II	MS III	MS IV	SPS I	SPS II	SPS III	SPS IV	MCS I	MCS II	MCS III	MCS IV
Uniformity of diameter (mm) ± SD	12.96 ± 0.05	12.98 ± 0.33	12.74 ± 0.25	12.64 ± 0.40	12.72 ± 0.20	12.60 ± 0.18	12.70 ± 0.39	12.82 ± 0.08	12.58 ± 0.13	12.76 ± 0.26	12.90 ± 0.70	12.96 ± 0.89
Uniformity of thickness (mm) ± SD	4.20 ± 0.10	4.06 ± 0.05	4.40 ± 0.23	3.90 ± 0.00	4.40 ± 0.33	3.3 ± 0.21	3.86 ± 0.15	3.66 ± 0.18	3.72 ± 0.16	3.94 ± 0.05	3.66 ± 0.18	4.14 ± 0.13
Uniformity of weight (g) ± SD	0.54 ± 0.03	0.53 ± 0.02	0.52 ± 0.02	0.49 ± 0.03	0.52 ± 0.03	0.45 ± 0.01	0.48 ± 0.03	0.46 ± 0.02	0.46 ± 0.02	0.45 ± 0.01	0.49 ± 0.02	0.50 ± 0.04
Crushing strength (KgF)	3.23	2.83	3.13	3.13	2.60	3.96	3.35	3.33	3.10	3.96	3.40	2.90
Friability test (%)	0.53	0.75	0.83	0.89	0.49	0.70	1.14	1.28	0.60	0.60	1.10	1.19
Disintegration time (min)	15.36	11.01	5.38	5.06	10.10	6.50	3.31	3.11	9.32	6.29	5.36	3.11

Key: M S = Maize starch B.P., SPS = Sweet potato starch, and MCS = Micro-crystalline starch While I, II, III and IV represents 2.5%, 5%, 7.5% and 10% disintegrant respectively.

results obtained for Hausner's ratio tallies with that of Carr's index regarding flow properties of the starch powders.

The hydration and swelling capacity of each of the starch powders as shown in table 3 implies that microcrystalline starch has the highest hydration and swelling capacity and can therefore be predicted based on this result and when the swelling as mechanism of disintegration is considered to be a better disintegrant than both maize starch B.P. and sweet potato starch. This is then followed by sweet potato starch while maize starch B.P. is the least. It is however important to note that there are other mechanisms of tablet disintegration apart from swelling.

Tablet thickness can vary with no change in weight because density of granulation and the pressure applied to tablets, as well as the speed of tablet compression^[13]. Not only is the tablet thickness and diameter important in producing tablets identical in appearance but also to ensure that every production lot will be usable with selected packaging components. Tablet thickness is also important in counting tablets using filling equipment.

tablet thickness also conforms to the specification which states that the range of tablet thickness should be between ± 5%^[13].

Table 5: Percentage concentration of drug dissolved at 50 minutes (DT₅₀)

Starch used	DT ₅₀ at 2.5% Disinteg-rant	DT ₅₀ at 5% Disinteg-rant	DT ₅₀ at 7.5% Disinteg-rant	DT ₅₀ at 10% Disinteg-rant
Maize starch	62.78	39.50	47.50	31.10
Sweet potato starch	27.00	25.50	32.00	26.00
Microcry-stalline starch	35.90	90.50	41.22	44.90

From the result of the uniformity of weight (table 4), the range of deviation of the tablets was within the range of 0.01-0.04. This implies that the tablets have less than 5% deviation as permitted for tablets weighing more than 250mg as stipulated by the pharmaceutical codex and principles of practice of Pharmaceutics^[14].

