

Original Research Article

The binding property of pregelatinized cocoyam starch on paracetamol tablets.

ABSTRACT

The binding properties of pregelatinized cocoyam starch were investigated. The starch was obtained by extraction using water maceration from the corms of xanthosoma sagittifolion obtained from a faringada market in plateau state, Nigeria. The cocoyam obtained was divided into two equal portions; one of the portions was pregelatinized while the other was not and then used separately as a binder in paracetamol granules and tablets formulations.

The tablets were produced by wet granulation method. The properties of the granules evaluated included; Flow Rate, Angle of Repose, Bulk and Tapped Densities, Hausner Ratio and Carr's compressibility. Tablet properties evaluated include; uniformly of thickness and diameter, uniformity of tablet and weight, disintegration time, dissolution profiles and friability test. The flow properties of these twelve batches were compared and the results indicate that the twelve batches have excellent flow properties.

The tablets produced from the granules of the twelve batches of paracetamol were found to have good physical appearance, hardness value and low disintegrating time.

Keywords : Binding properties, pregelatinization, granulation

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1.0 INTRODUCTION

Drugs are rarely administered solely as pure chemical substance but are always given in formulated preparations. They can vary from relatively simple solution to complex drug delivery systems, through the use of appropriate additive excipients in the formulation to provide varied and specialized pharmaceutical functions. Dosage forms can be classified in different ways. The basic types of dosage forms are the classification on the basis of the state of matter: solid, liquid and gaseous dosage forms. Dosage forms include tablet, cream, injectables, capsule, solutions etc.

Tablets may be defined as solid pharmaceutical dosage form containing drug substances with or without suitable diluents and prepared by either compression or molding methods. Tablet is still the most frequently administered dosage form for medical application (Olowosulu, Oyi, Isah& Ibrahim, 2011). There are different types of tablet, which may come in different shapes and sizes. The types include dispersible or effervescent, chewable, sublingual and buccal tablet, lozenges, and tablet for rectal or vaginal administration.

1.1 TABLET EXCIPIENTS

Excipients are no more considered as inert ingredients of formulation, but have a well-defined functional role. In addition to the active ingredient(s), a series of excipients are normally included in a tablet, their role is to ensure that the tableting operation can run satisfactorily and to ensure that the tablet of specified quality are prepared. However, excipient can affect the properties of a powder or the tablet in a series of ways and many substances used in tablet formulation can thus be described as multifunctional. The excipients include; lubricants, disintegrants, colourants, flavours and sweeteners, diluents, absorbents, binders and so on.

1.1.1 Reasons for excipients inclusion into dosage forms

- i. Aid processing of the dosage unit during manufacture.
- ii. Ease of administration to the target patient population(s) by the intended route and improved dosing compliance.
- iii. Protect, support, or enhance stability and or bioavailability.
- iv. Assist in product identification.

- v. Enhance any other attribute of the overall safety and effectiveness of the drug product during storage and use (Blechher, 1993).

1.1.2 Ideal properties of pharmaceutical excipient

The following general criteria are essential for excipients which should:

- i. Be pharmacologically inert
- ii. Be physically and chemically stable
- iii. Have no interference with drug bioavailability;
- iv. Have absence of pathogenic microbial organisms; and
- v. Be commercially available at relatively low cost (Armstrong, 1989).

In reality, no single excipient would satisfy all the criteria listed above, therefore, a compromise of the different requirements has to be made at some point. For example, although widely used in pharmaceutical tablet and capsule formulations as a diluent, lactose may not be suitable for patients who lack the intestinal enzyme lactase to break down the sugar, thus leading to the gastrointestinal tract symptoms such as cramps and diarrhea in such patients. The role of excipients varies substantially depending on the individual dosage form (Gowtham, 2013).

1.1.3 Binders

Binders are additives in tablet and formulation, to improve compatibility and flowability of powders during the granulation and compaction stages of manufacture (Symeko & Rhodes, 1995). Granules retain their integrity through encapsulation by binder and through the crystalline bridges, which form between the drug particles "(Herbert, 1989).

1.1.4 Disintegrants

Disintegrants are agents added to tablet formulations to promote the breakup of the tablet into smaller fragments in an aqueous environment, thereby increasing the available surface area and promoting a more rapid release of the drug substance (carter pharmaceutical, 2006),

Disintegrants act by mechanisms which include propagation of capillary effect within tablet pore structure, swelling in fluid to cause leaking of active drug (Alginic acid, sodium alginate) or melting to release active drug (Theobroma) oil in suppositories (Lowenthal, 1973).

1.1.5 Lubricants

Lubricants are substances that prevent ingredients from clumping together and from sticking to the tablet punches or capsule-filling machine. Lubricants also ensure that tablet formation can occur with low friction between the solid and die wall.

There are three interrelated types of pharmaceutical lubricating agent used in compression of tablets; Glidant, True lubricants and Anti-adherents.

- Glidants: - improve the flow characteristic of tablet granulation.
- True lubricants: - they reduce the friction between tablet surface and the die wall during and after compaction to ensure easy ejection of the tablet from the die.
- Anti-adherent: they reduce adhesion between tablet punch faces and tablet surfaces to prevent sticking of solid particles to punch surfaces (James, 1998).

1.1.6 Colorants.

Colorants are included in formulations to improve aesthetic elegance to increase their acceptability to patient due to attractive property it gives the product. They are classified into.

[a] Dyes- are soluble materials

[b] Lakes- are dyes adsorbed on aluminum hydroxide.

The use of colorants is optional and is regulated by the Agency for Food and Drug Control. Commonly used colorants include dried beet juice, caramels, carmine and turmeric. Colorants are included in tablet to increase their acceptability to patient due to attractive property it gives the product.

1.1.7 Flavors and Sweeteners.

In pharmaceutical formulations, flavor is an optional excipient and is essential in masking unpleasant tastes and providing the appealing tastes that make a drug palatable. Sweeteners are used to impart sweetness or pleasant taste to the preparation. They are frequently used in chewable tablets.

1.1.8 Diluents

Diluents also referred to as fillers or inert substances that are incorporated into the formulation to increase the bulk volume or the powdered drug making up the tablet. This increases the size of the tablet in order that it is of a size suitable for handling. Fillers are only necessary if the dose of drug per tablet is low and the tablet would otherwise be too small.

An Ideal filler, involves series of requirements such as should be chemically inert, non-hygroscopic, biocompatible, possess good biopharmaceutical properties for example; water soluble or hydrophilic, possess good technical properties (such as compatibility and dilution capacity), have an acceptable taste and should be cheap (Aulton, 2002).

1.2 STARCHES AS PHARMACEUTICAL EXCIPIENT

Starch possesses definite chemical structure and composition. It occurs widely as the major polysaccharide food reserve in seeds, swollen stems, tubers and roots of plants. Starch is present in these plant parts in the form of granule. It is the second most abundant compound synthesized by plant cells after cellulose, and exceeds cellulose in significance in terms of food value. Starch is a polysaccharide of glucose. It is stored in the plants as granules composed of amylose and amylopectin. Starch molecules produced by each plant have specific structures and compositions (for instance the length of glucose chains or the amylose/amylopectin ratio), and the protein content of the storage organs may vary significantly (Khalid, 2015).

Starch is colorless, odorless with slight characteristic taste, insoluble in water and alcohol. In pharmaceutical manufacture, starch is an important excipient that has been commonly employed because of its versatility and cheapness (Muazu et al, 2012).

Native starches were well explored as binders and disintegrants in solid dosage forms, but due to poor flow ability, their utilization is restricted. Most common form of modified starch i.e. Pregelatinized starch marketed under the name of Starch1500® are nowadays most preferred directly compressible excipients in pharmaceutical industry. Modified rice starch, starch acetate and corn starch, have been as established as multifunctional excipients in pharmaceutical industry (Bos, et al., 1992).

