KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

INVESTIGATION INTO THE USE OF THE FRUIT PULP OF *PARKIA BIGLOBOSA* (AFRICAN LOCUST BEAN) AS AN EXCIPIENT IN SOLID PHARMACEUTICAL DOSAGE FORMS

By

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DECLARATION

I here by declare that this submission is my own work towards 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 lovingly dedicated to my dear mother, Madam Odelia Lambon.

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ABSTRACT

The world today is increasingly interested in natural drugs and excipients. Natural materials have advantage over synthetic because they are relatively non toxic, less expensive and readily available. This study sought to process *Parkia biglobosa* fruit pulp, evaluate its physico-chemical and functional properties; formulate and assess its effects in tablets using Acacia gum and Sodium starch glycolate as reference binder and disintegrant, respectively in paracetamol tablet formulations.

The *P. biglobosa* fruits were obtained from four different locations in Northern Ghana and processed. The most suitable sample was selected as a representative sample based on their organoleptic properties and results of preliminary phytochemical and physicochemical tests. Further phytochemical analysis were then carried out on the chosen sample. The effects of the fruit pulp as a binder and disintegrant were investigated on paracetamol tablets formulations. Granules were formulated by the wet granulation method. The granules were compressed on manually controlled single punch tableting equiptment. Reference batches of tablets using Acacia gum as a binder and Sodium starch glycolate as a disintegrant were also prepared.

Post compression tablet parameters including: tablet thickness, uniformity of weight, friability, hardness, disintegration time and dissolution were assessed. The results of the phytochemical screening indicated presence of carbohydrates, reducing sugars, saponins and glycosides but were negative for alkaloids, starch and tannins. The *P. biglobosa* fruit pulp had a pH of 6.31 and was soluble in water but insoluble in organic solvents such as acetone, alcohol and chloroform. By all the indicators, Tapped density (0.24 g/ml), Bulk density (0.18 g/ml), Angle of repose (45.0^{o}), Hausner's ratio (1.67), Carr's index (40 %) the fruit pulp did not show satisfactory inherent flow properties. The particle size data revealed fine particles with a geometric mean diameter of 420 μm.

The fruit pulp had a very high water binding capacity (446 %) holding up to about five times its own weight of water and corroborates with its swelling profile (4.25) suggesting it could serve as a good disintegrant.

Its high moisture sorption value (42.50 %) however, indicates its susceptibility to atmospheric moisture and moisture induced changes which may affect flow, compression behaviour

and mechanical strength of tablets. The proximate data of *P. biglobosa* fruit pulp (moisture content 8.66 % , ash 2.40 % , crude fat 0.13, crude fibre 8.75 %, protein 6.64 % , carbohydrate 76.80 %, and sugar 3.66^{o}Brix) showed it could be a good source of macronutrients. The pasting profile of the *P. biglobosa* fruit pulp (pasting temperature 60.70^{o}C, breakdown viscosity 7.5 RVU, setback viscosity 15 RVU, peak viscosity 9.0 RVU and final viscosity 15.50 RVU) indicated the absence of starch and lack of inherent viscosity.

The tablets of all the batches had uniform thickness and passed the BP uniformity of weight test. The batches of tablets formulated with 1 %, 3 % w/w concentratons of *P. biglobosa* fruit pulp as binder (and 2 % w/w concentration of the fruit pulp as disintegrant) failed the BP hardness test. Tablets of with 1 % w/w concentration of the fruit pulp as binder failed the BP friability test. All others passed it. The tablets with *P. biglobosa* fruit pulp and Acacia gum as binders passed the BP disintegration test whiles those with the fruit pulp as disintegrant failed. Hence *P. biglobosa* fruit pulp may not be a good disintegrant. On the basis of drug release the tablets prepared with *P. biglobosa* fruit pulp as a binder at 5%w/w released over 90 percent of the drug within 45 minutes which compared well with the release profile of Acacia gum at the same binder concentration. Tablets with 5% w/w concentration of *P. biglobosa* pulp and Acacia gum showed comparative effectiveness as a binder to paracetamol powder. Thus *P. biglobosa* fruit pulp was found useful as a binder in the formulation of paracetamol tablets and demonstrated its potential for application in the pharmaceutical industry, especially as a thickener and binding agent.

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CHAPTER 1
INTRODUCTION

1.1 BACKGROUND

For the past decade there has been a growing awareness of the importance of non-timber forest products (NTFPs), for the role they play in the economy of many forest – dependent households, and also for their potential and importance to the economies of many developing countries. One common example is *Parkia biglobosa*. There is considerable interest concerning the optimal utilization of this resource base while at the same time protecting biodiversity and ensuring sustainability (Popoola and Maishanu, 1995). Knowledge of the potential utilization of these products and their transformation and commercialization, would favour their promotion.

Excipients are the non – therapeutic but vital components of drug delivery systems. They influence drug delivery through increased or decreased solubility, modified dissolution rates, absorption enhancement, ultimately leading to improved therapeutic activity (Ursino *et al*., 2011). Synthetic polymers offer a broad range of properties that can be reasonably well "built-in" by design and modified by altering polymer characteristics (Liu *et al*., 2007). Plant products are therefore attractive alternatives to synthetic products.

Excipients have also been found useful in formulating immediate and sustained release preparations. The ingredients or excipients used to make compressed tablets are numerous and can be classified by their use or function as: fillers, binders, disintegrants, lubricants, glidants, wetting agents, preservatives, colouring agents and flavouring agents. It is becoming increasingly apparent that there is an important relationship between the properties of the excipients and the dosage forms containing them. The advantages of natural plant – based excipients include that they are inexpensive, natural origin, environmental 'friendliness', fairly free from side effects, bioacceptable with a renewable source, local availability, better patient tolerance, as well as public acceptance. They improve

the natural economy by providing inexpensive formulation to people by using locally available material (Wade and Weller, 1994).

The cost of drug development drives the quest to search for low – cost ingredients and enabling companies to enhance their existing products in order to cope with the global challenges and completion. Novel excipients enable pharmaceutical companies to develop new drug delivery systems, improve efficiency, enhance functionality and reduce the cost of drugs (Manjanna *et al*., 2010). Furthermore, novel excipients offer patent holders opportunities to upgrade their products and thereby extend their patent lives. Development of excipients from natural sources which are known to be utilized for food consumption may reduce the regulatory requirements for approval.

Even agricultural wastes such as corn stalk, rice hulls and orange mesocarp have been recycled and microcrystalline cellulose produced from them (Ejikeme, 2008). Excipients from plant sources are appealing because plant resources are renewable and if maintained and harvested in a sustainable manner, they can be constant sources of raw materials (Beneke *et al*., 2009).

Parkia biglobosa (Mimosoideae - Leguminosae) commonly called African locust bean tree has long been widely recognized as an important indigenous fruit tree in anglophone and francophone West Africa (Oni, 1988).

A matured *P. biglobosa* bean pod contains yellow, dry and powdery pulp (locally known as 'Dorowa' in Hausa) in which dark brown or black seeds are embedded. The pulp which is rich in carbohydrates, minerals and vitamins (FAO, 1988) is licked for its sweet taste but only to a small extent.

Almost all drugs which are active orally are marketed as tablets, capsules or both. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation (Aulton, 1990). Today cosumers opt for the natural ingredients in food, drug and cosmetics as they believe that anything natural will be safer and devoid of side effects as compared to synthetic ones. While the *P. biglobosa* bean seed has been extensively studied (Addy *et al*., 1995), the yellow

dry fruit pulp has not attracted much attention (Odunfa,1986). As such little or no information is available concerning the use of the *P. biglobosa* fruit pulp as a pharmaceutical excipient.

This study sought to process *P. biglobosa* fruit pulp, evaluate its physicochemical and functional properties, formulate and assess its effects on tablets using Acacia gum and Sodium starch glycolate as reference binder and disintegrant , respectively, in paracetamol tablet formulations.

1.2 STATEMENT OF RESEARCH PROBLEMS

Natural excipients play a significant role in the formulation development of a new dosage forms as well as in human health care system. In recent years, natural plant excipient product segments are growing rapidly and it continues to remain an important source of new dosage formulation.

Natural products obtained from plants have diverse applications in drug delivery as disintegrants, suspending agents and as binders. There are some lesser known fruits whose functional properties have not been studied. One of such is the *P. biglobosa* fruit pulp. However, efficient utilization of any new excipient such as *P. biglobosa* fruit pulp requires enough information on its characteristics, functional, physicochemical and storage properties. There is no report available on the use of *P. biglobosa* fruit pulp as a pharmaceutical excipient in the literature. There has always been a search for better pharmaceutical excipients in the field of tableting technology because tablets have been the ruling dosage form for years.

1.3 JUSTIFICATION

For centuries, *P. biglobosa* tree has been an integral part of life in Northern Ghana. Each and every part of the tree (bark, leaves, root, seed, wood and fruit) serves a certain purpose. Most drugs locally produced are more expensive than imported ones. Patients tend to buy cheap drugs because they cannot afford to buy quality and expensive ones. The need therefore, for other potential sources of cheaper pharmaceutical excipients cannot be over emphasized. Due to limited supply and consequent increase in cost of traditional excipients a search for other lesser known naturally occurring excipients with the desired pharmaceutical properties is essential.

The evaluation of *P. biglobosa* fruit pulp as a possible raw material to be used as an excipient in solid pharmaceutical dosage forms will add to further studies on the fruit pulp and encourage cultivation and utilization in the pharmaceutical industry.

1.4 RESEARCH OBJECTIVE

The main objective of the study was to investigate the potential use of *Parkia biglobosa* fruit pulp as an excipient in solid pharmaceutical dosage forms.

1.5 SPECIFIC OBJECTIVES

The specific objectives of the study were to:

- Collect and process *Parkia biglobosa* fruit pulp.
- Determine the phytochemical properties of *Parkia biglobosa* fruit pulp.
- Determine the physicochemical properties of *Parkia biglobosa* fruit pulp.
- Determine the Proximate composition of *Parkia biglobosa* fruit pulp.
- Determine the binding property of *Parkia biglobosa* fruit pulp compared to the conventional binder (Acacia mucilage) using Paracetamol powder as active ingredient.
- Determine the disintegrating property of *Parkia biglobosa* fruit pulp compared to the conventional disintegrant (Sodium starch glycolate) using Paracetamol powder as active ingredient.
- Perform quality control tests on the paracetamol tablets produced.

CHAPTER 2

LITERATURE REVIEW

2.1 *PARKIA BIGLOBOSA*

2.1.1 Taxonomy

Parkia biglobosa (jacq.) Benth is a perennial deciduous tree from the sub – family Mimosoideae and family Leguminosae (Campbell – Platt, 1980).

2.1.2 Parkia species

Parkia is a genus of approximately thirty one species of leguminous trees through both the new world and old world tropics (Luckow and Hopkins, 1995). The genus is taxonomically most diverse in the rainforests of the Amazon Basin but four species are found in Africa and Madagascar and about ten in the Indo – Pacific region (Luckow and Hopkins, 1995).

Among the economically important species in the genus parkia is *Parkia clappertoniana*, popularly referred to as the West African locust bean (Yayock et al., 1988). The botanically related species of the African locust bean are *Parkia biglobosa*, *Parkia clappertonia*, *Parkia filicoidea* and *Parkia bicolor*. *Parkia biglobosa* and *Parkia filicoidea* are usually described as different while *Parkia clappertonia* is now considered the same as *P. biglobosa* and given as its synonym (FAO, 1988).

The main distinction between the first three species is the degree of division of their leaves. More recent monographic work has reduced the number of species present to two common ones, *P. biglobosa* and *P. bicolor*. *P. biglobosa* occurs commonly from Senegal across the region into Southern Sudan. *P. bicolor* occurs mainly as a forest species from Guinea to eastern Zaire. The third species, *P. filicoidea* is a species of central to eastern Africa with restricted and rare occurrence in highland locations of Ivory Coast, Ghana and Togo. Economic information on the genus parkia, in West Africa has in the past been more or less lumped in misinterpretation of the species under *P. filicoidea*. It is probably, that species names are interchangeable and usage are applicable, more or less, commonly to all (Burkill, 1995).

2.1.3 Local names

P. biglobosa is known by different names among ethnicities in different countries. However, the most common ones include; African locust bean, Monkey cutlass tree, fern leaf, two tall nitta – tree (English).

Arbre a farine, Arbre a fauve, caroubier African, nere, nerre (French).

Ner, Nete, Netto (Mandinka).

mkunde, mnienze (Swahili).

Dawadawa, Dorowa (Hausa). (Hopkins, 1983).

2.1.4 Description

P. biglobosa is a perennial deciduous tree with a height ranging from 7 to 20 m, although it can reach 30 m under exceptional conditions. Taproot often present, lateral roots up to10 – 20 m spreading from bole; bole usually straight and robust, cylindrical, up to 130 cm in diameter, often branching low; bark distinctly longitudinally fissured, often with more or less regular scales between the fissures, thick, ash - grey to grayish - brown, slash fibrous and reddish - brown, exuding an amber gum; crown dense, wide spreading and umbrella - shaped, consisting of heavy branches. Leaves alternate, bipinnately compound, up to 30 – 40 cm long, stipules absent; petiole 4 − 12.5 cm long, swollen at base and there with an orbicular gland; rachis with a caducous awn at apex, bearing up to 17 pairs of pinnae, with a gland between the terminal pinnae; pinnae with 13 – 60 pairs of leaflets; leaflets sessile, oblong, 8 – 30 mm. Inflourescence a pendulous head arranged racemosely; peduncle 10 – 35 cm long, turning salmon pink, many – flowered. Flowers bisexual, male or sterile, sessile but pseudopedkcellate by the fusion of the bases of calyx, corolla and stamens, calyx and corolla tubular; bisexual flowers in the distal portion of the capitulum (Burkill, 1995). The fruit is a linear - oblong pod. The pod is sub- cylindrical and compressed laterally in shape. Each pod contains 5 – 20 seeds, globose – ovoid, slightly compressed, 0.5 – 1.5 cm long,with distinct pleurogram on lateral face, testa hard, smooth glossy dark brown embedded in spongy, yellow endocarp (Hall *et al*.,1997). Bats are the primary pollinators of *P. biglobosa* (Hopkins,1983).

2.1.5 History of *Parkia biglobosa*

In 1757, Michel Adanson first recorded *P. biglobosa* during his collecting trips to Senegal and the Gambia. Although Adanson did not name the tree, in 1763 Nicolas Jacquin formally published the valid binomial name of *Mimosa biglobosa*. It is interesting to note that Jacquin's description and plant material came from tree specimens in the West Indies. The trees were presumably introduced from West Africa during the transatlantic slave trade. Palisot de Beauvois, a botanist who traveled both the WestIndies and West Africa, realized the link and described the species as *Inga biglobosa*. He published his discovery in 1816. Robert Brown in 1826 suggested renaming and reclassifying these plant materials under the same genus, *Parkia*, to commemorate Mungo Park. Park was a Scottish surgeon who explored western Africa in the 1790s following the course of the Niger River. Park had mentioned these trees by the local name *'nitta'*, in his 'Travels in the Interior Districts of Africa' published in 1799. In 1842, Bentham included Asian forms into the genus *Parkia* (Hall et al., 1997). Historical literature regarding *P. biglobosa* can be confusing with overlapping descriptions and names describing one species.

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2.1.6 Origin and distribution

P. biglobosa occurs in the belt between 5°N and 15°N from the Atlantic coast in Senegal to southern Sudan and Northern Uganda (Cambell – Platt, 1980). The tree is not normally cultivated but can be seen in the wild in the savannah region. It has a wide distribution ranging across the Sudan and Guinea savanna ecological zones. *P. biglobosa* is found in nineteen African countries: Senegal, The Gambia, Guinea Bissau, Guinea, Sierra Leone, Mali, La Côte d'Ivoire, Burkina Faso, Ghana,Togo, Benin, Niger, Nigeria, Cameroon, Chad, Central African Republic, Zaire, Sudan and Uganda (Hall *et al*.,1997). In Ghana the tree grows wild throughout the savanna to Sahel (Ejiofor and Okafor, 1996).

2.1.7 Diseases and pests

Insects or small rodents or livestock may damage the seedling, but they survive easily. Weevils and pyralid moths have been observed on the fruits; the moth eats both pulp and seed. Leaves are attacked by Lepidoptera of four families and timber is readily attacked by insects such as termites, marine borers and fungi.

Fungal attacks cause decolouration and considerably reduce the value of the wood (Hopkins, 1983).

2.1.8 Uses of *Parkia biglobosa*

P. biglobosa can be defined as Non - Timber forest products (NTFP), which includes wood energy (fuelwood and charcoal) and all other tangible products other than timber (Chandrasekharan, 1993). Products derived from *P. biglobosa* are food, medicine, glazes, animal fodder, soil amendments, charcoal, and firewood.

Food: The most significant product from *P. biglobosa* is food. The food products collected from *P. biglobosa* are especially important due to the seasonality of fruit maturation and food availability. In February or March, young green whole pods are roasted and eaten by men. In March and April, the beginning of 'hunger season' when other foods are becoming scarce, mature pods are collected for food. The seeds are used in preparation of *dawadawa*, a protein and fat rich food (Hall *et al*.,1997).

Mertz *et al* (2001) surveyed families in Burkina Faso on vegetable consumption and seasonality and found that in two villages, *dawadawa* was consumed in 78% and 85% of allmeals. *Dobulong*, the yellow starchy pulp that surrounds the seed, is an important food supplement rich in Vitamin C and carbohydrates. The dried powder is often mixed with water to produce a drink called *dozim* by the Dagbani tribe and *bololo* in Hausa (Hall *et al*.,1997).

The young pods of locust bean are cooked as a vegetable. The pods are also used as livestock feed. The young leaves are eaten as vegetable. The seeds are made into a condiment known as *dawadawa* in West Africa (Ajuebor *et al*., 2004). *Dawadawa* serves as source of protein. This condiment forms an important article of commerce in some towns and villages in Nigeria (Ibrahim and Antai, 1986) and Ghana. Progress has been made in research studies to optimize production of *dawadawa* (Ouoba *et al*., 2003). The organisms involve in the fermentation were mostly, species of the *bacillus subitilis* spectrum such as *Bacillus subtilis*, *Bacillus licheniforms* and *Bacillus pundus* and coagulase-negative *staphylococcus* species (Ogbedu and Okagbue,1988). Drink can be made from both the seeds and leaves (FAO, 1988).

In Sudan the dried reddish fruit pulp is both eaten with rice and meat and used in preparing fermented liquor. The seeds have been used as a substitute for coffee. In the Ivory Coast a much prized fat (soumera) is obtained from the fermented and roasted seeds (lrvine, 1961).

In Nigeria, the pulp is mixed with water and fermented to fine refreshing drink (Ibiyermi *et al*., 1998, Akoma *et al*., 2001). The flour has potential for cake making (FAO, 1988). It can be used as colour substitute in confectionary products (Puhan and Wiehing, 1996). The leaves mixed with cereal flour make food known as *dalambantani* in Hausa. In Ghana water is added to the pulp to produce a paste called *dozim* in Dagbani. It is made up into cakes for longer keeping (Burkill, 1995).

Fodder: The whole pods are eaten by domestic stock, including cattle. The young seedlings are nutritious and heavily browsed by livestock. An important attribute of P. biglobosa trees is that most of their leaves remain green throughout the dry season and branches are lopped and used as fodder. Seeds are rich in calcium, sodium, potassium and Phosphorus.

Apiculture: *P. biglobosa* attracts bees and is a popular tree among beekeepers.

Fuel: The branches are sometimes lopped for firewood.

Fibre: The pods and roots are used as sponges and as strings for musical instruments. There is a tough membrane inner lining to the husk. It is used by people in central Nigeria to rove into twine to fix arrow-heads and to bind the notched end. In northern Ghana, Nankani women wear strings of it dyed black with *Acacia nilotica* (Burkill, 1995).

Timber: The wood is whitish, moderately heavy, 580-640 kg/cubic m when air seasoned, relatively hard and solid; it smells unpleasant when newly felled, but seasoning does not take long and only occasionally causes shape distortion; easily worked by hand or power tools; nails, glues, varnishes and paints well; mainly useful as a light structural timber, for example, for vehicle bodies, agricultural implements, boxes, crates and barrels, furniture, mortars and pestles, bowls planks and carvings. The twigs are used to clean teeth whiles the bark stains mouth red and contains saponins that clean teeth.

Gum or resin: The mucilage from part of fruit is made into a fluid and used for hardening earth floors and to give a black glaze in pottery; gum exudate is

proteinaceous and contains as the constituent sugars galactose, arabinose, glucuro and 4-0-methyglucuronic acid.

Alcohol: The fruit pulp can be fermented into an alcoholic beverage (Booth, 1988).

Tannin or dyestuff: The husks of pods mixed with indigo improve the lustre of dye products. Ash prepared from the wood is used in dyeing for fixing the indigo. Seeds and bark contain tan and bark is used in tanning. An aqueous extract of the husk, sometime with the bark is used to harden laterite beaten floors and sides of indigo pits; on the outside walls of houses it forms a weather proof sealing layer; it also gives a gloss to pottery after firing. The bark contains 12-14 % tannins which makes leather dark brown (FAO, 1988).

Poison: The bark and pods contain piscicides; the alkaloid parkine that occurs in pods and bark may be responsible. The husks are used as fish poison and as a blue dye (FAO, 1988).

Economic: Economically the *P. biglobosa* tree provide income and employment to many household members in the savannah region, and particularly women who are more involved in processing and marketing of the tree products. Trading activities in the raw seeds, powered fruit pulp, the fermented food condiment (known as Dawadawa), charcoal and firewood among others provide reasonable income and employment. Trading in other small products like knife handles and those of hoes, axes and cutlasses also provide additional income sources (Tee *et al*., 2009).

Medicine: Different parts of the plant are used in indigenous medicine. The leaves and bark are used in treating worm; Bark is used as a mouthwash, vapour inhalant for toothache, or for ear complaints. It is macerated in baths for leprosy and used for bronchitis, pneumonia, skin infections, sores, ulcers, bilharzia, washes for fever, malaria, diarrhoea, violent colic and vomiting, sterility, venereal diseases, guinea worm, oedema and rickets, and as a poison antidote. Leaves are used in lotions for sore eyes, burns, haemorrhoids and toothache. Seed is taken for tension, and pulp for fevers, as a diuretic and as a mild purgative. Roots are used in a lotion for sore eyes rickets (FAO, 1988).

The pulp has been used in Europe as dietetic flour and is diuretic in action. It is prepared with honey as a refreshing emollient drink for children and for fever patients (lrvine, 1961). A bark decoction is used as a bath for fever. The root, less

the bark are dried and powered, mixed with shea butter and applied to the whole body of children in Ghana suffering from convulsions (Burkill, 1995).

Medicines derived from African locust bean are of value to a rural community that cannot afford or have access to "modern medicine". The importance of the tree and its products as medicine perhaps is the origin for its name. The name of the tree and food product, *dawadawa* is from Hausa, the lingua franca of West Africa, spoken by over fifty million in this part of the continent. Hausa borrowed a great number of words from Arabic, and greatly influenced its vocabulary (Salloum, 2001). In Swahili, a language also Arabic in origin, dawa is defined as medicament, anything supplied by a doctor, including charms and talisman used by native medicine men and Dawa ya miti-shamba is herbal medicine, made from leaves, bark, roots or trees (Swahili-English Dictionary, 1939).

Ecological: The tree play a vital role in nutrients recycling and erosion control. Also the tree acts as buffer against the effect of strong wind or water runoff that usually causes damage to the crops and soil. The whole tree improves soil fertility due to nitrogen fixation and the leaf. It is a common practice in The Gambia to pound the leaves and add them to the soil where groundnuts are being planted (lrvine, 1961). Leaf fall also contributes by adding organic matter to the soil beneath the tree. Farmers in the Gambia gather the leaves for use as fertilizers. In Burkina Faso, Mossi, Gourounsi, Gourmantché, Loi and Sénoufo tribes use the testa, by-products from *dawadawa* production, as fertilizers in their fields (Abbiw, 1990).

Other products: Burnt husks of the are added to tobacco to increase its pungency. Pulp is supposedly a water purifier but possibly just sweetens and disguises taste of foul water.

2.1.9 Chemical composition of *Parkia biglobosa* (African locust bean) fruit pulp.

The chemical composition of locust bean pulp varies with soil conditions and harvesting time (Puhan and Wiehing, 1996). Recently, Akoma *et al* (2001) reported that the pulp contained 85.5 g/100 g carbohydrate, 70.4 g/100 g reducing sugars, 13.0 g/100 fats, 1.0 g/100 g protein, 3.5 g/100 g ash and 1.0 g/100 g for other constituents. The pulp had been previously reported to contain 60 % carbohydrate, 20 % reducing sugars, 10-24 g/100 g sucrose and 2.9 mg/100 g vitamin C (Campbell-platt, 1980). Ibiyemi, *et al*

(1998) had also reported that the pulp contained 1.71% total sugar and 7.3 mg/100 g ascorbic acid. Gernah *et al*, (2007) also reported that the pulp contained a moisture content of 8.41%, protein 6.56 % fat 1.80 %, crude fibre 11.75 %, ash 4.18 %, carbohydrate of 67.30 %. Sugar content was found to be 9.00^{o}Brix; total carotenoids 49.175 ug/100 g and ascorbic acid of 191.20 mg/100 g.