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

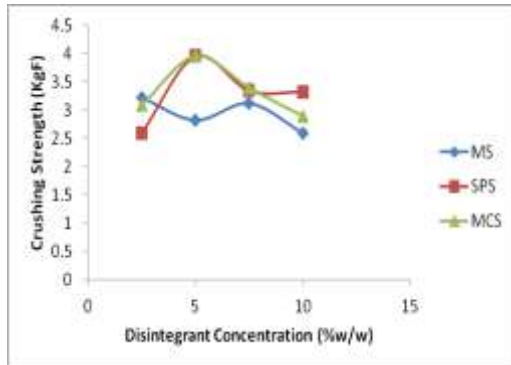
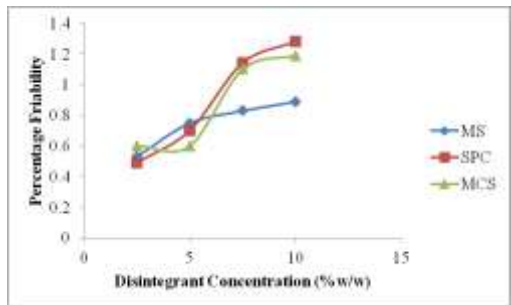


Figure 2: Effect of disintegrant concentration on friability of the paracetamol tablets formulated.



The crushing strength of majority of the batches of the tablets falls within the normal standard range for the crushing strength of tablets (i.e. 3-6 KgF). Two of the batches (SPS I and MCS III) however, failed the test (table 4). This therefore implies that to some certain extent, the twelve batches of the tablets can withstand mechanical stress.

Friability test is carried out to check the ability of the tablets to withstand the wear and tear during transportation. The tablets to be evaluated pass the test if the loss in weight is less than 1% as stipulated by the USP, 2008 [15]. Most of the batches of the tablets passed the friability test (table 5). Four batches however failed the test (SPS III, SPS IV, MCS III and MCS IV). This can be attributed to the high concentration of the disintegrants that is incorporated into those batches of tablets. It is therefore important to note that with increasing disintegrant concentration, the tablets become more friable as shown in figure 2.

Disintegration test measures the time required for a tablet to disintegrate when in contact with

Figure 3: Effect of disintegrant concentration on disintegration time of paracetamol tablet formulated.

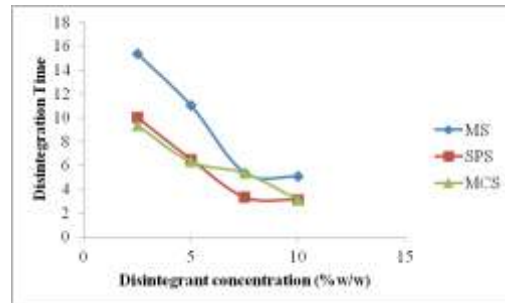
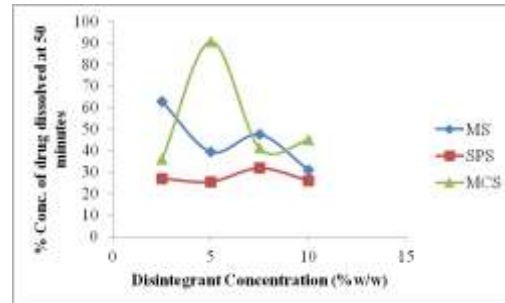


Figure 4: Effect of disintegrant concentration on percentage concentration of drug dissolved.



gastrointestinal fluids. This is the rate determining step in the processes of drug absorption as tablets must first disintegrate before it goes into solution [2].

All the batches of the tablets passed the test by disintegrating in less than 15 minutes as stipulated for uncoated tablets with the exception of the tablets containing 2.5%w/w maize starch BP which has a disintegration time of 15.36 minutes. This can be attributed to low concentration of disintegrant.

The rate of dissolution determines the rate and extent of absorption and subsequent therapeutic outcome of a drug. Table 5 shows the percentage concentration of drug dissolved at 50 minutes (DT₅₀). From the results, the percentage concentration of drug dissolved when microcrystalline starch was used as a disintegrant was found to be significant at DT₅₀ which is then followed by maize starch B.P. and sweet potato starch respectively as shown in figure 4.

It should however be noted that a tablet can disintegrate rapidly but still have delayed dissolution profile. This might be explained by the fact that tablet

may actually disintegrate into hard coarse particles from which dissolution may be slow^[16].

CONCLUSION

Conclusively, based on the results of the study conducted above, microcrystalline starch synthesized from sweet potato starch has a better disintegrant property in paracetamol tablet formulation compared to maize starch B.P. and sweet potato starch and can therefore be used as substitute (alternative) to both maize starch B.P. and sweet potato starch as disintegrant in paracetamol tablet formulation.

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