

**KWAME NKRUMAH UNIVERSITY OF SCIENCE AND
TECHNOLOGY**

KNUST

FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

DEPARTMENT OF PHARMACEUTICS

**EVALUATION OF ANACARDIUM OCCIDENTALE (CASHEW) GUM AS
A PHARMACEUTICAL EXCIPIENT**

**A THESIS SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES IN
PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE MASTER OF
PHILOSOPHY (MPHIL) PHARMACEUTICS DEGREE**

BY

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DECLARATION

This experimental work outlined in this thesis was carried out in the Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, KNUST. This work has not been submitted for any other degree

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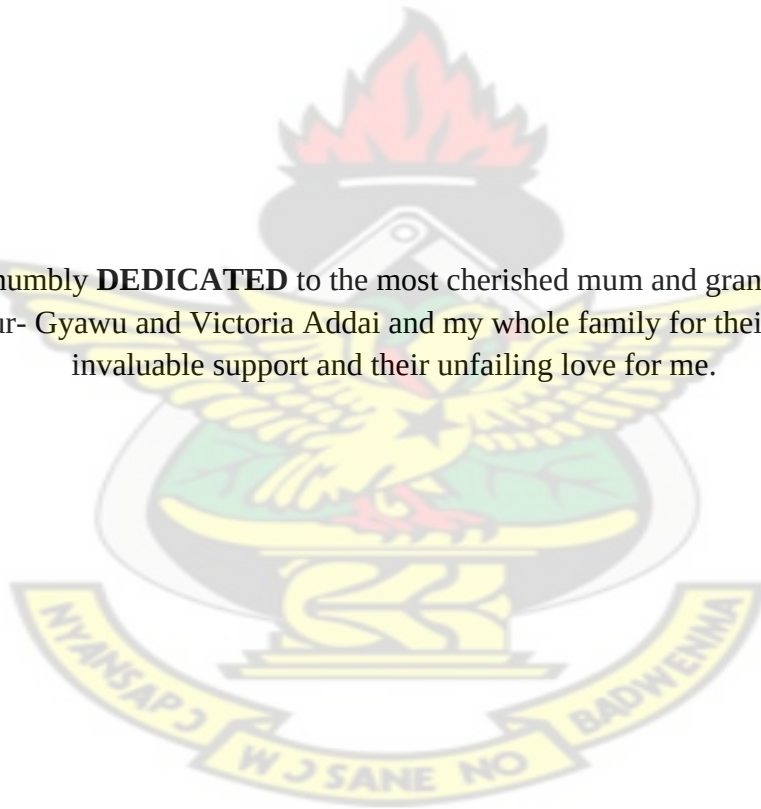
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DEDICATION

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This thesis is humbly **DEDICATED** to the most cherished mum and grand mum on earth, Georgina Baffour- Gyawu and Victoria Addai and my whole family for their constant prayers, invaluable support and their unfailing love for me.



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ABSTRACT

The current work deals with the study and development of *Anacardium occidentale* (Cashew) gum as a pharmaceutical excipient, namely: as a binding agent in tablet formulations, emulsifying agent in emulsions and as a suspending agent in suspensions. Crude and purified cashew gums were evaluated for their physicochemical properties and were found to be acidic in nature with satisfactory moisture content and insoluble matter. Atomic absorption spectrophotometric analysis of the gums showed that the crude gum had higher metallic ion content than the purified gum. This may be attributed to the purification process. The gums had relatively high levels of calcium, followed by magnesium, iron and zinc. Potassium and sodium were in trace amounts. Purified cashew gum was investigated as an emulsifying, suspending and binding agent. The emulsifying property of the gum was 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 stable 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 stable emulsions could be prepared with the mineral oil and fixed oil with ease but not with the volatile oil. All the emulsions prepared creamed readily, but creaming was reduced by homogenization and the addition of very low concentrations of Tween 80. The addition of a thickening agent worsened the creaming of the emulsions. The suspending property of the gum was investigated by assessing parameters such as rate of sedimentation, apparent viscosity and ease of redispersibility of zinc oxide suspensions prepared with different concentrations of cashew gum, compared to those prepared with xanthan gum. Suspensions were successfully prepared using the gum, but the sediment showed a tighter packing as the concentration of the gum used was increased. Xanthan gum which was used as the standard for comparison showed a better suspending action than cashew gum. Investigation of the gum as a binding agent in metronidazole tablets included the formulation of tablets with different concentrations of cashew gum using the wet granulation technique. The binding property of cashew 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 and dissolution rate determined. The granules had good flow properties as evidenced by their Hausner ratio and