1.2.1 The Plant Cocoyam

Botanical Description: *xanthoso masagittifolium* (L) Schott) is an herbaceous perennial (FAO, 2007). An indigenous plant to tropical South America (Tropilab® inc, 2007) that has corm or main underground stem in the form of rhizome from swollen secondary shoots or cormels, sprow (FAO, 2007). Generally, it resembles dasbeen (tard), with large leaves about 60.96cm wide of 76.2cm feet long the upper leaf surface is rather smooth and sometimes waxy, and the main stem which are sagittate and erect with long, ribbed petioles inflorescence sprout between the leaves in a spadix, with a white 12-15cm spathe which closes at its base in the form of a spherical chamber and opens at the

top into a concave lamina, the spadix is cylindrical, slightly longer than the spathe, with female flowers on lower portion, male flower on the upper portion and sterile flowers in the middle portion. The spices are rarely fertile and produce few viable seed.

xanthosomasagittifolium (L) Schott) is known by several common names among which are: English: tannia, tania, yautia, new cocoyam tanie} Spanish yautia. Malanga (Antiles), macas (mexico (yucaton), quiscarmote (Honduras), tiqiusque (costa Rica), Oto (Panama), Okamo (venezuela), uncucha (peru), gualuza (Bolivai), malangay (Columbia), Portuguese taiowa, mangareto, mangranto (brazil) French choucaribe (Anti(les): other languages queiquexque (mexico), tannia, taniera (Antillos), Sunin Honolulu, mondu (Tiv, Nigeria) (FAO, 2007; Tripolab® inc,2007).

Scientific Classification

Kingdom	Plantae
Division	Magnoliophyta
Class	Liliopsida
Order	Alismatales
Family	Araceae
Genus	Xanthosoma
Specie	X. sagittifolium
Bontical Name:	Xanthosoma sagittifolium(L) Schott.

1.2.2 Cultivation /Use

The planting material most commonly used are portion of the central corn. Others include; the cornels 'Seed' originating from virus;Free cultivations of stem tips. The ground for planting is ploughed and raced and moulds or ridges are formed for pitting the seed. The portion of the corn is placed at the depth of 6-7cm (FAO, 2007) at a distance of 1.6×1.6m (Wilson, 1980).

Xanthosoma sagittifolium is an important food crop in tropical areas, grown for its starchy tubers, which may be baked, mashed, fried or otherwise used as potatoes. Leaves are also eaten as greens (Stephens, 2003). There about 1530 calories in about 2.2kg (One pound) of malanga flour whose composition is approximately: 75.5% carbohydrate, 5.1% protein, 1.6% fat, 9.8% fiber, 1.22% water and 6.8% mineral (Special food™, 2007). The root can be milled into flour, since yautia is very hypoallergenic food and also high in calories (Tropilab® inc, 2007). The flour can be used to make

cookies, quick bread, loaf bread, pan cakes, bagels, muffins, doughnut, dumplings and so forth. Malaga flour is an excellent thickener for gravies, soups, stews and sauces (Special food™, 2007).

1.2.3 Cocoyam Starch

Cocoyam tubers contains considerable amount of starch (Jirarat et al, 2006). The starch extracted from Malanga appears as fine granule (Special food™, 2007), and thus offers smooth textured starch gel. The fine granule-starch is reported to improve binding and reduced breakage of snack product (Jirarat et al, 2006). According to a study of Elevina (2000), the amylase content of cocoyam starch determined by differential scanning calorimetry (DSC) as percentage w/w, dry basis starch is 106.9% (35.34 ± 0.65 by colorimetric method). The phosphorous and calcium contents of this starch are found to be $0.09 \pm 0.001 \text{mg}/100\text{g}$ and $280 \pm 0.02 \text{mg ca}^{++}/100\text{g}$ ($0.28 \pm 0.02\% \text{ca}^{++}$) starch dry basis (Elevina, 2000). According to this author, the higher the phosphorous content of a starch, the higher is its viscosity, while the calcium content confers an acid taste to the starch. Cocoyam starch as disintegrated can be incorporate in one of many ways:

- i. It can be all added to the other ingredients and the homogenous mix wet granulated (Rubinstein, 1998). Here all the starch acts intragranular.
- ii. The starch can be added in dry form all at once to the dried granules. This has the disadvantage of producing soft tablet as too much starch been the granules inhabits bonding (Rubinstein, 1998). The starch added in this form act extragranularly
- iii. About two-third of the starch can be added before wet granulation and the remainder added (in dry form) to the granules. It has the advantage of improving g the disintegration time of water repellent drugs, the starch acting as a pathway for entrance of water into the tablet. When this occurs, the granules are pushed apart due to the expansion of the localized high concentration of starch (Rubinstein, 1998). The starch added in this form act both intra and extragranularly, with the added advantage that, the extragranular starch aid the tablet breakup into granules to yield the individual drug particles (Audu-Peter & Gokum, 2005).

1.2.4 Pharmaceutical Use of Cocoyam Starch

Natural polymers are most commonly used as adjuvant in pharmaceutical preparations such as: thickeners, binders, emulsifier, suspending agents and grilling agents. These natural polymers obtained from various sources can be used in development of sustained release and controlled release formulations (Goswami et al., 2014).

1.2.5 Extraction of starch

The wet milling is the standard method of extracting pure starch from the raw material. After removing the impurities and other debris, separation of pure starch from other undesired components of the raw material like oil, highly-bound proteins and fibers is done through wet milling. When the insoluble starch is collected as its intact granules, it is referred to as native starch. However, at this step, the native starch is wash, dry and keeps for subsequent processing in to modified starches (Whistler R. 2009).

1.2.6 Advantages of Native Starch

Native starch as several advantages, some of which include the following:

- Economic: They are economic and their production cost is less than synthetic material.
- Easy availability: in many countries, they are produced due to their application in many industries.
- Non-toxic and Biocompatible: chemically, nearly all of these plant materials are carbohydrates in nature and compose of repeating monosaccharide unit. Hence, they are non-toxic.
- Biodegradable: naturally occurring polymers produced by all living organisms show no adverse effects on the environment or human being.
- Safe and devoid of side effect: they are from a natural source and hence, safe and without side effects (saviabh et al., 2015).

1.2.7 Disadvantages of Native Starch

Disadvantages of native starch include the following:

- Slow process: as the production rate depends upon the environment and many other factors which can't be change to any desirable extents, therefore natural polymers have a slow rate of production.
- Heavy metal contamination: there are probabilities of having heavy metal contamination, which is often associated with herbal excipients.
- Microbial contamination: there are chances of microbial contamination during production of natural polymers as they are expose to various external environments.

- Batch to batch variation: synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is completely dependent on environment and various physical factors which are not under any controlled procedure
- The uncontrolled rate of hydration: due to differences in the collection of natural materials of different times, as well as differences in region, species, and climatic condition; the percentage of chemical constituents present in a given materials may vary. (Savrabh et al., 2015)

1.3 MODIFICATION OF STARCH

Starch modification can be introduced by altering the structure including the hydrogen bonding in a controlled manner to enhance and extend their application in industrial prospective. The modification takes place at the molecular level and can be chemical, physical or enzymatic. Modified starches are typically used in food and pharmaceutical systems around the globe (Light, 1990).

1.3.1 Types of modified starches

Native starch can be modified in the following ways:

1.3.1.1 Chemical modification of starch

Cross-linking: Cross linking is the most important modified form that finds use in Industry. It involves replacement of hydrogen bond present between starch chains by stronger, permanent covalent bonds. Distarch phosphate or, adipate are the most commonly used cross-linked starch. Cross-linked starches offer acid, heat and shear stability over the native starch (Huijbrechts, 2008).

Stabilization: This process is used in conjunction with cross-linking. Stabilization is used to enhance shelf life through tolerance to temperature fluctuations (Lee, et al., 2002).

Acid hydrolysis: Acid reacts and de-polymerizes the amorphous regions of the granules such that when the starch is heated beyond its gelatinization temperature, the granules rupture quickly. This result in a hot lower viscosity cooked starch which becomes a stronger gel on cooking compared to the native parent starch (Jacobs, 1985).

Enzyme hydrolysis: Starch modified with amylase enzyme produces derivative with good adhesion property. The extent of enzyme hydrolysis determines the range of chain length

produced such as glucose, maltose, oligosaccharides and polysaccharides. α -amylases selectively and randomly attacks the 1,4-linkages of the starch to produce maltodextrins (Chiu, et al., 1997).

