WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

Volume 2, Issue 3, 906-920. Research Article ISSN 2278 – 4357

COMPARATIVE EVALUATION OF THE BINDING/DISINTEGRATING PROPERTIES OF *PLECTRANTHUS ESCULENTUS* STARCH

***Kemas, U.C., Nep, E.I., Ochekpe, N.A.**

Faculty of Pharmaceutical Sciences, University of Jos, Jos-Nigeria.

Article Received on
21 March 2013,

Revised on 20 April 2013,
Accepted on 29 May 2013

***Correspondence for Author:**

*** Kemas, U.C.**
Faculty of Pharmaceutical Sciences, University of Jos, Jos-Nigeria
kemas4ursula@gmail.com

ABSTRACT

The binding and disintegrating property of starch from tubers of *Plectranthus esculentus* was evaluated in chloroquine phosphate tablets at a use level of 5 %. This was compared with similar tablets formulated with maize or cassava starches as binder and disintegrant. The flow properties of the starch powder and granules formulated by wet granulation were evaluated. Tablets were compressed on a single station tabletting machine. Thereupon, tablet properties such as hardness friability and disintegration time of the tablets were evaluated. The starch powders exhibited flow parameters which were not satisfactory, but these were improved by wet granulation. All tablets passed the weight uniformity test. Tablets formulated using *P. esculentus* starch as binder gave a hardness value (7.33±0.5 KgF) lower than tablets formulated with maize or cassava starch as binder. All tablets had low friability values of less than 1% and tablets formulated with *P. esculentus* starch as binder were more rapidly disintegrating than the tablets formulated using maize or cassava starch as binder. The results from the *Invitro* drug release study however suggests that maize starch is preferable to *P.esculentus* starch when starch binders are indicated in solid dosage formulation. *P.esculentus* starch is also preferred to cassava starch in terms of disintegrating function.

Keywords: *P. esculentus* starch, disintegrant property, binder property, tablet formulation, chloroquine.

INTRODUCTION

The plant *P.esculentus* belongs to the mint family Lamiaceae, to which many aromatic plants belong. Despite this fact, this species is a kind of potatoes though it is not in the same family (Solanaceae) like the potatoes we commonly eat [1]. *P.esculentus* differs from most members of the Lamiaceae family because it produces tuberous organs at the base of the stem which are edible. The tubers are cultivated as source of food in parts of Africa, particularly in the middle belt and northern parts of Nigeria. The tubers are rich in vitamin A and iron than any other tuber and the leaves of this plant are used in the treatment of various ailments such as respiratory and digestive problems, although this has not been proven [2].The pharmaceutical significance of starch from this plant is not yet ascertained. The present investigation was aimed at extracting the starch from this plant and to evaluate the binding and disintegrating properties of the starch in chloroquine phosphate tablets.

MATERIALS AND METHOD

MATERIALS

The materials used as obtained from their manufacturers include the following: Maize starch, Chloroquine, procured from BDH chemicals, .England. Lactose, magnesium stearate was procured from May & Baker Ltd, Dagenham England. *P. esculentus* starch and Cassava starch was extracted in our laboratory. All equipments used are cited in the text.

EXTRACTION OF *P. ESCULENTUS* STARCH FROM THE TUBER

The tuber was first purchased from the local market (Heipang, Plateau state). The skin was peeled off to expose the white part which was then cut into several smaller pieces and washed in 0.1 % sodium metabisulphite before wet milling using a local wet mill. The paste was sieved using muslin bag and allowed to settle overnight. Thereafter, the supernatant was decanted leaving the paste that has settled at the bottom of the container. The paste collected at the bottom was then washed thoroughly with 0.1% sodium metabisulphite which served as a preservative until the paste became whitish. The washed paste was then air- dried for 72 hours. When properly dried, it was reduced using a mortar and pestle to break up the dried powder mass into smaller particles which was passed through a sieve size 250 µm and stored in an air-tight container.

