KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY.

PURIFICATION, PHYSICOCHEMICAL AND FORMULATION PROPERTIES OF SHEA (VITELLARIA PARADOXA) GUM.

A THESIS SUBMITTED IN
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To the

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By

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DECLARATION

The experimental work described in this thesis was carried out at the Department of Pharmaceutics, KNUST. This work has not been submitted for any other degree.

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DEDICATION

This thesis is dedicated to God Almighty. Without His help none of these would have been possible.

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I will like to thank God for how far He has brought me and also acknowledge the help of all persons in the department of Pharmaceutics especially my supervisor, Mr.S.L. Kipo, the head of department Mr. Francis Adu, other lecturers such as Prof. K. Ofori - Kwakye, Mr. Rapheal Johnson, Dr. Agyare and Miss Marian El-Duah for their various contributions towards the successful completion of this project. Not forgetting my dear collegues Mr. Ernest Obese and Miss Hilda Amekye for their encouragement and support through the programme. A special thank you goes to my family especially my dear loving Husband, Mr. Emmanuel Owusu-Sarfo for all their help. May God richly bless you all.

ABSTRACT

This study focused on the purification, physichochemical and formulation properties of Shea (*vitellaria paradoxa*) gum. The crude gum was purified and the yield obtained was 63.26%. Crude and purified Shea gums were evaluated for their physicochemical properties and were found to have satisfactory moisture content and insoluble matter. Atomic absorption spectrophotometric analysis of the gums showed that the crude gum had higher metallic ion and protein content than the purified gum which may be attributed to the purification process. The gums had relatively high levels of calcium, followed by magnesium, iron, zinc, potassuim and sodium. Different concentrations of the gum were analysed for their rheological properties and were found to exhibit pseudoplastic flow.The binding property of Shea gum was compared to that of acacia, a standard binding agent. The flow properties of the granules were evaluated and the physical properties of the compressed tablets, namely uniformity of weight, hardness, friability, and disintegration time, assay of content and dissolution rate determined. The granules had good flow properties as evidenced by their Hausner ratio, angle of repose and Carr's index values. The gum was successfully employed as a binding agent in Paracetamol tablet formulations with different concentrations of Shea gum and acacia gum at the same concentration. The study showed that Shea gum can be successfully employed as a binder at concentrations between 5% w/v and 20% w/v and the binding effect was found to be comparable to the binding effect of the same concentration of acacia.The suspending property of the gum was investigated by assessing parameters such as rate of sedimentation, apparent viscosity and ease of redispersibility of paracetamol suspensions prepared with concentrations of 1% w/v to 4% w/v shea gum and compared with those prepared with acacia gum at the same concentration. Suspensions were successfully prepared using the gum, but the sediment showed a tighter packing as the concentration of the gum used was increased. Shea gum proved more efficient as a suspending agent than acacia gum. The emulsifying property of the gum was also investigated by preparation of emulsions using different classes of oils and employing the wet and dry gum methods of preparation. The ratio of oil to water to gum for the preparation of primary emulsion was determined for the oils. The stability of the emulsions was assessed and an improvement in the stability was attempted using homogenization, a surface active agent, and the addition of a thickening agent. The results

obtained demonstrated that emulsions could be prepared with the mineral oil and fixed oil and volatile oil with ease. All the emulsions stabilized by homogenization creamed on the third day, but creaming was reduced by addition of very low concentrations of a thickening agent, xanthan gum at low concentrations of between 0.1% w/v and 0.2% w/v. The addition of a surface active agent (Tween 60) also reduced the creaming of the emulsions at low concentrations of between 0.001% w/v and 0.004% w/v.

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Chapter 1
INTRODUCTION

1.1 GENERAL INTRODUCTION

In our world today, natural substances are replacing their synthetic counterpart in every aspect of human life. Natural products are preferred in the food and cosmetic industries. The drug industry has not been spared of this trend, today the world is increasingly interested in natural drugs and excipients. This interest in natural product could be attributed to the numerous advantages they possess over synthetic materials. They are known to be less toxic, less expensive and readily available. In addition they are also easily modified to suit several drug delivery systems making them equally competitive with the synthetic materials available (Bhardwaj, et al. 2000.)

There are many kinds of natural products useful in pharmaceutical formulations. These include gums and mucilage, starches from various plants, natural sugars, agar, cellulose and many more.

These natural products are used pharmaceutically as binding agents, disintegrants, suspending agents, protective, colloids, thickening agents, gelling agents, bases in suppositories, stabilizers and coating materials.

Gums and mucilage are polysaccharide complexes formed from sugar and uronic acid units and are insoluble in alcohol but dissolve or swell in water. They are usually formed from the cell wall (for example, tragacanth) or deposited on it in successive layers. Gums are natural plant colloids that may be classified as anionic or non-ionic polysaccharides or salts of polysaccharides. They are translucent, amorphous substances that are frequently produced in higher plants as a protective after injury .The nature of the compounds involved influences the properties of different gums. Some plant gums, such as gum arabic are soluble in water, dissolving to give clear solutions. Others including gum tragacanth produce mucilage by absorption of large quantities of water (Girish. et.al, 2009). In recent years the Shea tree (*vitellaria paradoxa*) has gained importance as an economic crop because of the heavy demand for its butter both locally and internationally.

The Shea tree is readily available in Ghana, (the Northern, Upper East and Upper West regions) and extensively over the African continent (Coull, 1928). The stemof this tree has deep fissures some of which are usually covered with gums. In addition spots of injury on the stem are usually covered with gum suggesting that the gum can be obtained in large quantities from this plant hence it can serve as a cheaper replacement for the synthetic gums if found to be useful in pharmaceutical formulation. Other parts of the Shea tree including the gum from the trunk have been used traditionally. The Shea gum is used by women to mend broken calabashes (Wallace-Bruce, 1995).

In addition the gum is chewed as a gum and made into balls for children to play with. In Burkina Faso, Bobo musicians use it to repair cracked drums and punctured drumheads.

The gum contains only 15-25% of carotene and, therefore, is not suitable for the manufacture of rubber (Dissassomba.et.al, 2009).

However, the potential uses of this gum have being little investigated especially for pharmaceutical purposes. A review of literature revealed various uses of the different parts of the Shea tree. The most documented uses of the plant involves the butter obtained from the nuts.Shea butter is the main edible oil for the people of Northern Ghana, being the most important source of fatty acids and glycerol in their diet. It is an unguent for the skin. It also has anti-microbial properties, which gives it a place in herbal medicine (Fleury, 1981).

It is also used in the pharmaceutical and cosmetic industries as an important raw material and/or a precursor for the manufacture of soaps, candles, and cosmetics. Shea butter is used as a sedative or anodyne for the treatment of sprains, dislocations and the relief of minor aches and pains.

This study therefore focuses on the purification, physicochemical evaluation and evaluation of the formulation properties of the Shea gum.

1.2 JUSTIFICATION OF WORK

Pharmaceutical formulations are always made up of the active pharmaceutical agent and the excipients. The cost of most drugs are affected both component. With an increase in the cost of healthcare all over the world, it has become necessary for drug research to target natural excipient which are much cheaper compared to their synthetic counterparts in order to make drugs more affordable to patients.

Groups of natural products which find versatile use in the pharmaceutical industry as excipient are gums and mucilage. Gums and mucilages are employed in tablets, capsules, suspensions, emulsions, creams, lotions, ointments and many other formulations. As a result of these versatile uses coupled with the limited supply, the traditional hydrocolloids have a high cost. Hence the need for alternatives which are cheaper and readily available cannot be overemphasised.

Many gums such as acacia, cashew, albizia, xanthan, tragacanth, have been researched and are currently used in several formulations. However, others such as the Shea tree gum has not benefited from scientific research which would ultimately make it useful to the pharmaceutical industry. Meanwhile the shea tree gum is readily available all over the continent of Africa and in all the regions of Ghana. Almost all research on this tree has concentrated on the nuts which produce the oil used for the production of Shea butter.

The purification, physicochemical evaluation and the evaluation of formulation properties of the Shea tree gum provided in this study seeks to provide a basis for the use or rejection of the Shea gum as an alternative to traditional hydrocolloids in local drug manufacturing.

1.3 SCOPE OF RESEARCH

The research consists of:

- Purification of the crude gum
- Physicochemical evaluation of Shea gum
- Formulation of paracetamol tablets with different concentrations of the purified shea gum mucilage as a binder compared with same concentrations of acacia gum mucilage.
- Quality assessment of the paracetamol tablet formulated.
- Evaluation of the suspending abilities of the shea gum in paracetamol suspensions.
- Evaluation of the emulsifying property of the Shea gum.

Chapter 2

LITERATURE REVIEW

2.1 THE NATURE AND CLASSIFICATION OF GUMS

Natural gums are polysaccharides of natural origin, capable of causing a large viscosity increase in solution, even at small concentrations. In the food industry they are used as thickening agents, gelling agents, emulsifying agents, and stabilizers. In other industries, such as the pharmaceutical industry, they are also used as adhesives, binding agents, disintegrating agent, encapsulating agents, coating agent, flocculating agents, swelling agents, foam stabilizers, etc (Girish et.al,2009)

Natural gums can be classified according to their origin. They can also be classified as uncharged or ionic polymers (polyelectrolyte).

According to the origin gums can be classified as plant gums, gums from marine sources and gums obtained from bacteria fermentation Examples of these include;

Plant gums: gum Arabic, gum ghatti, karaya gum, chicle gum, gum tragacanth, mastic gum, locust bean gum, psyillium gum, spruce gum, glucomannan.

Marine gum: agar, algenic acid, carrageenan and sodium alginate

Gum from bacteria fermentation: gellan gum and xanthan gum

Gums are also classified based on their electrical properties, they may ionic or non-ionic depending on their electrical charges.

Ionic gum: karaya gum, gum ghatti, gum tragacanth, gellan gum, agar, algenic acid and carrageenan

Nonionic or uncharged gums; guar gum, locust bean gum, beta glucan, chicle gum, dammar gum, glucomannan, mastic gum, spruce gum, psyllium gum and tara gum (Girish. et.al,2009)

Gums of the ancient world were largely plant exudates. Many plant families include species that exude gums in greater or lesser degree. Gums may be exuded only in very small quantities and not be readily discernible, or they may be produced very copiously, forming large, conspicuous incrustations. Those produced in large amounts constitute the gums of the ancient world and even today constitute a significant 15-25% segment of the natural gums of commerce (Whistler, 1973).

Natural gums and resins are present either in the intercellular space (ducts or cavities) of the plant parts or as exudate produced due to injury. The ducts or cavities formed due to injury are called traumatic ducts/cavities. The causes of gum and resin formation and their biosynthesis are not fully understood. Poor soil, drought and other hostile environmental conditions promote their production. Gums and resins do not re-enter the metabolism of the plant in which they are produced and therefore, they are considered as by-products or end products of certain metabolic changes. It is suggested that gum formation may be a pathological response of the plants to protect the injured part by sealing the region to prevent water loss and infection. (Nair, 2011).

Plant gums may further be classified according to their solubility in water. They may be water soluble (true gums) such as acacia, guar gum and gum tragacanth or water insoluble gum such as chicle gum and mastic gum. The difference in water solubility has been attributed to the basic structure of the subunit of the polysaccharide chain. True plant gums are polysaccharides composed of many sugar subunits linked together while the poory soluble gums consist of branched sugar molecules. The degree of branching affects the solubility in water (Mantell, 1947).

2.2 PROPERTIES OF GUMS;

2.2.1 Physical properties

Gums consist of mixtures of similar, but not identical, molecules and different sources, methods of preparation, thermal processing and foodstuff environment (for example, salt content, pH and temperature) all affect the physical properties they exhibit. They are made up of mixtures of molecules with different molecular weights and no one molecule is likely to be conformationally identical or even structurally identical to any other . Therefore although there are general properties that may apply to almost all gums there are also some properties peculiar to the individual gums.

In the solid state, gums vary from almost colourless to various shade of yellow, amber and orange to dark brown. In commercial valuation of gums, strong preference is always shown for those that are light coloured (Robbins, 1988).

Certain gums when freshly secreted are virtually colourless. Colour is mainly due to the presence of impurities and tannins. Often it appears as the gum ages on the tree many substances are washed on it. True gums are generally scented or nearly so, differentiating them from some resins and oleo- resins that are distinctive in smell. They may be tasteless, and are in fact generally devoid of characteristic taste apart from being blandly mucilaginous. Some may be either sweet or bitter, depending on their botanical origin (Anekant. et.al, 2007).

Gums vary in hardness, which is obviously governed by the amount of moisture present. This generally ranges between 12 and 16 %. Density also proves variable. This may depend on the amount of air that may have been incorporated in the gum during formation. Most gums break with glassy fracture when properly dried, and may be readily pulverised. Gums are hygroscopic and will absorb moisture and become soft in humid atmosphere. This power to hold water or lose it may have an important repercussion in gum trade.

2.2.2 Chemical properties of gums

Gums, or hydrocolloids, are mainly long-chain, straight or branched polysaccharides that contain hydroxyl groups that can bond to water molecules. (Gelatin, a polymer of amino acids linked with peptide bonds, is also often described as a gum since it functions in a similar manner.) These chains can consist of 2,000 to over 10,000 monosaccharide units. The sugar monomers can contain linked side units, or substituent groups, such as sulfates, methyl ethers, esters and acetals. Gums can be neutral or anionic (negatively charged). It is this structure - the type and number of monosaccharides and their configuration and the type, number and location of the linked groups - that gives each gum its particular characteristics (Kuntz, 1999).

The chain length, or degree of polymerization (DP), influences a gum's viscosity and hydration rate. Longer molecules tend to produce higher viscosities and take longer to hydrate than shorter ones. A highly branched molecule takes up less space than a straight one with the same molecular weight, and therefore provides less viscosity. "As a hydrocolloid molecule becomes longer, it sweeps out a much greater volume as it randomly tumbles in solution, leading to increased collisions with its neighbors, which results in an increase in viscosity," . Longer molecules are slower to hydrate because they first need to

untangle from the adjoining molecules.

The number of side units per unit length of the monosaccharide chain is known as the degree of substitution (DS). The more substitution, the more the chains are held apart from each other. Because this prevents them from forming hydrogen bonds, they hydrate more quickly. The uniformity of this substitution also affects a gum's behavior. (Kuntz 1999).

2.2.3 Rheological and physical properties of gums

Most of the pharmaceutical uses of gums depend on their rheological properties; hence this property which varies from gum to gum is of great importance.

The differences in rheological behaviour of gums may be as a result of differences in botanical sources, climatic conditions of growth and collection, season of collection, age of exudates and treatment of gum after collection (Glicksman, 1969).

Each gum has unique flow properties which often affect their application particularly in liquid formulation since they impact these flow properties to the formulation they are incorporated. Solutions of different gums may exhibit different types of flow, some gums exhibit newtonian flow e.g. low viscosity type; some are dilatant e.g. furcellan; while others are pseudoplastic e.g. xanthan gum (Glicksman, 1969).

Solution of dilatant type gums become thicker when stressed and pseudoplastic ones get thinner when stressed. Xanthan gum has been reported to be the most pseudoplastic gum available (Rocks, 1971).

Most aqueous dispersions of gums show a decrease in viscosity as temperature increases, for instance the viscosity of solutions of carboxy methyl cellulose (CMC) reduces when the temperature is increased from 10 to 70°C. The opposite is true for gums such as xanthan gum which is reported to be resistant to temperature increase (Rocks, 1971).

Other factors that may affect the viscosity of gum solutions include changes in pH, age of gum solution, concentration of gum solution and the presence and amount of certain metallic ions such as calcium and magnesium.

2.3 OTHER PROPERTIES OF GUMS

2.3.1 pH

Plant gums may be acidic or neutral but most of them are acidic due to acidic groups such

as uronic acid unit. The pH of gum solutions range from 3-6, albizia gum ranges between 3.5 to 5 and that of tragacanth mucilage ranges between 5and 6.

Acidic gums are easily affected by changes in pH; meanwhile neutral gums are only slightly affected by pH changes. Some gums have molecules containing many carboxyl groups along their chains e.g. alginate and pectin these are precipitated at pH below 3 where free carboxyl groups are formed. Examples of gums with highly acidic substituent such as sulphuric acid group are carrageenan and furcellaran. Because the ionization of the sulphuric groups is not reduced much at low pH, such gums are stable in solutions of low pH. Gums that have neutral substituents along their linear chain tend to have increased viscosity and solution stability (Deman, 1999).

2.3.2 Concentration effect

The viscosities of gums tend to increase with increase in concentration. For most gums the relationship exhibited is logarithmic in nature at lower concentrations of up to 3 or 5 %. Gum mucilage exhibit typical pseudoplastic flow characteristics denoted by the decrease in viscosity with increase shear rate or shear stress. For most gums, the pseudoplasticity is exhibited at high concentrations and viscosities, whilst at lower viscosities and concentrations Newtonian flow is exhibited. Example, acacia gum mucilage does exhibit newtonian behaviours at concentrations up to 30 to 40 %, in which case the viscosity is not affected by the shear (Araujo, 1966). The pseudoplasticity is reversible, as the original viscosity is regained upon decreasing shear rate or removing the shear stress. The pseudoplasticity assists the suspending properties of the gum mucilage, in that the application of shear force will ease pourability, and yet allow the solution to its original viscosity upon cessation of the force (Davidson, 1980; Glinksman, 1969).

Gums are known to reduce the surface tension of water and the interfacial tension between oil and aqueous phases, hence their suspending and emulsifying properties. Some gums may be compatible with others and in most cases modification of properties occur and these are exploited to obtain optimum and conducive properties in their use and applications. For example acacia combines conveniently with tragacanth by lowering the viscosity of tragacanth which in turn produces emulsions with superior quality (Davidson, 1980).

2.4 PURIFICATION OF GUMS AND MUCILAGES

Gums for analysis are first purified by extraction with water. Dissolution may be accelerated using dilute acids or alkalis depending on the nature of the gums. If either dilute acid or water is employed, heating must be avoided since partial hydrolysis may occur in gums which contain heat labile sugar residues. Application of too much heat is inadvisable during alkali extraction, for although undesirable protein is thereby eliminated, decomposition of the uronic acid building units may occur.

The solution of the gum or mucilages is filtered to remove insoluble impurities and the polysaccharide removed by precipitating with alcohol. Repeated precipitation from acidified aqueous solutions with ethanol serves to remove inorganic ions and proteinaceous impurity. Elimination of inorganic ions may also be effected by electro dialysis or by passing an aqueous solution of the material through cation exchange resin.

Separation and purification can be achieved by crystallisation or precipitating from water. In this case, the polysaccharide is dissolved in hot or warm water, and the solution allowed cooling for the polymer to precipitate. Precipitation with alcohol and other organic solvents have been the main method used for the purification of gums and mucilages. The technique consists of dissolving the polysaccharide in water and adding ethanol gradually to effect precipitation. Although there is the tendency of co- precipitation, this disadvantage can be overcome to an extent by repeated fractional precipitation.

Fractional precipitation with salts has an advantage in that the tendency for co- precipitation is much less since salts have the effect of reducing hydrogen bonding. Fractional precipitation with complexing agents have also been found useful. Complexing agents such as phenols, borates, copper and aluminium ion form gelatinous complexes with mucilage. Some polysaccharides also have the tendency to precipitate others by forming complexes. Proteins used in fractional precipitation are the most selective method to and hold out considerable promise for the purification of polysaccharides (Smith and Montgomery, 1959). When gums contain considerable amount of protein, precipitation of the polysaccharide with ammonium sulphate or acetic acid may be advantageous since such procedure retains the proteins in the solution. The gum acetates may be purified by precipitation from acetone or chloroform solution with diethyl ether or petroleum ether and

the polysaccharide regenerated by deacylation with sodium hydroxide or potassium hydroxide. The purified products thus obtained dries prior to analysis by solvent exchange, azeotropic distillation of the water benzene- ethanol or by freeze- drying.

Freeze drying usually provides light amorphous white powders. When gums which contain moisture are dried by methods other than freeze drying, they often form hard, horny masses that are difficult to manipulate. It is not advisable to dry these polysaccharides by heating, for certain undesirable changes in solubility may develop and in the case of those gums containing acidic groups, hydrolysis and decomposition may occur (Smith and Montgomery, 1959).

2.5 DETECTION AND CHARACTERISATION OF GUMS AND MUCILAGES

The identification of a specimen of a gum or mucilage may be relatively simple if full use is made of the knowledge of the physicochemical properties of the gums and mucilage and the available techniques. In their natural state, single specimens of the gums may sometimes be recognised by physical appearance (size, shape, colour, brittleness, appearance on fracture etc.). The tough whitish opaque flakes, of tragacanth gum for example are easily identified and never confused with the clear, pale yellow or brownish appearance of the 'tears' of gum arabic (acacia), which fractures readily. However commercial samples of gums cannot be recognised in this way since most of them are used in the powdered form. Some can be recognised by the way they dissolve or disperse in water. Thus gum arabic dissolves in water easily and can be readily distinguished from tragacanth and khaya gums which partially dissolve in water.

The physical appearance and the rate of settling of the precipitate formed when aqueous solutions of the gum are treated with alcohol may also be used as a preliminary test for the identification of gums. It has been observed that albizia gum, having a highly branched spherical structure separates as a curdy precipitate which readily settles, where as tragacanth gum, which is linear in structure produces a stringy mucilaginous precipitate (Smith and Montgomery, 1959). The preliminary test may also include measurement of the specific optical rotation in either water or dilute alkali. The specific rotation of a suitable derivative of the gum, such as acetates, is also useful for the identification purposes. Infra-red analysis can also prove useful since various component sugars and glycosidic linkages

can often be distinguished (Barker et. al., 1956).

The technique of differential thermal analysis which was previously used for inorganic substances may well prove to be valuable analytical method in the study of gums and mucilage, since it had been well proven that carbohydrate polymers as well as oligosaccharides, having different glycolic linkage may be differentiated (Smith and Montgomery, 1959).

2.6 COMPOSITION OF GUM

2.6.1 Sugars, Sugar acids and their derivatives

Gums are known to be made up of polysaccharides which are composed of monosaccharides linked together in a long chain or in their free state, sugar acids in a bound or free state and also derivatives of sugar and sugar acids. These groups of compounds found in gums are generally classified into aldopentoses-(arabinose and D- xylose), aldohexoses- (D- glucose, D- mannose, D- galactose, L- galactose, 3,6- anhydr- D-galactose, 3,6- anhydro- L- galactose, etc.), ketohexoses- (D- fructose and D- tagatose), 6-deoxyhexoses- (L- fructose and L- rhamnose), uronic acids- (D- galactouronic acid, D-gluconic acid, etc) and hexitols- (D- mannitol) (Dror et. al., 2006).

2.6.2 Organic functional groups

Gums contain some ester groups such as acetyl and methoxyl residues. Other groups such as methyl groups are also present in some gums as derivatives of the sugar and sugar acids. Other functional groups are the anhydro and deoxy groups. The acetyl and methyl groups occur in gums such a karaya and khaya respectively.

2.6.3 Inorganic ions

Inorganic ions particularly metallic ions are also present in most gums as salts. Examples of such gums are albizia, acacia and tragacanth. These ions include sodium, potassium, calcium and magnesium, the commonly occurring being calcium followed by magnesium or potassium, with sodium being in traces. The calcium and magnesium contributes to the insolubility of some gums.

2.7 APPLICATIONS AND USES OF GUMS AND MUCILAGE

Gums find diverse application in pharmacy and are widely used as emulsifying and suspending agents, depending on their exhibited properties. Gum mucilage performs a stabilising function and imparts viscosity to emulsions thus reducing creaming. They are used to maintain insoluble solids in organic suspensions and to produce mucilaginous ointments and cosmetic hand creams. Acacia gum is used as a suspending agent, emulsifier, adhesive and binder in tabletting and demulcent in cough syrups (Ramsden, 2003). In tabletting, gums find use as adhesives or binders and also an excipient in the manufacture of pills and plasters. A number of plant gums have been used as binding agents in tablet formulations. They have been found useful in producing tablets of different mechanical strength and drug releasing properties for different pharmaceutical purposes. The fact that gums are naturally available, inexpensive and non toxic have also fostered interest in developing the gum for pharmaceutical use.

2.8 BOTANY AND SOURCE OF VITELLARIA PARADOXA

Family: Sapotaceae

Genus: *vitellaria*

Species: paradoxa

Synonyms: *Butyrospermum paradoxum, Lucuma paradoxa, Bassia parkii, Butyrospermum paradoxum, Butyrospermum parkii,, Lucuma paradoxa, Mimusops capitata ,Mimusops pachyclada .*

Common names: (Arabic) : lulu

(English) : bambouk butter tree, galam butter tree, Shea-butter tree

(French) : arbre a beurre, beurre de galam, beurre/graisse de karité, karité

(Fula) : balire, kareje

(German) : Schibutterbaum, Sheabutterbaum

(Hausa) : dan káraye, k'wara, kadanya, man ka'dai, man ka'danya

(Igbo) : okwuma

(Spanish) : tango

(Temne) : an-doni

(Yoruba): akúmalapa,emi-emi (Hall.et. al, 1996).

2.8.1 Botanic description

Vitellaria paradoxa is a small to medium-sized tree (min. 7) 10-15 (max. 25) m high; much branched, dense, spreading, round to hemispherical crown.

In mature trees the trunk is short, usually 3 to 4 m but exceptionally 8 m, with a diameter ranging from 0.3 to 1 m, but most frequently 0.6 m. Bark conspicuously thick, corky, horizontally and longitudinally deeply fissured; protects older trees against bush fires. Slash pale pink, secreting white latex, as do broken twigs or petioles. Leaves in dense clusters, spirally arranged at the end of stout twigs. They are covered by thick bark showing numerous leaf scars. Petioles are 5 to 15 cm long, leaves oblong. Juvenile leaves rust-red and pubescent, later coriaceous, glabrous and dark green, shining, 12 to 25 cm long and 4 to 7 cm wide, leaf margin wavy and bent. The flowers develop in the axils of scale leaves, at the extremities of dormant twigs, from buds formed 2 years previously. Inflorescence, a dense fascicle 5 to 7.5 cm in diameter, at the end of a flowering twig each usually contains 30 to 40 flowers, though 80 to 100 have been recorded. Individual flowers white or creamy-white, about 1.5 cm in diameter and subtended by scarious, brown, ovate or lanceolate bracteoles, which are abscised before flower opening. Fruit 5 to 8 cm long and 3 to 4 cm wide, elliptic, a yellow-green or yellow berry with thick butter-like, mucous pericarp; generally containing only one oval or round red-brown seed (the shea nut), surrounded by a fragile shining shell with a large, round, rough hilum on a broad base. The genus Vitellaria is considered by botanical authorities as monospecific, two subspecies are recognized ssp. paradoxa restricted to Western Africa and ssp. nilotica of Eastern Africa (Hall.et. al, 1996).