Oxidation: This is obtained by reacting the native starch with sodium hypochlorite or peroxide. Oxidized starch products are mainly used as surface sizing agent or coating binder and available in different viscosity grade (Forsell, et al., 1995).

Conversion: This is collective term for a range of chain cleavage reactions of starch. Typically includes acid hydrolysis, enzyme hydrolysis and oxidation (Wade, Weller, 1994).

1.3.1.2 Physical Modification of Starch

Pregelatinization of starch: It is the simplest starch modification, prepared by heating the slurry, roll drying, spray drying or, extrusion process. It maintains starch integrity while improving cold water thickening. This process is designed to enhance adhesiveness of starches. Pregelatinized starches exhibit good flow, binding and compressibility (Joshi, Neves, 2005), and therefore enhanced their pharmaceutical acceptability.

Annealing: This is carried out by soaking the native starch in excess water between 40 to 60% w/w between gelatinization temperatures for a specific period of time. Annealed starch has decreased swelling characteristics (Tester, et al. 1998), and the resultant enhanced crystalline structure does not rupture the starch granules (Coladebeye, et al, 2011).

1.3.4 Applications of Modified starches in Pharmaceuticals and Medical Industries: In recent years, pharmaceutical companies around the world widely use modified starches of various kinds in various stages of drug production or development technology. Excipient plays a very important role in solid dosage formulation by imparting mechanical strength, stability and tablet disintegration properties.

2.0 MATERIALS AND METHODS

2.1 MATERIALS

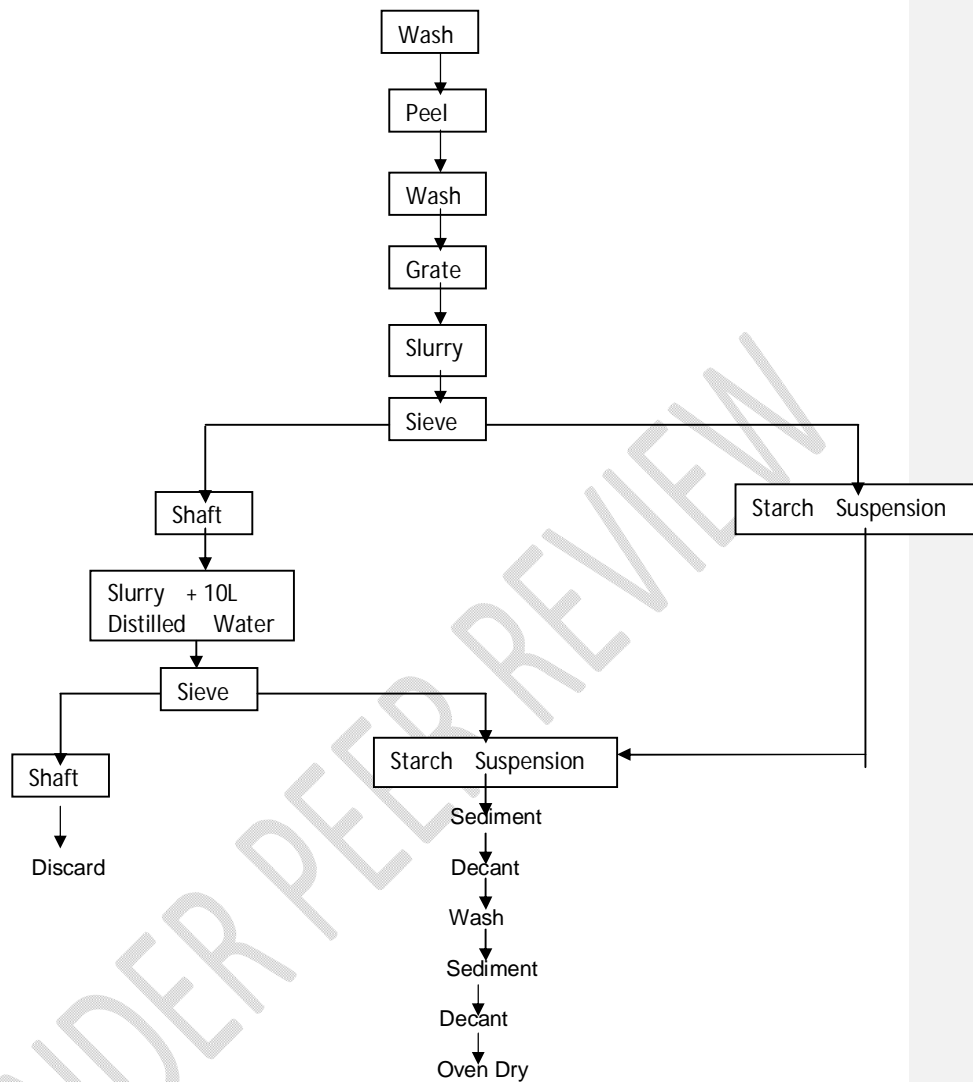
The following materials were used; Paracetamol, gum Tubers of cocoyam were purchased from Faringada market in Jos North Local Government Area

2.2 CHEMICALS

Paracetamol powder (PWD Bp 80, Rhone Doulenc France), maize starch, Philip Harms Reagent, batch 10139, England, Magnesium stearate (Gurr chemicals, GPR), All reagents were of analytical grade.

2.3 EXTRACTION OF COCOYAM STARCH

Tubers of cocoyam were purchased from Faringada market. It was peeled using a clean, sharp kitchen knife and cut into smaller chips. The chips were then properly washed with clean water and milled in a clean mortar after which the pop obtained was transferred into a clean bucket containing 20liters of clean water. With the aid of a clean muslin, the water (filtrate) was then separated from the chaff. The filtrate was further allowed to settle for 24hours after which the water was then separated from the starch. The starch obtained was dried in a hot air oven at 60°C for 2hours in order to remove the remaining moisture from the starch, and thus the starch (cocoyam starch) was then obtained and kept in an air tight bottle (Cavleset *al.*,1991)



Flowchart 1: EXTRACTION OF COCOYAM STARCH

2.4 PREPARATION OF PREGELATINIZED COCOYAM STARCH

The cocoyam starch was obtained using the same method as stated in 2.2 above. The starch was further made into slurry by weighing 50g and dispersed in 200ml of distilled water and was placed in water bath at 55°C for 15 minutes with slow mixing until a paste was obtained. The pregelatinized starch obtained was laid on ceramic crucible as a thin film and dried at 100°C for 24 hours. It was then milled into smaller bits and sieved through a mesh with size of 250µm and the resulting powder was stored in an air tight container.

2.5 PREPARATION OF PARACETAMOL GRANULES

The formula for preparing paracetamol granule containing cocoyam starch as a binder using a concentration of 3%, 6% and 9% is shown in Table 1. A total of two (2) fetches of paracetamol granules were made. In each case, using wet granulation method. The quantity of each ingredients required to make 50 tablets of paracetamol per batch was weighed.

Using an electronic balance, the quantity of lactose required was weighed into clean dry porcelain mortar. The quantity of paracetamol powder was weighed and mixed with the quantity of lactose in the mortar by geometric mixing and triturated with a pestle. Accurate amount of the binder (cocoyam starch) to be used per formulation was weighed and binder solution prepared depending on the concentration of binder to be used over batch. The binder solution was gradually added to the powder mix in the mortar. The powder mix was wet massed with the binder solution in the mortar to obtain a damp coherent mass, which was then screened through a suitable sieve of aperture 1700NM (Sieve no. 10) to form wet granules. The wet granule was dried at a temperature of 60°C in hot air oven for one hour. The dried granules were screened by passing them gently through sieve marked 16 or 20. The granules are stored in an air tight container for 24hours before evaluating for granules properties.

Binder Concentration of 3%, 6% and 9% for 50 tablets

Ingredient	Use	3%	6%	9%
Paracetamol	API	25g	25g	25g
Maize Starch (5%)	Disinter grant	1.5g	1.5g	1.5g
Cocoyam Starch	Binder	0.9g	1.8g	2.7g
Lactose Powder	Diluents	2.3g	1.4g	0.5g
Magnesium stearate (1%)	Lubricant	0.3g	0.3g	0.3g

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TABLE 1: Formula for Preparing Paracetamol Tablets

N.B:The binder to be used is cocoyam starch (modified and unmodified forms) at concentration of 3%, 6% and 9% Batch side.