Carr's index values. The gum was successfully employed as a binding agent in metronidazole tablet formulations with tablets of desired physical and release properties produced with different concentrations of cashew gum. Tablets produced from 30 % w/v cashew gum had similar characteristics to that produced from 20 % w/v acacia mucilage. The study shows that cashew gum can be successfully employed as a binder, emulsifying agent and a suspending agent in pharmaceutical formulations.

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ification of work, Scope of research

LITERATURE REVIEW

formation and classification of gums
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INTRODUCTION

The search for alternative products obtained from renewable sources has increased markedly in recent years and products that can be tapped over a long period of time will be preferred. If a nation could have a way of producing some of the basic ingredients that supports its local industries than importing, then it will be a better option.

Gums are natural exudates from the bark of trees and they have been of important pharmaceutical uses. Due to the limited supply and consequent sharply increased cost of traditional hydrocolloids, a search for other cheaper, naturally occurring gum with desired pharmaceutical properties is essential and timely.

Gum Arabic is the oldest and best known of all tree gum exudates from certain species of acacia, family Leguminosae. Gum Arabic in aqueous systems is used as an emulsifier, stabiliser, thickener etc. Other hydrocolloids are also used for this purpose, but gum Arabic is popular because of its ease of solution and performance, but its high cost has led to the assessment of other tree gums such as cashew gum for pharmaceutical uses.

Cashew gum has similar physicochemical and rheological properties like gum Arabic (Gyedu-Akoto et. al., 2008) and can therefore be used as a substitute for gum Arabic. Cashew gum is similar to gum Arabic in rheological properties and can be used in the pharmaceutical and cosmetic industries as agglutinant for capsules and pills.

There are a lot of cashew plantations in Ghana and the cashew plant produces a lot of gum. The cashew plant is mainly known for its nuts, which are used as food ingredients, but the fruit can also be utilised in the making of cashew wine. Cashew gum extraction represents one more source of revenue for the producer, in addition to the cashew nut and the peduncle, as well as an alternative for the utilisation of the non productive cashew trees in the face of decline or senescence.

JUSTIFICATION OF WORK

Gums and mucilages have a very wide application particularly in the pharmaceutical industry where they are used in emulsions, suspensions, lotions, creams, ointments, jellies, tablets, capsules, pills, suspensions and paste. Though studies have been made into the possible uses of gums in the pharmaceutical industry different materials such as polyvinyl pyrrolidone (PVP) are used as tablet binders. As a result of this, some drugs though locally produced are more expensive than imported drugs. Patients are therefore not able to afford these quality products and therefore resort to buying cheap medicines they find on the market regardless of their quality. The need therefore for other sources of cheaper pharmaceutical excipients can not be overemphasised. Gums are natural exudates from the bark of trees and they have been of important pharmaceutical uses. Due to the limited supply and consequent sharply increased cost of traditional hydrocolloids, a search for other cheaper, naturally occurring gum with desired pharmaceutical properties is essential and timely.

The evaluation of cashew gum as possible raw material to be used as an emulsifying, suspending and binding agent will add to the studies on this gum and encourage cultivation and use of this gum in the pharmaceutical industry.