EXTRACTION OF CASSAVA STARCH FROM THE TUBER

The method described by [3] was adopted for the extraction of cassava starch. Briefly, the intact cassava tubers and roots were first weighed and peeled, washed, cut into small sizes and then wet milled. The resulting product was mixed with distilled water. Fibers were separated by sieving through a 170-mesh screen. After washing for several times, starch was oven dried at 45 °C.

POWDER AND GRANULE PROPERTIES

Photomicrograph of the Starch of *P. esculentus*

Photomicrograph of starch was taken on Nikkon (Japan) microscope fitted with a camera. Slide of the power in glycerol was prepared on the microscope slide and placed on the stage and viewed with the aid of basic link system software connected to a computer

Flow Rate

A retort stand was set up in which a glass funnel was fixed to it at a height of 6.5 cm from the bottom. A 30 g quantity of the powder or granule was weighed and poured into the funnel closing the bottom with spatula and the stop clock was set. Immediately the spatula was removed, the stop clock was started. The time taken for the powder or granule to flow down completely was recorded. The flow rate was calculated using the equation.

$$\text{Flow rate} = \frac{weight\ of\ powder\ (g)}{time\ (\text{sec})}$$

Determination of Angle of Repose

This was determined using a retort stand, glass funnel and a plain paper. The powder or granule (30 g) was allowed to flow through a funnel on to a horizontal surface beneath. The angle of the conical heap so formed was determined by measuring the height and the radius from the base. This was done three times to get the mean (average). The angle of repose was calculated using.

$$\text{Tan } \theta = \frac{height\ (cm)}{radius\ (cm)}$$

Bulk and Tapped Densities

The bulk and tapped densities of the powder or granules were determined by pouring 30 g of the powder or granule into a 100 ML measuring cylinder. The initial volume was noted as volume for the bulk. The cylinder was tapped until there was no further reduction in volume. This was noted and recorded as the tapped volume. It was calculated using the equation;

$$\text{Bulk density} = \frac{weight\ (g)}{poured\ volume\ (cm3)}$$

$$\text{Tapped density} = \frac{weight\ (g)}{tapped\ volume\ (cm3)}$$

Hausner's Quotient and Carr's Compressibility

This was calculated using both the tapped and bulk density respectively in accordance with equation's below. Hausner's ratio gives insight into the degree of densification of powders which could occur during tabletting. It is important to note that the lower the ratio, the less propensity of the powder to density. This process may cause tablets which lack uniformity of active content and weight to be produced [4].

$$\text{Hausner's ratio} = \frac{tapped\ density}{bulk\ density}$$

$$\text{Carr's Compressibility index} = \frac{tapped\ density - bulk\ density}{tapped\ density} \times 100$$

Moisture Content

A 5 g quantity of the powder or granule was weighed and kept in the oven dryer (Gallenkamp Ltd, England) at a temperature of 105°C for three hours after which it was brought out and the weight taken to calculate percent loss on drying [5]. Moisture content was calculated using the equation.

$$\text{Moisture content} = \frac{wet\ weight - dry\ weight}{wet\ weight} \times 100$$

PREPARATION OF CHLOROQUINE GRANULES AND TABLET FORMULATION

The Chloroquine granules were formulated by wet granulation. The starch binder and disintegrants were used at concentrations of 5 % w/w. The composition of tablet formulation containing chloroquine is given in table 1. Briefly, the required amount of the active ingredient (chloroquine B.P), the diluent (lactose) and the binder/ disintegrant (*P. esculentus* starch, cassava or maize starch) was weighed and blended in a mortar using a pestle. The binder mucilage of maize starch was prepared using 5 ml of water and incorporated into the powder mix and triturated to give a damp but coherent mass. Coarse screening of the wet mass was done using a suitable sieve size 10 and dried in a hot air oven at 60 °C for 1 hour. Dry screening of the granule was done using sieve size number 16. The lubricant (Magnesium Stearate) were calculated and added prior to compression.

