EVALUATION OF STARCH FROM GHANAIAN SWEET POTATO VARIETIES AS EXCIPIENTS FOR SOLID ORAL DOSAGE FORMS

By

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DECLARATION

I hereby declare that this thesis is my own work for the Master of Philosophy degree in Pharmaceutics and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the university, except where due acknowledgement has been made in the text.

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DEDICATION

This work is dedicated to mymum, Madam Veronica Abena Achiaa, for her love, prayers and support which has brought me this far.

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ABSTRACT

The study sought to investigate the functional properties of starches obtained from four (4) new Ghanaian sweet potato varieties, in order to facilitate their exploitation as substitute excipients for the local pharmaceutical manufacturing industry. The varieties, namely: CRI Hi-starch, Sauti, Ogyefo and Faara were developed by way of introgression of desirable genes into adapted local germplasm, while their respective starches were obtained by wet separation techniques. Organoleptic properties ofthesweet potato root tubers and their starches, in addition to pre-formulation studies on the starches' physicochemical properties, proximate composition and pasting properties were undertaken in order to determine their suitability for pharmaceutical use. Furthermore, validation studies onthe sweet potato starches were carried out in order to determine their performance as pharmaceutical binder and disintegrant. Differences in the physicochemical properties, proximate composition, pasting properties and functional properties (as binder and disintegrant)for the four sweet potato starches were not significant. The Hi-starch sweet potato variety however had substantially high starch yield on fresh and dry weight basis (31.7 % fwb; 79.9 % dwb) and may becommercially suitable for industrial exploitation. Starches from all four sweet potato varieties were white in colour and predominantly fine (particle size < 75 µm). Granule shape of the sweet potato starches ranged from round to polygonal with mean diameter in the range of 14.2 - 16.3 µm. The sweet potato starches had higher bulk density (0.50 - 0.58g/cm^3), tapped density (0.75 - 0.82 g/cm^3) and true density (1.15 - 1.18g/cm^3) compared to a commercially available maize starch (0.40, 0.61 and 1.10g/cm^3, respectively). The sweet potato starches also had acidic pH (5.1 - 5.9), lower amylose content (22.3 - 26.2 %) and higher purity (97.37 - 97.84 %) compared to the commercial maize starch (5.2, 27.6 % and 96.82 %, respectively). Starch from all four sweet potato varieties had a 'type A' pasting pattern; which was characterized by a high swelling power, maximum granule fragmentation, low setback and final viscosities. The swellingcapacity of the sweet potato starches (694 - 762 BU) was comparable to that of a commercially available 'super disintegrant' [sodium starch glycolate (762 BU)], but higher than that of the commercial maize starch (451 BU). The tensile strength (tablet hardness) and friability of paracetamol tablets formulated with the sweet potato starches as binder were significantly better ($p < 0.05$) than similar compacts containing the commercial maize starch. The sweet potato starches also caused faster tablet disintegration and release of paracetamol.

The results established thesweet potato starches to be suitable for pharmaceuticaluse andthey were more robust as binder and disintegrant compared to the commercially available maize starch.

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CHAPTER ONE

INTRODUCTION

General introduction and justification of the research

The search for lesser known and under-utilized crops, not just as potentially valuable food security crops, but also as sources of excipients for the pharmaceutical industry has been a major focus for research in recent years. Pharmaceutical excipients refer to all materials other than the active drug or pro-drug essential to the manufacture and administration of the dosage form. A practical understanding of pharmaceutical excipients is essential to developing optimal, robust formulations and appropriate manufacturing processes (Chang and Chang, 2007). Starch, a key excipient in the manufacture of solid oral dosage forms such as tablets and capsules is a biopolymer and the major carbohydrate reserve in plants. It functions as a diluent, binder and or disintegrant in concentrations that depend on the quality or source of the starch.

For some time now, the Crop Research Institute (CRI) of Ghana has through genetic engineering and back crossing techniques developed new varieties of sweet potato with high food value, nutrient content and improved starch yield for the Ghanaian market (Dapaah *et al.*, 2005). It has been reported that genetic modifications of starch crops havein most cases led to the development of starches with improved and targeted functionality (Jobling, 2004). Such starches have been applied in the textile, paper, wood, petrochemical, food and beverage industries for various end uses (Graffham *et al.*, 1998). However, the possible applications of starch from these improved varieties from CRI as pharmaceutical excipients have not been exploited. It is envisaged that, genetic differences in the varieties would translate into physical and biochemical changes in the respective starch granules; which would ultimately influence their functional properties as pharmaceutical diluent, binder or disintegrant.

While studies on the physicochemical properties, proximate composition and pasting properties of starch generally help predict its nature, behaviour and industrial application, suitability for pharmaceutical use is determined by formulation and validation studies. For this reason, the code of Good Manufacturing Practice (cGMP) stipulates manufacturing process validation before use of new excipients. This helps decrease risks of processing problems, defect costs and regulatory non-compliance (Larsson *et al.*, 1997).

Starch granule size and size distribution are known to affect swelling and disintegrant

action, while its pH influence drug - excipient interaction. The pasting properties illustrate starch water binding capacity and the strength of hydrogen bonds that stabilize and maintain granule integrity. This can therefore be used to predict both binder and disintegrant quality. The amylose content gives an indication of not only the molecular composition, but also the crystalline - amorphous arrangement within the starch granule. This will ultimately influence starch swelling and disintegrant functionality. The proximate composition is important in establishing starch purity, as impurities such as proteins, soluble gums or latex, lipids and inorganic salts of phosphates can significantly alter starch functionality and lead to false characterization (Vasanthan, 2001).

In addition, studies on the flow and bulk properties of the starches as diluents, their adhesive or binder quality, and disintegrant properties as well as drug release capacity of formulations containing these starches could help validate their suitability for pharmaceutical use.

This study thus sought to investigate the functional properties of the sweet potato starches in order to facilitate their exploitation as substitute excipients for the local pharmaceutical manufacturing industry. This involved:

- Identification of sweet potato varieties with good starch yield for possible commercial exploitation.
- Determination of physicochemical and pasting properties of the extracted starches and prediction of their possible suitability for use as pharmaceutical excipients.
- Determination of proximate composition of thestarches and estimation of their purity.
- Assessment of the starches diluent quality.
- Determination of binder quality and optimum binder concentration of the starches in paracetamol tabletformulations.
- Determination of disintegrant quality and optimum disintegrant concentration of the starches in paracetamol tablet formulations.
- Determination of the starches influence as binder and disintegrant on in-vitro drug release from paracetamol tablets.

Paracetamol was used as a model drug due to its poor flow and compressibility, lack of inherent disintegrant capacity, as well as high capping and lamination tendencies (Okor, 2005; Mullarney and Hancock, 2004).

CHAPTER TWO

LITERATURE REVIEW

2.1 The sweet potatoplant

2.1.1 Taxonomy

The sweet potato [*Ipomoea batatas (L.) Lam.*] is a dicotyledonous plant of the family convolvulaceae. This family convolvulaceae contains approximately fifty (50) genera and more than 1200 species. Out of these, the sweet potato is the only member that is grown as a food crop (Edmond, 1971). Thesweet potato genus Ipomoeaalso includes several garden flowers called morning glories. In spite of itsname, sweet potato is not the same as potato (*Solanum tuberosum*); but they share the common order, Solanales(Woolfe, 1992; CIP, 2010).

2.1.2 Description

The plant is a herbaceous perennial vine, bearing alternate cordate or heart-shaped and palmately lobed leaves. They also bear medium-sized sympetalous flowers. The edible roottuber is long and tapered, with a smooth skin whose colour ranges from red, purple, brown and beige. Its flesh colour ranges from white through yellow, orange and purple (Villareal, 1982; Dapaah *et al.*, 2005).

2.1.3 Origin and distribution

The sweet potato is widely accepted to have originated from Latin America; from where it spread to other regions of the world including Africa. However, because of its versatility, the crop can be found in both warm temperate and tropical regions of the world. China accounts for over 80 % of global output, but on per capita basis, production is highest in countries where sweet potato is a major staple crop. This is led by Papua New Guinea at 550 kg, the Solomon Islands at 160 kg, Burundi and Rwanda at 130 kg and Uganda at 100 kg per person per year (Purseglove, 1991; Villareal, 1982).

2.1.4 Cultivation

Sweet potato can grow at altitudes ranging from sea level to 2500 meters. The plant does not tolerate frost. It however grows best at an average temperature of 24 °C (75 °F), abundant sunshine and warm nights. Annual rainfall of 750 - 1000 mm (30 - 39 inches) is considered most suitable, with a minimum of 500 mm (20 inches) in the growing season. The crop is sensitive to drought at the tuber initiation stage (50 - 60 days after planting),

and it is not tolerant to water-logging; as it may cause tuber rots and reduce growth of storage roots if aeration is poor. Depending on the cultivar and climatic conditions, root tubers mature in two to nine months. They are mostly propagated by stem or root cuttings or by adventitious roots called "slips" that grow out from the tuberous roots during storage. True seeds are used for breeding only (Ahn, 1993).

Though they can be grown on a variety of soils, well-drained, light and medium textured soils with a pH range of 4.5 - 7.0 are more favourable for the plant. They can also be grown in poor soils with little fertilizer. However, sweet potatoes are very sensitive to aluminum toxicity and will die within six weeks if lime is not applied at planting. In the tropics, the crop can be maintained in the ground and harvested as needed for market or home consumption (Lu and Sheng, 1990).

Sweet potatoes may be cured to improve storage, flavour and nutrition; and also to allow wounds on the periderm of the harvested root tuber to heal. Proper curing requires drying the freshly dug root tubers on the ground for two to three hours, then storage at 29 - 32 °C and 90 - 95 % relative humidity for 5 - 14 days. Cured sweet potatoes can keep for 13 months when stored at 13 - 15 °C and greater than 90 % relative humidity. Starch content of sweet potato depends on the variety as well as age during harvest. Harvesting at 120 days after planting is considered optimal to obtain a high starch as well as flour yield. Starch content is considerably reduced when harvesting is delayed at 150 days after planting (Antarlina and Kumalaningsih, 1990).

2.1.5 Cultivation in Ghana

Ghana has tropical climatic conditions with abundant sunshine and average annual temperature and rainfall of 26 °C (79 °F) and 736.6 mm (29 inches), respectively (Ghanaweb, 2012). This is conducive for the growth and cultivation of root and tuber crops such as sweet potato. However, challenges such as inadequate all year supply of tubers, agro-ecological barriers to crop cultivation, high tuber perishability, high per capita consumption, low crop yield and dry matter limit their exploitation for starch (Graffham *et al.*, 1998). Described as the world's most under-rated crop and best kept secret in agriculture (Villareal, 1982), sweet potato is increasingly becoming the third most important root and tuber crop after cassava and yam in Ghana; with an estimated annual production of 200,000 metric tons (Dapaah *et al.,* 2005). This is low when compared with output for the country's main staple crops such as cassava (9.7 million metric tonnes), yam (3.1 million metric tonnes) and maize (1.3 million metric tonnes)

[MOFA, 2003]. This notwithstanding, prospects for sweet potato cultivation and starch production are good as it can be produced in all four agro-ecological zones (viz. Guinea and Coastal savannas; Savanna or Forest transition and Forest zone) and even on marginal soils. Furthermore, its short maturity period (3 - 4 months) means that the crop can be supplied three times in a year.

Presently, sweet potato research and cultivation by small scale out-growers in Ghana is largely supported by donor interventions such as SASHA (Sweet potato Action for Security and Health in Africa) and SPHI (Sweet potato for Profit and Health Initiative). Aside their health promotion objectives, these interventions will in the long term contribute to increased commercialization of the crop for industrial starch.

2.1.6 Common sweet potato diseases and pest

In Ghana, common pests and diseases that attack the crop include *Cyclas* species, *Alcidodes* species, millipede and sweet potato virus complex disease (SPVD)[Otoo *et al.*, 2005]. In addition to these, a number of viral, plant and animal pests attack sweet potatoes at various stages of crop development (Table 2.1). This may affect crop yield and also enhance post harvest losses (Ames *et al.*, 1996).

Table 2.1: Common pest and diseases of the sweet potato plant

Scientific Name	Common Name	Group	Agronomic importance
Cyclas spp	Sweet potato weevil	Insect	Root, stem and foliage feeder
Euscepes postfasciatus	West Indian sweet potato weevil	Insect	Root and stem feeder
Blosyrus spp	Rough sweet potato weevil	Insect	Root and foliage feeder
Synanthedon spp	Clearwing moth	Insect	Root and stem feeder
Peloropus batatae	Peloropus weevil	Insect	Root and stem feeder
Omphisia anastomasalis	Sweet potato stem borer	Insect	Stem borer and feeder
Alcidodes spp	Stripped sweet potato weevil	Insect	Stem borer and feeder
Physomerus grossipes	Sweet potato bug	Insect	Stem borer and feeder
Phyllophaga spp	White grub	Insect	Root feeder
Acraea acerata	Sweet potato butterfly	Insect	Foliage feeder
Aspidomorpha spp	Tortoise shell beetles	Insect	Foliage feeder
Agrius convolvuli	Sweet potato hornworm	Insect	Foliage feeder
Brachmia convolvuli	Leaf folders	Insect	Foliage feeder

Scientific Name	Common Name	Group	Agronomic importance
Herpetogramma hipponalis	Leaf folders	Insect	Foliage feeder
Strobiderusa equatorialis	Strobiderus beetle	Insect	Foliage feeder
Spodoptera spp	Army worms	Insect	Foliage feeder
Aceria spp	Erinose mite	Mite	Foliage feeder
Aphis gossypi	Aphid	Insect	Virus transmitter and stem feeder
Bemisia tabaci	Whitefly	Insect	Virus transmitter and foliage feeder
Aphid transmitted Potyvirus	Sweet potato feathery mottle virus	Virus	Foliage disease
Whitefly transmitted Closterovirus	Sweet potato sunken vein virus	Virus	Foliage disease
Whitefly transmitted potyvirus	Sweet potato mild mottle virus	Virus	Foliage disease
Clostero-potyvirus	Sweet potato virus complex	Virus	Foliage disease
Erwinia chrysanthemi	Bacterial stem and root rot	Bacterium	Foliage and root disease
Pseudomonas solancearum	Bacterial wilt	Bacterium	Foliage and root disease
Streptomyces ipomoea	Soil rot	Bacterium	Foliage and root disease
Elsinoe batatas	Leaf and stem scab	Fungus	Foliage disease
Alternaria bataticola	Alternariosis/blight	Fungus	Foliage disease
Phomopsis ipomoea	Phomopsis Leaf spot	Fungus	Foliage disease
Fusarium spp	Fusarium wilt	Fungus	Foliage disease
Helicobasidium mompa	Violet root rot	Fungus	Foliage and root disease
Sclerotium rolfsii	Sclerotial blight	Fungus	Foliage and root disease
Ceratocystis fimbriata	Black rot	Fungus	Foliage and root disease
Meloidogyne spp	Root knot	Nematode	Foliage and root disease
Ditylenchus spp	Brown ring	Nematode	Root disease
Roytlenchulus reniformis	Reniformis nematode	Nematode	Foliage and root disease
Pratylenchulus spp	Lesion nematode	Nematode	Root disease

Source: Ames *et al.*, 1996

2.1.7 Nutritional value

Beside starch, sweet potatoes are rich in simple carbohydrates, dietary fibre, beta carotene (a vitamin A equivalent nutrient), vitamins C and B_6 (Table 2.2). They are considered to be more nutritious than potato and can be taken by diabetics as animal studies have shown it to help stabilize blood sugar levels and lower insulin resistance. This has been

attributed to its high dietary fibre content which slows down digestion and the release of sugar. The leaves and shoots of the plant can be eaten and have been shown to contain nutrient levels comparable to pork or beef (Collins and Walter, 1982; Villareal, 1982).

According to Bradbury and Holloway (1988), sweetpotato dry matter is composed of starch (70 %), total sugar (10 %), total protein (5 %), lipid (1 %), ash (3 %) and fibre (10 %). However, this composition varies widely because of differences in variety, soil type, pest and disease incidences and cultivation practices (Tian *et al*., 1991; Woolfe, 1992).

Table 2.2: Nutritional composition of fresh sweet potato root tubers

Nutritional value of raw sweet potato root tuber per 100 grams	
Energy	360 KJ (86 Kcal)
Carbohydrate	20.1 g
Starch	12.7 g
Sugars	4.2 g
Dietary fibre	3.0 g
Fat	0.1 g
Protein	1.6 g
Beta carotene	8.5 mg
Thiamine (vitamin B1)	0.1 mg
Riboflavin (vitamin B2)	0.1 mg
Niacin (vitamin B3)	0.6 mg
Pantothenic acid (vitamin B5)	0.8 mg
Pyridoxine (vitamin B6)	0.2 mg
Folate (vitamin B9)	11.0 µg
Ascorbic acid (vitamin C)	2.4 mg
Vitamin E	0.3 mg
Calcium (Ca)	30.0 mg
Iron (Fe)	0.6 mg
Copper (Cu)	0.2 mg
Magnesium (Mg)	25.0 mg
Phosphorus (P)	47.0 mg
Potassium (K)	337.0 mg
Sodium (Na)	55.0 mg
Zinc (Zn)	0.3 mg

Source: USDA, 2010

2.1.8 Uses and application of sweet potato

Sweet potato has many culinary uses in the countries and regions where they are grown. In Ghana, the root tubers may be deep fried or boiled and eaten as "Ampesi", with the leaves serving as substitute for cocoyam leaves ("kontomire"). The tubers and foliage are also used as feed for pigs, poultry and ruminants. The main economic importance of the sweet potato in China, which accounts for most of the world's output, is starch production from the root tubers. The starch is subsequently used to produce noodles by the food industry. The high vitamin A or beta carotene content of sweet potato, especially varieties with orange flesh, is encouraging their use in counteracting poor vision among malnourished and vitamin A deficient children (Otoo *et al.*, 2005; Tian *et al.*, 1991).

2.2 Biochemistry, sources and morphological properties of starch

Starches differ depending on their botanical source, biochemistry and morphological properties. Animal starch, also known as glycogen is not recommended for pharmaceutical use as concerns and risks of diseases such as transmissible spongiform encephalopathy (TSE) or bovine spongiform encephalopathy (BSE) and genetically modified organisms (GMO) are real (Chang and Chang, 2007).

2.2.1 Distribution and sources of starch

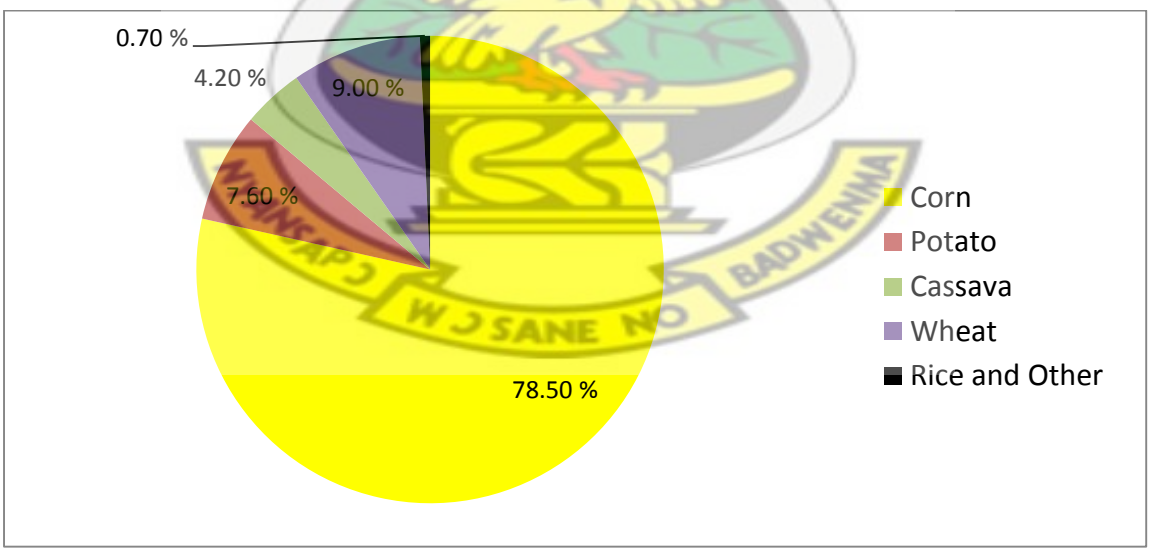


Figure 2.1:World wide starch production

Source: International Starch Institute, 2004

Starch is a biopolymer and the major carbohydrate reserve or storage energy in plants. They are found as granules in cereal grain seeds (e.g. corn, wheat, rice,sorghum), tubers

(e.g. potato, yam), roots (e.g. cassava, sweet potato, arrowroot), legume seeds (e.g. peas, beans, lentils), fruits (e.g. green bananas, unripe apples, green tomatoes), stem piths (e.g. sago, palm) and leaves (e.g. tobacco) [Chen *et al*., 2003]. Most of the 60 million metric tonnes of starch produced globally in 2004 were from corn or maize with other commonly used sources being wheat, potato, tapioca and rice (Figure 2.1).

2.2.1.1 Starch market and production in Ghana

There is a growing market and demand for starch by industries in Ghana (Table 2.3). This can be largely attributed to a rapidly expanding pharmaceutical manufacturing industry; even as the wood industry declines (Odoom-Domson and Vlosky, 2010). Maize, cassava and potato starches are the main starch sources utilized by industry in Ghana. However, most of the country's starch needs are imported, with the local pharmaceutical industry relying mostly on the cheaper, imported maize starch. Although, cassava and maize starches have been successfully produced locally, their prices are uncompetitive compared to imported starch. This is attributed in part to the high per capita consumption of these staples which affect raw material supplies and starch production cost (Graffham *et al.*, 1998).

Table 2.3: Starch market and consumption in Ghana

Sector	Market share (%)	Estimated quantity (tonnes/annum)
Textiles	40	1680
Pharmaceutical	20	840
Paper	10	420
Food	3	126
Plywood	27	1134
Total	100	4200

Source: Graffham *et al.*,1998

2.2.2 Starch granular shape and size distribution

Starch granules naturally exist in different ranges of size distribution, shapes and dimensions which depend on their botanical source, species, cultivar, genetic - environment interactions, growing and harvest conditions. The granule size varies from the tiny granules in rice and oat starches (1.5 - 9.0 μm) to the large ones in potato starch

(up to 100 μm). Mung bean starch has a relatively narrow size distribution while the broadest distribution is found for potato starch. Some cereal starches such as wheat, rye and barley show a bimodal size distribution. The small granules (called B-granules) are spherically shaped with a diameter below 10 μm and the large granules (called A-granules) are lenticular with a diameter around 20 μm (Eliasson and Gudmundsson, 1996). The size distribution determines its swelling functionality (Leach *et al*., 1959). Since their morphological characteristics show significant difference, most starches can be identified from their appearance under a light microscope (Table 2.4).

Table 2.4: Characteristics of some starch granules

Starch Source	Diameter range (μm)	Average diameter (μm)	Shape
Corn [(a)]	2 - 30	10	Round, Polygonal
Waxy Corn [(a)]	3 - 26	10	Round, polygonal
Wheat [(a)]	1 - 45	8	Round, lenticular
Potato [(a)]	5 - 100	28	Oval, spherical
Tapioca [(a)]	4 - 35	15	Oval, truncated
Mung bean [(b)]	7 - 26	NA	Oval, round
Sweet potato [(a)]	5 - 35	NA	Polygonal

Source: (a) Swinkels, 1985 NA: not available
(b) Hoover *et al.*, 1997

2.2.3 Starch granular structure and composition

Amylose and amylopectin are the two major polymers that constitute starch granules. The granules normally contain 70 – 80 % amylopectin and 20 – 30 % amylose molecules (Vorwerg *et al*., 2002). The structure and relative amount of both molecules play an important role in determining starch properties. The relative proportions of amylose to amylopectin depend on the source of the starch. High amylose corn starch (amylomaizes) for example contain over 50 % amylose whereas 'waxy' maize has almost none (less than 3 %) [Singh *et al.*, 2003]. Amylose and amylopectin are inherently incompatible molecules; amylose having lower molecular weight (~10^6 Daltons) with a relatively extended shape whereas amylopectin has huge (~10^8 Daltons) but compact molecules. The presence of amylose tends to reduce the crystallinity of the amylopectin and influence the ease of water penetration into the granules (Galliard and Bowler, 1987; Konstantinos, 2008).

2.2.4 Amylose

Amylose is primarily a linear chain of 500-20,000 D-glucose units linked by α-1→4 linkages. However, some amylose molecules have a few (about 0.3-0.5 %) α-1→6 branches (Takeda *et al.,* 1987; Hoover, 2001). When starch granules are heated to gelatinization, released amylose goes into solution. However, upon cooling of the starch paste or suspension, amylose chains coil into double helices and become insoluble in cold water. Hydrogen bonding between aligned chains causes retrogradation and release of bound water (syneresis). The double stranded crystallites are resistant to amylases and havea fairly hydrophobic structure of low solubility. Amylose forms a characteristic dark blue colour complex with iodine. It also forms complexes with various organic compounds such as butanol and fatty acids (Konstantinos, 2008). These complexes are essentially insoluble in water. The amylose content and degree of polymerization (DP) are important for the physical, chemical and functional properties of starch .The higher the amylose content, the lower is the swelling power and the smaller is the gel strength for the same starch concentration. To a certain extent, however, a smaller swelling power due to high amylose content can be counteracted by a larger granule size.

2.2.5 Amylopectin

Amylopectin structure is more complex since 4 – 5 % of the total linkages form branches. This branching is determined by enzymes and makes amylopectin more water soluble with higher bonding capacity. Amylopectin structure consists of three types of chains. The C chain carries the sole reducing group in the molecule to which the B - chains are attached, while the terminal A - chain is attached to the B - chain (Manners, 1989). In its native form, amylopectin is a semi-crystalline structure oriented radially in the starch granule to form concentric regions of alternating amorphous and crystalline lamellae. In the crystalline lamellae, amylopectin linear branches form double helices arranged in parallel with each other, while the amorphous lamellae regroup the molecule's branching points (Figure 2.2). Amylose molecules are found in the amorphous lamellae between the amylopectin crystallites. Typically, the crystalline and amorphous lamellae are 6nm and 4nm thick, respectively (Robin *et al.,* 1974). Some amylopectin (for example, from potato) has phosphate groups attached to hydroxyl groups, which increase starch hydrophilicity and swelling power.