2.6 EVALUATION OF GRANULE PROPERTIES

2.6.1 Flow Rate and Angle of Repose

A quantity of 10g of the selected size range of granule taken from each batch were introduced into plastic funnel with closed tip and with a measure orifice diameter, efflux, tube length and base diameter. The funnel was fixed at a constant height using a retort stand above a smooth measured paper board. The granules were allowed to flow undisturbed under gravity unto the paper board as a piece of paper used to cover the funnel tip was removed. The time of flow was determined. The height and diameter of the resulting cone were measured and the angle of repose which the heap of the powder makes with the horizontal plane was also determined from this equation;

$$\text{Angle of repose (F)} = \tan^{-1} (h/r)$$

The procedure was repeated five times for each batch of the granules and the main values recorded.

2.6.2 Moisture Content

A quantity of 10g of the granules from each batch was weighed and spread on a paper of measured dimension. The granules were dried in the cabinet at a temperature of 60C at intervals of 30minutes. The weights of the granules were determined at each interval and dried again until a constant weight was obtained. The moisture content was calculated based on lose of weight on a wet weight basis.

2.6.3 Tap and Bulk Densities

A 10g weight of granule per batch was weighed and transferred into a 100ml measuring cylinder and the volume occupied was recorded. The measuring cylinder containing the granules was tapped severally on a soft platform to determine the tapped volume. The procedure was repeated three (3) times and the mean bulk and tapped volume was determined. The bulk and tapped densities were calculated as a ratio of granule weight and respective volume.

2.6.4 Carr's Compressibility and Hausner's Quotient

Both the Carr's Compressibility and Hausner's Quotient were determined. Hausner's Quotient is related to the inter-particulate friction and is useful in the prediction of powder flow properties. The Hausner's Quotient is expressed as;

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

The effect binders would have on this physiochemical property of granules is to reduce the tapped density, increase the bulk density of the granules and then finally reduce the Hausner's Quotient which would then interpret to causing the granules to have good flowability properties because a reduction in Hausner's Quotient would lead to good flow of the granules. For Carr's Compressibility, this is the ability of the granules to decrease in volume under pressure.

$$\% \text{ Carr's Compressibility} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

The effect of binders on the compressibility of the granules is that on increasing the binder concentration, the volume of the granules is decreasing due to the formation of more unfilled voids leading to the increased tendency of the granules to compact thus, increasing the granule's compressibility and hence good flowability.

2.6.5 Tableting

The granules used for the preparation of batches of paracetamol tablets were prepared according to the formula in equation four (4). After evaluating the granule properties, the granules were screened again through sieve 80 was weight and 10% w/w was determined and kept in a different container.

A quantity of maize starch to be used per batch was weighed and mixed with the granules retained on sieve number 80. The quantity of magnesium stearate 8%w/w of the granule mass was weighed and mixed with the 10% weighed out to granules.

The mixture was then added to the granules in a manner resembling a tumble mix, that is, figure 1 kind of movement for 5minutes.

The granule mix were compressed into tablets using a single punch tablet machine with a suitable compression pressure of the die volume was adjusted to corresponded to the specified weight such that the tablet would contain 500g of paracetamol. The machine was operated manually to compress the granules into tablets. The batch size was 50 tablets and all batch of tablets produced were stored in an air tight bottle for 24hours before evaluating the tablet properties.

2.7 EVALUATION OF TABLETS

The tablets produced per batch were evaluated for tablet properties such as weight uniformity, hardness, friability, uniformity of diameter, disintegration and dissolution rate tests.

2.7.1 Weight Uniformity

Twenty (20) tablets were selected at random from each batch of tablets produced. The tablets were weighed individually and collectively using the métier P165 electronic balance. The mean weights were computed. According to the BP (2004) not more than two of the individual weight should deviate from the average weight by more than 5% for formulations of 666.67mg target tablet weight. The percentage coefficient of tablet weight variation (% CV) was calculated according to the equation:

$$\% \text{ coefficient of variation} = \frac{\text{standard deviation}}{\text{mean weight}} \times 100$$

$$\% \text{ coefficient of variation} = \frac{\text{standard deviation}}{\text{mean weight}} \times 100$$

2.7.2 Hardness Test

The Monsanto hardness tester was used to measure. The crushing strength of five (5) tablets selected at random from each batch. Each tablet was placed and held between a fixed avivil and a moving jaw and the load gradually increased until the tablet was crushed and mean hardness of the five tablets was determined and recorded.

2.7.3 Uniformity of Diameter and Thickness

Twenty tablets were randomly selected from each batch produced. The diameter and thickness of each tablets was measured using a Vernier caliper. The mean, standard deviation and coefficient of variation were calculated for each batch.

2.7.4 Friability Test

The friability of ten (10) tablets selected at random from each batch determine using the Roche friabilator (eagle scientific equipment, England) the tablets were weighed collectively using the meltler P165 electronic balance. The tablets were placed in a Roche friabilator and subjected to rotation at a speed of 25rpm for 4 minutes. The tablets were reweighed after the test and the percentage weigh loss or friability was calculated for each batch size from two weight values using the equation:

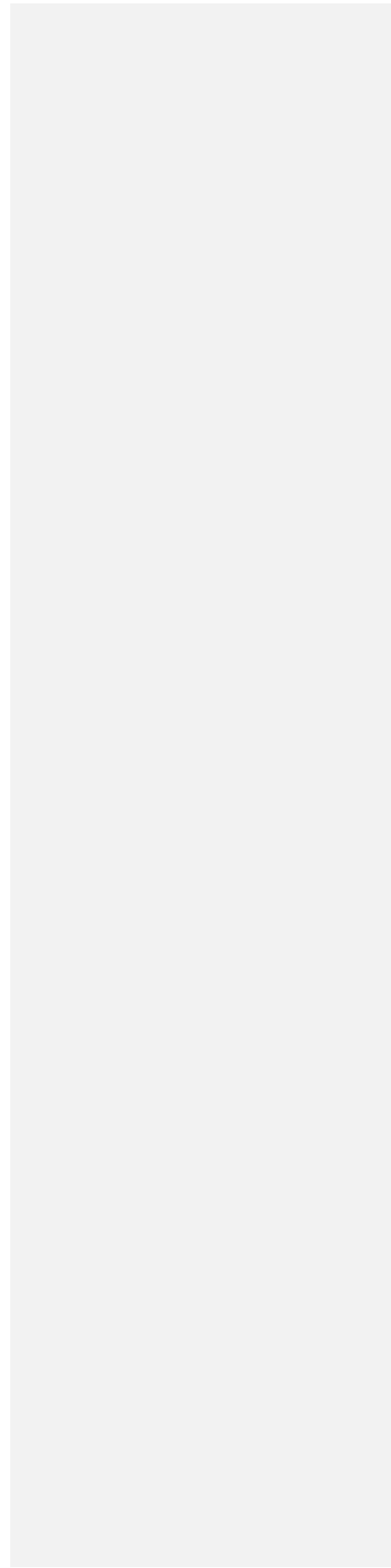
$$\% \text{ friability} = \frac{W_i - W_f}{W_i} \times 100$$

$$\% \text{ friability} = \frac{W_i - W_f}{W_i} \times 100$$

Where w_i =initial weight of the tablets before friabilation

w_f = final weight of the tablets after friabilation.

UNDER PEER REVIEW



2.7.5 Disintegration time

The disintegration apparatus (Eagle scientific limited, Nottingham England) was used in the test. The disintegration apparatus consists of 6 tubes and 0.1 Hydrochloric acid solutions as the disintegration medium.

Six tablets of approximately the same weight was selected from each batch and each of the tablets was placed in each of the six tubes which is raised and lowered at a constant frequency in a beaker containing 600ml of 0.1N hydrochloric acid solution maintained at 37°C (to mimic the gastric environment of the stomach). The time taken for the last tablet or its fragment to pass through the mash into the disintegrating medium is recorded.