Table 1A: PER TABLET FORMULA FOR CHLOROQUINE TABLETS USING *P. esculentus* STARCH AS BINDER.

Ingredients	Quantity
Chloroquine (mg)	250
Disintegrant: maize mg)	40
*Binder (mg)	20
Lactose	86
Magnesium stearate (mg)	4

***Test binders:** P. esculentus starch. ***Standards:** Maize starch, cassava starch.

Table 1B: PER TABLET FORMULA FOR CHLOROQUINE TABLETS USING *P.esculentus* STARCH AS DISINTEGRANTS

Ingredients	Quantity
Chloroquine (mg)	250
Binder: maize mg)	20
*Disintegrant (mg)	40
Lactose	86
Magnesium stearate (mg)	4

***Test Disintegrants:** P. esculentus starch. ***Standards:** Maize starch, cassava starch.

TABLET COMPRESSION

A single punch tabletting machine (Erweka, Germany) fitted with 12 mm punch and die set was used to compress the tablets. The required tablets weight is 400 mg and the compressed pressure used was 4.5 MT. The tablets were stored in a dessicator for 24 hrs before evaluation.

TABLET EVALUATION

Weight Uniformity

The weight uniformity test was carried out according to the B.P. (1988) [6] procedure. Ten tablets from each batch were randomly selected and weighed individually using a highly sensitive electronic balance (Mettler, Switzerland). Their average weight and the standard deviation from the average weight were determined. The percentage coefficient of tablet weight variation (% C.V) was calculated then calculated using;

$$\% \text{ C.V} = \frac{standard\ deviation}{average\ weight} \times 100$$

Tablet Thickness and Diameter

This was carried out by random selection of 10 tablets from each batch. The test was done by using Vernier Caliper, the thickness and diameters of the tablet were determined. The mean and standard deviation were calculated.

Hardness Test

The hardness of the tablets was determined using the Monsanto hardness tester from each batch. Tablets were selected at random and the pressure under which the tablet broke was determined.

This was done by placing the tablet between spindle and anvil of the tester and the calibrated scale is adjusted to zero after which a compression force is applied and the position on the scale at which the tablet broke was recorded in KgF [7]. The test was carried out in triplicate. The mean and standard deviation was thus calculated.

Friability Test

Ten tablets were picked at random from each batch, dusted and weighed using an electronic weighing balance. The friability test was carried out using the Roche friabilator. The instrument was set to rotate at a speed of 25 rpm for four minutes and stopped. The tablets were dusted and again reweighed. The percent losses were calculated using the equation below for each batch of the tablets [8].

$$\% \text{ Friability} = \frac{Wi - Wf}{Wi} \times 100$$

Wi = Initial weight of ten tablet, Wf = Final weight of ten tablets

Disintegration Time Test

The B.P (1988) method [6], was adopted. Eagle scientific disintegration apparatus (Eagle Scientific, England) and 0.1N hydrochloric acid was the dissolution medium maintained at 37.5 ± 0.1°C. The disintegration time test was done using six tablets from each batch. A tablet was introduced into each of the six tubes and then placed in a beaker containing 600 ml of the 0.1N Hydrochloric acid solution and agitated in water bath at 37°C. This was done for the various batches. As the tablets disintegrated, the granules passed through the mesh and

the end point was taken as when no particle was remaining at the bottom of the mesh and the time was recorded for each of the tablet.

In vitro Drug Release Studies

The release of drug from the chloroquine tablets was studied in 1000 ml of 0.1 N HCl using the USP II (paddle method) at 100 rpm and 37 ± 1°C equipped with a 40 mesh sinker. A 5 ml sample was withdrawn at time intervals of 5 minutes up to thirty minutes and thereafter every 10 minutes for the next thirty minutes. The withdrawn samples were filtered through syringe filters (pore size = 0.45 µm) before assaying for drug content using the UV-spectrophotometer at 344 nm. After withdrawal of sample, it was replaced with an equal volume (5 ml) of fresh 0.1N hydrochloric acid solution at same temperature.