2.2 SOLID PHARMACEUTICAL DOSAGE FORMS

This includes tablets, capsules, sachets and pills as well as a bulk or unit – dose powders and granules (Banker and Rhodes, 1990). Tablets and capsules currently account for the highest proportion of all drug presentations as a result of several factors, including their simplicity in good chemical, physical and microbiological stability as well as relatively low cost of manufacturing (Hess, 1985).

Over 80 % of the drugs formulated to produce systemic effects are produced as solid oral dosage forms and of this about 50 % are solids (tablets, capules and powders) (Banker and Rhodes, 1996).

The oral route is the most popular route for drug therapy. Orally administered solid dosage forms are a blend of pharmaceutical excipientssuch as diluents, binders, disintegrants, glidants, lubricants and Active Pharmaceutical Ingredients (APIs). The successful manufacture of pharmaceutically acceptable solid dosage products is dependent upon the ability to adequately mix and or granulate these materials to ensure that the resultant solid agglomerates possess high fluidity, compressibility and in addition avoid de-mixing during post-granulation processes, most notably during compression of tablets or filling of capsules. Also, the final characteristics of the dosage form such as drug dissolution, disintegration, porosity, friability and hardness are all significantly influenced by the properties of the powder blends used during their manufacture (Lieberman and Lachman, 1981).

During product manufacture, large volumes of powder are fed through production equipment/processes and it is essential to be able to accurately determine, define and control powder properties to ensure reproducible manufacture and consistent product performance. The agglomeration processes most typically used to ensure powder blends possess adequate fluid; cohesiveness and compressibility involve either wet or dry granulation.

The most common solid dosage forms in contemporary practice are tablets, which may be defined as "Unit forms of solid medicaments prepared by compaction". There are several reasons for the popularity of this group of dosage form;

- They employ the oral route of drug administration, which is generally the most acceptable route.
- They permit a high degree of accuracy.
- The dose of the active drug is contained in a relatively small volume. Thus a concentrated dosage form is produced, leading to the ease of packaging, transport, storage and administration (The Pharmaceutical Codex, 1994).

Tablets are divided into two general classes, whether they are made by compression or moulding. Compressed tablets are usually prepared by large-scale production method, while moulded tablets generally involve small-scale production method (Gennaro, 1995).

2.3 PHARMACEUTICAL EXCIPIENTS

The International Pharmaceutical Excipients Council (IPEC) defines excipient as any substance other than the active drug or prodrug that is included in the manufacturing process or is contained in a finished pharmaceutical dosage form which has been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing or aid manufacture, protect, support, enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance other attributes of the overall safety and effectiveness of the drug delivery system during storage or use (Robertson,1999).

Today's commercially available excipients provide a gamut of required functions, from processing aids that increase lubricity, enhance flowability, and improve compressibility and compatibility to agents that impact a specific functional property on the final product. The United States Pharmacopoeia (2007) categorizes excipients as binders, disintegrants, diluents, lubricants, glidants, emulsifying – solubilizing agents, sweetening agents and antimicrobial preservatives. In addition to their functional performance, ideally, excipients should be chemically stable, non – reactive with the drug and other excipients, inert in the human body, have low equipment and process sensitivity, have pleasing organoleptic properties, and be

well characterized and well accepted by the industry and regulatory agencies. Excipients are also categorized as compendial or noncompendial materials. Compendial excipients have composition consistent with monographs published in compendia such as United States Pharmacopoeia. Generally compendial excipients are the better characterized excipients and most likely to possess all the desirable qualities. These materials are recognized as preferred excipients for pharmaceutical formulations. Noncompendial excipients however, might also be applied in pharmaceutical formulations.

Excipient selection in the drug product – development phase focuses on desirable characteristics such as functionality, material consistency, regulatory acceptance, cost, availability and sources. It is also worthy of note that excipients are not totally inert to the human body and may contribute significantly to therapeutics in ameliorating many disease symptoms, leading to a synergistic treatment with or reduced side effects (Chang and Chang, 2007).

Excipients tend to be the largest components of many pharmaceutical formulations. They can be of natural or synthetic origin. Both synthetic and semi-synthetic products have enjoyed a long history of use, frequently thought of as offering unique properties and advantages over naturally derived compounds, including a low sensitivity to various ingredients or moisture, leading to more efficient and effective pharmaceutical products. Despite the many potential benefits of synthetic excipients, manufacturers must still address a number of challenges before their expanded implementation (Russell, 2004).

Natural polysaccharides, and their derivatives, represent a group of polymers that are widely used as excipients in the pharmaceutical industry in the formulation of solid, liquid and semisolid dosage forms in which they play different roles as disintegrants, binders, film formers, matrix formers or release modifiers, thickeners or viscosity enhancers, stabilizers, emulsifiers, suspending agents and muco adhesives (Beneke *et al.*, 2009).

The growing role and application of natural excipients in the pharmaceutical industry may be attributable not only to the fact that they are biodegradable and toxicologically harmless raw materials of low cost and relative abundance

compared to their synthetic ones (Malafaya *et al*., 2007, Malviya *et al*., 2011), but also because natural resources are renewable and if cultivated or harvested in a sustainable manner, they can provide a constant supply of raw material (Perepelkin, 2005). In the United States, an excipient that is 'generally recognized as safe', for its intended use can be exempted from premarket approval requirements of the Federal Food, Drug and Cosmetic Act (2002).

The ability of excipients to provide their intended function and perform through out the shelf life of the product must be established such that the information will justify the choice, concentration and characteristics that may influence the final product (EMEA, 2004). Since the ability of a natural polymer to provide its intended action mostly depends on its physical and chemical properties, such properties as solubility, water sorption, swelling capacity, pH, effect of temperature, and viscosity among others should be established for any such potential excipient. Acacia, tragacanth, albizia, guar gum are examples of natural polymers that have been used as excipients in pharmaceutical formulations (Martin *et al*., 1991).

Generally excipients should have no bioactivity, no reaction with the drug substance, no effect on the functions of other excipients, and no support of microbiological growth in the product (Banakar and Makoid, 1996).

Innovative and new excipients can therefore enable the development of new dosage forms, improve efficiency or reduce the cost of drugs (Frost and Sullivan, 2005).

2.3.1 TYPES OF EXCIPIENTS

2.3.1.1 Diluents (Fillers)

Diluents increase the volume of a formulation to prepare tablets of the desired size. Widely used fillers are lactose, dextrin, microcrystalline cellulose (Avicel PH® from FMC Corp. and Emococel® from Mendell), starch, pregelatinized starch, powdered sucrose, and calcium phosphate. The filler is selected based on various factors, such as the experience of the manufacturer in the preparation of other tablets, its cost, and compatibility with other formulation ingredients. For example, in the preparation of tablets or capsules of tetracycline, a calcium salt should not be used as a filler since calcium interferes with absorption of the antibiotic from the GI tract.

2.3.1.2 Binders (Adhesives)

Binders promote the adhesion of particles of the formulation. Such adhesion enables preparation of granules and maintains the integrity of the final tablet. Commonly used binding agents are Carboxymethylecellulose, Sodium cellulose, Microcrystalline cellulose (Avicel), Ethylcellulose, Hydroxypropyl methylcellulose, Karaya gum, Starch pregelatinized, Tragacanth, Methylcellulosse, Polypvinylpyrrolidone (Povidone), Acacia gum, Agar, Alginic acid, Guar gum, Gelatin, Dextrin, Glucose and Molasses (honey, sugar, syrups). Many of these are used as an aqueous solution in wet granulation (Kanig and Rudnic, 1984).

2.3.1.3 Lubricants and Glidants

Lubricant is a substance capable of reducing or preventing friction, heat and wear when introduced as a film between solid surfaces. It works by coating on the surface of particles, and thus preventing adhesion of the tablet material to the dies and punches. Lubricants play significant roles in the preparation of tablets;

- Lubricants improve the flow of granules in the hopper to the die cavity.
- Lubricants prevent sticking of tablet formulation to the punches and dies during formulation.
- Lubricants reduce the friction between the tablet and the die wall during the tablet's ejection from the tablet machine.
- Lubricants give sheen to the finished tablets.

A glidant is a substance that allows particles to move smoothly, continuously and effortlessly. Both lubricants and glidants have the same effect, but the ways they work are different. Unlike lubricant, glidant works by removing moisture and as a result enhancing flow. In tableting, a dry lubricant is generally added to the granules to cover each granule with lubricant. The most widely used lubricant is magnesium stearate which is also described as the most widely used excipient. Talc and glyceryl monostearate are also commonly used as lubricants. Fumed silicon dioxide is used as a glidant. Talc has both lubricant and glidant effects (Augsburger, 1990).

2.3.1.4 Disintegrating Agents

The breakup of the tablets to smaller particles is important for dissolution of the drug and subsequent bioavailability. Disintegrators promote such breakup. To rupture or breakup tablets, disintegrating agents must swell or expand on exposure to aqueous solution. Thus, the most effective disintegrating agents in most tablet systems are those with the highest water uptake property. In general, the more hydrophilic, the better the disintegrating agent. Examples of commonly used disintegrants includes Starches (corn and potato), Pregelatinized starch (Starch 1500®by Colorcon, Inc.), Sodium starch glycolate (Explotab® by Edward Mendell Co., Primojel® by Generichem Corp.), Sodium carboxymethylcellulose (CMC), Croscarmellose (Ac-Di-Sol® by FMC Corp.), Microcrystalline cellulose (Avicel PH® by FMC Corp.), Polyvinylpyrrolidone (PVP), Crospovidone (cross-linked PVP) (Polyplasdone XL® by GAF Corp., Kollidon CE 5050 by BASF Corp.), Cation-exchange resins, Clays and Magnesium aluminum silicate (Kanig and Rudnic, 1984)

2.3.1.5 Wetting Agents

A wetting agent is a surfactant (surface active agent) which allows easy spreading of water on the surface. It also makes water easy to displace air and spread over the surface inside the tablet. Surfactants have both polar and nonpolar groups. For this reason, they are also called amphiphiles. The amphiphilic property makes surfactants to possess a certain affinity to both polar and nonpolar solvents. The extent of the affinity to either polar or nonpolar solvent depends on the nature and the number of the polar and nonpolar groups present. Thus, a surfactant may be predominantly hydrophilic (water-loving), predominantly lipophilic (oil-loving), or well balanced between these two extremes (Lerk and Lagas, 1977).

2.4 PARTICLE SIZE AND SIZE DISTRIBUTION ANALYSIS

Size analysis of pharmaceutical products and their components is highly dependent on variables related to the particles themselves, the method of sampling, the technique of analysis and the means of expressing the data. The particles are susceptible to the influence of manufacturing, processing, compatibility, storage and intended use variables. The scale, context, and method of sampling require consideration to minimize bias in the particle size estimates. The technique of measuring characteristic dimensions of the particles inherently dictates the nature of the data

collected. In many cases statistical or mathematical distributions are fitted to the data as a means of expression, which may predispose the data to a particular interpretation. The dosage form and route of administration may necessitate the use of particles with unique characteristics and the adoption of specialized methods of analysis.

The measurement and expression of particle size is intimately bound with the shape and morphology of the constituent units that make up the ensemble of particles. The difficulties encountered when relating empirical information derived using different methods would not exist if the component particles were spherical. In the real world of pharmaceutics, particles are rarely (if ever) spherical and consequently it is important to understand the importance of particle shape and morphology (Burgess *et al*., 2004).

Particle size plays a critical role in the efficacy of a drug product. It can impact not only bioavailability, but also the process, and ultimately the final dosage form. The science of material characterization is relatively new, but having an understanding helps identify potential problems early, hopefully saving time and money. Particle size, although one of the most commonly used material characterization methods, is probably the most misunderstood. Problems can arise from factors as basic as the method of analysis (laser diffraction versus air jet sieve). For example, behaviour of the 'milled' API versus the 'unmilled', minor nuances such as lenses or screens used, refractive indices and dispersants can all have a major impact. Most companies would like to use similar excipients as those used in the brand, in achieving bioequivalence, particle size is often the major variable. Based on assumptions derived from the brand-name's dissolution profile and on the excipients listed on the label, target particle size specifications can be developed. It would be ideal if at least three distinct particle size distributions for the API could be supplied. These could then be screened quickly either by intrinsic dissolution (straight API formed in a slug) or dissolution of the formulated drug product.

There are several ways and methods for characterizing the size of a particle. However, particle size analysis is something of a paradoxical subject. Rumpf (1964) was one of the first to realize that the particle size distribution (PSD) significantly influences nearly every unit operation that involves mechanical processing of particles. Likewise,

in many of the unit operations in the pharmaceutical industry particle size monitoring and controlling has received much attention, since it has proven to affect vital quality parameters such as powder flow, drug release rate and dosage unit content uniformity (Kaerger *et al*., 2004; Liu *et al*., 2008). Hence, it is important to characterize the particles adequately. Additionally, the collection of a representative sample is of critical importance.

2.4.1 Particle size estimation methods

The growing need for particulate analysis and determination of PSD in the quality control of pharmaceutical products emphasizes the need for efficient and reproducible methods (Beaubien and Vanderwielen, 1980). Currently, several methods are available for PSD estimation, which includes both classical and modern instruments. Nevertheless, only objects of simple geometry (namely spheres) can be unambiguously described by a single numerical descriptor (Burgess *et al*, 2004). The sizing of irregularly shaped particles is typically expressed in terms of equivalent spherical diameters (Heywood, 1963).

2.4.1.1 Particle size estimation by analytical sieving

Particle size estimation by sieve analysis is the classical and least expensive method of particle sizing in the pharmaceutical industry. In sieving analysis, a sample is simply passed through wire meshes that have openings of various sizes and then the amount of the sample retained on each sieve is measured. Sieving is one of the fundamental methods for the classification of powders, and it is the method of choice for determining the size distribution of coarse powders (Brittain, 2002). Conducting analytical sieving for the classification of pharmaceutical materials has been fully described in General Test of the United States Pharmacopoeia (2009). The general method describes the use of both dry sieving method (Method I) and wet sieving method (Method II) procedures.

Sieve analysis represents the minimum square aperture through which the particle can pass and hence is greatly influenced by particle shape. Sieve analysis has its own drawbacks; longer measurement times give the particles ample time to orient themselves to fall through the sieve (Rawle, 1993). Particles having the form of thin flakes or long needles are difficult to sieve to finality, because they will only

pass the apertures when presented in a favorable position (Heywood, 1963). The general consensus is that sieving is most suitable for granular solids or powders whose average particle size exceeds about 50 µm.

2.4.1.2 Particle size estimation by microscopy

Optical microscopy, also known as static image analysis (SIA), is the only commonly used method in which individual particles are viewed and measured. Examination of a particle under a microscope provides a two dimensional image. An advantage of this method is that both size and qualitative or quantitative shape information can be obtained simultaneously (Houghton and Amidon, 1992). Particle shape has special importance for pharmaceutical powders, since it affects surface area, bulk density, permeability, flow characteristics and the pharmacological function (Staniforth and Hart, 1987). Various instruments exist for measuring individual particle dimensions of which image analysis is a widely applied technique. Optical microscopy is generally applied to particles of 1 µm and greater while the lower limit of estimation depends on the resolving power of the microscope.

The United States Pharmacopoeia (2009), General Test describes the particle characterization using optical microscopy. The General Test also states that "For irregularly shaped particles characterization of particle size must include information on particle shape". There are a number of diameters that can be measured in order to characterize particle size. The SIA technique is adequate enough for acquiring a general idea of particle shape, but it is insufficient when using particle shape analysis as a means to control a process. Unlike sieve analysis, both size and shape information are made available by the optical microscopy. However, the analysis is slow, tedious and often inaccurate due to operational error or bias if the visual investigation was manually performed (Yamamoto *et al*., 2004). Also, as relatively few particles are examined, there is a real danger of unrepresentative sampling; therefore limiting its suitability as a quality or production control technique.

2.4.1.3 Particle size estimation by laser diffraction

Laser diffraction (LD) particle size analysis is arguably the most popular particle size analysis technique within the pharmaceutical industry, especially in the quality control laboratories (Kelly *et al*., 2006). It offers a wide dynamic range and is very flexible. Dry powders can be measured directly. Other benefits are rapidity, typical analysis time of less than a minute, small sample requirement, repeatability for reliable results, and high resolution (Tinke *et al*., 2008). The Fraunhofer approximation, used in early diffraction instruments assumes that the particles being measured are opaque and scatter light at narrow angles. It is only true, however, when the particles are large compared to the wavelength of light (de Boer *et al*.,1987). As a result, it is only applicable to large particles and will give an incorrect assessment of the fine particle fraction. The Mie optical model provides a more rigorous solution for the calculation of PSDs from light scattering data. It predicts scattering intensities for all particles, small or large, transparent or opaque. The Mie optical model allows for primary scattering from the surface of the particle, with the intensity predicted by the refractive index difference between the particle and the dispersion medium (Merkus, 2009). Many international and national standards for using LD to analyze particulate matters in dry and wet forms have been established (Xu and DiGuida, 2003). Nevertheless, as an important argument, LD assumes particles to be spherical, which is in practice never the case. For smaller sample quantities, laser light scattering has become the method of choice for rapid and reproducible particle sizing (Ma *et al*., 2001). Recent advances in sophisticated data processing and automation have allowed LD to become the dominant method used in industrial PSD determination.

2.4.1.4 Particle size estimation using dynamic image analysis

Dynamic image analysis (DIA) is a recent and rapidly advancing technique and is currently being explored for its use in pharmaceutics (Yu and Hancock, 2008). Compared to other particle sizing techniques, DIA has the major advantage that the instrument provides images of fast moving particles and is sensitive to differences in size and shape characteristics; therefore, it is being increasingly applied to particle sizing in various processes (Rabinski and Thomas, 2004). The use of DIA has been found to be particularly suitable in sizing non-spherical particles This new DIA technique takes advantage of the progress in

microelectronics, such as fast frame grabbers (charge-coupled devices), and combines them with advanced image analysis algorithms to provide users a powerful means of obtaining both size and shape information of particles (Xu and DiGuida, 2003). A DIA instrument analyses images of the projected area and perimeter of each particle cross-section and based on the choice of size parameter provides a volume or number weighted size distribution of the entire particulate system. Additionally, the risk of bias caused by subjective sample selection is eliminated, since operator selection of images does not enter the measurement procedure. The results still depend on particle orientation, but the images are analyzed individually without any assumption of particle shape. Xu and DiGuida (2003) mentioned that in order to reduce the orientation effects, the particles in the sample may be circulated during measurement in which case, either each singe particle will be imaged multiple times, or many different particles will be imaged at different orientations. Random orientation provides a better representation of the sample and is the preferred method when true particle shape is critical to the efficacy of the final product. This method of reducing orientation effects has found its way into the designing of on-line and in-line DIA applications for pharmaceutical processes.

2.5 POWDER FLOW CHARACTERIZATION

Generally powder flowability has become an important topic and has been a subject of extensive research in the pharmaceutical industry, especially with respect to preformulation and development of solid dosage forms. A considerable effort has been spent in understanding and obtaining free flowing powders and granules for tablet and capsule manufacturing (Gold *et al*., 1966). The effects of poor flow, for instance, are observed in the weight variation of tablets (Fassihi and Kanfer, 1986) and in the filling performance of capsules (Tan and Newton, 1990). Hence, poor flow behaviour significantly influences the quality of the final product. Therefore, the pharmaceutical industry realized that an effective powder characterization is the only means of obtaining core knowledge that informs powder understanding and control. In response, many powder measurement methods have been developed. Powder characterization is also growing in importance because innovation in the industry is increasingly reliant on technological advancements, which intensify powder handling challenges. Highly potent actives incorporated in small proportions pose one set of issues with new delivery technologies, such as dry powder inhalers, another

(Freeman, 2010). Due to the complexity of powder flow and the various factors influencing flowability, no single measure is currently adequate for defining flow.

2.5.1 Factors influencing powder flow

Several factors are known to influence powder flow behaviour. Primary factors such as particle size and distribution, particle shape, surface energy, cohesion, adhesion and surface roughness have been shown to influence flowability (Podczeck and Miah,1996). Secondary or system variables for the degree of aeration and the level of moisture, will also have a profound impact (Freeman, 2010). Bonding index and internal friction coefficient can also be used as predictors of poor flow (Amidon *et al*., 2009). External conditions such as relative humidity of the environment, previous storage conditions, degree of consolidation also have a large impact on the flowability. When particle size is reduced to such a range that Van der Waals forces increasingly dominate then the powder behaviour will be affected. Particles larger than 250 µm are usually relatively free flowing, but as the size falls below 100 µm powders become cohesive and flow problems are likely to occur. Powders having a particle size of less than 10 µm are usually extremely cohesive and resist flow under gravity (Fan *et al*.,2005).

In general, gravitational forces may be dominant for particles having diameters of the magnitude of a millimeter whilst dispersion forces may be dominant for particles of the order of a micrometer. Particulate systems exhibiting narrower particle size distributions flow more easily compared to systems having a broader size distribution (Fan *et al*., 2005). Particles having a more irregular shape exhibit much higher porosities in powder beds than spherical particles both before and after tapping (Fukuoka and Kimura, 1992). Additionally, surface roughness can influence tablet compression pressure and adhesion of film coatings (Seitavuopio *et al*., 2006).

The sensitivity of a particulate system to environmental humidity is determined by its hygroscopicity, which is defined as the potential for and the rate of moisture uptake. In general, the higher the relative humidity, the more a solid will sorb water vapour at a higher uptake rate. As the moisture content of a powder increases, the adhesion and cohesion (Faqih *et al*., 2007) tend to increase. Even a small change in moisture content can substantially affect the frictional properties

(wall friction angle, internal angle of friction) of material (Marinelli and Carson, 1992). As a solid material remains at rest in a bin or hopper, it can become more cohesive and difficult flowing. Hopper and bin load levels, vibratory forces, time in storage, temperature of storage as well as the intrinsic cohesiveness of the material will alter a material flow characteristics (Howard, 2007).

2.5.2 Flow characterization methods

Measuring an array of powder properties is essential because powders have many characteristics. There is a variety of simple techniques that attempt to quantify powder flow. The compendia methods include measurement of angle of repose, bulk and tapped density Hausner ratio (Hausner, 1967) or Carr's compressibility index (Carr, 1965), flow through an orifice and the shear properties. Innovative flow characterization methods such as cohesivity determination under unconfined conditions (Faqih *et al*., 2006), dielectric imaging (Dyakowski *et al*., 1999), atomic force microscopy (Weth *et al*., 2001) and penetrometry (Zatloukal and Sklubalova, 2007) are a result of technological advances. Cowell *et al* (2005) and Freeman (2007) used a powder rheometer (Manumit powder rheometer and FT4 powder rheometer respectively) to measure axial and rotational forces acting on the rheometer blade while the propeller is penetrating a bed of powder. Someresearchers utilize powder avalanching to determine flow characteristics. By measuring chaotic powder avalanches inside a rotating drum Kaye *et al* (1995) and Hancock *et al* (2004) were able to investigate the rheological behaviour of powders and powder mixtures. This avalanching characterization method appears to be promising for manufacturing related studies.

2.5.2.1 Angle of repose

The angle of repose has long been used to characterize bulk powders. Angle of repose is a characteristic related to inter-particulate friction or resistance to movement between particles. When a powder is allowed to flow through a funnel onto a horizontal plane, it forms a cone. The angle between the side of the cone and the horizontal plane is referred to as the angle of repose. The angle of repose can be reported as the 'drained angle of repose' or the 'dynamic angle of repose.' The four most common methods in use until recently are; fixed height cone, fixed base cone,

tilting table and rotating cylinder. A free flowing powder will form a cone with shallow sides, and hence a low angle of repose, while a cohesive powder will form a cone with steeper sides. Since the angle of repose measurements are highly dependent on the testing conditions, it is not a very robust means of quantifying powder flow (United States Pharmacopoeia, 2009).

Table 2.1 describes the different angle of repose values and the corresponding flow characteristics. As a rough guide, angles less than 30° are usually indicative of good flow, while powders with angles greater than 40° are likely to be problematic. Although the measurement of angle of repose has sometimes met industrial and academic needs for a simple and quick test, Geldart *et al* (1990) pointed out that there was no general agreement as to the best design or size of equipment, for the way that a test should be done, or the optimum amount of powder that should be used.