2.9 RESEARCH AND DEVELOPMENT OF THE SHEA TREE AND ITS PRODUCTS

The shea tree, formerly Butryospermum paradoxum, is now called Vitellaria paradoxa. Many vernacular names are used for Vitellaria, which is a reflection of its extensive range of occurrence – nearly 5,000 km from Senegal (west) to Uganda (east) across the African Continent. The nomenclature history and synonymy of the shea tree followed a very tortuous evolution since the oldest specimen was first collected by Mungo Park on May 26, 1797 before eventually arriving at the name vitellaria with subspecies paradoxa and nilotica.

It usually grows to an average height of about 15 m with profuse branches and a thick waxy and deeply fissured bark that makes it fire resistant. The shea tree grows naturally in the wild in the dry Savannah belt of West Africa from Senegal in the west to Sudan in the east, and onto the foothills of the Ethiopian highlands. It occurs in 19 countries across the African continent, namely Benin, Ghana, Chad, Burkina Faso, Cameroon, Central African Republic, Ethiopia, Guinea Bissau, Cote D'Ivoire, Mali, Niger, Nigeria, Senegal, Sierra Leone, Sudan, Togo Uganda, Zaire and Guinea.

In Ghana, it occurs extensively in the Guinea savannah and less abundantly in the Sudan Savannah. The Shea tree occurs over almost the entire area of Northern Ghana, over about 77,670 square kilometers in Western Dagomba, Southern Mamprusi, Western Gonja, Lawra, Tumu, Wa and Nanumba with Eastern Gonja having the densest stands.

There is also a sparse Shea tree cover found in Brong-Ahafo, Ashanti, and the Eastern and Volta regions in the south of the country (Frimpong and Adomako, 1989, FAO Report 1988a).

The trees of Shea are ravaged by annual bush-fires that usually burn the undergrowth and cause stunted growth of the trees in the wild. Under these conditions, the trees attain heights of only 6.1 meters and girths of about 61 cm. (Hill, 1930). However, under protected conditions (e.g. on cultivated lands and on the fringes of settlements) the trees can reach heights of about 15 meters and girths of 175 cm. The trees grow slowly from seeds, taking about 30 years to reach maturity (Dalziel, 1937), but limiting or stressful conditions such as bush-fires and harsh weather can reduce this. The Shea tree has no capacity for vegetative regeneration and can only be propagated by seed.

The Shea tree also has a great, untapped capacity for producing copious amounts of sap that can constitute an important source of raw material for the gum and rubber industry. Hence this project seeks to investigate the pharmaceutical uses of this sap.

The trees begin to bear fruits at maturity and start flowering by early November, with picking or gathering lasting from April to August every year. When the shea fruits ripen, they fall under their own weight to the floor and are gathered by hand. The fruit, which is green in color, has a fleshy edible pulp, which contains 0.7-1.3 g of protein and 41.2 g of carbohydrate and is very sweet. The fruit pulp is a particularly rich source of ascorbic acid: 196.1 mg/100 g compared with 50 mg/100 g in oranges. The iron and calcium content compares favorably with raspberries: 1.93mg/100g as against 0.92 mg/100 g for iron, and 36.4 mg/100 g as against 26 mg/100 g for calcium, reports that B vitamins are also present. The sugar content varies from 3-6%, equally distributed between glucose, fructose and sucrose (Frimpong and Adomako, 1989)

In northern Ghana the fruits contribute to food security, particularly for the rural poor, especially since their ripening coincides with the lean season of food production.

2.10 USES OF SHEA BUTTER

The shea nut serves as the main source of livelihood for the rural women and children who are engaged in its gathering. Shea butter is the main edible oil for the people of Northern Ghana, being the most important source of fatty acids and glycerol in their diet. It also has anti-microbial properties, which gives it a place in herbal medicine. It is also used in the pharmaceutical and cosmetic industries as an important raw material and/or a base for the manufacture of ointments, suppositories, soaps, candles, and cosmetics. Shea butter is used as a sedative for the treatment of sprains, dislocations and the relief of minor aches and pains (Marchand, 1988).

Other important uses include its use as an anti-microbial agent for promotion of rapid healing of wounds, as releasing agent in bread baking and as a lubricant for donkey carts. Its by-products, the brown solid that is left after extracting the oil and the hard protective shell, are used as a water-proofing material on the walls of mud-buildings to protect them from the eroding forces of the wind and rain. Poor quality butter is not only applied to earthen walls but also to doors, windows, and even beehives as a waterproofing agent. In

a traditional setting, shea butter of poor quality is used as an illuminant (or fuel, in lamps or as candles) (Marchand, 1988).

2.11 OTHER TRADITIONAL USES OF SHEA BUTTER

As a cosmetic, it is used as a moisturizer, for dressing hair (Dalziel, 1937, Ezema & Ogujiofor, 1992) and for protection against the weather and sun. It is used as a rub to relieve rheumatic and joint pains and is applied to activate healing in wounds and in cases of dislocation, swelling and bruising. It is widely used to treat skin problems such as dryness, sunburn, burns, ulcers and dermatitis and to massage pregnant women and small children (Marchand, 1988).

Having a high melting point of between (32- 45°C) and being close to body temperature are attributes that make it particularly suitable as a base for ointments and medicines. It is also used to treat horses internally and externally for girth galls and other sores. The healing properties of shea butter are believed to be partly attributable to the presence of allantoin, a substance known to stimulate the growth of healthy tissue in ulcerous wounds (Wallace-Bruce, 1995). It is used as "white oil" to anoint the dead in Niger, and is placed in traditional ritual shrines.

Refuse water from production of shea butter is used as a termite repellent (Dalziel, 1937). In Burkina Faso, shea butter is used to protect against insect (Callosobruchus maculatus) damage to cowpeas (Vigna sp.). Research has shown that after treatment with shea butter a reduction occurs in the life span and fertility of the insects and hence the infestation rate. Shea butter, however, is not as effective as cottonseed or groundnut oil (Pereira, 1983; Owusu-Manu, 1991).

2.12 USES OF OTHER PARTS OF THE SHEA TREE

2.12.1 Flowers, fruit and nuts

Some ethnic groups make the flowers into edible fritters. The fruit pulp, being a valuable food source, is also taken for its slightly laxative properties (Soladoye et al., 1989). Although not widespread, shea nut cake is used for cattle feed (Salunkhe et al, 1992), and also eaten raw by children (Faegri, 1966; Farinu, 1986). The residual meal, as in the case with shea butter, is also used as a waterproofing agent to repair and mend cracks in the

exterior walls of mud huts, windows, doors and traditional beehives. The sticky black residue, which remains after the clarification of the butter, is used for filling cracks in hut walls (Greenwood, 1929; Marchand, 1988) and as a substitute for kerosene when lighting firewood (Wallance-Bruce, 1995). The husks reportedly make a good mulch and fertiliser (FAO, 1988b), and are also used as fuel on three stone fires.

2.12.2 Foliage

Leaves are used as medicine to treat stomachache in children (Millee, 1984). A decoction of young leaves is used as a vapor bath for headaches in Ghana. The leaves in water form a frothy opalescent liquid, with which the patient's head is bathed. A leaf decoction is also used as an eye bath (Abbiw, 1990). The leaves are a source of saponin, which lathers in water and can be used for washing (Abbiw, 1990). When a woman goes into labor, branches may be hung in the doorway of her hut to protect the newborn baby. Branches may also be used for covering the dead prior to their burial.

2.12.3 Roots

The roots are used as chewing sticks in Nigeria, most commonly in savannah areas (Isawumi, 1978). Roots and root bark are ground to a paste and taken orally to cure jaundice (Ampofo, 1983). These are also used for treatment of diarrhoea and stomachache (Millee, 1984). Mixed with tobacco, the roots are used as a poison by the Jukun of Northern Nigeria. Chronic sores in horses are treated with boiled and pounded root bark (Dalziel, 1937).

2.12.4 Bark

Infusions of the bark have shown to have selective anti-microbial properties, as being effective against Sarcina lutha and Staphylococcus aureas but not mycobacterium phlei (Malcolm & Sofowora, 1969). Macerated with the bark of Ceiba pentandra, and salt, bark infusions have been used to treat cattle with worms in the Tenda region of Senegal and Guinea. The infusions have been used to treat leprosy in Guinea Bissau (Dalziel, 1937) and for gastric problems (Booth and Wickens, 1988) as well as for diarrhoea or dysentery (Soladoye et al., 1989). A bark decoction is used in the Cote d'Ivoire in baths and

therapeutic sitz-baths to facilitate delivery of women in labour, and is drunk to encourage lactation after delivery (Abbiw, 1990; Soladoye et al., 1989). However, in northern Nigeria such a concoction is said to be lethal, (Dalziel, 1937).

A bark infusion is used as an eyewash to neutralise the venom of the spitting cobra (Soladoye et al 1989) and also, in Ghana, as a footbath to help extract jiggers.

Greenwood in 1929, noted that the stripping of bark for medicinal purposes may have a severe impact on the health of shea trees and may even be fatal. The wood is only used when individual trees are not valued for butter production. The latex is heated and mixed with palm oil to make glue (Hall et al., 1996). It is chewed as a gum and made into balls for children to play with. In Burkina Faso, Bobo musicians use it to repair cracked drums and punctured drumheads (Millee, 1984). It contains only 15-25% of carotene and, therefore, is not suitable for the manufacture of rubber.

2.13 POSSIBLE USES OF GUM IN PHARMACEUTICAL FOMULATION

2.13.1 Oral solid dosage forms

Active ingredients often require the help of additives in order to be formulated into various dosage forms. These additives are included to play various functions such as increasing the bulk, improving stability of the product, improving appearance and taste, enhancing the release of the active ingredient, etc.

Additives should possess certain properties in order to be able to perform their task satisfactorily, hence it is extremely important to evaluate their abilities before it can be used commercially.

2.13.2 Tablets as a dosage form

Tablets may be defined as a solid pharmaceutical dosage form containing drug substance with or without suitable excipients and prepared either by compression or moulding methods. Tablets remain popular as dosage form because of the advantages afforded both to the manufacturer (e.g., simplicity and economy of preparation, stability and convenience in packaging, shipping and dispensing) and the patient (accuracy of dosage, compactness, portability and ease of administration) (Aulton, 1994). Tablet technology has undergone great improvement. Factors affecting the availability of the right kind of tablets are always

being considered together with factors affecting raw materials, facilities, personnel, validated processes and equipment, packaging and the controls.

2.13.3 Tablet ingredients

In addition to the active or therapeutic ingredient, tablets contain a number of inert materials; these are known as additives or excipients. They may be classified according to the part they play in the finished tablet. The first group contain those which help to impart satisfactory processing and compression characteristics to the formulation. These include diluents, binders, glidants and lubricants. The second group of added substances help to give additional desirable physical characteristics to the finished tablet. Included in this group are disintegrants, colours etc.

2.13.3.1 Diluents

Frequently the single dose of the active ingredient is so small and inert substances are added to increase the bulk in order to make the tablet a practical size for compression. Diluents used for this purpose include dicalcium phosphate, calcium sulphate, lactose, cellulose, kaolin, dry starch and powdered sugar (Allen. et.al, 2004)

2.13.3.2 Binders

These are agents used to impart cohesive qualities to the powdered materials. They impart cohesiveness to the tablet formulation which insures the tablet remaining intact after compression as well as improving the free flowing qualities by the formulation of granules of desired hardness and size. Materials commonly used as binders include starch, gelatin, and sugars. Natural and synthetic gums which have been used include acacia, sodium alginate, panwar gum, ghatti gum, carboxymethylcellulose, methyl cellulose and polyvinylpyrrolidine (Raymond.et.al, 2003)

The quantity of binder used has considerable influence on the characteristics of the compressed tablet. The use of too much binder or too strong a binder will make a hard tablet which will not disintegrate easily and will cause excessive wear of punches and dies. The binders may be added as powder or in the form of mucilage which consist of the

binding agent and a granulating fluid intended to be removed after granulation by drying (Raymond et al,2003).

2.13.3.3 Lubricants

Lubricants have a number of functions in tablet manufacture. They prevent adhesion of tablet material to the surface of dies and punches, reduce inter particle friction, facilitate ejection of the tablets from the die cavity and may improve the rate of flow of the tablet granulation.

Commonly used lubricants include talc, magnesium stearate, calcium stearate hydrogenated vegetable oil and polyethylene glycol (Raymond.et.al, 2003)

In selecting a lubricant, proper attention must be given to its compatibility with the drug agent.

2.13.3.4 Glidants

A glidant is a substance which improves flow characteristics of a powder mixture. These materials are normally added in the dry state just prior to compression. Colloidal silicon dioxide is the most commonly used at usually low concentrations.

2.13.3.5 Disintegrants

A disintegrant is a substance or mixture of substances, added to a tablet to facilitate its break up or disintegration after administration. The active ingredient must be released from the tablet matrix efficiently as possible for its rapid dissolution. Materials serving as disintegrants have been classified chemically as starches, clays, cellulose, algins, gums and cross linked polymers. The oldest and still the most popular disintegrants are corn and potato starch which have been well dried and powdered. A group of materials known as super disintegrants have gained popularity as disintegrating agents. The name comes from the low levels at which they are very effective. Examples are croscarmelose and crospovidone. The method of addition of the disintegrant in the course of granulation is also of much importance (Raymond.et.al, 2003)

2.14 TABLET CHARACTERISTICS

Compressed tablet are characterized by some specifications which include diameter size, shape thickness, weight, hardness, disintegration time, friability and dissolution characteristics.

2.14.1 Tablet Hardness and Friability

The resistance of the tablet to chipping, abrasion or breakage under conditions of storage, transportation and handling before usage depend on its hardness. Hardness determinations are made throughout the tablet runs to determine the need for pressure adjustment on the tabletting machine. A tablet property related to hardness is friability. This parameter assesses the ability of the tablet to withstand abrasion in packaging, handling and shipping.

2.14.2 Uniformity of Dosage Forms

Tablet Weight: The volumetric fill of the die cavity determines the weight of the compressed tablet. The weight of the tablet is the quantity of the granulation which contains the labelled amount of the therapeutic agent. The tablet weights must conform to the set standards as in the USP or BP.

Content Uniformity: Each tablet must contain the intended drug quantity with little variation among the tablets in a batch. The drug quantity per tablet of average weight is determined analytically and compared to standards as set in the monographs.

2.14.3 Tablet Disintegration:

To be absorbed, a drug substance must go into solution, but the disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrate into particles. It is therefore recognised that the in vitro tablet disintegration test does not necessarily bear a relationship to the in vivo action of the tablet. The maximum disintegration time often set at 15 minutes for uncoated tablets and 60 minutes for coated tablet. This test does not apply to depot tablets, lozenges and chewable tablets.

2.14.4 Dissolution

For certain tablets, the monographs require direct compliance with limits on dissolution rather than disintegration. Since drug absorption and physiological availability depend on having the drug in dissolved state, suitable dissolution characteristics are an important property of a satisfactory tablet. Like the disintegration test, the dissolution test is for measuring the amount of time required for a given percentage of the drug substances in a tablet to go into solution under a specified set of conditions, is an in vitro test. It is intended to provide a step towards the evaluation of the physiological availability of the drug.

2.14.4.1 Models for Statistical analysis of dissolution data

A simple model independent approach uses a difference factor (f_1) and a similarity factor (f_2) to compare dissolution profiles. The difference factor calculates the percent difference between the two curves at each time point and is a measurement of the relative error between the two curves. It is expressed as:

$$f_2 = 50 + \log \{[1+ (1/n) \sum t=1 * n (Rt-Tt) 2]-0.5 *100\} \ldots\ldots\ldots \text{(Mathiowitz)}$$

Where n = the number of time points

R is the dissolution value of the reference (prechange) batch at time t

Tt is the dissolution value of the test (postchange) batch t at time t.

The similarity factor is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent dissolution between the two curves. This model independent method is most suitable for dissolution profile comparison when three to four or more dissolution time points are available.

Dissolution efficiency (DE) on the other hand is a parameter for evaluation of in-vitro dissolution data. It is expressed as the area under dissolution curve up to a certain time 't' expressed as percentage of the area of the rectangle described by 100 percent dissolution at the same time (Mauralidhar et al,2011).

This concept was proposed by khan and Rhodes and is defined as follows

$$DE = \{(\int_0^t Y.dt) / Y_{100}.(t_2-t_1)\} \times 100$$

Where y is the percentage of dissolved product. DE is then the area under the dissolution curve between time points t_1 and t_2 expressed as a precentage of the curve maximum dissolution. Y_{100} over the same period (Costa and Sausa lobo, 2001) .

2.14.5 Stability

The stability of the drug substances is investigated when developing the formulation. A suitable method of preparation must be chosen for the tabletting of sensitive substances. The stability control proceeds after production by periodic examination of stored reference sample of production batches. Tablets generally have a long shelf life. The physico-chemical properties of the tablet should also be studied during storage.

2.15 METHODS OF PREPARATION OF TABLETS

2.15.1 Granulation

Granulation is the process in which primary powder particles are made to adhere to form larger, multiparticle entities called granules. Pharmaceutical granules typically have a size range between 0.2 and 4.0 mm, depending on their subsequent use. In the majority of cases this will be in the production of tablets or capsules, when granules will be made as an intermediate product and have a typical size range between 0.2 and 0.5 mm, but larger granules are used as a dosage form in their own right (Aulton,1994).

2.15.1.1 Reasons for granulation

Granulation is done for many reasons some of which are outlined below

- To prevent segregation of the constituents of the powder mix.
- To improve the flow properties of the mix
- To improve the compaction characteristics of the mix
- Materials which are slightly hygroscopic may adhere and form a cake if stored as a powder.Granulation may reduce this hazard, as the granules will be able to absorb some moisture and yet retain their flowability because of their size.
- Granules, being denser than the parent powder mix, occupy less volume per unit weight. They are therefore more convenient for storage or shipment (Aulton, 1994).

2.15.2 Methods of granulation

Granulation methods can be divided into two types: **wet** methods, which use a liquid in the process, and ***dry*** methods in which no liquid is used.

2.15.2.1 Wet granulation

The most widely use and most general method of tablet preparation is the wet granulation method. Wet granulation is a process of using a liquid binder or adhesive to the powder mixture. The amount of liquid can be properly managed, and over wetting will cause the granules to be too hard and under wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with than other solvents.

2.15.3 Dry granulation

This process is used when the product needed to be granulated may be sensitive to moisture and heat. Dry granulation can be conducted on a press using slugging tooling or on a roller compactor commonly referred to as a chilsonator. Dry granulation equipment offers a wide range of pressure and roll types to attain proper densification. However, the process may require repeated compaction steps to attain the proper granule end point.

Process times are often reduced and equipment requirements are streamlined; therefore the cost is reduced. However, dry granulation often produces a higher percentage of fines or non compacted products, which could compromise the quality or create yield problems for the tablet. It requires drugs or excipients with cohesive properties.

Some granular chemicals are suitable for direct compression (free flowing) e.g. Potassium chloride. Tabletting excipients with good flow characteristics and compressibility allow for direct compression of a variety of drugs.

2.16 FLOW PROPERTIES OF GRANULES

Practically every solid used in pharmacy must be handled as a powder at some stage and this handling is greatly facilitated if the powder is free flowing. This study of the flow and deformation of powders is the science of rheology and is analogous in some respect to the rheology of liquid systems. However, since a powder mass consist of discrete particles;

there is an absence of the continuity found in liquids.

There are different methods used to determine the flow properties of powders or granules. These methods are generally grouped into two; direct and indirect methods. The indirect methods include angle of repose, shear cell determination, bulk density measurement etc. The direct methods include Hopper flow rate and recording flow meter (Aulton,1994).

1.4.5.1 ANGLE OF REPOSE

There are many different methods of determining the angle of repose. The different methods may produce different values of angle of repose for the same powder. For this reason angles of repose tend to be variable and are not always representative of flow under specific conditions. As a general guide, powders with angles of repose greater than 50° have satisfactory flow properties whereas angles close to 25° correspond to very good flow properties. The different methods for determining angles of repose are:

- Fixed height method
- Fixed base method
- Tilting table

1.4.5.2 BULK DENSITY MEASUREMENTS

The bulk density of a powder is dependent on particle packing and changes as the powder consolidates. A given mass of granules in a measuring cylinder will have an initial volume, V_o. After tapping for some specific amount of time, it attains a final volume, V_f.

The change in volume occurring when void space diminishes is known as 'packing down'. An initial density can be calculated knowing the initial bulk density or fluff or paired bulk density, D_o. The final density can also be calculated. This is known as the final bulk density or equilibrium or tapped or consolidated bulk density, D^f

Hausner found that the ratio D^f / D^o was related to interparticulate friction and such could be used to predict powder flow properties. Hausner showed that powders with low interparticulate friction had ratios of approximately 1.2, whereas more cohesive, less free-flowing ones had ratios greater than 1.6 (Aulton, 1994, Hausner, 1967.).

Carr's index

Carr developed another method of measuring powder flow from bulk density measurements. Carr's index is also known as percentage compressibility and is calculated as % Compressibility = $(D_f - D_o / D_f) \times 100$ (Carr, 1965)

2.17 SUSPENSIONS

Suspensions may be defined as a two phase system consisting of an undissolved or immiscible material dispersed in a vehicle (solid, liquid or gas). They may also be defined as preparation containing finely divided drug particles distributed somewhat uniformly throughout a vehicle in which the drug exhibits a minimum degree of solubility Pharmaceutical suspensions tend to be coarse dispersions rather than true colloids, although there are many sub-micrometre polymer dispersions available. Drugs in suspension are prepared mainly for oral, intramuscular or subcutaneous use, but suspensions of drugs are also used as reservoirs in transdermal patch preparations and in conventional topical formulations (Florence and Atwood, 2005). The problems that arise when a drug is dispersed in a liquid include sedimentation, caking (leading to difficulty in resuspension), flocculation and particle growth (through dissolution and recrystallisation). In practice we wish to avoid the problems of aggregation of particles in suspensions and in many lyophilised preparations and to ensure their efficient redispersion on reconstitution with water or other media. Adhesion of suspension particles to container walls has also been identified as a problem, particularly with low-dose drugs. Formulation of pharmaceutical suspensions to minimise caking can be achieved by the production of flocculated systems. A flocculate, or floc, is a cluster of particles held together in a loose open structure; a suspension consisting of particles in this state is termed flocculated (Florence and Atwood, 2005).

In suspensions, the particle size of the constituents of the drug product has diameters greater than 0.1 micrometer and some of the particles exhibit Brownian motion. Generally pharmaceutical suspensions contain aqueous dispersion but in some cases they may be oily or organic phase (Aulton, 1994).

Suspensions may be classified into different groups:

- **Orally administered mixtures**

  Patients who have problems swallowing solid dosage forms require drugs to be dispersed in a liquid. Oral suspensions permit the formulation of poorly soluble drugs in the form of liquid dosage form. Finely divided solids like kaolin, magnesium carbonate, etc., when administered in the form of suspensions will be available to a higher surface area for adsorptive and neutralising actions in the gastrointestinal tract.

- **Topical suspensions**

  These suspensions are meant for external application and therefore should be free of gritty particles. Their consistency may range from fluid to paste. Example of fluid suspension is calamine lotion and zinc cream has a consistency of a semi solid.

- **Parenteral preparation**

  These suspensions should be sterile and should possess property of syringability. Parenteral suspensions are used to control the rate of absorption. As the absorption rate of the drug is dependent on the dissolution rate of the solid. Therefore by varying the size of the dispersed solid particles the duration and absorption can be controlled. Some vaccines such as the cholera vaccine are formulated as dispersions of killed microorganisms.

- **Ophthalmic suspension**

  These should also be sterile and should possess very fine particles. Drugs which are are not stable in aqueous solution, are formulated as stable suspensions using non aqueous solvents. For example, fractionated coconut oil is used for dispersing tetracycline hydrochloride for ophthalmic use.

2.17.1 Properties of suspensions

- Suspension should have good pour ability to ensure ease of removal of dose from container.
- They should have good physical appearance
- They should have uniform particle size distribution.
- There should be ease of redispersion of settled solid particles.

- They should be physically and chemically stable
- They should be resistant against microbial contamination.

Viscosity and particle size are important factors to consider since they affect the nature of suspensions. Addition of electrolytes to a suspension decreases the thickness of the double layer and reduces electroviscous effects, an effect reflected in the reduced viscosity of the suspension (Florence and Atwood, 2005).
The following factors are significant in suspensions.

- Particle size distribution
- Specific surface area
- Inhibition of crystal growth
- Changes in polymorphic formulations

The formulator must ensure that these and other properties do not change significantly during storage.

2.17.2 Stability of suspensions

Physical stability of suspensions may be defined as the condition in which the particles do not aggregate and in which they remain uniformly distributed throughout the dispersion. Since the ideal situation is seldom realised, it is appropriate to add additives, which are added to achieve ease in resuspension by a moderate amount of agitation. Additives such as carboxymethylcellulose, microcrystalline cellulose, aluminium magnesium silicate (Veegum), sodium alginate (Manucol) and sodium starch(Primojel). Pregelatinised starches, Primojel and Veegum, are promising alternatives to the traditional compound tragacanth powder often used as suspension stability. (Florence and Attwood, 2005)

2.17.3 Interfacial properties of suspensions

Flocculated particles are weakly bonded, settle rapidly, do not form cake, and are easily re suspended. Flocs tend to fall together producing a distinct barrier between the sediment and the supernatant liquids. The liquid above the sediment is clear because even the small particles present in the system are associated with the flocs.

- **Degree of flocculation**

It is important to ensure that the product exhibit the correct degree of flocculation. Under flocculation will give those properties which are associated with deflocculated systems. Over flocculation may be irreversible. The product will look inelegant and its viscosity may

be high resulting in difficult redispersion. Flocculation degree can be controlled by the use of flocculating agents and by particle size control (Aulton,1994)

2.17.3.1 FLOCCULATING AGENTS

- **Electrolytes**

These act as flocculating agents by reducing the electric barrier between the particles as evidenced by a decrease in the zeta potential and the formation of a bridge between the particles so as to link them together in a loosely arranged structure.

The most widely used electrolytes include the sodium salts of phosphate, acetates and citrates and the concentration chosen will be that which produces the desired degree of flocculation. Excessive electrolyte may cause charge reversal on each particle thus forming a deflocculated system.

- **Surfactants**

Both ionic and non ionic have been used to bring about flocculation of suspended particles. Their concentration should not however exceed the critical micelle concentration in this case.