Statistical Analysis

The data will be analyzed using two-way ANOVA (Instat software, Graph Pad, San Diego, CA).

RESULTS AND DISCUSSION

POWDER AND GRANULE PROPERTIES

Percentage Yield of P. *esculentus* Starch

The percentage yield *of P. esculentus* starch obtained after extraction was 36.6%

Photomicrograph of P. *esculentus* Starch

Figure 1 shows the photomicrograph of starch obtained from the tubers of *P. esculentus.* The particles of *P.esculentus* starch are more or less irregular in shape. It has been reported that the shapes of starch particles may have an effect on the ability of the particles to rearrange themselves under compaction.

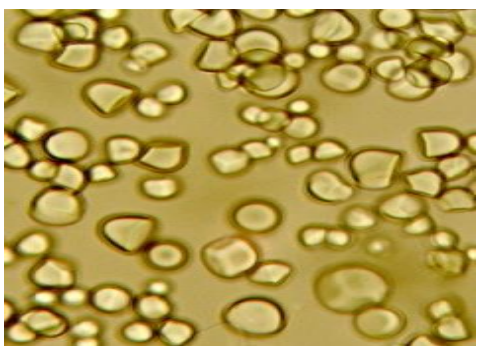

Figure 1: Photomicrograph of P. *esculentus* starch

Moisture Content

The moisture content of the powders and granules are shown in tables 2A and 2B respectively. The moisture content of the powders (table 2A) was within 8.89- 15.3 %. Maize starch has the least moisture content in the order Maize starch<*P.esculentus* starch<Cassava starch. Most pharmaceutical materials are not completely free from moisture but contain some residual water, the amount may vary with temperature and humidity of the ambient air to which they are exposed [9]. Tablet granules have superior compaction properties with a small amount (1-2%) of residual moisture [9].

Bulked and Tapped Densities

The bulk and tapped densities of the starch powder, binder/disintegrants and their granules are shown in table 2A, 2B and 2C. The tapped density which is indicative of the powder packing properties was seen to be higher than the bulk density. *P. esculentus* was seen to have the lowest bulk and tapped densities compared to maize and cassava starch. This implies the particles of *P. esculentus* starch do not easily pack to fill up voids within the powder bed compared to maize and cassava starch. The same trend was observed with the granules. From (Table 2B and 2C) the bulk and tapped density was observed to decrease for the granules compared to the powders and this was due to the introduction of binder solution during wet granulation to form larger granules which resulted in larger void spaces in between the granules [10]. This decrease in densities increases the flow properties of the granules compared to the powders due to the resultant increase in particle size which leads to decrease in surface free energy of the granule and frictional forces between the granules [11].

Angle of Repose, Hausner's Ratio and Carr's Compressibility Index

These are all indirect methods used in predicting powder flow properties under specific conditions. Hausner's ratio is an indicative of inter-particle friction while Carr’s index shows the aptitude of a material to diminish in volume. As the values of these indices increases the flow of the powder decreases. In general a Hausner’s ratio less than 1.25 which is equivalent to 20% Carr's compressibility index indicates good flow while that greater than 1.5 equivalent to 33% Carr's compressibility index indicates poor flow [12]. Angle of repose is a measure of the powder resistance to flow under gravity due to frictional forces resulting from the surface properties of the granules. Usually, when it is less than or equal to 30° indicates free flowing powders while that greater than or equal to 40° suggests a poor flowing powder.

The results for flow parameters of the powders and granules are shown in table 2A, 2B and 2C. The powder flow properties suggest that maize starch, cassava and *P.esculentus* starch powder have poor flow characteristics and may require granulation or modification to improve the flow of the powder. Thereupon granulation, an improvement in the flow parameters is obvious (table 2B and 2C).