SCOPE OF RESEARCH

The work would essentially consist of:

- Physicochemical characterisation of cashew gum
- Investigation of the emulsifying property of the gum
- Formulation and stabilization of emulsions prepared with cashew gum
- Investigation of the suspending properties of the gum
- Formulation of metronidazole tablets with different concentrations of cashew gum mucilage as binder as compared to Acacia gum mucilage.
- Evaluation of the physicochemical properties of the tablets

CHAPTER ONE

LITERATURE REVIEW

1.1.0 THE ORIGIN, FORMATION AND CLASSIFICATION OF GUMS

Gums and mucilages are polysaccharide complexes formed from sugar and uronic units. They are insoluble in alcohol but dissolve or swell in water (Irvin 1961). The polysaccharide may be produced naturally from plants or produced synthetically. Natural gums are obtained as exudates or extractives from various plants and plant parts (Trease and Evans, 1983). The gum exudates are obtained mainly from the bark of stems, branches and roots of plants. Examples of gum include khaya, albizia, guar, acacia, tragacanth and xanthan, among others. They are products of normal plant metabolism and may serve as food reserves or act as agents of holding water. Various sea weeds also produce gums such as agar and carrageenan which are obtained by extraction.

The basis and reason for gum formation and exudation of gums are still not fully understood and many theories have been formulated to explain the phenomenon. One theory suggests that the gum formation is a protective mechanism resulting from a pathological condition. Other proposed theories believe that gums are normal physiological metabolites of plants. Some evidence on acacia trees favours the former theory. Healthy acacia trees, grown under favourable conditions of moisture, soil and temperature, do not produce any gum. When grown under adverse conditions offered by high elevations, heat and lack of moisture, the secretion of gum is favoured (Blunt, 1962). Others believe that gums are synthesised as a result of infection of the plant by microorganism in an effort to seal off the infected section of the plant and prevent further invasion of tissue (Aulton, 1990).

The formation of gum has also been attributed to fungi attacking the plant and releasing enzymes that penetrate the tissue and transform the constituent cellulose materials of the cell wall into gum. For example, the parasite *Stereum purpureum*, which causes lead disease, induces plum trees to produce a considerable amount of gum at the site where the parasite grows. Yet another theory claims the formation of gums caused by bacterial action and suggests that specific bacteria are capable of producing different kinds gums (Aulton, 1990). The most reasonable explanation however seems to be the simplest one, namely that the plant produces the gum in order to seal of the injured part, primarily to prevent infection. This concept is supported by the fact that gums are produced immediately by gum producing

plants once they are injured deliberately. Gums and mucilages are said by some to arise from starch, whilst others suggest that they are produced at the expense of cellulose or hydrocellulose (Thaysen and Bunker, 1972; Smith and Montgomery, 1959).

An interesting observation made is that all the neutral sugars in some gums are indeed present in the tissues of the tree in the free state (Smith and Montgomery, 1959). Gums in general may be classified as acidic, neutral or basic. Natural gums are either acidic or neutral. No basic gum occurs in nature. Examples of acidic gums are acacia, tragacanth and albizia gums. Examples of neutral gums are asparagus gum and plantago seed gums.

Gum are also classified into natural (examples are: acacia, tragacanth and xanthan), modified or semi- synthetic (examples are: carboxymethylcellulose, and microcrystalline cellulose) and synthetic (example are: carboxypolymethylene and colloidal silicon dioxide.) Gums are sometimes classified as either water swellable (example albizia) or water soluble (example acacia).

1.2.0 DISTRIBUTION OF GUMS IN THE PLANT KINGDOM

Gums are relatively abundant in nature. The leguminosae family provides most of the commercially important gums. Example of such gums include; gum arabic found from Acacia specie found in Africa, Australia and Asia and tragacanth, found in Asia and Iran. The plant families Anacardiaceae, Combristaceae, Meliaceae, Rosaceae and Rutaceae are also known for their capacity for gum production (Smith and Montgomery, 1959).