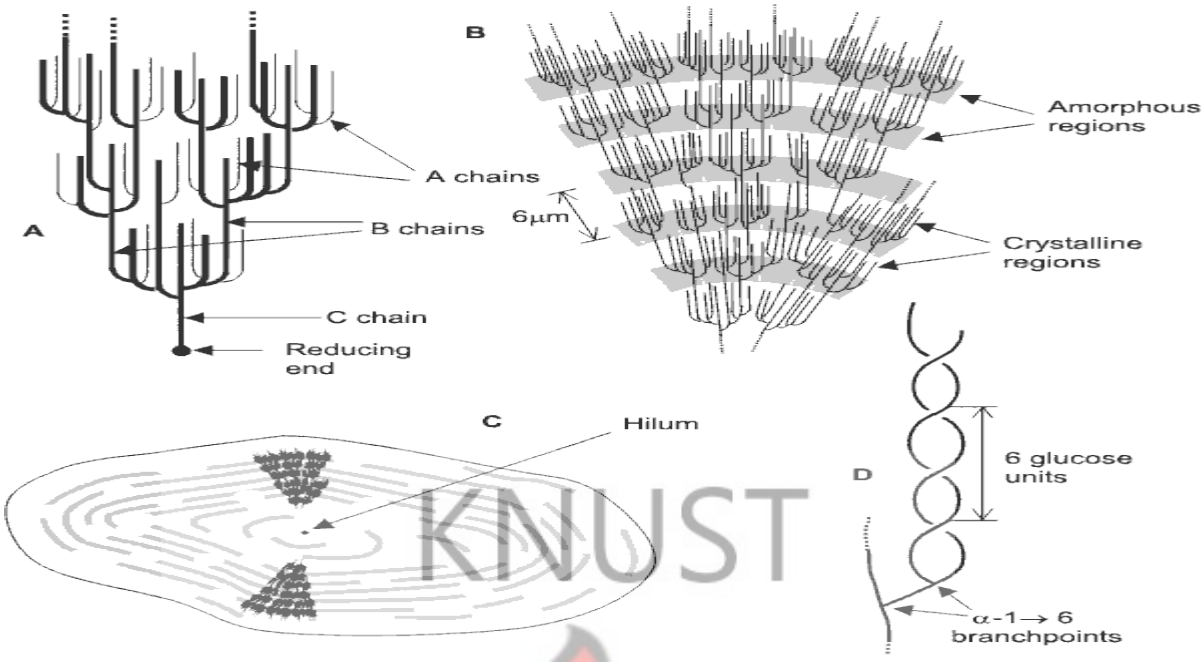


Figure 2.2: Structure of amylopectin:

A - Shows the essential features of amylopectin. **B**- Organization of the amorphous and crystalline regions. **C** - Orientation of amylopectin molecules in an idealized granule. **D** - Double helix structure responsible for granule crystallinity.

Source: Chaplin, 2010.

2.2.6 Starch modification and functionality

Physical, chemical, biochemical and thermal modifications of starch are known to enhance and extend their application in diverse industries. The alterations take place at the molecular level with little or no change taking place in the superficial appearance of the granule. The enzyme amylase for instance, has been thought to preferentially attack the more amorphous region of starch granules compared to the crystalline regions. On the contrary, inter chain associations and the compact organization of the amorphous regions of high amylose starches resist penetration by amylase. Thus waxy starches which are more crystalline are more easily hydrolyzed by amylase than normal starches which in turn are more hydrolyzed than high amylose starches (Konstantinos, 2008). Many functional derivatives of starch for specific end uses include cross-linked, oxidized, acetylated, hydroxypropylated, glycolated, hydrolyzed or soluble starch, partially and fully gelatinized starch. It has also been reported that genetic modification of starch crops can lead to the development of starches with improved and targeted functionality (Jobling, 2004).

2.3 Starch extraction and purity

Plant materials differ in their tissue structure and composition; hence different protocols are used for starch isolation. However, all established protocols are based on either of the following two procedures for starch isolation: (1) grain steeping, wet grinding and starch recovery or (2) dough making, dough washing and starch recovery (Wolf, 1964). Softer plant materials like tubers and roots unlike grains do not require water steeping to facilitate grinding. Hard materials like grains may be dry milled into flour, but this result in starch granule damage which ultimately affects physicochemical properties. The dough washing process is specifically used for isolation of starch from wheat flour. The higher density of starch compared to water is exploited in isolating starch from the plant material and washing it to reduce water soluble impurities. The wet starch obtained is dried at temperatures not exceeding 40 ^{o}C to prevent annealing of the starch granules which can affect its functionality and industrial application. Successful characterization of starch depends greatly upon the purity of the isolate. A good representative sample should contain more than 96 % (w/w) starch and be devoid of other plant components, such as fibre (soluble and insoluble), protein and lipids. These impurities, especially soluble gums, proteins and lipids influence starch properties and lead to false characterization (Vasanthan, 2001).

2.4 Minor components of starch extracts

Proteins, phosphate, lipids, moisture and ash are present in small amounts within thestarch granules. Based on their location, these components can be classified either as particulate material, surface components or internal components. Particulate materials are fragments of non-starch materials. These components may interfere with the starch separation process and cause impurity in the final starch or in products prepared thereafter. The amount of particulate material in these products is dependent on the source, separation process and the extent of starch purification. Surface components are materials that are associated with the surface of granules and may be removed by extraction procedure without disrupting the granule internal structure (Galliard and Bowler, 1987). Surface starch granule proteins are loosely associated with the surface of granules and can be extracted using alkaline solution to form salt. The main components of surface lipids are triglycerides, free fatty acids, glycolipids and phospholipids. These surface lipids can be separated using appropriate solvents like methanol and chloroform. Internal components are materials that are buried within the starch granules and require

more rigorous extraction. The amount of these components varies among different sources of starch. Even though they are present in small amounts, these components play important roles in the physicochemical properties of starch.

2.4.1 Phosphate

Phosphorus is usually present in starch as phosphate monoesters, phospholipids or inorganic phosphate (Taggart, 2004). Root and tuber starches usually contain higher amount of phosphorus than cereal starches. Phosphate monoesters could contribute to high viscosity, high transparency and water binding capacity of starches. Repulsion between phosphate groups on adjacent amylopectin chains may increase the hydration by weakening the extent of bonding between the crystalline domains (Galliard and Bowler, 1987; BeMiller and Whistler, 1996). In addition, phosphate monoester on long B-chains of amylopectin may decrease the gelatinization temperature by decreasing the interaction between double helices (Jane *et al.*, 1997). The small amounts of phosphorus as phospholipids present in cereal starch tend to form complex with amylose and long branched chain of amylopectin which result in limited swelling (Taggart, 2004). Aside phosphates, sodium and hydroxyl ions have been shown to significantly increase starch swelling (Mistry and Eckhoff, 1992).

2.4.2 Lipids

Compared to tuber and legume starches, cereal starches are believed to contain higher levels of lipids associated with amylose. Since these lipids occupy the same site within amylose helices, their presence may interfere with the determination of amylose content measured using iodine-binding method. Under estimation may result from failure to remove amylose complexed lipids (Singh *et al.*, 2003). Surface lipids affect the diffusion of water into starch granules and may reduce water binding capacity, swelling and solubilization of starches. In addition, surface lipids may also create undesirable flavours by oxidation of unsaturated lipid. This lipid layer may also prevent amylose from contributing to the thickening power of gelatinized starch by forming complex with amylose in starch paste. Moreover, surface lipid may create an opaque or cloudy starch paste and film due to the presence of insoluble starch-lipid complexes (Swinkels, 1985; Craig *et al.*, 1989).

2.4.3 Proteins

Starch protein content includes enzymes and varies depending on the botanical source. In general, cereal starches have higher protein content than tuber and root starches. The

presence of protein can cause unwanted colour in starch and starch hydrolysis products via Maillard's reaction; where amino acid groups react with reducing sugars (Cui, 2005). Moreover, proteins can affect the pasting or gelatinization process in different ways depending on their degree of polymerization, ability to retain water and their interaction capacity with starch molecules and granule surface. They may increase pasting temperature and overall viscosity due to the formation of cross links with starch molecules (Ribotta and Rosell, 2010; Lim and Narsimhan, 2006).

2.4.4 Latex and mucilage

Tubers and roots contain latex and mucilage which are viscous polysaccharide polymers. These substances are mainly composed of water-soluble glycoproteins containing a number of different sugars such as L-arabinose, D-galactose, L-rhamnose and D-xylose. The latex of sweet potato has been shown to be a natural defense against insect pests. Due to the presence of high amount of hydroxyl groups, latex and mucilage have good water binding capacity (Maurice *et al*., 1994). Sweet potato latex also possesses angiotensin converting enzyme (ACE) inhibitory activity and antioxidant activity against hydroxyl and peroxyl radicals. Substances that inhibit ACE activity are clinically used in hypertension management (Ames *et al*., 1996).

2.5 Starch gelatinization and pasting

Native starches undergo transformation at both granular and molecular levels when heated in the presence of water. At the molecular level, uncoiling of amylose chains in the amorphous regions and disruption of hydrogen bonds maintaining the crystalline order allow hydroxyl groups of water to freely bond to that of the starch polymers. Gelatinization and pasting respectively describes hydration within the granule and the irreversible granule swelling that build viscosity. When starch granules are heated above the gelatinization temperature, they absorb water and swell causing an increase in viscosity. The temperature at the onset of this rise in viscosity is considered as the pasting temperature. Usually, the pasting temperature (i.e. temperature at which the viscosity has increased by about 20 Brabender units) is higher than the gelatinization temperature (i.e. temperature at which bonds within starch molecules break down). This implies that starch granules are first gelatinized, after which the viscosity begins to rise till the Brabender viscoamylograph is able to detect and record (Mudford and Ward, 2008). Lower pasting temperature results in faster and irreversible granule swelling. The viscosity of the paste increases with further increase in temperature to a point where the number of swollen,

intact starch granules is maximum; referred to as the peak viscosity (PV) and considered to be indicative of water binding capacity. Granules may rupture during further heating, resulting in a decrease of viscosity as amylose leaches out. During the holding period at 95 ºC, the sample is subjected to mechanical shear stress which usually leads to further disruption of starch granules causing amylose and amylopectin leaching. Leached out amylose molecules are more or less aligned in the direction of flow, which contributes to the breakdown (BD) in viscosity. The break down therefore explains the resistance of a starch paste to viscosity breakdown as shear is applied. A low value indicates an improved organization within the starch granules. This gives the starch a longer paste to peak time; and hence swells more gradually with little susceptibility to mechanical damage (Wiesenborn *et al*., 1994; Li and Yeh, 2001). As the sample is subsequently cooled down to 50 ºC, reordering of amylose chains results in an increase in viscosity until a gel is formed, which is defined as setback (SB). This parameter is related to the retrogradation of the amylose chains. The viscosity at the end of the test is defined as final or cold paste viscosity (FV). Pasting properties of starch varies depending on botanical source, amylose to amylopectin ratio, concentration of lipids, residual proteins, granular size and size distribution, effects of phosphate groups and instrument operating conditions. In general, lower amylose content corresponds to higher paste peak viscosity and higher resistance to retrogradation (Philips and Williams, 2000; Konstantinos, 2008).

According to Schoch and Maywald (1968), starch paste viscosity patterns can be classified into four (4) types: 'type A', which shows a high pasting peak followed by rapid and major thinning or breakdown in viscosity; 'type B', which shows a lower pasting peak and much less thinning or breakdown in viscosity; 'type C', which shows no pasting peak but rather a very high viscosity which remains constant or increases during cooking; and 'type D', in which the amount of starch must be increased two or threefold to give a significant hotpaste viscosity of 'type C'.

2.6 Solid oral dosage forms

Oral delivery is the preferred route for drug administration as it is more natural and less invasive than other traditional routes such as intravenous and intramuscular injection. It is the largest and the oldest segment of the total drug delivery marketdominated mainly by tablets. Excipients and production methods employed in the manufacture of solid oral dosage forms can influence the pharmacokinetic profile of the drug, hence due consideration (with respect to their functional and pharmaceutical properties) should be

exercised in selecting them (Chang and Chang, 2007).

2.7 Desirable properties of pharmaceutical raw materials

Pharmaceutical formulations are composed of one or more medicaments and a variety of excipients. Irrespective of the type of tablet or solid oral dosage form being prepared, the raw materials must have desirable properties such as particle size, moisture content, crystalline form, consistency, purity and acceptable tableting index to assure product quality.

2.7.1 Particle size

Particle size distribution, shape and density influence powder flow, segregation and dissolution. Fine powders (particle size < 75 μm) are cohesive, poor flowing and easily adheres to surfaces while particles larger than 250 μm are usually free flowing. Flow properties are enhanced when regular shaped, smooth particles with a narrow size distribution are employed. Uneven powder flow, besides causing weight uniformity problems can result in excessive air entrapment in the powder which may promote capping and lamination of tablets. Uneven flow may also occur as a result of particle friction with die wall; and this causes lubrication problems with concomitant dust contamination risks during powder transfer. Powders and granulations with more than 30 % fines virtually turns product into dust which would be lost, thus affecting tablet yield. Smaller particles generally have high solubility and dissolution rate because of the large surface area exposed to solvent action (Gilbert and Christopher, 2002). Particle size also influences the uniformity of dosage or content of very potent drugs and is greater with smaller particles because of the greater number of particles constituting the dose. The importance of particle size came to the fore in 1939 and 1940 when the toxicity of phenothiazine to codling moth larvae and its anthelmintic properties were respectively investigated. In both instances, reduction in particle size increased the activity of the drug (Alexander and Attwood, 2006).

2.7.2 Moisture content / Losses on drying

One significant parameter that contributes to the behaviour of many tablet formulations is the level of moisture present during manufacture as well as that residual in the product. High residual moisture content has adverse effects on product stability as accelerated aging and crystal transformation may occur. Low moisture content on the other hand, may increase the incidence of capping and lamination in tablets (Gilbert and Christopher, 2002).

2.7.3 Crystalline form

The crystalline form of an excipient affects its stability and tableting index while that of a drug determines its efficacy and clinical response. Different polymorphic forms and crystal habits may have a pronounced effect on bioavailability of some drugs due to their different dissolution rates. The crystalline form may also affect the compactibility and mechanical strength of tablets (Gilbert and Christopher, 2002).

2.7.4 Tableting index

Table 2.5: Hiestand compaction indices for some drugs and excipients

Material	Compaction index		
	BI	**BFI**	**SI**
Acetaminophen[(a)]	0.7	0.90	4.16
Phenacetin[(a)]	2.8	0.90	1.88
Aspirin[(b)]	1.5	0.16	1.11
Ibuprofen[(b)] A	1.9	0.05	0.98
Ibuprofen B	1.8	0.57	1.51
Ibuprofen C	2.7	0.45	1.21
Mannitol[(b)] A	0.8	0.19	2.18
Mannitol B	0.5	0.15	2.26
Corn Starch[(b)] NF	0.4	0.26	2.48
Pregelatinized starch	1.8	0.14	2.02
Pregelatinized compressible starch	1.2	0.02	2.08
Modified (1500) starch	1.5	0.27	2.30

Source: (a) Mullarney and Hancock (2004)

(b) Hiestand *et al*., (1977)

Poorly compressible materials produce soft tablets while brittle crystalline materials yield brittle tablets. Hiestand quantified the compaction properties of pharmaceutical powders using three indices (Table 2.5). The strain index (SI) as a measure of internal entropy or strain associated with a material when compacted. The bonding index (BI) as a measure of the material's ability to form bonds and undergo plastic deformation to produce a suitable tablet. The third index, the brittle fracture index (BFI) as a measure of the

brittleness of a material and its compact. A material's desirability is based on the outcome of all three indices (Gilbert and Christopher, 2002). Normal materials (e.g. Phenacetin) compress in a viscoelastic manner to form compacts. Special case materials (e.g. Paracetamol or acetaminophen powder) have low effective angle of internal friction (EAIF), low compact dynamic indentation hardness and low compact tensile strength. Such materials are exceptionally poor for tableting as a result of having hard particles that interact very weakly to form compacts. They tend to consolidate through particle rearrangement rather than by plastic deformation (Mullarney and Hancock, 2004).

2.7.5 Consistency

Differences in raw material quality may result when procured from different sources and such differences may affect tablet production and quality. It is therefore imperative to source materials from recognized approved vendors so as to monitor and assure quality.

2.7.6 Purity

Microbial contamination and impurities such as acetylsalicylic anhydride in aspirin affect product toxicity and dissolution of aspirin tablets. Materials of natural origin such as starch and gelatin usually have high microbial contamination but a manufacturing process like drying in wet granulation reduces this considerably (Gilbert and Christopher, 2002).

2.8 Tablet dosage forms

Tablets are solid pharmaceutical dosage forms containing one or more drug substance with or without suitable excipients. They are prepared either by compression or moulding. Compressed tablets are prepared by applying high pressure on powder or granules while moulded tablets are obtained with low pressure on moist powder mass. Moulding is now generally reserved for laboratory and small scale production while commercial production is done solely by compression. Tablets remain popular as dosage form because of the advantages afforded to both manufacturer (viz. simplicity and economy of preparation, stability and convenience in packaging, shipping and dispensing) and patient (accuracy of dosage, compactness, portability and ease of administration). The irritant effect of some drugs like aspirin on GI mucosa, bioavailability problems resulting from slow disintegration and dissolution, age, conscious state of patient and emesis limit tablet usage. Ideally, a well compressed tablet should have good physical appearance and hardness so as to be able to withstand the rigours of packaging and handling. It should also have acceptable weight and content uniformity. In addition, there should be

reproducibility and predictability in the release of the active ingredient from the tablet whilst still maintaining physical and chemical stability during its shelf life. In order to facilitate tablet handling during manufacture and achieve targeted content uniformity, the tablet size and weight are usually kept above 2 - 3 mm and 50 mg, respectively (Mukesh, 2009).

2.9 Types and classes of compressed tablets

There are different types of compressed tablets depending on the route of administration, functions, drug delivery systems and methods of manufacture (Mukesh, 2009).

2.9.1 Oral tablets for ingestion

Depending on the class of the active pharmaceutical ingredient, condition for which it is indicated, excipients used in the formulationand manufacturing process employed, different types of oral tablet dosage forms exist.

2.9.1.1 Conventional compressed tablets

These are standard uncoated tablets produced from a single compression cycle. They may be used for local action in the gastro-intestinal tract or for systemic effect.

2.9.1.2 Multiple compressed tablets

These are multiple-layered or compression coated tablets produced by more than one compression cycle. They are formulated either to separate physically and chemically incompatible ingredients or produce repeat or prolonged action.

2.9.1.3 Modified or controlled release tablets

These are compressed tablets formulated to release the drug slowly over a prolonged or extended period of time, thus reducing dosage frequency and improving patient compliance.

2.9.1.4 Coated tablets

Coating help mask the unpleasant taste of some active pharmaceutical ingredients (APIs), eliminate API irritation of gastric mucosa, protect APIs sensitive to low pH and oxygen degradation and ensure site specific release of undiluted APIs such as intestinal antibacterial and vermifuges. Common examples of coated tablets include sugar coated, film coated and enteric coated tablets.

2.9.1.5 Chewable tablets:

Chewable tablets are attractive alternative for patients who are unable to swallow whole tablets or for children who have not yet learnt to swallow tablets. Antacid tablets besides being too large to swallow, are chewed to provide quick relief as their activity is related to particle size.

2.9.2 Tablets used in the oral cavity

The oral mucosa offers an attractive route of administration for systemic drug delivery. The buccal mucosa like other transmucosal routes such as the linings of the nose, rectum, vagina and eyes has rich blood supply and is relatively permeable; bypassing hepatic first pass metabolism and enzymatic degradation associated with per oral administration of peptide and protein drugs. In addition, the oral mucosa is robust, shows short recovery times after stress or damage and the virtual lack of Langerhans cells makes the oral mucosa tolerant to potential allergens (Shojaei, 1998). Tablets administered by this route include:

2.9.2.1 Buccal and sublingual tablets

These tablets are to be respectively placed in the buccal pouch and under the tongue to allow quick systemicdrug absorption and action. The tablets are usually small and flat, compressed lightly to keep them soft and contain API whose only satisfactory non parenteral application is this route e.g. glyceryl trinitrate.

2.9.2.2 Orodispersible tablets

Orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed.

2.9.2.3 Troches and lozenges

These are small, circular, sugar or fruit flavoured tablets intended to dissolve in the mouth for local action within the mouth and throat.

2.9.2.4 Dental cones

These tablets are designed to be loosely packed into the empty socket remaining following a tooth extraction. They are formulated to dissolve or erode slowly and either inhibit bacteria proliferation orreduce bleeding.

2.9.3 Tablets administered by other routes

2.9.3.1 Implantation tablets

They are sterile formulation without excipients and made hard with large particle size to achieve gradual drug release lasting between a month and a year. The tablets may be pellet, cylindrical or rosette shaped with diameter not more than 8 mm and are inserted into subcutaneous tissue by surgical procedures.

2.9.3.2 Vaginal tablets

These tablets undergo slow dissolution and drug release in the vaginal cavity. They generally release antibacterial, antiseptics or astringents to treat vaginal infections or release steroids for systemic absorption.

2.9.4 Tablets used to prepare solution

2.9.4.1 Effervescent tablets

These tablets contain active pharmaceutical ingredients (APIs) with limited stability in liquid dosage forms and provide quick onset of action when dispersed and immediately administered orally. The tablet is quickly disintegrated by the liberation of CO_2 from the interaction between tartaric or citric acid with alkali metal carbonates or bicarbonates in the presence of water.

2.9.4.2 Hypodermic tablets

These tablets contain one or more readily water soluble ingredients and are intended to be dissolved by sterile water for injection. The clear solution formed is subsequently administered parenterally. They were widely used by rural physicians due to its portability.

2.9.4.3 Tablettriturates

Tablet triturates are small water soluble tablets (30 - 250 mg each), containing small amounts of potent drugs and are now prepared mainly by compression using minimal pressure.

2.10 Methods for preparing tablet dosage form

Tablets may be prepared by any of the following three methods:

2.10.1 Direct compression

The direct compression process is the most economical and uses the least number of steps. The drug is blended with a variety of excipients, subsequently lubricated and directly compressed into a tablet. Less than 20 % of active pharmaceutical materials can be directly compressed into tablets as the majority lack flow, cohesion or lubricating properties necessary for direct compression (Shangraw, 1989).

2.10.2 Drygranulation

This process involves processing the drug substance with excipients using a "slugging" or "compaction" technique followed by "granulation sizing" and final blending with additional excipients prior to tablet compression or capsule shell filling. Dry granulation is simpler than wet granulation and is most preferred when moisture or heat sensitivity is a concern. It however produces higher percentage of fine granules which can compromise the quality or create yield problems for the tablet (Gilbert and Christopher, 2002; Aulton, 2001).

2.10.3 Wet granulation

Wet granulation employs a liquid binder to agglomerate the powder mixture. The process involves processing the drug substance with excipients and a solvent in which a binder may be dissolved to produce a granulation. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. The granulation is subsequently dried, sized and blended with additional excipients prior to tablet compression or capsule shell filling. Though it requires the highest number of steps, it is the most utilized method of preparing tablet dosage form (Carter, 2003).

2.11 Excipients for tablet formulation

Most pharmaceutically active ingredients or drugs are poorly compressible, cohesive and easily adhere to substrates. Others are administered in low doses, hence require the presence of pharmacologically inactive ingredients (otherwise known as excipients) to not only give them adequate bulk for administration but also provide other functions such as compressibility and flowability to the tablet formulation. Excipients may be classified as compendial (i.e., have composition consistent with monographs published in compendia such as USP-NF) or non compendial. Quality-by-design concepts emphasize the need for characterizing material properties (e.g. micromeritic, chemical, thermal, rheological and

mechanical properties) and elucidate their vital role in formulation and manufacturing processes. Excipient selection in the drug product development phase focuses on the desirable characteristics (e.g. functionality, material consistency, regulatory acceptance, cost, availability and sources)and that imprudent selection of excipients and excipient vendors may lead to process development problems. Excipients play crucial roles in the design of the delivery system; determining its quality and performance and are therefore characterized based on their roles or functions (Chang and Chang, 2007). Some routinely used excipients include:

2.11.1 Binders or granulating agents

The binder holds or glues drug particles and other excipients together in agglomerates to form granules of desired bulk or capsule slugs or tablets. Good binders assessed by compressibility under pressure, have high plasticity, low elasticity and small particle size. Small particle size facilitates even distribution of the binder through the interparticulate voids to enhance tablet crushing strength. They also have low hygroscopicity as excessive uptake of moisture (> 5 %) or high moisture content can lead to instability and sticking during tablet production. The quantity and quality of binder used has considerable influence on the characteristics of compressed tablets. Excessive amounts of binder produces very hard tablets which fail to disintegrate and also cause punch wear. Higher binding capacity reduces binder use levels and the compression force required to form a hard, non-friable tablet. As binding capacity of the binder increases, disintegrating time of tablet increases and this counteract rapid disintegration (Mukesh, 2009). Native starch granules are usually pregelatinized or gelatinized to form paste (in wet granulations) at concentrations of between 5 - 20 % w/w. Cellulose derivatives such as microcrystalline cellulose, natural gums such as acacia and synthetic polymers like polyvinylpyrrolidone are other examples of pharmaceutical binders (Murali and Durig, 2008).

2.11.2 Diluents or fillers

Diluent is the pharmaceutical term for filler, used in tablet and capsule formulations to add bulk or weight, thus giving them a practical size (at least 50 mg) for administration. They are most useful in formulations containing low dose APIs and ultimately influence the quality and technological properties of the mass being tableted or encapsulated. They may have additional functionality such as aiding in compaction and powder flow or increasing density (Lefevre and Quettier, 2001). The solubility and compression characteristics of fillers affect both rate and mechanism of tablet disintegration. Soluble

fillersare likely to dissolve rather than aid tablets disintegrate; and may cause an increase in viscosity of the penetrating fluid which tends to reduce effectiveness of strongly swelling disintegrating agents (Mukesh, 2009). Insoluble diluents produce rapid disintegration with adequate amount of disintegrants. Apart from starch, other carbohydrates like mannitol, lactose, sorbitol and cellulose derivatives have been successfully used as tablet diluent. Usual range of diluent usage may vary from between 5 - 80 %.

2.11.3 Disintegrants

Disintegrating agents are used to cause granules, tablets or capsule contents to break apart to enhance the availability of drug substance for dissolution and absorption. An ideal disintegrant has poor solubility, poor gel formation, good hydration capacity, good moulding and flow properties; and should have no tendency to form complexes with the drugs (Carter, 2002). Disintegrating agents can be added either prior to granulation (intragranular) or prior to compression (after granulation i.e. extragranular) or at both processing steps. Extragranular fraction of disintegrant (usually, 50 % of total disintegrant requirements) facilitates breakup of tablets to granules. The intragranular addition of disintegrants produces further erosion of the granules to fine particles. Five mechanisms affecting tablet disintegration are as follows:

2.11.3.1 Swelling

Although not all effective disintegrants swell in contact with water, swelling is believed to be a mechanism by which certain disintegrating agents (such as starch) impart their disintegrating effect. By swelling in contact with water the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart (Carter, 2002).

2.11.3.2 Porosity and capillary action (wicking)

Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart (Carter, 2002).

2.11.3.3 Deformation

Starch grains are generally thought to be “elastic” in nature, thus even when deformed under pressure will return to their original shape when that pressure is removed. The compression forces involved in commercial tableting are believed to deform these grains more permanently and are thus said to be “energy rich”. This energy is released upon exposure to water giving them higher swelling ability than native starch grains that have not been deformed under pressure (Carter, 2002).

2.11.3.4 Repulsion

Repulsion is secondary to wicking and it is thought to be due to the generation of electrical charges among particles when water is drawn into the tablet. Repulsion between similar charged particles leads to tablet break up (Murali and Durig, 2008).

2.11.3.5 Chemical reaction (acid - base reaction)

Tablet disintegration may result from the inclusion of citric acid or tartaric acid together with sodium or potassium bicarbonate and sodium or potassium carbonate. These react in contact with water to liberate carbon dioxide that disrupts the tablet (Mukesh, 2009).