- **Polymers**

Hydrophilic polymers also act as protective colloids and particles coated in this manner are less prone to cake than are uncoated particles. Examples include; gelatine, starch, alginates, cellulose derivatives, gums such as tragacanth and silicates (Aulton, 1994)

2.17.4 Quality control test for suspensions

2.17.4.1 Sedimentation Volume

The sedimentation volume is the simple ratio of the height of sediment to the initial height of the suspension. The higher the value better is the suspendability.

Sedimentation volume (F) or height (H) for flocculated suspensions

$F = V_u / V_o$ ---------- (A)

Where, V_u = final or ultimate volume of sediment, V_o = original volume of suspension before settling.

Sedimentation volume is a ratio of the final or ultimate volume of sediment (Vu) to the original volume of sediment (V_o) before settling.

Some times 'F' is represented as 'Vs' and as expressed as percentage. Similarly when a measuring cylinder is used to measure the volume $F = H_u / H_O$

Where, H_u = final or ultimate height of sediment, H_O = original height of suspension before settling.

Sedimentation volume can have values ranging from less than 1 to greater than1; F is normally less than 1. F = 1, such product is said to be in flocculation equilibrium. And show no clear supernatant on standing.

Sedimentation volume ($F_¥$) for deflocculated suspension

$F_¥ = V_¥ / V_O$

Where, $F_¥$ = sedimentation volume of deflocculated suspension, $V_¥$ = sediment volume of completely deflocculated suspension. (Sediment volume ultimate relatively small)

V_O = original volume of suspension.

The sedimentation volume gives only a qualitative account of flocculation.

2.17.4.2 Flocculated Suspensions

In flocculated suspension, formed flocs (loose aggregates) will cause increase in sedimentation rate due to increase in size of sedimenting particles. Hence, flocculated suspensions sediment more rapidly. Here, the sedimentation depends not only on the size of the flocs but also on the porosity of flocs. In flocculated suspension the loose structure of the rapidly sedimenting flocs tends to preseve the sediment, which contains an appreciable amount of entrapped liquid. The volume of final sediment is thus relatively large and is easily redispersed by agitation (Florence and Atwood, 2005)

2.17.4.3 Deflocculated suspensions

In deflocculated suspension, individual particles are settling, so rate of sedimentation is slow which prevents entrapping of liquid medium which makes it difficult to re-disperse by agitation. This phenomenon is also called 'cracking' or 'claying'. In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquid so supernatant appears cloudy whereas in flocculated suspension, even the smallest particles are involved in flocs, so the supernatant does not appear cloudy. However the small particles eventually settle with time (Aulton, 1994.).

2.17.4.4 Redispersibility

Redispersibility is the major consideration in assessing the acceptability of a suspension. The measurement of the sedimentation volume and its ease of redispersion form two of the most common basic evaluative procedures. .

2.17.4.5 Particle size and size distribution

It is of importance to study the changes for absolute particle size and particle size distribution. It is performed by optical microscopy, sedimentation by using Andreasen apparatus and Coulter counter apparatus. None of these methods is direct methods. However microscopic method allows the observer to view the actual particles. The sedimentation method yields a particle size relative to the rate at which particles settle through a suspending medium.It is Important to analyse the particle size of suspensions since the size of dispersed particles affect their rate of sedimentation.

2.17.4.6 Rheological studies

Rheologic methods can help in determining the settling behaviour of the suspension. Brookfield viscometer with variable shear stress control can be used for evaluating viscosity of suspensions. It consist of T-bar spindle which is lowered into the suspension and the dial reading is noted which is a measure of resistance the spindle meets at various levels in the suspension. This technique also indicates in which level of the suspension the structure is greater due to particles aggregates. Data obtained on aged and stored suspension reveals whether changes have taken place in suspensions upon storage. Suspensions may exhibit pseudoplatic, plastic or Newtonian flow depending on its viscosity (Florence andAtwood 2005).

2.18 EMULSIONS

An emulsion is a mixture of two or more liquids that are normally immiscible . Emulsions are part of a more general class of two-phase systems of matter called colloids. Although the terms colloid and emulsion are sometimes used interchangeably, emulsion is used when both the dispersed and the continuous phase are liquid. In an emulsion, one liquid (the

dispersed phase) is dispersed in the other (the continuous phase). Emulsions are biphasic systems consisting of two immiscible liquids, one of which (the dispersed phase is finely subdivided and uniformly dispersed as droplets throughout the other phase (the dispersion medium). The dispersed phase is also called the internal phase and the dispersion medium as external phase. These immiscible liquids are made miscible by adding a third substance known as emulsifying agent such as xanthan gum. They stabilize the system by forming a thin film around the globules of the dispersed phase (Aulton, 1994).

Advantages

- They can mask the bitter taste and odour of drugs thereby making them more palatable. E.g. castor oil, cod-liver oil etc.
- They can be used to prolong the release of the drug thereby providing sustained release action.
- Essential nutrients like carbohydrates and fats and vitamins can all be emulsified and can be administered to bed ridden patients as sterile intravenous emulsions
- Emulsions provide protection to drugs which are susceptible to oxidation or hydrolysis
- Intravenous emulsions of contrast media have been developed to assist in diagnosis.
- Emulsions are used widely to formulate externally used products like lotions and liniments.

Types of Emulsions

- Oil in water
- Water in oil
- Multiple emulsion
- Micro emulsions (Florence and Attwood.2005)

Oil in water emulsion(o/w); in these emulsions the water is the dispersion medium while the oil is the dispersed phase

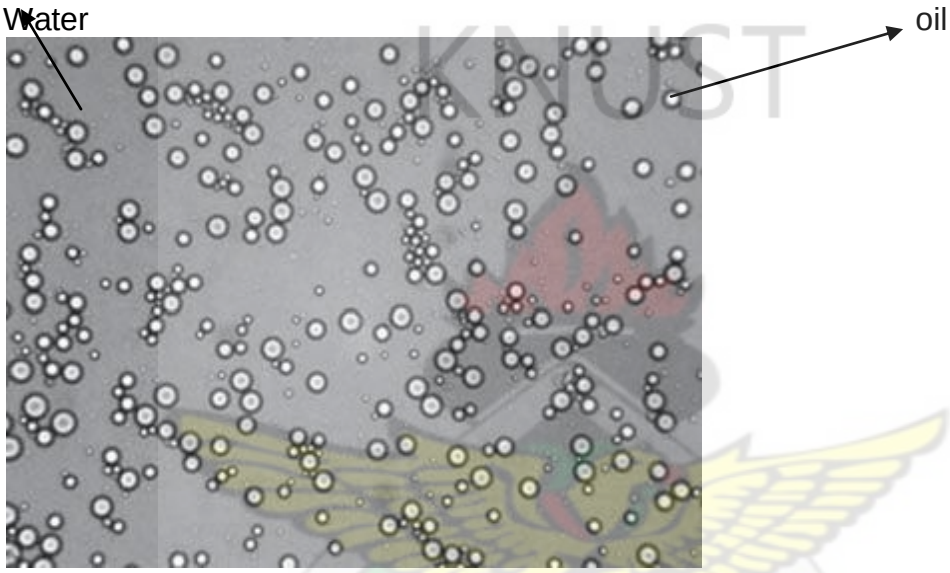

Figure 2-1 Oil in water emulsion

Water in oil emulsion (w/o); here the oil is the dispersion medium and the water is the dispersed phase. Water-in-oil emulsions in which a water-soluble drug is dissolved in the aqueous phase may be injected by the subcutaneous or intramuscular routes to produce a delayed action preparation, as to escape the drug have to diffuse through the oil to reach the tissue fluids. The main disadvantage of a w/o emulsion is generally its high viscosity, brought about through the influence of the oil on the bulk viscosity.

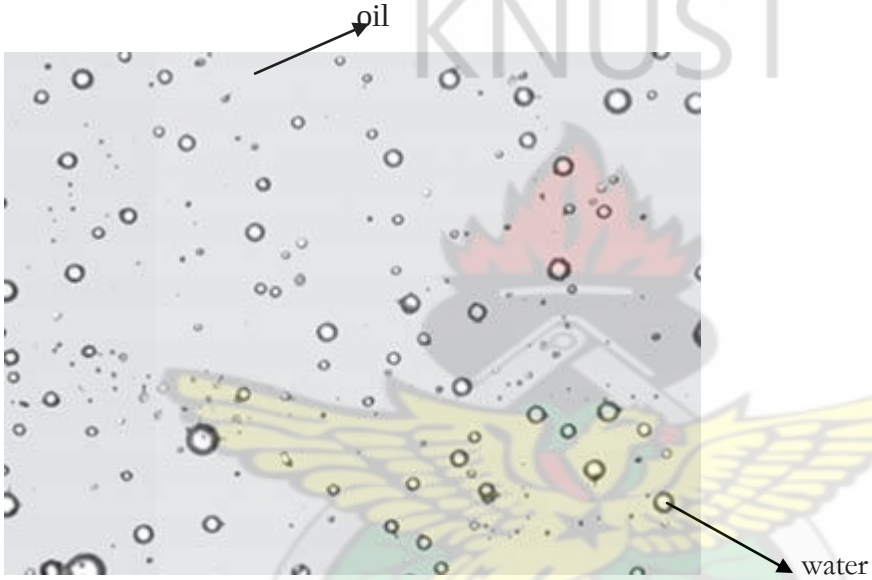

Figure 2-2 Water in oil emulsion

Multiple emulsion; Multiple emulsions are emulsions whose disperse phase contains droplets of another phase . Water-in-oil-in-water(w/o/w) or o/w/o emulsions may be prepared, both forms being of interest as drug delivery systems (Florence and Atwood,2005) .

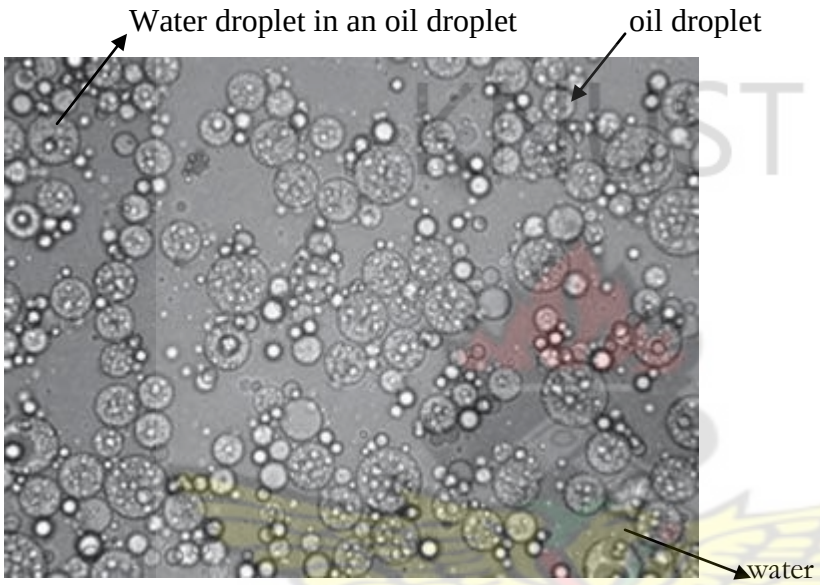

Figure 2-3 Multiple emulsion

Microemulsion; Microemulsions consist of apparently homogeneous transparent systems of low viscosity which contain a high percentage of both oil and water and high concentrations (15–25%) of emulsifier mixture. Microemulsions form spontaneously when the components are mixed in the appropriate ratios and are thermodynamically stable. In their simplest form, microemulsions are small droplets (diameter 5–140 nm) of one liquid dispersed throughout another by virtue of the presence of a fairly large concentration of a suitable combination of surfactants. They can be dispersions of oil droplets in water (o/w) or water droplets in oil (w/o) (Florence and Atwood, 2005).

EMUSIFYING AGENTS; The inclusion of an emulsifying agent or agents is necessary to facilitate actual emulsification during manufacture, and also to ensure emulsion stability during the shelf-life of the product. There are many types of emulgent available, but for convenience they can be divided into two main classifications: synthetic or

semisynthetic surface-active agents, and naturally occurring materials and their derivatives (Aulton, 1994).

Synthetic and semisynthetic surface active agents

There are four main categories of these materials, depending on their ionization in aqueous solutions:anionic, cationic, non-ionic and amphoteric.

Anionic surfactants

In aqueous solutions these compounds dissociate to form negatively charged anions that are responsible for their emulsifying ability. They are widely used because of their cheapness, but because of their toxicity they are only used for externally applied preparations.

Alkali metal and ammonium soaps; Emulgents in this group consist mainly of the sodium, potassium or ammonium salts of long-chain fatty acids, such as sodium stearate.They produce stable o/w emulsions but may in some instances require the presence of an auxiliary nonionic emulsifying agent in order to form complex monomolecular film at the oil/water interface. Because in acidic conditions, these materials will precipitate out as the free fatty acids, they are most efficient in an alkaline medium.This type of emulgent can also be formed in situ during the manufacture of the product by reacting an alkali such as potassium, sodium or ammonium sodium or ammonium hydroxide with a fatty acid(Aulton,1994) .

Cationic surfactants

In aqueous solutions these materials dissociate to form positively charged cations that provide the emulsifying properties. The most important group of cationic emulgents consists of the quaternary ammonium compounds. Although these materials are widely used for their disinfectant and preservative properties, they are also useful o/w emulsifiers. Like many anionic emulgents, if used on their own they will produce only poor emulsions, but if used with non-ionic oil-soluble auxiliary emulgents they will form stable preparations.Because of the toxicity of cationic surfactants they tend to be used only for the formulation of antiseptic creams, where the cationic nature of the emulgent is

also responsible for the product's antiseptic properties. Cationic emulsifying agents are incompatible with anionic surface-active agents and polyvalent anions, and are unstable at high pH. The most useful of these cationic emulgents is cetrimide (cetyl trimethylammonium bromide). Cetrimide is used at a concentration of 0.5% with 5% cetostearyl alcohol for the formulation of Cetrimide Cream BP (Aulton, 1994)

Non-ionic surfactants; These products range from oil-soluble compounds stabilizing w/o emulsions to water-soluble materials giving o/w products. It is usual for a combination of a water-soluble with an oil-soluble emulgent to be used in order to obtain the complex interfacial film necessary for optimum emulsion stability. Non-ionic emulgents are particularly useful because of their low toxicity and irritancy; some can therefore be used for orally and parenterally administered preparations. They also have a greater degree of compatibility with other materials than do anionic or cationic emulgents, and are less sensitive to changes in pH or to the addition of electrolytes. They do, however, tend to be more expensive.

Glycol and glycerol esters Glyceryl monostearate(a polyhydric alcohol fatty acid ester) is a strongly hydrophobic material that produces weak w/o emulsions.The addition of small amounts of sodium, potassium or triethanolamine salts of suitable fatty acids will produce a 'self-emulsifying' glyceryl monostearate,which is a useful o/w emulsifier. Self-emulsifying monostearin is glyceryl monostearate to which anionic soaps (usually oleate or stearate) have been added. This combination is used to stabilize Hydrocortisone Lotion.

Sorbitan esters These are produced by the esterification of one or more of the hydroxyl groups of sorbitan with either lauric, oleic, palmitic or stearic acids.This range of surfactants exhibits lipophilic properties and tend to form w/o emulsions. They are, however, much more widely used with polysorbates to produce either o/w or w/o emulsions.

.*Polysorbates* Polyethylene glycol derivatives of the sorbitan esters give us polysorbates. Polysorbates are generally used in conjunction with the corresponding sorbitan ester to form a complex condensed film at the oil/water interface. Other non-ionic oil-soluble materials, such as glyceryl monostearate, cetyl or stearyl alcohol or propylene glycol monostearate, can be incorporated with polysorbates to produce 'self-emulsifying'

preparations. For example, Polawax contains cetylalcohol with a polyoxyethylene sorbitan ester.

Amphoteric surfactants

This type possesses both positively and negatively charged groups, depending on the pH of the system.They are cationic at low pH and anionic at high pH. Although they are not widely used as emulsifying agents, one example, lecithin, is used to stabilize intravenous fat emulsions (Aulton,1994).

Naturally occurring materials and their derivatives

Naturally occurring materials often suffer from two main disadvantages: they show considerable batch-to-batch variation in composition and hence in emulsifying properties and many are susceptible to bacterial or mould growth. For these reasons they are not widely used in manufactured products requiring a long shelf-life, but rather for extemporaneously prepared emulsions designed for use within a few days of manufacture.

Polysaccharides

The most important emulsifying agent in this group is acacia. This stabilizes o/w emulsions by forming a strong multimolecular film round each oil globule, and so coalescence is retarded by the presence of a hydrophilic barrier between the oil and water phases. Because of its low viscosity, creaming will occur readily and therefore a suspending agent such as tragacanth or sodium alginate can also be included. Because of its sticky nature the use of acacia is limited to products for internal use (Aulton, 1994).

2.18.1 Methods for preparing emulsions

The methods commonly used to prepare emulsions can be divided into two categories:

2.18.1.1 Bottle Method

This method is employed for preparing emulsions containing volatile and other non-viscous oils. Both dry gum and wet gum methods can be employed for the preparation. As volatile oils have a low viscosity as compared to fixed oils, they require comparatively large quantity of gum for emulsification. In this method, oil or water is first shaken thoroughly and vigorously with the calculated amount of gum. Once this has emulsified completely, the

second liquid (either oil or water) is then added all at once and the bottle is again shaken vigorously to form the primary emulsion. More of the water is added in small portions with constant agitation after each addition to produce the final volume.

2.18.1.2 Trituration Method

This method consists of dry gum method and wet gum method.

- **Dry Gum Method**- In this method the oil is first triturated with gum with a little amount of water to form the primary emulsion. The trituration is continued till a characteristic 'clicking' sound is heard and a thick white cream is formed. Once the primary emulsion is formed, the remaining quantity of water is slowly added to form the final emulsion.
- **Wet Gum** Method- As the name implies, in this method first gum and water are triturated together to form a mucilage. The required quantity of oil is then added gradually in small proportions with thorough trituration to form the primary emulsion. Once the primary emulsion has been formed remaining quantity of water is added to make the final emulsion.

2.18.2 Instabilities in emulsions

An emulsion is a thermodynamically unstable preparation so care has to be taken that the chemical as well as the physical stability of the preparation remains intact throughout the shelf life. There should be no appreciable change in the mean particle size or the size distribution of the droplets of the dispersed phase and secondly droplets of the dispersed phase should remain uniformly distributed throughout the system. Instabilities seen in emulsion are discussed below.

2.18.2.1 Creaming

An emulsion is said to cream when the oil or fat rises to the surface, but remains in the form of globules, which may be redistributed throughout the dispersion medium by shaking. An oil of low viscosity tends to cream more readily than one of high viscosity. Increasing the viscosity of the medium decreases the tendency to cream. Creaming is a reversible phenomenon which can be corrected by mild shaking. (Florence and Attwood 2005).

The factors affecting creaming are best described by Stoke's law

$V = 2r^2 (d_1-d_2) g/9\hat{I}\cdot$

Where V = rate of creaming

r = radius of globules

d_1 = density of dispersed phase

d_2 = density of dispersion medium

g = gravitational constant

$\hat{I}\cdot$ = viscosity of the dispersion medium

The following approaches can be used for decreasing Creaming

- **Reduction of globule size:** According to Stoke's law, rate of creaming is directly proportional to the size of globules. The bigger the size of the globules, the more the creaming. Therefore in order to minimize creaming, globule size should be reduced by homogenization.
- **Increasing the viscosity of the continuous phase:** Rate of creaming is inversely proportional to the viscosity of the continuous phase i.e. more the viscosity of the continuous phase, less will the problem of creaming. Therefore to avoid creaming in emulsions, the viscosity of the continuous phase should be increased by adding suitable viscosity enhancers like gum acacia, tragacanth etc. (Florence and Attwood 2005)

2.18.2.2 Cracking

Occasionally, it happens that an emulsion cracks during preparation, i.e., the primary emulsion does not become white but acquires an oily translucent appearance. In such a case, it is impossible to dilute the emulsion nucleus with water and the oil separates out. Cracking of emulsion can be due to addition of an incompatible emulsifying agent, chemical or microbial decomposition of emulsifying agent, addition of electrolytes, exposure to increased or reduced temperature or change in pH.

2.18.2.3 Phase Inversion

In phase inversion o/w type emulsion changes into w/o type and vice versa. It is a physical instability. It may be brought about by the addition of an electrolyte or by changing the phase volume ratio or by temperature changes. Phase inversion can be minimized by using the proper emulsifying agent in adequate concentration, keeping the concentration of

dispersed phase between 30 to 60 % and by storing the emulsion in a cool place (Florence and Attwood. 2005)

Chapter 3

MATERIALS AND METHODS

3.1 MATERIALS AND METHODS

Materials

Crude Shea gum was used for the study. The crude gum was obtained from the Bolgatanga plantation as natural exudates from the stem bark of the plant *vitellaria paradoxa* family, sapotaceae in the Upper East Region of Ghana. It was authenticated at the Cocoa Research Institute of Ghana (CRIG) Subsidiary Research Substation for the Shea tree at Bole in the Northern Region.

3.1.1 Reagents

Concentrated hydrochloric acid was obtained from Phillip Harris plc (Shenstone, England). 96 % ethanol, diethyl ether, perchloric and acid were obtained from the chemical store of the Department of Pharmaceutics and the Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences, KNUST, Kumasi.

3.1.2 Equipment and apparatus

Buchi distillation unit k-314, Bibby digital burette Trohm pH meter, mortar and pestle, , Sartorius Electrical Balance, perkin Elmer Analyst400 Atomic absorption Spectrophotometer (Shidmazu Corporation), Brookfield Viscometer Model DV-I+, Retsch laboratory sieves, USP-ED-2L, Photometer model PF P7(Jenway, United Kingdom), WA 210 Analytical balance, Electrolab Disintegrating Tester USP- ED-2L SOTAX Friabilator (USP), Cecil CE 8020 UV machine and Erweka Dissolution Apparatus, (type DT 6, GmbH Heusenstamm, Germany).

METHODS

3.2 PURIFICATION OF SHEA GUM

The method used by Ofori Kwakye et al, 2010 was modified and used for the purification of the gum. The crude gum was dried in the air for 4 weeks until it became sufficiently brittle. The bark and other extraneous materials were scraped manually and the gum was separated from the extraneous materials. The crude gum was further processed by powdering in a porcelain mortar with pestle. Parts of the powdered gum were used in some of the subsequent test and analysis as crude shea gum powder.

To purify the gum, 100 g of the crude gum powder was hydrated in 200 ml of distilled water for fourteen days with intermittent stirring to allow enough time for dissolution of the gum material. Using a piece of calico linen the mixture was then strained into a basin. The filtrate was re-filtered to ensure that all debris were removed. Thereafter the gum was precipitated with 96 % ethanol. About 400 ml of 96 % ethanol was used to precipitate 100 g of the gum. The precipitated gum was filtered and washed with di- ethyl ether and dried in the hot air oven at 40^{o}C for about 24 hours. The dried purified gum was pulverized using a mortar and pestle and sieved through sieve number 80. The purified gum was stored in airtight container.

3.3 EXAMINATION OF PHYSICAL PROPERTIES OF SHEA GUM

3.3.1 Macroscopic properties of shea gum

In evaluating the macroscopic properties of Shea gum, its colour, shape, size, odour and taste were observed.

3.3.2 Moisture content of the gum

The method used was that described by Mahmud et al, (2008). Two (2) grams of powdered crude Shea gum was weighed accurately into a dry porcelain crucible. The gum was allowed to dry in a desiccator and weighed daily until a constant weight was obtained (after 5days). The weight of the crucible and the gum were recorded. This determination was done in triplicate. The moisture content or loss on drying was expressed as a percentage of the Shea gum sample. The entire process was repeated for the purified shea gum.

3.3.3 Insoluble matter in crude and purified gum

Two grams (2.0 g) each of the crude and purified gums were separately weighed into a 250 ml round bottom flask. To each was added 100 ml of water followed by the addition of 14 ml of 2M HCl. The mixture was boiled gently for 15 minutes, while shaking frequently, and filtered whilst hot through number 4 sintered glass filters. The residue was then washed with hot water and air dried to constant weight. The weight of the insoluble matter was expressed as a percentage of the initial weight (British Pharmacopea, 2009).

3.3.4 Determination of swelling capacity of gum

Five grams of the purified gum powder was placed in a 100 ml capacity measuring cylinder and tapped 200 times after which the volume of gum was noted (Vo). Distilled water was added to the 80 ml mark and left to stand for 24 hours after which the new volume obtained was recorded as V_1. This process was carried out in triplicate and the swelling capacity was calculated as the ratio of final volume to initial volume (Mahmud et al, 2008).

3.3.5 Determination of the hydration capacity/ water retention capacity of gum.

One gram of purified shea gum was placed in a thermofisher laboratory bench top(low speed, 80-2) centrifuge tube and covered with 10 ml of purified water. The tube was manually shaken intermittently over a two hour period and left to stand for 30 minutes. This was then centrifuged at 3000 rpm for 10 minutes. The supernatant was decanted and the weight of the gum after uptake of water and centrifugation was determined (Xg) (Oyi et al, 2010).

3.4 FLOW PROPERTIES OF THE PURIFIED GUM

3.4.1 Bulk and tapped density determination

Ten grams of purified shea gum was weighed into a 100 ml measuring cylinder. The initial volume was recorded as the bulk volume (V_b). The bottom of the cylinder was tapped 200 times and the volume obtained was recorded as the tapped volume (V_t). This process was repeated in triplicate. The bulk and tapped densities were calculated as the ratio of the mass of gum to respective volumes (Aulton,1994).

3.4.2 Hausner's ratio

The hausner's ratio was calculated as a ratio of the tapped density to the bulk densities

Hausner's ratio = $\frac{\text{tapped density}}{\text{Bulk density}}$ (Aulton, 1994)

3.4.3 Compressibility index

The compressibility index was determined according to the Carr's index which is calculated as follows

Carr's index= $\frac{\text{Tapped density- bulk density}}{\text{Tapped density}} \times 100$ (Aulton, 1994)

3.4.4 Angle of repose

The static angle of repose was measured according to the fixed funnel and free standing cone method. A funnel was clamped with its tip 2 cm above a paper placed on a flat horizontal surface.

The purified gum powder was carefully poured through the funnel until the apex of the cone formed just reached the tip of the funnel. The height (h),of the powder cones were determined and the mean diameters (D), of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation.

$\text{Tan}\Theta = 2h/D$ (Aulton, 1994)

3.5 DETERMINATION OF APPROXIMATE SOLUBILITY OF SHEA GUM IN VARIOUS SOLVENT

The solubility of shea gum was determined in cold and hot distilled water, acetone, chloroform and ethanol. 10 mg sample each of gum was added to 10 ml each of the above mentioned solvents and left overnight. 5 ml of the clear supernatants were taken in small pre-weighed evaporating dishes and heated to dryness over a digital thermostatic water bath. The weights of the dried residue with reference to the volume of the solutions were determined using a digital top loading balance and recorded (Vijetha et al 2010).