It can be seen from the results (Table 2B and 2C) that the flow properties of the granules of *P.esculentus* starch binder/disintegrant demonstrated good flow. The recorded value's for angle of repose, Carr's compressibility and Hausner's ratio decreases for the granules, indicating an improvement in the flow properties of the granules over the powders, due to reduce cohesive forces of the larger granules formed during wet granulation. Although the flow parameters indicate that flow of both powders and granules is only fair, these can be further improved by the addition of glidants and lubricants [13].

TABLE 2A: Physicochemical Properties of the Starch Powders Used as Binder/ Disintegrant.

(Mean ± S.D)

	P.esculentus starch	Maize	Cassava
Bulk Density (g/cm^3)	0.44±0.01	0.53±0.01	0.60±0.01
Tapped Density (g/cm^3)	0.73±0.01	0.76±0.01	0.80±0.01
Carr's Compressibility (%)	40.1±5.36	30.4±1.75	24.8±0.85
Angle of Repose (°)	39.9±0.89	53.3±0.27	46.2±0.07
Hausner's Ratio	1.68±0.15	1.44±0.04	1.33±0.02
Moisture Content (%)	11.1±0.77	8.89±0.29	15.3±0.57

TABLE 2B: Effect of Type of Starch Binder on the Physicochemical Properties of Granules (n=3, Mean ± S.D)

	P. esculentus starch	Maize	Cassava
Bulk Density (g/cm^3)	0.47±0.01	0.47±0.01	0.53±0.01
Tapped Density (g/cm^3)	0.52±0.01	0.53±0.01	0.6±0.02
Carr's Compressibility (%)	9.1±1.52	11.8±0.91	11.5±2.29
Angle of Repose (°)	29.78±0.33	27.7±0.21	29.7±0.66
Hausner's Ratio	1.1±0.02	1.13±0.01	1.13±0.03
Moisture Content (%)	1.89±1.44	2.16±1.55	1.35±0.55

TABLE 2C: Effect of Type of Starch Disintegrant on the Physicochemical Properties of Granules (n=3, Mean ± S.D)

	P. esculentus starch	Maize	Cassava
Bulk Density (g/cm^3)	0.47±0.01	0.46±0.01	0.47±0.01
Tapped Density (g/cm^3)	0.51±0.01	0.52±0.01	0.51±0.01
Carr's Compressibility (%)	8.53±1.11	12.2±1.02	7.84±2.85
Angle of Repose (°)	29.1±0.82	28.9±0.10	29.7±0.78
Hausner's Ratio	1.09±0.01	1.14±0.01	1.09±0.03
Moisture Content (%)	0.06±0.01	0.05±0.01	0.06±0.01

PHYSICOCHEMICAL PROPERTIES OF CHLOROQUINE TABLETS

Weight Uniformity

The individual weight of the tablets (tables 3 and 4) does not deviate from the mean more than is permitted since all showed a low coefficient of variation below 5% according to the standard in the national pharmacopoeias for tablets greater than 324 mg. Compliance with the standard ensures that uniformity of dosage is achieved across all the batches [14].

Tablet Thickness and Diameter

The diameter and thickness of the tablets (tables 3 and 4) was uniform across all the batches. This eliminate the doubt of tablet of dissimilar appearance being of same potency and also it is expected that tablet of uniform diameter and thickness will not differ markedly in weight. The % C.V allowed for tablet diameter and thickness is ±5 depending on the size of the tablet [15]. From the result obtained, all the batches of tablets formulated with the different starches gave values below 5%.

Tablet Hardness

The results show that tablets containing *P.esculentus* starch as binder (table 3) had no significant difference (P>0.05) compared to tablets containing maize or cassava starch as binder. When the different starches were applied as disintegrants in chloroquine phosphate tablets, although same binder was used for all batches, the hardness of the tablets were different (table 4). Despite the fact that tablets containing maize starch disintegrant gave tablets of recommended hardness (4-7 KgF) for uncoated conventional tablets [15], the tablets were nonetheless not as hard as tablets containing *P.esculentus* or cassava starch disintegrants.