2.7.6 Dissolution Rate Test

Tablets of equal weight selected from each batch were used. A six station RC-6 dissolution tester fitted with paddles with 0.1N hydrochloric acid as the dissolution medium mounted a temperature of 36 – 38° c operating at 49 – 51rpm. A single tablet was dropped into the basket filled to the paddle in the beaker containing 1liter of 0.1N hydrochloric acid solution under forced convection arising from the stirring rod. At regular time interval of 5 minutes, samples of the dissolution medium (5ml) withdrawn and replaced immediately with equal volume of 0.1N hydrochloric acid solution using a syringe. The absorbance of the withdrawn samples will be taken using UV-vis spectrophotometer at a predetermined wave length between 240-260nm, the analysis was repeated for one tablet batches and the absorbance obtained. The equivalent drug concentration determined in each case from a standard Beer's plot or calibration curve

2.7.7 Determination of Beer's Plot

A standard calibration curve was derived by plotting standard paracetamol concentrations against absorbance.

0.1g of paracetamol powder was weight using the métier P165, electronic balance (meter instrument, Zurich Switzerland) and dissolved in 100mls of 0.1N hydrochloric acid solution. This is the stock solution of concentration 1mg%. 0.1ml of stock solution was made up to 100ml with 0.1N hydrochloric acid solution to make 0.1mg%. 2ml of stock solution was again made up to give 0.2mg%. The same procedure was carried out using 0.3ml, 0.4ml, 0.5ml and 0.6ml; of the stock solution and made up to

100ml using 0.1N hydrochloric acid solution to give concentration of 0.3mg%, 0.4mg%, 0.5mg%, and 0.6mg respectively.

The absorbance of each concentration of paracetamol was taken using Jenway 6305 spectrophotometer at a predetermined wavelength of 262nm. The values obtained were plotted to give the Beer's plot.

3.0 RESULTS

3.1 PHYSICOCHEMICAL PROPERTIES OF PREGELATINIZED STARCH

	White cocoyam	Red cocoyam
Flow rate (g/s)	1000	869.57
Angle of repose (Degree)	18.26	18.77
Bulk density (g/ml)	0.73	0.67
Tapped Density(g/ml)	1.00	0.97
Hausner's Quotient	1.37	1.45
Carr's compressibility %	27.00	30.93

Table 2: Physicochemical properties of pregelatinized starch

3.2 PHYSICOCHEMICAL PROPERTIES OF GRANULES

The results obtained from analysis in respect to Flow rate, Angle of repose, Bulk density, Tapped density, Hausner's Quotient and Carr's compressibility are tabulated below for different batches.

BATCH	Flow Rate (g/sec) ±SD	Angle of Repose (°)±SD	Bulk Density (g/ml) ±SD	Tapped Density (g/ml) ±SD	Hausner's Quotients	Carr's compressibility (%) ±SD
1.1.1						
IA	1.70(0.07)	28(0.04)	0.31(0.01)	0.37(0.01)	1.194(0.01)	16.22(0.9)
IIA	1.21(0)	27(0.07)	0.30(0.02)	0.36(0.01)	1.200(0.02)	16.67(0.7)
IIIA	1.54(0.07)	26(0.6)	0.31(0.02)	0.35(0.01)	1.129(0.01)	11.43(0.7)
IB	1.34(1.4)	28(0.07)	0.31(0.01)	0.36(0.01)	1.161(0.01)	13.89(0.7)
IIB	1.25(0.07)	28(0.4)	0.29(0.02)	0.36(0.01)	1.241(0.02)	19.44(0.07)
IIIB	1.57(1.4)	27(0.07)	0.29(0.02)	0.34(0.01)	1.172(0.01)	14.71(0.8)

Table 3: Effect of White Cocoyam Starch as Binders on the Physicochemical Properties of

Paracetamol Granules

KEY

- IA = 3% Native Starch
- IIA = 6% Native Starch
- IIIA = 9% Native Starch
- IB = 3% Pregelatinized Starch
- IIB = 6% Pregelatinized Starch
- IIIB = 9% Pregelatinized Starch
- SD = Standard Deviation

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The results obtained from analysis in respect to flow rate, Angle of repose, Bulk density, tapped density, Hausner's Quotient and Carr's compressibility are tabulated below for different batches

BATCH	Flow Rate (g/sec) ±SD	Angle of Repose (°)±SD	Bulk Density (g/ml) ±SD	Tapped Density (g/ml) ±SD	Hausner's Quotient±SD	Carr's compressibility (%) ±SD
IA	1.30(0.07)	27(0.6)	0.40(0.01)	0.45(0.07)	1.125(0.01)	11.11(0.07)
IIA	1.18(1.55)	28(0.8)	0.40(0.02)	0.46(0.01)	1.150(0.01)	13.04(0.07)
IIIA	1.58(0.35)	27(0.04)	0.40(0.01)	0.49(0.01)	1.225(0.02)	18.37(0.6)
IB	1.21(1.00)	26(0.07)	0.38(0.02)	0.45(0.07)	1.184(0.01)	15.56(0.07)
IIB	1.27(0.07)	26(0.07)	0.41(0.02)	0.47(0.01)	1.146(0.02)	12.77(0.4)
IIIB	1.27(0)	27(0.4)	0.41(0.01)	0.47(0.01)	1.146(0.02)	12.77(0.07)

Table 4: Effect of Red Cocoyam Starch as binder on the Physicochemical Properties of Paracetamol Granules.