The sources of commercially useful gums can be summarised as follow

- Marine gums – agar, alginate, carrageenan
- Microbial gums – dextrans and xanthans
- Seed gums – locust bean, psyllium
- Shrubs or tree exudates - acacia, tragacanth, khaya

1.2.1 PHYSICAL AND CHEMICAL PROPERTIES OF GUMS

The physical properties of gums are of primary importance in determining their uses and commercial value. These properties may differ considerably depending on the botanical source of the gum. Gums from the same specie when collected from plants growing under

different climatic and edaphic conditions or even collected from the same plant at different seasons of the year, show considerable difference in their physical properties. Another factor that affects the physical properties of gums is the treatment gums receive after collection such as washing, drying and bleaching in the sun as well as storage conditions.

1.2.1.1 COLOUR AND FORM

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. 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.

1.2.1.2 TASTE AND SMELL

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.

1.2.1.3 HARDNESS AND DENSITY

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.

1.2.1.4 POLARISATION

In aqueous solutions, most gums are usually weakly laevorotatory.

1.2.1.5 SOLUBILITY

For their solubility in water most gums like albizia, kyaya and tragacanth swell in water to give viscous or gel like solutions, whilst other gums like acacia literally dissolve in water. A lot of gums cannot be dissolved in water at concentrations higher than 5 % because of their very high viscosities. Gum arabic however can yield solutions up to 50 % concentrations. Gums are generally insoluble in oil and in most organic solvents. They may be soluble in aqueous ethanol, up to a limit of about 60 % ethanol. Limited solubility can also be obtained with glycerol and ethylene glycol. The gums that swell in water usually have a soluble portion and insoluble portion.

The overall solubility properties of gums can be improved by freeze drying or by the purification of the gum (Aspinal et. al., 1956). The purification involves dissolving the gum in 4 % sodium hydroxide, acidifying with hydrochloric acid and precipitating with ethanol. The purified gum in contrast with the crude gum is readily soluble in water. There is great loss in viscosity after purification (Meyer, 1950).

1.2.2 METHODS USED FOR THE 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).

1.2.3 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; Meyer, 1950). 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., 1959).

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).

1.2.3.1 RHEOLOGICAL AND PHYSICAL PROPERTIES OF GUMS

The physical properties and the appearance of natural gums are of utmost importance in determining the commercial value and their end use. These vary considerably with gums of different botanical source, and there are even substantial differences in gum from the same specie when collected from plants growing under different climatic conditions or even collected from the same plant at different seasons of the year. The physical properties may also be affected by age of the exudates and the treatment of the gum after collection, which may involve washing, drying, sun – bleaching and storage conditions (Glicksman, 1969).

Natural gums are exuded in varieties of shapes and forms, the best known being the tear drop or globular shapes of acacia gum. Other characteristic shapes are flakes or threadlike ribbons as with tragacanth, still others resemble stalactites and after collection and fracturing, yield irregular rod- shaped fragments as seen in khaya gums. The surface of most of gums is perfectly smooth when fresh but may become rough or covered with small cracks or striations upon weathering, resulting in an opaque appearance. These fissures or striations are often restricted to the surface, but may be deep in some gums. The colour of gums in their natural

forms varies from almost water white (colourless) through shades of yellow, amber, pink and orange to dark brown. Many gums when first secreted appear to be colourless, and it is believed that colour is due mainly to the presence of various types of impurities. Colour often appears as the gum ages upon the tree or as it is dried or heated. Colour often appears as the gum ages upon the tree or as it is dried or heated. The presence of tannins also account for the dark gums yielded by certain trees.

The water soluble gums are usually odourless and in this respect differ markedly from the oil soluble resinous exudates which have distinctive smells. The gums are usually tasteless and bland, except for some species which have sweet carbohydrate taste and some types that have been contaminated. Gums contaminated with tannins usually have a harsh, bitter flavour that is a serious disadvantage. Gums vary in hardness but, since this is usually dependent on the amount of moisture present, this therefore cannot be used as a mean of classification (Glinksman 1969).

1.2.3.2 pH AND OTHER PROPERTIES OF GUMS

Natural gums are mostly acidic with a few being neutral. The acidity is due to the presence of uronic acid unit in addition to the sugar polymer. The pH of gum solutions range from 3-6, albizia gum ranges between 3.5 to 5 and that of tragacanth mucilage ranges between 5 and 6.