3.6 SPECTROPHOTOMETRIC ANALYSIS OF METALLIC ION CONTENT OF SHEA GUM

3.6.1 Wet Digestion of Gum

The first step involved the elimination of the inorganic materials present in the gum through the procedure of wet washing. One (1) gram of the sample was weighed into a 250 ml beaker. Twenty five mililitres (25 ml) of concentrated nitric acid was added and the beaker covered with a watch glass. The sample was digested with great care on a hot plate in a fumed chamber until the solution was pale yellow. The solution was cooled and 1 ml Perchloric acid (70 % $HClO_4$) added. The digestion was continued until the solution was colourless or nearly so (the evolution of dense white fumes indicated the removal of nitric acid). When the digestion was completed, the solution was cooled slightly and 30 ml of distilled water added. The mixture was brought to the boil for about 10 minutes and filtered hot into a 100 ml volumetric flask using a Whatman No. 4 filter paper. The solution was then made to the mark with distilled water (Ofori Kwakye et al, 2010).

3.6.2 Determination of Calcium (Ca), Magnesium (Mg), Zinc (Zn) and Iron (Fe) Content

One (1) mililitre of the digest was used to determine the content of Ca, Mg, Zn and Fe in the sample using the Perking Elmer Precisely A Analyst 400 Atomic Absorption Spectrophotometer (AAS) fitted with an acetylene flame. The AAS was fitted with Zn and Fe EDL lamps and Mg and Ca CHCL lamps set at wavelengths of 213.86 λ, 248.33 λ, 285.21 λ, and 422.67 λ respectively. The determination was done in triplicate (Ofori Kwakye et al, 2010).

3.6.3 Determination of Sodium (Na) and Potassium (K) Content

Two (2) mililitres of the digest was used in the determination of sodium and potassium using the Flame Photometric method. The photometer (Jenway, United Kingdom) model PF P7 with methane gas was used. The determination was done in triplicate (Ofori Kwakye et al, 2010).

3.7 DETERMINATION OF PROTEIN CONTENT

This was done using the Kjeldahl method (Anderson, 1986) which entails converting the nitrogen content of the gum into free ammonia by steam distillation of a digest solution in the presence of excess alkali (NaOH).

3.7.1 Wet digestion of gum sample;

The first step involved the elimination of the inorganic materials present in the gum through the procedure of wet washing. 0.2 grams of the sample was weighed into a 250 ml beaker. Twenty five mililitres (25 ml) of concentrated nitric acid was added and the beaker covered with a watch glass. The sample was digested with great care on a hot plate in a fumed chamber until the solution was pale yellow. The solution was cooled and 1ml Perchloric acid (70 % $HClO_4$) added. The digestion was continued until the solution was colourless or nearly so (the evolution of dense white fumes indicated the removal of nitric acid). When the digestion was completed, the solution was cooled slightly and 30 ml of distilled water added. The mixture was brought to the boil for about 10 minutes and filtered hot into a 100 ml volumetric flask using a Whatman No. 4 filter paper. The solution was then made to the mark with distilled water. 5 ml aliquot of sample digest solution above was transferred into the Buchi distillation apparatus. 5 ml of 40% sodium hydroxide and 100 ml of distilled water were added to the 5 ml sample in the distillation apparatus. The mixture was then distilled and the resulting distillate was collected into a conical flask containing 5 ml of 2% boric acid with drops of mixed indicator (methyl red and bromocresol).

This was then titrated with 0.01M HCl using a digital burette until the mixture changed from its initial green colour to the reddish endpoint. The titration was done in triplicate and the titre values recorded. The nitrogen content was then calculated.

3.8 pH OF PURIFIED GUM MUCILAGE

Purified gum mucilage was prepared with distilled water to a concentration of 2 % w/v. The pH of the mucilage was determined using a standardized pH meter at 26 ^{o}C. The pH was determined in triplicate and the average was calculated.

3.9 PHYTOCHEMICAL SCREENING OF GUM

The methods described by Onwukaemea et al, 2007 was modified and employed to determine the phyto chemical constituents of the gum.

3.9.1 Fehling's test for reducing sugars

A small amount of the gum was dispersed in about 2 ml of water in a test tube.1ml of fehling's solution A and B was added and the mixture was shaken and heated in a water bath for 10 minutes. The colour obtained was recorded. A brick red precipitate indicated the presence of reducing sugars.

3.9.2 Frothing test for saponins

The purified gum powder was dispersed in about 2ml of water and the resulting dispersion was heated on a water bath until it began to boil. The dispersion was shaken vigorously and left to stand for 10 minutes. The presence of a thick persistent froth indicated the presence of saponins.

3.9.3 Test for flavanoids

A small quantity of gum powder was placed in a test tube. About 2 ml of dilute NaOH was added followed by 2 ml of dilute HCl. The colour and the solubility of the gum after this was used to confirm the presence or absence of flavanoids.

3.9.4 Test for tannins

A small quantity of the gum was dispersed in about 2 ml of water in a test tube. This was followed by the addition of 15% $FeCl_3$ solution. The colour of the solution was used to determine the type of tannins present.

3.9.5 Test for alkaloids

A small quantity of gum is dispersed in water. About 2 ml of dragendroff's reagent was added. The presence or absence of colour of the precipitate formed was noted.

3.9.6 Test for carbohydrate

Molisch reagent was added to the gum mucilage a violet ring at the junction of the two liquid indicates the presence of a carbohydrate.

3.9.7 Test for gums

Ruthenium red was added to the gum mucilage. A red colour indicates the presence of a gum (Evans, 1989).

3.10 RHEOLOGICAL PROPERTIES OF GUM

3.10.1 Flow curves of various concentration of shea gum

Mucilages of five different concentrations of shea gum; 2%, 5%, 10%, 15% and 20% were prepared using distilled water. The viscosities of these samples were then determined at different shear rates; 0.5, 1, 1.5, 2, 2.5 and 3 rpm using a Brookfield viscometer at a room temperature (26^{o}C) (Gyedu-Akoto et al,2007).

3.10.2 Effect of concentration on viscosity of gum mucilage

Mucilages of six different concentrations of acacia and shea gum, namely: 5 % w/v, 10 %w/v, 15 %w/v, 20 % w/v, 30 % w/v, and 40 % w/v were prepared using distilled water. The viscosity of the samples were determined at shear rate of one rpm using a Brookfield viscometer (spindle number 2) (Gyedu-Akoto et al,2007).

3.10.3 Effect of temperature on viscosity of gum mucilage

20 % w/v of purified shea gum mucilage was prepared in distilled water and the viscosity determined with a Brookfield viscometer at different temperatures; 25^{o}C, 30^{o}C,35 ^{o}C, 45^{o}C, 60^{o}C and 80^{o}C(Gyedu-Akoto et al,2007).

3.10.4 Effect of pH on the viscosity of mucilage

One litre of 20%w/v gum mucilage was prepared using distilled water. This was then divided into five portions each of 200 ml. These portions were labelled A, B, C, D and E respectively according to their desired pH values. The pH of all the five portions were pre determined and recorded. These pH values were altered to the desired pH by the gradual addition of 0.1M HCl

or 0.1M NaOH to obtain the desired pH. To the bottles labelled A and B, 0.1M HCL was added to each until the pH of 3 and 5 were obtained respectively. To portions D and E, 0.1M NaOH was added gradually until pH values of of 9 and 11 were obtained. The portion labelled C was maintained at its initial pH since the pH of the mucilage was within the neutral pH desired. This was followed by the determination of the viscosities of each sample. The viscosities of the five samples were determined at shear rate of one rpm and recorded (Cornway and Nep, 2005).

3.10.5 Effect of electrolyte on viscosity of gums

To determine the effect of the ion content on the viscosity of the purified shea gum, 600 ml of 20 % gum dispersion was prepared and divided into three portions labelled A, B and C.

The initial viscosities of all three portions were determined at shear rate of one rpm using Brookfield viscometer spindle 2 at 27 ^{o}C.

To Sample A, molar solutions of $AlCl_3$ in the range of 0.125 M to 1.5 M were added gradually and the viscosity determined after each addition. This process was repeated for the B and C portions using molar solutions of $CaCl_2$ and KCl. The results were recorded; tabulated and appropriate graphs were drawn (Conway and Nep, 2010).

3.11 MICROBIAL QUALITY OF CRUDE AND PURIFIED GUM

Purified shea gum (0.1g) were dissolved separately in 10 ml of sterile water and 1 ml of the mucilage was inoculated into a previously stabilised MacConkey agar, mannitol salt agar, cetrimide agar, sabauraud plus streptomycin agar and bismuth sulphite agar. The inoculated agars were incubated at 37 °C for 48 hours and growth of specific organisms depending on the selective media that was used was read as present or not present. All the experiments were duplicated (Asantewa et al,2011).

3.12 FORMULATION PROPERTIES OF SHEA GUM

3.12.1 Tablet formulation

3.12.1.1 Preparation of Shea mucilage

five grams of Shea gum was weighed into a clean porcelain mortar and triturated. Small amounts of distilled water were added until uniform mucilage was formed. The mucilage was then transferred into a clean tarred bottle and made up to the 100 ml mark with distilled water to obtain 5 % w/v shea mucilage. A similar process was followed to obtain a concentrations 10 %w/v, 15 % w/v and 20 %w/v. The mucilage was used as the binder in the preparation of the various batches of granules.

3.12.1.2 Preparation of acacia mucilage

The acacia gum mucilage was prepared by following the same procedure as the Shea mucilage using different amounts of the gum to prepare 5 % w/v, 10 %w/v, 15 %w/v and 20 % w/ v.

3.12.1.3 Preparation of granules

The wet granulation method was employed and the batch size was 100 tablets for each concentration of mucilage.Quantities of the paracetamol powder, lactose and maize starch stated in the table below, were dry mixed in a porcelain mortar and moistened with appropriate amounts of binder solution to produce a wet powder mass containing different concentrations of shea gum. The wet mass was then screened with sieve number eight. The screened mass was dried in an oven at sixty degrees for about an hour after which the dried mass was screened using sieve number sixteen to obtain dry granules for compression into tablet.

Table 3-1 General formulae for the preparation of paracetamol tablet

Ingredients	Quantity per tablet/mg	Quantity per batch/g
Paracetamol	500	50
Lactose	40	6.49
Maize starch (1%)	15.6	5.06
Binder	??	??
Talc(1%)	1.3	0.13

Table 3-2 Total volume of shea gum mucilage used

Concentration %w/v	Volume of binder used/ ml	Weight of binder per tablet/g	Weight of binder per batch/g
5	25.00	0.0125	1.25
10	22.00	0.0220	2.20
15	17.00	0.0255	2.55
20	5.0	0.0100	1.00

Table 3-3 Total volume of acacia mucilage used

Concentration %w/v	Volume used/ml	Weight of binder per tablet/g	Weight of binder per batch/g
5	23	0.0150	1.15
10	22	0.0220	2.2
15	20	0.03	3.0
20	7	0.0140	1.4

3.13 FLOW PROPERTIES OF GRANULES

About 30 g of granules was weighed and poured through a funnel into a 100 ml measuring cylinder. The cylinder was then lightly tapped twice to collect all the granules sticking on the wall of the cylinder. The initial volume, V_o was recorded.

The cylinder was tapped from a height of 2.5 cm 50 times on a wooden bench top to attain a constant volume reading from the cylinder, V_f

The initial density was calculated as the initial bulk density or fluff or paired bulk density, D_o that is, mass/V_o. The final density was also calculated as the final bulk density or equilibrium or tapped or consolidated bulk density, D_f that is, mass/ Vo. The ratio D_f / D_o was calculated as the Hausner's ratio. And Carr's index also known as percentage compressibility was calculated as $(D_f – Do/D_f)$ x 100%

The Hausner ratio and the Carr's index, which are measures of interparticle friction and the potential powder arch or bridge strength and stability, respectively, are used widely to estimate the flow properties of powders. The angle of repose of the granules was determined using the fixed height method (Aulton 1994).

3.14 COMPRESSION OF GRANULES

The granules obtained were compressed using a single punch tablet press. For each batch 100 tablets were compressed using a die volume of 550 mg to 560 mg.

3.15 QUALITY COMPLIANCE TESTS ON TABLETS

3.15.1 Uniformity of weight test

Twenty (20) tablets from each batch were randomly selected and weighed together; the tablets were then weighed individually. The weight of each tablet was subtracted from the mean tablet weight (of twenty tablets) and the percentage deviation of each tablet from the mean was also calculated (British Pharmacopoeia, 2009).

3.15.2 Friabilty test

Tablets of total weight greater than 6 g was dedusted and weighed initially (Wo). The tablets were then placed in the drum of the friabilator and all the parameters set on the machine. The

drum rotated and tumbled the tablets for four minutes. The tablets were collected dusted again and its final weight, W_f taken and the percentage weight loss calculated as (Wo – W_f/Wo) x 100. The tablets were observed for cleavages, breakages and cracks (USP – NF XXIII, 2002).

3.15.3 Hardness test

Ten tablets were selected randomly from the different batches of the tablets prepared. Each tablet was placed in between the test jaws of the hardness tester . Initiation of the test causes the motorized test jaw to drive forward towards the tablet, thus constantly increasing the pressure applied to the tablet by the two jaws. At the moment of breakage, the force used to break the tablet was displayed digitally, and the value displayed was recorded as the breaking strength in Newton (N) and converted to kilogram, thus: 1 kilogram is equal to 9.80 Newton (USP – NF XXIII, 2002).

3.15.4 Disintegration test

One (1) dosage unit was placed in each of the 6 tubes of the basket of a disintegration apparatus. The apparatus was operated using distilled water as the medium, maintained at 37 ± 0.5 °C. The machine was switched on and the rack with tubes moved up and down in the immersion fluid, until all tablets disintegrated in each of the tubes. The time for the last tablet to disintegrate and pass through the mesh was then recorded. This test was done in triplicate for each batch of tablet (British Pharmacopoeia, 2009).

3.15.5 Dissolution test

3.15.5.1 Calibration of UV spectrophotometer

Appropriate amounts of paracetamol powder was dissolved in phosphate buffer of pH 5.8 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 247 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.

3.15.5.2 Dissolution testing

Nine hundred (900) mililitres of the dissolution medium (phosphate buffer pH 5.8) was placed in each of the seven vessels of the USP Dissolution apparatus. The dissolution medium was equilibrated to 37 ± 0.5 °C, and the paddle speed set at 100 revolutions per minute. One dosage unit was placed in each of the six vessels of the dissolution machine and operated at the specified speed. Care was taken to exclude air bubbles from the surface of the dosage unit. At specified time intervals of 5 minutes, 10 minutes, 15 minutes , 20 minutes, 25minutes, 30minutes, 40 minutes, and 45 minutes, 10 ml samples were withdrawn from a zone midway between the surface of the dissolution medium and the top of the rotating paddle blade, not less than 1 cm from the vessel wall and filtered into a labelled test tube.. To replace the 10 ml sample withdrawn, 10 ml of fresh dissolution medium from the seventh vessel was added to the beaker from which the volume was withdrawn. Five mililitres portions of the filtrate were diluted 10 times. The filtrate was analysed by UV spectrophotometer at a wavelength of 247 nm using a 1cm cell and phosphate buffer pH 5.8 as blank solution.

Using the equation obtained from the calibration curve, the concentration of paracetamol in samples taken at time 5,10,15,20,25,30,35,40 and 45 minutes were calculated and the percentage release values were then calculated. A plot of the cumulative percentage drug release against time was then obtained and results analysed using Microsoft Office Excel and GraphPad Prism.

3.15.5.3 Statistical Analysis of Dissolution Data

Dissolution at time 15 minutes (t_{15}) and time for 85% dissolution ($D_{85\%}$)

Statistical test conducted on the dissolution data was done using the graph pad prism.

The test included 'T' test comparing each test concentration against the equivalent standard (5% Shea vs. 5% acacia). The above was followed by the determination of the similarity factor (F_2) dissolution efficiencies of the various batches.

The similarity factor was determined using the equation

$$= 50 + \log \{[1+ (1/n) \sum_{t=1} * n (R_t-T_t)^2]^{-0.5} *100\}$$

Where f_2 = similarity factor

n = time points

R_t = cumulative percentage dissolved at time t for the reference

Tt = cumulative percentage dissolved at time t for the test (Suvakanta *et al.*, 2010)

3.15.6 Drug Content Determination:

Ten tablets were powdered and a weight of the powder containg 250 mg of paracetamol in tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 5.8) was added and shaken for 10 minutes. Thereafter, the volume was made up to 100ml with buffer. Subsequently, the solution in the volumetric flask was filtered and 1ml of the filtrate was diluted and analyzed at 247 nm using UV visible spectrophotometer to obtain the absorbance . The absorbance was used to obtain the amount of drug in the fluid analysed with the help of the equation below;

A= abc where A = Absorbance, a = molar absorptivity, b = path length c = concentration of drug. The amount of drug obtained was the multiplied by the dilution factor to obtain the actual content of paracetamol present in the paracetamol tablet. (British Pharmacopeia, 2009).

3.16 SUSPENDING PROPERTY OF SHEA GUM

The purified gum was investigated for its possible suspending ability. This was done by incorporating different concentrations of the gum into paracetamol suspension and the suspensions produced were compared to suspensions containing standard suspending agent (acacia gum). Parameters measured include sedimentation volume, apparent viscosity and ease of re dispersibilty.The methods described by Asantewa et.al (2011) were adopted.

3.16.1 Preparation of Paracetamol Suspension

The paracetamol suspensions (2.4%w/v) were prepared using 1.0 - 4%w/v Acacia and purified shea gum powders. Double Strength Chloroform Water and benzoic acid 0.1 % were employed as a preservative for the suspensions. The solid components were triturated finely in a porcelain mortar with a pestle. The suspending agents (Acacia and Shea gum) were added to the powdered components and triturated until homogeneous slurry was obtained. This was then transferred into a 100 ml measuring cylinder. The mortar was rinsed with the preservative mixture and added to the suspension in the measuring cylinder and topped up to volume.

Table 3-4 Formular for preparation of paracetamol suspension

Ingredient	Quantity
Paracetamol powder	2.4g
Benzoic acid (0.1%w/v)	0.1g
Chloroform water (d/s)	50ml
Acacia mucilage (1%w/v)	10ml
Water to	100ml

3.17 RHEOLOGICAL TEST ON SUSPENSIONS

3.17.1 Flow time and apparent Viscosity

Suspensions containing 1.0% w/v to 4% w/v acacia and shea gum as suspending agent were prepared and the time required for each suspension sample to flow through a 10 ml pipette was determined using a stop watch and the apparent viscosity (η) was calculated using the equation: Flow rate = (mls^{-1}) = Volume of pipette (ml) /flow time/sec. The suspensions were stored for seven days and the procedure above was repeated for the stored suspensions. The flow rates of the fresh and stored suspensions were determined using the equation above.

3.18 SEDIMENTATION VOLUME AND RATES

Quality and stability of the suspensions were assessed by determining parameters such as sedimentation volume and rates.

3.18.1 Sedimentation Volume

Suspensions containing 1.0% w/v to 4% w/v acacia and shea gum as suspending agent were prepared. Each suspension (50 ml) was stored in a 50 ml-measuring cylinder for 42 days at room temperature (28°C). Observations were made at every hour for 6 hours on the first day and then every 72 hours for 42 days. The sedimentation volume, F (%), was then calculated using the following equation: $F = 100Vu/Vo$, where Vu is the ultimate volume of the sediment and Vo is the original volume

3.18.2 Redispersion

Suspensions containing 1.0% w/v to 4% w/v acacia and shea gum as suspending agent were prepared. Fixed volume of each suspension (50 ml) was kept in a measuring cylinders each labeled with it's concencentration and it was to be stored at room temperature (28 °C.) for 42 days. After the specified number of days, the measuring cylinders were shaken vigorously to redistribute the sediment and the ease of redispersion was recorded.

3.19 DETERMINING THE RATIO FOR PREPARATION OF STABLE PRIMARY EMULSIONS USING DIFFERENT OILS

Different ratios of oil, water and gum were investigated to find the most stable primary emulsion using a fixed oil, volatile oil and mineral oil i.e. castor oil, peppermint oil and paraffin oil respectively. The ratio of oil to water to gum used in finding an appropriate ratio for preparation of stable primary emulsions were recorded(Asantewa et al, 2011)

3.19.1 Preparation of primary emulsion by dry gum method

A specified amount of oil was measured and a specified amount of the purified gum was weighed and triturated together in a mortar and the specified volume of water was added. On trituration the hearing of the cracking sound showed the formation of the primary emulsion. The formed primary emulsion was observed for its consistency and the separation of the water and oil (Asantewa et al, 2011)

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3.19.2 Preparation of primary emulsion by wet gum method

A specified amount of water was measured and a specified amount of the purified gum was weighed and triturated together in a mortar and the specified volume of oil was added gradually whilst triturating. On trituration the hearing of the cracking sound showed the formation of the primary emulsion. The formed primary emulsion was observed for its consistency and the separation of the water and oil (Asantewa et al,2011).

Sample calculation for the preparation of primary emulsion out of fixed oil using the ratio: 4:2:1 that is. Oil: Water: Gum.

Volume of emulsion to be prepared = 100 ml

Total percentage of oil = 25%

Therefore volume of oil is 25 ml. using the ratio of 4:2:1 was to be used to prepare the emulsion, then the volume of water = 12.5 ml and that of the gum = 6.25 g. This calculation was repeated for the various ratios that were used in determining the stable ratio.

Table 3-5 Ratios for Fixed Oil

OIL	WATER	GUM
4	2	1
3	2	1
4	2	1.5
3	1	2
5	2	1
2	3	2
3	1.5	1

Table 3-6 Ratios for Mineral Oil

OIL	WATER	GUM
3	2	1
4	2	1
4	2	2
5	3	2
5	3	3
2	3	2
3	1	2
3	1	1

Table 3-7 Ratios for Volatile Oil

OIL	WATER	GUM
2	2	1
5	4	5
1	1	1
3	2	2.5

3.20 PREPARATION OF MINERAL OIL EMULSION FOR STABILISATION

Using a ratio of 5: 3:2 for oil: water: gum respectively for mineral oil, 25 ml of paraffin oil was measured and 10 g of previously weighed purified cashew gum was added and triturated. 15 ml of water was added to the gum-oil mixture and triturated thoroughly until a cracking sound was heard indicating the formation of the primary emulsion. A little amount of water was added to

the primary emulsion to make it pourable, it was then transferred into an already tarred plain bottle and the mortar qualitatively rinsed with purified water and added. It was then made up to volume with purified water to 100ml mark. This was repeated for all the ratios and that of the other oils (Asantewa et al, 2011).

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3.20.1 Stabilisation by homogenisation

Emulsion were prepared as described in section 2.19.2 was transferred into a domestic blender and homogenised for three minutes. It was then transferred into plain bottles and covered.

3.20.2 Stabilisation by addition of a thickening agent

25 ml of mineral oil was measured and 10 g of the gum was added and triturated. 15 ml of water was added to the gum-oil mixture and triturated thoroughly to form the primary emulsion. After the formation of the primary emulsion, an already prepared 40ml xanthan gum suspension of concentrations 0.025 % w/v, 0.05 % w/v, 0.075 % w/v, 0.1 % w/v, 0.2 % w/v, 0.3 % w/v, 0.4 % w/v and 0.5 % w/v was added to the primary emulsion and transferred into an already tarred plain bottle and the mortar was rinsed thoroughly and added to make up to 100 ml after which it was homogenised. It was then transferred into a plain bottle covered and stored (Asantewa et al, 2011).

3.20.3 Stabilisation by reducing interfacial tension using Tween 60

25 ml of mineral oil was measured and 10 g of the gum was added and triturated. Different solutions of tween 60 were prepared, namely: 0.05 % v/v, 0.025 % v/v, 0.024 % v/v, 0.022 % v/v, 0.018 % v/v, 0.015 % v/v, 0.0125 % v/v. 15 ml tween 60 aqueous solutions were added to the gum - oil mixture and triturated hard until the cracking sound was heard, to form the primary emulsion. A little amount of purified water was added to the primary emulsion to make it pourable, it was then transferred into an already tarred plain bottle and the mortar rinsed and added. It was then made up to 100 ml volume with water and homogenised and transferred into a plain bottle and tightly covered (Asantewa et al,2011).