KEY

IA = 3% Native Starch

IIA = 6% Native Starch

IIIA = 9% Native Starch

IB = 3% Pregelatinized Starch

IIB = 6% Pregelatinized Starch

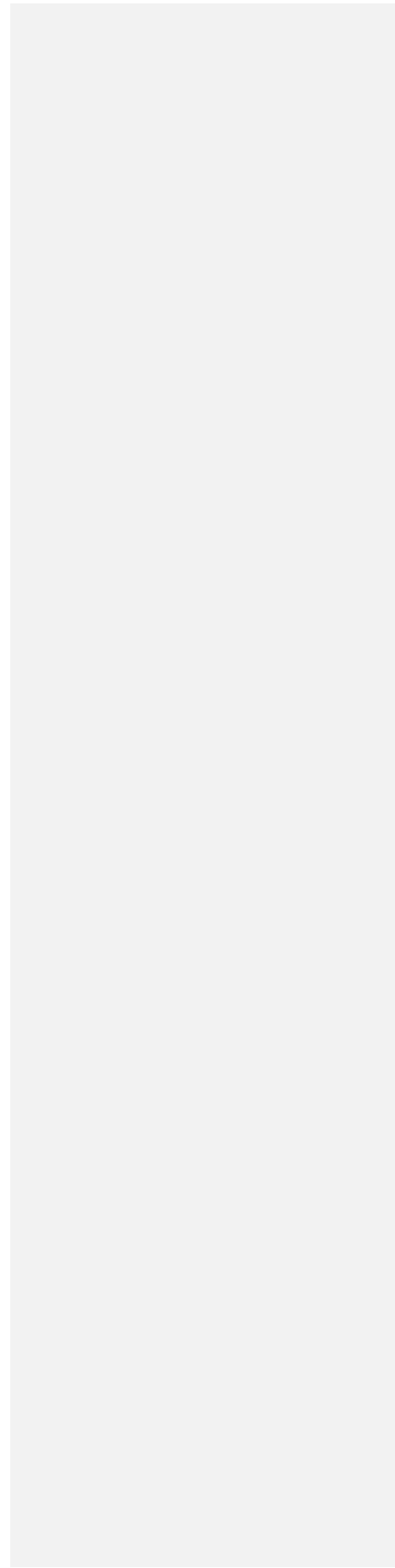
IIIB = 9% Pregelatinized Starch

SD = Standard Deviation

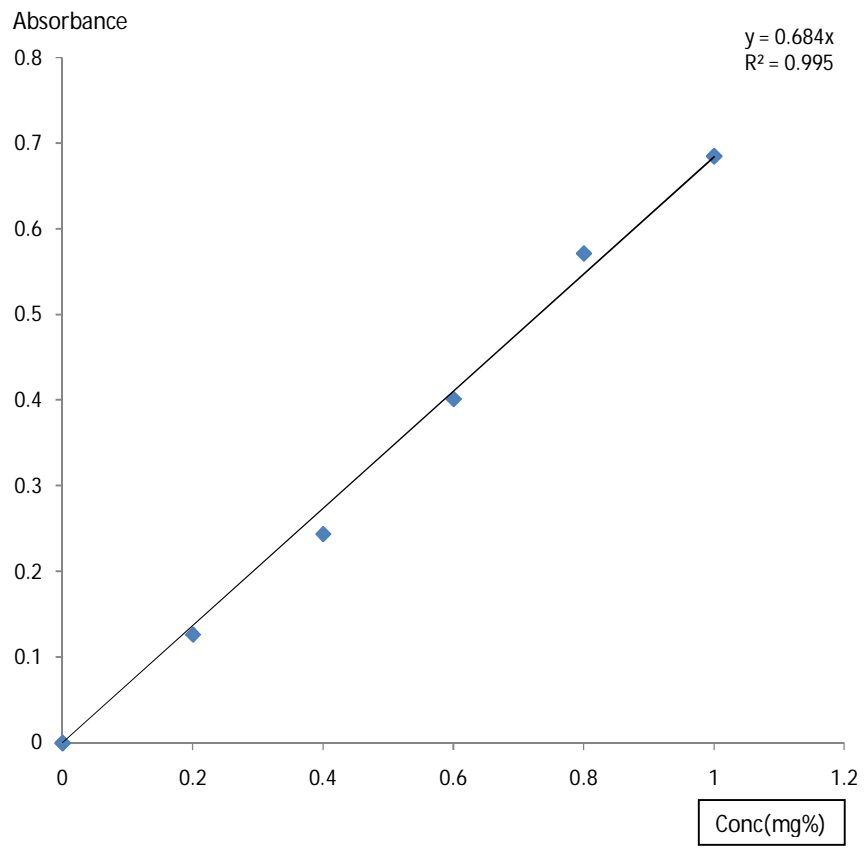
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DISSOLUTION PROFILES OF PARACETAMOL TABLETS

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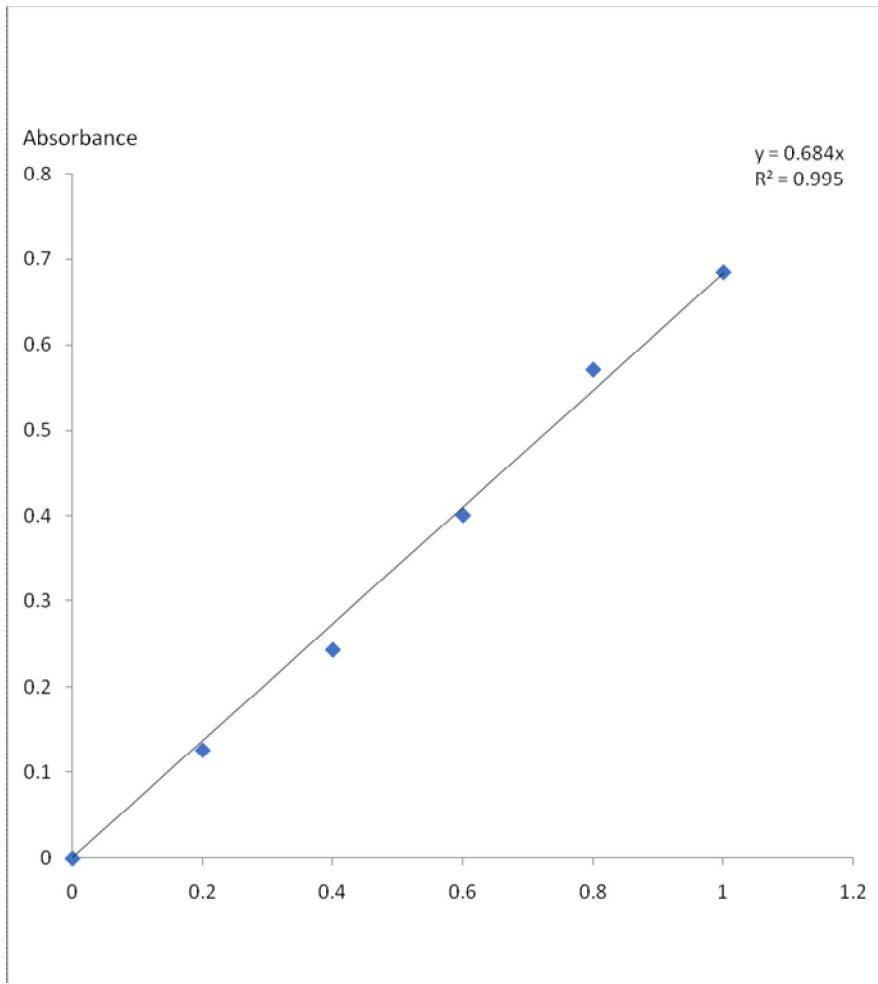


Fig. 1: Beer's plot of acetaminophen in 0.1N hydrochloric acid at 290nm and 37±1

Batch	IA	IIA	IIIA	IB	IIB	IIIB

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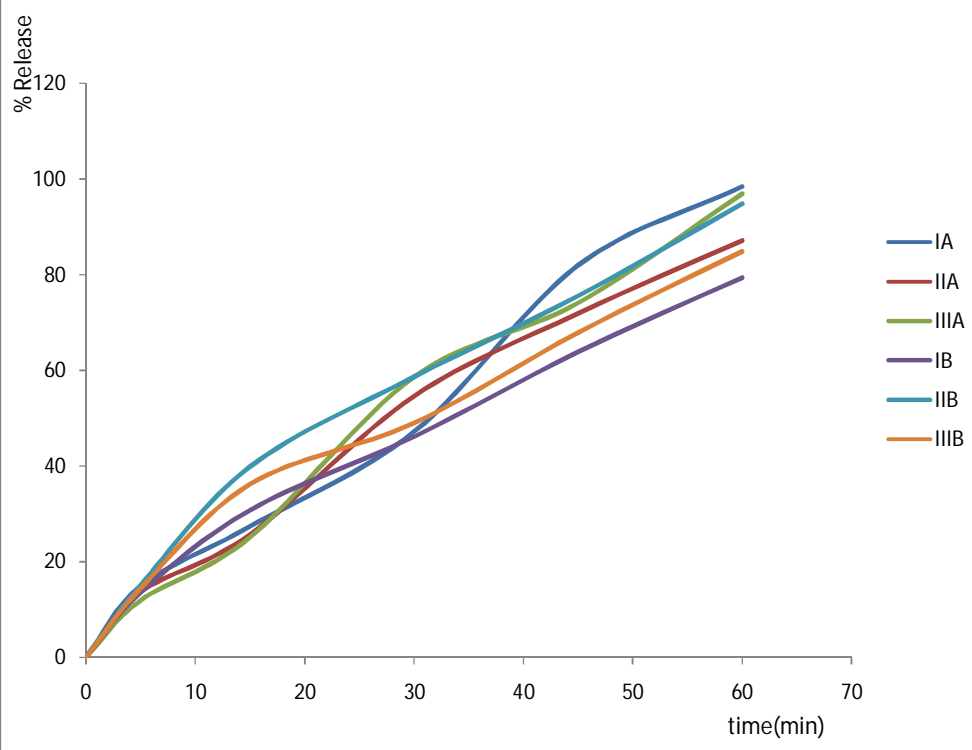
Time(min)	% Release	% Release	% Release	% Release	% Release	% Release
5	14.9	13.6	11.9	13.6	15.1	14.4
15	27.4	25.7	25.1	30.8	39.9	36.2
30	47.2	54.6	58.6	46.2	58.7	49.0
45	82.0	71.9	74.7	63.9	75.6	67.9
60	98.5	87.2	96.9	79.5	94.9	84.9

Table 7: Dissolution Profile of Paracetamol Tablets (white cocoyam starch).