Table 2.1. Flowability scale

Flow character	Angle of repose	Compressibility index	Hausner's ratio
Excellent	25 – 30	≤10	1.00 – 1.11
Good	31 – 35	11 – 15	1.12 – 1.18
Fair	36 – 40	16 – 20	1.19 – 1.25
Passable	41 – 45	21 – 25	1.26 – 1.34
Poor	46 – 55	26 -31	1.35 – 1.45
Very poor	56 – 65	32 – 37	1.46 – 1.59
Very, very poor	> 66	>38	>1.60

(United States Pharmacopoeia, 2009).

2.5.2.2 Bulk, tapped and true densities

Bulk density is the mass per unit volume of a loosely packed powder bed. The volume includes the spaces between particles as well as the envelope volume of the particles themselves. The bulk density is an essential parameter for process development and solid dosage manufacturing, since it is used to determine the capacity of mixers and hoppers. Tapped density is the bulk density of a powder that has been compacted by tapping for a definite period of time. The tapped

density of a powder represents its random dense packing. Tapped density values are generally higher for more regularly shaped particles (spheres) as compared to irregularly shaped particles such as needles (Amidon *et al*., 2009). The true density of a substance is the average mass of the particles divided by the solid volume, exclusive of all voids that are not a fundamental part of the molecular packing arrangement. The true density is independent of the method of determination. A powder can only possess a single true density, but it can have many different bulk density values, depending on the way in which the particles are packed and depending on the bed porosity.

2.5.2.3 Carr's compressibility index and Hausner's ratio

Carr's compressibility index (CI) or simply Carr's index is a measure of the capacity of the powder to consolidate. It is a measure of the relative importance of the inter-particulate interactions. In a free flowing powder, such interactions are generally less significant and the bulk and tapped densities will be closer in value and vice versa (Amidon *et al*., 2009). These differences in particle interactions are reflected in the Carr's index. Compressibility index can be expressed as below, where Vo is the untapped apparent volume and Vf is the tapped apparent volume.

$$CI\ (\%) = 100\ \{\frac{Vo - Vf}{Vo}\}$$

It is easy to calculate the CI once bulk and tapped density measurements are available. Fassihi and Kanfer (1986) found that for directly compressible pharmaceutical powders, when the compressibility index exceeded a value of about 20% a significant increase in tablet weight variation resulted irrespective of the powder flow rate. Podczeck and Newton (1999) demonstrated a correlation between the minimum coefficient of (capsule) fill weight variation and CI. Lee *et al* (2000) demonstrated that the Carr's index is related to the mean time to avalanche. The Hausner ratio is closely related to CI and can be calculated according to the relation below.

Hausner's Ratio (HR) = {Vo/Vf}

The higher the Hausner's ratio, the poorer the flow. The generally accepted scale of flowability for Carr's index and Hausner ratio is given in Table2.1. Carr's index and

Hausner ratio continue to be used, in combination with other tests, to characterize and predict the flow of pharmaceutical excipients and formulations.

2.5.2.4 Flow through an orifice

Flow through an orifice is an important measure of powder flow characteristics because of its wide application in several of the pharmaceutical solid dosage manufacturing process. Such processes include granules or powders flow through the opening in a hopper or bin used to feed powder to tabletting and capsule filling machines or sachet filling machines. Because of its importance in producing unit doses, the behaviour of particles being fed through an orifice has been extensively studied. Flow rate through an orifice is generally measured as the mass of material per unit time flowing from containers such as cylinders, funnels, and hoppers. However, determination of flow rate through an orifice provides useful information only with free flowing powders. Dahlinder *et al* (1982) reported that, for cohesive materials the minimum orifice diameter necessary to induce free flow was a better index of flowability. Beverloo's correlation (Beverloo *et al*., 1961) is perhaps the most reliable for general calculations of mass flow rate in a silo. The Beverloo's correlation can be expressed as;

$$W = C\rho_b\sqrt{g}(Do - kd)^{5/2}$$

Where, W is the mass flow rate of particles, C is an empirical constant, ρb is the bulk density of powder, g is the acceleration due to gravity, Do is the hopper orifice diameter, k is an empirical constant for particle shape, and d is the mean particle diameter. C and k are dimensionless constants and C takes values between 0.55 and 0.65 whereas k takes a value of approximately 1.5 ± 0.1 (Ahn *et al*., 2008). However, the Beverloo's correlation fails when the particle size is great enough for mechanical blocking of the orifice to occur and this happens when the particle diameter is about one-sixth of the orifice diameter. Besides, the flow rate is different for small and large orifices. In conclusion, the Beverloo's correlation is reliable in the range $Do/6 > d > 400$ µm. Beverloo's correlation applies well with large powder quantities flowing out of a hopper or silo, but it may not be applicable for small powder quantities.

2.5.3 Flowability of binary powder mixtures

Flowability of binary powder mixtures consisting of coarse and fine materials is essentially complex, since flow properties are not only influenced by the physico-chemical material factors, but also to a great extent by the particle packing. The particles in multi-component mixtures can assume various packing organizations. The simplest pharmaceutically relevant mixture is binary blends of a drug with an excipient. Such blends provide packing of multisized particles for which empirical equations were derived to calculate the packing density (Yu and Standish, 1987). The prediction of the packing properties is even more complex, if interaction between the particles is assumed. Thus, the physics of binary particle mixtures is still not well understood (Crowder and Hickey, 2000). However, the packing organization defines the material flow properties. These technical blend properties can greatly change, if the packing organization is altered at different mixture ratios. Such changes of flowability with different mixing ratios are important to understand. It is a required knowledge to adequately formulate pharmaceutical powder blends that need designing quality into the product (Storme-Paris *et al*., 2009; Sun *et al*., 2009).

2.5. 4 Effect of fines on flow properties of binary mixtures

In the context of solid dosage forms, addition of fines is usually done to improve flowability of powders. These materials are extremely fine and are added in small quantities of up to 1% w/w (Elbicki and Tardos, 1998). These fine particles generally have poor flowability due to the cohesion force arising mainly from Van der Waals attraction. The addition of a flow agent is an effective way to improve the flowability (Valverde *et al*., 2000). Lefebvre *et al* (1988) pointed out that if the amount of smaller (disintegrant) particles in a binary mixture was continuously increased, a more or less critical concentration was observed for which the mechanical properties such as flowability and compressibility of the mixture and the resulting tablets changed. Kaerger *et al* (2004) investigated the effect of size and shape of paracetamol particles on the flow and compressibility behaviour of binary blends in microcrystalline cellulose. The authors concluded that small, spherical drug particles may result in improvement in the bulk density, densification and compactibility of the binary blends.

In a similar study, Soppela *et al* (2010) reported that the flowability of the binary blends was affected both by the amount of paracetamol and the physical properties of microcrystalline cellulose and additional factors such as charging, surface moisture, carrier payload and particle size. In conclusion, powder flowability is per se a unique field and requires much attention for better understanding of the flow characteristics. All current techniques for determining powder flow are based on different principles and have advantages and disadvantages (Prescott and Barnum 2000).

2.6 PASTING PROPERTIES OF FLOURS

Pasting properties is an important index in determining the cooking qualities of flours (PBIP, 1995). Pasting occurs after or simultaneously with gelatinization. Pasting properties of flours are important indicators of how the flour will behave during processing. Pasting and viscosity are commonly measured using the Rapid Visco Analyzer (RVA).

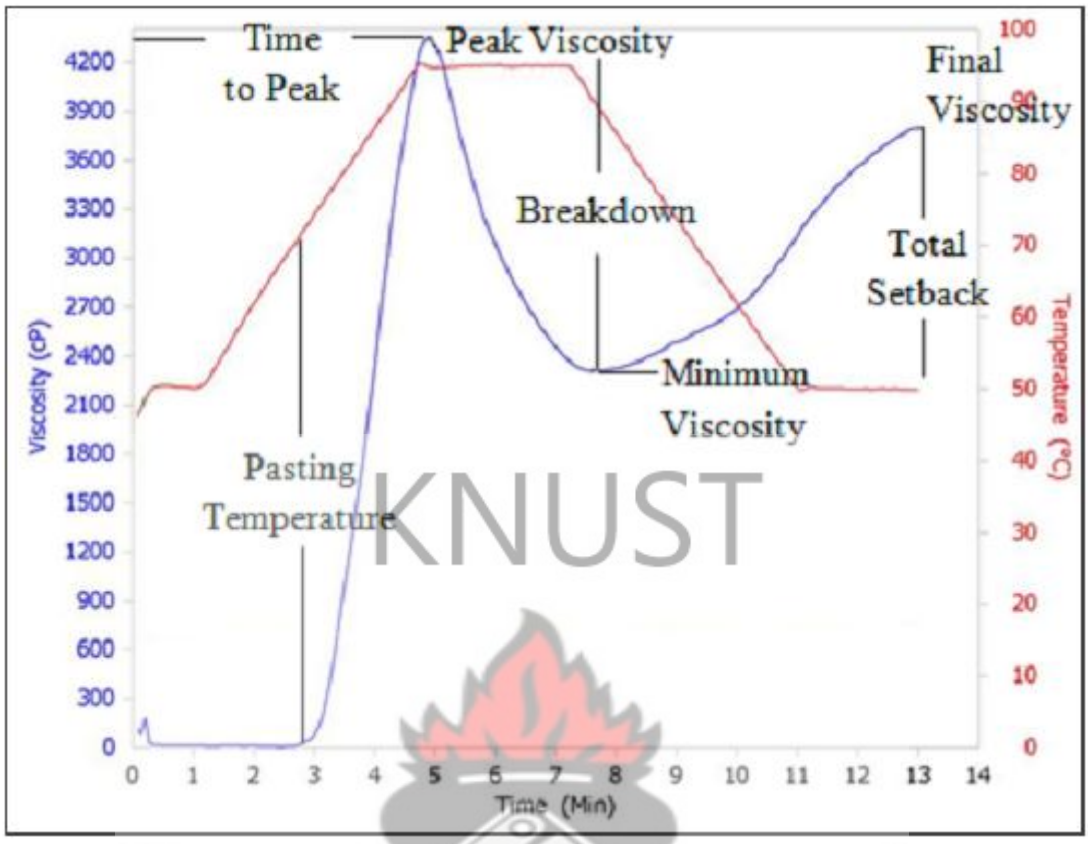

Figure 2.1 Typical Pasting Curve of Starch as Measured by RVA.

In the RVA test, starch is mixed with water to allow for hydration and held for a short time above ambient temperature. Heating proceeds, resulting in swelling of starch granules. As heating continues, an increase in viscosity can be observed, which reflects the process of pasting. Continued heating of starch in excess water with stirring causes the granules to further swell, the amylase to leach more, and the granules to disintegrate, forming a viscous material called paste (BeMiller, 2007). The temperature at the onset of viscosity increase is termed pasting temperature. Viscosity increases with continued heating, until the rate of granule swelling equals the rate of granule collapse, which is referred to as the peak viscosity (PV). PV reflects the swellling extent or water binding capacity of starch and often correlates with final product quality since the swollen and collapsed granules relate to texture of cooked starch. Once PV is achieved, a drop in viscosity, or breakdown, is observed as a result of disintegration of granules. Break-down is a measure of the ease of disrupting swollen starch granules and suggests the degree of stability during cooking (Adebowale and Lawal, 2003).

Minimum viscosity, also called hot paste viscosity, holding strength, or trough, marks the end of the holding stage at the maximum temperature of the RVA test. Cooling stage begins and viscosity again rises (setback) which is caused by retrogradation of starch, particularly amylose. Setback is an indicator of final product texture and is linked to syneresis or weeping during freeze-thaw cycles. Viscosity normally stabilizes at a final viscosity or cold paste viscosity, which is related to the capacity of starch to form viscous paste or gel after cooking and cooling (Batey, 2007). Other components naturally present in the starchy material or additives interact with starch and influence pasting behavior (Newport Scientific, 1998). The presence of proteins were indicated to confer shear strength and gelatinized paste rigidity to rice starch (Xie *et al*., 2008). Beta-glucans added to rice starch also reportedly increase the paste viscosities (Banchathanakij and Suphantharika, 2009).

2.7 FORMULATION OF SOLID PHARMACEUTICAL DOSAGE FORMS

2.7.1 GRANULATION

Granulation is the process in which small particles are made to form larger, physically strong agglomerates in which the original particles can still be identified. In the majority of cases this will be used in the production of tablets or capsules, when granules will be made as an intermediate product, but granules may also be used as a dosage form. The general reasons for granulation is to prevent segregation of the constituents in the powder mix, to provide better control of drug content uniformity at low drug concentrations, to improve the flow properties of the mix, to improve the compression characteristics of the mix, to make the surface of particles and the tablet hydrophilic and to reduce the harmful toxic dust (Faure *et al*., 2001).

Several granulation techniques exist. The most common ones are wet granulation using either high-shear mixing or fluid-bed processing. However, dry granulation has recently increased in popularity (Kleinebudde, 2004). Technical innovations that improve existing processes can have considerable impact on development times and contribute to improved material processability of the end product. Granulation literature is extensive and describes applications within many industries (Mort *et al*., 2001).

2.7.1.1 Dry granulation

In the dry methods of granulation the primary powder particles are aggregated under high pressure. There are two main processes. Either a large tablet (known as a 'slug') is produced in a heavy-duty tabletting press (a process known as 'slugging') or the powder is squeezed between two rollers to produce a sheet of material ('roller compaction'). In both cases these intermediate products are broken using a suitable milling technique to produce granularmaterial, which is usually sieved to separate the desired size fraction. The unused fine material may be reworked to avoid waste. This dry method may beused for drugs that do not compress well after wet granulation, or those which are sensitive to moisture (Gergely, 1981).

2.7.1.2 Wet granulation

Wet granulation or agglomeration of powders proceeds by agitation of a powder or powder mix in the presence of a liquid, usually an aqueous binder or solution or water if the binder has been premixed with the dry powder. Granule formation and growth proceed because of effects of mobile liquid bondings formed between the primary particles (Swarbrick and Boylan, 1993).

When powders are very fine, fluffy, will not stay blended, or will not compress, then they must be granulated. A fluffy powder means that the required quantity of powder physically will not fit into the die cavity on the tablet press. The volume of fill (bulk density) is greater than that which is mechanically allowed. Wet granulation is one of the most common ways to granulate. The process can be very simple or very complex depending on the characteristics of the powders, the final objective of tablet making, and the equipment that is available. Some powders require the addition of only small amounts of a liquid solution to form granules. The liquid solution can be either aqueous based or organic based. Aqueous solutions have the advantage of being safer to deal with than organic base. Although some granulation processes require only water, many actives are not compatible with water. Water mixed into the powders can form bonds between powder particles that are strong enough to lock them together. However, once the water dries, the powders may fall apart. Therefore, water may not be strong enough to create and hold a bond. In such instances, a liquid solution that includes a binder (pharmaceutical glue) is required (Tousey, 2002). Wet granulation has a

number of advantages over the other granulation methods, but it is not suitable for hydrolysable and or thermolabile drugs such as antibiotics (Aulton, 1988).

Wet granulation is the most widely used manufacturing process in the pharmaceutical industry. In general wet granulation is done using a binder liquid consisting mostly of water and some polymer. The particle growth occurs by liquid bridging of powders and when water evaporates, the binder solidifies between the particles, forming a strong solid bond (Newitt and Conway-Jones, 1958). These bonds must be sufficiently strong to prevent breakdown of the granule to powder in subsequent handling operations (Summers 1988). The mechanisms of bonding in the wet state depend on capillary and viscous interparticle fluid forces or interfacial forces between particles (Augsberger and Vuppala 1997). During wet granulation each state of liquid content in the agglomerate represents a progressive increase in the moisture content, with a corresponding change in capillary forces. In practice, more than one bonding mechanism may be acting simultaneously.

According to Iveson *et al* (2001) wet granulation behaviour can be determined by three sets of rate processes: 1) wetting and nucleation; 2) consolidation and growth; and 3) breakage and attrition. Wetting and nucleation is the process of bringing liquid binder into contact with dry powder and trying to distribute this liquid uniformly throughout the powder to give a distribution of nuclei granules. Whenever material in the granulator collides and sticks together granule growth occurs. Two large granules can be united to form a larger granule or fine material can be stuck onto the surface of large pre-existing granules. When granules collide with other granules and equipment surfaces they gradually consolidate and this reduces their size and porosity. The granules gradually consolidate during agitation, and that increases their liquid pore saturation and alters their mechanical properties. Granule consolidation and liquid saturation might depend strongly on the formulation and binder properties. Breakage of wet granules will influence and may control the final granule size distribution. Attrition of dried granules leads to the production of dusty fines.

Typically wet granulation processing takes place in one of two types of closed granulating systems: fluid bed granulators or high shear mixers (Faure *et al*., 2001).

The properties of the granule are influenced by the manufacturing process, for example the granules formed in high shear mixers are harder and denser than those obtained in fluid bed granulation. Predicting the appropriate amount of water added to powders is important but difficult, since suitable moisture content varies with pharmaceutical formulations, due to powder properties. The amount of liquid required for a wet granulation process depends on a large number of factors, such as material properties, liquid characteristics and the mode of action of the equipment (Kristensen and Schaefer, 1987). For example, a crystalline substance can be dissolved in the granulating solution during the wet massing phase. The size of crystals produced in the recrystallization could be changed from the original. This may modify the dissolution rate and drug bioavailability. According to Mackaplow *et al* (2000) dry lactose granule size distribution was more dependent on the amount of added water than the primary particle size. This was attributed to the increased size and number of recrystallized lactose bridges holding the dried lactose particles together.

In wet granulation, drying or dehydration is required as a process of removing part of the water conbtained in a solid by thermal methods to obtain the moisture level best suited to the subsequent process (Terrier de la Chaise and LePerdriel, 1972). Drying is essentially a process of simultaneous heat and mass transfer. Heat, necessary for evaporation, is transferred from the surroundings to the particle surfaces by convection and from there further into the particle by conduction. On the surface water evaporates and passes on by convection to the surroundings. The three most common drying methods for pharmaceutical granules are tray drying, fluid-bed drying and vacuum drying (Van Scoik *et al*., 1993).

2.7.1.3 Direct compression

Direct compression is the process by which tablets are compressed directly from mixtures of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure, thus making pretreatment such as wet granulation unnecessary. Few drugs can be directly compressed into tablets of acceptable quality, but a number of materials are available which are directly compressible and which can serve as tablet diluents

(Shangraw *et al*., 1981).Most direct compression formulations consist of three basic types of ingredients

• An inert carrier (e.g., lactose) to provide volume for final dosage;

• A filler (e.g., microcrystalline cellulose) to form tablets; and

• The active ingredient(s).

These ingredients are mixed in a blender (Prescott and Hossfeld, 1994).

2.8 ASSESSMENT OF COMPRESSED TABLETS

The need for precisely defined and acceptable specifications for production control during manufacturing processes and for the final products, in order to assure reproducibility in the wide context of drug safety, is recognized. This is required not only by the pharmaceutical industry but also by national drug regulatory bodies and international organizations actively concerned with the quality control of medicines. The assurance of quality of medicines is the primary responsibility of the manufacturers (internal quality control).

However, it is recognized in most countries that the national health authorities must exercise comprehensive surveillance by legislative methods over pharmaceutical manufacturers within their jurisdiction, in order to ensure observance of good manufacturing practices and quality control of products. During research, development and formulation, physicochemical analysis and analytical profiles of drug substances provide good quality control data on which good decisions can be established (Deasy *et al*., 1976). Assessment of quality, safety and efficacy onstitutes an important component of pharmaceutical product evaluation, which is based on quality control tests. Tablets must have some apparent features, like certain amount of hardness and resistance to friability to withstand mechanical shocks encountered during their production, packaging and handling prior to use. In addition to these apparent features, they must meet other physical specifications and quantity standards. These include criteria for tablet dosage form uniformity (weight variation, content uniformity), disintegration, and drug dissolution (Howard *et al*., 1999; Lachman *et al*.,1990). All are tablet properties that can be utilized as parameters for drug quality control. Each property will influence

the other as hardness has influence on both friability and drug dissolution (Souto *et al*., 1989).

2.8.1 Hardness and Friability

Tablets require certain degree of strength and resistance to friability to withstand mechanical shocks of handling during manufacturing, packaging, shipping and utilization by the patient. Adequate tablet hardness and friability are necessary requisites for customer acceptance (Getie *et al*., 1998) and have adequate impact on drug product quality. There are factors, which may alter tablet hardness and friability. These are changes in particle size, distribution of the granulation mix and lubricants. Large particles of low density will produce softer tablets whereas smaller particles of high density granules will produce relatively stronger tablets (Lachman *et al*., 1990, James 1996). Studies with Phenobarbital tablets quality control showed that duration of mixing with lubricant, maximal compression force and compression rate have influence on various properties of the tablets. These variables of tablet manufacturing process are found to have a marked influence on hardness, friability, disintegration, and dissolution properties (Souto *et al*., 1989, Shah *et al*., 1977).

2.8.2 Weight variation

Weight variation requirements may be applied where the product to be tested contains 50 mg or more of an active ingredient comprising 50% or more, by weight, of the dosage form unit, and otherwise content uniformity. The United States Pharmacopoeia (USP) contains a test for the determination of dosage form uniformity for uncoated tablets. Ten tablets are weighed individually and the average weight calculated. The tablet weight of each tablet is then subtracted from the mean weight and the percentage deviation of each tablet from the mean calculated (Kovacs *et al*., 1980).

2.8.3 Disintegration Test

For the active medicinal agent in a tablet to become fully available for absorption, the tablet must first disintegrate and discharge the drug to the body fluids for dissolution. Tablet disintegration also provides drug particles with an increased surface area for localized activity within the gastrointestinal tract

(Howard *et al*., 1999). Before a tablet goes into solution it must breakdown into smaller particles or granules by the process of disintegration. Complete tablet disintegration is the state in which any residue of the tablet is a soft mass having no palpably firm core.

Disintegration testing is more appropriate when a relationship to dissolution has been established and it is a limiting factor of drug dissolution, particularly with low aqueous solubility drugs likecarbamazepine. For tablets to be disintegrated, it is necessary to overcome the cohesive forces introduced into the mass by compression and by any binder present, which is usually practised by incorporating disintegrants. Disintegration could be affected by formulation factors and properties and concentration of excipients, in particular. Studies done on paracetamol and oxytetracycline tablets revealed that variations with various formulation and processing variablesand excipients lead to variations in physical properties like disintegration (Lachman *et al*., 1990; Esezobo, 1985).

Porosity, hydrophilicity, swelling ability of particles and interparticle forces are important factors for tablet disintegration. Tablet porosity is related to water absorption, which is an important step of disintegration process. There are factors related to the inner structure of the tablets and hydrophilicity of excipients affecting wettability of the formulation and playing a vital role in the process of disintegration (Lopez-Solis *et al*., 2001; Bi *et al*., 1999).

2.8.4 Dissolution Test

Dissolution is defined as the process by which a solid substance enters the solvent to yield solution, that is, the process by which a solid substance dissolves (Banakar, 1992). This means that the tablets must break down into smaller particles through disintegration and render greater surface area to the dissolving media to bring the tablets into solution. Dissolution is required for absorption and must be related to the availability of the drug to the body (Aulton, 2002). The amount of drug substance that goes into solution per unit time under tandardized conditions is called dissolution rate. This depends on several factors like ageing, excipient type (surfactants, disintegrants), tablet integrity and other drugs. Some excipients like sorbitol and sodium lauryl sulfate increase dissolution rate. A study with paracetamol tablet showed that mode of excipient incorporation also influences

the rate of dissolution. External addition of aerosil led to increased dissolution rate while internal addition resulted in decreased dissolution rate of the tablet (Esezobo,1985; Gordon *et al*., 1993).

Dissolution tests are employed to establish the quality of drug products, mostly tablets and capsules, based on in - vitro drug release characteristics of these products. In reality, a dissolution test may be considered as a simple extraction step in a vessel with a stirrer. Most of the commonly used apparatuses in this regard are known as paddle and basket apparatuses, in which a round bottom vessel containing a stirrer referred to as paddle (an inverted T – shaped bar) or small wired cage (known as basket), respectively, are used (United States Pharmacopoeia, 2009).

The quality of an oral drug product (tablet and capsule) is based on the fact that the drug will be released from a product in a predictable and reproducible manner and dissolved in the fluid present in the human gastrointestinal (GI) tract, in particular, small intestine. Thus, this *in vivo* drug dissolution step, also interchangeably referred to as drug release, becomes a critical step for developing a product and later assessing its quality.

Since drug absorption depends on the drug in the dissolved state, the dissolution property is highly important for bioavailability. If the rate of dissolution is lower than the rate of absorption (that is, if the rate of dissolution is the rate-limiting step), then the dissolution rate determines the bioavailability. The therapeutic effect of different formulations of the same drug depends on the rates at which the drug is released (Banakar and Makoid,1996).