TABLE 3: Effect of Binder Type on Tablet Properties (n=3, Mean ± S.D)

	P.esculentus starch	Maize starch	Cassava starch
Diameter	11.95±0.0	11.97±0.0	11.96±0.0
Thickness	3.40±0.1	3.35±0.1	3.39±0.0
Weight variation (% C.V)	399.0±10.4 (0.026)	400.0±4.47 (0.011)	398.0±11.7 (0.029)
Hardness	7.33±0.5	9.33±0.5	9.33±1.7
Friability	0.82±0.2	0.78±0.2	4.39±2.5
Disintegration Time	5.00±0.0	9.00±0.9	19.00±1.7

TABLE 4: Effect of Disintegrant Type on Tablet Properties (Mean ± S.D)

	P.esculentus starch	Maize starch	Cassava starch
Diameter	11.98±0.0	11.97±0.1	11.95±0.1
Thickness	3.37±0.0	3.36±0.1	3.36±0.0
Weight variation (% C.V)	402±8.7 (0.022)	400±8.9 (0.022)	401±5.4 (0.013)
Hardness	9.67±0.5	5.93±0.7	9.33±0.9
Friability	0.65±0.2	0.98±0.4	0.34±0.2
Disintegration Time	4.67±0.5	2.33±0.5	6.33±1.3

Friability

The results (tables 3 and 4) show that all the tablets had a weight loss of less than 1% across all the batches, which is acceptable according to the standard in the British Pharmacopeia, implying that the tablets can withstand handling and transportation conditions without much reduction in weight and change in appearance of the tablets. It must be noted that while tablets containing maize starch were not as hard as tablets containing *P.esculentus* or cassava starch, there was no significant variation in the friability of the tablets ($P>0.05$). Friability values of less than 1% show efficiency of dosage form formulation and development [16].

Disintegration Time

The British Pharmacopoeia recommends a disintegration time of not more than 15 min for conventional (plain uncoated) tablets. From table 3, tablets containing *P.esculentus* and maize starch binders disintegrated within 15 min and therefore pass the disintegration time test for conventional tablets. Such tablets will be expected upon oral administration to disintegrate

within expected time to release the pharmaceutical active for systemic absorption. The speed with which this disintegration will occur can be seen to vary with the type of starch binder. Although cassava starch displayed a remarkable delay in tablet disintegration time which was extremely significant (P<0.001) when compared to maize or *P.esculentus* starch, it therefore exhibit good binding properties and will probably be applied at low concentrations in conventional tablets formulations. *P. esculentus* starch however gave tablets of lowest hardness values when applied as binder, the tablets however exhibited a disintegration time that is faster than maize and cassava starch-containing tablets. These results show a relationship between hardness and disintegration time of the tablets which is expected.

The effect of type of disintegrant on the tablet disintegration time is shown in table 4. The tablets formulated with the different starch disintegrants disintegrated within the 15 min recommended for uncoated conventional immediate release tablets. However, tablets containing maize starch as disintegrant gave the shortest disintegration time. The order of rapid tablet disintegration was:

Maize starch > *P.esculentus* starch > Cassava starch.

This result show that maize starch when incorporated in tablet formulations will promote rapid disintegration of the dosage form compared to cassava and *P.esculentus* starch. The mechanism of disintegration has been reported [15]. The disintegrant action of starch is attributable to a combination of capillary action followed by rapid swelling when in contact with moisture. Capillarity may increase the rate at which water is introduced into the tablet and it is influenced by the porosity of the tablet.