Tablet disintegration is believed to be mostly due to inter-relationships between different mechanisms. Native starch, depending on their botanical source may be used as a disintegrant in concentrations of between 5 - 10 % w/w (Carter, 2003).

2.11.4 Lubricants, anti-adherents and glidants

Lubricants prevent sticking of powders to equipment used to compress tablets or fill capsule shells (i.e. tablet punches and dies, encapsulating dosators or tamping pins). Anti-adherents unlike lubricants are more effective in preventing adhesion to blender and hopper surfaces while glidants are used to reduce inter-particle friction thereby improving flow characteristics. Respective examples include magnesium stearate, talc and fumed silicon dioxide. Only a limited number of drugs and excipients do not require lubrication; and these include acetyl salicylic acid, starch and microcrystalline cellulose (Carter, 2001).

2.11.5 Adsorbents

Adsorbents facilitate the incorporation of liquid medicaments like volatile oils into solid dosage forms. Adsorption is a surface phenomenon and is influenced by the available surface area on the solid. The most efficient adsorbents are very small particles. These

materials often have low bulk densities with poor flow and compaction properties. Most commonly used adsorbents are silica, microcrystalline cellulose, starch, carbonates, talc, magnesium oxide, tricalcium phosphate, magnesium aluminum silicate and clays (McCarty, 2003).

2.12 Considerations for excipients selection in a formulation

Many guidelines exist to aid in the selection of non toxic excipients. They include: Inactive Ingredient Guide (IIG), Generally Regarded as Safe (GRAS), Handbook of Pharmaceutical Excipients (HOPE), Food Chemicals Codex (FCC) and Code of Federal Regulations (CFR). Though excipients are usually regarded as non toxic, there are examples of known excipient induced toxicities which include renal failure and death from diethylene glycol, osmotic diarrhoea caused by ingested mannitol, hypersensitivity reactions from lanolin and cardio toxicity induced by propylene glycol (Chang and Chang, 2007). Considerations for selecting excipients in a formulation include:

2.12.1 Composition of reference product

Compendia and product labels (if available) often list qualitative composition of formulations which can be followed to achieve a desired product quality.

2.12.2 Requirement for specific excipients

Formulations start out simple as the number of excipients are kept low, with additional, specialized excipients being incorporated as needed through experimental trials. In addition, the quantity of each excipient should be minimized and multifunctional excipients given preference over unifunctional excipients.

2.12.3 Drug - excipient compatibility

Drug characterization and pre-formulation studies may exclude specific excipients due to potential incompatibility or stability issues.

2.12.4 Influence on drug substance release

Depending on the drug substance, certain excipients may be selected due to their effect at enhancing or retarding the release of the drug substance to produce the desired “in-vitro” dissolution release profile.

2.12.5 Formulation process

Certain excipients are specialized for direct mixing processes whereas others are more suitable for wet granulation processes.

2.12.6 Availability

Excipients most readily available are usually selected over excipients that may be equally adequate but not readily available.

2.12.7 Experience

Formulators usually select excipients with which they have the most experience, even though there may be equivalent excipients to perform the same function.

2.12.8 Cost

With two functionally equivalent, equally available excipients, the cheaper of the two may be selected (Carter, 2003; Mukesh, 2009).

2.13 Powder flowability and flow properties

Powder flowability refers to the ability of powders and other bulk solids like granules to flow in a desired manner in a specific piece of equipment. The flow properties on the other hand refer to specific bulk characteristics and properties of a powder which affect flow and which are measurable (e.g. density, compressibility, cohesive strength, permeability, internal friction and wall friction). Flowability is a factor for several processes (e.g. powder transfer, storage, blending and compaction) in the pharmaceutical industry. A high degreeof powder flowability ensures smooth powder flow into the press which minimizes air pockets in the die and ensures weight consistency and tablet stability. High flow also improves reproducibility of feed parameters to give tablets of consistent hardness, friability and dissolution rates. The flowability also improves powder permeability, allowing rapid air release during compression, thus eliminating problems such as capping and splitting. Finally, free flowing powders fill dies in a shorter time thus allowing high production speeds and process efficiency. The reverse of these desirable production outcomes listed is observed when poor flow, characterized by ratholing and arching of the powder mass occurs. Flow behaviour is multi dimensional, relying generally on the physical properties of the particle, properties of the bulk powder and processing equipment or environment; hence more than one test is used to quantify flowability. Four commonly reported methods for testing powder flow are: angle of

repose, compressibility or hausner's ratio, flow rate through an orifice and shear cell (Prescott and Barnum, 2000).

2.13.1 Angle of repose

The angle of repose is a constant three dimensional angle assumed by a cone-like pile of material formed as powder flows onto a surface. It is a function of interparticulate friction or resistance to movement between particles sliding down the adjacent surfaces of the powder cone. Flatter cones are formed when the strength of interparticle forces are weak. The more acute the angle of repose (or the flatter the cone), the better the flowability of the material. Although there is some variation in the qualitative description of powder flow using the angle of repose, there are examples in the literature of formulations with an angle of repose in the range of 40 - 50° that were manufactured satisfactorily. When an angle of repose exceeds 50°, the flow will be problematic and is rarely acceptable for manufacturing purposes. The use of a common fixed base with a retaining lip eliminates variability introduced by using different surfaces and uncontrolled powder spread (USP, 1990).

2.13.2 Compressibility index and Hausner's ratio

Compressibility Index (or Carr's index) and Hausner's ratio are closely related. Both are based on the comparison of bulk density and tapped density or poured volume and tapped volume. These two parameters are influenced by variables such as particle size distribution, true density, particle shape, and cohesiveness due to surface forces including moisture. The Hausner's ratio and Carr's index are respectively measures of interparticle friction and the impact of tapping on particle packing and their potential to form an arch or bridge to impede powder flow. Compressibility index is thus defined as the percentage change in volume induced by tapping asample of fixed mass. Hausner ratio is simply the unsettled volume divided by the tapped volume.

The tapped density of a material can thus be used to predict both its flow properties and its compressibility or aptitude to diminish in volume. In general, powders that are less affected by tapping have better flow properties (Staniforth, 1996; Copley, 2008). Specified limits for the various flow indices are listed in Table 2.6.

Table 2.6: Scale of powder flowability

Angle of repose (degrees)	Compressibility index (%)	Hausner's ratio	Flow Character
25 - 30	< 10	1.00 - 1.11	Excellent
31 - 35	11 - 15	1.12 - 1.18	Good
36 - 40	16 - 20	1.19 - 1.25	Fair – aid not needed
41 - 45	21 - 25	1.26 - 1.34	Passable – may hang up
46 - 55	26 - 31	1.35 - 1.45	Poor – must agitate, vibrate
56 - 65	32 - 37	1.46 - 1.59	Very Poor
> 66	> 38	> 1.60	Extremely Poor

Source: USP, 1990; Copley, 2008

2.14 Physical specifications of compressed tablets

When compressed tablets are prepared, various physical specifications are examined (for quality control). They should be controlled to assure not only the outward appearance of the product but also its therapeutic efficacy. The factors to be examined include shape, weight, score (or groove), imprinting, colour, hardness (or breaking strength), disintegration, dissolution and content uniformity.

The shapes of the compressed tablets differ widely; they can be round, oblong or triangular. Tablets may be flat or have varying degree of convexity depending on the contours of the punches such as flat face, shallow cup, standard cup, deep cup or modified ball. Some tablets are scored or grooved in halves, thirds or quadrants. This allows fairly accurate breaking of the tablet for the administration of a partial amount. In general scored tablets are grooved on a single side. Tablet shapes and size are determined by the die and punches used for the compression of the tablet. Tablets may be imprinted with a symbol of the manufacturer to denote the company, the product or both. To make imprinted tablets, punches having impressions are used. Punches with raised impressions will produce recessed (embossed) impressions on the tablets and vice versa. By the food and drugs administration of the United States (FDA) regulation (effective 1995), all solid dosage forms for human consumption must be imprinted with product specific identification codes. Code imprints, in conjunction with a product's size, shape and colour permit the unique identification of a drug product and its manufacturer or distributor. Code imprints may contain any combination of letters and numbers or the

product's national drug code number. They may also contain any marks, symbols, logos or monograms assigned by the drug company to the product. Each product's imprint must be registered with the FDA.

Tablets should be made sufficiently hard to resist breaking during packaging, shipment and normal handling. At the same time, tablets should be soft enough to disintegrate and dissolve properly after administration. It is a common practice in hospitals and extended care facilities to crush tablets to mix with food or drink for easy swallowing. Some tablets such as enteric coated tablets, controlled release tablets and sublingual or buccal tablets should not be crushed, since the release characteristics of the drug from the dosage form and subsequently the drug absorption could adversely affect the patient's welfare (Well and Aulton, 1996; Gilbert and Christopher, 2002).

2.15 Compendial and Non-compendial quality tests on tablets

Compendial tests are officially described in the pharmacopoeias while non-compendial tests are based on a manufacture's own product specifications. Analysts prefer to use compendial methods, if available, as the results are easier to be accepted by third parties including regulatory agencies. Compendial and non compendial tests are employed by manufacturers to control product quality. Official tests described by the BP and USP include weight and content uniformity (uniformity of dosage unit), disintegration, dissolution and friability tests.

2.15.1 Quality control tests

2.15.1.1 Tablet thickness

Tablet thickness is important for packaging and patient administration (swallowing). It is determined by the diameter of the die, amount of fill permitted to enter the die and the force or pressure applied during compression. Tablet thickness may be measured manually by a micrometer or by automatic equipment.

2.15.1.2 Tablet hardness

Tablets should be sufficiently hard to resist breaking during normal handling, packaging and shipping, yet soft enough to disintegrate properly after swallowing. Hardness is controlled by the pressure applied during the compression stage. The test measures the crushing strength defined as the compressional force applied diametrically (through diameter) to a tablet which just fractures it. Normal tablet hardness ranges from 4 - 6 Kgf

(1 Kgf = 9.80665 Newton). However, certain tablets such as lozenges and buccal tablets that are intended to dissolve slowly, show deliberate higher hardness values (Alfonso, 1990).

2.15.1.3 Uniformity of dosage unit (weight and content uniformity)

This test is done to ensure a constant dose of drug between individual tablets. Weight uniformity or mass variation test is performed when the drug forms a greater part of the tablet, as any variation in weight obviously indicates a variation in the active ingredient. Tablets pass the test if only two (2) or less of the individual weights deviate from the average weight by more than the percentages shown in Table 2.7 and none deviate by more than twice that percentage.

Uniformity of content is performed for uncoated tablets with a content of active substance less than 2 mg or 2 % of the total mass. Excipients form the greater part of the tablet weight and correlation between tablet weight and amount of the API can therefore be poor. The test is also applicable to coated tablets other than film coated tablets regardless of drug content. If the test for uniformity of content is prescribed, the test for uniformity of weight is not required.

Table 2.7: Limits of weight uniformity

Pharmaceutical form	Average weight	Deviation
Tablets	80 mg or less	10 %
	> 80 mg - < 250 mg	7.5 %
	250 mg or more	5 %

Source: BP, 2007

2.15.1.4 Friability test:

Measurement of tablet friability supplements other physical strength measurements such as tablet breaking force. For tablets with a unit mass equal to or less than 650 mg, a sample of whole tablets corresponding as near as possible to 6.5 g are taken. For tablets with a unit mass of more than 650 mg, a sample of ten (10) whole tablets is taken. Generally, the test is run once. If no obvious cracks or broken tablets are present in the sample after tumbling; and a maximum weight loss of not more than 1 % is found, the

tablets pass the test. Normally when capping occurs, friability values are not calculated (BP, 2007).

2.15.1.5 Disintegration test

For the drug to be fully available for absorption, the tablet must first disintegrate and discharge the drug to the body fluid for dissolution. Disintegration is also important for drugs acting locally in the GIT without absorption. It regulates their onset of action and availability. All tablets and capsules must pass a test for disintegration except chewable tablets, troches and modified or extended release tablets. Tablets meet the requirement if no fragments remain on the screen after the specified time in the monograph. Exception is allowed for fragments of insoluble coating or capsule shell and soft mass having no palpably firm core. The procedure is applied to six or more tablets. TheBritish Pharmacopoeia recommends a disintegration time of 15 minutes or less for uncoated tablets (BP, 2007).

2.15.1.6 Dissolution test:

Dissolution is a more meaningful quality attribute than disintegration testing (especially for drugs of limited water solubility) and therefore, dissolution test is a standard requirement for all tablets and capsules. It is performed in-process (during production) and on the final product. Uncoated or coated tablets for which a requirement for dissolution is included in the individual monograph, the requirement for disintegration does not apply. Media used in dissolution testing may be purified water, simulated gastric fluid, simulated intestinal fluid or others. Organic solvents are not recommended. Seven official dissolution test apparatuses are present in the USP; however, the most commonly used are USP apparatus I (basket) and USP apparatus II (paddle). For conventional release dosage forms tested under reasonable and justified test conditions, the British Pharmacopoeia recommends that at least 75 % of the active substance should be released in 45 minutes (BP, 2007).

CHAPTER THREE

EXPERIMENTATION

3.1 MATERIALS

3.1.1 Pharmaceutical raw materials

Pharmaceutical grade materials used in the paracetamol tablet formulations included:

- Maize starch BP (Riddhi Siddhi Gluco Biols limited, India),
- Paracetamol BP (Anqui Lu'an Pharmaceuticals, China),
- Mannitol BP (Gayatri Bio Organics Limited, India),
- Sodium starch glycolate BP (Vasa Pharmachem PVT limited, India),
- Povidone BP (Boai Nky Pharmaceutical limited, China) and
- Magnesium stearate BP (Legend Industries, India).

They were all kindly supplied by the raw material stores of Tradewinds Chemist Limited, Kumasi.

3.1.2 Reagents

Analytical grade reagents used in carrying out the investigations included:

- Ethanol 96 % (Sasol chemical Industries limited, South Africa)
- Copper sulphate (BDH Laboratory suppliers, England),
- Sodium sulphate (BDH Laboratory suppliers, England),
- Glacial acetic acid (BDH Laboratory suppliers, England),
- Sodium hydroxide (BDH Laboratory suppliers, England),
- Potassium orthophosphate (BDH Laboratory suppliers, England),
- Iodine crystals (BDH Laboratory suppliers, England),
- Potassium Iodide (BDH Laboratory suppliers, England),
- Petroleum ether (BDH Laboratory suppliers, England),
- Conc. Sulphuric acid (Merck KGaA, Germany),
- Conc. Hydrochloric acid (Merck KGaA, Germany),
- Boric acid (Merck KGaA, Germany),
- Xylene (Merck KGaA, Germany).
- Amylose starch 70 % (BDH Laboratory suppliers, England)

- Distilled water, deionized water andready made buffers of pH 4.0, 7.0 and 9.0 were all supplied by the quality control department, Tradewinds Chemist Limited, Kumasi.

3.1.3 Equipment and apparatus

Equipment and apparatus used in carrying out the investigations included:

- A domestic food blender (Sharp corporation - Japan),
- Laboratory test sieves (ASTME II, Retsch - Germany),
- Hot air oven (Gallenkamp Oven 300 Plus series, United Kingdom),
- Muffle furnace (Gallenkamp - United Kingdom),
- Moisture analyser (MB-45, Ohaus - Switzerland),
- Brabender Viscograph-E viscoamylograph (Brabender OHG - Germany),
- Analytical balance (Vic-212, Sartorius group - Canada),
- Sieve shaker (AS-200 Basic, Retsch - Germany),
- Clifton bench centrifuge (Nickel Electro - England),
- pH meter (UD-95, Universal enterprises - India),
- Light microscope (CX-41, Olympus corporation - Japan),
- Single punch tablet press (DP-30, Pharmao Industries - China),
- Digital caliper (CD-8 CSX, Mitutoyo corporation - Japan),
- Monsanto tablet hardness tester (VEEGO HT-01, Progressive Instruments - India)
- Friabilator (TA-20, Erweka - Germany),
- Disintegration apparatus (ZT-4, Erweka - Germany),
- BP apparatus II (paddle) dissolution machine (DBK Instruments - India),
- UV Spectrophotometer (Pharmaspec UV-1700, Shimadzu Corporation - Japan).
- Other accessory apparatus or equipments used included: density bottle or pycnometer, desiccator, porcelain crucible, motar and pestle, general purpose glassware, hot water bath and thermometer.

3.1.4 Sweet potato root tubers

Fresh root tubers of four (4) sweet potato cultivars were obtained from the Crop Research Institute (CRI) of the Council for Scientific and Industrial Research (CSIR), Fumesua - Kumasi. They were identified and averred to be the root tubers of CRI-Sauti, CRI-Hi-starch (“Fufu Santom”), CRI-Ogyefo (Mugande) and CRI-Faara. The identification and

authentication were undertaken by Dr. Ted Carrey, the regional sweet potato breeder at the International Potato Center (CIP), Fumesua - Kumasi. The tubers were harvested five (5) months after planting and starch extraction undertaken within fourteen (14) days.

3.2 METHODS

3.2.1 Organoleptic properties of fresh sweet potato root tubers

The organoleptic properties of fresh sweet potato root tubers were determined by visual, gustatory and textural evaluations. The amount of latex produced by 300 g fresh root tubers when sectioned was ascertained using the following criteria: Sections with virtually no latex produced (less than 1 ml) were given a score of zero (0); those with small amounts of latex (1 - 2 ml) were scored three (3), while those with higher volumes of latex production (3 - 5 ml) were scored seven (7) [Brabet *et al*., 1998].

3.2.2 Tuber dry matter

The sweet potato root tubers were washed with tap water and cut into small pieces (about 0.5cm^2). Two sub-samples of 100 g each were dried in a hot air oven (Gallenkamp 300 Plus series, UK) at 105 ^oC until constant weight. The dry matter content was estimated from the relationship:

$$\% \text{ Dry matter} = \frac{\text{Dry weight}}{\text{Fresh weight}} \times 100$$

3.2.3 Starch extraction

A wet separation technique was used to extract starch from fresh root tubers of the sweet potato varieties (Brabet *et al*., 1998). The tubers were washed, peeled and defective parts removed. These were then sliced, diced and weighed. They were then blended with equal volumes of tap water (1:1 v/v)in a food blender at maximum speed for 5 minutes. The slurry obtained was filtered through a nylon mesh (2 mm) and the marc resuspended twice in tap water (1:2 v/v), macerated and filtered in the same way. The three filtrates were pooled, passed through a 250µm laboratory test sieve (ASTME II, Retsch – Germany) and the volume adjusted to 20 L with tap water. Starch was allowed to settle undisturbed for 3 hours at room temperature and the supernatant discarded. The starch was resuspended in 10 L of tap water, filtered through a 75µm sieve to remove fibrous materials and allowed to settle for 1 hour. The settled starch was subsequently washed twice in 10 L of deionized water,dried in a hot air oven at 40 ^oC for 48 hours and weighed. The dried starch was ground with a mortar and pestle, passed through a 250 µm sieve, sealed in polyethylene bags and stored in air-tight plastic containers at room temperature until used further.

3.2.4 Moisture content of the dried starch

Residual moisture content of the dried starch samples were determined thermo-gravimetrically using a moisture analyser (MB-45, Ohaus – Switzerland). 1 g quantities of starch powder were spread out on the pan,dried at 105 ^{o}C for 10 minutes and complete moisture loss observed as a plateau peak. The weight difference was determined and expressed as percent moisture content.

3.2.5. Starch yield on fresh weight basis (fwb)

The starch yield on fresh weight basis was calculated as a ratio of weight of starch (g) to weight of fresh root tubers (g) taking 14% as standard moisture content as follows:

$$\text{Percent (\%) Starch yield from fresh root tubers} = \frac{\text{Weight of dried starch}}{\text{Weight of peeled tubers}} \times 100$$

$$\text{Starch yield on fwb} = \frac{(14\\%) \times (\%\ \text{starch yield from fresh root tubers})}{\text{Moisture content of dried starch}}$$

3.2.6 Starch yield on dry weight basis (dwb)

The starch yield on dry weight basis was calculated using the relationship:

$$\text{Starch yield on dwb} = \frac{\text{Starch yield on fwb}}{\%\ \text{Dry matter}} \times 100$$

3.2.7 Identification and organoleptic tests for sweet potato starches

Methods and procedures described in the United States Pharmacopoeia and British Pharmacopoeia were used for starch identification and organoleptic evaluations (USP, 1990; BP, 2007).

3.2.7.1 Identification test

Approximately 2 ml of distilled water was added to 1 g of starch powder to prepare a smooth mixture. The mixture was added to 15 ml of boiling water and heated gently for 2 minutes. The clarity of jelly formed when the slurry was allowed to coolas well as any further change in colour of the slurry upon addition of iodinetest solution (TS), were observed and recorded.

3.2.7.2 Organoleptic characteristics

Organoleptic tests were carried out by sensory evaluations. The texture, colour, odour and taste of powdered sweet potato and commercial maize starches were assessed.

3.2.8 Microscopy

3.2.8.1 Calibration of eyepiece / ocular micrometer

A 2.0 mm stage micrometer with a basic graduation of 10 µm was placed on the stage of the light microscope and the graduations brought into focus at a magnification of x100. The eyepiece micrometer was fitted into one of the barrels of the two eyepieces and the lens carefully refitted. Graduations on the two micrometers (stage and eye piece) were aligned and the number of ocular divisions between two coinciding graduations on both stage and eyepiece micrometers were counted. The corresponding number of stage micrometer divisions was multiplied by 10 µm and the product divided by the number of ocular divisions. This gave the value of one ocular or eyepiece micrometer graduation at x100 magnification. A conversion factor (given below) was applied when counting was done at a different magnification.

$$\text{Conversion factor} = \frac{100 \times \text{value of one ocular division}}{\text{New magnification}}$$

3.2.8.2 Estimation of starch granule diameter and size range

A 1 % w/v starch suspension was prepared by weighing 0.25 g of starch into a 25 ml volumetric flask. A mixture containing equal volumes of distilled water and glycerol was added (with concurrent shaking of the flask) to the 25 ml mark. A few drops of the starch suspension obtained was placed on a slide and observed under the microscope at low and high power magnifications (x400 and x1000, respectively). The mean granule diameter from fifty (50) randomly selected granules was estimated at low power magnification with the calibrated eye piece micrometer. The determinations were in triplicates. The range of granular size distribution was determined from the smallest and largest granules enumerated.

3.2.9 Physicochemical and powder properties of the sweet potato starches

3.2.9.1 Bulk properties

The procedures employed by Obitte and Chukwu, 2007 were used in the determination of true density, bulk density and tapped density of the powdered starches.

3.2.9.1.1 True density

True density of the pulverized starches was determined by fluid displacement (using xylene as the displacement fluid). The weight of an empty 50 ml pycnometer (W_1) was recorded and subsequently filled with xylene to the mark. The cover was replaced, excess fluid wiped off and the weight of fluid that filled the bottle (W_3) noted. About 5 ml of the fluid was withdrawn from the bottle and 0.5 g of starch (W_2) transferred into it. The fluid level was raised to the mark on neck of the density bottle with fresh xylene, stoppered and the weight of fluid and starch (W_4) recorded. The true density was then calculated using the relation:

$$\text{True density } (g/cm^3) = \frac{W_2 W_3}{50(W_2 - W_4 + W_3)}$$

3.2.9.1.2 Bulk density

Starch powder of weight 10 g was placed in a 25 ml measuring cylinder. The upper surface was carefully flattened out and the volume noted. Bulk density was then calculated using the relation:

$$\text{Bulk density } (D_0)\ g/cm^3 = \frac{\text{Weight of starch}}{\text{Bulk volume}}$$

3.2.9.1.3 Tapped density

The 10 g starch powder in section **3.2.9.1.2** above was gently tapped 150 times on a padded bench (till no further reduction in powder volume) and the final volume noted. Tapped or final bulk density was calculated using the relation:

$$\text{Tapped density } (D_f)\ g/cm^3 = \frac{\text{Weight of starch}}{\text{Tapped volume}}$$

3.2.9.1.4 Average diameter and particle size distribution of the starch powders

A sieving method employed by Ohwoavworhua and Adelakun, 2005 was used in analyzing particle size of the starch powders. Three test sieves ranging from 250 µm to 75 µm and a pan were arranged in descending order on the sieve shaker. 20 g of starch powder was placed on the top sieve (250 µm) and the set-up shaken at amplitude 70 for 5 minutes. The weight of material retained on each sieve was determined. The average diameter was computed using the relation:

$$\text{Average diameter} = \sum \frac{[(\%\text{retained}) \times (\text{mean aperture})]}{100}$$

3.2.9.2 Starch powder flow properties

Methods described in the United States Pharmacopoeia were used in the determination of Angle of repose, Hausner's ratio and Carr's compressibility index (USP, 1990).

3.2.9.2.1 Angle of repose

A funnel was clamped with its tip 2 cm above a 9 cm wide petri dish. The starch powders were allowed to flow through the funnel until the apex of the powder cone thus formed just touched the tip of the funnel. The mean diameter (D) of the base of the powder cone was determined and the tangent of the angle of repose (θ) was calculated using the relation:

$$\tan \theta = \frac{2h}{D}$$

Where, h is the height of the heap of powder; from which the angle of repose was ascertained.

3.2.9.2.2 Hausner's ratio

This was calculated as the ratio of tapped density to bulk density of the starches.

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

3.2.9.2.3 Carr's compressibility index

Carr's index was calculated from the bulk and tapped density data using the relation:

$$\text{Carr's index} = \frac{[\text{Tapped density} - \text{bulk density}] \times 100}{\text{Tapped density}}$$

3.2.9.3 pH

The pH of the starches was determined using procedures described in the British Pharmacopoeia (BP, 2007). The pH meter was first standardized using standard buffers 4.0, 7.0 and 9.0. Subsequently, 5 g of starch was weighed into a 50 ml volumetric flask and 25 ml of freshly boiled, cooled deionized water added. The mixture was agitated for 1 minute and the starch suspension allowed to settle in a 50 ml beaker for 15 minutes. The pH of the supernatant was then determined potentiometrically with a pH meter.

3.2.9.4 Moisture sorption capacity

2 g of dried starch powder was accurately weighed and evenly spread on a 90 mm wide petri dish. The samples were then placed in a desiccator containing distilled water in its reservoir (Relative Humidity ≥ 100%) and kept at room temperature for 5 days. Weight gained by the exposed powders at the end of the period was recorded. The amount of water sorbed was calculated from the weight difference (Ohwoavworhua and Adelakun., 2005).

$$\% \text{ Moisture sorption} = \left[\frac{\text{Final weight (g)} - \text{Initial weight (g)}}{\text{Initial weight (g)}}\right] \times 100$$

3.2.9.5 Amylose content

To 0.1 g of each starch sample was added 1mlof ethanol (96%) and 9ml of NaOH (1 M). The mixture was solubilized by heating in a boiling water bath for 10 minutes. 1 ml of the solution was diluted to 10 ml with distilled water. To 0.5 ml of this diluted solution was added 0.1 ml acetic acid (1 M) and 0.2 ml of iodine test solution (0.2 g I_2 + 2.0 g KI in 100 ml of distilled water). The resultant dark blue solution was made up to 10 ml with distilled water and allowed to stand for 20 minutes for complete colour development. The solution was vortexed for 5 minutes and its absorbance read on a UV spectrophotometer (Pharmaspec UV - 1700) at 620 nm. Corn starch containing 70 % amylose was used as standard to estimate the amylose content of the samples (Ellis *et al*., 2003). Percentage content of amylose was estimatedusing the relationship:

$$\text{Percent (\%) Amylose} = \frac{\text{\% Amylose of standard x Absorbance of sample}}{\text{Absorbance of standard}} \times 100$$

3.2.10 Proximate composition and purity of the starches

The methods described by the Association of Official Analytical Chemists (AOAC, 1990) were used to estimate the amount of crude fat, protein, fibre, ash and total carbohydrate in the starch powders. The purity of starch was estimated from the total carbohydrate content (Vasanthan, 2001).