Batch	IA	IJA	IIIA	IB	IIB	IIIB
Time(min)	% Release	% Release	% Release	% Release	% Release	% Release
5	7.0	13.1	14.6	16.2	14.1	14.8
15	15.2	25.0	31.4	34.3	30.0	36.7
30	30.7	52.0	58.6	63.1	57.8	64.0
45	53.1	69.4	72.0	72.1	76.6	77.8
60	76.9	88.0	96.9	94.8	97.7	98.4

Table 8: Dissolution Profile of Paracetamol Tablets (red cocoyam starch)

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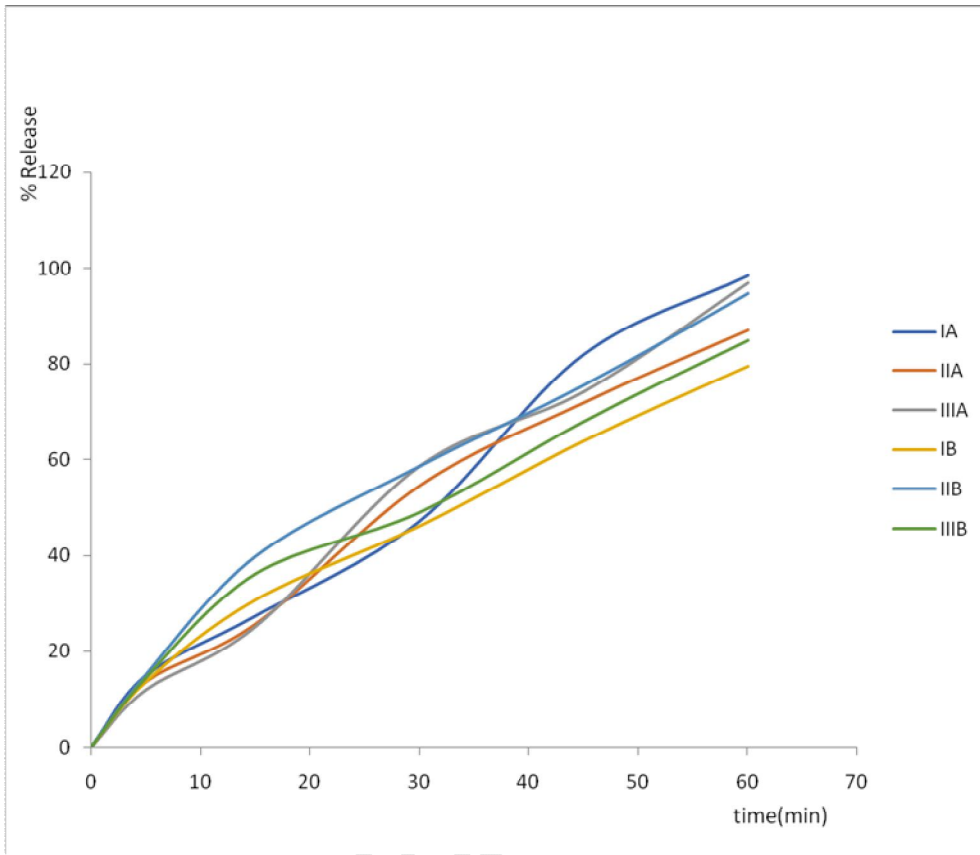
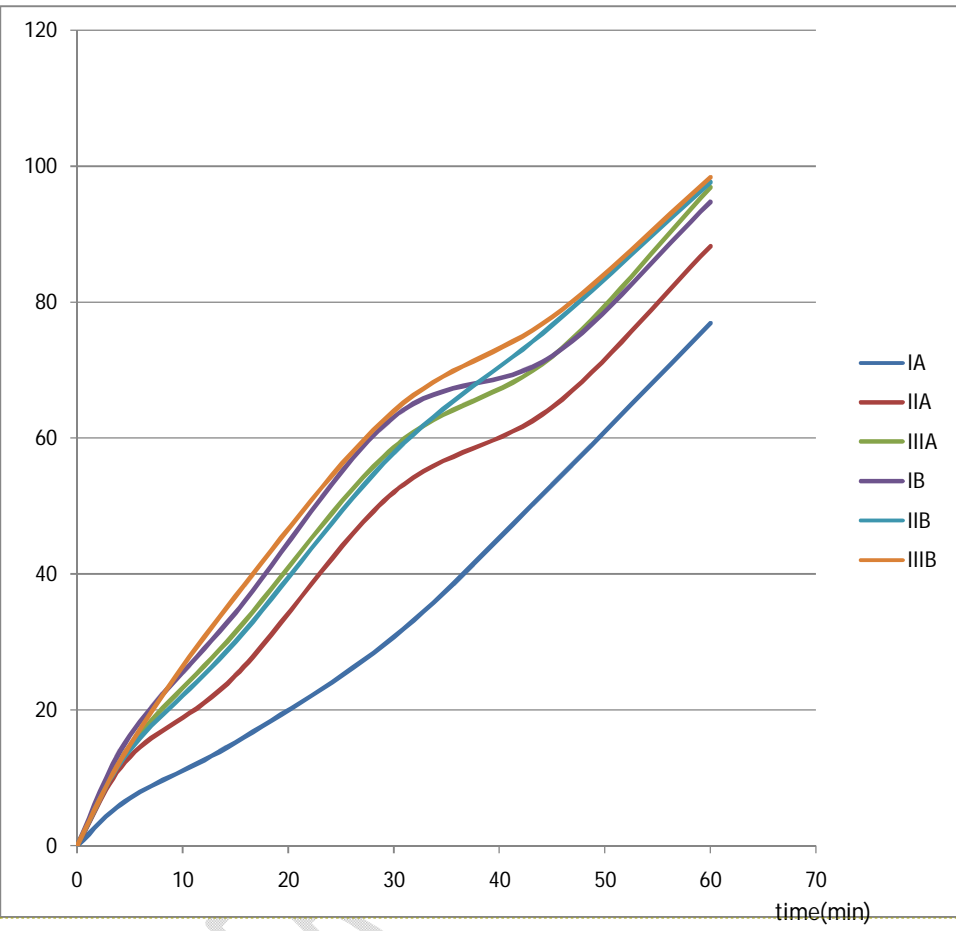


Fig. 2: dissolution profile of paracetamol tablet (white cocoyam starch)

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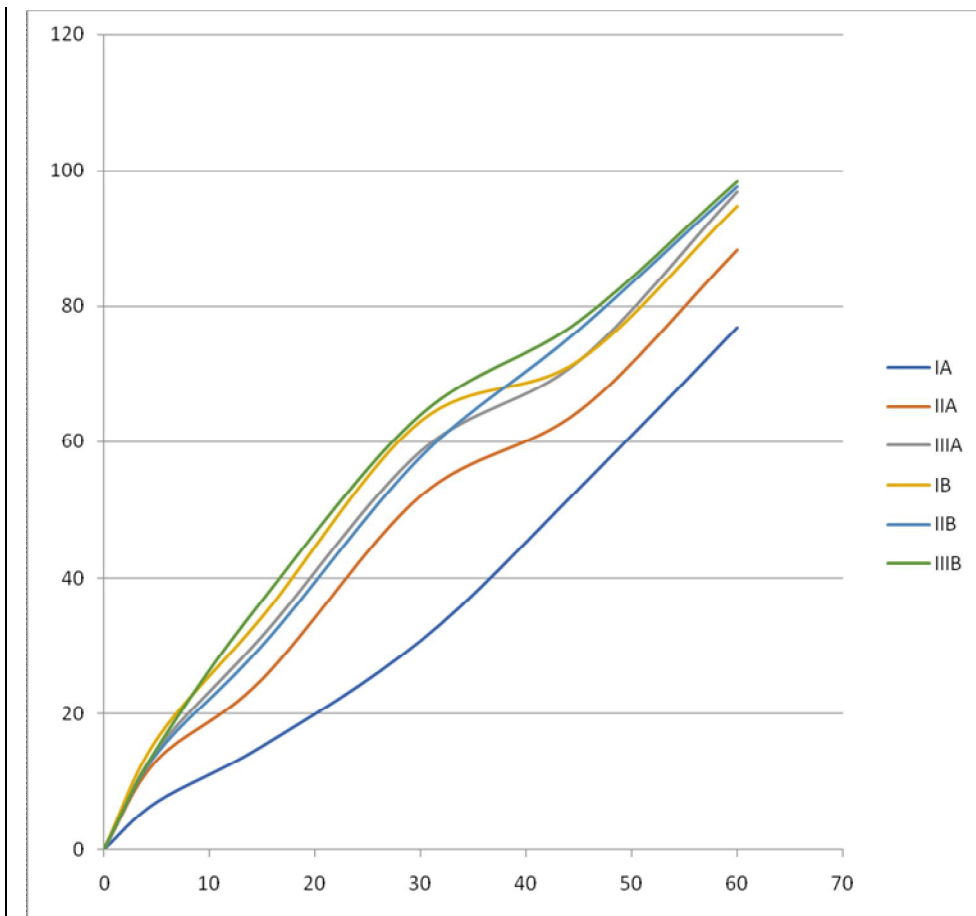