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Chapter 4

RESULTS

4.1 PERCENTAGE YIELD OF SHEA GUM

Weight of crude gum used = 100 g

Weight of purified gum obtained = 63.26 g

The percentage yield of purification process is given by:

$$\frac{\text{Final weight of gum (after purification)}}{\text{Initial weight of gum (before purification)}} \times 100$$

Hence for shea gum

$$\text{Percentage yield} = \frac{63.26\ \text{g}}{100\ \text{g}} \times 100 = 63.26\ \%$$

Percentage yield= 63.26%

4.2 PHYSICAL PROPERTIES OF SHEA GUM

4.2.1 Macroscopic properties of the gum

Table 4-1 Macroscopic properties of crude shea gum

Property	crude gum	purified gum
Colour	Off white, pale pink	Off white or cream
Odour	Characteristic	Characteristic
Taste	Bland	Bland
Surface appearance	Somewhat smooth surface	-
Form and Shape	Irregular tear	-
Fractures	Only very dry ones fracture easily	-

4.2.2 Moisture content of crude and purified gum

4.2.2.1 ***Crude gum***;

Sample calculation

Weight of Petri dish alone = 35.46 g

Weight of Petri dish and gum= 36.46 g

Weight of Petri dish and gum after drying = 36.30g

Loss on drying = 0.16g

% loss/ moisture content = 0.16/1 ×100 = 16%

Moisture content of crude gum = 16%

4.2.2.2 ***Purified gum***;

Weight of petri dish alone = 35.60g

Weight of Petri dish and purified gum = 36.62g

Weight Petri dish and gum after drying = 36.52g

Weight loss = 0.1g

%loss/ moisture content = 0.1/1.02 × 100 =9.80%

Moisture content of purified gum = 9.80%

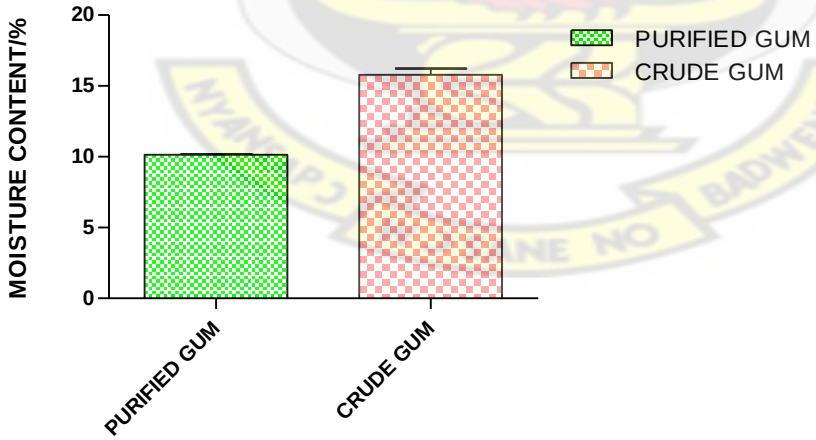

Figure 4-1 Moisture content of crude and purified Shea gum

4.2.3 Insoluble matter of shea gum

Sample calculation

Initial Weight of crude gum = 2.0 g

Weight of residue = 0.0048 g

Insoluble matter = $\frac{0.0048 \times 100}{2.0} = 0.240\%$

Initial weight of purified shea gum = 2.0 g

Weight of residue = 0.0033g

Insoluble matter = $\frac{0.0033 \times 100}{2.0} = 0.165\%$

Table 4-2 Insoluble matter of shea gum

Gum	Insoluble matter (%)
Purified gum	0.165 ± 0.020
Crude gum	0.240 ± 0.205

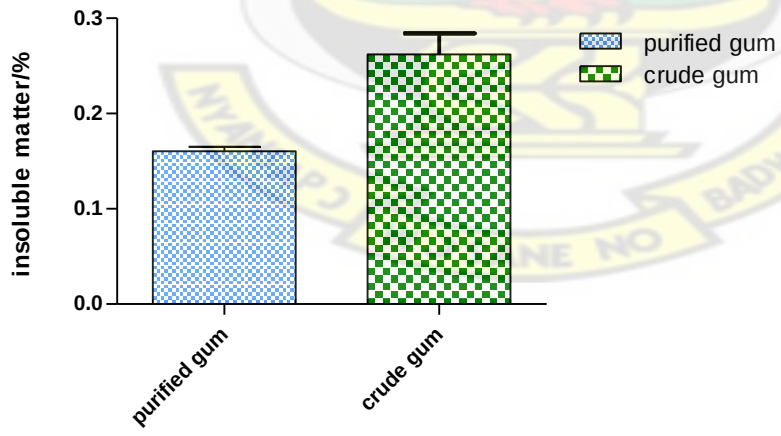

Figure 4-2 Insoluble matter of crude and purified Shea gum

4.2.4 SWELLING CAPACITY OF PURIFIED GUM

Table 4-3 Change in volume of gum upon swelling

No. of test	Test 1	Test 2	Test 3	Average/ml
V_1/ml	92	91	92	91.67
V_0/ml	80	80	80	80

$V_{0=}$ initial volume

$V_{1=}$ volume after swelling

Swelling capacity $\Phi = v_1/v_0$

$\Phi = 91.67/80 = 1.15$

Swelling capacity of purified gum = 1.15

4.2.5 HYDRATION CAPACITY OF PURIFIED GUM

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Table 4-4 Change in weight of gum after hydration

Test	Test 1	Test 2
Wt of test tube +1g before test/g	13.14	13.06
Wt of test tube +1g gum after test./g	14.98	14.97
Difference/g	1.84	1.91

Average difference = 1.87g± 0.021

Hydration capacity = 1.875/1 = 1.875

Hydration capacity of purified gum = 1.875 ± 0.021

4.2.6 Flow properties of purified shea gum

Table 4-5 Flow properties of purified shea gum

Mass= 10g				average values
Initial volume/ v_0/ml	19	19	17	18.33
Tapped volume/v_1/ml	16	17	15	16
Bulk density/g/ml	0.5263	0.5263	0.5882	0.5469
Tapped density/g/ml	0.625	0.5882	0.6666	0.6266
Hausner's ratio	1.1875	1.1176	1.3077	1.2043
Compressibility index/ %	15.79	10.52	11.77	12.69

4.2.6.1 Angle of repose of purified gum

Table 4-6 Angle of repose of purified gum

Height of cone/cm	1.5	1.2	1.4
Diameter of cone/cm	9	9.5	9
Angle of repose Θ	18.4^0	14.17^0	17.28^0

Average angle of repose = $16.62^0 \pm 0.020$

Sample calculation;

$\tan\Theta = 2h/D$

h= height of cone

D= diameter of cone

$\tan\Theta = \frac{1.5(2)}{9}$

$\tan\Theta = 0.3333$

$\Theta = \tan^{-1} = 18.4^0$

4.2.7 Solubility profile of crude and purified gum.

Table 4-7 Solubility profile of shea gum

Liquid	Crude gum	Weight/ml/g/ml	Purified Gum	Weight/ml/g/ml
Water (cold)	Insoluble	0.0030	Sparingly soluble	0.090
hot water	Sparingly Soluble	0.0200	Soluble	1.200
Conc. HCl	Soluble	0.1000	Soluble	1.0250
Ethanol 96%	Insoluble	0.0040	Insoluble	0.0067
Chloroform	soluble	0.4000	Sparingly soluble	0.0340
Chloroform water	Sparingly Soluble	0.0200	Sparingly soluble	0.0430
10% NaCl	Insoluble	0.0004	Insoluble	0.0009
100% acetone	Insoluble	0.0005	Insoluble	0.0007

4.3

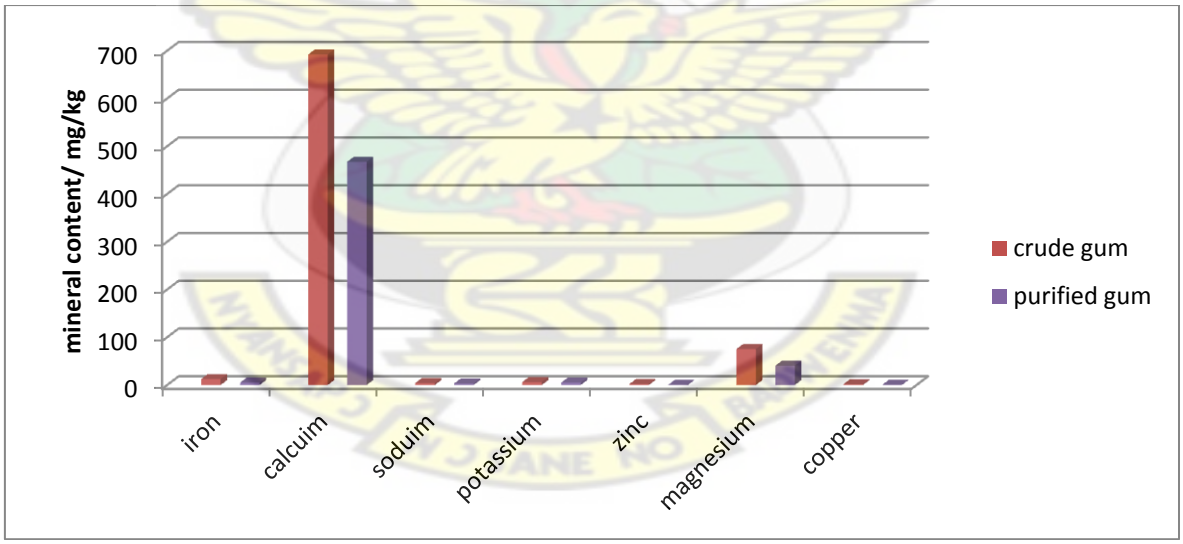

Figure 4-3 Mineral ion content of shea gum

4.3.1 Protein content of gum

Table 4-8 Protein content of purified and crude gum

Test	Test 1	Test 2	Test 3
Titre value/ ml	0.51	0.47	0.47
%Nitrogen/%	0.714	0.658	0.658
% Protein/%	4.463	4.113	4.113
% protein of crude gum	8.741	8.080	8.080

$$\%N = \frac{\text{Titre value} \times 14 \times 100 \times V \times 0.01}{1000 \times w \times al}$$

V= final volume of digestion = 100ml

w = weight of sample taken in grams

al = aliquot of the solution taken for analysis

0.01 = morality of acid used

14 = molar weight of nitrogen

% protein content = %Nitrogen content ×protein factor(6.25)

Sample calculation

$$\%N = \frac{0.51 \times 14 \times 100 \times 100 \times 0.01}{0.2 \times 5 \times 1000}$$

$$\%N = \frac{714}{1000} = 0.714$$

% protein = 0.714×6.25= 4.463

$$\text{Average\% protein} = \frac{4.463+4.113+4.113}{3}$$

Average%protein= 4.230%

4.4 pH OF PURIFIED GUM

Table 4-9 pH of purified gum

pH /FIRST TEST	pH/SECOND TEST	pH/THIRD TEST
7.30	**6.90**	**7.20**

Average pH = 7.133

4.5 PHYTOCHEMICAL CONSTITUENTS OF PURIFIED SHEA GUM

Table 4-10 Phytochemical constituents of purified gum

Test	**Observation**	**Inference**
Reducing sugars	Change from blue colour to red	Presence of reducing sugars
saponins	No frothing only bubbles	Absence of saponins
Tannins	No blue-black precipitate	Tannins absent
Flavanoids	Yellow solution changed to colourless	Flavanoids present
Alkaloids	yellow colour present	Alkaloids present
Molich test	A voilet ring at thejunction of the mucilage and the reagent	Carbohydrates present
Test for gum	Red colour observed	The sample is a gum

4.6 RHEOLOGICAL PROPERTIES OF PURIFIED GUM

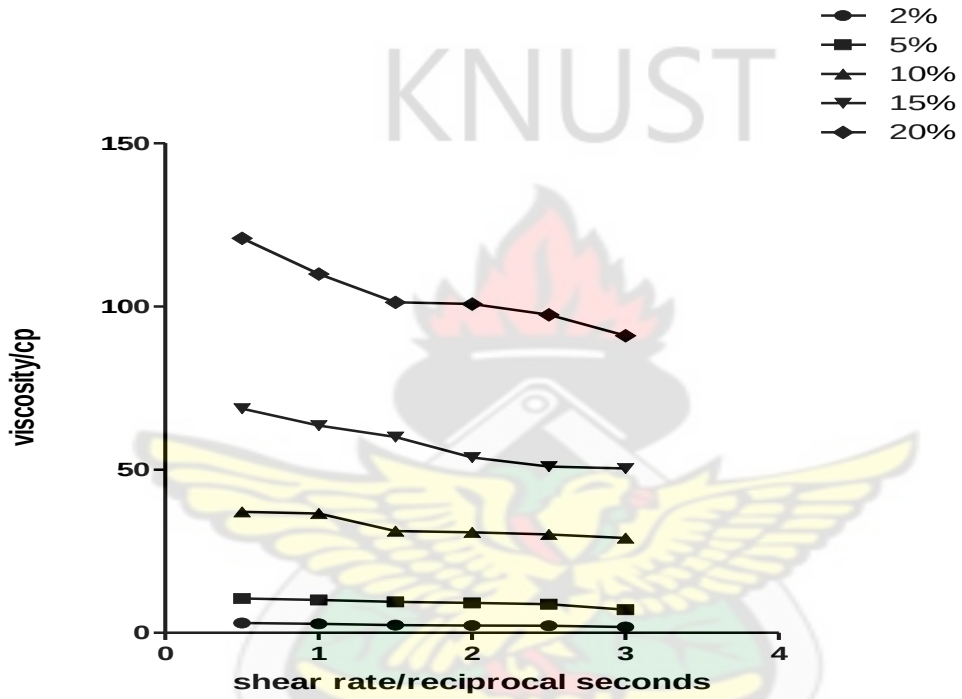

Figure 4-4 Flow curves of various concentrations of shea gum mucilage

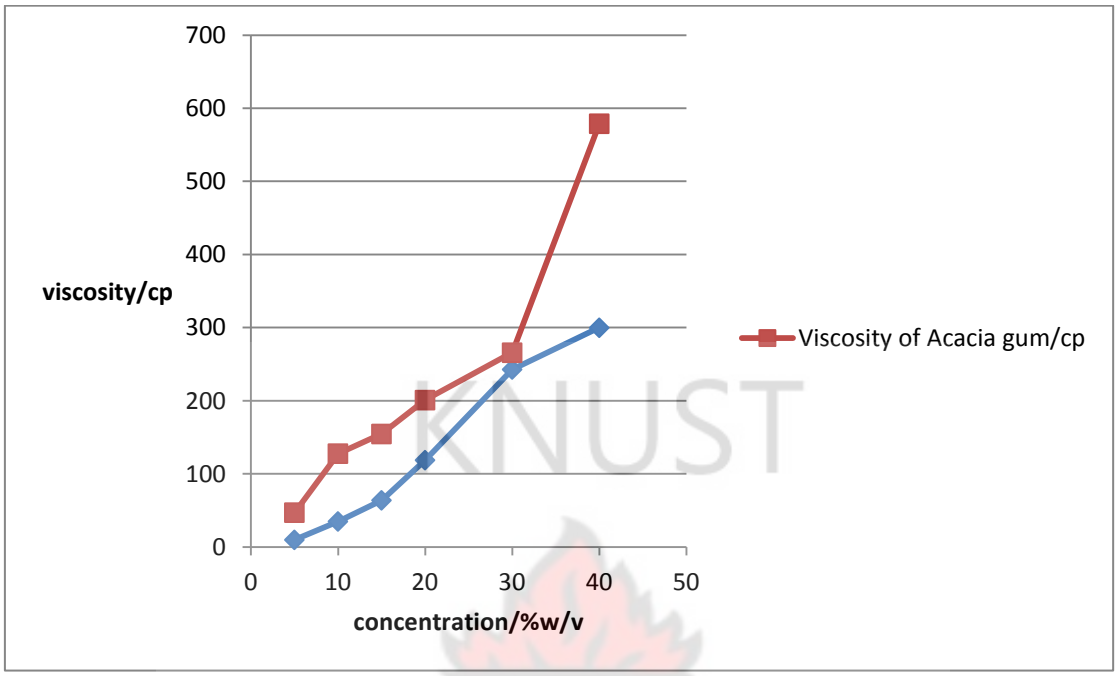

Figure 4-5 Relationship between viscosity and concentration of gum mucilage

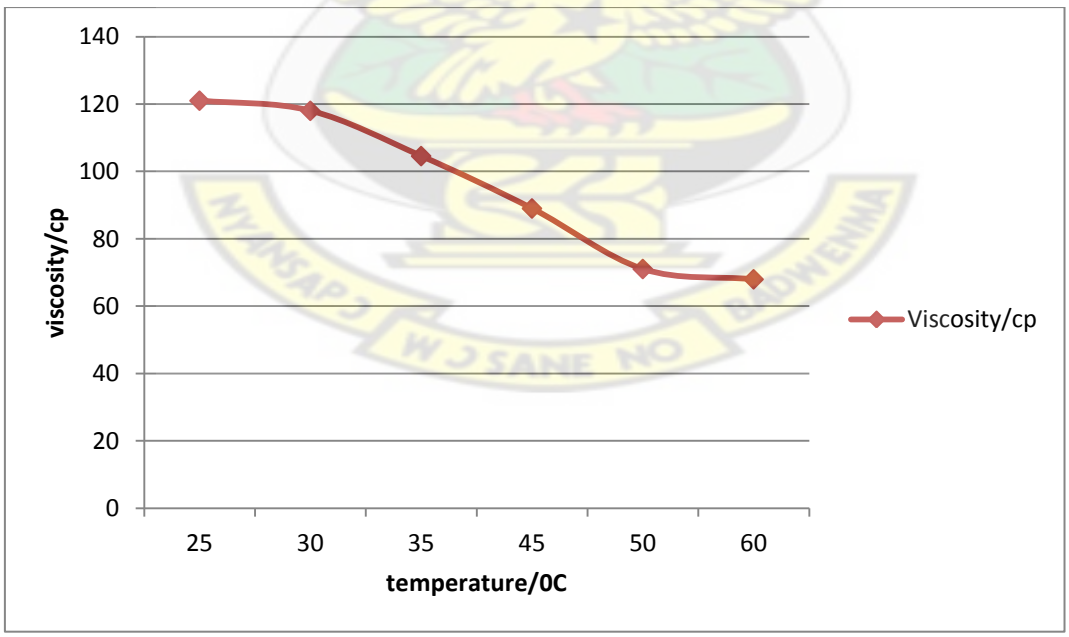

Figure 4-6 Effect of temperature on viscosity

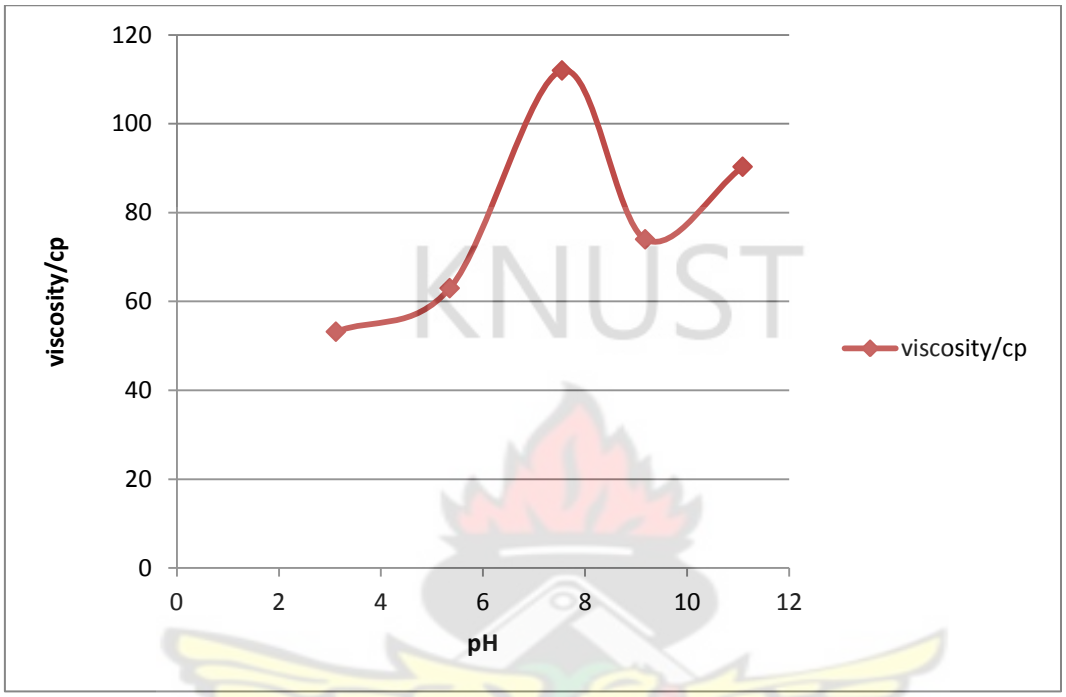

Figure 4-7 Effect of pH on viscosity

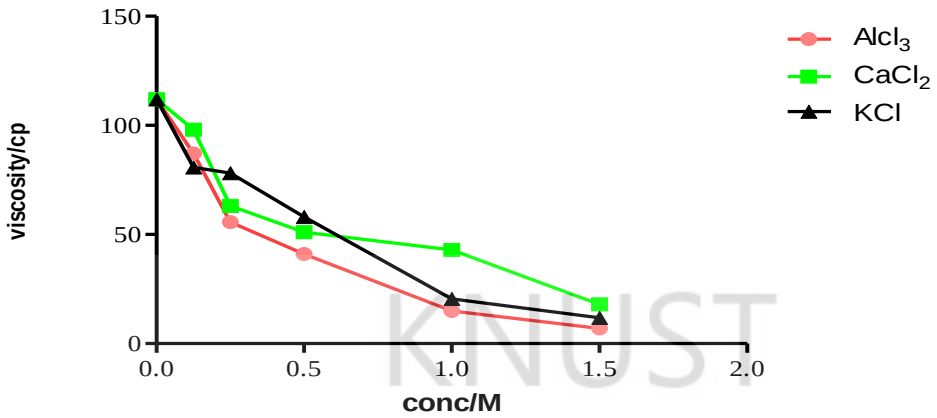

Figure 4-8 Effect of electrolyte on viscosity of shea gum

4.7MICROBIAL QUALITY OF CRUDE AND PURIFIED SHEA GUM

Table 4-11 Microbial quality of crude gum

Selective culture medium	Results	Inference
MacConkey Agar	-	*E.coli* absent
Mannitol Salt Agar	+	Presumptive pathogenic staphylococci present
Bismuth Sulphite Agar	+	Salmonella present
Cetrimide Agar	-	Pseudomonas absent
Sabouraud Agar+ Streptomycin	+	Fungi present

Table 4-12 Microbial quality of purified shea gum

Selective culture medium	Results	Inference
Mac Conkey Agar	-	*E.coli* absent
Mannitol Salt Agar	-	Presumptive pathogenic staphylococci absent
Bismuth Sulphite Agar	-	Salmonella absent
Cetrimide Agar	-	Pseudomonas absent
Sabauraud Agar+ Streptomycin	+	Fungi present

4.8 FORMULATION PROPERTIES OF SHEA GUM

4.8.1 Nature of granules

The granules formulated had a uniform proportion of coarse and fine and was also well dried.

4.8.2 Flow properties of granules

Table 4-13 Bulk volume and tapped volume of granules containing shea and acacia gum mucilage

Granules	Weight of granules(g)	Initial Volume/ml(Vo)	Tapped Volume(V_f)
5% shea	30.00	65.00	54.00
5% acacia	30.00	62.00	55.00
10% shea	30.00	62.50	59.50
10% acacia	30.00	63.50	57.00
15% shea	30.00	63.50	58.50
15% acacia	30.00	65.00	60.50
20% shea	30.00	65.50	60.00
20% acacia	30.00	66.00	63.50

Table 4-14 Flow properties of granules containing acacia and shea mucilage

Granules	Bulk Density (Do)	Tapped Density (D_f)	Hausner's ratio	% Compressibility
5% Shea	0.462	0.555	1.201	16.756
5% acacia	0.484	0.545	1.126	11.119
10% Shea	0.480	0.504	1.050	4.762
10% acacia	0.472	0.526	1.114	10.266
15% Shea	0.472	0.513	1.086	7.992
15% acacia	0.461	0.496	1.075	7.056
20% Shea	0.458	0.500	1.030	8.400
20% acacia	0.455	0.472	1.037	3.602

Sample calculation

$$\text{Hausner's ratio} = \frac{D_f}{D_O}$$

$$= \frac{0.555}{0.462} = 1.201$$

$$\%\text{Compressibility} = \frac{\text{Tapped density- bulk density} \times 100}{\text{Tapped density}}$$

$$= \frac{0.555-0.462 \times 100}{0.555}$$

% Compressibility = 16.756%

Table 4-15 Angle of repose of granules

Batch	1st determination./ x^0	2nd determination./x^0	3rd determination/x^0.	Mean angle of repose/x^0
5% shea	12.40	12.00	10.12	11.50
5% acacia	15.12	13.17	15.28	14.52
10% shea	13.01	13.17	13.31	13.16
10% acacia	10.21	10.32	10.19	10.24
15% shea	16.30	16.00	16.94	16.41
15% acacia	16.45	16.97	16.81	16.74
20% shea	18.03	18.90	18.51	18.48
20% acacia	17.46	17.09	17.96	17.50

4.8.3 Uniformity of weight of tablets

CALCULATION

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

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

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

Table 4-16 Summary of results of uniformity of weight of tablets containig various concentrations of acacia gum as binder

Tablet no.	% Deviation For 5% acacia	%Deviation for10%acacia	%Deviation for15%acacia	%Deviation for 20%acacia
1	-0.159	0.018	0.908	-0.231
2	-0.515	-0.338	-1.584	-0.160
3	-0.3550	-0.267	1.050	-1.050
4	0.284	-0.018	-0.213	0.160
5	0.017	-0.196	-0.516	-0.285
6	0.071	-0.338	-0.374	-0.124
7	-0.248	-0.089	-0.178	-0.142
8	-0.142	-0.125	-0.125	-0.249
9	0.000	0.569	0.996	-0.142
10	-0.231	0.000	1.085	-0.302
11	0.319	-0.214	-0.320	-0.373
12	-0.0353	-2.398	-0.907	-0.249
13	0.000	-0.302	-0.231	-0.213
14	-0.195	0.017	-0.338	0.516
15	0.000	-0.480	-0.071	0.391
16	-0.089	-0.719	-0.142	0.605
17	-0.142	0.925	-0.036	-0.107
18	-0.159	0.267	0.160	0.089
19	0.177	0.195	0.036	-0.195
20	-0.159	0.303	0.231	0.018
Mean weight	0.5629g	0.5619	0.5619	0.5623
Stdev	0.0015	0.0005	0.0005	0.0007

Table 4-17 Summary of results of uniformity of weight of tablets containig various concentrations of shea gum as binder

Tablet no.	%Deviation For 5% shea	%Deviation Of 10%shea	%Deviation Of 15%shea	%Deviation Of 20%shea
1	0.178	-0.125	-0.266	-0.140
2	0.000	-0.089	0.053	-0.035
3	0.357	-0.142	0.000	-0.089
4	-0.090	-0.053	-0.195	0.000
5	0.036	-0.142	0.017	-0.570
6	0.071	0.071	-0.088	0.089
7	0.000	-0.071	0.017	0.000
8	0.054	0.107	-0.071	-0.053
9	-1.071	0.089	0.088	-0.089
10	0.268	-0.053	0.035	-0.035
11	-0.089	-0.106	0.000	0.018
12	0.089	-0.196	0.017	0.266
13	0.089	-0.196	0.124	-0.035
14	-0.089	-0.214	-0.053	0.000
15	-0.054	-0.142	0.071	0.106
16	0.571	-0.053	0.159	0.159
17	0.036	0.017	-0.053	0.035
18	0.249	0.000	0.088	0.266
19	-0.089	0.071	0.035	0.018
20	0.012	0.125	-0.230	0.089
Mean weight	0.5605g	0.5615	0.5640	0.5645
Stdev	0.0012	0.0052	0.0009	0.0017