3.2.10.1 Crude fat

To a 2 g quantity of starch powder wrapped in a 125 mm Whatman filter paper and placed in the extraction chamber of a soxhlet apparatuswas added 200 ml of petroleum ether. The crude fat was extracted from the sample with heating of the solvent for 8 hours.

Majority of the solvent was recovered from the extract (at the end of the process) while the residual solvent containing the crude fat was dried in an air oven at 105 ^{o}C to constant weight. The amount of crude fat present was estimated using the relation:

$$\text{Percent (\%) Fat} = \frac{\text{Weight of residue}}{\text{Weight of starch}} \times 100$$

3.2.10.2 Crude Protein

To a 2 g quantity of starch powder in aKjeldahl flask was added 25 ml of concentrated sulphuric acid and a mixture of 0.5 g anhydrous sodium sulphate and copper sulphate (1:1) to catalyze and speed up the digestion process. The starch powder was digested until it was clear. This converted any nitrogen in starch (with the exception of nitrates and nitrites) into ammonium; and other organic matter to carbon dioxide and water.

$$\text{Starch} \xrightarrow[\text{Heat, catalyst}]{\text{Sulphuric acid}} (NH_4)_2SO_4 \quad (1)$$

The mixture was allowed to cool and 10 ml of the digested starch neutralized with 18 ml of 40 % NaOH. This converted the ammonium sulphate into ammonia gas:

$$(NH_4)_2SO_4 + 2NaOH \longrightarrow 2NH_3 + 2H_2O + Na_2SO_4 \quad (2)$$

A conical flask (connected to the digestion flask by a tube) containing 25 ml of 2 % boric acid and 2 - 3 drops of a mixed indicator (methylene blue and methylene red) was used to receive the ammonia gas. The low pH of the solution in the receiving flask converted the ammonia gas into ammonium ion, and boric acid to borate ion.

$$NH_3 + H_3BO_3 \longrightarrow NH_4^+ + H_2BO_3^- \quad (3)$$

The content of the conical flask was then titrated with 0.1 M HCl to a faint pink colour (end point) and the titre value recorded. A blank sample was run concurrently to take into account any residual nitrogen present in the reagents used to carry out the analysis. The concentration of hydrogen ions required to reach the end point is equivalent to the concentration of nitrogen that was in the starch (equation 3). The amount of protein in the starch samples were estimated taking 6.25 as the conversion factor from the following relations:

$$\text{\% Total nitrogen (N)} = \frac{100 \times (V_A - V_B) \times N_A \times 0.014}{W \times 10 \text{ ml of sample}} \times 100$$

Where; V_A and V_B are the titration volumes of the sample and blank

N_A and W are the normality of acid and weight of sample respectively.

Percent (%) Protein = conversion factor (6.25) x % N

3.2.10.3 Crude fibre

2 g of starch powder was defatted as in section **3.2.10.1** above. The defatted starch was transferred to a flat-bottom flask and 200 ml of 1.25 % H_2SO_4 added. The flask was connected to a condenser, placed on a hot plate and refluxed for 30 minutes after the first drop of condensate. The content of the flask was then filtered through a clean cheese cloth and the residue washed with boiling water until filtrate was no longer acidic. The residue was quantitatively transferred back into the flask and refluxed for 30 minutes with 200 ml of 1.25 % NaOH. The contents of the flask was again filtered through cheese cloth and washed with boiling water until filtrate was no longer basic. The residue was transferred into a dry crucible and dried in an air oven at 105 ^oC for 4 hours. The weight of residue was noted before being combusted at 600 ^oC in a muffle furnace for 2 hours. The crucible was allowed to cool and the weight of ash noted. The percentage of crude fibre present was then calculated by difference in weight.

$$\text{Percent (\%) Fibre} = \frac{[\text{weight of dry insoluble residue} - \text{weight of ash}]}{\text{Weight of sample}} \times 100$$

3.2.10.4 Ash content

2 g of starch powder was spread out in a pre-weighed porcelain crucible. It was combusted at 600 $^oC$for 2 hours in a muffle furnace. It was then allowed to cool and the weight of residue recorded.

$$\text{Percent (\%) Ash} = \frac{\text{weight of residue}}{\text{weight of sample}} \times 100$$

3.2.10.5 Carbohydrate content

The carbohydrate content was determined by subtracting all the other proximate determinations including percentage moisture from 100 %.

Percent (%) Carbohydrate = 100 – (% moisture + % crude fat + % crude protein + % crude fibre + % ash)

3.2.10.6 Starch purity

The purity of starch extracted from the sweet potato root tubers was estimated using the relation:

$$\text{Percent (\%) Starch Purity} = \left[\frac{\text{\% Carbohydrate}}{(100 - \text{\% Moisture})}\right] \times 100$$

3.2.11 Pasting profile and characteristics of the starches

Starch samples (40 g) were suspended in 420 ml of distilled water and transferred into the measuring bowl of the Brabender Viscograph-E (Brabender OHG - Germany). The test was run at a speed of 75 revolutions per minute (rpm) with a measuring range of 0 cmg to 1000 cmg. The temperature profile of the analysis rose from 50 °C to 95 °C at a rate of 1.5 °C per minute, held at 95 °C for 15 minutes, subsequently declined to 50 °C at the same rate and held for 15 minutes. The pasting characteristics were then determined from the time, temperature and viscosityat the various stages of starch granule gelatinization. The pasting temperature (P_{temp}), time from onset of pasting to peak viscosity (P_{time}), peak viscosity (PV), viscosity at the end of the holding time at 95 ^{o}C (hot paste viscosity, HPV), viscosity at the end of the holding time at 50 ^{o}C (final or cold paste viscosity, FV), the drop in peak or maximum viscosity at the end of heating cycle (break down, BD) and the rise in viscosity at the end of the cooling cycle (set back, SB) were recorded. The tests were in triplicates and the viscosities measured in Brabender units (BU). It should be noted that the Brabender viscoamylograph does not measure true viscosity. It gives only a numerical value related to an apparent viscosity (Mistry and Eckhoff, 1992).

Commercial maize starch and sodium starch glycolate were used as standard binder and disintegrant, respectively.

3.2.12 Pharmaceutical evaluations

The purity of paracetamol powder used in the study was verified using a procedure described in the British Pharmacopoeia (BP, 2007). In addition, the quality of the starches as pharmaceutical diluent, binder and disintegrant were investigated; and their influence on in-vitro drug release from the dosage form (dissolution) evaluated.

3.2.12.1 Determination of paracetamol purity

To 0.15 g of paracetamol powder was added 50 ml of 0.1 M sodium hydroxide. The solution was diluted with 100 ml of distilled water, shaken for 15 minutes and sufficient

water added to produce 200 ml. The solution was filtered and 10 ml of the filtrate diluted to 100 ml with water. 10 ml of the resulting solution was added to 10 ml of 0.1 M sodium hydroxide, and then diluted to 100 ml with water. Absorbanceof the resulting solution which was expected to contain 0.00075 % w/v paracetamol was measured at 257 nm on a UV spectrophotometer (Pharmaspec UV - 1700). Content of paracetamol was calculated taking 715 as the value of A (1%, 1 cm) from the Beer-Lambert's equation as follows:

$A = abc$

Where; A = absorbance a = absorptivity b = thickness of cell c = concentration

$$\text{Percent (\%) Purity of Paracetamol} = \frac{\text{Absorptivity of samplex } 100}{\text{Specific absorptivity of paracetamol (i.e. 715)}}$$

3.2.12.2 Evaluation of the sweet potato starches as tablet binder

Table 3.2.1: Composition of paracetamol tablets for binder quality evaluation of the sweet potato starches.

Ingredients	**Quantities for the different concentrations of sweet potato starch as binder**				**Quantities for the reference binder**
	3 % w/w	5 % w/w	8 % w/w	12 % w/w	5 % w/w
Sweet potato starch (Paste binder)	17.25 mg 3.45 g *	28.75 mg 5.75 g *	46.00 mg 9.20 g *	69.00 mg 13.80 g *	- -
Maize starch (reference binder)	- -	- -	- -	- -	28.75 mg 5.75 g *
Paracetamol	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *
Mannitol (diluent)	50.05 mg 10.01 g *	38.55 mg 7.71 g *	21.30 mg 4.26 g *	- -	38.55 mg 7.71 g *
Magnesium stearate (lubricant)	1.70 mg 0.34 g	1.70 mg 0.34 g	1.70 mg 0.34 g	- -	1.70 mg 0.34 g
Na starch glycolate (disintegrant)	6.00 mg 1.20 g *	6.00 mg 1.20 g *	6.00 mg 1.20 g *	6.00 mg 1.20 g *	6.00 mg 1.20 g *
Total for 1 tablet **Total for 200 tablets**	**575 mg** **115 g ***	**575 mg** **115 g ***	**575 mg** **115 g ***	**575 mg** **115 g ***	**575 mg** **115 g ***

* Represents scaled quantities (x200)

Granules for paracetamol tablets were formulated using paste from the various sweet potato starches as binder in four different concentrations of 3 %, 5 %, 8 % and 12 % w/w. Mannitol was used as a diluent to adjust tablet weight. The starch pastes were prepared by

dispersing appropriate quantities of starch powder in 10 ml of distilled water. 15 ml of boiling water was added to the suspension which was subsequently heated until the starch was fully gelatinized to form a paste. The pastes obtained were used to wet the powder mass and granulate appropriate mixtures of paracetamol and mannitol; adding more water where necessary. The wet masses were screened with a mesh 12 (1700 µm) sieve and dried at 60 ^{o}C in a hot air oven for 90 minutes to amoisture content of 1.20 ± 0.30 %. The dried granules were screened with a mesh 16 (1180 µm) sieve. 1 % w/w sodium starch glycolate and 0.3 % w/w magnesium stearate were incorporated as extragranular disintegrant and lubricant respectively, and the mixture thoroughly blended.

The paracetamol granules were then compressed into tablets using a manually controlled single punch tableting machine (DP -30, Pharmao industries). The tableting machine was fitted with concave punches with 12 mm diameter and a fixed compression load of 11 kN was applied. All the tablets were compressed to a fill weight of 575 mg and formulations for an investigational batch of 200 tablets were made in each case.

A reference batch of paracetamol tablets were also compressed from a formulation containing 5 % w/w maize starch as binder.

3.2.12.2.1 Bulk and tapped density of the paracetamol granules

The bulk and tapped densities of paracetamol granules formed after the wet granulation process were determined as in sections **3.2.9.1.2** and **3.2.9.1.3**, respectively to determine their suitability before compression.

3.2.12.2.2 Weight uniformity of the paracetamol tablets

Twenty (20) tablets from each investigational batch were randomly selected, weighed together and the mean tablet weight noted. The tablets were then weighed individually and the weight of each tablet subtracted from the mean tablet weight. The percentage deviation of each tablet from the mean was then calculated.

$$\text{Percentage weight deviation} = \left[\frac{\text{Individual tablet weight} - \text{Mean tablet weight}}{\text{Mean tablet weight}} \right] \times 100$$

3.2.12.2.3 Thickness uniformity of the paracetamol tablets

The thicknesses of ten (10) paracetamol tablets from each batch were individually determined with the aid of an electronic vernier caliper (CD-8 CSX, Mitutoyo

Corporation). The mean and standard deviations were determined for all the tablet batches compressed.

3.2.12.2.4 Tablet hardness

Tablet hardness was determined using a manually operated Monsanto hardness tester (VEEGO HT-01, Progressive Instruments). Ten (10) tablets wererandomly selected from the different batches of tablets andeach positioned verticallyon the lower immovable anvil of the machine. The upper anvil was gently moved down by rotating the head screw in anticlockwise direction, such that the two anvils just hold the tablet vertically. The main and follow pointers on the gauge were then set to zero and diametral load manually applied to the tablet by moving the head screw anticlockwise at a rate of 0.1 kg per turn. Hardness values ofthe paracetamol tablets were recorded on the gauge in kg/cm^2 (1 kg/cm^2 or $kgf/cm^2 \equiv 98066.5\ N/m^2$or Pascal) by the follow pointer, while the main pointer went back to zero after the tablets cracked or crushed.

3.2.12.2.5 Tablet friability

The friability of eleven(11) tablets approximately weighing 6.5 g was determined in a friabilator (TA-20, Erweka). The drum was rotated at 25 rotations per minute (rpm) for 4 minutes. Loss of tablet weight with respect to the initial weight was then calculated after the tablets were de-dusted and observed for capping and lamination.

$$\% \text{ Weight loss} = \left[\frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \right] \times 100$$

3.2.12.3 Evaluation of the sweet potato starches as tablet disintegrant

The sweet potato starches were each used as extra-granular disintegrant in four different concentrations of 1 %, 3 %, 6 % and 9 % w/w. Povidone (3.45 g) as a standard binder was dissolved in 25 ml of distilled waterand the solution used to granulate appropriate mixtures of paracetamol powder and mannitol. The resulting wet masses were screened with a mesh 12 sieve (1700 µm) and dried at 60 ºC for 90 minutes. The dried granules were then screened with a mesh 16 (1180 µm) sieve and the respective concentrations of sweet potato starch as disintegrant and 0.3 % w/w magnesium stearate as lubricant incorporated. The powders were then thoroughly blended.All the paracetamol tablets were compressed to a fill weight of 575 mg and formulations for an investigational batch of 200 tablets made in each case. Uniformity of weight and thickness for the compressed tablets were determined as in sections **3.2.12.2.2** and **3.2.12.2.3**, respectively.

A reference batch of paracetamol tablets were also compressed from a formulation containing 3 % w/w maize starch as disintegrant.

Table 3.2.2: Composition of paracetamol tabletsfor disintegrant qualityevaluation of the sweet potato starches.

Ingredients	**Quantities for the different concentrations of sweet potato starch as disintegrant**				**Quantities for the reference disintegrant**
	1 % w/w	3 % w/w	6 % w/w	9 % w/w	3 % w/w
Sweet potato starch (disintegrant)	5.75 mg 1.15 g *	17.25mg 3.45 g *	34.5 mg 6.9 g *	51.75 mg 10.35 g *	- -
Maize starch (reference disintegrant)	- -	- -	- -	- -	17.25mg 3.45 g *
Paracetamol	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *	500.00 mg 100.00 g *
Mannitol (diluent)	50.30 mg 10.06 g *	38.80 mg 7.76 g *	21.55 mg 4.31 g *	4.30 mg 0.86 g *	38.80 mg 7.76 g *
Povidone K-30 (binder)	17.25mg 3.45 g *	17.25mg 3.45 g *	17.25mg 3.45 g *	17.25mg 3.45 g *	17.25mg 3.45 g *
Magnesium stearate	1.70 mg 0.34 g	1.70 mg 0.34 g	1.70 mg 0.34 g	1.70 mg 0.34 g	1.70 mg 0.34 g
Total for 1 tablet **Total for 200 tablets**	**575 mg** **115 g***	**575 mg** **115 g***	**575 mg** **115 g***	**575 mg** **115 g***	**575 mg** **115 g***

* Represents scaled quantities (x200)

3.2.12.3.1 Disintegration time test

The disintegration time of tablets with extra-granular sweet potato starch as disintegrant was determined according to the procedure described in the British Pharmacopoeia (BP, 2007). A tablet was placed in each of the six tubes of the disintegration apparatus (ZT-4, Erweka) and the time taken for all tablets to completely disintegrate in distilled water maintained at 37 ± 2 ^{o}C was determined.

3.2.12.4 Influence of the starches as binder and disintegrant on in-vitro drug dissolution

Two sets of paracetamol tablets which respectively contained 5 % w/w of the different sweet potato starches as binder (Table 3.2.1) and 3 % w/w of the sweet potato starches as disintegrant (Table 3.2.2) were selected for these evaluations against paracetamol tablets containing similar concentrations of maize starch as reference.

3.2.12.4.1 Calibration curve of the UV Spectrophotometer

The UV spectrophotometer (Pharmaspec UV-1700, Shimadzu corporation) was calibrated using the following concentrations of paracetamol; 0.0001 %, 0.0002 %, 0.0004 %, 0.0008 % and 0.001 % w/vin 0.1M NaOH. The absorbances of these solutions were determined at 257 nm and a calibration curve ascertained. The resultant regression equation was subsequently used to estimate amount of drug released from the uncoated tablets.

3.2.12.4.2 Dissolution test

The test was carried out as described in the British Pharmacopoeia (BP, 2007), using the BP apparatus II (paddle) dissolution machine (DBK Instruments). 900 ml of Phosphate buffer (pH 5.8) was placed in each of the six vessels of the dissolution apparatus and maintained at 37 ± 0.5 °C with a paddle speed of 50 revolutions per minute. A tablet was carefully placed into each vessel in a way that excluded air bubbles from its surface. 20 ml samples were withdrawn from a zone midway between the surface of the dissolution medium and the top of the rotating paddle blade, not less than 1 cm from the vessel wall at specified time intervals of 5, 10, 15, 30, 45 and 60 minutes. 20 ml of fresh dissolution medium maintained at 37 ± 0.5 °Cwas used to replace each sample withdrawn. The withdrawn samples were filtered with Whatman filter paper and 0.90 ml of each filtrate diluted to 50 ml with 0.1 M NaOH. The absorbances of the resultant solutions were measured at 257 nm onthe UV spectrophotometer (Pharmaspec UV-1700, Shimadzu corporation). A solution of 0.1 M NaOH was used in the reference cell of the UV spectrophotometer. The absorbances were used to determine the total content of paracetamol released from the calibration curve. A graph of percentage drug released against time was then plotted to establish the dissolution profile of paracetamol from the uncoated tablets.

3.2.12.4.3 Calculations

The regression equation showing the relationship between drug concentration and absorbance was:

$y = 689.7x + (-0.017)$ $(r^2 = 0.9999)$

Where; y = absorbance at 257 nm and x = concentration of drug released. Using paracetamol tablets containing Hi-starch as paste binder as example, 0.90 ml

aliquots taken after 5 minutes whose average absorbances were 0.405 nm, the concentration of drug released (X) was computed as follows:

$$X = \frac{0.405 + 0.017}{689.7}$$

X = 0.000612 % w/v

Diluting this volume to 50 ml gives a dilution factor of 55.556; while tablet weight ratio (actual weight :expected weight) was 1.0 as approximately 575 mg tablets were used for the test.

The actual amount of drug released into the medium after 5 minutes was thus computed as:

X = 0.000612 x 55.556 x 1.0

X = 0.034 % w/v

Assuming 100 % release, a 575 mg tablet containing 0.500 g of paracetamol in the 900 ml dissolution medium will give medium concentration (X_m) of:

$$X_m = \frac{0.500}{900} \times 100$$

X_m = 0.0556 % w/v

The percentage (%) drug released (X) is thus given as:

$$X = \frac{0.034}{0.0556} \times 100$$

X = 61.2 %

3.2.13 Statistical analysis

The results were expressed as Mean ± SD. GraphPad Prism version 5.01 for Windows (GraphPad Software Inc., San Diego - California) was used for the statistical analysis. One-way analysis of variance (ANOVA) with Newman-Keuls and Bartlett's post tests were performed to determine differences between starch sample variables. Possible correlations of starch properties were ascertained by Pearson's correlation tests. Determinations with values of $p < 0.05$ were considered significant.

3.3 RESULTS

3.3.1 Organoleptic properties of fresh sweet potato root tubers

Table 3.3.1: Sensory evaluations of fresh sweet potato root tubers

Cultivar	Skin colour	Flesh colour	Taste	Texture	Latex exudate
Hi-Starch	Creamy-brown	Cream	Mildly sweet	Firm	7
Sauti	Cream	Yellow	"	"	3
Ogyefo	Purple	White	"	"	0
Faara	Purple	Cream	"	"	7

3.3.2 Tuber dry matter

Table 3.3.2: Dry matter content of fresh sweet potato root tubers

Cultivar	Dry matter content (%)
Hi-Starch	39.6 ± 0.42^{a}
Sauti	40.0 ± 0.31^{a}
Ogyefo	39.5 ± 0.50^{a}
Faara	36.4 ± 0.24^{a}

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

3.3.3 Starch extraction and yield

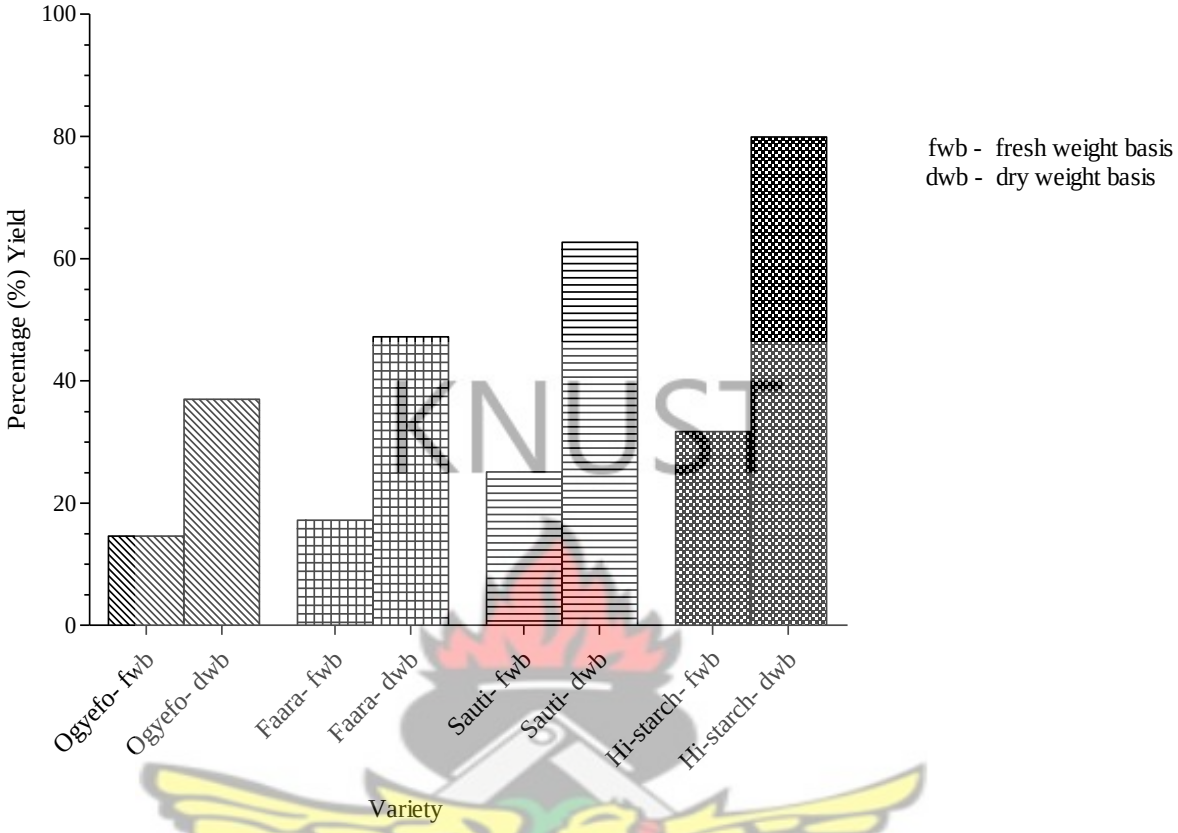


Figure 3.3.1: Starch Yield from the four Sweet potato varieties

3.3.4 Moisture content

Table 3.3.3: Moisture content and yield of the dried starches

Starch	Moisture content (%)	Yield (%)	
		fwb	dwb
Hi-Starch	10.93 ± 0.21[a]	31.7	79.9
Sauti	12.77 ± 0.21[a]	25.1	62.7
Ogyefo	13.13 ± 0.31[a]	14.6	37.0
Faara	10.03 ± 0.16[a]	17.2	47.2
Maize	12.70 ± 0.23[a]	-	-

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

3.3.5 Identification and Organoleptic tests for starch

Table 3.3.4: Starch identification test

Starch	Test	Observation	Inference
Hi-Starch	2 drops of iodine test solution was added to 15 ml of starch paste	Translucent paste turns dark blue	Powder complied with the BP and USP identification test for starch
Sauti	"	"	"
Ogyefo	"	"	"
Faara	"	"	"
Maize	"	"	"

Table 3.3.5: Starch organoleptic test

Starch	Test	Observation	Inference
Hi-Starch	Starch powder was observed for texture, colour, odour and taste	Appeared as fine, white, odourless powder with a bland taste	Powder complied with the BP and USP organoleptic test for starch
Sauti	"	"	"
Ogyefo	"	"	"
Faara	"	"	"
Maize	"	"	"

3.3.6 Microscopy

Table 3.3.6: Shape, size and size distribution of the starch granules

Starch	Shape	Diameter range (µm)	Mean granule diameter (µm)
Hi-Starch	Round, polygonal	7.0 - 45.0	16.3 ± 1.0[a]
Sauti	"	5.0 - 35.0	14.2 ± 0.9[a]
Ogyefo	"	4.0 - 42.5	14.4 ± 1.1[a]
Faara	"	3.5 - 35.0	13.6 ± 1.0[a]
Maize	"	2.5 - 22.5	9.1 ± 0.6[d]