CHAPTER 3
EXPERIMENTATION

3.1 MATERIALS

3.1.1 Plant Material

The dry fruit pods of *Parkia biglobosa* were collected from four (4) different locations in Ghana namely; Bunkpurugu in the Bunkpurugu/Yunyoo District, in the Northern Region, Wiid at Bawku in the Bawku District, in the Upper East Region, Jirapa in the Jirapa/Lambushi District, in the Upper West Region and Dawadawa No.1 in the Kintampo District, in the Brong Ahafo Region during the March/April, 2011 fruiting season. The fruits were packed in jute bags. The fruits were authenticated by Mr. G. H. Sam of the Department of Herbal Medicine, Faculty of Pharmacy and Pharmaceutical Sciences KNUST where a voucher specimen of each sample was deposited. They were then stored in a cool dry place in the laboratory store room until used.

3.2 REAGENTS/CHEMICALS

Chemicals

Potassium hydrogen phosphate, Iodine crystals, Potassium iodide, Paracetamol powder, Sodium starch glycolate, Copper II sulphate, Acacia powder, Sodium hydroxide and Magnesium stearate were all obtained from BDH Laboratory Chemicals Limited, Poole, England.

Reagents

Hydrochloric acid, Acetone, Alpha naphthol, Sulphuric acid, Phloroglucinol, Ferric chloride, Dragendoff's reagent, Glacial acetic acid, Ethylacetate, Methanol, Lead acetate, Methyl red solution, Bromocresol green (0.1%),Fehling's solution, Resorcinol, Petroleum ether 60^{o}, Chloroform and Ethanol ; all obtained from BDH Laboratory Chemicals Limited, Poole, England were also used in these experimentations.

3.3 EQUIPMENT AND APPARATUS

Equipment/ Apparatus

- Clifton laboratory centrifuge — Nickel – Electro Ltd., England
- Ultra sonic bath — Nickel – Electro Ltd., England.
- Retsch sieve shaker — AS 200; Retsch GmbH, Haan, Germany.
- Abbe Refractometer Model 2 WA – J — Shanghai Optical Instrument, China.
- Microprocessor pH meter — HANNA Instruments, pH 210, Romania.
- Gallenhamp Oven 300 plus series — England.
- Brabender Viscoamylograph Viskograph — EBrabender Instrument Inc. Duisburg, Germany.
- DP30 Single punch tablet press — Pharmao Industries Co.Ltd, China.
- Digital analytical balance — Adam Equipment Co. Ltd. Milton Keynes, UK.
- Mitutoyo Vernier caliper — Mitutoyo Japan.
- Monsanto hardness tester — Manesty machines Ltd., England.
- Erweka friability test apparatus — Erweka friability machine TA 20, Germany.
- Disintegration rate test unit — Erweka disintegration machine, Germany.
- BP Paddle Dissolution Test Apparatus — G.B. Caleva Limited, Dorset, England.
- Spectrophotometer — Perkin Elmer spectrophotometer, Massachusetts, USA.

3.4 METHODS

3.4.1 Processing of *Parkia biglobosa* fruit pulp flour

The *P. biglobosa* fruit pods were sorted, cleaned, and split open manually. The yellow pulp along with attached seeds was removed, sun dried for 3 days and pounded lightly in a mortar with a pestle. The pulp was separated from the seeds and pounded thoroughly and sieved through 40 mesh sieve. The fruit pulp samples (500g each) were packed in high density polyethylene (HDPE) bags and labeled A, B, C, and D representing the various locations; Bunkpurugu, Wiid, Jirapa and Kintampo, respectively and stored in a refrigerator until required. The physical, chemical and functional properties of the pulp flour were determined.

3.4.2 Macroscopic and organoleptic properties of *Parkia biglobosa* fruit pulp

The macroscopic and organoleptic properties of the *P. biglobosa* fruit pulp samples obtained were evaluated by observing specified characteristics of the fruit pulp for any marked differences among them viz, appearance, colour, taste, odour and flavour.

3.4.3 Phytochemical analysis

The Phytochemical tests conducted on the fruit pulp were: carbohydrate test, tests for reducing sugars, deoxy sugar, ketones, pentoses, starch, tannins, glycosides, saponins, alkaloids and flavonoids.

3.4.3.1 Molisch's Test: To a solution of each of the samples was added a few grain's of α-naphthol and conc. H_2SO_4 poured gently down the side of the test tube. A purple colour indicate a positive test. A ring formation with the conc. H_2SO_4 gently poured in to form a layer below the aqueous solution indicate the presence of soluble carbohydrate (Trease and Evans, 1983).

3.4.3.2 Fehling's Test (Reducing sugars): A small portion of each of the samples was shaken with distilled water and filtered. The filtrate was boiled with drops of Fehling's solution A and B for 2 minutes. An orange-red precipitate on boiling with Fehling's solution indicate the presence of reducing sugars (Trease and Evans, 1983).

3.4.3.3 Keller-killiani Test (Glycosides): A small quantity of each of the samples was diluted in 5 ml of distilled water. 2 ml of glacial acetic acid containing one drop of ferric chloride solution was added to each. This was underlayed with 1 ml of concentrated sulfuric acid. A redish brown ring is formed at the interface and upper layer turns bluish green on standing indicates the presence of a deoxy sugar characteristic of cardiac glycosides (Trease and Evans, 1983).

3.4.3.4 Iodine Test (Starch): To 0.1g of each of the samples was added about 1 ml of iodine solution. A blue - black colour formation indicate the presence of starch (Trease and Evans, 1983).

3.4.3.5 Tannins:

3.4.3.5.1 Ferric Chloride Test: A small quantity of each sample was boiled in 10 ml of water in a test tube and then filtered while hot and a few drops of 0.1% ferric chloride solution were added to the filtrate. A brownish g reen or a blue-black colouration indicate a positive test (Odebiyi and Sofowora, 1978).

3.4.3.5.2 Lead Acetate Test: A small quantity of each sample was placed in a test tube and diluted with 5 ml of distilled water. Few drops of a 1% solution of lead acetate were added to each. A yellow or red precipitate indicate a positive test (Trease and Evans, 1983).

3.4.3.6 Selivanoff's Test (Ketones): Few crystals of resorcinol were added to a solution of each sample and warmed on a water bath with an equal volume of conc. HCl. The development of a rose colour indicate the presence of ketones (Trease and Evans, 1983).

3.4.3.7 Pentoses: A solution of each sample was heated in a test tube with an equal volume of HCl containing a little phloroglucinol. Formation of a red colour indicated the presence of pentoses (Trease and Evans, 1983).

3.4.3.8 Saponins: A small quantity of each sample was boiled with 5 ml of distilled water, filtered and cooled (Trease and Evans, 1983).

3.4.3.8.1 Frothing: To the filtrate (2.5 ml) of each sample, about 10 ml of distilled water was added and shaken vigorously for 2 minutes. Frothing observed indicated a positive test.

3.4.3.8.2 Emulsification: To the filtrate (2.5 ml) of each sample was added 3 drops of olive oil and shaken vigorously for 2 minutes. An emulsified layer indicated a positive test.

3.4.3.9 Alkaloids: A Small quantity of each sample was stirred with 5 mL of 1% hydrochloric acid for five minutes on a water bath and then filtered. Of the filtrate of each sample was divided into two portions. Mayer's reagent was added to one portion; occurrence of creamy white precipitate was taken as positive. To the second portion few drops of Dragendorff's reagent were added and appearance of orange red precipitate was regarded as positive for the presence of alkaloids (Harborne, 1973; Trease and Evans, 1983).

3.4.3.10 Flavonoids: Three methods were used to determine the presence of flavonoids in the extracts (Sofowora, 1993; Harborne, 1973).

3.4.3.10.1 Method-1: Dilute ammonia solution (5 ml) was added to aqueous filtrate of each sample followed by addition of 1ml concentrated H_2SO_4 acid. A yellow colouration that disappeared on standing indicated the presence of flavonoids.

3.4.3.10.2 Method 2: Few drops of 1% aluminium solution were added to aqueous filtrate of each sample. Formation of a yellow coloration indicated the presence of flavonoids.

3.4.3.10.3 Method 3: A small portion of the each sample was heated with 10 ml of ethyl acetate over a steam bath for 3 min. The mixture was filtered and 4 ml of the filtrate was shaken with 1 ml of dilute ammonia solution. Formation of a yellow coloration indicated the presence of flavonoids.

3.4.4 PHYSICOCHEMICAL CHARACTERIZATION OF *PARKIA BIGLOBOSA* FRUIT PULP.

3.4.4.1 Solubility Test

The *P. biglobosa* fruit pulp was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with standard specifications (British Pharmacopoeia, 2004).

3.4.4.2 pH Determination

This was done by shaking 1% $^{w}/_{v}$ dispersion of the sample in water for 5 minutes and the pH determined using a digital pH meter (Anoop *et al*., 2010).

3.4.4.3 Particle size determination of *Parikia biglobosa* pulp flour

Particle size determination was carried out by weighing 150 g of the powdered sample which was shaken through a stark of sieves consisting of aperture size 75 to 850 μm arrange in descending order with a collector pan at the bottom on an electromagnetic sieve shaker. The percentage weight of the flour retained on each sieve was determined (Sefa-Dedeh, 1989). The ease of passage of the flour particles in each of the mesh is an indication of the particle size.

3.4.4.4 Powder flow characterization

3.4.4.4.1 Angle of Repose

The static angle of repose (Ɵ) was measured according to the fixed funnel and free standing method. A funnel was clumped with its tip 2cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the angle of repose calculated using the equation: $\tan \theta = 2h/D$ (Anoop *et al.*, 2010).

3.4.4.4.2 Bulk and Tap Densities

Ten gram (10 g) of sample was weighed into 50ml graduated measuring cylinder and the volume, V, occupied by each of the samples without tapping was noted. After 150 taps on the table, the occupied volume V_{150} was noted. The bulk and

tap densities were calculated as the ratio of weight to volume (Vand V_{150} respectively).
(Annop *et al*., 2010).

3.4.4.4.3 Hausner's Ratio

The Hausner's ratio was calculated as the ratio of tapped density to bulk density of the samples.

$$\text{Hauser's ratio} = \frac{\text{Tapped density (Dt)}}{\text{Bulk density (Db)}}$$

3.4.4.4.4 Carr's Compressibility Index (%)

Carr's index was calculated using the equation

$$\text{Carr's index (\% compressibility)} = \frac{\text{Tapped density (Dt) – bulk density (Db)}}{\text{Tapped density (Dt)}} \times 100$$

(Annop et *al*., 2010)

3.4.4.5 SWELLING CAPACITY

Swelling power was determined with the method described by Leach *et al* (1959) with modification for small samples. One gram of the sample was mixed with 10ml distilled water in a centrifuge tube and heated at 80ºC for 30 minutes. The mixture was continually shaken during the heating period. After heating, the suspension was centrifuged at 3000 rpm for 10 minutes. The supernatant was decanted and the weight of the paste taken. The swelling power was calculated as:

$$\text{Swelling power} = \frac{\text{wt of paste}}{\text{Wt of dry sample}}$$

3.4.4.6 MOISTURE SORPTION CAPACITY

Two gram (2 g) of each sample material was accurately weighed and evenly distributed over the surface of a 70 mm tarred petri dish. The samples were then placed in a large desiccator containing distilled water on its reservoir (RH= 100 %) at room temperature and the weight gained by the exposed samples at the end of a five day period was recorded and the amount of water sorbed was calculated from the weight difference (Ohwoavworhua *et al*., 2004).

3.4.4.7 WATER BINDING CAPACITY

Water binding capacity was determined using modified method of Medcaf and Gilles (1965). 1.0 g of sample was suspended in 10 ml of distilled water and was centrifuged for 10 minutes at 3000 rpm. Then the weight of the centrifuge tube and content was determined after decanting the water and allowed to drain; the bound water was determined by the change in weight. It was calculated by the formula below.

$$\text{Water binding capacity (WBC)} = \frac{\text{Bound water (g)}}{\text{Wt of sample (g)}} \times 100$$

3.4.5 PROXIMATE PROPERTIES OF *PARKIA BIGLOBOSA* FRUIT PULP

Moisture, Ash, Fat, Fibre, crude protein and carbohydrate and sugar contents were determined by the AOAC official methods (AOAC, 1990). Carbohydrate content was calculated by difference.

3.4.5.1 Moisture Content

Two gram (2 g) of *P. biglobosa* pulp powder was weighed accurately into three previously ignited and weighed crucibles. The crucibles were placed in an oven thermostatically controlled at 105^{o}C for 5hours after which they were removed and placed in desiccators to cool. They were each weighed and the moisture content determined (AOAC, 1990).

3.4.5.2 Ash Value

Two gram (2 g) of *P. biglobosa* pulp powder was weighed accurately into three previously ignited and weighed crucibles and placed in a muffle furnace (pre – heated to 450^{o}C) for 2 hours to incinerate after which the crucibles were removed and transferred directly into desiccators and allowed to cool. They were each weighed and the percentage ash determined (AOAC, 1990).

3.4.5.3 Crude Fat

Two gram (2 g) of *P. biglobosa* pulp powder was wrapped in a 22 x 80 mm filter paper an placed in a thimble with a small ball of cotton wool to prevent loss of the samples. The thimble was then transferred into a previously dried (hot oven at 100^{0}C), 250 ml round bottom flask and weighed accurately. Antibumbing granules

(asbestos) were also added. 150 ml of petroleum spirit, (60 – 80°) was added to the flask and the apparatus assembled (distillation apparatus). A quick fit condenser was connected to the soxhlet extractor and refluxed for 4 hours on high heat on a heating mantle. The flask was removed and the spirit evaporated on a steam bath. The flask and fat was heated for 30 minutes in an oven at 103°C. after which it was removed and cooled to room temperature in a desiccator. It was weighed and the weight of fat obtain determined (AOAC, 1990).

3.4.5.4 Crude Fibre

The *P. biglobosa* pulp sample obtained from crude fat determination was transferred to a 750 ml Erlenmeyer flask and 0.5 g of asbestos added. 200 ml of 1.25 % H_2SO_4 solution was also added and the flask immediately set on a hot plate and a condenser connected. The content was boiled until the sample was thoroughly wet. The flask was removed after 30 minutes and the contents filtered immediately through a linen cloth in a funnel and washed with boiling water until washings were no longer acidic. The asbestos was washed back into the flask with 200 ml of 1.25 % NaOH and refluxed for 30 minutes. It was filtered through linen cloth and washed thoroughly with boiling water. The residue was transferred to the funnel with water and washed with 15ml alcohol. It was transferred into a crucible and the contents dried for 1 hour at 100°C in an oven. This was removed and cooled in a desiccator and reweighed. The crucible was ignited in an electric furnace for 30 minutes, cooled and reweighed. The percentage of crude fibre present was then determined (AOAC, 1990).

3.4.5.5 Protein

(a) Digestion

Two gram (2 g) of *P. biglobosa* pulp sample was weighed accurately into a digestion flask and a half selenium based catalyst tablet with a few anti – bumping agent (asbestos) added. 25 ml of concentrated H_2S0_4 solution was added and shaken so that the entire sample was thoroughly wet. The flask was placed on digestion burner and heated slowly until bottling ceases and the resulting solution clear. It was cooled to room temperature. The digested sample solution was transferred into a 100 ml volumetric flask and made up to volume with distilled water.

(b) Distillation

The distillation apparatus was flushed out before use, by boiling the distilled water in a steam generator of the apparatus with the connections arranged to circulate through the inner decomposition flask and out through the condenser, for 10 minutes. 25 ml of 2 % boric acid was pipetted into a 250 ml conical flask and 2 drops of mixed indicator added. The liquid was drained from the steamtrap. The conical flask with its content was placed under the condenser in such a position that the tip of the condenser was completely immersed in solution. The stopcock of the steamjacket was opened and the 10 ml of digested sample transferred into it. Excess of 40 % NaOH (20 ml) was added to the decomposition flask. The funnel stopcock was closed. The liberated ammonia was driven into the collection flask by shutting the stopcock on the steam trap outlet. The boric acid changed to bluish green as soon as it came into contact with the ammonia and the distillation continued for 5 minutes. The receiving flask was lowered so that the condenser tip was just above the liquid. The end of the condenser was washed with a little distilled water and distillation continued for another 30 seconds.

c) Titration

The nitrogen in the distillate was determined by titrating with 0.1N HCl solution. The acid was added until the solution was colourless. Additional acid was added until the solution changed to pink. The same procedure was repeated for blank determination (without the sample being analysed).

(d) Calculation

The crude protein was determined using the equation below.

$$\% \text{ Total Nitrogen} = \frac{100 \times (V_A - V_B) \times N_A \times 0.01401 \times 100}{W \times 10}$$

Where, V_A = vol. of standard acid used in titration

V_B = vol. of standard acid used in blank

N_A = normality of acid (HCl)

W = weight in grams of sample (AOAC,1990).

3.4.5.6 Carbohydrate

Carbohydrate percentage was obtained by difference usingthe fresh weight derived data and the following equation: % carbohydrate = 100 – (% protein + % fat + % ash + % moisture + % fibre)

3.4.5.7 Sugar

Abbe Refractometer, reading in (^{o}Brix) units with a sugar content scale between 0 – 95 % Brix was used for the determination.

The water circulating in the refractometer was adjusted at 20 ± 0.5^{o}C so that it registers for distilled water a soluble solid (sucrose) content of zero and allowed to flow to bring the prism of the refractometer to the same temperature which remained constant during the determination. Two gram (2 g) of the sample was accurately weighed on an analytical balance, mixed with 100ml of distilled water in a beaker and heated to boiling and allowed to boil gently for 2 – 3 minutes. It was cooled and mixed thoroughly. It was then filtered and 3 drops were put on the fixed prism of the refractometer and immediately adjusted the movable prism until the line dividing the light and dark parts of the surface was brought in the field of view and the value of sugar content read directly (AOAC, 1990).

3.4.6 PASTING CHARACTERISTICS *PARKIA BIGLOBOSA* FRUIT PULP

A smooth paste was made of the prepared flour using 40 g of the *P. biglobosa* flour in 420 ml distilled water for viscoelastic analysis using Brabender Viscoamylograph equipped with a 1000 cmg sensitivity carriage. The smooth paste was heated at a rate of 1.5^{o}Cmin^{-1} to 95^{o}C and maintained for 15 minutes. It was then cooled at same temperature range and maintained for 15 minutes. Viscosity profile indices were recorded for pasting temperature, peak temperature, peak viscosity, viscosity at the end of the holding time at 95^{o}C, viscosity at the end of the holding time at 50^{o}C, breakdown and setback viscosities (Mazurs *et al.*,1957).

3.4.7 FORMULATION AND PREPARATION OF PARACETAMOL TABLETS

Wet granulation method was used to prepare granules for the compression of tablets containing various concentrations of *P. biglobosa* pulp as binder. The formulation was developed by using paracetamol BP as model drug.

The composition of the different formulations used contained 500 mg paracetamol per tablet with a batch size of 100 tablets of 600 mg weight. All ingredients were mixed manually in a mortar and water was used as granulating fluid. The wet mass obtained was then passed manually through a number 12 mesh sieve. The granules were dried at 60ºC for 30 minutes in a hot air oven. The dried granules were passed through sieve number 16 and were compressed by using single punch tablet machine. Before each compression, the punch and die surfaces were lubricated with a 1% dispersion of magnesium stearate in chloroform to prevent sticking and allow easy ejection of tablets from the die. Two sets (A and B) of formulations were prepared . Set A had six batches (Table 3.1). The first five (A_1 – A_5) had standard ingredient but with varying concentrations (1 %, 3 %, 5 %, 8 %, 12 % w/w respectively) of the *P. biglobosa* fruit pulp as binder whilst the sixth batch (A_6) had Acacia gum (5 % w/w) as reference binder. Mannitol was used as a diluent to adjust tablet weight. Set B had five batches (Table 3.2). The first four (B_1 – B_4) made of standard ingredients but with different concentrations (of 2 %, 4 %, 6 % and 8 % w/w) respectively, of the *P. biglobosa* as disintegrant and the fifth had 4%w/w Sodium starch glycolate as reference disintegrant.

Table 3.1 Composition of paracetamol tablet formulation with varying concentration of *Parkia biglobosa* fruit pulp as a binder.

Ingredients	Weight of Ingredients (mg)					
	Batches					
	A1	A2	A3	A4	A5	A6
Paracetamol	500	500	500	500	500	500
Parkia biglobosa fruit pulp	6 (1)	18 (3)	30 (5)	48 (8)	72 (12)	-
Manitol	70	58	42	28	4	46
Sodium starch glycolate (4 % w/w)	24	24	24	24	24	24
Acacia gum	-	-	-	-	-	30 (5)
Total weight per tablet (mg)	600	600	600	600	600	600

Key: Figure in brackets represent concentration of binder (% w/w).

Table 3.2 Composition of paracetamol tablet formulation with varying concentration of *Parkia biglobosa* fruit pulp as disintegrant.

Ingredients	Weight of ingredients (mg)				
	Batches				
	B1	B2	B3	B4	B5
Paracetamol	500	500	500	500	500
Parkia biglobosa fruit pulp	12 (2%)	24 (4%)	36 (6%)	48 (8%)	-
Polyvinylpyrrolidone (PVP) (3 % w/w)	12	12	12	12	18
Manitol	76	64	52	40	58
Sodium starch glycolate	-	-	-	-	24 (4%)
Total weight per tablet (mg)	600	600	600	600	600

Key: Figure in brackets represent concentration of disintegrant (% w/w).

3.4.8 ASSESSMENT OF PARACETAMOL TABLETS

3.4.8.1 Uniformity of weight

Twenty tablets were taken at random from each batch and their weights were determined individually and collectively on a digital weighing balance. The average weight of each batch was determined. The deviation of each of the individual tablets in each batch from the average weight of the sample was determined. The percentage deviation was also calculated. For a sample to pass the uniformity of weight test not more than two of the individual weights should deviate from the average weight by more than the percentage deviation shown in the table below and none should deviate by more than twice that percentage (British Pharmacopoeia, 2007).

Table 3.3 Limit of uniformity of weight scale.

Pharmaceutical form	Average tablet weight	Percentage deviation
Tablets (uncoated)	80mg or less	10
	More than 80mg and less than 250mg	7.5
	250mg or more	5

(British Pharmacopoeia, 2007)

3.4.8.2 Thickness of tablets

The thickness of six tablets of each batch was measured using Mitutoyo Vernier caliper and average thickness for each sample determined.

3.4.8.3 Hardness Test

The load (Newtons) required to diametrically break a tablet was determined at room temperature using Monsanto hardness tester. Ten tablets randomly selected from each batch were used for the test. It was ensured that all fragments of broken tablets were removed before the next determination. The hardness values were read from a graduated scale in kg/cm^2 after the tablets cracked or crushed (1 kg/cm^2 or $kgf/cm^2 \equiv 98066.5\ N/m^2$ or Pascal).

3.4.8.4 Friability Test

The friability of the tablets was determined with a scientific Erweka Friability Test Apparatus. Twenty tablets were randomly selected and weighed on a digital analytical balance and the weight recorded. The tablets were placed in the transparent drum of the apparatus and set to rotate at 100 revolutions per minute (rpm). The weight of dedusted tablets after the test was taken and the difference in weight expressed as a percentage of the initial weight (British Pharmacopoeia, 2007).

3.4.8.5 Disintegration Test

Disintegration rate test for six tablets selected at random from each batch was determined using a disintegration rate test unit. The apparatus was operated using distilled water as the medium and immersion fluid and maintained at 37 ± 2ºC. One tablet was placed in each of the six tubes of the disintegration basket. The time taken for all tablet particles in each unit to pass through the mesh was recorded. All measurements were made in duplicates.

3.4.8.6 Calibration

Appropriate amounts of pure Paracetamol powder was dissolved in 0.1 M NaOH to produce 0.0001 % w/v, 0.0002 % w/v, 0.0003 % w/v, 0.0004 % w/v and 0.0005 % w/v solutions. The absorbances of these solutions were determined at 257 nm. A calibration curve showing the relationship between concentration and absorbance was plotted and the equation and correlation values of the curve generated from the scatter plot.

3.4.8.7 In vitro drug release (dissolution test)

The dissolution of the compressed tablets was determined using a BP Paddle Dissolution Test Apparatus. For each batch of Paracetamol tablets, the test conditions were: 900 ml of phosphate buffer pH 5.8 at 37.0 ± 0.50ºC as dissolution medium and a paddle speed of 50 rpm.