4.8.4 Friability test for tablet prepared shea gum

Sample calculation for 5% shea

Intial weight= 6.150g

Final weight = 6.100g

$$\% \text{ loss} = \frac{\text{initial weight} - \text{final weight}}{\text{Initial weight}} \times 100$$

$$\% \text{ loss} = \frac{6.15 - 6.10}{6.10} \times 100$$

% Loss = 0.8130%

Table 4-18 Friability test for tablet prepared with shea gum

FRIABILITY TEST						
GUM CONC. /% w/v	INITIAL WEIGHT/ g	FINAL WEIGHT/g	LOSS/g	LOSS/ INITAL WEIGHT	% LOSS	AVE.% LOSS
5% shea	6.150	6.100	0.05	0.00813	0.81	0.73
	6.200	6.160	0.04	0.0064	0.65	
10% Shea	6.2910	6.2730	0.0180	0.0029	0.29	0.53
	7.369	7.313	0.056	0.0076	0.76	
15% shea	7.453	7.417	0.036	0.0048	0.48	0.44
	7.459	7.429	0.03	0.0040	0.40	
20% Shea	7.483	7.412	0.071	0.009	0.95	0.87
	7.456	7.397	0.059	0.008	0.79	

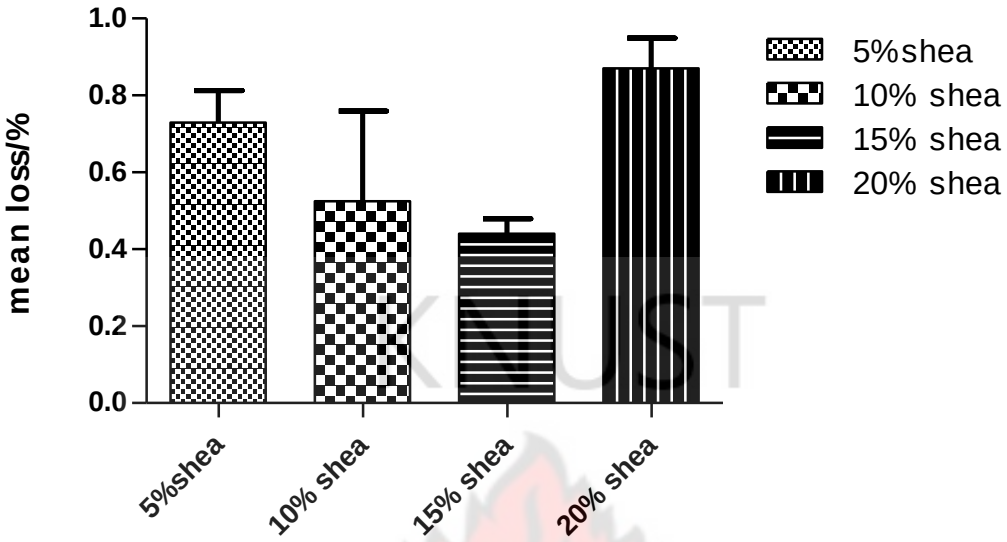

Figure 4-9 Friability of tablets formulated with shea mucilage

Table 4-19 Friability test for tablet prepared with acacia gum

Gum conc/%w/v	Initial weight/g	Final weight/g	Loss/g	%loss	Mean %loss
5% acacia	6.0700	6.0100	0.0600	0.99	0.58±0.412
	6.1705	6.1597	0.0108	0.18	
10% acacia	6.0700	6.010	0.0600	0.99	0.58±0.123
	6.1705	6.1597	0.0108	0.18	
15% acacia	7.1700	7.1600	0.0100	0.13	0.19±0.019
	7.0670	7.0489	0.0181	0.26	
20% acacia	7.1212	7.1102	0.0110	0.15	0.21± 0.0158
	7.1093	7.0891	0.0202	0.28	

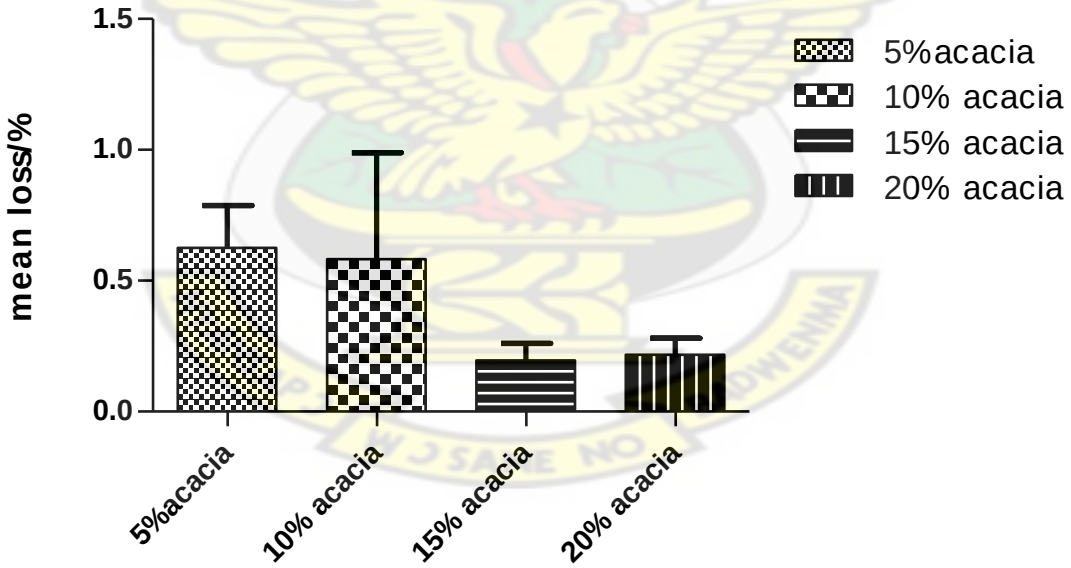

Figure 4-10 Friability of tablet formulated with acacia mucilage

4.8.5 Hardness of tablet formulated with shea gum.

Table 4-20 Relationship between hardness and concentration of gum mucilage

orce/kg						
	Shea gum			Acacia gum		
Gum Conc. /% w/v	First determination	Second determination	Average	First determination	Second determination	Average
5%	4.45	4.65	4.55	4.13	4.13	4.13
10%	5.52	5.56	5.54	5.23	5.28	5.25
15%	6.17	6.17	6.17	5.54	5.52	5.53
20%	6.98	6.95	6.96	6.18	6.15	6.16

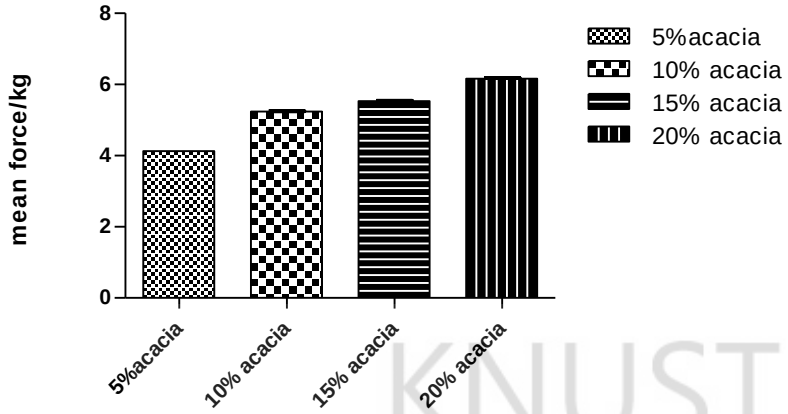

Figure 4-11 Relationship between concentration of acacia and hardness of tablet

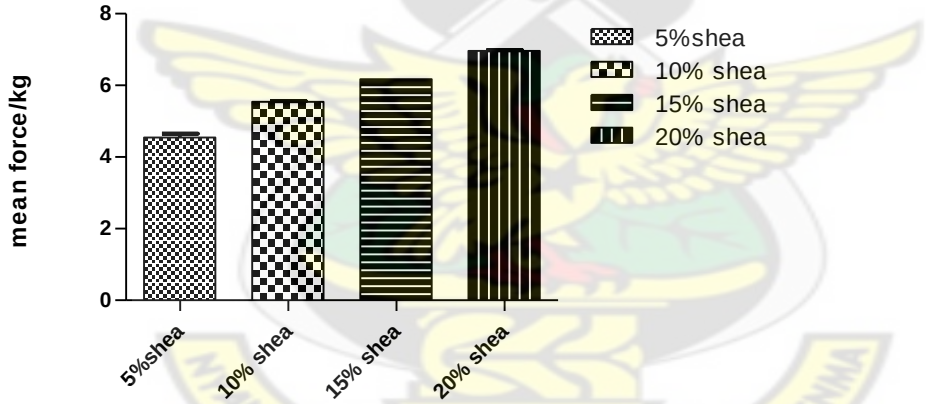

Figure 4-12 Relationship between shea gum mucilage and hardness of tablet

4.8.6 Disintegration time for paracetamol tablets formulated.

Table 4-21 Effect of shea gum concentration on Disintegration time of Paracetamol Formulations

	Disintegration Time			
Gum concentration	T1/min	T2/ min	T3/ min	Average / min
5% shea	3.00	3.10	3.03	3.17 ± 0.187
10% shea	4.20	4.23	4.20	4.21 ± 0.014
15% shea	5.49	5.37	5.40	5.42 ± 0.062
20% shea	7.08	7.12	7.01.	7.07 ± 0.045

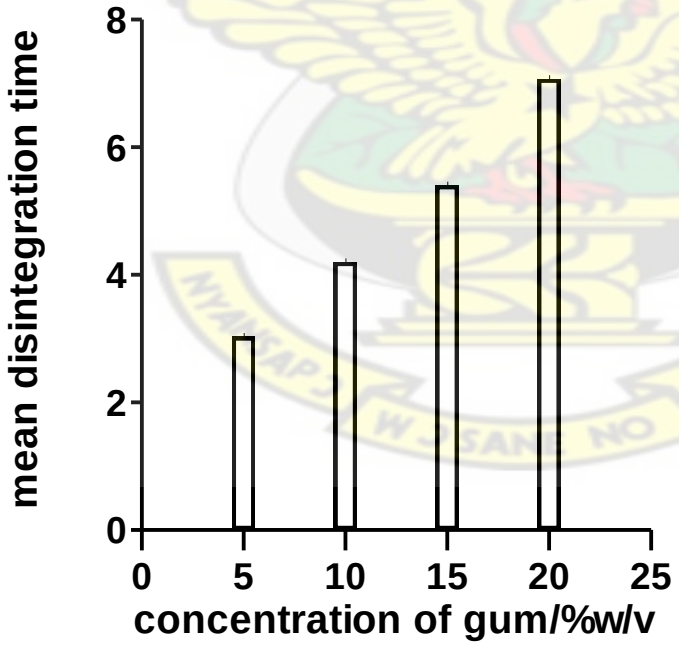

Figure 4-13 Relationship between shea gum concentration and disintegration time

Table 4-22 Effect of acacia concentration on disintegration time of paracetamol tablet

Concentration of Gum	Disintegration time			
	$time_1$/min	$time_2$/min	$time_3$/min	$time_{ave}$/ min
5% acacia	4.30	4.35	4.35	4.33±0.029
10%acacia	6.06	6.03	6.10	6.06±0.035
15% acacia	7.19	7.17	7.14	7.16±0.025
20%acacia	8.12	8.13	8.09	8.11±0.028

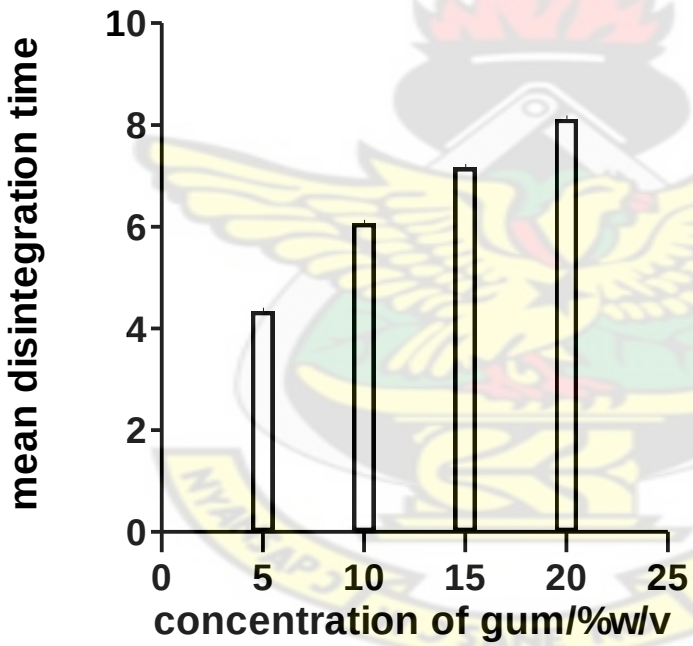

Figure 4-14 Relation ship between concentration of acacia gum and disintegration time

Dissolution profile of paracetamol tablets formulated with different gum concentrations

Blank used: phosphate buffer (pH 5.8)

Table 4-23 Absorbance of pure Paracetamol in Phosphate buffer pH 5.8

Concentration %w/v	
0.0001	0.194 ± 0.002
0.0002	0.253 ± 0.003
0.0004	0.431 ± 0.002
0.0006	0.566 ± 0.003
0.0008	0.709. ± 0.003
0.0010	0.885 ± 0.165

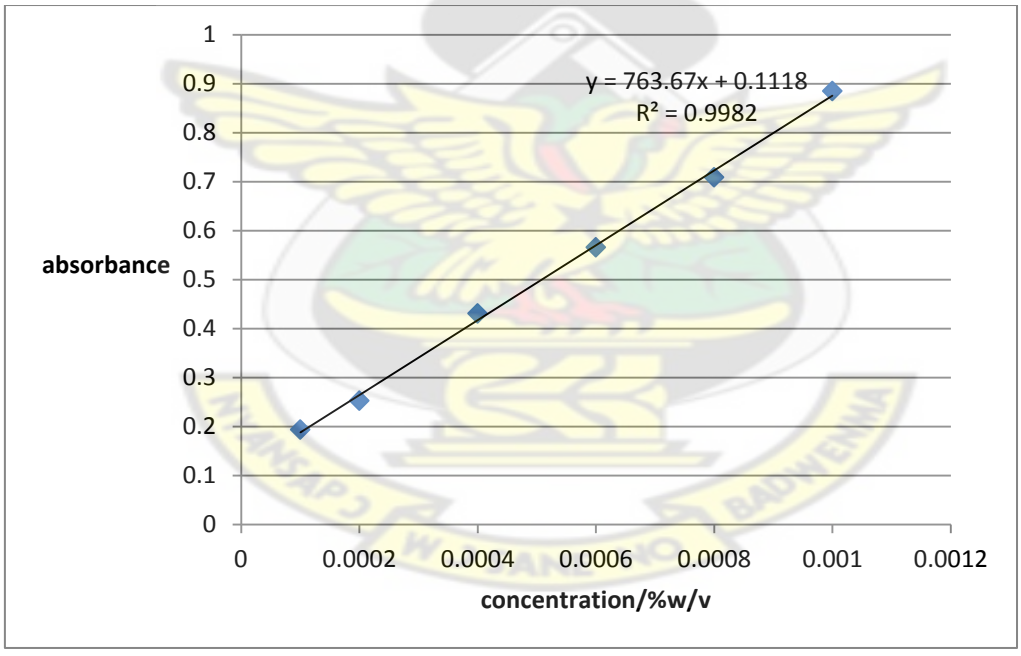

Figure 4-15 Calibration curve for pure paracetamol

Calculation of concentration of paracetamol

From the calibration curve the equation of the graph of pure paracetamol powder dissolved in phosphate buffer pH 5.8 :

R^2= 0.9982 where y= absorbance, and x = concentration

Hence x = y-0.1118/763.67

Thus for a tablet having an absorbance of 0.715

Its concentration, x = 0.715 - 0.1118/ 763.67

X = 0.0007898

7.898×10^{-4} w/v

Hence 7.898×10^{-4} g of paracetamol = 100 ml

? = 900 ml

(900/100) x 7.898×10^{-4} = 7.1086×10^{-3} g

Multiplying 'x' by the dilution factor of 50 gives the concentration of drug dissolved.

$7.898 \times 10^{-4} \times 50$ = 0.35543 g was contained in 10 ml of solution taken

Calculation of percentage release

Assuming that there is a 100% release, then the total amount of drug released will be

500mg of paracetamole in 900 ml of solution

Then, % release = $\frac{0.35543 \times 100}{0.5}$

= 71.09%

Amount released after 10 minutes

Absorbance after 10 minutes = 0.828

Its concentration , x = 0.828 - 0.1118/ 763.67

X = 0.000937

9.3784×10^{-4} w/v

Hence 7.898×10^{-4} g of paracetamol = 100 ml

? = 900 ml

(900/100) x 9.378x 10^{-4} = 8.4405×10^{-3} g

8.4405×10^{-3} g × 50 = 0.4220 g

But at after 5 minutes 10ml of medium was withdrawn and filtered

Hence if at 5 minutes 900ml of dissolution medium contained 7.1086×10^{-3} g

Then the 10ml withdrawn contained (10/900)×7.1086×10^{-3} = 7.8984×10^{-5} g

Therefore total cumulative amount released at 10 minutes =

0.4220g+ 7.8984×10^{-5} = 0.4221g

Cumulative % release = $\frac{0.4221\times100}{0.5}$

= 84.42%

This calculation procedure was used to obtain all concentration and percentage release recorded in the table below.

Table 4-24 Drug release profiles for different batches of tablet

	Cumulative percentage drug release from different batches of paracetamol tablets/%							
Time/ mins	5% shea	5%acacia	10%shea	10%acacia	15%shea	15%acacia	20%shea	20%acacia
5	71.64 ± 0.062	79.56 ± 0.031	68.26 ± 0.031	70.43 ± 0.105	62.47 ± 0.104	72.44 ± 0.045	52.05 ± 0.03	67.09 ± 0.24
10	88.19 ± 0.155	90.18 ± 0.006	81.78 ± 0.026	87.75 ± 0.362	77.04 ± 0.020	77.44 ± 1.119	67.54 ± 0.046	73.29 ± 0.085
15	92.87 ± 0.050	94.11 ± 0.759	88.20 ± 0.035	93.10 ± 0.089	85.63 ± 0.020	86.35 ± 0.214	80.12 ± 0.021	76.06 ± 0.057
20	95.14 ± 0.015	94.76 ± 0.631	90.04 ± 0.025	94.48 ± 0.422	92.86 ± 0.015	89.35 ± 0.040	89.69 ± 0.015	83.70 ± 0.699
25	98.14 ± 0.061	96.35 ± 0.32	95.45 ± 0.042	95.32 ± 0.279	96.90 ± 0.006	93.29 ± 0.153	95.45 ± 0.010	89.38 ± 0.220
30	98.72 ±	98.04 ± 0.11	97.82 ± 0.015	97.12 ± 0.030	97.16 ± 0.021	93.31 ± 0.615	97.15 ± 0.026	92.87 ± 0.368
35	98.93 ± 0.020	98.31 ± 0.13	98.94 ± 0.015	98.68 ± 0.040	97.97 ± 0.006	95.85 ± 0.04	97.53 ± 0.025	95.31 ± 0.524
40	99.19 ± 0.021	98.33 ± 0.53	98.96 ± 0.006	98.82 ± 0.025	98.13 ± 0.015	95.95 ± 0.026	97.83 ± 0.025	95.15 ± 0.139

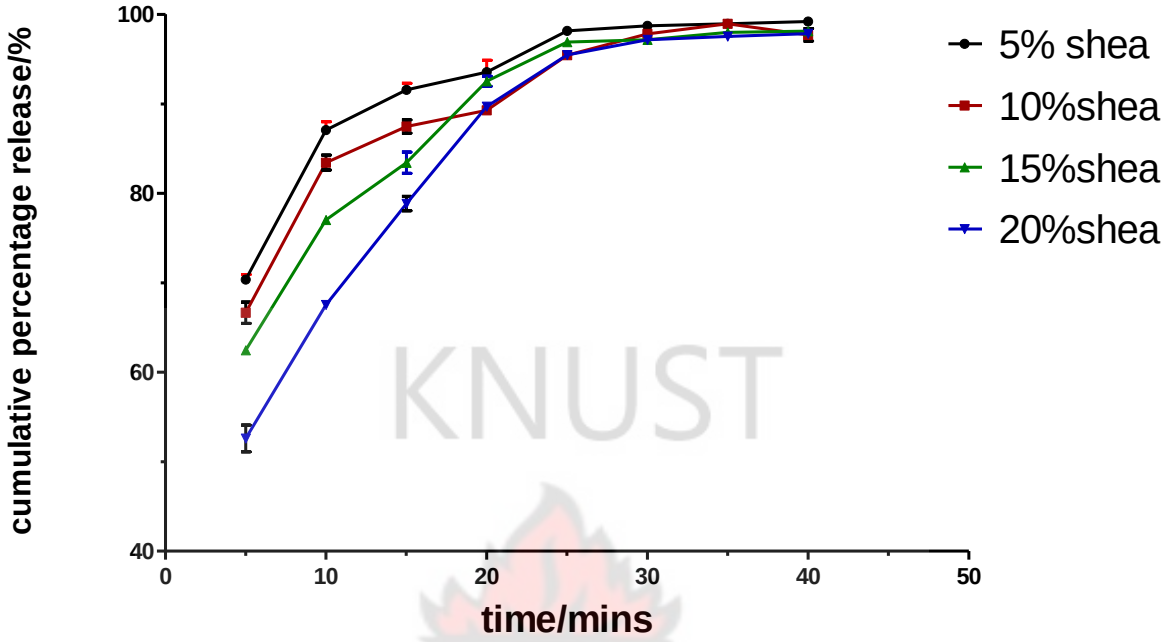

Figure 4-16 Dissolution profile of Paracetamol tablet formulated with shea gum

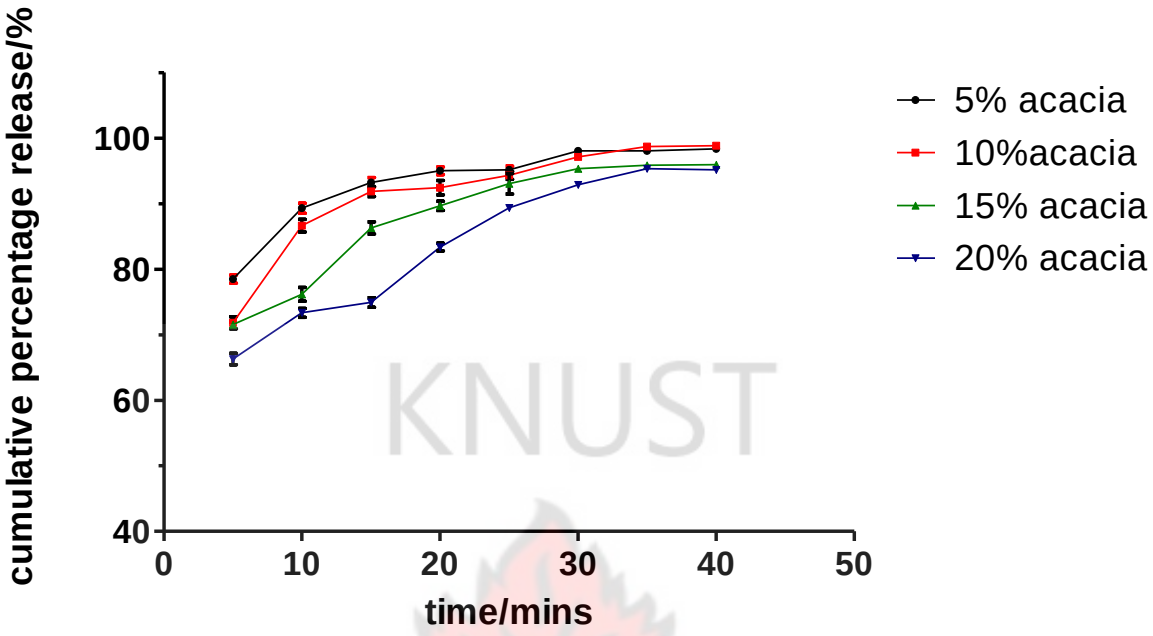

Figure 4-17 Dissolution profile for paracetamol tablets formulated with acacia gum

4.8.7 Statistical analysis of dissolution data

Table 4-25 Statistical analysis of dissolution data

Batch of tablet	Dissolution at 15min (t_{15}) /%	Time for 85% dissolution(D_{85}) / minutes	Dissolution efficiency (DE)/ %
5% Shea	92.87	9.63	94.98
5%acacia	94.11	9.43	96.00
10% shea	88.20	14.46	91.77
10% acacia	93.10	9.77	94.11
15%shea	85.63	14.89	91.39
15% acacia	86.35	14.77	92.55
20%shea	80.12	15.94	87.97
20%acacia	76.06	20.31	88.69

T_{15} = percentage of paracetamol dissolved after 15 minutes

D_{85} = Time required for 85% of the content of paracetamol to dissolve

DE= Dissolution efficiency = $\{(_0\int^t Y.dt) / Y_{100}.(t_2-t_1)\}\times 100$

$(_0\int^t Y.dt)$ = area under the dissolution curve(AUC)

Y= the percentage dissolved at t_2

t_2= time for all active ingredient to dissolve

.t_1= time at which first sample was withdrawn.

Sample calculation

5% Shea

AUC = 3291

AUC was determined using graph pad prism.

Y= 99%

$$DE= \frac{3291\times 100}{99(40-5)}$$

= 94.98%

Table 4-26 Comparative analysis of test and standard

Concentration of gum	'P' Value	Similarity factor (F_2)
5%Shea vs 5% acacia	0.5162	51.4939
10%shea vs 10% acacia	0.7191	51.4683
15% Shea vs 15% acacia	0.8531	51.366
20%shea vs 20% acacia	0.8345	51.1577

'P' Values were obtained after performing anova test using graph pad prism.

P value gives an idea of whether the means of the paired samples are actually significantly different.

P value	Meaning
< 0.001	Extremely significant
0.001 to 0.01	Very significant
0.01 to 0.05	Significant
>0.05	Not significant

The similarity factor was determined using the equation

$$= 50 + \log \{[1+ (1/n) \sum_{t=1} * n (R_t-T_t)^2]^{-0.5} *100\}$$

Where f_2 = similarity factor

n = time points

R_t = cumulative percentage dissolved at time t for the reference

Tt = cumulative percentage dissolved at time t for the test

Results displayed in table above was obtained by employing this formulae on an excel work sheet to generate the similarity factors.

4.8.8 Results of assay of batches of paracetamol tablet prepared

Table 4-27 Content of Paracetamol in tablet prepared

Batch of tablet	% Paracetamol content for three determinations			Mean% content
5% shea	100.40	100.61	100.37	100.46±0.131
10% shea	103.00	103.15	103.25	103.13±0.126
15% shea	101.83	101.96	101.90	101.89±0.065
20%shea	100.98	100.85	100.97	100.93±0.070
5%acacia	98.75	98.72	98.70	98.72±0.025
10% acacia	101.80	101.11	101.91	101.60±0.43
15% acacia	100.78	101.10	101.94	101.27±0.599
20% acacia	100.17	100.15	100.17	100.16±0.012

4.9 RHEOLOGICAL PROPERTIES OF SUSPENSIONS CONTAINING SHEA GUM IN COMPARISON TO ACACIA GUM

4.9.1 Apparent viscosity of suspensions containing Shea and acacia gum

Apparent viscosity was determined by

Flow rate/ apparent viscosity = (mls^{-1}) = Volume of pipette (ml) /flow time/sec

Volume of pipette 10 ml

Apparent viscosity = 10/9.3 =1.07529 mls^{-1}

This calculation was used to generate the fiqures in the table below.