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

3.3.7 Physicochemical and powder properties of the starches

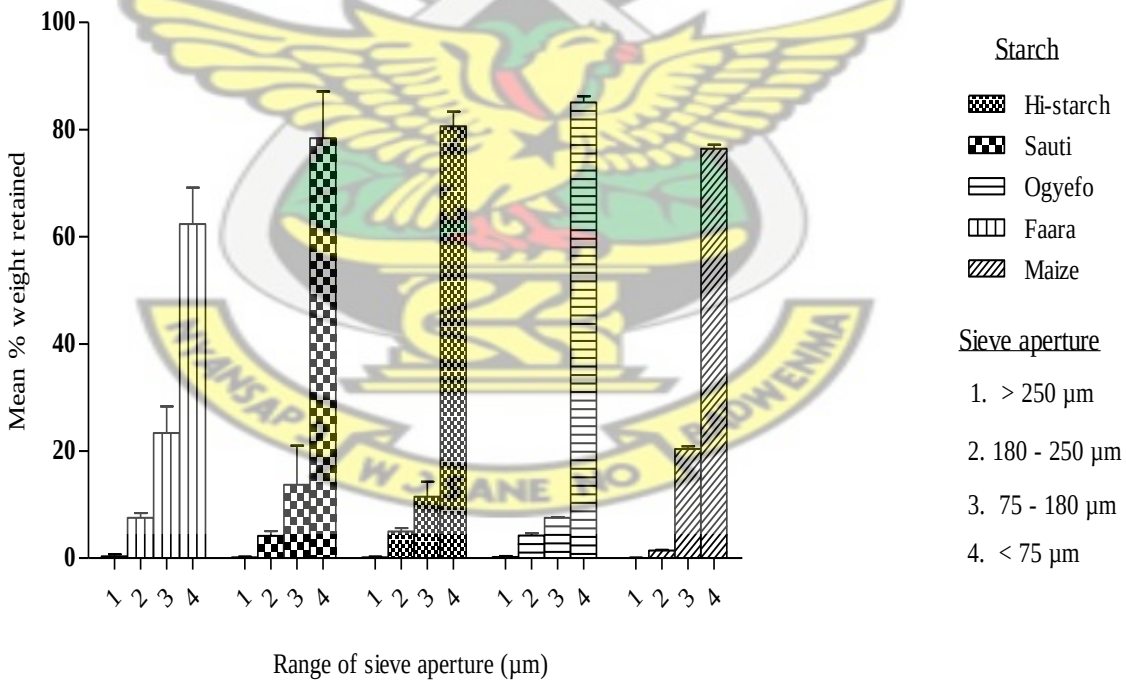


Figure 3.3.2: Particle size distribution of the dried pulverized starch

Table 3.3.7: Particle size and size distribution of the powdered starches

Starch	Sieve aperture (µm)	Weight of starch retained (Mean ± SD) (%)	Starch particle diameter (Mean ± SD) (µm)
Faara	> 250	0.35 ± 0.35	93.6 ± 3.92[a]
	180 - 250	7.55 ± 0.85	
	75 - 180	23.40 ± 4.95	
	< 75	62.40 ± 6.75	
Sauti	> 250	0.15 ± 0.15	85.4 ± 5.00[a]
	180 - 250	4.15 ± 0.88	
	75 - 180	13.70 ± 7.33	
	< 75	78.40 ± 8.75	
H-starch	> 250	0.15 ± 0.15	86.2 ± 3.25[a]
	180 - 250	5.00 ± 0.65	
	75 - 180	11.50 ± 2.78	
	< 75	80.60 ± 2.75	
Ogyefo	> 250	0.20 ± 0.20	83.0 ± 0.51[a]
	180 - 250	4.20 ± 0.45	
	75 - 180	7.55 ± 0.10	
	< 75	85.10 ± 1.10	
Maize	> 250	0.05 ± 0.05	86.4 ± 0.48[a]
	180 - 250	1.40 ± 0.15	
	75 - 180	20.40 ± 0.50	
	< 75	76.40 ± 0.80	

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

Table 3.3.8: Bulk properties of the starches

Parameter	Starch				
	Hi-starch	Sauti	Ogyefo	Faara	Maize
Bulk Properties:					
True density (g/cm^3)	1.15 ± 0.02^a	1.16 ± 0.03^a	1.18 ± 0.02^a	1.16 ± 0.03^a	1.10 ± 0.03^b
Bulk density (g/cm^3)	0.53 ± 0.00^a	0.50 ± 0.02^a	0.55 ± 0.01^a	0.58 ± 0.01^a	0.40 ± 0.01^b
Tapped density (g/cm^3)	0.75 ± 0.01^a	0.79 ± 0.02^a	0.80 ± 0.01^a	0.82 ± 0.02^a	0.61 ± 0.00^b

Means followed by the same superscript in a row are not significantly different at $p < 0.05$

Table 3.3.9: Flow property and behaviour of the starches

Parameter	Starch				
	Hi-starch	Sauti	Ogyefo	Faara	Maize
Flow Properties:					
Angle of repose [NMT 40 °]	40.4 ± 1.20^a	38.7 ± 1.45^a	37.6 ± 1.10^a	36.1 ± 0.80^a	36.9 ± 1.85^a
Hausner's ratio [NMT 1.25]	1.42 ± 0.09^a	1.58 ± 0.13^a	1.45 ± 0.18^a	1.41 ± 0.12^a	1.53 ± 0.10^a
Compressibility index [NMT20 %]	29.3 ± 0.18^a	36.7 ± 0.21^a	31.3 ± 0.19^a	29.3 ± 0.27^a	34.4 ± 0.32^a

Means followed by the same superscript in a row are not significantly different at $p < 0.05$

NMT- Not More Than

Table 3.3.10: pH and moisture sorption capacity of the starches

Parameter	Starch				
	Hi-starch	Sauti	Ogyefo	Faara	Maize
pH	5.9 ± 0.10[a]	5.8 ± 0.05[a]	5.1 ± 0.04[a]	5.6 ± 0.04[a]	5.2 ± 0.03[a]
Moisture sorption capacity (%)	7.50 ± 1.00[a]	6.50 ± 0.50[a]	6.50 ± 1.00[a]	7.50 ± 1.00[a]	5.75 ± 0.25[a]

Means followed by the same superscript in a row are not significantly different at $p < 0.05$

3.3.8 Amylose content

Table 3.3.11: Calorimetric estimation of starch amylose content

Starch	Mean absorbance	Amylose content (%)
Hi-starch	0.346 ± 0.004	22.3 ± 0.26[a]
Sauti	0.395 ± 0.006	25.4 ± 0.39[b]
Ogyefo	0.407 ± 0.002	26.2 ± 0.13[c]
Faara	0.393 ± 0.003	25.3 ± 0.19[b]
Maize	0.429 ± 0.002	27.6 ± 0.13[d]

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

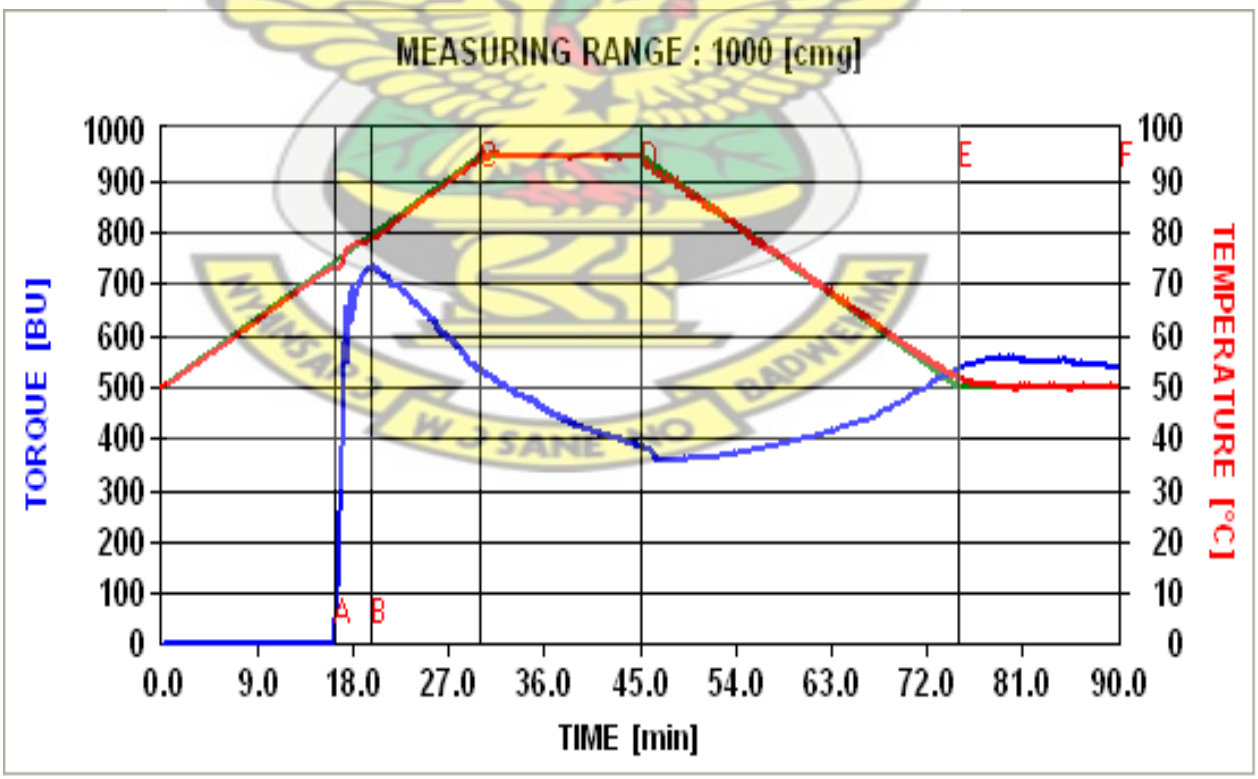
3.3.9 Proximate composition

Table 3.3.12: Proximate composition and purity of the starches

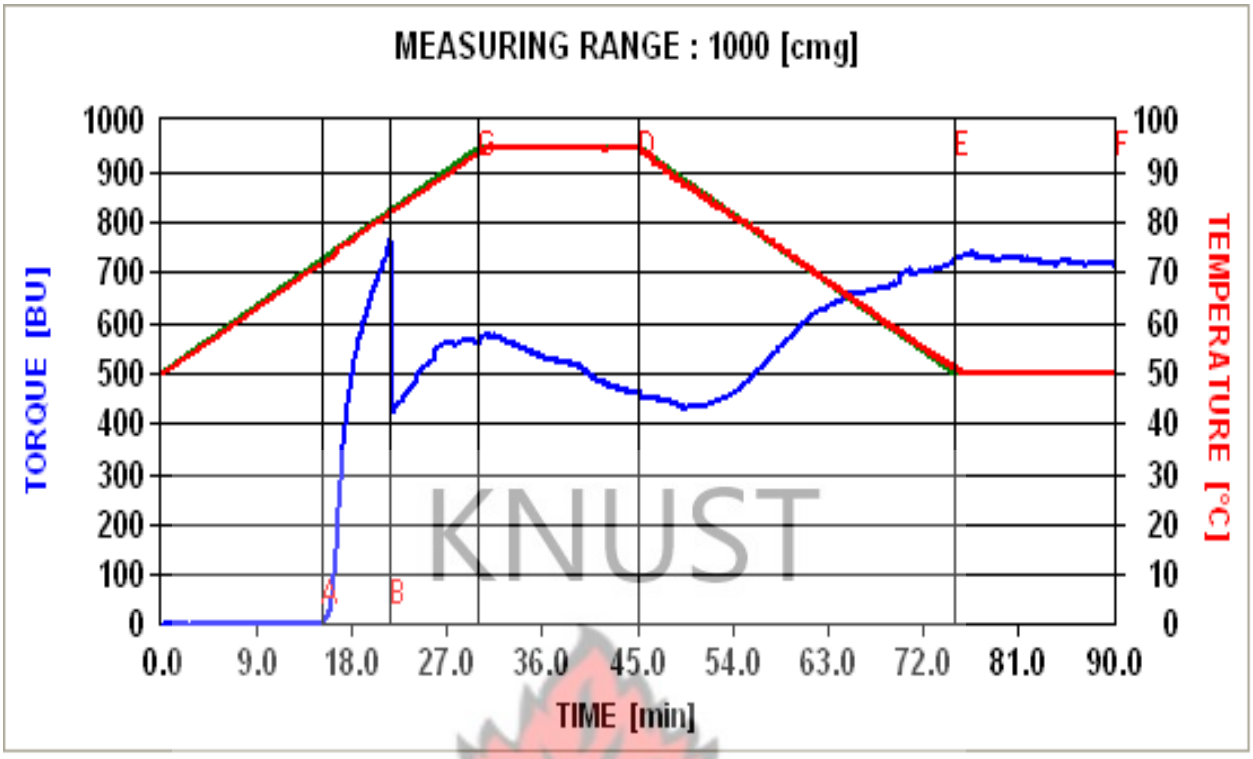
Starch	Parameter					
	Ash (%)	Fat (%)	Fibre (%)	Protein (%)	Carbohydrate (%)	Purity (%)
Hi-Starch	0.57 ± 0.11a	0.32 ± 0.07[a]	0.09 ± 0.02[a]	0.94 ± 0.15[a]	87.15 ± 0.23[a]	97.84 ± 0.38[a]
Sauti	0.54 ± 0.26[a]	0.44 ± 0.12[a]	0.07 ± 0.01[a]	1.24 ± 0.11[a]	84.94 ± 0.25[a]	97.37 ± 0.37[a]
Ogyefo	0.10 ± 0.03[a]	0.54 ± 0.10[a]	0.04 ± 0.01[a]	1.36 ± 0.09[a]	84.83 ± 0.19[a]	97.65 ± 0.37[a]
Faara	0.49 ± 0.08[a]	0.45 ± 0.10[a]	0.16 ± 0.03[a]	1.14 ± 0.20[a]	87.73 ± 0.21[a]	97.51 ± 0.34[a]
Maize	0.43 ± 0.13[a]	1.22 ± 0.09[d]	0.12 ± 0.02[a]	1.01 ± 0.10[a]	84.52 ± 0.20[a]	96.82 ± 0.15[a]

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

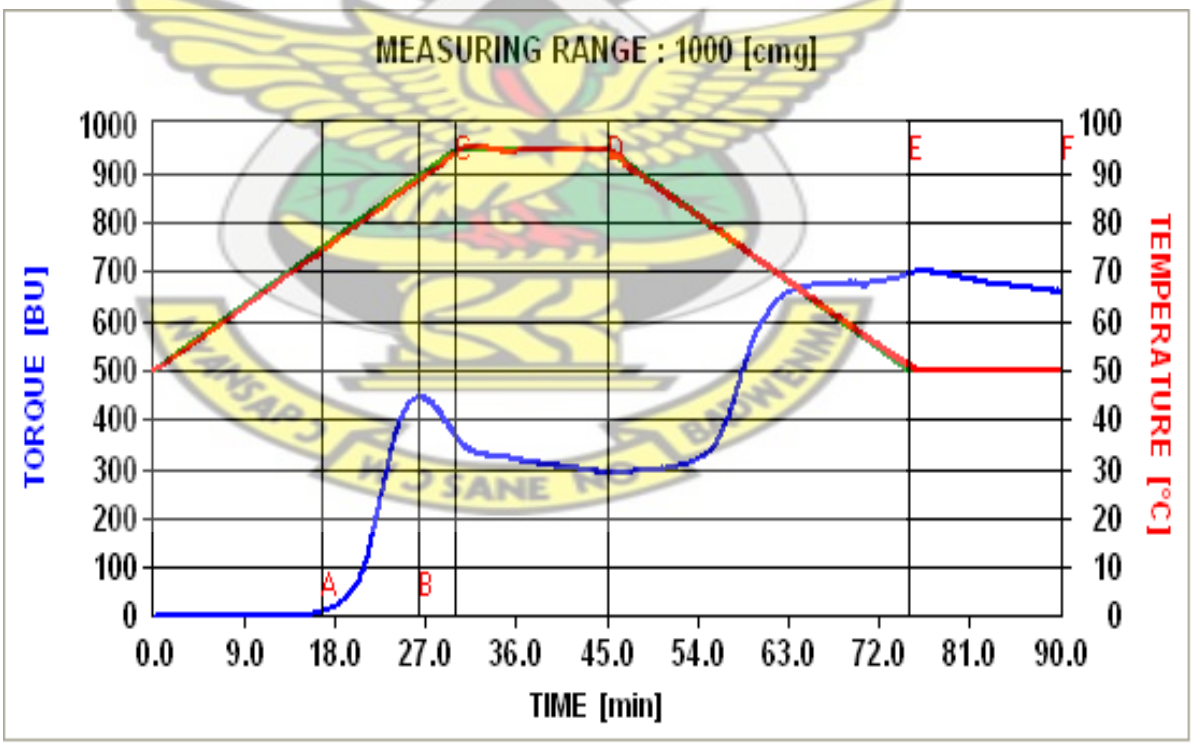
3.3.10 Pasting profile and characteristics of the starches



Sweet potato starch (Hi-starch)



Na starch glycolate



Maize starch

Figure 3.3.3: Amylogram of sweet potato and commercial maize starches after complete heating and cooling cycles.

Table 3.3.13: Starch pasting properties

Starch	Pasting Parameters					
	P_{temp} (ºC)	P_{time} (Minutes)	PV (BU)	BD (BU)	SB (BU)	FV (BU)
Hi-starch	72.9 ± 0.01[a]	3.25 ± 0.05[a]	734 ± 04[a]	348 ± 07[a]	152 ± 03[a]	538 ± 05[a]
Sauti	75.6 ± 0.00[b]	1.13 ± 0.03[b]	729 ± 21[a]	326 ± 30[a]	142 ± 09[a]	514 ± 08[a]
Ogyefo	75.8 ± 0.00[b]	1.15 ± 0.00[b]	694 ± 15[a]	213 ± 27[b]	164 ± 03[a]	638 ± 02[b]
Faara	75.1 ± 0.00[c]	1.28 ± 0.08[c]	762 ± 28[a]	421 ± 01[c]	102 ± 07[b]	435 ± 16[c]
Maize	74.2 ± 0.20[d]	9.38 ± 0.08[g]	451 ± 04[g]	157 ± 04[g]	407 ± 05[g]	667 ± 06[g]
Na Starchglycolate	72.1 ± 0.05[e]	6.13 ± 0.13[h]	762 ± 05[a]	324 ± 17[a]	251 ± 18[h]	679 ± 36[g]

Means followed by the same superscript in a column are not significantly different at $p < 0.05$

3.3.11 Pharmaceutical evaluations

3.3.11.1 Paracetamol purity

Table 3.3.14: Percentage purity of the paracetamol powder

Batch Number: 100602A / Sample Number	Mean absorbance	Purity (%)	Average Purity (%)	Reference (%)
I	0.533 ± 0.005	99.4	100.4	99.0 - 101.0
II	0.542 ± 0.003	101.1		
III	0.540 ± 0.004	100.7		

3.3.11.2 Evaluation of the sweet potato starches as tablet binder

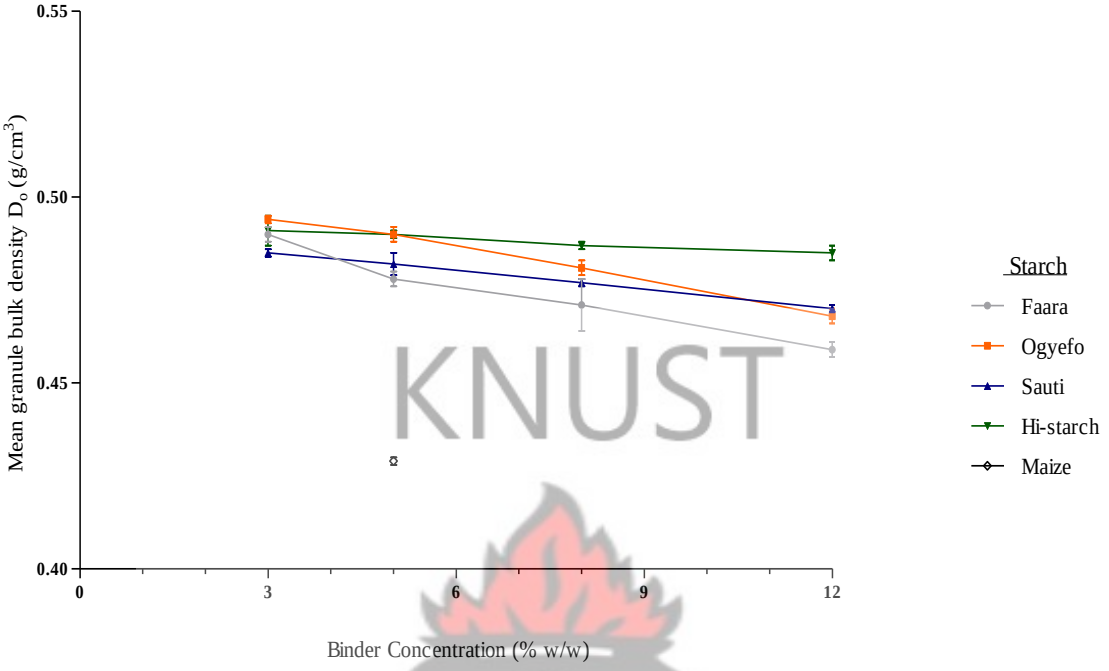


Figure 3.3.4: Bulk density of paracetamol granules at different starch binder concentrations

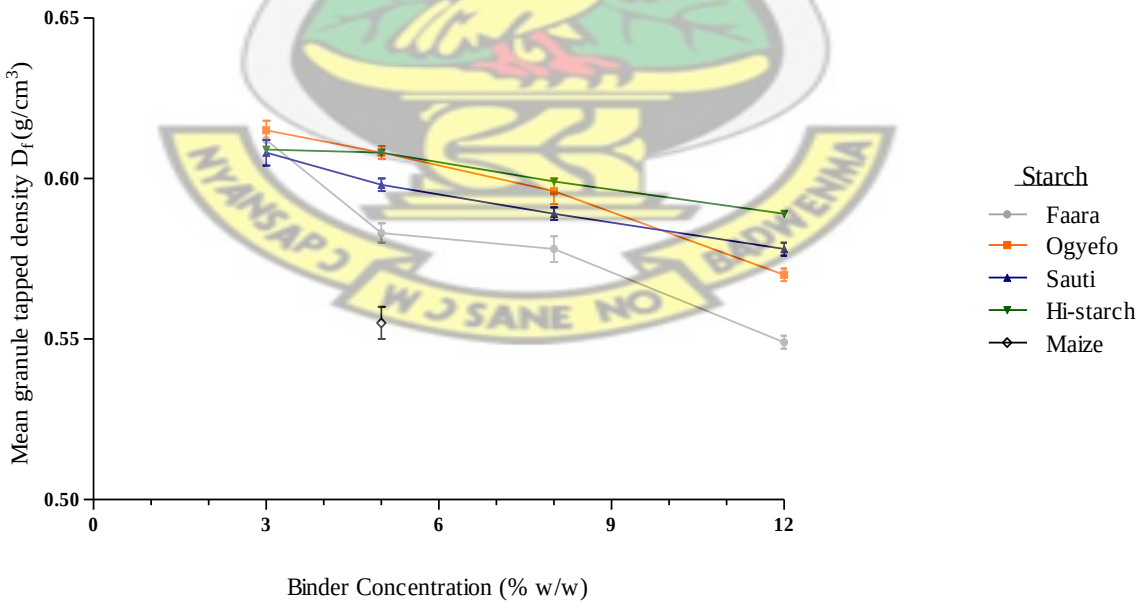


Figure 3.3.5 : Tapped density of paracetamol granules at different starch binder concentrations

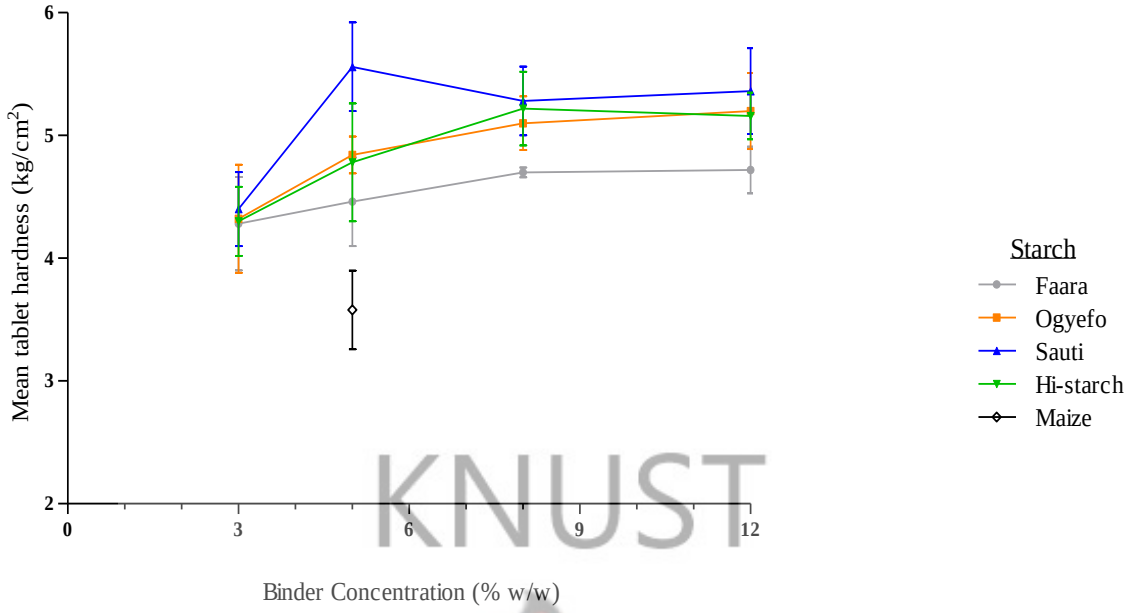


Figure 3.3.6: Comparing hardness of paracetamol tablets at different starch binder concentrations

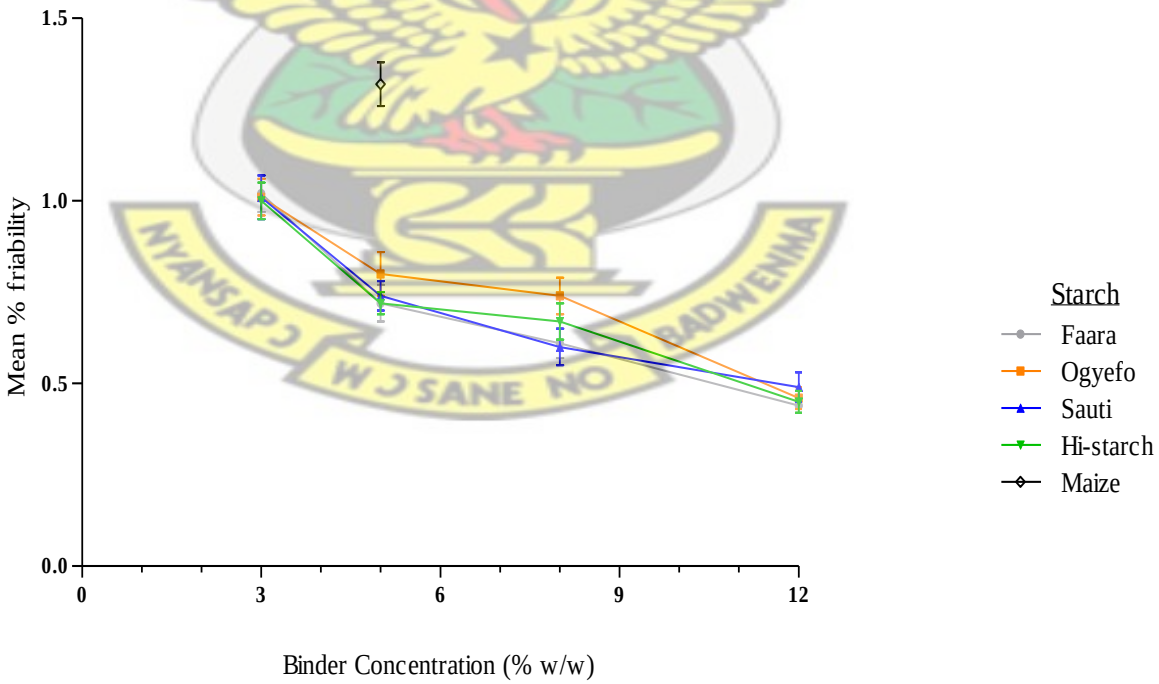


Figure 3.3.7: Comparing friability of paracetamol tablets at different starch binder concentrations

Table 3.3.15: Compaction properties of formulations with the sweet potato starches as binder