Each of the vessels contained 900 ml of the prepared buffer. The apparatus was then set up with paddles and for each test, a tablet was carefully introduced into each of the eight vessels of the apparatus. 10 ml samples were withdrawn at 5,

10, 15, 30, 45 and 60 minute intervals, 10ml of fresh dissolution medium was used to replace each volume withdrawn immediately to maintain the sink condition. The dissolution was carried out for 1 hour. Each sample withdrawn was filtered and 0.90ml of each filtrate diluted to 50 ml with 0.1M NaOH. The diluted solution was expected to contain 0.00075 % w/v paracetamol before being assayed spectrophotometrically at 257 nm, using 0.1M NaOH in the reference cell. The amount of drug (paracetamol) released was then determined from the calibration curve. A graph of percentage drug released against time was plotted to establish the dissolution profile of paracetamol from the uncoated tablets.

3.4.9 Statistical Analysis

The determinations were undertaken in duplicates (except where indicated) and the results expressed as mean ± standard deviation. One – Way Analysis of variance (ANOVA) and Post hoc multiple comparisons were carried out using Tukey's Multiple comparison test. The level of significance used in all tests was $p<0.05$. The data generated was analysed using the statiscal package provided by GraphPad Prism version 5.01 for Windows (GraphPad Software Inc. San Diego California).

3.5 RESULTS AND CALCULATIONS

3.5.1 Physical properties of *Parkia biglobosa* fruit pulp .

Table 3.4 Macroscopic and organoleptic properties of *P. biglobosa* fruit pulp samples.

Physical properties	Observation			
	Sample A	Sample B	Sample C	Sample D
Appearance	Yellow	Bright yellow	Bright yellow	Deep yellow
Taste	Sweet	Sweet	Sweet	Sweetest
Odour	Characteristic	Characteristic	Characteristic	Characteristic
Flavour	Desirable	Desirable	Desirable	Most Desirable

3.5.2 Phytochemical properties of *Parkia biglobosa* fruit pulp samples.

Table 3.5 Phytochemical properties of *P. biglobosa* fruit pulp samples.

No	Test	Observation			
		Sample A	Sample B	Sample C	Sample D
1	Molisch's test for Carbohydrate	+	+	+	+
2	Selivanoff's test for Ketones	+	+	+	+
3	Pentoses test	+	+	+	+
4	Keller-Killiani test for Deoxy – sugars	+	+	+	+
5	Test for starch	-	-	-	-
6	Test for Tannins	-	-	-	-
7	Test for Glycosides	+	+	+	+
8	Test for Saponins	+	+	+	+
9	Test for Alkaloids	-	-	-	-
10	Fehling's test for reducing sugars	+	+	+	+
11	Test for Flavonoids	+	+	+	+

Key: Present = + : Absent = -

3.5.3 Particle size and size distribution estimation of *Parkia biglobosa* fruit pulp powder.

Table 3.6 Results of the sieving analysis of the selected *P. biglobosa* fruit pulp.

Particle size range (μm)	Particle size mean (μm)	Frequency (%)
> 850	850.0	0
425 – 850	637.5	33.97
250 – 425	337.5	78.27
180 – 250	215.0	97.26
75 – 180	127.5	99.39
75 – 0	75	0
d_{geo} (μm)		420
S_{geo} (μm)		1.43

3.5.4 Physicochemical properties of the *Parkia biglobosa* fruit pulp.

Table 3.7 Results of the determined physicochemical properties of the *P. biglobosa* fruit pulp.

Parameters	*Parkia biglobosa fruit pulp*	Reference
Solubility	Soluble in water, sparingly soluble in chloroforrn and insoluble in acetone, alcohol.	
pH	6.31	
Angle of repose	45.0^0	$\leq 30^0$
Bulk density (g/ml)	0.18	≤ 1.2
Tapped density (g/ml)	0.24	≤ 0.45
Hausner's ratio	1.67	≤ 1.25
CompressibilityIndex (%)	40.0	$\leq 35\%$
Particle size (μm)	420	
Swelling power (g/g)	4.25	
Moisture sorption capacity (%)	42.50	
Water binding capacity (%)	446	

3.5.5 Proximate properties of the *Parkia biglobosa* fruit pulp

Table 3.8 Results of the proximate composition of the *P. biglobosa* fruit pulp.

Parameters	Values (%)
Moisture content	8.66 ± 0.01
Ash content	2.40 ± 0.06
Fat content	0.13 ± 0.01
Crude fibre	8.75 ± 0.01
Protein	6.64 ± 0.01
Carbohydrate	76.80 ± 0.07
Sugar content(^{o}Brix)	3.66 ± 0.01

3.5.6 Pasting characteristics of the *Parkia biglobosa* fruit pulp and acacia gum.

Table 3.9 Results of the pasting analysis of the *P. biglobosa* fruit pulp and Acacia gum.

Sample	Peak viscosity (RVU)	Final viscosity (RVU)	Breakdown (BU)	Set back viscosity (RVU)	Peak time (min.)	Pasting temp. (^{o}C)
P.biglobosa fruit pulp	9.0 ±7.07	15.5 ±3.54	7.5 ± 4.95	15.0 ± 1.41	7.08 ± 8.59	60.70 ± 12.02
Acacia gum	5.5 ± 0.71	7.0 ± 1.41	0.0±0.00	1.5 ± 0.71	21.53±30.44	72.35 ± 31.61

3.5.7 Analysis of the compressed paracetamol tablets

Table 3.10 The Thickness of the formulated tablets with varying concentration of *P. biglobosa* fruit pulp or Acacia gum as binder.

Binder	Formulation code (%w/w)	Tablet thickness (mm)
P. biglobosa fruit pulp	A_1	6.2 – 6.3
	A_2	6.2 – 6.3
	A_3	6.2 – 6.3
	A_4	6.2 – 6.3
	A_5	6.2 – 6.3
Acacia gum	A_6	6.2 – 6.3

Table 3.10.1 The Thickness of formulated tablets with varying concentration of *P. biglobosa* fruit pulp or Sodium starch glycolate as disintegrant.

Disintegrant	Formulation code (% w/w)	Tablet thickness
P. biglobosa fruit pulp	B_1	6.2 – 6.3
	B_2	6.2 – 6.3
	B_3	6.2 – 6.3
	B_4	6.2 – 6.3
Sodium starch glycolate	B_5	6.2 – 6.3

Table 3.11 Results of the uniformity of weight test of formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or Acacia gum as binder.

Binder	Batches	Weight of 20 tablets/g (X)	Numb. of tablets that Deviated By > ± 5% (%)	Inference
P. biglobosa fruit pulp	A_1	11.949	0	Passed
	A_2	12.003	0.	Passed
	A_3	12.049	0	Passed
	A_4	12.038	0	Passed
	A_5	11.923	0	Passed
Acacia gum	A_6	12.100	0	Passed

Table 3.11.1 Results of the uniformity of weight test of formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp pulp or Sodium starch glycolate as disintegrant.

Disintegrant	Formulation (% w/w)	Weight of 20 tablets/g (X)	Numb. of tablets that Deviated By > ± 5% (%)	Inference
P. biglobosa fruit pulp	B_1	11.967	0	Passed
	B_2	11.984	0	Passed
	B_3	11.909	0	Passed
	B_4	11.948	0	Passed
Sodium starch glycolate	B_5	12.074	0	Passed

Table 3.12 Results of the hardness test for the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or Acacia gum as binder.

Binder	Formulation code (% w/w)	Force for 10 tablets (N)	Mean (N)	Minimum Force (N)	Maximum Force (N)	Inference
P.biglobosa fruit pulp	A_1	220.50	22.05 ± 3.01	19.60	24.47	Failed
	A_2	303.80	30.38 ± 2.51	29.40	34.30	Failed
	A_3	408.30	40.83 ± 2.73	39.20	44.10	Passed
	A_4	499.80	49.98 ± 3.34	44.10	53.90	Passed
	A_5	543.90	54.39 ± 3.83	49.00	58.80	Passed
Acacia gum	A_6	460.60	46.06 ± 4.13	39.20	53.90	Passed

Table 3.12.1 Results of the hardness test for the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or sodium starch glycolate as disintegrant.

Disintegrant	Formulation Code (% w/w)	Force for 10 tablets (N)	Mean (N)	Minimum Force (N)	Maximum Force (N)	Inference
P. biglobosa fruit pulp	B_1	441.00	44.10 ± 3.10	35.93	49.00	Failed
	B_2	447.87	44.79 ± 4.92	39.20	52.27	Passed
	B_3	452.42	44.24 ± 5.98	39.20	55.53	Passed
	B_4	450.80	45.08 ± 6.21	39.20	52.27	Passed
Sodium starch glycolate	B_5	444.27	44.43 ± 5.24	39.20	55.90	Passed

Table 3.13 Results of the friability test of the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or acacia gum as binder.

Binder	Number of tablets	Formulation code (% w/w)	Weight of tablets beforeTest (g)	Weight of tablets after test (g)	% of weight loss	Inference
P. biglobosa fruit pulp	20	A_1	9.22	9.10	1.27 ± 0.05	Failed
		A_2	9.22	9.14	0.78 ± 0.08	Passed
		A_3	9.21	9.16	0.60 ± 0.08	Passed
		A_4	9.24	9.21	0.11 ± 0.00	Passed
		A_5	9.22	9.20	0.11 ± 0.00	Passed
Acacia gum	20	A_6	9.43	9.39	0.37 ± 0.07	Passed

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Table 3.13.1 Results of the friability test of the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or sodium starch glycolate as disintegrant.

Disintegrant	Number of tablets	Formulation code (% w/w)	Weight of tablets before test(g)	Weight of tables after test (g)	% of weight loss	Inference
P. biglobosa fruit pulp	20	B_1	9.19	9.15	0.45 ± 0.08	Passed
		B_2	9.17	9.14	0.27 ± 0.05	Passed
		B_3	9.20	9.15	0.53 ± 0.03	Passed
		B_4	9.18	9.22	0.78 ± 0.03	Passed
Sodium starch glycolate	20	B_5		9.13	0.44 ± 0.08	Passed

Table 3.14 Results of the disintegration test of the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or acacia gum as binder.

Binder	Formulation (% w/w)	Disintegration time (min.)	Outcome
P. biglobosa fruit pulp	A_1	0.74 ± 2.12	Passed
	A_2	1.52 ± 0.02	Passed
	A_3	3.30 ± 0.03	Passed
	A_4	9.04 ± 0.03	Passed
	A_5	10.24 ± 0.02	Passed
Acacia gum	A_6	1.39 ± 0.01	Passed

Table 3.14.1 Results of the disintegration test of the formulated paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp or sodium starch glycolate as disintegrant.

Disintegrant	Formulation (% w/w)	Disintegration time (min.)	Outcome
P. biglobosa fruit pulp	B_1	80.83 ± 2.12	Failed
	B_2	53.67 ± 2.83	Failed
	B_3	26.50 ± 1.65	Failed
	B_4	29.00 ± 1.42	Failed
Sodium starch glycolate	B_5	3.49 ± 0.35	Passed

Table 3.15 The U.V Absorbance of pure paracetamol of varying concentration in 0.1M NaOH at 257nm .

Concentration (%w/v)	Absorbance (nm)			
	1	2	3	Mean
0.0001	0.062	0.055	0.053	0.057 ± 0.005
0.0002	0.230	0.229	0.229	0.229 ± 0.001
0.0003	0.240	0.242	0.238	0.240 ± 0.002
0.0004	0.288	0.287	0.289	0.288 ± 0.001
0.0005	0.336	0.349	0.349	0.345 ± 0.008

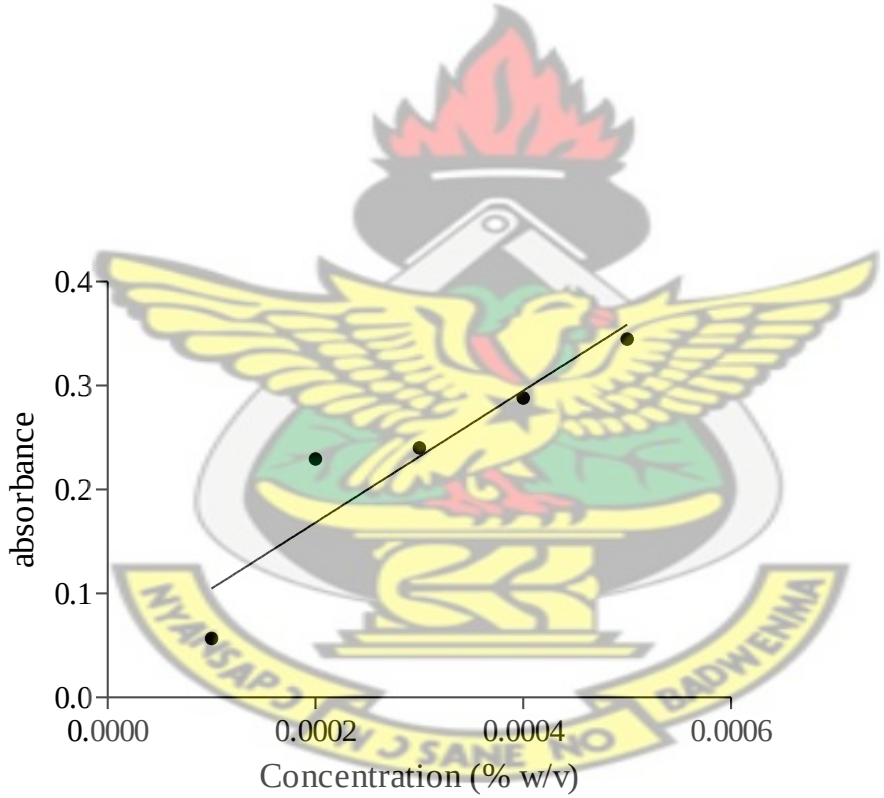


Figure 3.1 Graph of U.V absorbance against concentration of pure paracetamol powder in 0.1M NaOH solution (Calibration curve)

Table 3.16 Drug release profile of the formulated paracetamol tablets with 5 % w/w *P. biglobosa* fruit pulp as binder.

Time/ min	Mean absorbance	Concentration % w/v	Concentration x Dilution factor	Percentage release
5	0.455 ± 0.003	0.000652	0.0347	86.68
10	0.478 ± 0.005	0.000689	0.0366	91.59
15	0.500 ± 0.003	0.000724	0.0385	96.20
30	0.504 ± 0.006	0.000729	0.0388	96.70
45	0.491 ± 0.004	0.000708	0.0377	94.21
60	0.481 ± 0.004	0.000693	0.0368	92.08

Table 3.17 Drug release profile of formulated paracetamol tablets with 5 % w/w acacia gum as binder.

Time/ min	Mean absorbance	Concentration (% w/v)	Concentration x Dilution factor	Percentage release (%)
5	0.403 ± 0.003	0.000571	0.0304	75.88
10	0.422 ± 0.005	0.000600	0.0319	79.72
15	0.459 ± 0.005	0.000658	0.0350	87.51
30	0.484 ± 0.004	0.000697	0.0371	92.71
45	0.494 ± 0.006	0.000719	0.0383	95.29
60	0.488 ± 0.006	0.000704	0.0375	93.61

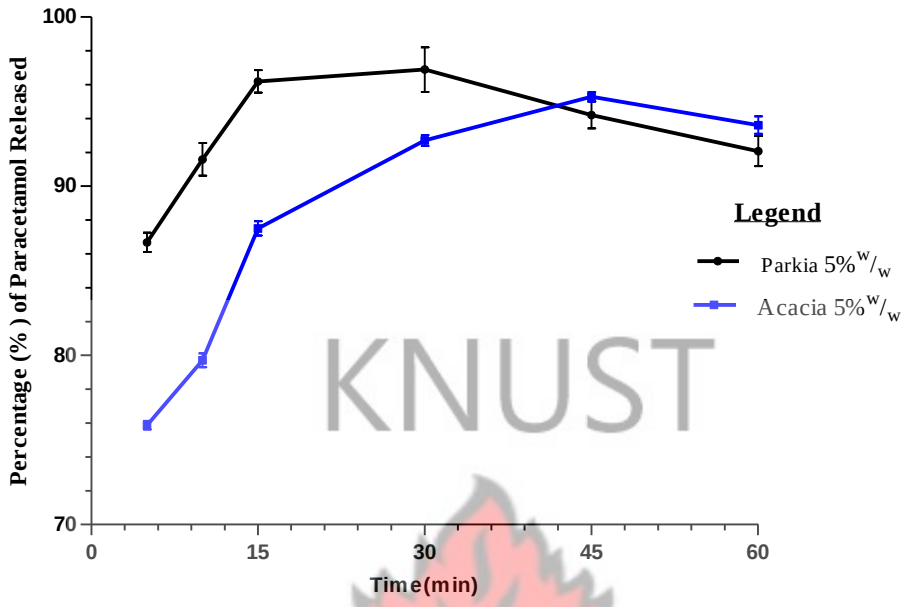


Figure 3.2 Graph of percentage drug release of the formulated Paracetamol tablets against time.

3.6 DISCUSSION

3.6.1 The organoleptic properties of the *Parkia biglobosa* fruit pulp.

Organoleptic properties are important considerations for development of a solid oral dosage form that can influence consumer preference and compliance. The *Parkia biglobosa* fruit pulp samples had characteristic odour , yellow colour and sweet taste (Table 3.4) with sample D (sample collected from Dawadawa Number 1) showing the best physical properties; hence selected as a representative sample for further studies. Also, sample D showed the physical properties that the rural households require and use when selecting *P. biglobosa* fruits for keeps and use especially during the arid season. However, there were no marked differences among the samples indicating that the different vegetation locations had little effect on the physical properties.

3.6.2 The Phytochemical properties of the *Parkia biglobosa* fruit pulp.

The preliminary Phytochemical screening (Table 3.5) of the *P. biglobosa* fruit pulp samples showed the presence of carbohydrates, reducing sugars, saponins and glycosides in all the samples. However, alkaloids, starch and tannins were absent. It could be observed that there were no differences in the Phytochemical properties exbihited by the four *P. biglobosa* fruit samples. This suggests that the different vegetational locations had little or no effect on the Phytochemical composition of the samples.

3.6.3 The physicochemical properties of the *Parkia biglobosa* fruit pulp.

3.6.3.1 Solubility and pH

The *P. biglobosa* fruit pulp flour was soluble in water, sparingly soluble in chloroform, insoluble in acetone, and alcohol (table 3.7).

The pH value obtained for the *P. biglobosa* fruit pulp was 6.31. This is higher than the pH of 5.22 reported earlier by Gernah *et al* (2007). Knowledge of the pH of an excipient is an important parameter in determining its suitability in formulation since the stability and physiological activity of most preparations depends on pH (Luiz *et al*., 2005). The near neutral pH of the *P. biglobosa* fruit

pulp implies that when used in uncoated tablets, it may be less irritating to the gastrointestinal tract.

3.6.3.2 Particle Size and size distribution of the *Parkia biglobosa* fruit pulp

Particle size and particle size distribution affects the compactibility and rearrangement of particles (Virtanen *et al*., 2010). Although there are exceptions, the flowproperties of an excipient will improve when the particle sizes are large. However large particle sizes lead to less strong tablets due to the fact that they have low surface areas for bond formation as compared to smaller particles (Sun and Himmdspach, 2006). Therefore an optimal particle size and size distribution will be required to obtain good flow properties, compaction, and hardness and also reduce weight variation. The size distribution of a powdered material can be specified two parameters namely the geometric mean diameter (d_{geo}) and the geometric standard deviation (s_{geo}). From the particle size data obtained (Table 3.6), the *P. biglobosa* fruit pulp showed geometric mean diameter of 420µm and geometric standard deviation of 1.43. The geometric mean diameter obtained suggests that the particles of the pulp are relatively fine and the flour may exhibit cohesiveness whilst the geometric standard deviation value suggests that the pulp flour may have a wide particle size range and can be made useful in pharmaceutical preparations that require wide range of particle size.

3.6.3.3 Powder flow properties of the *Parkia biglobosa* fruit pulp

The bulk and tapped densities of the *P. biglobosa* fruit pulp were found to be 0.18g/ml and 24 g/ml respectively (Table 3.7). Bulk density is an essential parameter for process development and solid dosage manufacturing. It is used to determine the capacity of mixers and hoppers (Amidon *et al*., 2009). It is also a measure of heaviness of flour (Adejuyitan *et al*., 2009) and an important parameter that determines the suitability of flours for ease of packaging and transportation (Shittu *et al*., 2005). Aulton (1990) specifies that for good flow, bulk density values should be less then 1.2. It can be observed that the value obtained for the bulk density of the fruit pulp was lower than the 1.2 specified. This suggests that the pulp may likely have a good flowability. The tapped density of a powder represents its random dense packaging. Tapped densities values are generally higher for more

regularly shaped particles (spheres) as compared to irregularly shaped particles such as needles (Amidon *et al*., 2009). Hence the tapped density value obtained for the *P. biglobosa* fruit pulp suggests that the flour may have more irregularly shaped particles.

Hausner's ratio greater than 1.67 is indicative of poor flowability whiles values less than 1.25 show good flowability (Aulton, 1990). The Hausner's ratio value obtained for the *P. biglobosa* fruit pulp (1.67) was higher than the reference value of 1.25 indicating poor flow property. Hausner's ratio is an indication of interparticle friction.

Carr's compressibility index is a measure of the capacity of powder to consolidate. It is also a measure of the relative importance of the interparticulate interactions (Amidon *et al*., 2009). A compressibility index greater than 35% is considered to be an indication of poor flowability and below 16% an indication of good flowability (Aulton, 1990). The results obtained for the *P. biglobosa* fruit pulp showed a compressibility index of 40% (Table 3.7). This indicated that the fruit pulp powder did not show satisfactory flow property.

The angle of repose of the *P. biglobosa* fruit pulp was 45^{o}. This high value confirms the poor flowability of the fruit pulp since values greater than 30^{o} are indicative of poor flowability and cohesiveness and vice versa (Aulton, 1990). These results observed could be attributed to the particle size of the materials. Materials having smaller particle sizes equivalent to fine powders corresponds to poor flowbaility due to increased interparticle friction. Therefore, the addition of a glidant or flow agent could be necessary to improve the flowability of such powders.

From table 3.7 the water binding capacity of the *P. biglobosa* fruit pulp was 446%. This indicates that the fruit pulp is capable of absorbing about five times its own weight of water. The high water binding capacity could also be a reflection of the amorphous nature of the fruit pulp.

Swelling is generally accepted as an indication of tablet disintegration ability (Caramell, 1991). The swelling capacity of the *P. biglobosa* fruit pulp was 4.25 g/g (Table 3.7). Thus, if the *P. biglobosa* fruit pulp was incorporated in a tablet

formulation as a disintegrant it would probably produce disintegration capillary action or wicking and swelling. Also the relatively high hydration and swelling capacity of the fruit pulp could possibly be due to high powder porosity (Guyot – Herman, 1992) and may suggest that it could to be agood disintegrant. The high water binding capacity corroborates the high swelling profile of the pulp.

Moisture sorption value obtained for the *P. biglobosa* fruit pulp was 42.50%. Moisture sorption capacity is a measure of the moisture sensitivity of material. The value obtained was high. This could be due to the hydrophilic nature of the molecules of the powders. This may also indicate a possible higher susceptibility to moisture induced changes (Addikwu, 1998) which may affect flow, compression behaviour and mechanical strength of tablets (Hancock and Shamblin, 1998). The results is therefore, indicative of the sensitivity of the fruit pulp to atmospheric moisture and should be stored in air – tight containers.

3.6.4 Proximate composition of the *Parkia biglobosa* fruit pulp

The moisture content of the *P. biglobosa* fruit pulp was 8.66% (Table 3.8) comparable to 8.41% reported by Gernah *et al* (2007). This indicates that the fruit pulp may be less prone to microbial attack, less interaction with moisture sensitive drugs and high ability to absorb water to facilitate disintegration. The value obtained was within the limit of 4 % - 12 % reported by Olayemi (2008). The low moisture content of the fruit pulp also indicate better shelf stability and quality of the flour. According to Gernah *et al* (2007) low moisture content of flours is an indication that they can be stored in a tight container for a long time without spoilage.

The percent ash content of the *P. biglobosa* fruit pulp obtained was 2.40 %. This is higher than the 1.0 % obtained for the fruit pulp of the Meditarranean species by Stein (1982) but within the range for most legumes (2.0 % - 5.0 %) as reported by Gernah *et al* (2007). It is a commonly applied parameter for detection of impurities adulteration and substitution. The low ash content value obtained for the fruit pulp therefore, indicate low levels of contamination during gathering and handling of the fruit pulp.

Crude fat was found to be 0.13 % in the *P. biglobosa* fruit pulp. The value obtained is in conformity with those reported for most legumes. Ihekoronye and Ngoddy (1985) reported that most legumes have less than 3.0 % fat with lentils having as low as of 0.60 %. Stein (1982) also reported a fat content of 0.50 % in the Mediterranean speces. This low fat content is an indication that the fruit pulp can be stored for long periods at right temperature and moisture without undergoing rancidification, which is characteristic of many legumes.