Table 4-28 Flow time of suspensions containing Shea and acacia gum

Gum	Conc/ %w/v	Flow time for freshly prepared suspension/s	Apparent viscosity of freshly prepared suspension/ $mlss^{-1}$	Flow time for stored suspensions/s	Apparent viscosity of stored suspensions/ $mlss^{-1}$
Shea gum	1.0	9.3±0.361	1.08	17.53±0.231	0.570
	2.0	11.5±0.200	0.87	28.27±2.146	0.35
	3.0	14.7±0.300	0.68	44.10±0.436	0.23
	4.0	16.23±0.416	0.62	97.10±0.361	0.10
Acacia gum	1.0	7.67±0.252	1.30	10.53±0.252	0.95
	2.0	10.07±0.058	0.99	24.50±0.200	0.41
	3.0	15.46±0.289	0.65	33.73±0.153	0.29
	4.0	16.60±0.265	0.60	63.63±0.306	0.16

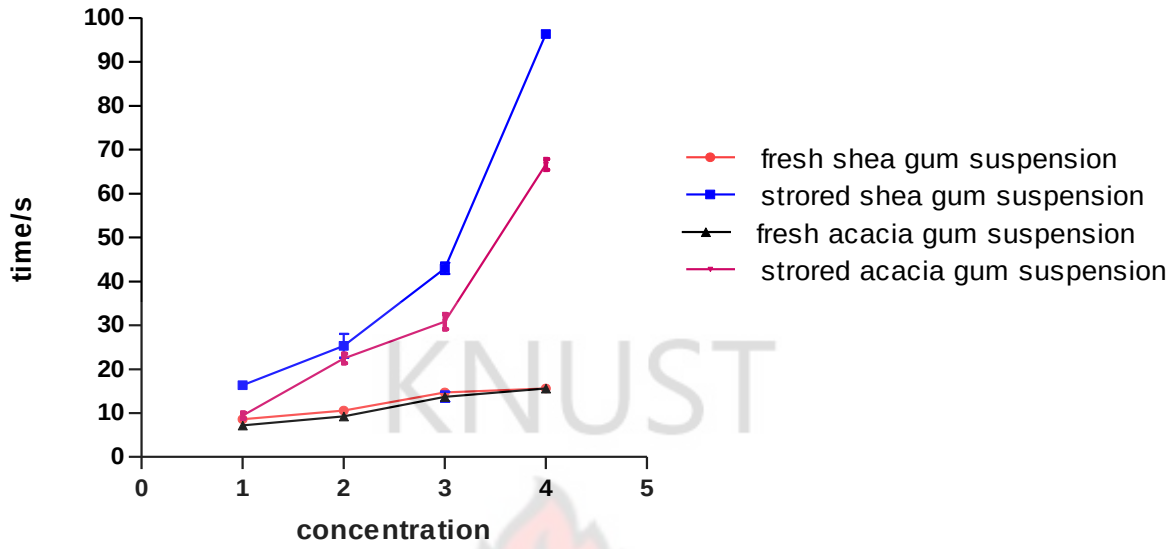

Figure 4-18 Flow time for freshly prepared and stored suspensions of acacia and shea gum

4.9.2 Sedimentation volume

4.9.2.1Relationship between sedimentation volume and concentration of gum used over a period of 6hours

ACACIA GUM SHEA GUM

Table 4-29 Sedimentation volume of suspension over a period of 6 hours

	Acacia gum				Shea gum			
Conc./%w/v of gum used	1.0	2.0	3.0	4.0	1.0	2.0	3.0	4.0
Time/ hours	Vol/%	Vol/%	Vol/%	Vol/%	Vol/%	Vol/%	Vol/%	Vol/%
0	50ml	50	50	50	50	50	50	50
1	33ml	48	45	56	27	31	40	47
2	30	42	40	54	25	28	33	43
3	24	35	33	47	20	23	31	41
4	20	35	32	45	16	18	27	41
5	20	25	32	43	16	15	23	38
6	20	35	32	42	13	15	21	37

Vol/% = Volume of sediment obtained after specified time in percentage

4.9.2.2Relationship between volume of sediments and concentration over a period of 42days

Table 4-30 Sedimentation volume of acacia gum suspension over 42 days

Conc./%w/v	1.0	2.0	3.0	4.0
Time/days	Vol/%	Vol/%	Vol/%	Vol/%
0	50.0	50.0	50.0	50.0
3	12.0	30.0	24.0	40.0
6	12.0	27.0	21.0	38.0
9	12.0	27.0	19.0	37.0
12	12.0	27.0	19.0	37.0
15	12.0	25.0	19.0	34.0
18	12.0	25.0	19.0	30.0
21	12.0	25.0	19.0	30.0
24	12.0	25.0	19.0	30.0
27	12.0	25.0	19.0	30.0
30	12.0	25.0	19.0	30.0
33	12.0	25.0	19.0	30.0
36	12.0	25.0	19.0	30.0
39	12.0	25.0	19.0	30.0
42	12.0	25.0	19.0	30.0

Table 4-31 Sedimentation volume of shea gum suspension over 42 days

Conc./%w/v	1.0	2.0	3.0	4.0
Time/days	Vol/%	Vol/%	Vol/%	Vol/%
0	50.0	50.0	50.0	50.0
3	11.0	13.0	20.0	34.0
6	10.0	12.0	18.0	30.0
9	10.0	10.0	17.0	28.0
12	10.0	10.0	17.0	28.0
15	10.0	10.0	17.0	28.0
18	10.0	10.0	17.0	28.0
21	10.0	10.0	17.0	28.0
24	10.0	10.0	17.0	28.0
27	10.0	10.0	17.0	28.0
30	10.0	10.0	17.0	27.0
33	10.0	10.0	17.0	27.0
36	10.0	10.0	17.0	27.0
39	10.0	10.0	17.0	27.0
42	10.0	10.0	17.0	27.0

4.9.3 Redispersibility of suspensions

Table 4-32 Summary of Redispersibility of acacia gum suspension after 42 days

Concentration (% w/v)	acacia gum suspension
1.0	Redisperses easily after shaking
2.0	Redisperses easily after shaking
3.0	Redisperse easily after shaking
4.0	Redisperses after vigorous shaking

Table 4-33 Summary of Redispersibility of shea gum suspension after 42 days

Concentration (% w/v)	shea gum suspension
1.0	Redisperses easily after shaking
2.0	Redisperses easily after shaking
3.0	Redisperses after vigorous shaking
4.0	Redisperses after vigorous shaking

Figure 4-19 Acacia suspension before redispersion

Figure 4-20 Acacia suspension after redispersion

Figure 4-21 Shea suspension before redispersion

Figure 4-22 Shea suspensions after redispersion

4.10 EMULSIFYING PROPERTIES OF SHEA GUM

4.10.1 Stability ratio of primary emulsion for fixed oil, volatile oil and mineral oil.

Table 4-34 Stability ratio of primary emulsion prepared with a Mineral oil

Oil	Water	Gum	Result
3	2	1	Cracked
3	1	1	Cracked
4	2	2	Cracked
4	3	2	Cracked
4	3	3	Cracked
5	3	2	Cracked
5	2	3	Formed and stable
5	1	3	Gum hardened out
5	2	2	Formed but less stable

Table 4-35 Stability ratio of primary emulsion prepared with a Fixed oil

Oil	Water	Gum	Result
4	2	1	Cracked
4	1	1	Cracked
3	2	1.5	Cracked
3	1	2	Cracked
3	2	1	Cracked
4	2	2	Formed and stable
4	1.5	2	Formed but less stable

Table 4-36 Stability ratio of primary emulsion prepared with a Volatile oil

Oil	Water	Gum	Result
2	2	1	Cracked
2	1	1	Cracked
3	1	2	Gum hardened out
3	1	3	Formed, less stable
3	1	4	Formed and stable

Figure 4-23 Stability ratios for primary emulsions prepared with volatile oil, fixed oil and mineral oil.

4.10.2 Stabilisation of emulsion

4.10.2.1 Stabilisation by homogenisation

The emulsions creamed after the 3rd day

4.10.2.2 Stabilisation with xanthan gum + homogenisation

Table 4-37 Stabilisation with xanthan gum + homogenisation

Concentration of xanthan gum (% w/v)	Results
0.01	Creaming
0.02	Creaming
0.04	Marked Creaming
0.08	Marked Creaming
0.10	Marked Creaming
0.20	Marked Creaming
0.40	Marked Creaming
0.80	Marked Creaming

4.10.2.3 Stabilisation by reducing interfacial tension with Tween 60

Table 4-38 Stabilisation by reducing interfacial tension with Tween 60

Concentration of Tween 60 (% w/v)	Results
0.001	Less creaming compared with others
0.002	Less creaming compared with others
0.004	Reduced creaming gum not thrown out
0.008	
0.010	Creaming was very visible with two layer
0.020	marked creaming, gum not thrown out onto the surface of emulsion
0.040	
0.080	
0.100	

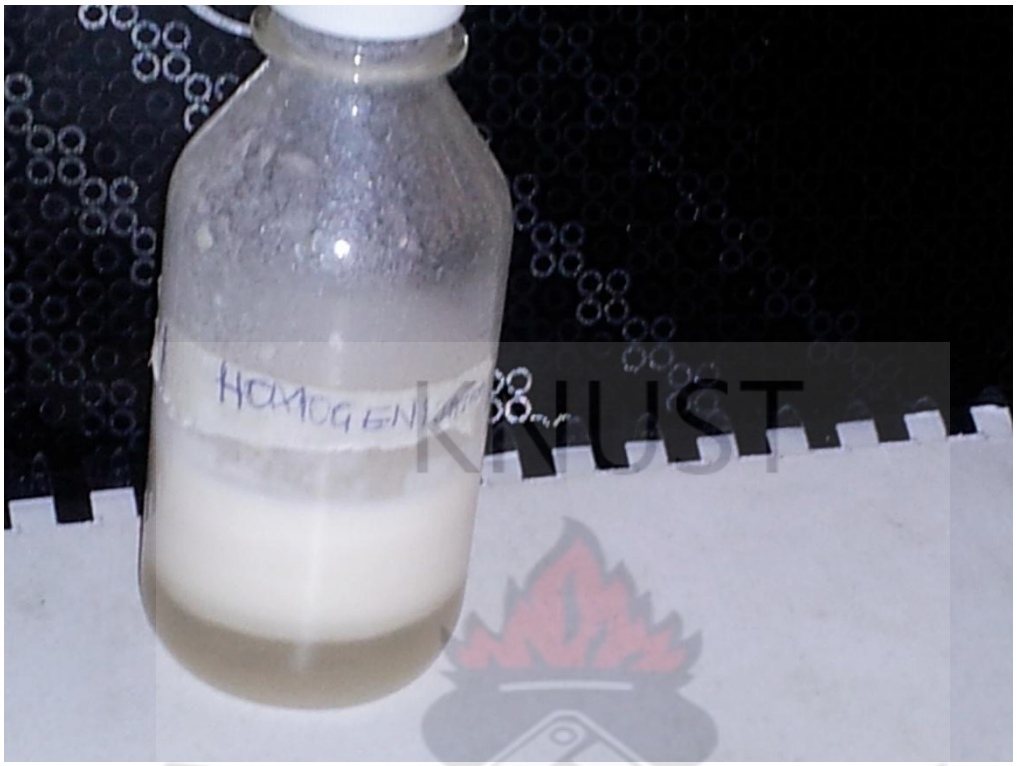

Figure 4-24 Stabilization by homogenization

Figure 4-25 Stabilization with xanthan gum

Figure 4-26 Stabilization with Tween 60

Chapter 5

DISCUSSION

5.1 PERCENTAGE YIELD OF GUM

After the purification process the percentage yield obtained was 63.26% which implies that the non gum constituents and contaminants constituted about 36.74%. The yield was good considering the fact that the crude gum was collected from dry bark of the Shea tree as scraps. Also the purification process can be said to have been successful. Crude gums are generally known to contain among other things chlorophyll or pigments, dirt, debris and scraps of bark. These constituents should be removed during purification before the gum can be used industrially.

5.2 PHYSICOCHEMICAL PROPERTIES OF SHEA GUM

5.2.1 Macroscopic properties of gum

Macroscopic properties such as colour odour, shape, taste and texture are perculiar to the type of gum and are often used to identify both the crude and purified gum. From Table 4-1 the crude gum was observed to be pale pink or off white in colour, irregular shaped tears and it did not fracture easily, only the very dry ones fractured easily. The colour of gum is dependent on how long it sticks to the tree after it has been exudated. If collected immediately the gum is usually lightly coloured but when allowed to remain stacked to the tree for some time tannins accumulate causing the colour to deepen. (Smith and Montgomery, 1959). The crude shea gum was observed to be very elastic and as such only very dry ones fractured with irregular tears. Both the crude and purified gum had a characteristic smell and a bland taste, the bland taste of the purified gum makes it a suitable candidate for the pharmaceutical industry since it will not affect the taste of the final product.

5.2.2 Moisture content of crude and purified gum

The moisture content of the crude and purified shea gum was found to be 16% and 9.80% respectively. According to the U.S.P (2002) and the B.P (2008), the moisture content should

not exceed 15%w/w. Hence the purified gum complies with this standard whiles the crude has a higher moisture content. The difference in the moisture content of crude and purified gum shows that the purification process was successful in reducing the amount of moisture in the crude gum which makes the purified gum more pharmaceutically acceptable and suitable for moisture sensitive drugs. Given suitable temperature, moisture will lead to activation of enzymes and the proliferation of microorganism, there by affecting its shelf life. It is important to investigate for the moisture content of a material because the economic value or importance of a material for the pharmaceutical industries lies not only on the cheap and readily availability of the excipient but the optimization of production processes such as drying packaging and storage.(Sonnergard ,1999).

5.2.3 Insoluble matter

The content of insoluble matter is a measure of the amount of contaminants or impurities such as sand, small particles of stones e.t.c present in the sample from collection or handling. According to the B.P and U.S.P the permissible limit is 0.5%w/w. From Table 4-2 the insoluble matter content of the crude gum was 0.240 and that of the purified gum was 0.165%. although both figures falls within the stated limits, it evident that the purification process helped to remove some impurities since the content of insoluble matter of the purified gum was less than that of the crude gum.

5.2.4 Swelling and hydration capacity

The purified shea gum had a swelling capacity of 1.15 (from Table 4-3) indicating it's hydrophilic nature and also its ability to swell into a gel and release the embedded drug. The swelling index gives an idea of the binding or disintegrating property of the gum. However the hydration capacity on the other hand suggests how the gum retains water or how rapid water penetrates the gum. The hydration capacity of the gum was obtained as 1.875 which means it retains about 87% of its weight of water in less than three hours hence water penetration is rapid meaning it can help potentiate the action of disintegrants in tablet (Oyi.et.al, 2010).

5.2.5 Flow properties of purified Shea gum.

To help assess the flow properties of the purified gum, the following parameters were investigated; bulk density, tapped density, Hausner's ratio, angle of repose and compressibility index. Bulk and tapped densities give an insight of the packaging and arrangement of the particles and the compaction profile of the gum powder.

The results of the bulk and tapped densities shown in Table 4-5 indicated that there was a reduction in volume due to packing under applied pressure from tapping. This could be attributed to the regular shape and smooth texture which promotes closer packing of particles.

The Hausner's ratio and Carr's index gives an idea of the densification that will occur during tabletting. As the values of these indices increase, the flow of powders decreases giving more likelihood for weight variation (Stanifforth, 1996).

From Table 4-5and 4-6 the Hausner's ratio, angle of repose and the Carr's index were found to be 1.204, 16.62^0 and 12.69 %, all these figures showed that the gum powder had a good flow or was free flowing meaning that the amount of glidant required to improve flow will be minimal. The results also suggest that granules prepared with shea gum will require minmium amount of glidant for free flow from the hopper during compression (Aulton, 1994).

5.2.6 Solubility of Shea gum

The crude shea gum was found to be insoluble in cold water, acetone and ethanol but it was soluble in chloroform and hydrochloric acid (concentrated). It was found to be sparingly soluble in hot water and chloroform water.

The purified gum was also found to be soluble in concentrated hydrochloric acid , but insoluble in ethanol and acetone. It was sparingly soluble in chloroform water, chloroform and in both cold and hot water. This suggests that the solubility of the purified gum in water both cold and hot was improved after purification. This could be as a result of the removal of certain ions such as calcium which when present in large amount causes aqueous insolubilities of gums.

5.2.7 Mineral ion content of shea gum.

Metallic ion content of the purified and crude Shea gum is shown on figure 4-3, it revealed that the purification process affected the ion content of the gum since the levels of all the

ions decreased after purification. Very high levels of certain metals such as copper (Cu^{2+}) when ingested can be poisonous. The levels of copper in both the crude and purified gum were found to be low and in fact the lowest of all the cations analysed, hence it is less likely to be poisonous when ingested since the according to the WHO guidline the acceptable limit for copper is 1.3mg/l. Determination of the metallic ion content of the gums is important because the levels of some metals such as calcium (Ca^{2+}) and magnesium (Mg^{2+}) affects physical properties such as aqueous solubility and viscosity of the gum revealed that, both the crude and the purified forms of the gum contained varying amounts of metallic ions. The dominant ion in both samples was Calcium, followed by Magnesium and then Iron. The levels of Sodium, Potassium, Zinc and copper were very low. The content of Ca^{2+} in the crude gum was markedly reduced from 692.31mg/kg in crude to 467.43mg/kg in purified gum. The reduction may account in the reduction of viscosity of the gum after purification. In addition, high levels of magnesium contribute to the aqueous solubility of gums, the levels of magnesium was also reduced from 75.32mg/kg to 40.43mg/kg. The reduction may also give a good explanation to the change in aqueous solubility of the gum after purification since the crude gum was insoluble in water but the purified gum was sparingly soluble.

5.2.8 Protein content of purified Shea gum;

Dickinson in 2003 indicated that the carbohydrate structure of hydrocolloid gums does not contain a significant proportion of hydrophobic groups, so the emulsifying capability of polysaccharides is most likely dependent on the surface active protein attached to it.

The protein content of the crude and purified gum was 8.30% and 4.23%. The content of protein was reduced to almost half of its original value after purification which could reduce the emulsifying ability of shea gum drastically. However, the amount remaining may still help in the gum's emulsifying ability. The protein content of polysaccharides plays an important role in its emulsion stabilizing function. The emulsion stabilizing capacity of most hydrocolloids decrease as it associated protein is removed (Dickinson 2003).

5.2.9 Phytochemical constituents of purified shea gum

Phytochemical test carried out shea gum confirmed the absence of alkaloid, tannins and saponins. A violet ring was formed at junction of two liquids on reaction with Molisch's reagent indicating the presence of carbohydrates. Gum could reduce Fehling's solution, so

the sugars present were reducing sugars. On treatment of the mucilage with ruthenium red it showed red colouration confirming the obtained product as a gum. The results of phytochemical screening of gum are summarized in Table 4-10.

5.2.10 Rheological behaviour of purified Shea gum

The viscosity of the purified Shea gum mucilage increased with an increase in concentration at the same shear rate. According to Figure 4-5, this increase was not linear.

When the shear rates were varied for the different concentrations, the viscosity of gum dispersion decreased with an increase in shear rate. At high shear rates the decrease in viscosity can be attributed to decreasing number of chain entanglement (Cui and Qi, 2005.)

The flow curves obtained in Figure 4-4 were that of a pseudoplastic flow. The gum mucilage can therefore be said to exhibit shear thinning behaviour. This property may aid its function as a suspending agent. However, at low concentrations (2 %w/vand 5 %w/v) however, the curve was almost linear meaning that the gum is less viscous at these concentrations. Hence, at low concentrations the shea gum may exhibit Newtonian flow.

Generally many gum mucilages are known to be non-Newtonian and exhibit pseudoplastic flow (Shama. et.al, 2007), but the variations in viscosity of different concentrations may be as a result in the differences in cohesiveness of the molecules with an increase in concentration. Usually, molecules in a fluid have different shapes and sizes. The force required to move these molecules in the fluid is determined by their type of bond, shape and size. The flow properties of concentrated mucilage with insufficient liquid to completely fill the voids between the particles results in a three phase mixture; solid, liquid and air. The presence of air makes the material compressible, and therefore the more the mucilage is compressed, the greater the viscosity (Brookfield Eng. Labs Inc.Lab. Manual, 2007). This probably explains why the Shea mucilage has a higher viscosity value which is more viscous at a concentration of 10 %w/v compared with 2 and 5 %w/v mucilage concentrations.

5.2.10.1 The effect of temperature and pH on the viscosity of purified Shea gum;

Most fluid viscosities decrease as temperature increases. The effect of temperature on the apparent viscocity of 20%w/v shea gum mucilage is shown in Figure 4-6.

At any given shear rate the viscosity of the gum decreased with an increase in temperarture and vice versa. At a given shear stress polymer chain entanglement or disentanglement determines flow rate. Temperature causes disentanglement which leads to a decrease in viscosity (Cui and Qi, 2005).

The effect of pH on viscosity of Shea gum is shown in Figure 4-7. From the fiqure the viscosity of the gum peaks at a pH of 7.55 but drops sharply below pH of 6 and above 7. The gum viscosity is therefore highest in pH of 7 to 7.55.

5.2.10.2 Effect of electrolyte on the viscosity of shea gum

The effect of electrolyte type on the viscosity of a 20%w/v is shown in Figure 4-8, the gradient of decrease of viscosities of the gum increased with increasing valency of the electrolyte. The decreased in viscosities were very sharp initially but later became gentle, which suggests that shea gum may be very sensititive to electrolyte change. Aluminuim chloride was more effective in decreasing the viscosity of the gum compared to calcium chloride which in turn was more effective than potassium chloride. The decrease in the viscosity of gums brought about by electrolytes is proportional to the concentration as well as the valence of the cation (Venor-Carter and Sherman, 1980).

5.2.11 Microbial quality of crude and purified gum

The microbial quality of the gum was assessed, because pharmaceutical excipients need to meet the requirement for microbial quality (B.P 2008). From the current work done it was realised that, purification had a significant effect on the microbial quality of the gum. From Table 4.11 it was observed that, the crude gum did not have *E.coli and Pseudomonas aeruginosa* present but was found to contain pathogenic Staphylococci, salmonella and fungi. But after purification the pathogenic staphylococci and salmonella were removed and were absent in the purified gum. Both gums had fungi present but fungal growth was scanty on the purified gum plate but profuse on the crude gum plate. This could be attributed to the purification process. Purification therefore is an important process in gum processing and the purified gum had high microbial quality than the crude Shea gum. The purified gum is therefore more likely to meet the criteria for microbial quality of pharmaceutical excipients than the crude gum. Crude and purified Shea tree gums at high

concentrations were tested for their antimicrobial activity against bacteria, and fungi. Shea gum presented no activity on the studied organisms.

5.3 FORMULATION PROPERTIES OF SHEA GUM

5.3.1 Tablet binding properties of shea gum

5.3.1.1 Flow properties of granules

As mentioned above the flow properties of a mass of granules is important to ensure uniform die filling during compression which will ultimately lead to uniform weight of the tablets compressed. Hausner's ratio and compressibility index are measures of the flow properties of granules. Hausner's ratio of 1.2 and below indicates low interparticle friction while ratio greater than 1.6 indicates high interparticulate fiction and less free flowing particles. On the other hand Carr's index of 5 to 15% indicates free flowing granules (Aulton, 1994). From Table 4-13 and 4-14, it was found that all the batches of granules were free flowing since they all had Hausner's ratio and Carr's indices lying within the above stated standards. This confirms the shea gum's good flowing properties which were impacted to the granules prepared. Hence, the granules when compressed will be less likely to have uniformity of weight problems due to the flow rate of granules or rate of die filling.

5.3.1.2 Quality assessment of Paracetamol tablets

The uniformity of weight test gives an indication of how the weights of the individual tablets are scattered about the average weight. By B.P (2008) standards, the permitted percentage deviation for tablets of weight greater than 250 mg is 5 % and not more than two of the individual tablets should deviate from the average weight by more than the permitted percentage deviation and none should deviate by twice the permitted deviation. From Tables 4-16 and 4-17, none of the tablets failed the uniformity of weight test. Although all batches passed, for the batches containing acacia, the standard deviation of 5% acacia from the mean weight was found to be 0.0015 which was the highest compared with the others, meaning that the tablets deviate more from the mean.the other batches have less significant deviations from the mean weight. This means that the batch containing 5% acacia is likely to have less uniform weight distribution.

For the tablets containing shea gum the batch with the highest deviation from the mean weight was 10% shea with a standard deviation of 0.0052 while the batch with the lowest deviation was 15% shea with a deviation of 0.0009, hence the 15% shea will be a preferable choice with respect to minimum weight variation. However unlike the bacthes containing acacia, the batches containg 5% and 20% the shea gum also had relatively high standard deviation. Meaning that all the batches containing the shea gum are more likely to have weight variations compared to the tablet containing same concentration of acacia gum.

The uniformity of weights observed in the batches containing different concentrationof Shea and Acacia gum as binders could be attributed to the good flow properties of the granules. Should weights differ there may be variations in disintegration, dissolution and possibly content of active ingredient.

The effect of binder concentration on tablet hardness and friability are shown in Tables 4-18 to 4-20. According to the BP 2008, The minimum force required to crush an uncoated tablet should be 4 kg whiles the maximum should be 15 kg, from the results all the batches passed hence the tablets are hard enough to withstand breakage and soft enough to release the embedded drug. Moreover, an increase in binder concentration increased the hardness of tablets, however, for the same concentration of Shea and acacia gum mucilage for example 5% w/v of acacia and Shea gum the tablets containing the Shea mucilage were found to be harder than that containing acacia mucilage. This trend runs through the other batches, but for all of them the differences were minimal and may not be significant.

An increase in binder concentration enhances the formation of stronger interparticulate bonds between the granules during compression in a tabletting machine. This implies that the tablets would offer greater resistance to shock and abrasion since there is a stronger adhesive bonding of the granules at high binder concentrations.