In vitro Drug Release Studies

The dissolution profiles of chloroquine tablets containing *P.esculentus* starch, maize and cassava starch as binder at 5% w/w are shown in figures 3. The results show that all batches of tablets gave maximum release of the API within 45 min of study. The time taken for the tablets to release 50% of the API (t_{50}) is also shown in figure 4. The result show that maize starch release 50% of the drug faster than *P. esculentus* starch (native). The order of increasing t_{50} is maize starch < *P.esculentus* starch (native) < cassava starch (fig 9). The result indicates that *P. esculentus* starch may be more effective as a binder (at a concentration of 50% w/w) in chloroquine phosphate tablets than maize starch. It is however not as effective as cassava starch in delaying the release of the API from tablets. Therefore cassava starch is significantly different (P<0.01) from native *P.esculentus* starch which also has a

significant difference (P<0.01) from maize starch. Although a tablet can disintegrate (table 3) but still have delayed dissolution in the case of *P.esculentus* starch, this can be explained by the fact that although disintegration could be rapid, the tablet may actually disintegrate into hard coarse particles from which dissolution may be slow. Rubeinstein and Wells [17] and Iwuagwu *et al* [4] have demonstrated that the particle size and subsequently the surface area into which a tablet disintegrates correlates with the dissolution time of the active drug.

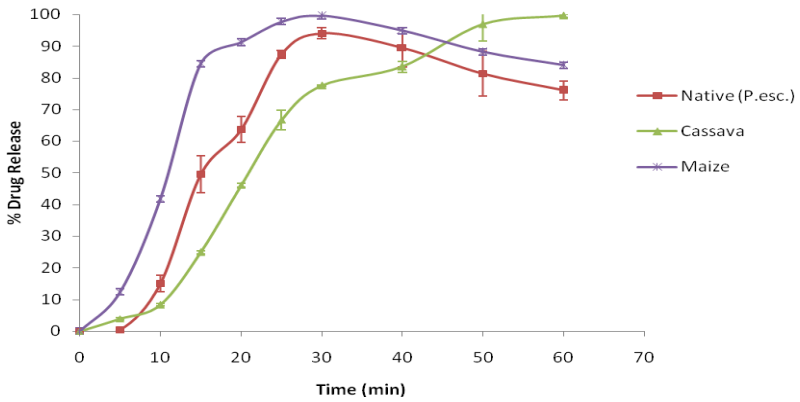

Fig 3: Release profiles of chloroquine phosphate from tablets containing 5% w/w of native *P.esculentus* starch, Maize or Cassava starch as binder in 0.1 N HCl (pH 1.0) solution at 37±1 ^{o}C (n=3, mean±s.d).

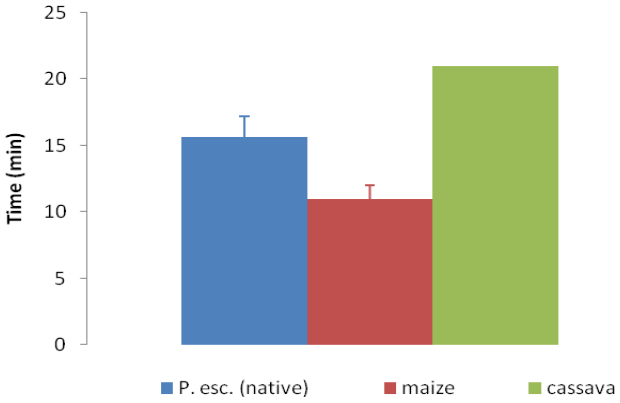

Fig. 4: Time taken to release 50% (t_{50}) of API when P. esculentus starch (native), maize or cassava starch was used as binder (mean ± s.d)

CONCLUSION

The results from the present study suggest that *P. esculentus* starch at 5 %w/w use level produces tablets with friability values of less than 1% which is indicative of efficiency of dosage form formulation. The tablets were of recommended hardness but also disintegrate

faster than similar tablets formulated using maize or cassava starch as binder. From the *Invitro* drug release studies, the present study indicates that despite the fact that maize starch may not be preferable to *P. esculentus* starch when binder action in solid dosage forms is desired, it is however not better than cassava starch as a binder. Therefore *P.esculentus* starch may require chemical modification to improve its binding characteristics. Similarly *P.esculentus* starch may be perfectly applied as disintegrant in tablets compared to cassava starch.