Crude fibre of 8.75 % obtained for the *P. biglobosa* fruit pulp was low compared to 22.73 % reported by Dahouenon – Ahoussi *et al* (2012). Though crude fibre does not contribute nutrients or energy it is a source of dietary fiber. This makes the fruit pulp a poor source of fibre.

The protein content of the *P. biglobosa* fruit pulp was found to be 6.64 % which is higher than 4.29 % reported by Dahouenon – Ahoussi *et al* (2012) and comparable to 6.56 % reported by Gernah *et al* (2007).

The major component of the *P. biglobosa* fruit pulp obtained was carbohydrate with a value of 76.80 %. In their study of the composition of *P. biglobosa* fruit pulp Akoma *et al* (2001) found the content of carbohydrate to be 67.30%. The high content of carbohydrate can explain the noticeable sweet taste of the pulp. The carbohydrate content obtained seem to support the findings of Uwaegbute (1996) that the *P. biglobosa* fruit pulp contains more carbohydrates than the seeds. Though proteins and fats also provide energy, carbohydrates are much cheaper and more easily digested and absorbed (Fox and Cameron, 1989). With this content of carbohydrate the fruit pulp is a potential food source of energy (Muller, 1988). Apart from imparting sweetness carbohydrates act as a preservative when present in high concentration by making water unavailable to microorganisms.

The sugar content of the *P. biglobosa* fruit pulp obtained was 3.66^{o}Brix. Sugars (example sucrose, glucose and fructose) are abundantly used as basic ingredients in the food industry and as excipients in the pharmaceutical industry due to the quality attributes they contribute to the final products, such as sweet taste, flavour, texture, binder, bulking agent and carrier function of active pharmaceutical

components (Ballinger,1971). Therefore, the *P. biglobosa* fruit pulp may be a potential ingredient in the pharmaceutical industry due to its high sugar content.

3.6. 5 Pasting profile of the *Parkia biglobosa* fruit pulp

The *P. biglobosa* fruit pulp exhibited low pasting peak viscosity of 9.0 rapid viscosity units (RVU) (Table 3.9). Acacia gum produced a lower value of 5.5RVU compared to the *P. biglobosa* pulp. The low peak viscosity of the fruit pulp could be attributed to high cation content that may be contained in the pulp. The presence of cations has been reported by Zobel (1984) to decrease viscosity of the pulp. The pasting temperature obtained for the *P. biglobosa* fruit pulp was 60.70ºC and that of Acacia gum was 72.35ºC. The pasting temperature gives an indication of how fast flour swell (Liang and King, 2003). The relatively high pasting temperature of the fruit pulp (60.70ºC) and that of Acacia gum (72.35ºC) could be attributed probably to strong associative forces in the pulp powder and the gum as such forces are known to be responsible for viscosity stability (Henshaw *et al*., 1996). The ability of flour to imbibe water and swell is primarily dependent on the pasting temperature (Dreher and Berry, 1983). Hence in the presence of water and heat, the fruit pulp and gum may swell and form paste by imbibing water. The *P. biglobosa* fruit pulp showed high breakdown, setback and final viscosities of 7.5 RVU, 15.0 RVU and 15.5 RVU respectively compared to 0.0 RVU, 1.5 RVU and 7.0 RVU respectively obtained for Acacia gum. The low setback values obtained for the fruit pulp and the gum suggests that paste formed from them may have cohesive property. The low breakdown viscosity of the fruit pulp suggests that the pulp may have undergone a low degree of swelling but this was not evident in the swelling capacity of the fruit pulp; a rather high swelling capacity was obtained. The pasting profile of the *P. biglobosa* fruit pulp and the Acacia gum is expected since the fruit pulp and the gum are not starches. Pasting properties are known to be influenced by the degree and type of molecular association in the material. Though starch is widely distributed in plants (occurring in seeds, fruits, stem, pith, roots and leaves), a lack of viscosity development in the Brabender viscoamylograph for the *P. biglobosa* fruit pulp only suggests absence of starch which was confirmed by the negative results shown by the Iodine test in the Phytochemical analysis (Table 3.5).

3.6.6 Analysis of the formulated tablets

The post compression evaluation of the tablets showed that the tablets of all the various formulations showed uniform thickness (Table 3.9). The compendial specification for uniformity of weight states that for tablets weighing more than 250 mg, weights for not more than two tablets should deviate from the average weight by more than 5 % (BP, 2007). The percentage deviation of 20 tablets of each formulation was found to be remarkably consistent and none of the individual tablet weights deviated by more than ± 5 % (Table 3.10) and hence all the tablet formulations of both the *P. biglobosa* fruit pulp and Acacia gum passed the BP uniformity of weight test.

Crushing strength test shows the ability of tablets to withstand pressure or stress during handling, packaging and transportation. The hardness of the tablets of the different formulations varied ranging from 27.77 N to 52.27 N (Table 3.12). The results showed that increasing the content of *P. biglobosa* fruit pulp as binder in the formulation resulted in an increase in the hardness of the tablets. Since hardness greater than 39.2 N (4kg/cm^2) and less than 73.5 N (15kg/cm^2) is considered acceptable, all the tablets except those of batches A_1 and A_2 with *P. biglobosa* fruit pulp concentration of 1% and 3%w/w as binder showed the desired hardness. It could be due to formation of more solid bonds within the tablets due to the increase in binding effects of the *P. biglobosa* fruit pulp which conferred resistance to tablet fracture and abration (United States Pharmacopoeia, 2007). The differences in hardness of the tablets with varying concentration of the *P. biglobosa* fruit pulp as binder were significant ($p < 0.0001$). However, the differences in hardness observed between the tablets with concentrations of 5 %, 8 % and 12 % w/w of the *P. biglobosa* fruit pulp as binder and tablets with 5 % w/w concentration of Acacia gum as binder were not significant ($p > 0.05$). It was observed that tablets with 5 % binder concentration of *P. biglobosa* fruit pulp compared well to the Acacia gum tablets. Therefore, tablets with binder concentrations of 1% and 3 % w/w of the *P. biglobosa* fruit pulp did not comply with the specification and hence failed the BP hardness test. This could be attributed to low binder concentration and formation of weak solid bonds within the tablets. It could be explained from the

results that increasing *P. biglobosa* fruit pulp concentration as binder increases particle cohesiveness and results in harder tablets. Tablets of both the fruit pulp and Sodium starch glycolate as disintegrants also passed the BP hardness test except those with 2 % w/w disintegrant concentration of the pulp (Batch B_1) (Table 3.12.1). This could also be attributed to the low disintegrant concentration of *P. biglobosa* fruit pulp since there was an observed increase in hardness with increase in concentration of *P. biglobosa* as disintegrant. The differences in hardness of the all tablets with varying concentrations of the fruit pulp as disintegrant and those of Sodium starch glycolate were not significant ($p > 0.05$) except tablets of batch B_1 with 2 % disintegrant concentration of the fruit pulp. It was also observed that tablets hardness increased marginally as concentration of *P. biglobosa* fruit pulp as disintegrant increased.

The tablets with *P. biglobosa* fruit pulp at 4 % w/w disintegrant concentration compared favourably with those of Sodium starch glycolate at the same concentration.

The tablets with 1% w/w binder concentration of *P. biglobosa* fruit pulp showed friability value of 1.27 % (Table 3.13) but the BP specifies a friability limit of not more than 1 %. This implies that the tablets did not comply with the BP specifications and hence failed the friability test. This could be due to the formation of rougher surface of the tablets during compression. Since the rougher the surface of a tablet the more friable it will be.

Tablets with 3 %, 5 %, 8 % and 12 % w/w concentration of *P. biglobosa* fruit pulp and that of Acacia gum at 5% concentration as binders passed the friability test. The differences in friability of the tablets with varying concentrations of *P. biglobosa* fruit pulp as binder and those of Acacia gum were significant ($p < 0.0001$). Also tablets with 8 % and 12 % w/w concentration of the fruit pulp as binder had the lowest friability value of 0.11 % compared to the 0.37 % obtained for Acacia gum. It could be observed that tablets with 5 % w/w concentration were more friable than those with Acacia gum as binder at the same concentration. It could also be observed that friability of the prepared tablets with *P. biglobosa* fruit pulp decreased as the concentration of the fruit pulp as binder increases. All the tablets with the *P. biglobosa* fruit pulp and the Sodium starch glycolate as disintegrants did meet the required BP specification for friability

though they showed significant ($p < 0.0001$) differences in friabilities (Table 3.13.1). The tablets with 4%w/w concentration of *P. biglobosa* pulp as disintegrant was less friable than those of Sodium starch glycolate at the same concentration. The friability marginally increased as the concentration of the *P. biglobosa* fruit pulp as disintegrant increased.

The disintegration time of the formulated Paracetamol tablets with varying concentration of *P. biglobosa* fruit pulp and that of Acacia gum at 5%w/w concentration as binder were found to be less than 15 minutes (Table 3.14). This could be attributed to the mechanical strength of the tablets. The higher the binder concentration the harder the tablets, hence the observed increase in disintegration time with increase in binder concentration. The differences in disintegration times of the tablets of different concentrations of the *P. biglobosa* pulp as binder were significant ($p < 0.0001$). The BP (2007) specification for disintegration states that uncoated tablets should disintegrate within 15 minutes. Hence tablets of both the *P. biglobosa* fruit pulp and the Acacia gum as binders passed the disintegration test.

The disintegration times obtained for tablets of varying concentration of the *P. biglobosa* fruit pulp as disintegrant showed a decrease in disintegration time ranging from 80.83 minutes to 29 minutes with increase disintegrant concentration (3.14.1) but did not meet the BP specification for disintegration. This could be attributed to the hardness of the tablets. It could also be due to the effect of the fruit pulp incorporated as disintegrant. From the results the *P. biglobosa* fruit pulp produced harder tablets than the Sodium starch glycolate tablets at 4 % w/w disintegrant concentration.

Generally the *P. biglobosa* pulp tablets produced hard tablets at the various disintegrant concentrations hence the high disintegration times observed. The differences in disintegration times between the tablets of the different concentrations of *P. biglobosa* fruit pulp as disintegrant compared to those of Sodium starch glycolate were significant ($p < 0.0001$). Sodium starch glycolate tablets at 4%w/w disintegrant concentration met the BP specification for disintegration of uncoated tablets. Sodium starch glycolate is likely to possess inherent disintegrating property and hence initiate distintegrantion by swelling and capillary action. The

as disintegrant does not conform to the swelling capacity and water binding capacity observed for the fruit pulp. This may probably be because the *P. biglobosa* fruit pulp fruit pulp tablets disintegrated by other mechanism either than swelling and capillary action. It appeared that the fruit pulp may not be self-disintegrating. From the results obtained the *P. biglobosa* fruit pulp may not be a good disintegrant.

Disintegration of tablets plays a vital role in the dissolution process. The tablets of both the *P. biglobosa* fruit pulp and the Acacia gum as binders (5 % w/w) released over 70 % of the drug in 5 minutes. Paracetamol is classified under the biopharmaceutical classification system (BCSclass III) high solubility and low permeability, though, it may be said to have properties of BCS class I-high solubility and high permeability (Kalantzi *et al*., 2006), this may explain the rapid releases within 5 minutes from tablets of the *P. biglobosa* fruit pulp and the Acacia gum. Also the ablets prepared with *P. biglobosa* fruit pulp pulp as a binder (5 % w/w) released over 90 percent of the drug within 45 minutes (figure3.2) comparable to the amount of released for the tablets with Acacia gum at the same binder concentration. This may be due to the disintegration times observed for both samples. The difference in dissolution rates between the *P. biglobosa* fruit pulp tablets and that of Acacia gum at 5 % w/w binder concentration was significant ($p < 0.05$).

The United States Pharmacopoeia and British Pharmacopoeia states that the quantity of drug releases should not be less than 85 % of the labeled amount of paracetamol in 45 minutes. Hence the tablets formulated with *P. biglobosa* fruit pulp and Acacia gum as binders complied with the specification. It could therefore, be said that the *P. biglobosa* fruit pulp and Acacia gum showed comparative effectiveness at 5%w/w concentration as binders to paracetamol tablets

3.7 CONCLUSION

The *P. biglobosa* fruit pulp samples collected from the four locations, all had the same characteristic odour with a yellow colour and a sweet taste, as well as the preliminary screening showed that all the had the same phytochemical composition.

The *P. biglobosa* fruit pulp was soluble in water but insoluble in ethanol and organic solvents. The pH of the fruit pulp with a near neutral pH and may be less irritating to the gastrointestinal tract hence may be suitable as an excipient in oral tablets.

From the results the particles of the fruit pulp showed low geometric mean diameter (d_{geo}) of 420 μm. *P. biglobosa* fruit pulp demonstrated poor flowability.

The hydration , swelling and moisture sorption capacities of *P. biglobosa* fruit pulp were found to be high.

The proximate composition of the fruit pulp confirmed it as a good source of macronutrients. However, the pasting properties of the showed lack of inherent viscosity and absence of starch.

The evaluation of the formulated tablets showed that all tablets had uniform thickness and also passed the British Pharmacopoeia uniformity of weight test. The tablets with 1% and 3% w/w concentrations of the fruit pulp as binder failed the BP hardness test whiles those with 1 % w/w binder concentration failed the friability test. Hardness slightly increased and friability decreased as concentration of binder increased. The tabletd with 2 % w/w concentration of the fruit pulp as disintegrant failed the hardness test. Hardness slightly increased and friability also increased as disintegrant concentration increased. The tablets with varying concentration of the fruit pulp as binder met the BP specification for disintegration while those with varying concentration of the fruit pulp as disintegrant failed the BP disintegration test. Hence it may not be a good disintegrant. Also the disintegration time increased with increase in concentration of the fruit pulp as binder whiles disintegration time decreased with increasing concentration of the fruit as disintegrant. The tablets with 5 % w/w concentration of fruit pulp passed the BP dissolution test for tablets specifying that not less than 80 % was released after 45 minutes. The *P. biglobosa* fruit pulp

and Acacia gum showed comparative effectiveness as a binding agent at 5% w/w. Hence *P. biglobosa* fruit pulp could be a good binder for the pharmaceutical industry especially in the manufacture of solid dosage forms.

3.8 RECOMMENDATION

- *P. Boglobosa* plant is not normally cultivated and there is no conservation measures in place to prevent it from extinction hence the need for studies on its cultivation and conservation.
- There should be studies into the use of excipients from natural polymeric excipients and their modifications in finding cheap, biodegrable and ecofriendly excipients.
- Formulation of matrix tablets using *P. Boglobosa* fruit pulp can be attempted.

REFERENCES

Abbiw, D.K. (1990). Useful Plants of Ghana.Intermediate Technology Publications And the Royal Botanic Gardens, Kew. UK. p. 337.

Addy, E.O.U. Salami, C.I .I.,gboeli, L.C and Remana, H.S. ((1995). Effect of processing on nutrient composition and antinutritive substance of African locust bean (*Parkia filicoidea*) and baobab seed (*Adansonia digitata*) Plant foods. Hum Nutr 48: 113 – 117.

Adebowale, K.O and Lawal, O.S. (2003). Microstructure, physicochemical properties and retrogradation behavior of Mucuna bean (Mucuna pruriens) starch on heat moisture treatments. *Food Hydrocolloids* 17:265–272.

Adejuyitan , J.A. Otunola E T, Akande, E .A., Bolarinwa, I .F., Oladokun, F .M. (2009). Some physicochemical properties of flour obtained from fermentation of Tigernut (*Cyperus esculentus*). *Food Sci*. 3(2):51 – 55.

Adikwu, M.U. (1998). Moleculer weight and Amylose/Amylopectin ratio of Starch From *Gladiolus Actinomorphantus*. *Nig.J.Nat. Prod. and Med. Vol.* 02 54 – 56.

Ahn, H. Basaranoglu, Z., Yilmaz, M., Bugutekin, A., Gül, M.Z. (2008). Experimental Investigation of granular flow through an . orifice. Powder Technol. 186, 65-71.

Ajuebor, N. (2004). Performance evaluation of locust bean dehuller/separator for dawadawa production. *Nig Food J* 22:203 – 210.

Akoma, O.O., Basaranoglu, Z., Yilmaz M., Bugutekin A., Gül M.Z. (2001). Physicochemical attributes of wine produced from the yellow pulp of *Parkia boglobosa* using traditional juice extraction techniques. *Nig Food* J 19:76 -79.

Amidon, G.E., Secreast, P.J., Mudie, D. (2009). Particle, powder, and compact characterization. In: Developing solid oral dosage forms: pharmaceutical theory and practice. Academic press, Burlington, USA, pp. 169.

Anoop, K.S., Selvam, P.R., Sivakuma, T. (2010). Isolation, characterization and formulation properties of a new plant gum obtained from *mangifera indica*. *Int JPharm Biomed Res* 2010 1(2), 35 – 41.

Association of Analytical Chemists (AOAC). (1990). Official Methods of Analysis, Washington D.C. Association of Official Analytical Chemists.

Augsburger, L.L. and Vuppala, M.K. (1997). Theory of granulation. In Handbook of pharmaceutical granulation technology, Parikh D M (ed.), Marcel Dekker Inc., New York, USA, pp. 7-24.

Augsburger, L.A. (1990). Hard and soft gelatin capsules. In Modern Pharmaceutics, G.S Banker and C.T Rhodes, Marcel Dekker: New York, NY, 441–490.

Aulton, M.E. (2002). Pharmaceutics, The science of dosage form design, 2nd edn., Harcoust publishers Ltd., London, pp.18 – 21.

Aulton, M.E.(1990). Pharmaceutics, The Science of Dosage form Design. Churchill Livingstone, 1990, p. 610 – 612

Aulton, M.E. (1988). The Science of Dosage Form Design, 1st ed., pp: 4, 304, 309,654

Azokpota, P., Hounhouigan, D.J., Nago, M.C. (2006). Microbiological and chemical changes during the fermentation of African locust bean (Parkia biglobosa) to produce afitin , iru and sonru, three traditional condiments produced in Benin. International Journal of Food Microbiology, 107:304-309

Ballinger, R.A. (1971). A History of Sugar Marketing. Agricultural Economic Report No. 197. Washington, D.C.: United States Department of Agriculture, Economic Research Service.

Banakar, U.V. (1992). Pharmaceutical dissolution testing, Marcel Dekker, Inc. New York, pp.1 – 8, 347 – 421.

Banakar, U.V. and Makoid, M.C. (1996). Pharmaceutical issues in drug development in The Drug Development Process. Increasing Efficiency and Cost-Effectiveness. Marcel Dekker: New York, NY, 117–168.

Banchathanakij, R.and Suphantharika, M. (2009). Effect of different β - glucans on the gelatinisation and retrogradation of rice starch. *Food Chemistry* 114:514.

Banker, G.S. and Rhodes, C.T. (1990). Modern pharmaceutics 2nd.Edn. In: Drugs and the Pharmaceutical Sciences.Vol.40 New York, Marcel Dekker Inc.

Batey, I.L. (2007). Interpretation of RVA Curves. In: The RVA handbook, G.B. Crosbie, A.S. Ross (Ed.), American Association of Cereal Chemists, St. Paul, MN. pp. 19-30.

Beaubien, L.J. and Vanderwielen, A.J. (1980). Particle size analysis of pharmaceutical powders. *J. Pharm. Sci.*, 69, 651-655.

BeMiller, J.N. (2007). Carbohydrate chemistry for food scientists, 2nd ed. AACC International: St. Paul, MN. pp.389.

Beneke, C.E., Viljoen, A.M., Hamman, J.H. (2009). Polymeric Plant – derived Excipients in Drug Delivery. 14: 2602 – 2620.

Beverloo, W.A., Leniger, HA., van de Velde, J. (1961). The flow of granular solids through orifices. *Chem. Eng. Sci*. 15, 260-269.

Booth, F.E.M. and Wickens, G.E. (1988). Non-timber uses of selected arid zone trees and shrubs in Africa. FAO Conservation Guide 19. Food and Agriculture Organization of the United Nations. Rome. pp 103-109.

Bi, Y.X., Sunada, H., Yonezawa, Y and Danjo, K. (1990). Evaluation of rapidly disintegrating tablets prepared by a direct compression method. Drug dev. Ind. Pharm. 25: 571 – 581.

British Pharmacopoeia, Her Majesty's Stationery Office, London, UK, 2007.

British Pharmacopoeia, Her Majesty's Stationery Office, London, UK, 2004.

Brittain, H.G. (2002). Particle size distribution, Part III. Determination by analytical sieving. *Pharm. Technol.* 56-64.

Burgess, D.J., Duffy, E., Etzler, F., Hickey, A.J. (2004). Particle size analysis: AAPS workshop report, cosponsored by the Food and Drug Administration and the United States Pharmacopeia. AAPS J., 6, Article 20.

Burkill, H. M. (1995). Usefull Plants of West Tropical Africa. Families J – L,Vol 3. BPC Wheatons Ltd. p. 256 – 257;359 – 360.

Caramella, C. (1991). Novel methods for disintegrant characterization, part 1. *Pharm Technol*. pp 48 – 56.

Campbell – Platt, G. (1980). African locust bean (*Parkia species*) and its African fermented food products, Dawadawa. *Ecol. Food Nut.*,9: 123 – 132.

Carr, R.L. (1965). Evaluating flow properties of solids. *Chem. Eng.* 72, 69-72.

Chakraberty, R .E and Eka, O. U. (1978). Studies on hydrocyanic acid, oxalic acid and phytate contents of food stuffs. W Afr J Biol and Appl Chem. 21:50 - 59

Chandrasekharan , C. (1993). Issues Involved in the Sustainable Development of Non-Wood Forest Products. Paper prepared for the Expert Consultation on Non-Wood Forest Products for English-Speaking African Countries. Arusha, Tanzania, 17-22 Oct. 1993.

Chang, D. and Chang, R.K. (2007). Review of Current Issues in Pharmaceutical Excipients.*Pharm. Technol.* 6. 1 – 12.

Cowell, A,. McGlinchey, D., Ansell, R. (2005). A CFD analysis of the Stable Microsystems Powder Flow Analyser with an experimental comparison. Abstract, Particulate Systems Analysis, Stratford upon Avon.

Crowder, T.M. and Hickey, A.J. (2000). The physics of powder flow: Applied to Pharmaceutical solids, *Pharm. Technol.*, 50-58.

Dahlinder, L.E., Johansson, M., Sjogren, J. (1982). Comparison of methods for evaluation of flow properties of powders and granulates. Drug Dev. *Ind. Pharm.* 8, 455-461.

Dhahouenon – Ahoussi, E., Adjou, S.E., Lozes Yehouenou, L.L., Hounye, R., Famy, N., Soumanou, M.M., Sohounhloue, D.C.K. (2012). Nutritional and Microbiological Characterization of pulp powder of locust bean (*Parkia biglobosa*) used as a supplement in infant feeding in Northern Benin. *African Journal of Food Science* vol. 6(9) pp. 232 – 238.

Deasy, P.B. and Timoney, R.F. (1976). The Quality control of medicines. Elsevier scientific publishing company, New York, pp.1, 3.

de Boer, G.B.J., de Weerd, C., Thoenes, D., Goossens, H.W.J. (1987). Laser diffraction spectrometry: Fraunhofer diffraction versus Mie scattering. Part. Part. Syst. Charact. 4, 14-19.

Department of Health and Human Services.Food and Drug Administration,21 CFR Part170.3, April, 2002

Dreher, M. I. and Berry, J. W. (1983). Buffalo gourd root starch. Part 1. Properties and structure. *Starch /Starke*.35:76 – 81.

Dyakowski, T. Luke, S.P., Ostrowski, K.L, Williams, R.A. (1999). On-line monitoring of dense phase flow using real-time dielectric imaging. Powder Technol. 104, 287-295.

Elbicki, J.M. and Tardos, G.I. (1998). The influence of fines on the flowability of alumina Powdersin test hoppers. Powder Handling and Processing 10, 147-149.

Ejiofor, M.A.N. and Okafor, J .C. (1996). Prospect for commercial exploitation .of Nigerian trees,vegetables, fruits and seeds through food and industrial products formation.Intern Tree Crops J 9: 129 - 199

EMEA. (2004). European Medicines Agency 'ICHQ8 Pharmaceutical Development' p. 4 – 5.

Esezobo, S. (1985). The effect of some excipients on the physical properties of a paracetamol tablet formulation. J Pharm Pharmaco.137: 193 – 194.

Fan, A., Parlerla, S., Carlson, G., Ladipo, D., Dukich, J., Capella, R. (2005). Effect of particle size distribution and flow property of powder blend on tablet weight variation. Am. *Pharm. Rev*. 8, 73-78.

FAO.(1988). Traditional Food plants. FAO, Food and Nutrition paper. No. 42.pp.388 – 393.