Starch	Binder concentration (% w/w)	Bulk density of paracetamol granules (g/cm^3)	Tapped density of paracetamol granules (g/cm^3)	Tablet Hardness (kg/cm^2)	Tablet Friability (%)
Hi-starch	3.0	0.491 ± 0.004	0.609 ± 0.001	4.30 ± 0.28	1.00 ± 0.05
	5.0	0.490 ± 0.001	0.608 ± 0.001	4.78 ± 0.48	0.72 ± 0.03
	8.0	0.487 ± 0.001	0.599 ± 0.001	5.22 ± 0.30	0.67 ± 0.05
	12.0	0.485 ± 0.002	0.578 ± 0.002	5.16 ± 0.19	0.45 ± 0.03
Faara	3.0	0.490 ± 0.002	0.612 ± 0.001	4.28 ± 0.38	1.02 ± 0.05
	5.0	0.478 ± 0.002	0.583 ± 0.003	4.46 ± 0.36	0.72 ± 0.05
	8.0	0.471 ± 0.007	0.578 ± 0.004	4.70 ± 0.04	0.61 ± 0.04
	12.0	0.459 ± 0.002	0.549 ± 0.002	4.72 ± 0.19	0.44 ± 0.04
Ogyefo	3.0	0.494 ± 0.001	0.615 ± 0.003	4.32 ± 0.44	1.01 ± 0.05
	5.0	0.490 ± 0.002	0.608 ± 0.002	4.84 ± 0.15	0.80 ± 0.06
	8.0	0.481 ± 0.002	0.596 ± 0.004	5.10 ± 0.22	0.74 ± 0.05
	12.0	0.468 ± 0.002	0.570 ± 0.002	5.20 ± 0.31	0.46 ± 0.03
Sauti	3.0	0.485 ± 0.001	0.608 ± 0.004	4.40 ± 0.30	1.01 ± 0.06
	5.0	0.482 ± 0.003	0.598 ± 0.002	5.56 ± 0.36	0.74 ± 0.04
	8.0	0.477 ± 0.001	0.589 ± 0.002	5.28 ± 0.28	0.60 ± 0.05
	12.0	0.470 ± 0.001	0.578 ± 0.002	5.36 ± 0.35	0.49 ± 0.04
Maize starch	5.0	0.429 ± 0.001	0.555 ± 0.005	3.58 ± 0.32	1.32 ± 0.06

3.3.11.3 Evaluation of the sweet potato starches as tablet disintegrant

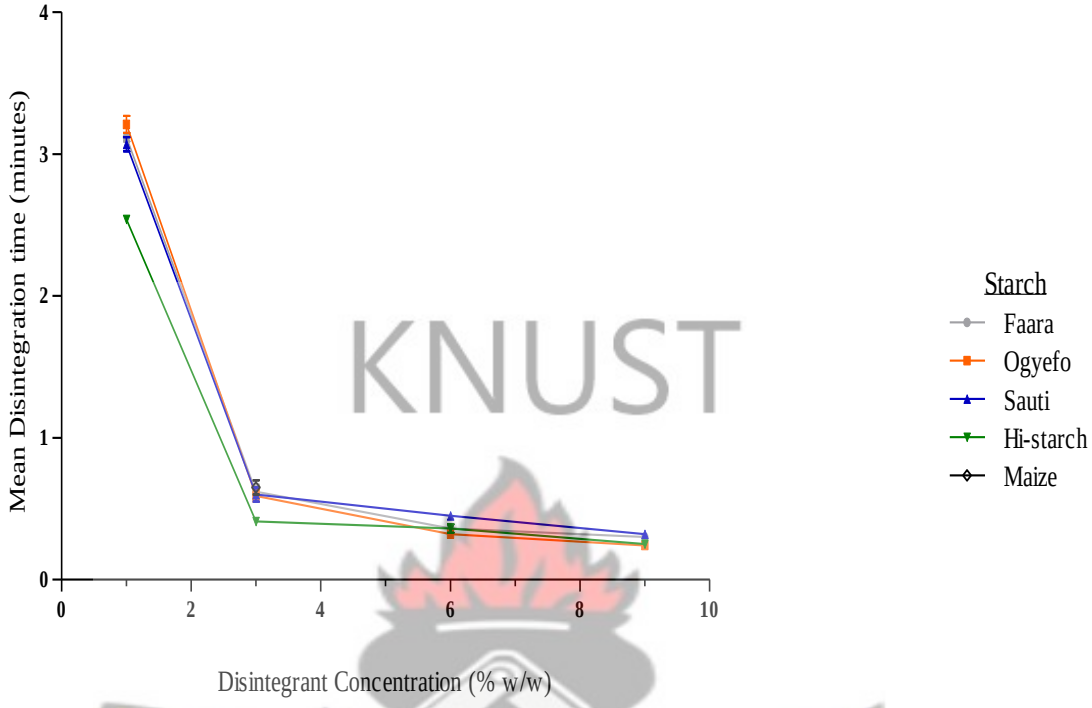


Figure 3.3.8: Comparing disintegrant strength of the starches at different extra-granular concentrations

Table 3.3.16: Disintegration time profile of formulations with the sweet potato starches as disintegrant

Starch	Mean Disintegration time (minutes) for paracetamol tablets at different extragranular starch concentrations			
	1 % w/w	3 % w/w	6 % w/w	9 % w/w
Faara	3.12 ± 0.03	0.62 ± 0.05	0.36 ± 0.03	0.30 ± 0.02
Ogyefo	3.21 ± 0.06	0.59 ± 0.04	0.32 ± 0.02	0.24 ± 0.01
Sauti	3.07 ± 0.05	0.60 ± 0.05	0.45 ± 0.02	0.32 ± 0.02
Hi-starch	2.54 ± 0.01	0.41 ± 0.02	0.36 ± 0.03	0.25 ± 0.02
Maize starch	-	0.65 ± 0.05	-	-

Disintegration time not more than 15 minutes (BP, 2007)

3.3.11.4 Quality control evaluations of the paracetamol tablets

Table 3.3.17: Uniformity of weight and thickness for the paracetamol tablets

Tablet batches for binder quality evaluations	Mean weight of 20 tablets (g)	Mean weight of 1 tablet (g)	Mean weight deviation (%)	Mean tablet thickness (mm)
Hi-starch	11.66 ± 0.16	0.583 ± 0.008	1.39 ± 0.28	6.35 ± 0.03
Sauti	11.58 ± 0.10	0.579 ± 0.005	1.87 ± 0.20	6.32 ± 0.01
Ogyefo	11.42 ± 0.22	0.571 ± 0.011	1.91 ± 0.33	6.28 ± 0.04
Faara	11.44 ± 0.06	0.572 ± 0.003	1.52 ± 0.16	6.27 ± 0.03
Maize starch	11.53 ± 0.12	0.577 ± 0.006	1.04 ± 0.27	6.30 ± 0.02
Tablet batches for disintegrant quality evaluations	**Mean weight of 20 tablets (g)**	**Mean weight of 1 tablet (g)**	**Mean percentage weight deviation (%)**	**Mean tablet thickness (mm)**
Hi-starch	11.37 ± 0.14	0.569 ± 0.007	1.22 ± 0.31	6.28 ± 0.02
Sauti	11.41 ± 0.08	0.571 ± 0.004	1.70 ± 0.25	6.31 ± 0.04
Ogyefo	11.69 ± 0.18	0.585 ± 0.009	1.57 ± 0.19	6.35 ± 0.05
Faara	11.55 ± 0.08	0.578 ± 0.004	2.16 ± 0.36	6.29 ± 0.03
Maize starch	11.39 ± 0.20	0.570 ± 0.010	1.89 ± 0.22	6.25 ± 0.03

3.3.11.5 Influence of the starches as disintegrantand binder on in-vitro drug release

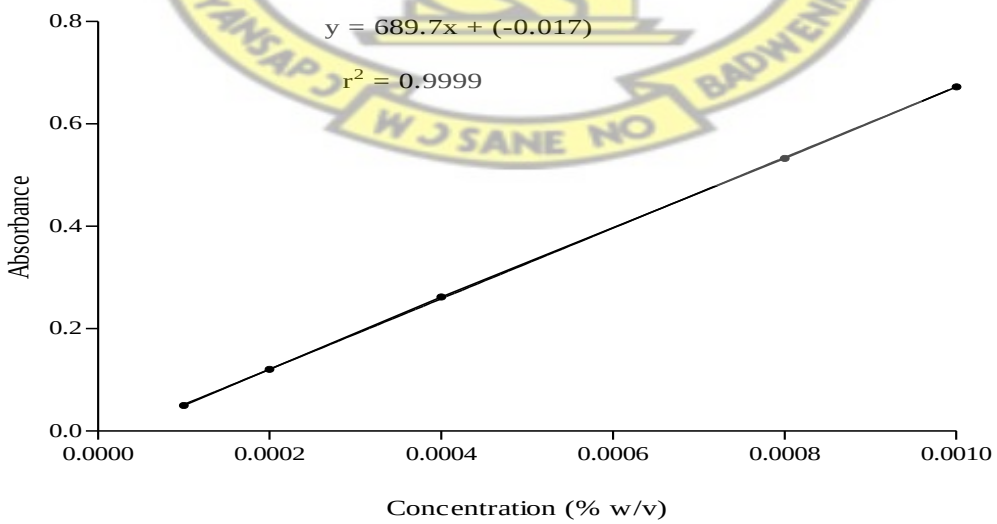


Figure 3.3.9: Calibration of the UV Spectrophotometer with Paracetamol BP

Table 3.3 18: UV absorbance of Paracetamol BP at a wavelength of 257 nm

Paracetamol Concentration (% w/v)	Mean absorbance
0.0001	0.050 ± 0.003
0.0002	0.121 ± 0.002
0.0004	0.262 ± 0.002
0.0008	0.533 ± 0.001
0.0010	0.673 ± 0.002

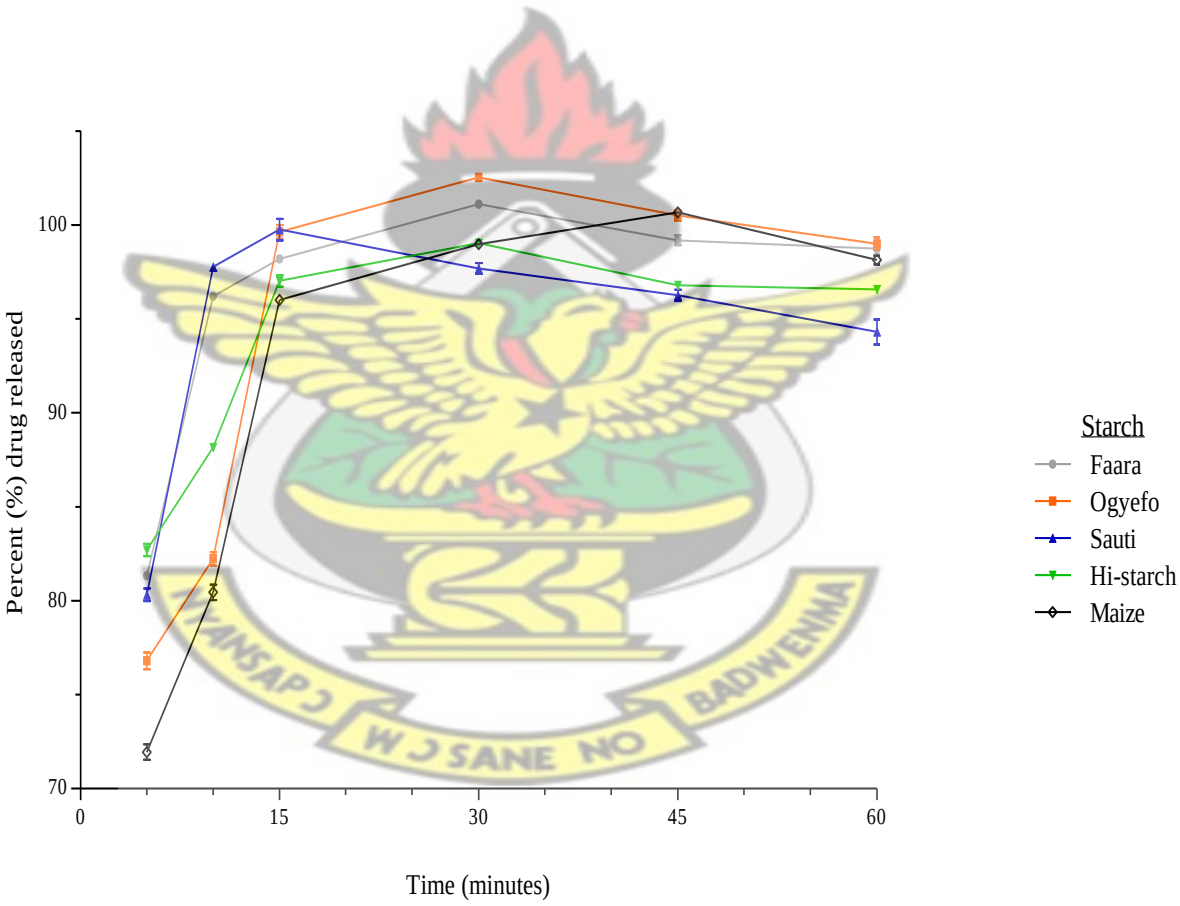


Figure 3.3.10: Comparing the starches influence as extra-granular disintegrant on in-vitro drug release

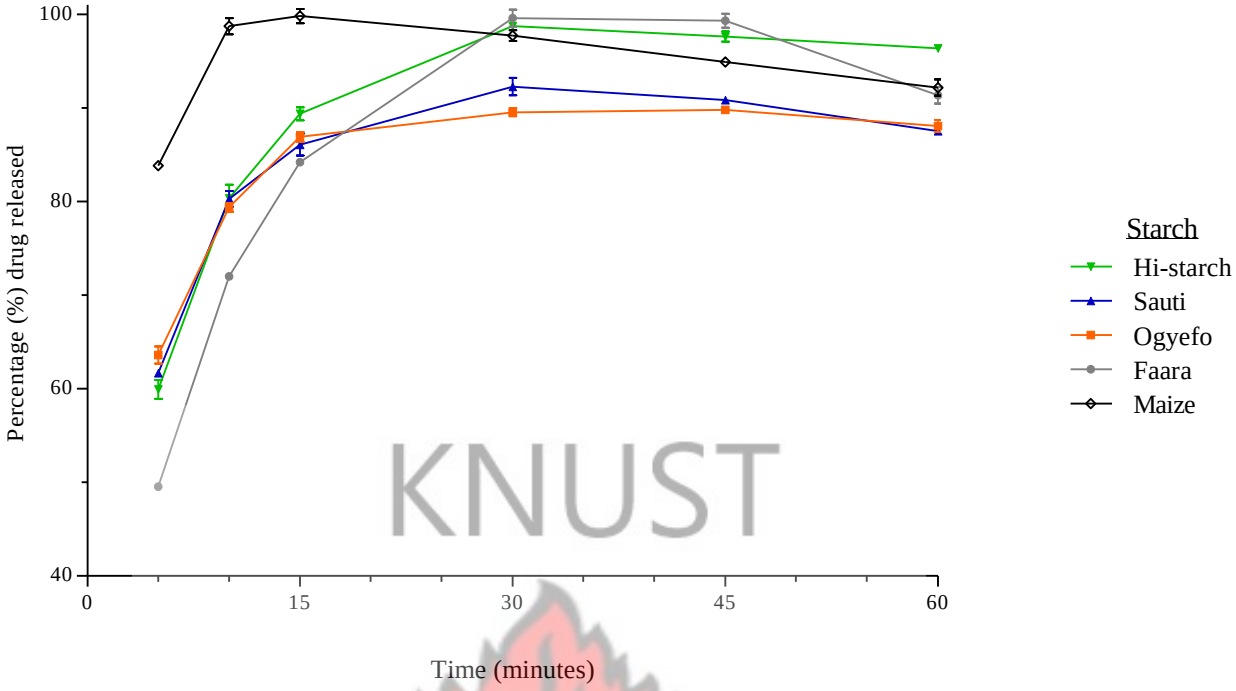


Figure 3.3.11: Comparing the starches influence as paste binder on in-vitro drug release

Table 3.3.19: The sweet potato starches influence on rate of in-vitro drug release from the paracetamol tablet formulations

Starch as 5 % w/w Binder	**Percentage (%) drug released at specified time intervals**					
	5 minutes	**10 minutes**	**15 minutes**	**30 minutes**	**45 minutes**	**60 minutes**
Hi-starch	61.2 ± 2.43	80.4 ± 3.57	89.4 ± 1.71	98.7 ± 0.30	97.6 ± 1.32	96.4 ± 0.65
Sauti	61.7 ± 0.43	80.3 ± 2.09	86.1 ± 2.89	92.3 ± 2.29	90.8 ± 0.37	87.5 ± 0.59
Ogyefo	63.6 ± 2.24	79.4 ± 1.14	86.9 ± 1.29	89.5 ± 1.03	89.8 ± 0.83	88.1 ± 1.57
Faara	49.5 ± 0.23	72.0 ± 0.75	84.2 ± 0.57	99.6 ± 2.25	99.3 ± 1.85	91.4 ± 2.15
Maize starch	83.9 ± 0.72	98.7 ± 2.10	99.8 ± 1.85	97.7 ± 1.41	94.9 ± 0.75	92.2 ± 2.10
Starch as 3 % w/w Disintegrant	**5 minutes**	**10 minutes**	**15 minutes**	**30 minutes**	**45 minutes**	**60 minutes**
Hi-starch	82.7 ± 0.87	88.2 ± 0.39	97.0 ± 0.73	99.0 ± 0.37	96.8 ± 0.30	96.6 ± 0.41
Sauti	80.3 ± 0.84	97.8 ± 0.52	99.8 ± 1.39	97.7 ± 0.73	96.3 ± 0.72	94.3 ± 1.64
Ogyefo	76.8 ± 1.11	82.2 ± 0.87	99.6 ± 0.91	102.5 ± 0.37	100.5 ± 0.69	99.0 ± 0.84
Faara	81.3 ± 0.48	96.2 ± 0.33	98.2 ± 0.42	101.1 ± 0.25	99.2 ± 0.64	98.7 ± 0.77
Maize starch	72.0 ± 0.99	80.5 ± 1.01	96.0 ± 0.35	99.0 ± 0.43	100.7 ± 0.50	98.1 ± 0.56

3.4 DISCUSSION

3.4.1 Organoleptic properties of the fresh sweet potato root tubers

The skin and flesh colourof the four used sweet potato varieties were different, but on the contrary, the taste and texture were similar (Table 3.3.1). White, cream and yellow flesh sweet potato varieties are known to be most suitable for the starch industry as their pigments have negligible impact on starch colour (Brabet *et al*., 1998). There was a relatively high content of simple sugars and carbohydrates in the sweet potato root tubers whichmay possibly account for their mild sweet taste; though this could negatively affect starch content and yield (USDA, 2010). Additionally, sweet potato root tubers with high dry matter content tend to have firm texture as tuber water content is relatively lower (Woolfe, 1992). Firm textured tubers (as observed for these sweet potato varieties) are preferred by the starch industry as they tend to have high starch yield.

The amount of latex produced was high in the Hi-starch and Faara varieties (Table 3.3.1). High latex contamination can enhance water binding capacity and adhesive or binder property of the starch. It may however reduce flow properties as it causes adhesion to substrates. The differences in skin and flesh colour as well as quantities of latex produced possibly reflected variability in genetic traits.

3.4.2 Tuber dry matter and starch yield

All the four sweet potato varieties had high dry matter content ranging between 36.4 - 40.0 % (Table 3.3.2). There are reports of a positive correlation between tuber dry matter content and starch yield (Tsakama *et al*., 2010). However, the correlation observed in this study was not significant. Starch yield is known to be affected by not only the crop variety, but also the degree of association of granules with fibre and the method of extraction (Rahman *et al*., 2003). The sweet potato starch industry usually requires root tubers with dry matter content higher than 30 % for economic viability (Mok *et al*., 1997). In addition, starch yield greater than 70 % on dwb is deemed to be good enough for the industry (Tsakama *et al*., 2010). The investigations confirmed Hi-starch variety as a truly high starch yielding genotype (31.7 % fwb; 79.9 % dwb) compared to the other three varieties (Figure 3.3.1, Table 3.3.3).

3.4.3 Moisture content of the starches

Residual moisture content of starches from the four sweet potato varieties were less than 15 %, the upper limit recommended by the British Pharmacopoeia, 2007 (Table 3.3.3). Starch moisture content is known to be largely influenced by its hygroscopicity, crystallinity, drying temperature and duration, particle size, humidity and the velocity of moist air (Nokhodchi, 2005). High starch moisture content (> 15 %) could have adverse effects on its quality. It promotes the growth of moulds and results in reduced shelf life. It may also affect starch quantity and market value as a result of high losses on drying. Optimal levels ofmoisture in starch (5 - 10 %) have been shown to be essential in producing compacts with high tensile strength and low friability (Aulton, 2001).

3.4.4 Identification and Organoleptic tests for the starches

Starches of the sweet potato and commercial maize had characteristic taste, texture, odour and colour (Tables 3.3.4 and 3.3.5). Starch amylose is reported to form a characteristic dark blue colour complex with iodine (Konstantinos, 2008). This colour complex observed in the investigations confirmed the identity of materials obtained from the wet separation process as starch.

3.4.5 Microscopy

The microscopy revealed various shapes and sizes for the starch granules. The sweet potato starch granules as well as that of the commercial maize starch were either round, irregularly round or polygonal in shape (Table 3.3.6). The mean diameter of the sweet potato starch granules (13.6 - 16.3 µm), although not significantly different among the varieties, was significantly larger ($p < 0.0001$) than that of the commercial maize starch (9.1µm) [Table 3.3.6]. These results seem consistent with reports of some sweet potato starches having larger sized granules than maize starch (Swinkels, 1985; Chen *et al*., 2003). Starch granule size and size distribution contribute to the temperature and rate of gelatinization. There are reports of less molecular bonding with faster swelling in larger starch granules (Tsakama *et al*., 2010). Such starch granules would therefore be of interest to the pharmaceutical manufacturing industry as their high swelling capacity will make them stronger tablet disintegrants (Carter, 2002).

3.4.6 Physicochemical and powder properties of the starches

The physical and chemical properties showed differences in bulk and flow properties as well as acidity and hygroscopicityof the sweet potato and commercial maize starches.

The bulk properties describe the density, consolidation and flow of a powder mass (Staniforth, 1996). The sweet potato starch powders had higher true density (1.15 - 1.18), bulk density (0.50 - 0.58) and tapped density (0.75 - 0.82) compared to values of 1.10, 0.40 and 0.61, respectively recorded for the commercial maize starch (Table 3.3.7). Differences in bulk properties of starch from the four sweet potato varieties were however not significant. High density materials have high diluent power as they substantially reduce volume of thepowder mass while improving consolidation and flow (Aulton, 2001). The sweet potato starches are therefore expected to be relatively stronger as diluent in the manufacture of solid oral dosage forms compared to the commercial maize starch.

All starches evaluated had similar mean particle size (83.0 - 93.6µm) [Table 3.3.8] and size distribution (< 75- 250 µm) [Fig. 3.3.2]. Generally, fine powders (particle size < 75 µm) are known to have poor flow which negatively affect uniformity of the dosage unit thus limiting their application in direct compressions.

In addition, thesweet potato starches like the commercial maize starch had high angle of repose (36.1 - 40.4), hausner's ratio (1.41 - 1.58) and compressibility index (29.3 - 36.7) [Table 3.3.9]. The high indices of powder flowability observed, confirmed reports of native starches generally having poor flow properties (Shangraw, 1989; Kolling, 2005). They would therefore be ideal for wet granulations, where improved granule flow (as a result of the increased powder density) allows smooth tablet compression (Gilbert and Christopher, 2002).

The pH of the sweet potato starches (5.1 - 5.9) was acidic and similar to a pH value of 5.2 recorded for the commercial maize starch (Table 3.3.10). The starches should therefore be used with caution in formulations of low dose alkaline drugs to prevent drug - excipient interaction. On the other hand, effectiveness of other excipients such as the parabens, which act as antimicrobial preservatives may however be enhanced as they are more active in acidic conditions (Woods, 2001). The British Pharmacopoeia recommends a pH range of 4.0 - 7.0 for starch (BP, 2007).

The moisture sorption capacity estimates a material's hygroscopicity as well as its moisture sensitivity. The moisture sorption capacity of the sweet potato starches (6.5 - 7.5 %) was not significantly different among the varieties and from that of the commercial maize starch (5.75 %) [Table 3.3.10]. High moisture sorption (> 5 %) by a dry powdered material may improve the flow, compression characteristics, and hardness of granules and

tablets. It may however cause materials with adhesive properties to stick to punch surfaces. Furthermore, the stability of moisture sensitive APIs would be adversely affected leading to reduced product shelf life (Nokhodchi, 2005). Moisture sorption by starch has been attributed to interactions between free hydroxyl groups of amylose and amylopectin hexose moieties and that of water molecules (Sair and Fetzer, 1944). In addition to the interactions, amylopectin structure has been shown to physically trap water, hence giving starches with a high amylopectin ratio higher moisture sorption potential (Rebar *et al*., 1984).

3.4.7 Amylose content of the starches

The amylose content gives an estimate of starch's other molecular component, amylopectin. Sauti and Faara starches had similar amylose content (25.4 and 25.3 %, respectively) which was significantly different from that of Hi-starch (22.3 %) and Ogyefo starch (26.2 %). The sweet potato starches however recorded significantly lower amylose content than the commercial maize starch (27.6 %) [Table 3.3.11]. Starch amylose has been reported to form a complex with lipids which in turn inhibit granule swelling and disintegrant potential (Wiesenborn *et al*., 1996). On the other hand, starch amylopectin is reported to enhance granule swelling as a result of repulsion between phosphate groups on adjacent amylopectin chains (Galliard and Bowler, 1987; BeMiller and Whistler, 1996). Sweet potato starches with amylose content ranging between 18.6 - 27.1 % have been reported (Brabet *et al*., 1998). The sweet potato starches having higher amylopectin ratio are therefore expected to exert stronger disintegrant action compared to the commercial maize starch.

3.4.8 Proximate composition and purity of the starches

The proximate composition is a major determinant of starch purity. It determines the presence of all other contaminants or impurities other than pure starch.

The ash content of the sweet potato starches investigated and the commercial maize starch were lower than 0.6 % w/w, the upper limit recommended by the British Pharmacopoeia (Table 3.3.12). The ash content indicates amount of insoluble salts and complexes in starch. Presence of inorganic salts and ions of phosphorous, sodium, iodine and hydroxyl groups in starch have been reported to contribute significantly to starch granule swelling and gelatinization (Mistry and Eckhoff, 1992).

The sweet potato starches had significantly lower ($p < 0.0004$) lipid content (0.32 - 0.54 %) than the commercial maize starch (1.22 %), although differences among the varieties was not significant (Table 3.3.12). Low starch lipid content (< 1%) is recommended as higher quantities form complexes with amylose to inhibit starch swelling and solubility; hence reduce disintegrant effects (Moorthy, 2002). A high starch lipid content may also have adverse effects on its binder quality as itincreases the hydrophobicity of the polymers (amylose and amylopectin) [Carter, 2001].