The maximum permitted loss in weight of a batch of tablets subjected to friability testing is 1 % (British Pharmacopoeia, 2009)

In general the tablet showed good friability profiles since all had friability values of less than one. The friability of tablet is dependent on the amount and nature of gum used as binder therefore as the concentration of gum increased the friability of the tablets decreased and vice versa. Considering the difference between tablets formulated with the same

concentration of the shea gum and the standard gum (acacia) will bring out the effect of the nature of the gum on the parameters assessed.

It was observed that at the same concentration the tablets containing the acacia were found to be less friable than that containing the shea gum.

Disintegration is a crucial step in drug release from immediate release tablets. The rate of disintegration is directly proportional to the rate of dissolution (Bi. et al. 1999). The rate of disintegration is influenced by the penetration of water into the tablets which is also dependent on the porosity of the tablets. When the porosity is high, disintegration is hardly influenced by tablet formulation but when porosity is low then disintegration will be affected by the excipients (Bi. et al., 1999).

From Tables 4-21 and 4-22 the tablets were observed to have an increasing disintegration time with an increase in concentration of gum. According to the B.P. uncoated tablets should dinintegrate within 15 mins. All the batches passed the test but there were difference in the disintegration times although batches of different types and concentrations contained the same quantity of the same disintegrant (starch). Generally the tablets containing shea gum disintegrated faster than that of acacia this may be due to their higher friability in comparison to the tablets containing acacia since the more friable tablets may be more porous. However, there various mechanism for the disintegration of tablets. The main mechanisms of disintegration proposed are swelling of disintegrant resulting in development of swelling force, capillary action and annihilation of intermolecular forces resulting in development of a repulsive force between particles. Some pharmaceutical excipients have inherent ability to disintegrate due to annihilation of bonds. (Ngwulala.et.al, 2010).The above mentioned mechanism may also explain the trend observed in the results.

5.3.1.3Dissolution profile of Paracetamol tablet

Dissolution is a very important step which determines the rate and extent of absorption and subsequent therapeutic outcome of a drug embedded in a tablet. The factors that affect dissolution include type and concentration of binder, hardness, surface area, distance of diffusion, solubility of the drug, manufacturing process (wet granulation, dry granulation or direct compression) and diluents (Jacob and Plein , 2006)

According to the USP (2008), 85 % of the contents of Parscetamol tablets should be released in a medium in 30 minutes. Since paracetamol is an analgesic and antipyretic agent, a fast release will be expected for effective reduction of raised temperature and pain. Dissolution studies can give an idea of the amount of drug available for absorption after oral administration. Drugs with poor dissolution profiles will not be easily available in the body system or target organ/tissues to elicit therapeutic effect.

The comparative *in vitro* dissolution profiles of the various batches of paracetamol tablets formulated with the shea and acacia gums are shown in Figures 4-16 and 4-17. The *in vitro* dissolution profiles were found to be varying for each batch, but within the prescribed limit. The dissolution at 15 minutes (t15 min, %) and 85 % of dissolution (D 85 %, min) were also determined (Table 4-26). For the dissolution at 15 minutes, it was observed that the values decreased with increasing concentration of both the shea and acacia gum. The batch containing 5% shea realeased the highest amount(92.87%) of the active ingredient within 15 minutes making most effective within the stipulated 15 minutes while the batch containing 20% shea released the least amount (80.12%) of the active ingredient making it the least effective within 15 minutes.

For the time for 85% release the vice versa was observed, as the concentration of gum increased the time for 85% release increased with the batch containing 5% shea being the fastest with D 85%min of 9.63 minutes while the batch with 20% shea was the slowest with a D 85 % min of 20.31minutes.

The dissolution efficiency proposed by Anderson et al, 1998 was also determined for the batches to ascertain which batch will be effective in releasing the drug for its therapeutic effect. According to Anderson the higher the dissolution efficiency, the more efficient the tablet is at releasing it's embedded drug.It was observed that the batch containing the 5% shea had the highest dissolution efficiency compared to the other batches but in general the efficiency decreased with increasing concentration of the shea gum. From the above analysis all other parameters being constant it can be said that for effective release of the drug from the tablet the 5% shea gum mucilage will be preffered as a binder.

In addition, the dissolution of the tablets containing the shea gum was compared with that containing acacia using the similarity factors. Similarity factors of between 50 and 100 ensure sameness while similarity factors outside of this range means the batches are

significantly different. From Table 4-25, 5% shea was compared with 5% acacia and the similarity factor was 51.4939 meaning that they can be said to be similar and are likely to possess similar dissolution characteristics. Hence the 5% shea could be substituted for the 5% acacia as a binder in the formulation of the tablets. The other batches were also found to have similarity factors within the stated range and can also be said to be similar to the same concentration of the standard acacia. The 'P' values were also found which proved that the dissolution profile of the same concentrations of shea and acacia were not significantly different since all the 'P' values obtained were found to be greater than 0.05.

5.3.1.4 Content of active ingredient

The results for the content of active ingredients is shown in Table 4-27 according to the B.P. 2008, the content of paracetamol tablet should be 95% to 105% of the stated amount.
All the batches of tablets analyzed passed the test. Therefore, the assay results ascertain the presence and compendial quality of paracetamol in all these products .But, the paracetamol content in the batches of paracetamol tablets, formulated with 5% acacia is significantly less compared with all the batches of paracetamol tablets.

5.3.2 Shea gum as suspending agent

Shea gum was also investigated as a suspending agent. The suspending ability of shea gum was assessed in comparison to that of acacia gum at the same concentration. Acacia gum was found to be a better suspending agent than that of shea gum. The parameters that were assessed were flow time, apparent viscosity of fresh and stored suspensions, and the rate of sedimentation over time and ease of redispersibility.

5.3.2.1 Rheology

Different concentrations of acacia gum suspensions and shea gum were prepared and their flow times and apparent viscosities were determined as a function of their viscosity. From Table 4-28 it was observed that, the flow time of the freshly prepared acacia gum suspension increased gradually with increasing concentration of gum. The time frame was between 7.76 seconds to 16.230 seconds for 1% gum concentration to 4% gum concentration. For shea gum, the time frame was 9.3 seconds to 16.23 seconds representing a similar trend to that of acacia .For the apparent viscosity, the trend did not

differ much for the two types of gum but for both types the apparent viscosities increased with an increase in gum concentration. The apparent viscosity of the freshly prepared suspensions were found to be higher than the stored suspensions meaning that actual viscosity of the stored gum mucilage is higher than that of the freshly prepared . Generally natural polysaccharides may show a reduction in viscosity of their dispersions or solutions with age due bacteria or mould growth, however some gum needs a long time to hydrate and for such gums the actual viscosities increase on storage (Conway 2010). From the results it can be said that Shea and acacia gum belongs to the later group of gum since its actual viscosity increase upon storage.

Looking at Table 4-28, there was increase in the flow time of acacia gum suspensions as the storage time increased. For example, for 1% acacia suspension that is freshly prepared the flow time was 7.63 seconds but after storage had a flow time of 10.53 seconds and that of shea gum at the same concentration was 9.3 seconds before storage and 17.53 seconds after storage. That shows an increase in viscosity of the suspension. Some gums are well hydrated with time and their suspending ability increased with time.

For the same concentration of the both shea and acacia, the shea suspension was observed to have a lower apparent viscosity compared with the acacia gum. Therefore, from the above discussion, the suspendability of the shea gum is likely to be better than that of the acacia gum since the former will have a higher actual viscosity and will be able to keep the suspended particles longer in suspension for a dose to be poured compared with the later.

From Tables 4-29 and 4-31 it can also be observed that the sedimentation volume measured over six hours decreased with time. Sedimentation in the shea gum suspensions were lower than that of acacia gum suspensions.

On storage for 42 days and redispersed, the ease of redispersibilty was observed to decrease with an increase in gum concentration for both shea and acacia gum. Hence as the concentration of gum increased the possibility of caking of suspended particles increased making redispersibility difficult. However, at the same concentration of both gums for example at 1% w/v of both acacia and shea gum, it was observed that the shea gum suspension was easier to disperse than the acacia gum suspension.

5.3.2.2 Volume of sediment

The volume of sediment was recorded for the first 6 hours and in every three days. For 1 %w/v shea gum suspensions, the final volume of sediment was reached by the 6th day, 2 %w/v shea gum was reached on the ninth day, 3 %w/v shea gum was reached on the 9th day and 4 %w/v was reached on the 30th day. Hence the 4 % shea suspension suspended the particles in suspensions for longer time compared to the other concentrations. There was no practical change in the volume of sediment until the 42nd day. The volume of sediment for acacia gum suspension was always lower than that of shea gum suspension.

Before redispersion, the supernatant was clear as seen in Figure 4-21, for shea gum suspension, but that of acacia was cloudier as seen in Figure 4-19. After storage and redispersion of acacia gum suspensions, the rate of sedimentation decreased drastically as compared to that of the freshly prepared suspension. This goes to show that the suspending ability of acacia gum increases with time. With the redispersion of shea gum suspension, there was not much change in the rate of sedimentation, but the marked observation was that, some particles were still suspended but was still not comparable to acacia gum.

5.3.2.3 Ease of Redispersion

Concentration of shea gum suspension between 1% w/v and 2% w/v were easily redispersed, but the higher concentration, that is those above 2 %w/v were done with much difficulty. This can be attributed to tighter packing of the particles. With acacia gum only the 4 % concentration dispersed with much difficulty, the rest were easily dispersed .The addition of deflocculating agent may reduce the tight packing nature of the shea gum. In all the acacia gum was a better suspending agent than the shea gum.

5.3.3 Shea gum as a emulsifying agent

Gums are normally used as emulsifying agents. Shea gum was investigated for its emulsifying property. Different ratios of oil, water and gum were used for the preparation of primary emulsions out of fixed oil, mineral oil and volatile oil. The mineral oil used was paraffin oil, the fixed oil was arachis oil and the volatile oil used was peppermint oil. From Tables 4-34 – 4-36, the ratio of oil to water to gum for the preparation of primary emulsions, determined for fixed oil was 4:2:2 , for mineral oil was 5:2:3 and that of volatile

oil was 3:1:4. Different ratios were studied and the above recorded values were the ratios that gave stable primary emulsions. The ratios determined broke down on standing for a short time. After the primary emulsions were prepared and made up to volume, the major observation made was that, all the emulsions were creaming (two distinct layers were seen – a clear liquid at the bottom and a milky layer at the top).

A lot of approaches are adopted in the reduction of the rate of creaming in emulsions. Creaming is not as bad as cracking (where the oil separates from water). Creaming is a reversible process unlike cracking and emulsion is reformed on shaking the bottle.

Homogenisation, addition of a thickening agent or reduction of the interfacial tension with a surfactant are methods used to reduce creaming in emulsions. All the emulsions prepared were homogenised, but creaming was still observed after the third day.

When a thicking agent (xanthan gum) was added in various concentrations between 0.1 and 0.8%w/v it was observed that all the emulsions exhibited marked creaming with the exception of those containing 0.1% and 0.2%w/v xanthan gum. This may implies that from concentrations of 0.3 upwards the xanthan gum displaced the shea gum as an emulsifying agent leading to the marked creaming observed. Hence xanthan gum may be used to stabilize the emulsions but only small concentration of between 0.1% and 0.2% should be used. The stabilization was also done using Tween 60 to reduce the interfacial tension. A similar trend to that observed for the xanthan gum was observed. The tween was more effective at stabilizing the emulsions at lower concentrations than at higher concentration.

The shea gum can therefore act as an emulsifying agent and the creaming can be reduced by the addition of a low concentrations (0.1-0.2%w/v) of a thickening agent (xanthan gum) or a surface active agent(Tween 60 at concentrations between 0.001-0.004%v/v).

Chapter 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

- Crude shea gum was successfully purified with a percentage yield of 63.26 %
- The physicochemical and formulation properties of the purified shea gum were assessed and the results proved that the gum could be of use in pharmaceutical dosage forms such as tablets, suspensions and emulsions.
- The purified shea gum can be used as an effective binding agent at concentrations of 5 %w/v to 20 %w/v. The binding effect of the gum is comparable or similar to acacia at the same concentrations.
- The shea gum was found to have suspending abilities but these suspending abilities were better compared to the same concentration of acacia with respect to the parameters measured.
- The purified shea gum had emulsifying abilities, producing primary emulsion of mineral, volatile and fixed oil with ratio of oil, water and gum obtained as 5:2:3, 3:1:4 and 4:2:2 respectively for the various types of oils. Creaming can be reduced in the emulsions by addition of low concentrations of xanthan gum (0.1 % to 0.2 %) and tween 60 (0.001 - 0.004 %w/v)

6.2 RECOMMENDATIONS

- Further work on the gum should explore other methods of purification which will improve upon physicochemical properties such as the viscosity and protein content in order to improve it suspending and emulsifying abilities.
- Further work on the purified gum in combination with other gums may also uncover improved suspending, emulsifying and binding abilities
- The use of the crude gum as a coating agent should also be looked at.

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APPENDIX

1. . 0.1M HCl solution - 0.84ml of Conc. HCl was measured into a 100ml volumetric already containing some amount of distilled water, the measuring cylinder was rinsed qualitatively and quantitatively into the volumetric flask. The solution was made up to volume to produce 100ml.

   NB: Higher volumes were prepared in the dissolution test, i.e. 5000ml of 0.1M HCl
2. Preparation of 2% gum mucilage: 2g of gum was weighed into a conical flask. Sufficient water was added to produce 100ml of mucilage amidst shaking.
3. Preparation of Acacia 10 %w/v mucilage – 10 g of acacia gum was weighed into a clean mortar. 100ml of distilled water was measured and added to the gum gradually, whilst triturating, until the whole quantity of water was added and uniform mucilage was formed.

   This method was used in the preparation of the Shea gum mucilages for the rheological assessment and the preparation of the paracetamol tablets.

Table 6-1 Insoluble matter and moisture content of purified and crud shea gum

Gum	Insoluble matter (%)	Moisture content (%)
Purified gum	0.165 ± 0.020	10.00 ± 0.26
Crude gum	0.240 ± 0.205	16.01 ± 0.61

Table 6-2 Metallic Ion Content of shea gum

Mineral/mg/kg	**Crude gum**	**Purified gum**
Iron	12.51	5 .000
Calcium	692.31	467.4
Sodium	4.21	3. 32
Potassium	6.28	5.21
Zinc	2.012	0. 510
Magnesium	75.32	40.43
Copper	1.84	0. 65

Table 6-3 Effect of pH change on viscosity of shea gum mucilage

pH	*Viscosity/ cp*			
	First	*second*	*third*	*average/ cp*
3.12	53.4	52.6	53.6	53.2
5.35	61	67	61	63
7.55	112	112	112	112
9.18	75	70	77	74
11.09	90	90	91	90.3

Table 6-4 Effect of change of rate of shear on viscosity of shea gum

Shear rate/rpm	*Viscosity of 2%w/v/cp*	*Viscosity of 5%w/v/cp*	*Viscosity of 10%w/v/cp*	*Viscosity of 15%w/v/cp*	*Viscosity of 20%w/v/cp*
0.5	3.0	10.50	37.10	68.70	120.90
1.0	2.77	10.10	37.10	63.50	109.91
1.5	2.36	9.48	31.20	60.01	101.29
2.0	2.21	9.19	30.82	53.71	100.29
2.5	2.20	8.79	30.17	50.96	97.40
3.0	1.81	7.09	29.06	50.36	91.02

Table 6-5 Effect of temperature on shea gum mucilage

Temperature/^{o}C	Viscosity/cp
25	121.01
30	118.00
35	104.56
45	89.01
50	71.04
60	67.98

Table 6-6 The effect of concentration on the viscosity of shea and acacia gum mucilage

Concentration of gum %w/v	Viscosity of shea gum/ cp	Viscosity of Acacia gum/cp
5	10.00	47.21
10	35.16	127.89
15	64.06	154.76
20	119.00	201.1
30	243.01	265.90
40	300.05	579.03

Table 6-7 Uniformity of weight of paracetamol tablets formulated with 5% shea gum mucilage

Tablet no.	Tablet weight(Ag)	(A-B)g	(A-B)g/B)	Percentage deviation
1	0.5615	0.001	0.0017	0.178
2	0.5605	0.000	0.000	0.000
3	0.5607	0.0020	0.0036	0.357
4	0.5600	-0.0005	-0.0009	-0.090
5	0.5603	-0.0002	0.0004	0.036
6	0.5609	0.0004	0.0071	0.071
7	0.5605	0.0000	0.0000	0.000
8	0.5608	0.0003	0.0053	0.054
9	0.5601	-0.0004	-0.0071	-1.071
10	0.5620	0.0150	0.0268	0.268
11	0.5600	-0.0005	-0.0089	-0.089
12	0.5610	0.0005	0.0089	0.089
13	0.5610	0.0005	0.0089	0.089
14	0.5600	-0.0005	-0.0089	-0.089
15	0.5602	-0.0003	-0.0054	-0.054
16	0.5637	0.032	0.057	0.571
17	0.5607	0.0002	0.0035	0.036
18	0.5619	0.0140	0.0249	0.249
19	0.5600	-0.0005	-0.0089	-0.089
20	0.5612	0.0007	0.0012	0.012
Total	11.210g			
Average	0.5605g			
Stdev	0.0012			

Table 6-8 Uniformity of weight of paracetamol tablet formulated with 10% shea gum mucilage

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5608	-0.0007	-0.0012	-0.125
2	0.5610	-0.0005	-0.0089	-0.089
3	0.5607	-0.0008	-0.0142	-0.142
4	0.5612	-0.0003	-0.0053	-0.053
5	0.5607	-0.0008	-0.0142	-0.142
6	0.5619	0.0004	0.0071	0.071
7	0.5611	-0.0004	-0.0071	-0.071
8	0.5621	0.0006	0.0010	0.107
9	0.5620	0.0005	0.0089	0.089
10	0.5612	-0.0003	-0.0053	-0.053
11	0.5609	-0.0006	-0.0010	-0.106
12	0.5604	-0.0011	-0.0019	-0.196
13	0.5604	-0.0011	-0.0019	-0.196
14	0.5603	-0.0012	-0.0021	-0.214
15	0.5607	-0.0008	-0.0142	-0.142
16	0.5612	-0.0003	-0.0053	-0.053
17	0.5616	0.0001	0.0001	0.017
18	0.5615	0.0000	0.0000	0.000
19	0.5619	0.0004	0.0071	0.071
20	0.5622	0.0007	0.012	0.125
Total		11.230g		
Average		0.5615g		
Stdev		0.0052		

Table 6-9 Uniformity of weight of paracetamol tablets formulated with 15% shea gum mucilage

Tablet no.	Tablet weight(A)g	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5625	-0.0015	-0.0026	-0.266
2	0.5643	0.003	0.0053	0.053
3	0.5640	0.0000	0.0000	0.000
4	0.5629	-0.0011	-0.0195	-0.195
5	0.5641	0.0001	0.0017	0.017
6	0.5635	-0.0005	-0.0088	-0.088
7	0.5641	0.0001	0.0017	0.017
8	0.5636	-0.0004	-0.0071	-0.071
9	0.5645	0.0005	0.0088	0.088
10	0.5642	0.0002	0.0035	0.035
11	0.5640	0.0000	0.0000	0.000
12	0.5639	-0.0001	-0.0017	0.017
13	0.5647	0.0007	0.0012	0.124
14	0.5637	-0.0003	-0.0053	-0.053
15	0.5644	0.0004	0.0007	0.071
16	0.5649	0.0009	0.0159	0.159
17	0.5637	-0.0003	-0.0053	-0.053
18	0.5645	0.0005	0.0088	0.088
19	0.5642	0.0002	0.0035	0.035
20	0.5627	-0.0013	-0.0230	-0.230
Total	11.2806g			
Average	0.5640g			
Stdev	0.0009			

Table 6-10 Uniformity of weight of paracetamol tablets formulated with 20% shea gum mucilage

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5637	-0.0008	-0.0014	-0.14
2	0.5643	-0.0002	-0.0003	-0.035
3	0.5640	-0.0005	-0.0008	-0.089
4	0.5645	0.0000	0.0000	0.000
5	0.5613	-0.0032	-0.0057	-0.57
6	0.5650	0.0005	0.0008	0.089
7	0.5645	0.000	0.000	0.000
8	0.5642	-0.0003	-0.0005	-0.053
9	0.5640	-0.0005	-0.0008	-0.089
10	0.5643	-0.0002	-0.0003	-0.035
11	0.5646	0.0001	0.0001	0.018
12	0.5660	0.0015	0.0027	0.266
13	0.5643	-0.0002	-0.0003	-0.035
14	0.5645	0.000	0.000	0.000
15	0.5651	0.0006	0.0010	0.106
16	0.5654	0.0009	0.0015	0.159
17	0.5647	0.0002	0.0003	0.035
18	0.5660	0.0015	0.0026	0.266
19	0.5646	0.0001	0.0001	0.018
20	0.5650	0.0004	0.0008	0.089
Total	11.290g			
Average	0.5645			
Stdev	0.0017			

Table 6-11 Uniformity of weight of paracetamol tablets formulated with 5% acacia gum mucilage

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5620	-0.0009	-0.0015	-0.159
2	0.5600	-0.0029	-0.0051	-0.515
3	0.5609	0.0020	0.0035	-0.3550
4	0.5645	0.0016	0.0028	0.284
5	0.5630	0.0001	0.0001	0.017
6	0.5625	-0.0004	-0.0007	0.071
7	0.5615	-0.0014	-0.0024	-0.248
8	0.5621	-0.0008	-0.0014	-0.142
9	0.5629	0.0000	0.0000	0.000
10	0.5616	-0.0013	-0.0023	-0.231
11	0.5647	0.0018	0.0032	0.319
12	0.5627	-0.0002	-0.0003	-0.0353
13	0.5629	0.0000	0.0000	0.000
14	0.5618	-0.0011	-0.0019	-0.195
15	0.5629	0.0000	0.0000	0.000
16	0.5624	-0.0005	-0.0008	-0.089
17	0.5621	-0.0008	-0.0014	-0.142
18	0.5620	-0.0009	-0.0015	-0.159
19	0.5619	-0.001	-0.0017	0.177
20	0.5620	-0.0009	-0.0015	-0.159
Total			11.258	
Average			0.5629g	
Stdev			0.0015	

Table 6-12 Uniformity of weight of paracetamol tablets formulated with 10% acacia gum mucilage

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5620	0.0004	0.0001	0.018
2	0.5600	-0.0019	-0.0034	-0.338
3	0.5604	-0.0015	-0.0026	-0.267
4	0.5618	-0.0001	-0.0017	-0.018
5	0.5608	-0.0011	-0.0019	-0.196
6	0.5600	-0.0019	-0.0034	-0.338
7	0.5614	-0.0005	-0.0088	-0.089
8	0.5612	-0.0007	-0.0012	-0.125
9	0.5651	0.0032	0.0056	0.569
10	0.5619	0.0000	0.0000	0.000
11	0.5607	-0.0012	-0.0021	-0.214
12	0.5619	-0.010	-0.024	-2.398
13	0.5602	-0.0017	-0.0030	-0.302
14	0.5620	0.0001	0.0001	0.017
15	0.5660	-0.002	-0.005	-0.480
16	0.5601	-0.003	-0.007	-0.719
17	0.5671	0.0053	0.0092	0.925
18	0.5634	0.0015	0.0026	0.267
19	0.5630	0.0011	0.0019	0.195
20	0.5602	-0.0017	-0.0030	0.303
Total	11.2392g			
Average	0.5619g			
Stdev	0.0005			

Table 6-13 Uniformity of weight of paracetamol tablets formulated with 15% acacia gum mucilage.

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5670	0.0051	0.0090	0.908
2	0.5530	-0.0089	-0.0158	-1.584
3	0.5678	0.0059	0.0105	1.050
4	0.5607	-0.0012	-0.0021	-0.213
5	0.5590	-0.0029	-0.0052	-0.516
6	0.5598	-0.0021	-0.0037	-0.374
7	0.5609	-0.001	-0.0017	-0.178
8	0.5612	-0.0004	-0.0021	-0.125
9	0.5675	0.0056	0.0099	0.996
10	0.5680	0.0061	0.0108	1.085
11	0.5601	-0.0018	-0.0032	-0.320
12	0.5670	-0.0051	-0.0091	-0.907
13	0.5632	-0.0013	-0.0023	-0.231
14	0.5600	-0.0019	-0.0034	-0.338
15	0.5615	-0.0004	-0.0007	-0.071
16	0.5627	-0.0008	-0.0014	-0.142
17	0.5617	-0.0002	-0.0003	-0.036
18	0.5628	0.0009	0.0016	0.160
19	0.5621	0.0002	0.0003	0.036
20	0.5632	0.0013	0.0023	0.231
Total	11.2392g			
Average	0.5619g			
Stdev	0.0005			

Table 6-14 Uniformity of weight of paracetamol tablets formulated with 20% acacia gum mucilage

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.5610	-0.0013	-0.0023	-0.231
2	0.5614	-0.0009	-0.0016	-0.160
3	0.5621	-0.0059	-0.0105	-1.050
4	0.5632	0.0009	0.0016	0.160
5	0.5607	-0.0016	-0.0028	-0.285
6	0.5616	-0.0007	-0.0012	-0.124
7	0.5631	-0.0008	-0.0014	-0.142
8	0.5609	-0.0014	-0.0025	-0.249
9	0.5615	-0.0008	-0.0014	-0.142
10	0.5606	-0.0017	-0.0030	-0.302
11	0.5602	-0.0021	-0.0037	-0.373
12	0.5637	-0.0014	-0.0025	-0.249
13	0.5635	-0.0012	-0.0021	-0.213
14	0.5652	0.0029	0.0051	0.516
15	0.5645	0.0022	0.0039	0.391
16	0.5657	0.0034	0.0060	0.605
17	0.5617	-0.0006	-0.0011	-0.107
18	0.5628	0.0005	0.0008	0.089
19	0.5612	-0.0011	-0.0019	-0.195
20	0.5624	0.0001	0.0001	0.018
Total	11.247g			
Average	0.5623g			
Stdev	0.0007			

Table 6-15 Friability of tablet containing acacia gum

Gum Conc/ %w/v	Initial weight/g	Final weight/g	Loss/G	intial Weight/g	%Loss	Ave.%Loss
5% acacia	6.3302	6.3009	0.0293	0.0046	0.4629	
	6.3000	6.2504	0.0496	0.0079	0.7873	0.6251
10% acacia	6.0700	6.010	0.0600	0.0098	0.9885	
	6.1705	6.1597	0.0108	0.0017	0.1750	0.5818
15%acacia	7.1700	7.1600	0.0100	0.0013	0.1300	
	7.0670	7.0489	0.0181	0.0026	0.2610	0.1955
20% acacia	7.1212	7.1102	0.0110	0.0015	0.1545	
	7.1093	7.0891	0.0202	0.0028	0.2800	0.2172