REFERENCES

1. Allemann, J., Robbertse, P. and Hammes, P. (2003). Organographic and anatomical evidence that the edible storage organs of *Plectranthus esculentus* N.E.Br. (Lamiaceae) are stem tubers. *Field Crop. Res*. Volume 83: pages 35-39
2. Kyesmu, P.M. (1994).*Plectranthus esculentus* N.E.Br.A minor tuber crop in need of rescue from extinction. *Lamiales Newsletter*, 4:3-4.
3. Mbougueng, P.D., Tenin, D., Scher, J. and Tchiegang, C. (2012). Influence of acetylation on physicochemical, functional and thermal properties of potato and cassava starches. International Journal of Food Engineering, v, 108, p. 320-326.
4. Iwuagwu, M.A., Onyekweli, A.O. and Obiorah, B.A. (2001). Physicochemical properties of paracetamol tablets marketed in Benin City. Nig. J. Pharm. Vol. 32 Jan-Mar, 49-51.
5. Musa, H., Muazu, J.and Bhatia, P.G. (2008) Evaluation of fonio (digitaria exilis) starch as a binder in paracetamol tablets. *Nigerian Journal of Pharmaceutical Sciences Vol. 7.*
6. British Pharmacopiae, 1988.
7. Satyam, G., Singh, S., Garg, G., Pawar, V. and Sharma, P.K. (2008). Isolation and evaluation of binding property of sago starch in paracetamol tablet.International Journal of Pharma Research and Development. IJPRD/2010/PUB/ARTI/VOV-2/ISSUE-1/MAR/008.
8. Singh, A.V. (2009).Evaluation of binder property of moth bean in compressed solid dosage form. International Journal of Pham tech Research. April-June,volume 2, no 2.
9. Aulton, M.E. (2007). Tablets and Compaction. In: Aulton's pharmaceutics: the design and manufacture of medicines, 3rd edition, Oxford: Churchill Livingstone Elsevier; 442-478.
10. Esezobo. S. (1986).Evaluation of Sweet potato starch as a binder and disintegrant for paracetamol tablets. *Nig. Jour. Pharm. Sci*. Vol. 2, 2, 44-51.
11. Iwuagwu, M.A., Nwanshai, C.A. and Iseghohi, F.E. (1986). Investigations into the Binding and Disintegrant properties of starches from selected Dioscoreaceae plants, Nig.

J .Pharm. Sci. Vol 2, 2, 10-22.

12. Martins, A., Swarbrick, J. and Cammarata, A. (1983). Micromeritics. In: Chun, A.H., (illus), *Physical pharmacy: Physical Chemical Principles in the Pharmaceutical Sciences* (third edition), Philadelphia: Lippincott Williams & Wilkins, pp. 423 – 453.
13. Staniforth, J.N. and Aulton, M.E. (2007). Powder flow. In: Aulton's Pharmaceutics. The design of medicines. Aulton, M.E., (Ed.), 3rd edn. Harcourt Publishers Ltd. Philadelphia USA, pp: 169-179.
14. Molke, M.D., Majid, I. and Rao, K.S. (2010). Formulation and Evaluation of Verapamil HCL Gastroretentive Floating Tablet from matrices prepared using Compritol ATO. Research Journal of Pharmaceutical, Biological and Chemical Sciences.Volume 1 Issue 3 Page 429.
15. Rudnic, E. M. and Schwartz, J.B. (2005). "Oral Solid Dosage form" Remington. The Science and Practice of Pharmacy.21st edition. Pp 889 -918.
16. Pranati, S., Rishabha, M. and Giriraj T. K. (2010). Formulation and Evaluation of Paracetamol tablets to assess binding property of orange peel pectin. *International Journal of Pharmaceutical Sciences Review and Research* Volume 3, Issue 1, Pp30- 34.
17. Rubinstein, M.H. and Wells, J.I. (1997).Generated surface area measurement of disintegrating tablets. *J. Pharm. Pharmacol*. 29 (6), 363-366.