The protein content of the sweet potato starches (0.94 - 1.36 %) was not significantly different from that of the commercial maize starch (1.01 %) and among the varieties (Table 3.3.12). High protein content can affect starch gelatinization in diverse ways depending on the degree of polymerization, ability to retain water and their interaction capacity with starch molecules and granule surface (Liang and King, 2003; Ribotta and Rosell, 2010). Low starch protein content (< 0.2 %) is thus recommended (Mistry and Eckhoff, 1992; Chen *et al*., 2003) as higher quantities observed in these starches can influence their functional properties and result in false characterization (Vasanthan, 2001).

The carbohydrate content as an indirect measure of purity of the sweet potato starches was high (84.83 - 87.73 %) and comparable to that of the commercial maize starch (84.52 %) [Table 3.3.12]. This ultimately resulted in the high purity observed for the sweet potato starches (97.37 - 97.84 % w/w). A good starch material for pharmaceutical application should contain more than 96 % w/w starch and as much as possible, be devoid of other plant components such as fibre, protein and lipids (Vasanthan, 2001).

3.4.9 Pasting profile and properties of the starches

The pasting properties illustrate the molecular changes and stages starch granules undergo when heated in excess water. They estimate starch water binding capacity and the strength of bonds in the starch granule. They can therefore be used to predict both binder and disintegrant quality. Starch pasting properties are known to be influenced by the amylose, lipid, protein and mineral content, as well as the granule size and size distribution (Peroni *et al.*, 2006).

All the sweet potato starches exhibited “type A” pasting profiles that were characterized by a high peak viscosity and a low final viscosity (Figure 3.3.3). These characteristics are Indicative of high starch granule swelling (hence high disintegrant capacity) and

maximum starch granule fragmentation with low set back (hence high adhesive capacity).

The commercial maize starch on the other hand exhibited a"type B" pasting profile characterized by a medium peak viscosity and a high final viscosity. These characteristics were indicative of reduced starch granule swelling (hencelow disintegrant capacity) and limited starch granule fragmentation with high set back (hence low adhesive capacity) [Schoch and Maywald, 1968]. Sodium starch glycolate (a modified maize starch and a pharmaceutical 'super disintegrant') however exhibited a hybrid profile. It was characterized by a high peak viscosity of "type A" curves and a high final viscosity of "type B" curves. These characteristics are respectively indicative of enhanced disintegrant capacity and diminished adhesive capacity (Fig. 3.3.3).

The sweet potato starches had similar pasting temperatures (P_{temp}) as that of the commercial maize starches (Table 3.3.13). They however attained maximum viscosity within a significantly ($p < 0.0001$) shorter time (1.13 - 3.25 minutes) than maize starch (9.38 minutes) and starch glycolate (6.13 minutes). There are reports of a positive correlation between P_{temp} and time to reach maximum viscosity (P_{time}). Lower pasting temperatures generally correspond with faster starch granule swelling, hence a shorter time to reach maximum viscosity (Liang and King, 2003). However, P_{temp} is only an estimate of the gelatinization temperature which actually breaks starch bonds (Ward and Mudford, 2008); hence a correlation may not always be established. The shorter P_{time} of the sweet potato starches compared to the commercial maize starches however indicated weaker associative forces and cross-links within granules of the former (Akinwande *et al*., 2007; Tsakama *et al*., 2010). Strong intermolecular associations between starch polymers (as observed in the commercial maize starch) reduce bonding sites on their hexose monomers for hydroxyl groups of water to interact with (Beery and Ladisch, 2001). Thus, the sweet potato starch granules would most likely have higher affinity for water andpotentially act as stronger tablet disintegrant than the commercial maize starches.

The significantly shorter P_{time} ($p < 0.0001$) of sodium starch glycolate compared to maize starch gave credence to earlier findings ascribing weak intermolecular bonds as an underlining factor affecting starch hydration. Bonds stabilizingthe integrity of maize starch granules are believed to be weakened, when hydrophilic Na^+ and CH_3COO^-groups are incorporated into their hexose monomers during commercial production of starch glycolate (Mistry and Eckhoff, 1992). Thus, the fraction of starch glycolate granules with

the substituted groups after attaining high peak viscosity (PV) in a relatively shorter time (approximately 20 minutes) and temperature (approximately 80 ^{o}C) experienced a sharp and substantial break down in viscosity. On the other hand, a second relatively lower peak viscosity observed on the sodium starch glycolate amylogram in an approximate time and temperature of 30 minutes and 95 ^{o}C respectively, could be attributed to the un-substituted and smaller granule fractions. Such granule fractions with stronger hydrogen bonds experienced a gradual rise in viscosity with limited break down even at such a higher temperature (Fig. 3.3.3 and Appendix C).

Peak viscosity (PV) of the sweet potato starches (694 - 762 BU) and starch glycolate (762 BU) were significantly higher ($p < 0.0001$) than that of maize starch (451 BU). Differences in PV among starches from the four sweet potato varieties were not significant (Table 3.3.13). However, there was a significant positive correlation between PV and mean granule diameter of the starches ($r = 0.93$, $p < 0.007$). The peak viscosity is indicative of the swelling and disintegrant capacity of starch, as at this point, the number of swollen intact starch granules is maximum (Ribotta and Rosell, 2010). Similarity in PV values of the sweet potato starches and sodium starch glycolate (a 'super disintegrant') therefore portends the disintegrant value of the former.

The breakdown in viscosity (BD) of the sweet potato starches (213 - 421 BU) and starch glycolate (324 BU) were significantly higher ($p < 0.0001$) than maize starch (157 BU) [Table 3.3.13]. Hi-starch and Sauti starches however had similar BD values (348 and 326 BU, respectively) which were significantly different ($p < 0.05$) from that of Ogyefo (213 BU) and Faara (421 BU). The BD represents resistance to fragmentation of swollen starch granules as shear stress is applied (Wiesenborn *et al*., 1994) such that materials with high resistance show low BD. A high BD (low resistance) will increase paste adhesiveness as a result of maximum starch granule fragmentation and release of amylose and amylopectin. These polymers acting as binding agents in solid oral dosage forms are expected to confer stronger binding properties to the sweet potato starches compared to the commercial maize starch.

The setback (SB) viscosity of the sweet potato starches (102 - 164 BU) which showed little variation among the varieties was significantly lower ($p < 0.0001$) than that of maize starch (407 BU) and starch glycolate (251 BU) [Table 3.3.13]. This culminated in lower final viscosity (FV) for the sweet potato starches (435 - 638 BU) and higher FV for maize starch (667 BU) and starch glycolate (679 BU). The SB is indicative of retrogradation or

re-association of starch polymers as the paste cools (Bemiller and Whistler, 1996; Singh *et al*., 2003). High amylose starches (as in the maize) have been found to re-associate more readily than high amylopectin starches (as in the sweet potato varieties). Re-association of amylose chains reduces available hydroxyl bonding sites on the polymer thus reducing its contribution to paste adhesiveness.

Final viscosity (FV) on the other hand, predicts ease of binder spreadability in a powder mixture such that highly viscous pastes are less uniformly distributed compared to pastes and mucilages of low viscosity (Mukesh, 2009). The sweet potato starches formed pastes of relatively lower FV and would thus be uniformly distributed (Table 3.3.13). For highly viscous paste binders (as in the maize starch), higher shearing stresses are required (by mixers) for uniform distribution in powder mixtures. Granules produced by such viscous pastes are usually brittle and the resultant tablets compressed are easily friable (Marquardt *et al*., 1997). The sweet potato starches are therefore expected to be stronger binding agents in solid oral dosage forms compared to the commercial maize starch.

3.4.10 Pharmaceutical evaluations

3.4.10.1 ParacetamolPurity

Purity of the model drug used to assess binder and disintegrant quality of the starches was high (100.4%) [Table 3.3.14]. This confirmed the powdered material whose specific absorptivity was approximately 715, to be paracetamol. Purity of a drug is essential in assuring optimum release and bioavailability. The British Pharmacopoeia recommends a purity range of 99.0 - 101.0 % for paracetamol powder (BP, 2007).

3.4.10.2 Evaluation of the sweetpotato starches as tablet binder

The bulk density (0.482 - 0.490 g/cm^3) and tapped density (0.583 - 0.608g/cm^3) of paracetamol granules prepared using the sweet potato starches as binder, were significantly higher ($p < 0.05$), compared to the commercial maize starch (0.429 and 0.555g/cm^3, respectively) [Table 3.3.15]. The bulk and tapped densities of paracetamol granules prepared using the sweet potato starches as binder did not however show any notable differences (Figures 3.3.4 and 3.3.5). Higher granule bulk density results when a strongly adhesive binder agglomerates more particles of the drug. This reduces volume of the powder mass as particle size and weight increases. Narrow differences between granule bulk density and tapped density (as observed for the sweet potato starch granulations) signify enhanced consolidation and flow. This ensures the compressionof

tablets with uniform weight and minimum density variations (Aulton, 2001; Nokhodchi, 2005).

Paracetamol tablets with the sweet potato starches as binder were significantly ($p < 0.05$) harder (4.46 - 5.56 kg/cm^2) and less friable (0.72 - 0.80 %) compared to similar compacts containingthe commercial maize starch (3.58 kg/cm^2 and 1.32 %, respectively) [Table 3.3.15]. The differences in tablet hardness and friability among compacts prepared using the sweet potato starches as binder were however not significant (Figures3.3.6 and 3.3.7). The tensile strength and mechanical integrity of tablets are known to improve significantly when low density regions or voids are eliminated (Mukesh, 2009). Void elimination has been demonstrated to reduce incidences of tablet capping and lamination; and may be achieved if the material has either high binding capacity (as was in the case of the sweet potato starches) or if the compression load or quantity of binder is increased (Okor, 2005). Conventional compressed tablets of acceptable hardness (4 - 6 kg/cm^2) and friability (≤ 1%) are essential for handling during packaging, transportation and administration (Alfonso, 1990; Gilbert and Christopher, 2002).

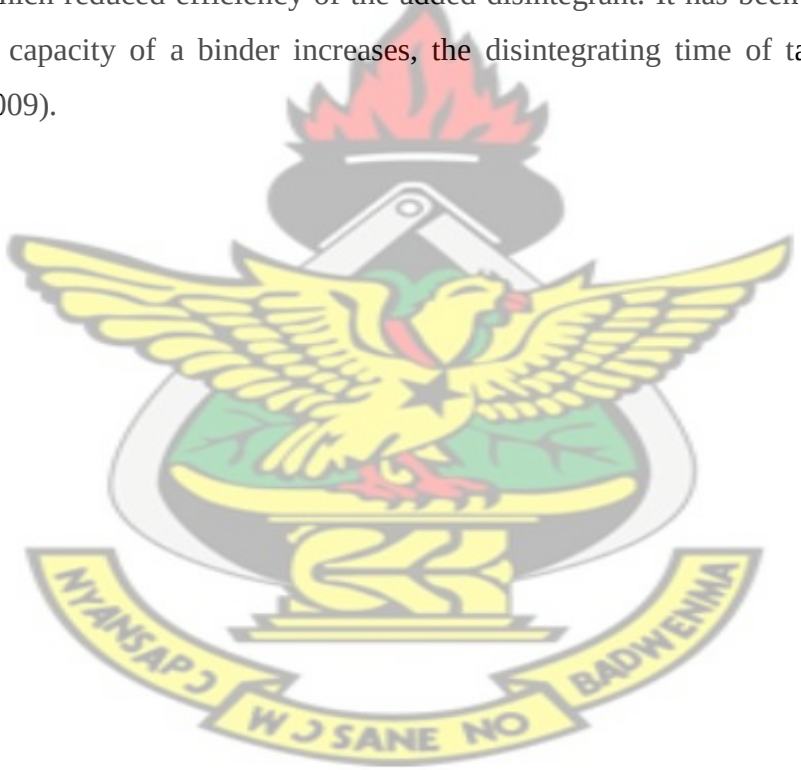
3.4.10.3 Evaluation of the sweet potato starches as tablet disintegrant

The disintegration time of paracetamol tablets containing the sweet potato starches as disintegrant was marginally faster than compacts containing the commercial maize starch (Table 3.3.16). The disintegration time of paracetamol tablets containing the sweet potato starches as disintegrant did not also show any significant differences (Fig. 3.3.8). Starch granules as extra-granular disintegrant undergo deformation during high pressure tablet compression; and these swell maximally in aqueous fluids to cause tablet disintegration (Carter, 2002). The sweet potato starch granules with weaker intermolecular bonds (as illustrated by their shorter $P_{time,}$ Table 3.3.13), are therefore likely to deform more readily compared to the commercial maize starch. Furthermore, a sugar alcohol such as mannitol, used as diluent is likely to dissolve (rather than aid tablet disintegration) and cause an increase in viscosity of the penetrating fluid. This tends to reduce effectiveness of strongly swelling disintegrating agents like the sweet potato starches (Mukesh, 2009). The British Pharmacopoeia recommends a disintegration time of 15 minutes or less for immediate release tablets (BP, 2007).

3.4.10.4 Influence of the starches asdisintegrantand binder on in-vitro drug release

Paracetamol tablets containing the sweet potato starches as extra-granular disintegrant released the drug faster (especially during the first 15 minutes) than similar compacts

containing maize starch (Fig. 3.3.10). On the other hand, paracetamol tablets containing the sweet potato starches as paste binder, slowly released the drug (during the first 15 minutes) compared to compacts containing maize starch (Fig. 3.3.11). The differences in drug release pattern from compacts containing starch from the sweet potato varieties (either as binder or disintegrant) was however not significant. The pattern of in-vitro dissolution and drug release closely followed that of tablet disintegration. Tablets which disintegrated quickly released paracetamol faster than tablets which took a longer time to disintegrate. The sweet potato starch granules having high swelling capacity (as shown by their high PV, Table 3.3.13) therefore caused relatively faster tablet disintegration and release of the drug. Furthermore, the sweet potato starches having high binding capacity (as demonstrated by their high BD, low SB and FV, Table 3.3.13), formed harder compacts which reduced efficiency of the added disintegrant. It has been reported thatas the binding capacity of a binder increases, the disintegrating time of tablets increases (Mukesh, 2009).



3.5 CONCLUSIONS

All four Ghanaian sweet potato varieties used had high dry matter content (> 30 %), although significant differences existed in the organoleptic properties of their root tubers. Faara and Ogyefo varieties had similar starch yields which were significantly lower than that of Sauti and Hi-starch varieties. The yield from Hi-starch variety was significantly high (> 70 % dwb) to potentially merit commercial exploitation. The residual moisture content of all the sweet potato starches was within limits specified by the official monographs (< 15 % w/w).

Although the granular shapes were similar, all the sweet potato starches had significantly larger granule sizeand size distribution than the commercial maize starch. Thesweet potato starches were also found to be significantly denser and with lower amylose content than commercial maize starch, but like the latter, they had fine particle size, poor flow, acidic pH and high moisture sorption capacity.

The sweet potato starches were of high purity (> 96 % w/w) with lower levels of ash, fat and fibre, although the protein content (like that of the commercial maize starch) was high (> 0.2 % w/w).

Thesweet potato starches also exhibited a 'type A' pasting pattern characterized by high granule swellingand fragmentation, while that of the commercial maize starch was 'type B' with limited granule swellingand fragmentation.

Furthermore, the sweet potato starches with superior bulk properties as in higher true density, bulk and tapped densities presented them as possibly more robust and effective diluents compared to the commercial maize starch.

The sweet potato starches were also superior to the commercial maize starch as tablet binder and could be effectively applied in concentrations of between 3 - 8 % w/w.

The sweet potato starcheswere also effectively applied as disintegrant in concentrations of 1 - 3 % w/w, and in addition, demonstrated stronger disintegrant capacitycompared to the commercial maize starch.

The superior disintegrant capacity of the sweet potato starches compared to the commercial maize starch helped ensure faster in-vitro drug dissolution and release.

All in all, the sweet potato starches exhibited properties suitable for use as pharmaceutical excipients in oral tablet dosage forms. However, by virtue of superior yield, starch from the Hi-starch variety would be commercially viable as a substitute pharmaceutical diluent, binder and disintegrant in local drug manufacture.

Although these sweet potato varieties and their starches are used in the food industry and their nutritional value well investigated, this is the first report of their suitability as excipients for use in the pharmaceutical industry and the possible commercial viability of the Hi-starch variety. It is also the first report of their superiority as binder and disintegrant compared to commercial maize starch in oral tablets.

3.6 RECOMMENDATIONS

Further work on granule modification of starch from the high yielding Hi-starch variety in order to further enhance its swelling and disintegrant capacity; and as a modified release matrix are quite appropriate and sound as these could add on and improve their exploitation as pharmaceutical excipients.

Furthermore, feasibility studies on the commercial viability of local starch production from the Hi-starch variety should be conducted to ascertain its prospects.

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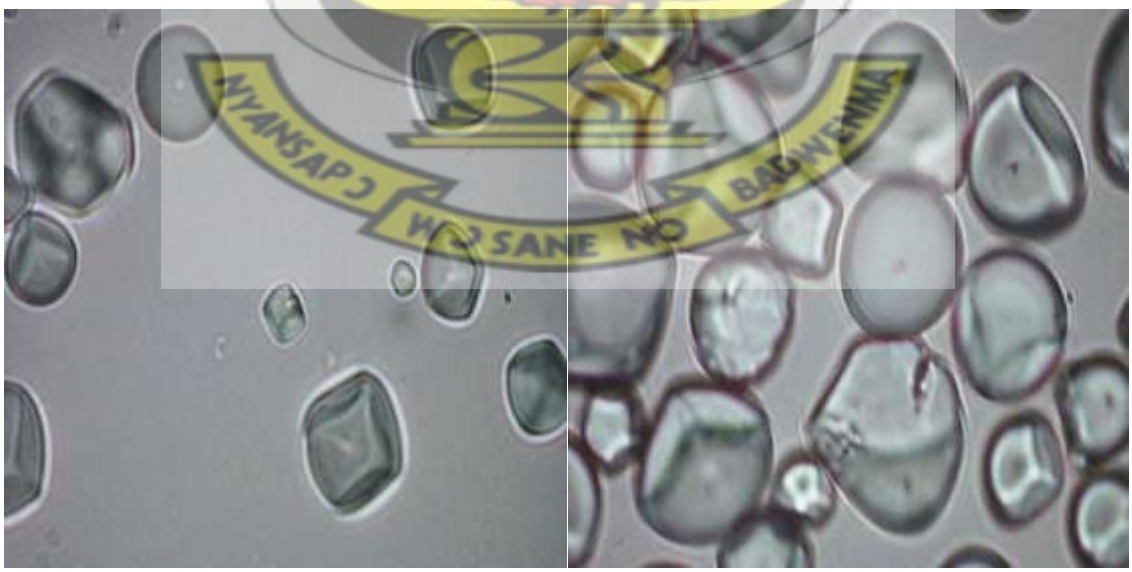
APPENDICES

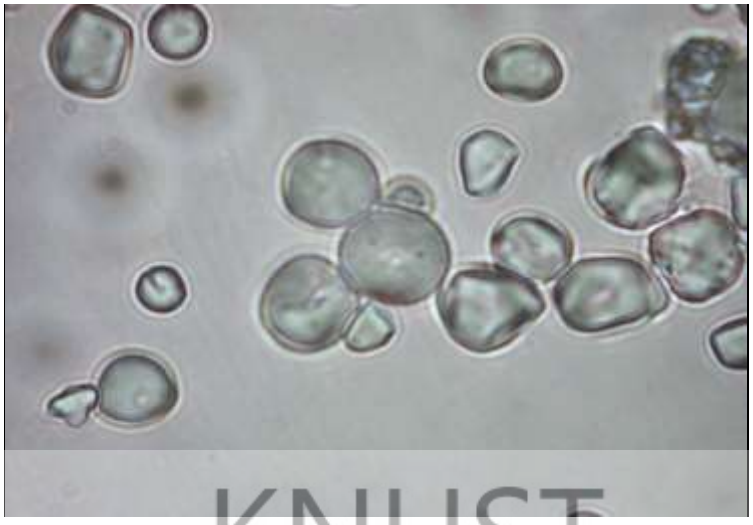
APPENDIX A

Photomicrographs of sweet potato and commercial maize starch granules at low and high power magnifications (x400 and x1000, respectively)

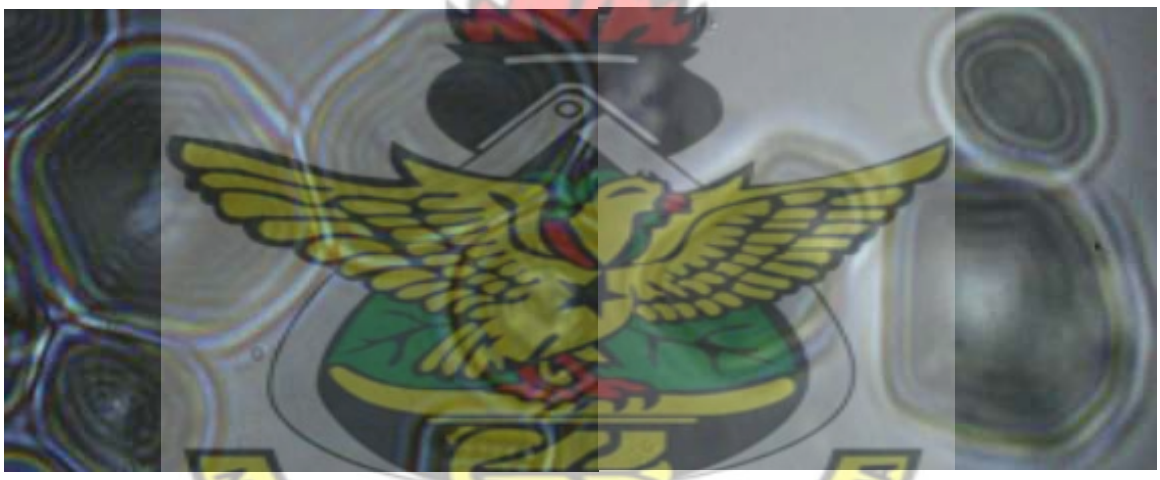
Faara starchgranules (x400) **Hi-starch starch granules (x400)**



Ogyefo starch granules (x400) **Sauti starch granules (x400)**



Maize starch granules (x400)



Hi-starch granules (x1000) **Maize starch granules (x1000)**

APPENDIX B

Photomicrograph of fully hydrated, intact sweet potato starch granule at low and high power magnifications (x400 and x1000, respectively)

Fully hydrated Hi-starch granule (x400) **Fully hydrated Hi-starch granule (x1000)**

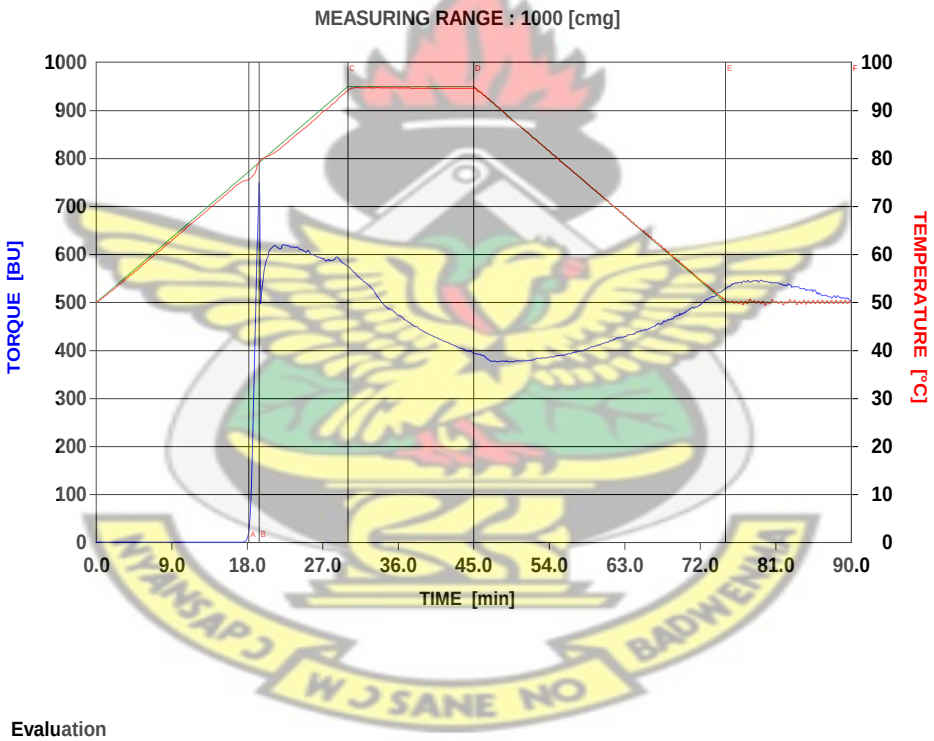
APPENDIX C

Amylograms of the sweet potato and commercial maize starches

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/2/2011	
Sample	:	SAUTI STARCH (A)		Method	:	METHOD 1	
Moisture	:	14.23	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40.1	[g]
Water	:	420	[ml]	Corr. to 14%	:	419.8	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

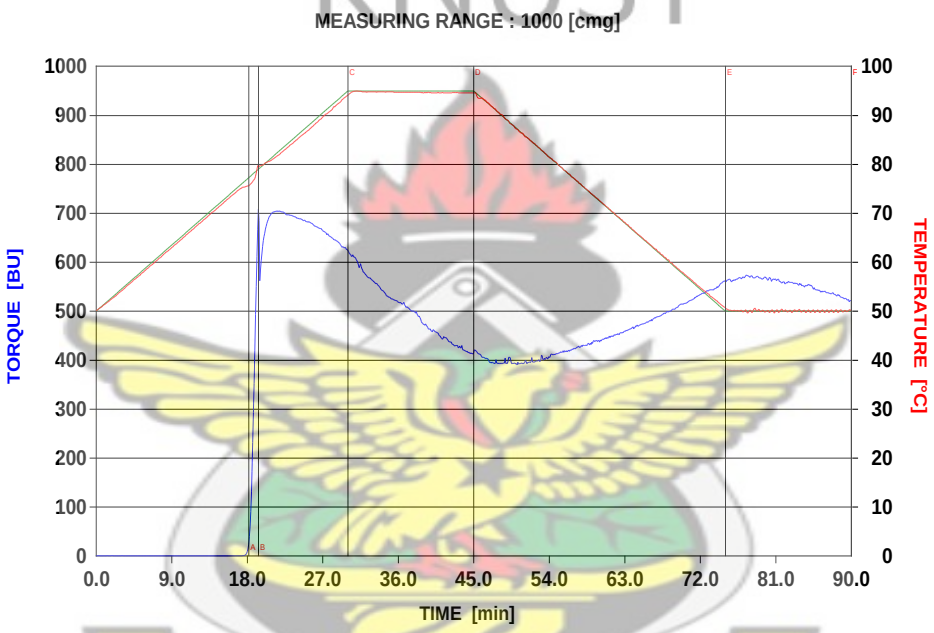
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:18:10	21	75.6
B	Maximum viscosity	00:19:25	750	79.2
C	Start of holding period	00:30:00	575	94.1
D	Start of cooling period	00:45:00	394	94.6
E	End of cooling period	01:15:00	528	50.5
F	End of final holding period	01:30:00	506	50.0
B-D	Breakdown		355	
E-D	Setback		133	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/2/2011	
Sample	:	SAUTI STARCH (B)		Method	:	METHOD 1	
Moisture	:	14.23	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40.1	[g]
Water	:	420	[ml]	Corr. to 14%	:	419.8	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