Faqih, A.M., Chaudhuri, B., Alexander, A.W., Davies, C., Muzzio, F.J., Tomassone, M.S. (2006). An experimental/computational approach for examining unconfined cohesive powder flow.*Int. J. Pharm.* 324, 116-127.

Faqih, A.M., Mehrotra, A., Hammond, S.V., Muzzio, F.J. (2007). Effect of moisture and magnesium stearate concentration on flow properties of cohesive granular materials. *Int. J. Pharm.* 336,338-345.

Fassihi, A.R. and Kanfer, I. (1986). Effect of compressibility and powder flow properties on tablet weight variation, Drug Dev. *Ind. Pharm.* 12, 1947-1966.

Faure, A., York, P., Rowe, R.C. (2001). Process control and scale-up of pharmaceutical wet granulation processes: a review. *Eur. J. Pharm. Biopharm*.2001, 52, 269–277.

Fox, B. A. and Cameron, A .G. (1989). Food Science, Nutrition and Health, 15th Ed. Edward Arnold, London.

Freeman, R.F. (2007). Measuring the flow properties of consolidated, conditioned and aerated powders: a comparative study using a powder rheometer. Powder Technol. 174, 25-33.

Freeman, T. (2010). The importance of powder characterization.*Pharma.Technol. Eur*. 22 (6), 21-26.

Frost and Sullivan. (2005). "Strategic Analysis of Pharmaceutical Excipients in Europe". http://www.marketresearch.com/product/display.asp?productid

Fukuoka, E. and Kimura, S. (1992). Cohesion of particulate solids, VIII. Influence of particle shape on compression by tapping. Chem. Pharm. Bull. 40, 2805-2809.

Geldart, D., Abdullah, E.C., Verlinden, A. (2009). Characterization of dry powders. Powder Technol. 190, 70-74.

Geldart, D., Mallet, M.F., Rolfe, N. (1990). Assessing the flowability of powders using angle of repose. Powder Handling and Proc., 2, 341-346.

Gennero, R.G. (1995). Remington: The Science and Practice of Pharmacy, 19th ed. Vol. II, p.1615. Review. Volume 3 Number 10

Gergely, G. (1981). Granulation –a new approach. *MfgChem.Aerosol* News, 52, 43.

Gernah, D.I., Atolagbe, M.O., Echegwo, C.C. (2007). Nutritional composition of the African locust bean (*Parkia biglobosa*) fruit pulp.*Nig. Food J.* 25(1): 190-196

Getie, M. and Gebre – Mariam, T. (1998). In vitro comparative evaluation of some tablets available in drug retail outlets of Addis Ababa: physical properties, content uniformity and dissolution profiles. Eth Pharm J. 16: 22 – 24.

Gold, G., Duvall, R.N., Palermo, B.T. (1996). Powder flow studies I: Instrumentation and applications, *J. Pharm. Sci.* 55:1133-1136.

Gordon, M.S., Rudraraju ,V.S., Dani, K., Chowhan, Z.T (1993). Effects of the mode of super disintegrant incorporation on dissolution in wet granulated tablets. *J Pharm Sci*. 82: 220 – 226.

Guyot – Herman, A.M. (1992). Tablet disintegration and disintegrating agents, STP. Pharm Sci 2 (6):445 – 462.

Hall, J.B,. Tomlinson, H.F., Oni, P.I., Buchy, M., Aebischer, D.P. (1997). *Parkia biglobosa*. A Monograph. School of Agricultural and Forest Sciences.University of Wales, Bangor, U.K.

Hancock, B.C. and Shamblin, S.L.(1998). Water vapour Sorption by Pharmaceutical Sugar Pharm.Sci.Technol. Today; (8): 345 – 351

Hancock, B.C., Vukovinsky, K.E., Brolley, B., Grimsey, I., Hedden, D., Olsofsky, A., Doherty, R.A . (2004). Development of a robust procedure for assessing powder flow using a commercial avalanche testing instrument, *J. Pharm.Biomed.Anal.*35, 979-990.

Harborne, J.B . (1973). Phytochemical Methods.Chapman and Hall Ltd., London , pp.49-188. Herourat D, Sangwin RS, Finiaux MA.

Hausner, H.H. (1967). Friction conditions in a mass of metal powder. *Int. J. Powder*. Metall. 3, 7-13

Heffels, C.M.G., Verheijen, P.J.T., Heitzmann, D., Scarlett, B. (1996). Correction of the effect of particle shape on the size distribution measured with a laser diffraction instrument. Pat. Part. Syst. Charact. 13, 271-279.

Henshaw, F .O., Mcwatters, K.H, Oguntunde, A., Philips, R. P. (1996). Pasting properties of cowpea flour: Effect of soaking and decortications method. *J Agric.and Food Chem.* 44(7): 1864 – 1870.

Hess, H. (1985). Pharmaceutical dosage forms and their use, Bern, Hans Hubers publishers.

Heywood, H. (1963). The evaluation of powders. *J. Pharm. Pharmacol*. 15, 56T-74T.

Hopkins, H.C.(1983). The Taxonomy, Reproductive Biology and Economic Potential of *Parkia* (Leguminosae: Mimosoideae) in Africa and Madagascar. Botanical Journal of the Linnean Society. 87: 135-137.

Houghton, M.E. and Amidon G.E. (1992). Microscopic characterization of particle size and shape: An inexpensive and versatile method. Pharm. Res., 9, 856-859.

Howard, C.A., Loyd, V.A., Nicholas, G.P. (1999). Pharmaceutical dosage forms and drug delivery systems. (eds), 7th edn. Lippincott Williams and Wilkins, New York, pp. 203-9.

Howard, S.A. (2007). Solids: Flow properties, In: Encyclopedia of pharmaceutical technology. Informa Healthcare, USA. pp 3275-3296.

Ibiyemi, S .A., Abiodun, A., Akanyi, S. A. (1988). *Adasonia digitata*and *Parkia filicoidea* fruit pulps for the soft drink industry. Food Chem.28 (2):111- 116.

Ibrahim, M. H and Antai, S.P.(1986). Chemical changes during the fermentation of African locust bean (*parkia filicoidea* welw) seed for production of dadawa. Plant Foods Hum Nutr 30:179 – 184.

Ihekoronye, I.A and Ngoddy, P. O. (1985). Integrated Food Science and Technology for the Tropics. Macmillan, London. pp.125 – 364.

Irvine, F .R. (1961). The woody plants of Ghana, Oxford University Press, London, p.868.

Iveson, S.M., Litster, J.D., Hapgood, K., Ennis, B.J. (2001). Nucleation growth and breakage phenomena in agitated wet granulation process: a review.*Powder Technol.*, 117, 3–39.

James, I.W. (1996). Tablet Testing. In: Encyclopedia of Pharmaceutical Technology. James S, James CB. (eds), Vol. 14, Marcel Dekker, Inc., New York. pp. 411 – 412.

Kaerger, J.S., Edge, S., Price, R. (2004). Influence of particle size and shape on flowability and compactibility of binary mixtures of paracetamol and microcrystalline cellulose. *Eur. J. Pharm. Sci.* 22, 173-179.

Kalantzi, L., Reppas, C., Dressman, J.B., Amidon, G.L., Junginger, H.E., Midha, K.K., Shah, V.P., Stavchansky, S.A., *Barends, D.M. (2006). Biowaive rmonographs for immediate release solid oral dosage forms: Acetaminophen (paracetamol). *J. Pharm. Sci.*, 95(1):4-14.

Kanigm J.L and Rudnic, E.M. (1984). "The mechanisms of disintegrant action" Pharm Tech. April 50–63.

Kaye, B.H., Gratton-Liimatainen, J., Faddis, N. (1995). Studying the avalanching behaviour of a powder in a rotating disc, Part. Part. Syst. Charact. 12, 232-236.

Kelly, R.N., DiSante, K.J., Stranzl, E., Kazanjian, J.A., Bowen, P., Matsuyama, T., Gabas, N. (2006). Graphical comparison of image analysis and laser diffraction particle size analysis data obtained from the measurements of nonspherical particle systems. AAPS *PharmSciTech* 7, Article 69.

Kleinebudde, P. (2004). Roll compaction/dry granulation: pharmaceutical applications. *Eur J Pharm Biopharm*;58:317-26.

Kovacs, I., Hadady, K.K., Darbai, M.J. (1980). Application of content uniformity test to tablet preparations. Pharmazie. 35: 609 – 612.

Kristensen, H.G. and Schaefer, T. (1987). Granulation: A Review on Pharmaceutical Wet-Granulation. Drug Dev. *Ind. Pharm.*, 13(4-5):803-872.

Lachman, L. and Schwarts, J.B. (1990). Pharmaceutical dosage forms, Tablets. (eds), 2nd edn., vol.2, Marcel Dekker, Inc. USA. pp 201-25, 246-313, 349-570.

Leach, H.W., McCowen, L. D, Schoch, T. J. (1959). Structure of the starch granules. In: Swelling and solubility patterns of various starches. Cereal Chem.36: 534 – 544.

Lee, Y.S.L., Poynter, R., Podczeck, F., Newton, J.M. (2000). Development of a dual approach to assess powder flow from avalanching behaviour, AAPS PharmSciTech. 1 (3), Article 21.

Lefebvre, C., Barthelemy, C., Guyot-Hermann, A.M., Guyot, J.C. (1988). An attempt at bringing to light a "phase inversion" in a binary mixture of two dimensional rounded particles. Drug. Dev. *Ind. Pharm* 14, 2443-2465.

Lerk, C. F. and Lagas, M. (1977). 'The wettability of pharmaceutically useful powders.' Acta Pharm. Technol.23:21 – 27.

Liang, X. and King, J. M. (2003). Pasting and Crystalline property difference of commercial and isolated rice starch with added amino acids. *Journal of FoodScience*. 68(3):832 -838

Lieberman, H.A and Lachman, L. (1981). *Pharmaceutical dosage forms: tablets*. 2nd Edn.vol. 2. New York, NY:Marcel Dekker.

Liu, L.X., Marziano, I., Bentham, A.C., Litster, J.D., White, E.T., Howes, T. (2008). Effect of particle properties on the flowability of ibuprofen powders. *Int. J. Pharm.*,362, 109-117.

Liu, M., Fan, J., Wang, K., He, Z. (2007). Synthesis, charcacterization and evaluation of phosphate cross linked konjac glucomanan hydrogels for colon targeted drug delivery. Drug Deliv. 14: 397 - -02

Lopez – Solis, J. and Villafuerte – Robles, L. (2001). Effect of disintegrants with different hygroscopicity on dissolution of norfloxacin/pharmatose DCLII tablets. *Int. J. Pharm*. 216: 127 – 216.

Luiz, A., George, G., Pedro, P., Peter, C. (2005). Dry Granulation and Compression of spray – Dried Plant Extracts. *AAPS Pharm Sci. Tech.* 6(3);45.

Lukow, M. and Hopkins, F.C.H. (1995). A Cladistic Analysis of Parkia (Leguminosae; Mimosoideae): *American journal of Botany*; vol. 82, No. 10.1300 – 1320.

Ma, Z., Merkus, H.G., van der Veen, H.G., Wong, M., Scarlett, B. (2001). On-line measurement of particle size and shape using laser diffraction. Part. Part. Syst. Charact. 18, 243-247.

Mackaplow, M.B., Rosen, L.A., Michaels, J.N. (2000). Effect of primary particle size on the granule growth and end point determination in high-shear wet granulation. Powder Technol. 119, 14 – 25.

Malafaya, P.B., Silva, G.A., Reis, R.L. (2007). Natural – origin polymers as carriera and scaffolds fobiomolecules and cell delivery in tissue engineering applications. *Adv. Drug. Deliv. Rev*. 59207 - 59233

Malviya, R., Srivastava, P., Kulkarni, G.T. (2011). Applications of Mucilages in Drug Delivery - A Review. Advances in Biological Research 5: 1-7.

Marinelli, J. and Carson, J.W. (1992). Solve solids flow problems in bins, hoppers and feeders. Chemical Engineering Progress, 88, 22-28.

Martin, A., Swarbrick, J., Cammarataa, A. (1991). In; Physical Pharmacy (3rd edn.) pp. 465, 544 – 553.

Mazurs, E.G., Schoch, T.J., Kite, F.E. (1957). Graphical analysis of the brabender viscosity curves of various starches. Cereal Chem. 34(3): 141 – 153.

Medcalf, D.G and Gillies, K.A. (1965). Wheat starches 1: comparison of physicochemical properties. Journal of Cereal Chemistry.42:558 – 562.

Merkus, H.G. (2009). "Laser Diffraction" in Particle Size Measurements: Fundamentals, Practice, Quality. Springer: Netherlands. pp 259-285.

Miyazaki, S., Yamagichi, H., Takada, M., Hou, W.M., Tacheichi, Y., Yasubuchi, H. (1990). Pharmaceutical applications of biomedical polymers. XXIX. Preliminary study on film dosage form prepared from chitosan for oral drug delivery. Acta Pharm. Nord. (2):401 – 406.

Mort, P.R., Capeci, S.W, Holder, J.W. (2001). Control of agglomerate attributes in a continuous binder-agglomeration process. Powder Technol., 117, 173–176.

Muller, H. G. (1988). An Introduction to Tropical Food Science. Cambridge University Press, Cambridge, pp16 – 46, 112 – 118.

Newitt, D.M. and Conway-Jones, J.M. (1958). A contribution to the theory and practice of granulation. Trans. Inst. Chem. Eng., 36, 422–442.

Newport Scientific. (1998). Applications manual for the Rapid Visco Analyzer. Newport Scientific Pty. Ltd., Warriewood NSW, Australia.

Odebiyi, O. O. and Sofowora, E. A. (1978). Phytochemical screening of Nigerian Medical Plants II.*Lloydia* 41: 2234-2246.

Odunfa, S .A. (1986). Dawadawa. In: legume based fermented foods. Eds: Reddy, N.R, Pierson, N.D and Salunkhe, D.K, Bolaratun, CRC press; pp. 174 – 185.

Ogbadu, L .J. and Okagbue, R. R. (1988). Fermentation of African locust beans (*Parkia biglobosa*), Involvement of different species of Bacillus species. *J FoodMicrobiol* 5:195 – 199.

Ohwoavworhua, F.O., Kunle, O.O., Ofoefule, S.I. (2004). Extraction and characterization of microcrystalline cellulose derived from Luffa cylindrical plant. Afri. J. Pharm. Res. Dev. 1 (1): 1 – 6.

Olayemi, M.A and Olaniyi, A. A. (2008). Bioavailability profile of a commercially available sustained-release ketoprofen capsules in Nigerians: Effect of food. *The Nigerian Clinical Review Journal, 73, July/Aug, 13-19.*

Ouoba, L. I.I., Rechinger, K .B., Barkholt, V., Piawara, B., Traore, A. S., Jakobsen, M. (2003). Degradation of proteins during the fermentation of African locust bean (*Parkia biglobosa*) by strains of *Bacillus subtilis* and *Bacillus pumillus* for production of *soumbala*. *J Appl Microbiol* 94:396 – 402.

PBIP. (1995). Plantain and Banana Improvement Program 1994 Annual Report. Crop Improvement Division, International Institute of Tropical Agriculture, Nigeria.

Perepelkin, K.E. (2005). Polymeric materials of the future based on renewable plant resources and biotechnologies. Fibre Chemistry 37: 417-430.

Petterson, S. and Knudsen, J. (2001). Floral Scent and Nectar Production in *Parkia biglobosa* Jacq. (Leguminosae: Mimosoideae). Botanical Journal of the Linnean Society.135: 97-106.

Podczeck, F. and Miah, Y. (1996). The influence of particle size and shape on the angle of internal friction and the flow factor of unlubricated and lubricated powders. *Int.J. Pharm.* 144, 187-194.

Pharmaceutical Codex (1994). 12th ed. London Pharmaceutical Press, pp.2,5.

Podczeck, F. and Newton , J.M. (1999). Powder filling into hard gelatin capsules on a tamp filling machine. *Int. J. Pharm.* 185, 237-254.

Popoola, L. and ,Maishanu ,H. (1995).Socio – economic values of some potential farm forestry species in Sokoto State. Proceeding of the 24th Annual Conference of the Forestry Association of Nigeria. Kaduna, Oduwaiye, E.A .(Edn.),pp:109 -119.

Prescott, J.K. and Barnum , R.A. (2000). On powder flowability.Pharma. Technol. 24, 60 –84.

Prescott, J.K and Hossfeld, R.J. (1994). Maintaining product uniformity and uninterrupted flow to Direct-Compression tableting process. Pharm. Tech., 18(6): 99-114.

Puhan, J and Weilinga, O. C. (1996). Physicochemical analysis of locust bean seeds. *Ecol Food Nutr* 29(3): 199 – 205.

Rabinski, G. and Thomas, D. (2004). Dynamic digital image analysis: emerging technology for particle characterization. Water Sci. Technol. 50, 19-26.

Rawle, A.F. (1993). Basic principles of particle size analysis" application note MRK038, Malvern instruments, Malvern, UK. www.malvern.co.uk.

Robertson, M. (1999).'Regulatory issues with excipients'. *International Journal of Pharmaceutics*,187(2):273 – 276.

Rumpf, H. and Ebert, F. (1964). Darstellung von Kornverteilunsen zur Ausdeutung Der Gesetzmassigkeit der Zerkleinerungswirkung von Zerkleinrungsmaschinen. *Chem. Ing. Techn*. 36, 523 – 557.

Russell, R. (2004). Synthetic excipient challenge all-natural organics offer advantages/challenges to developer and formulators. Pharmaceutical Technology 38-50.

Salloum, H. (2001). The Odyssey of Arabic Language and Its Script. The Vocabula Review.Volume 3 Number 10.

Sefa – Dedeh, S. (1989). Effects of particle size on some physicochemical characteristics of 'agbelima' (Cassava dough) and corn dough. Tropical Science.29: 21 – 22.

Seitavuopio, P., Heinämäki, J., Rantanen, J., Yliruusi1, J. (2006). Monitoring tablet surface roughness during the film coating process. AAPS PharmSciTech. 7, Article 31, E1-E6.

Shah, A.C. and Meodozeniec, A.R. (1977). Mechanism of lubrication: Influence of duration of lubricant – excipient mixing on processing characters of powders and properties of compressed tablets. J pharm Sci. 66: 1377 – 8.

Shangraw, R.F., Wallace, J.W., Bowers, F.M. (1981). In: The Pharmaceutical Codex. (1994), 12th ed. London Pharmaceutical Press, pp. 9-10.

Shittu, T.A., Sanni, L.O., Awonorin, S.O., Maziya-Dixon, B., Dixon, A. (2005). Use of multivariate techniques in studying flour making characteristics of some Cassava Mosaic Disease resistant cassava clones. African Crop Science Conference Proceedings, Vol. 7. pp. 621-630 .

Sofowora, A .(1993). Medicinal Plants and Traditional Medicine in Africa. Spectrum Books Ltd., Ibadan, Nigeria, pp. 191-289.

Soppela, I., Airaksinen, S., Murtomaa, M., Tenho, M., Hatara, J., Raikkonen, H. (2010). Investigation of the powder flow behaviour of binary mixtures of microcrystalline celluloses and paracetamol. J. Excipients and Food Chem. 1, 55-67.

Souto, C., Gomez-Amoza, J.L, Landin, M., Vila-Jato, J.L,, Concheiro, A., Martinez-Pacheco, R. (1989). Use of the crushing strength parameter for quality control of phenobarbital-microcrystalline cellulose tablets. Farmaco.44: 731-7.

Staniforth, J.N. and Hart, J.P.(1987). Particle size characterization for pharmaceuticals. Anal. Proc. 24, 78-80.

Stein, R. (1982). Locust B; Gum In: Food Hydrocolloids. Volume III.Ed. M. Glicksman, ORC Press, Inc. Florida, U. S. A, p. 61 – 170.

Storme-Paris, I., Clarot, I., Esposito, S., Chaumeil, J.C., Nicolas, A., Brion, F., Rieutord, A., Chaminade, P. (2009). Near infrared spectroscopy homogeneity preformulation process, a real-life application, *Eur. J. Pharm. Biopharm.* 72, 189-198.

Summers, M.P. (1988). Granulation. In: Pharmaceutics, The science of dosage forms design, Aulton M.E (ed.), Churchill Livingstone, New York, p. 616-628.

Sun, C. and Himmelspach, M.W. (2006). Reduced tablet ability of roller compacted granules as a result of granule size enlargement. *J. Pharmac. Sci.*, 95(1): 200-206.

Sun, C.C., Hou, H., Gao, P., Ma, C., Medina, C., Alvarez, F.J. (2009). Development of a high drug load tablet formulation based on assessment of powder manufacturability: moving towards quality by design, *J. Pharm. Sci.* 98, 239-247.

Swahili – English Dictionary. (1939). Inter – Teritorial Language Committee for the East African Dependencies under the direction of Frederick Johnson. Nairobi, Kenya. Oxford University Press.p. 481 – 676.

Swarbrick, J. and Boylan, C.J. (1993). Encyclopedia of Pharmaceutical Technology, Marcel Deckker Inc. Vol. 7, p. 126.

Tan, S.B. and Newton, J.M.(1990). Powder flowability as an indication of capsule filling performance. Int J Pharm. 61: 145 – 155.

Terrier de la Chaise, B.and LePerdriel, F. (1972). The drying of granules. Pharma Int. 6: 16-22

Tinke, A.P., Carnicer, A., Govoreanu, R., Scheltjens, G., Lauwerysen, L., Mertens, N. (2008). Particle shape and orientation in laser diffraction and static image analysis: size distribution analysis of micrometer sized rectangular particles. *Powder Technol.* 186, 154-167.

Tousey, M. D. (2002). The Granulation Process 101; Basic Technologies for Tablet Making. Pharmaceutical Technology, Tableting and Granulation. pp. 8 – 13.

Trease, G.E. and Evans, W.V. (1983). Drugs of Biological Origin. In Pharmacognosy 12thedn. United Kingdom:Balliere Tindall, pp.309 – 540.

United States Pharmacopoeia (2009). General Test USP 32–NF 27, (U.S. Pharmacopeial Convention, Rockville, MD), pp. 302−304, 307−310, 688−691.

United States Pharmacopeia (2007). 30th Edition, National Formulary 25th ed., United States Pharmacopeia Convection, Rockville, MD, USA.

Uwaegbute, A .C. (1996). African Locust Beans In: Food from Legumes and Oil seeds. (E. Nwok3 la and J. A. Smart, eds.). Chapman and Hall, London. pp. 124 – 129.

Valverde, J.M. (2000). Avalanches in fine, cohesive powders. Physical Review E 62, 6851-6860.

Van Scoik, K., Zoglio, M.A., Carstensen, J.T. (1993).Drying and driers. In: Encyclopedia of pharmaceutical technology, Swarbrick J and Boylan JC (eds.). Marcel Dekker, Inc., New York, pp. 485-515.

Virtanen, S., Antikainen, O., Räikkönen, H,, Yliruusi, J. (2010). Granule size distribution of tablets", *J. Pharmac. Sci*., 99(4): 2061-2069.

Wade, A. and Weller, P. J. (1994). Handbook of Pharmaceutical Excipients 11th edn. The Pharmaceutical press: London. pp. 426 – 428.

Weth, M., Hoffman, M,, Kuhn, J., Frick, J. (2001). Measurement of attractive forces between single aerogel powder particles and the correlation with powder flow. *J. Non-Cryst*. Solids 285, 236-243.

Xie, L., Chen, N., Duan, B., Zhu, Z., Liao, X. (2008). Impact of proteins on pasting and cooking properties of waxy and non-waxy rice. *Journal of Cereal Science* 47:372–379.

Xu, R. and Andreina Di Guida, O. (2003). Comparison of sizing small particles using different technologies. Powder Technol. 132,145-153.

Yamamoto, N., Shinozuka, Y., Kumagai, K., Fujii, M., Yanagisawa, Y. (2004). Particle size distribution quantification by microscopic observation. *J. Aerosol. Sci.*, 35,1225 - 1234.

Yayock, J .Y., Lombin, G.,Owonubi, J .J. (1988). Crop science and Production in Warm Climates 4th Edn, Macmillan Intermediate Agriculture Series. Macmillan publishers Ltd. London. pp. 256 – 257.

Yu, A.W and Standish, N. (1987). Porosity calculation of multi-component mixtures of spherical particles, Powder Technol. 52, 233-241.

Yu, L.X. (2008). Pharmaceutical quality by design: product and process development, understanding, and control. Pharm. Res. 25, 781-791.

Zatloukal Z. and Sklubalova Z. (2007). Penetrometry and estimation of the flow rate of powder excipients. Pharmazie. 62, 185-189.

Zobel, H. F. (1984). 'Starch gelatinization and mechanical properties' In Starches: Chemistry and Technology,2nd ed., R.L. Whistler, J.N. Benwiller, E.F.Paschal (Eds), pp. 286 – 287, Academic Press, New Y ork.