Fig. 3: dissolution profile of paracetamol tablet (Red cocoyam starch)

4.0 DISCUSSION

4.1 PHYSICOCHEMICAL PROPERTIES OF COCOYAM STARCH SAMPLES

The granules formed when the pregelatinized starch was used gave flow rates that are similar to the native starch. Also, there is no significant difference between white and red cocoyam native starch which are 1.70g/sec, 1.21g/sec, 1.54g/sec, and 1.3-g/sec, 1.18g/sec, 1.58g/sec respectively at the concentration of binder as 3%, 6% and 9% respectively. The pregelatinized starch of the white cocoyam and red cocoyam starch also have the same range of flow rate which are 1.34g/sec, 1.25g/sec, 1.57g/sec and 1.21g/sec, 1.27g/sec, 1.27g/sec respectively with the red cocoyam starch having slightly improved flow rate (generally the flow rate of all the batches are good, it shows that the

granules will flow well and flow will not constitute a problem during tableting). The development of flow through an orifice is important to flow because certain pattern of flow may be blocked during downward and outward movement of granules through the orifice and this may be affected by particle size and shape, additives, moisture content and method of pouring into the funnel.

For angle of repose, since angle of repose of about 25° or less than 30° indicate good flow, this implies that all of the batches produced granules with relatively good flow.

The results also show that the batches of white cocoyam have a lower bulk and tapped density than that of red cocoyam starch. There was similarity of bulk and tapped density within the batches of white cocoyam and also within the red cocoyam batches. It was observed that the bulk density was greater than the tapped density. This is expected since part of the bed volume which consisted of voids, when tapped, there was a change from open to close packing within the powder bed. The bed diminished in volume since the void was eliminated.

Values of Hausner's quotient and Carr's compressibility less than 1.25 (or 20% Carr's compressibility) indicates good flow behavior (James Well, 2002) while greater than 1.25 (or 33% Carr's compressibility) indicate a poor flow behavior.

This shows that all the batches of white cocoyam and red cocoyam starch (native and pregelatinized) show a good flow behavior and acceptable result with red cocoyam starch both native and pregelatinized starch having a better flow behavior. There was no significant difference between the concentration of both white cocoyam starch and red cocoyam starch. Carr's compressibility value of between 5-21% is generally accepted, values between 5-15% have been given to produce excellent flow while those with 18-21% have fair flow.

4.2 SOME PHYSICAL PROPERTIES OF PARACETAMOL TABLET

Tablet size and mechanical strength

The thickness of the tablet is often directly related to tablet hardness and can be used as an initial control of this parameter. During the routine compression of tablet, changes in thickness often can indicate problem in flow through the feeder or faulty deposition of granulation in the die. Tablets, which are too thin, are liable to break easily and those, which are too thick, may give difficulty in swallowing.

The results from table 5 and 6 show that Batch IIIA of both white cocoyam and Red cocoyam starch have hardness values of 9.2kgf and 10.3kgf respectively in terms of binder efficiency. The more the binding efficiency of binder, the harder the tablets.

The degree of hardness of tablets depends on its physical size and shapes together with the characteristics of the chemicals that go into the formulation and the pressure applied during compression. If the tablets are too soft, it may not withstand the necessary multiple shocks occurring during handling, shipping and dispensing. If it is initially too hard, it may not disintegrate in the requisite period of time.

In the pharmaceutical industry, a 4kg "crushing strength" is considered minimal and this value usually should not exceed 7kgf. This implies that all the batches of modified and unmodified of white cocoyam starch and red cocoyam starch fall above the normal acceptable range.

Table 5 and 6 shows the friability test result for white and red cocoyam starch (modified and unmodified). Generally, friability decreases with increasing binder concentration and increasing with decreasing granules sizes. Friction and shock are the forces that most often cause tablets to chip, cap and break. The tablet friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion, handling and shipping. The loss due to abrasion is a measure of tablet friability. A maximum weight loss of not more than 1% of the weight of the tablets being tested during friability test is considered generally acceptable and any broken or smashed tablets are not picked up. From the observation made from results gotten, it implies that the tablets in all the batches are of poor compact.

Weight uniformity is also an essential property to be considered during tablet compression as it helps to ensure all tablets in the same batch are of uniform weight. Granule size and granule flow-ability are some of the factors that affect tablet weight. According to Remington, 2005, an average weight greater than 638mg with SD of not more than 5% are indicative of good uniformity of weight and thickness. Also. It is expected that the average weights from the batches should fall within the range of 570mg to 630mg and not more than 2 tablets should fall outside this limit (U.S.P) and from table 5 and 6, all batches are within the range.

Disintegration Rate

Disintegration involves the rapid breaking up of tablet into small fragments to ensure that the tablet releases its active ingredient when exposed to the appropriate condition. It also measures the ease with which the bonds formed during compression are broken down, a short disintegration time indicates that the bonds are easily broken while long disintegration time is due to formation of strong bonds which takes longer time to break (Shok et al, 1992). Table 5 and 6 shows the disintegration time obtained from white and red cocoyam starch (modified and unmodified). All the batches having fairly good disintegration time in the range 1.42min to 2.11min except for batch IA of red cocoyam starch that failed the test with 27.59min. The time required for uncoated tablet to disintegrate is 15min (B.P, 1988).

Dissolution Rate Test

The concentration of binder and method of incorporation affect the time of dissolution of paracetamol tablets: apart from Batch IA of red cocoyam starch (unmodified) they all had a fast release of paracetamol.

Generally, disintegration time is known to affect the release rate of tablet formulations. The longer the disintegration of the tablets, the lower the rate of dissolution vice versa. As such, the rate of dissolution parameters can further be corroborated with the results obtained from disintegration rates and this shows that there is no significant difference between pregelatinized and unmodified starch and between white cocoyam and red cocoyam starches with the binders release at least 50% of the total drug content within 30 minutes but batch IA of red cocoyam starch shows the least release of the total drug content of 30.7% at 30 minutes. This Batch has observed from disintegration rate result also seems to have a prolonged disintegration time of 27.59min.

4.4 CONCLUSION

From the evaluation of the binding properties of pregelatinized cocoyam starch on paracetamol tablets the following conclusions can be drawn based on this study.

- Pregelatinized cocoyam starch did not have excellent flow
- Pregelatinized cocoyam starch did not have significant effect in comparison to the native one

- There was no significant variation across the concentration of the binders of both white and red cocoyam starch of both native and pregelatinized

In summary, there was pregelatinized cocoyam starch have similarity with native cocoyam starch with red cocoyam starch having a better flow rate than white cocoyam starch.

APPENDIX

1. Flow Rate =
$$\frac{\text{granule weight (g)}}{\text{time taken for flow (s)}}$$
2. Bulk Density =
$$\frac{\text{granule weight (g)}}{\text{bulk volume (cm}^3\text{)}}$$
3. Tapped Density =
$$\frac{\text{granule weight (g)}}{\text{tapped volume (cm}^3\text{)}}$$
4. Carr's Compressibility (%) =
$$\frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100$$
5. Hausner's quotient =
$$\frac{\text{tapped density}}{\text{bulk density}}$$
6. Angle of repose =
$$\tan^{-1} \frac{\text{height of granules}}{\text{radius of granules}}$$
7. Tensile strength =
$$\frac{2P}{\pi DT}$$
 - P = Tablet Hardness
 - D = Tablet Diameter
 - T = Table thickness

8. Binding capacity =

$$\frac{\text{crushing strength (hardness)}}{\text{table thickness}}$$

9. % Standard deviation =

$$\frac{\sqrt{\frac{\sum(x-\bar{x})^2}{n-1}}}{\bar{x}} \times 100$$

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