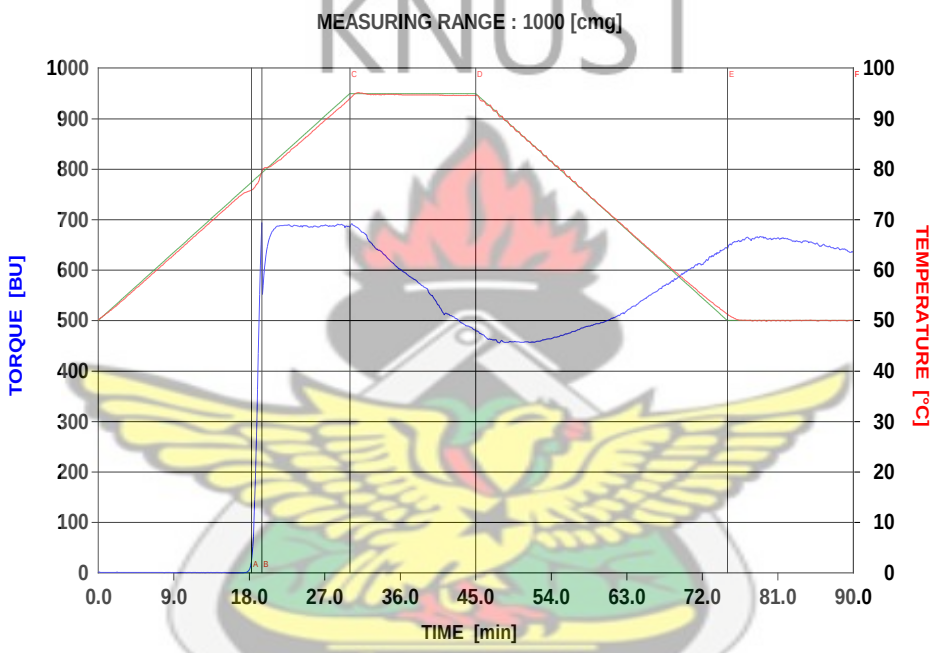
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:18:10	24	75.6
B	Maximum viscosity	00:19:20	708	79.7
C	Start of holding period	00:30:00	624	94.1
D	Start of cooling period	00:45:00	415	94.6
E	End of cooling period	01:15:00	561	50.7
F	End of final holding period	01:30:00	521	50.0
B-D	Breakdown		296	
E-D	Setback		150	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/2/2011	
Sample	:	OGYEFO STARCH (A)		Method	:	METHOD 1	
Moisture	:	14.19	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40	[g]
Water	:	420	[ml]	Corr. to 14%	:	420	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

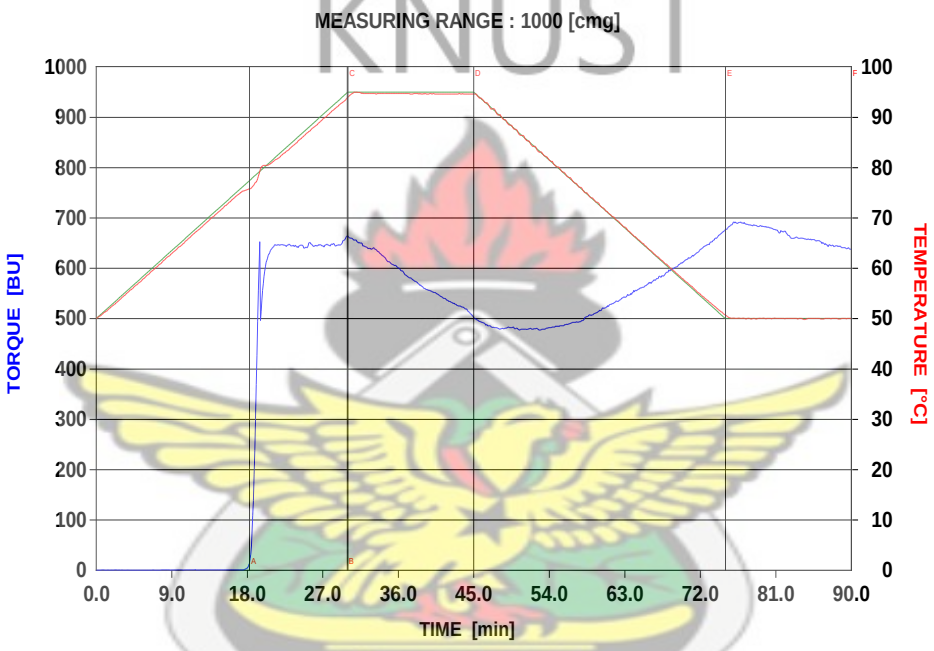
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:18:15	21	75.8
B	Maximum viscosity	00:19:30	694	79.5
C	Start of holding period	00:30:00	685	94.0
D	Start of cooling period	00:45:00	480	94.6
E	End of cooling period	01:15:00	642	51.3
F	End of final holding period	01:30:00	635	50.0
B-D	Breakdown		213	
E-D	Setback		164	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/8/2011	
Sample	:	OGYEFO STARCH (B)		Method	:	METHOD 1	
Moisture	:	14.19	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40	[g]
Water	:	420	[ml]	Corr. to 14%	:	420	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

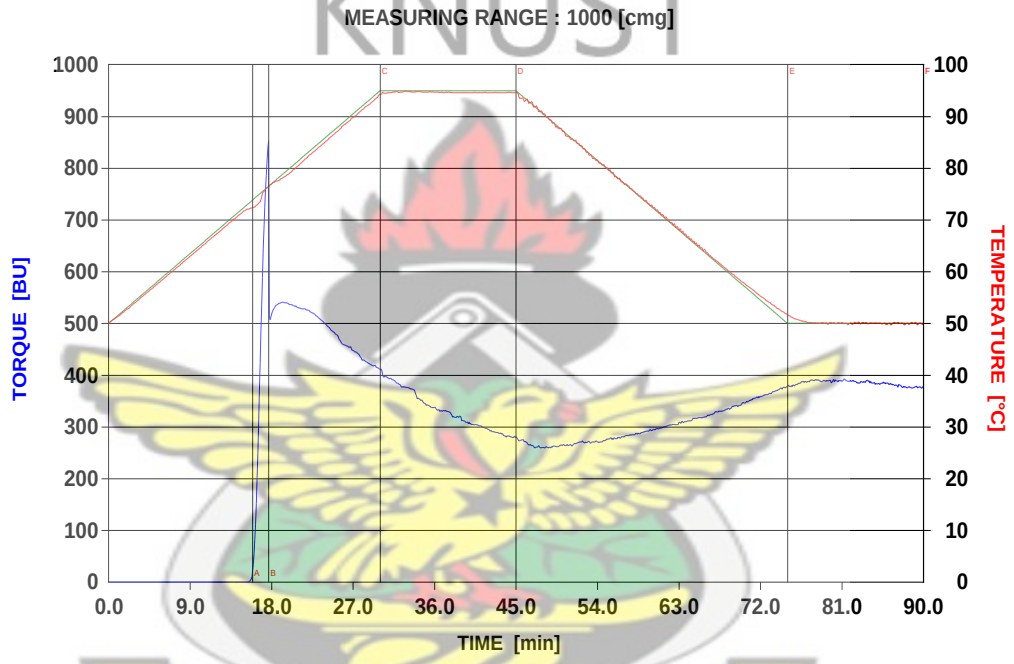
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:18:15	13	75.8
B	Maximum viscosity	00:29:55	664	93.8
C	Start of holding period	00:30:00	664	94.0
D	Start of cooling period	00:45:00	502	94.6
E	End of cooling period	01:15:00	677	50.7
F	End of final holding period	01:30:00	638	50.0
B-D	Breakdown		159	
E-D	Setback		170	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/9/2011	
Sample	:	PURIFIED STARCH(A)		Method	:	METHOD 1	
Moisture	:	13.52	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.7	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.2	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

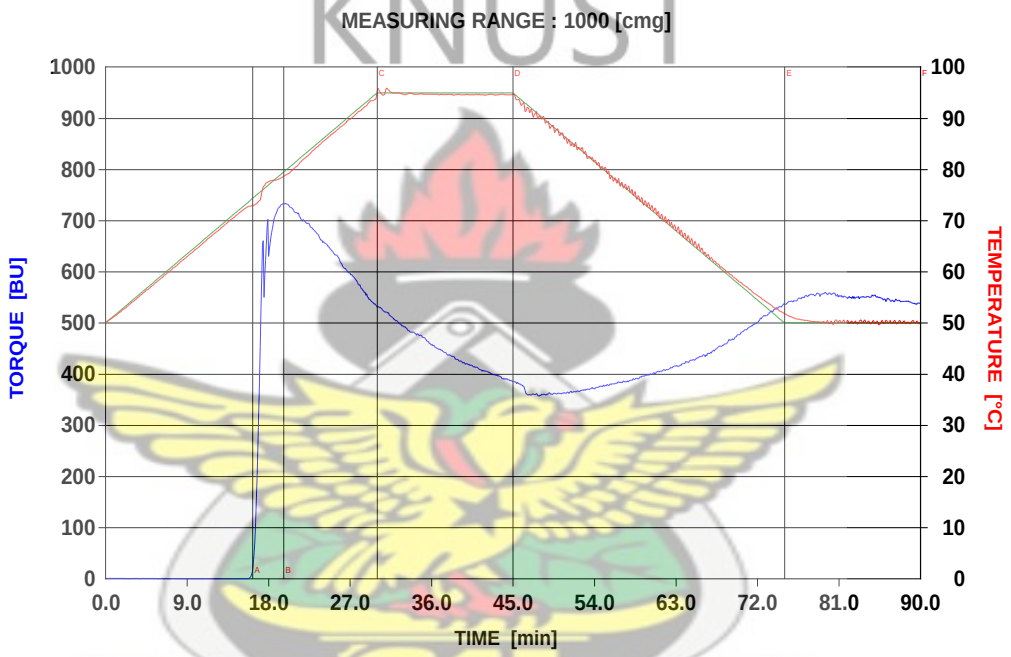
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:15:55	22	72.3
B	Maximum viscosity	00:17:40	853	76.4
C	Start of holding period	00:30:00	411	94.2
D	Start of cooling period	00:45:00	281	94.6
E	End of cooling period	01:15:00	378	51.7
F	End of final holding period	01:30:00	379	50.0
B-D	Breakdown		574	
E-D	Setback		99	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/9/2011	
Sample	:	HIGH STARCH II		Method	:	METHOD 1	
Moisture	:	12.76	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.4	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.6	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

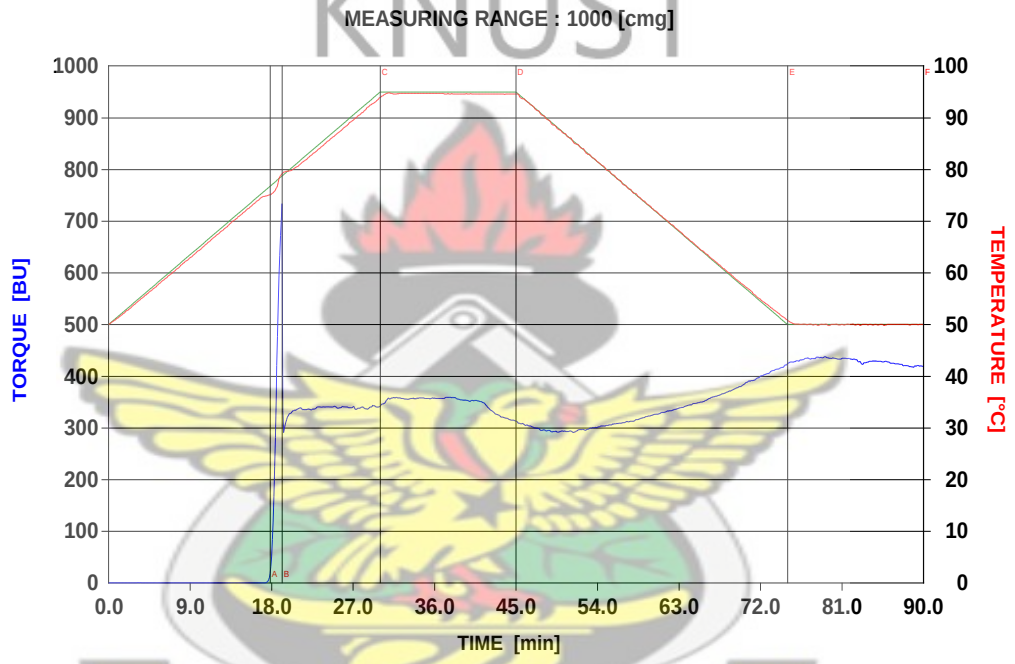
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:16:15	16	72.9
B	Maximum viscosity	00:19:40	734	78.6
C	Start of holding period	00:30:00	531	95.3
D	Start of cooling period	00:45:00	386	94.6
E	End of cooling period	01:15:00	537	51.8
F	End of final holding period	01:30:00	538	50.2
B-D	Breakdown		348	
E-D	Setback		152	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/10/2011	
Sample	:	FAARA STARCH (A)		Method	:	METHOH 1	
Moisture	:	12.41	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.2	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.7	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:17:50	18	75.1
B	Maximum viscosity	00:19:10	734	79.2
C	Start of holding period	00:30:00	342	93.9
D	Start of cooling period	00:45:00	313	94.6
E	End of cooling period	01:15:00	425	50.8
F	End of final holding period	01:30:00	419	50.0
B-D	Breakdown		420	
E-D	Setback		108	

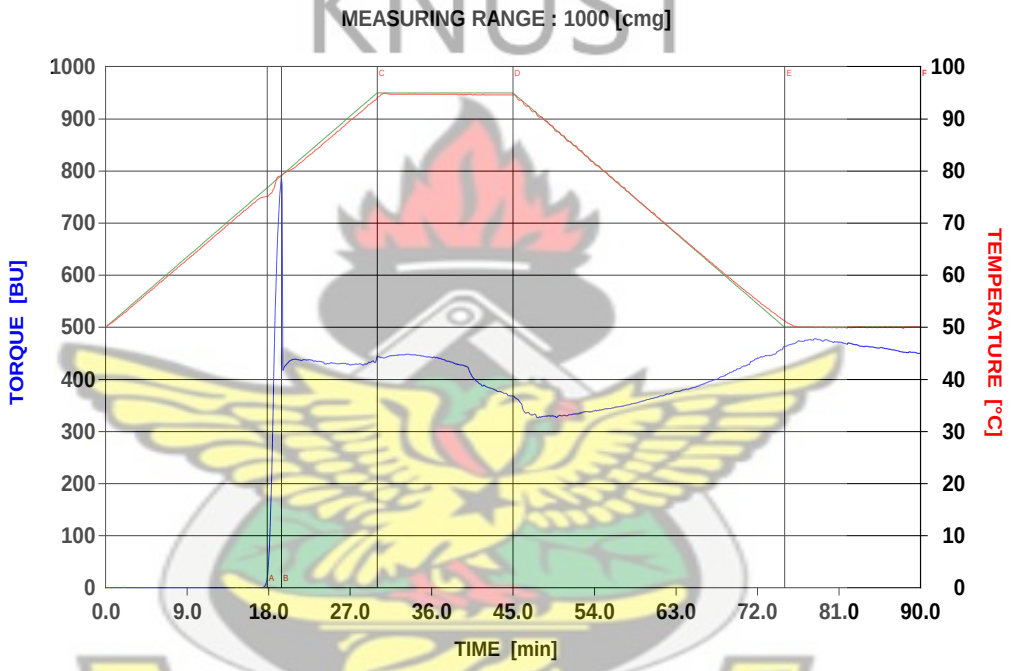
File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/10/2011	
Sample	:	FAARA STARCH (B)		Method	:	METHOH 1	
Moisture	:	12.41	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.2	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.7	[ml]
Note	:						
Note	:						

Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

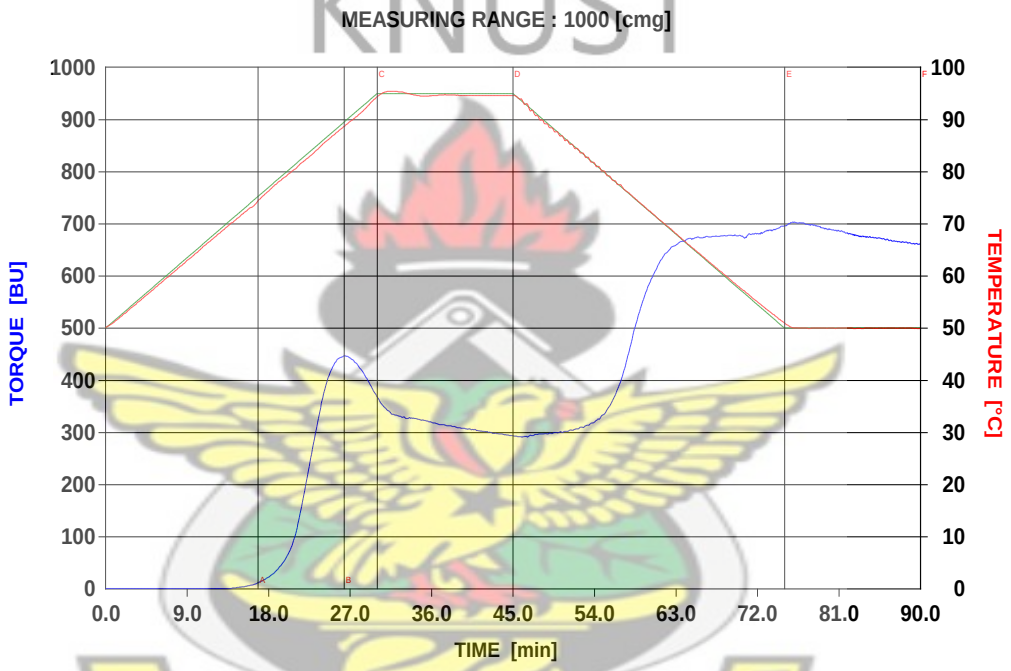
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:17:50	16	75.1
B	Maximum viscosity	00:19:25	790	79.1
C	Start of holding period	00:30:00	444	94.0
D	Start of cooling period	00:45:00	368	94.6
E	End of cooling period	01:15:00	463	51.2
F	End of final holding period	01:30:00	450	50.0
B-D	Breakdown		422	
E-D	Setback		95	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/9/2011	
Sample	:	RISI MAIZE STARCH		Method	:	METHOD 1	
Moisture	:	12.79	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.4	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.6	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

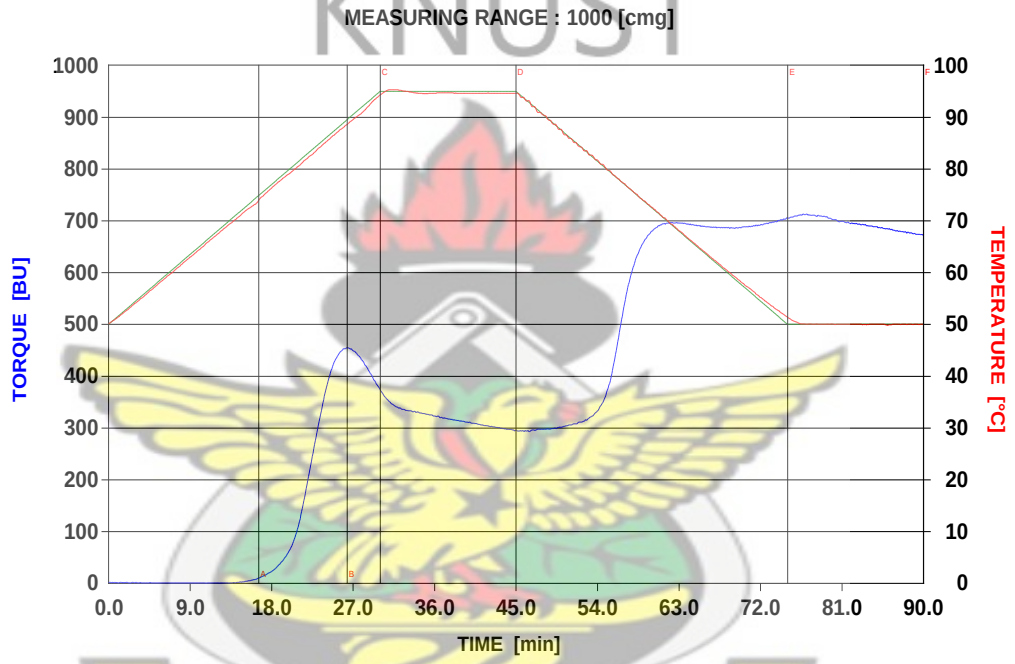
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:16:50	12	74.4
B	Maximum viscosity	00:26:20	447	88.7
C	Start of holding period	00:30:00	368	94.4
D	Start of cooling period	00:45:00	294	94.6
E	End of cooling period	01:15:00	696	51.0
F	End of final holding period	01:30:00	661	50.0
B-D	Breakdown		153	
E-D	Setback		402	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	11/9/2011	
Sample	:	RISI MAIZE STARCH(B)		Method	:	METHOD 1	
Moisture	:	12.79	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	39.4	[g]
Water	:	420	[ml]	Corr. to 14%	:	420.6	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

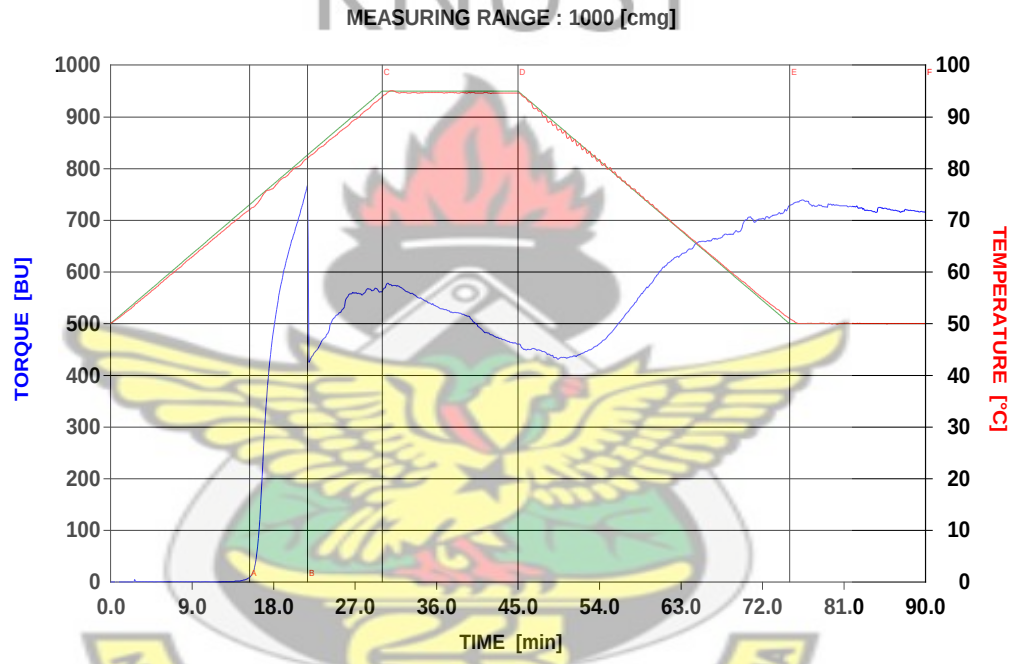
Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:16:35	10	73.9
B	Maximum viscosity	00:26:20	455	88.6
C	Start of holding period	00:30:00	374	94.3
D	Start of cooling period	00:45:00	296	94.6
E	End of cooling period	01:15:00	706	51.4
F	End of final holding period	01:30:00	673	50.0
B-D	Breakdown		160	
E-D	Setback		411	

File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	12/20/2011	
Sample	:	STARCH GLYCOLLATE (A)		Method	:	METHOH 1	
Moisture	:	14.14	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40	[g]
Water	:	420	[ml]	Corr. to 14%	:	420	[ml]
Note	:						
Note	:						
Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:15:20	9	72.1
B	Maximum viscosity	00:21:45	767	82.0
C	Start of holding period	00:30:00	561	93.9
D	Start of cooling period	00:45:00	460	94.6
E	End of cooling period	01:15:00	728	51.0
F	End of final holding period	01:30:00	715	50.0
B-D	Breakdown		307	
E-D	Setback		268	

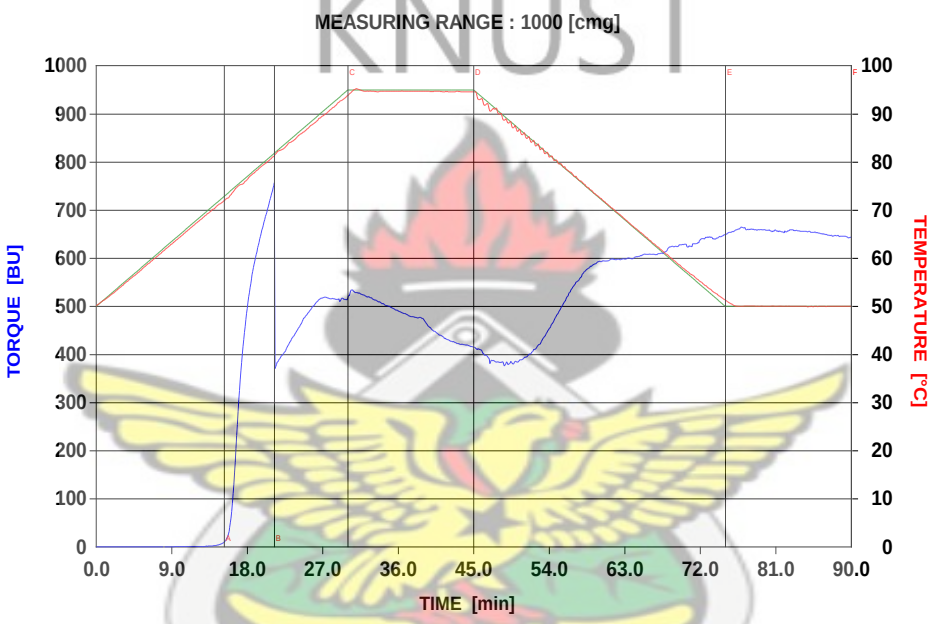
File : Measurement V: 2.3.16

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	12/20/2011	
Sample	:	STARCH GLYCOLLATE (B)		Method	:	METHOH 1	
Moisture	:	14.14	[%]	Correction	:	14	[%]
Sample weight	:	40	[g]	Corr. to 14%	:	40	[g]
Water	:	420	[ml]	Corr. to 14%	:	420	[ml]
Note	:						
Note	:						

Speed	:	75	[1/min]	Meas. range	:	1000	[cmg]
Start temperature	:	50	[°C]	Heat./Cool. rate	:	1.5	[°C/min]
Max. temperature	:	95	[°C]	Upp. hold. time	:	15	[min]
End temperature	:	50	[°C]	Fin. hold. time	:	15	[min]



Evaluation

Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:15:15	10	72.0
B	Maximum viscosity	00:21:15	757	81.3
C	Start of holding period	00:30:00	518	93.8
D	Start of cooling period	00:45:00	415	94.6
E	End of cooling period	01:15:00	649	51.3
F	End of final holding period	01:30:00	643	50.0
B-D	Breakdown		341	
E-D	Setback		233	

File : Measurement V: 2.3.16