APPENDICES

APPENDIX I: Particle size and size distribution determination of *Parkia biglobosa* fruit pulp.

Sieve Size	Aperture Size (µm)	Range of Aperture (µm)	Midpoint of Range (µm)	Weight Retained (g)	Percentage Weight Retained (%)	Cumulative Percentage Oversize
20	>850	7850	850. 0	–	–	–
40	425	425 – 850	637.5	1.05	0.70	0.70
60	250	250 – 425	337.5	106.49	70.99	71.69
80	180	180 – 250	215.0	29.97	19.98	91.67
200	75	75 – 180	127.5	29.97	7.90	99.57
Pan	–	< 75	75	–	–	–

Total weight of powder = 150g

Percentage weight retained = $^{\text{wt retained}}/_{\text{Total wt}}$ x 100

For sieve 40, percentage wt retained = $^{1.05}/_{150}$ x 100% = 0.70%

From the log probability graph

50% size ⟶ 300 µm

16% size ⟶ 400 µm

Geometric mean diameter, d_{geo} = 300 µm

Geometric standard deviation, d_{geo} = $^{16\% \text{ oversize}}/_{50\% \text{ size}}$ = $^{400}/_{300}$ = 1.3333

Calculation of equivalent spherical diameter, using Hatch – Choate equation

1. Mean Surface Diameter, ds

   $\log ds = \log d_{geo} - 4.6052 \log^2 \sigma_{geo}$

   $\log ds = \log 300 - 4.6052 \log^2 1.3333$

   $\log ds = 2.41525$

   $ds = \text{antilog } 2.41525$

   $ds = 254.24\ \mu m$

   Mean surface diameter = 254.24μm

APPENDIX II : Phytochemical properties of the *P **bigobosa*** fruit pulp samples.

No.	Test	Observation			
		Sample A	**Sample B**	**Sample C**	**Sample D**
1	Carbohydrate test (Molisch's test)	A purple ring formed at the junction of two layers observed.	A purple ring formed at the junction of two layers observed.	A purple ring formed at the junction of two layers observed.	A purple ring formed at the junction of two layers observed.
2	Selivanoff's test for Ketones	A rose red colour formed.	A rose red colour formed.	A rose red colour formed.	A rose red colour formed.
3	Pentoses test	Red colour formed.	Red colour formed.	Red colour formed.	Red colour formed.
4	Keller-Killiani test for Deoxy – sugars	Two layers formed. Upper layer turned bluish green on standing.	Two layers formed. Upper layer turned bluish green on standing..	Two layers formed. Upper layer turned bluish green on standing.	Two layers formed. Upper layer turned bluish green on standing.
5	Test for starch	No blue □ black colour formed.	No blue □ black colour formed.	No blue □ black colour formed.	No blue □ black colour formed.
6	Test for Tannins	No brownish green colour formed.	No brownish green colour formed.	No brownish green colour formed.	No brownish green colour formed.
7	Test for Glycosides	A redish brown ring is formed at the interface of two layers.	A redish brown ring is formed at the interface of two layers.	A redish brown ring is formed at the interface of two layers.	A redish brown ring is formed at the interface of two layers.
8	Test for Saponins	Frothing observed.	Frothing observed.	Frothing observed.	Frothing observed.
	Test for	No creamy	No creamy white	No creamy white	No creamy

9	Alkaloids	white precipitate formed.	precipitate formed.	precipitate formed.	white precipitate formed.
10	Fehling's test	Brick red precipitate formed.	Brick red precipitate formed.	Brick red precipitate formed.	Brick red precipitate formed.
11	Test for Flavonoids	A yellow colouration observed.	A yellow colouration observed.	A yellow colouration observed.	A yellow colouration observed.

APPENDIX III: **Calculation for flowability properties**

ANGLE OF REPOSE

Diameter of funnel = 10cm

Diameter of funnel tip = 0.8cm

Length of funnel stem = 9.0cm

Height of cone formed = 1.9cm + 1.8cm

Average = $^{1.9 + 1.8}/_{2}$ = 1.85cm

Diameter of cone formed = 4.2cm + 4.4cm

Average = $^{4.2 + 4.4}/_{2}$ = 4.3cm

Tan ɵ = $2h/_{D}$

Angle of repose = Tan ɵ = $^{2x1.85}/_{4.3}$ = 0.8605

ɵ = $Tan^{-1}0.8605$ = 40.71°

BULK DENSITY

Initial bulk volume (Vo) = 49ml

Final bulk volume (tapped), Vt = 32ml + $32^{ml}/_{2}$ = 32.ml

Weight of sample (m) = 7.0g

Bulk density (Db) = $^{M}/_{Vo}$ = $^{7.0}/_{49}$ = 0.1429

Tapped density (Dt) = $^{M}/_{Vt}$ = $^{7.0g}/_{32ml}$ = 0.2188

Hausner's ratio = $^{Dt}/_{Db}$ = $^{0.2188}/_{0.1429}$ = 1.531

Carr's compressibility index = $^{Dt - Dh}/_{Dt}$ x 100 = $^{0.2188 - 0.1429}/_{0.2188}$ x 100 = 34.69%

APPENDIX IV: **Calculation for swelling capacity**

Volume of distilled water = 10ml

Weight of sample = 1g

Weight of empty tube I = 12.84g

Weight of empty tube II = 13.15g

Volume of supernatant I = 5.2ml

Volume of supernatant II = 5.2ml

Weight of paste + tube I = 17.05g

Weight of paste + tube II = 17.43g

Weight of paste I =17.05g – 12.84g = 4.21g

Weight of paste II = 17.43g – 13.15g = 4.30g

Average = $\frac{4.21 + 4.30}{2}$ = 4.26g

Swelling power = $\frac{\text{Wt of paste}}{\text{Wt of dry sample}} = \frac{4.26}{1}$ = 4.26

APPENDIX V: **Calculation for water binding capacity (WBC)**

Volume of distilled water = 10ml

Weight of sample = 1g

Weight of empty tube I = 13.53g

Weight of empty tube II = 9.09g

Volume of supernatant I = 7.0ml

Volume of supernatant II = 7.0ml

Weight of paste + tube I = 17.70g

Weight of paste + tube II = 13.20g

Weight of paste I = 17.70g – 13.53g = 4.17g

Weight of paste II = 13.20g – 9.09g = 4.11g

Average = 4.17 + 4.11/2 = 4.14

Water binding capacity = $^{\text{Bond Water (g)}}/_{\text{Wtof sample}}$ x 100 = $^{4.14}/_{1}$ x 100

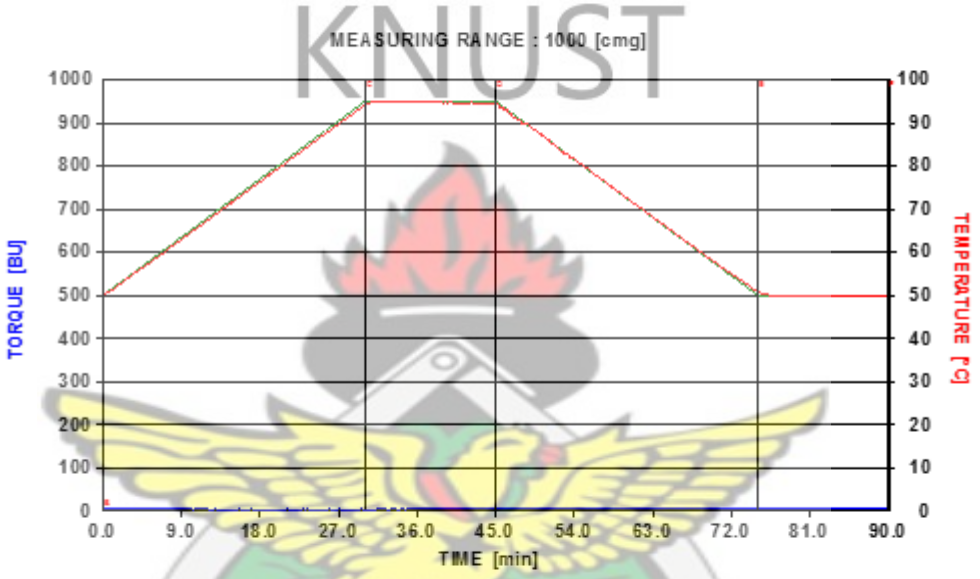
= 414%

APPENDIX VI: Pasting curve of Acacia gum as measured by RVA.

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS		Date	:	12/23/2011	
Sample	:	Acacia		Method	:	METHOH 1	
Moisture	:	12.35	[%]	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	00:00:05	5	50.1
B	Maximum viscosity	00:00:00	5	50.0
C	Start of holding period	00:30:00	3	94.2
D	Start of cooling period	00:45:00	4	94.6
E	End of cooling period	01:15:00	7	50.9
F	End of final holding period	01:30:00	6	49.9
B-D	Breakdown		0	
E-D	Setback		1	

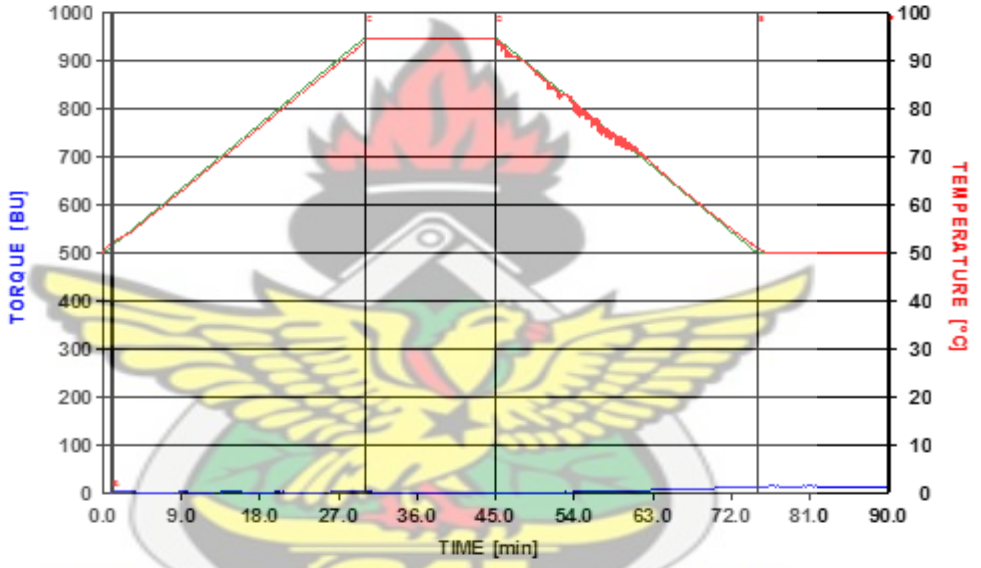
APPENDIX VII: Pasting curve of *Parkia* fruit pulp as measured by RVA.

BRABENDER VISCOGRAPH

Parameter

Operator	:	APOLLONIUS	Date	:	12/21/2011
Sample	:	PARKIA FRUIT PULP	Method	:	METHOH 1
Moisture	:	10.0 [%]	Correction	:	14 [%]
Sample weight	:	40 [g]	Corr. to 14%	:	38.2 [g]
Water	:	420 [ml]	Corr. to 14%	:	421.7 [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]

MEASURING RANGE : 1000 [cmg]



Evaluation

Point	Name	Time [HH:MM:SS]	Torque [BU]	Temperature [°C]
A	Beginning of gelatinization	00:01:05	3	52.4
B	Maximum viscosity	00:01:00	4	52.2
C	Start of holding period	00:30:00	2	94.2
D	Start of cooling period	00:45:00	0	94.7
E	End of cooling period	01:15:00	14	51.1
F	End of final holding period	01:30:00	13	49.9
B-D	Breakdown		4	
E-D	Setback		14	

File : Measurement V: 2.3.16

APPENDIX VIII: Calculation of uniformity of weight test

The percentage deviations of the tablets from the mean were calculated using:

Weight of 20 tablets = Xg

Average weight of 20 tablets = Xg/20 = B

$$\text{Percentage deviation} = \frac{A - B}{B} \times 100,$$

Where, A = Initial weight of tablets, B = Average weight of 20 tablets

APPENDIX IX: Uniformity of weight of paracetamol tablets formulated with 1%w/w *P. biglobosa* fruit pulp as binder.

Tablet no.	Tablet weight (Ag)	(A-B)g	(A-B) /B g	Percentage deviation
1	0.597	0.000	0.0000	0.000
2	0.603	0.006	0.0134	1.342
3	0.599	0.002	0.0045	0.450
4	0.602	0.005	0.0112	1.120
5	0.597	0.000	0.0000	0.000
6	0.605	0.008	0.0179	1.790
7	0.592	-0.005	-0.0112	-1.120
8	0.593	-0.004	-0.0089	0.890
9	0.594	-0.003	-0.0067	-0.670
10	0.591	-0.006	-0.0134	-1.342
11	0.600	0.003	0.0067	0.670
12	0.595	-0.002	-0.0045	-0.450
13	0.599	0.002	0.0045	0.450
14	0.595	-0.002	-0.0045	-0.450
15	0.593	-0.004	-0.0089	-0.890
16	0.595	-0.002	-0.0045	-0.450
17	0.598	0.001	0.0022	0.220
18	0.596	-0.001	-0.0022	0.220
19	0.600	0.003	0.0067	0.670
20	0.604	0.007	0.0157	1.570
Total	11.949			
Average	0.597			
Stand. dev.	0.004			

APPENDIX XI : Uniformity of weight of paracetamol tablets formulated with 5%w/w Acacia gum as binder.

Tablet no.	Tablet weight (Ag)	(A-B)g	(A-B) /B g	Percentage deviation
1	0.603	-0.002	-0.0044	-0.440
2	0.594	-0.011	-0.0242	-2.418
3	0.591	-0.014	-0.0308	-3.077
4	0.594	-0.011	-0.0242	-2.418
5	0.603	-0.002	-0.0044	-0.440
6	0.608	0.003	0.0066	0.660
7	0.609	0.004	0.0088	0.880
8	0.609	0.004	0.0088	0.880
9	0.611	0.006	0.0132	1.320
10	0.460	0.005	0.0110	1.100
11	0.610	0.005	0.0110	1.100
12	0.609	0.004	0.0088	0.880
13	0.608	0.003	0.0066	0.660
14	0.606	0.001	0.0022	0.220
15	0.606	0.001	0.0022	0.220
16	0.457	0.002	0.0044	-0.440
17	0.607	0.002	0.0044	-0.440
18	0.604	-0.001	-0.0022	0.220
19	0.604	-0.001	-0.0022	0.220
20	0.607	0.002	0.0044	0.0044
Total	12.10			
Average	0.605			
Stand. dev.	0.0057			

APPENDIX XII : Uniformity of weight of paracetamol tablets formulated with 2% w/w *P. biglobosa* fruit pulp as disintegrant.

Tablet no.	Tablet weight (Ag)	(A-B)g	(A-B) /B g	Percentage deviation
1	0.601	0.002	0.0033	0.330
2	0.600	0.001	0.0017	0.170
3	0.599	0.000	0.0000	0.000
4	0.598	0.001	0.0017	0.170
5	0.596	-0.003	-0.0050	-0.500
6	0.595	-0.004	-0.0067	0.670
7	0.597	-0.002	-0.0033	-0.330
8	0.600	0.001	0.0017	0.170
9	0.594	-0.005	-0.0083	-0.830
10	0.599	0.000	0.0000	0.000
11	0.596	-0.003	-0.0050	-0.500
12	0.598	-0.001	0.0017	0.170
13	0.599	0.000	0.0000	0.000
14	0.597	-0.001	-0.0022	-0.220
15	0.598	-0.001	-0.0017	0.170
16	0.593	-0.006	-0.0100	-1.000
17	0.605	0.006	0.0100	1.000
18	0.603	0.004	0.0067	0.670
19	0.602	0.003	0.0050	0.500
20	0.600	0.001	0.0017	0.170
Total	11.97			
Average	0.599			
Stand. dev.	0.003			

APPENDIX XIII : Uniformity of weight of paracetamol tablets formulated with 4% w/w Sodium starch glycolate as disintegrant.

Tablet no.	Tablet weight (Ag)	(A-B)g	(A-B) /B g	Percentage deviation
1	0.604	0.000	0.0000	0.000
2	0.597	0.007	-0.0154	-1.540
3	0.602	-0.002	-0.0044	-0.440
4	0.604	0.000	0.0000	0.000
5	0.601	-0.003	-0.0066	-0.660
6	0.602	-0.002	-0.0044	-0.440
7	0.606	0.002	0.0044	0.440
8	0.602	-0.002	-0.0044	-0.440
9	0.609	0.005	0.0110	1.100
10	0.602	-0.002	-0.0044	-0.440
11	0.600	-0.004	-0.0088	-0.880
12	0.606	0.002	0.0044	0.440
13	0.604	0.000	0.0000	0.000
14	0.603	-0.001	-0.0022	-0.220
15	0.606	0.002	0.0044	0.440
16	0.606	0.002	0.0044	0.440
17	0.604	0.000	0.0000	0.000
18	0.601	-0.003	-0.0066	-0.660
19	0.607	0.003	0.0066	0.660
20	0.608	0.004	0.0088	0.880
Total	12.07			
Average	0.604			
Stand. dev.	0.003			

APPENDIX XIV: Preparation of 0.1M NaOH solution

Molecular weight of NaOH = 40g/mol

40g NaOH in 1000ml ≡ 1M

4g NaOH in 1000ml ≡ 0.1M

8g NaOH in 2000ml ≡ 0.1M

Assay of NaOH ≡ 99%

99% ≡ 8g NaOH

100% ≡ 100/99 x 8g = 8.08g

Preparation of various concentrations of paracetamol solution with 0.1M NaOH

i. For 0.0001% solution

0.1X = 0.0001 x 50

X = 0.0001 x 50/0.1 = 0.05ml

ii. For 0.0002% solution

0.1X = 0.0002 x 50

X = 0.0002 x 50/0.1 = 0.1ml

iii. For 0.0003% solution

0.1X = 0.0003 x 50

X = 0.0003 x 50/0.1 = 0.15ml

iv. For 0.0004% solution

0.1X = 0.0004 x 50

X = 0.0004 x 50/0.1 = 0.2ml

v. For 0.0005% solution

0.1X = 0.0005 x 50

X = 0.0005 x 50/0.1 = 0.25ml

APPENDIX XV: Preparation of phosphate buffer pH 5.8

Preparation of 0.2M KH_2PO_4 solution

Molecular weight of Potassium dihydrogen phosphate (KH_2PO_4) =136.09g/mol

136.09g KH_2PO_4 ≡ 1000ml 1M

952.63g KH_2PO_4 ≡ 7000ml 1M

190.53g KH_2PO_4 ≡ 7000ml 0.2M

Assay of KH_2PO_4 ≡ 99.5%

If 99.5% ≡ 190.53g KH_2PO_4

100% ≡ 100/99.5 x 190.53 = 191.48g KH_2PO_4

Preparation of 0.2M NaOH solution

Molecular weight of NaOH = 40g/mol

40g NaOH ≡ 1000ml 1M

280g NaOH ≡ 7000ml 1M

56g NaOH ≡ 7000ml 0.2M

Assay of NaOH ≡ 99%

99% ≡ 56g NaOH

100% ≡ 100/99 x 56g = 56.57g

APPENDIX XVI: UV Absorbance of the formulated paracetamol tablets with 5%w/w *P. biglobosa* fruit pulp as binder..

Form.	Time/min.	Absorbance (nm)						Mean
		1	2	3	4	5	6	
Parkia	5	0.456	0.451	0.458	0.452	0.455	0.456	0.455±0.003
biglobosa	10	0.471	0.474	0.480	0.480	0.483	0.481	0.478±0.005
fruit pulp	15	0.496	0.499	0.498	0.502	0.501	0.505	0.500±0.003
	30	0.510	0.503	0.512	0.501	0.499	0.496	0.504±0.006
	45	0.484	0.493	0.490	0.492	0.495	0.490	0.491±0.004
	60	0.479	0.486	0.485	0.475	0.480	0.478	0.481±0.004
Acacia	5	0.402	0.402	0.403	0.409	0.401	0.402	0.403±0.003
gum	10	0.425	0.426	0.423	0.417	0.414	0.424	0.422±0.005
	15	0.455	0.456	0.453	0.460	0.466	0.462	0.459±0.005
	30	0.480	0.481	0.482	0.489	0.487	0.482	0.484±0.004
	45	0.493	0.492	0.495	0.496	0.500	0.499	0.494±0.006
	60	0.487	0.484	0.482	0.486	0.499	0.489	0.488±0.006

APPENDIX XVII: Calculation for invitro drug release of the formulated paracetamol tablets

The U.V absorption calibration curve of Paracetamol in 0.1M NaOH over a concentration range 0.0001 – 0.0005 yielded a linear regression equation of y = 634.7x + 0.041(where y is the absorbance and x is the concentration in mg/ml) with narrow confidence interval and correlation of 0.863.

Using linear regression equation below,

y = 634.7x + 0.041 r^2 = 0.863, where y is the absorbance and x is the concentration in mg/ml with r being the correlation.

For an aliquot of 0.94ml with absorbance of 0.456nm

Conc. x = $\frac{0.456 - 0.041}{634.7} = 6.54 \times 10^{-4}$

Actual amount of drug released = conc. x dilution factor (50/0.94)

= $6.54 \times 10^{-4} \times 53.19$

= 0.0346 % w/v

Assuming 100 % release, conc. of drug in 900 ml medium

= 900ml ≡ 0.360g

100ml ≡ $\frac{100 \times 0.360}{900}$ = 0.040 % w/v

% released = 0.0348 / 0.040 = 87 %

APPENDIX XVIII: Drug release profile of the formulated paracetamol tablets with 5 % w/w *P. biglobosa* fruit pulp as binder.

Formulation	Time/min.	Percentage (%) Drug release						
		1	2	3	4	5	6	Mean
P. biglobosa fruit pulp	5	87.00	85.90	87.40	86.10	86.70	87.00	86.68 ± 0.58
	10	90.09	90.72	91.97	91.97	92.60	92.18	91.59 ± 0.97
	15	95.33	95.95	95.75	96.58	96.37	97.21	96.20 ± 0.67
	30	98.26	96.79	98.68	96.37	95.95	95.33	96.70 ± 1.32
	45	92.81	94.69	94.07	94.49	95.12	94.07	94.21 ± 0.79
	60	91.76	93.23	93.02	90.93	91.97	91.56	92.08 ± 0.88
Acacia gum	5	75.63	75.63	75.84	77.10	75.42	75.63	75.88 ± 0.61
	10	80.45	80.66	80.03	78.77	78.15	80.24	79.72 ± 1.01
	15	86.74	86.95	86.32	87.78	89.04	88.20	87.51 ± 1.02
	30	91.97	92.18	92.39	93.86	93.44	92.39	92.71 ± 0.76
	45	94.69	94.49	95.12	95.33	96.16	95.95	95.29 ± 0.67
	60	93.44	92.81	92.39	93.23	95.95	93.86	93.61 ± 1.25

APPENDIX XIV : Summary of analysis of formulated tablets with varying concentrations of *P. biglobosa* as binder (Reference: Acacia gum).

Binder	Batches	Thickness (mm)	Hardness (N)	Friability (%)	Disintegration time (min.)	Drug release value (%)
P. biglobosa fruit pulp	A_1	6.2 – 6.3	19.60	1.27 ± 0.05	0.74±2.12	94.00
	A_2	6.2 – 6.3	29.40	0.78 ± 0.08	1.52±0.02	
	A_3	6.2 – 6.3	39.20	0.60 ± 0.08	3.30±0.03	
	A_4	6.2 – 6.3	44.10	0.11 ± 0.00	9.04±0.03	
	A_5	6.2 – 6.3	49.00	0.11 ± 0.00	10.24±0.02	
Acacia gum	A_6	6.2 – 6.3	39.20	0.37 ± 0.07	1.39±0.01	95.00

APPENDIX XV: Summary of analysis of formulated tablets with varying concentrations of *P. biglobosa* as disintegrant (Reference: Sodium starch glycolate).

Disintergrant	Batches	Thickness (mm)	Hardness (N)	Friability (%)	Disintegration time (min.)
Parkia biglobosa fruit pulp	B_1	6.2 – 6.3	35.93	0.45 ± 0.08	80.83 ± 2.12
	B_2	6.2 – 6.3	39.20	0.27 ± 0.05	53.67 ± 2.83
	B_3	6.2 – 6.3	39.20	0.53 ± 0.03	26.50 ± 1.65
	B_4	6.2 – 6.3	39.20	0.78 ± 0.03	29.00 ± 1.42
Sodium starch glycolate	B_5	6.2 – 6.3	39.20	0.44 ± 0.08	3.49 ± 0.35