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).

1.2.3.3 VISCOSITY AND RHEOLOGICAL PROPERTIES OF GUMS

Many useful industrial and pharmaceutical applications of gums are based on the viscous character of their solutions. Whereas most gums like khaya form highly viscous solutions at low concentrations of about 1 to 5 %, acacia gum is unique in that it is extremely soluble and not very viscous at low concentrations. High viscosities are not obtained until concentrations of about 40 to 50 % are obtained. Like other physical properties, viscosity and rheological

properties of the gum exudates are affected by the age of the parent tree, the climatic conditions or amount of rainfall or sunshine, pH and its variation, ageing of the gum, or mucilage and concentration of mucilage (Davidson, 1980; Glicksman, 1969).

1.2.3.4 EFFECT OF TEMPERATURE

Elevated temperature has viscosity thinning effect on fully hydrated gum. Upon cooling the gum revert to nearly their original viscosities, indicating that the elevated temperature does not degrade the macro molecules structurally. It has also been shown that as temperature is increased, the relative viscosity and density of gum solution is decreased (Taft and Malm, 1931).

1.2.3.5 EFFECT OF AGING

Studies on acacia show that all solutions undergo a decrease in viscosity with age. Unpreserved solutions show the greatest drop in viscosity while solutions preserved with benzoic acid (0.2 %) exhibit the smallest loss of viscosity (Davidson, 1980). Thus the decrease of viscosity with time can be minimised by the addition of preservatives. This phenomenon is common with almost all gums but the stability with respect to viscosity with time differs from gum to gum. The decrease in viscosity with time of aqueous solutions of some gums is probably due to enzymic degradation or microbial degradation or spontaneous depolymerisation (Smith and Montgomery, 1959).

1.2.3.6 EFFECT OF CONCENTRATION

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).

1.2.3.7 EFFECT OF OTHER FACTORS

Gum solutions are polymerised by ultrasonic waves and continued exposure to ultrasonic vibrations release monosaccharides, thereby reducing the viscosity (Mantell, 1947). Also mechanical grinding of gums, a process usually practised in commerce leads to molecular breakdown. This is revealed by the fact that solutions made from unground pieces of khaya gum are more viscous than those of the same concentration made from the powdered gum (Dror et. al., 2006).

1.2.4 CHEMICAL AND STRUCTURAL PROPERTIES OF GUMS

The physical properties manifested by the various gums and for that matter their use in the pharmaceutical and other industries depends on their structural and chemical composition of the gum. The chemical properties involve the constituent sugars and the sugar acids of the polysaccharides, the presence of other organic and functional groups and also the presence of inorganic ions. The chemical reactivity of the gum with other chemical substance also constitutes a chemical property.

1.2.4.1 SUGARS, SUGAR ACIDS AND THEIR DERIVATIVES

Gums and mucilage have been found to be made up of polysaccharides which are composed of sugars in a bound or 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).

1.2.4.2 ORGANIC FUCTIONAL GROUPS

Gums and mucilage have been found to contain some ester groups such as methoxyl and acetyl residues. Alkyl 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 as karaya and khaya respectively.

1.2.4.3 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.

1.2.5 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.

1.2.6.0 ANACARDIUM OCCIDENTALE- BOTANY AND SOURCE

Family: Anacardiaceae

Genus: *Anacardium* (Rickson, 1998)

Species: *occidentale*

Synonyms: *Acajuba occidentalis*, *Anacardium microcarpum*, *Cassuvium pomiverum*

Common name: cashew,

It is found mainly in cashew growing districts like Sampa, Wenchi, Bole, Jirapa and cashew plantations like Ejura farms in Ghana

Parts Used: Leaves, bark, fruit, nut

Description

Native to Brazil, it also grows in tropical areas of Central and South America and in the West Indies in tropical forests and grasslands. The evergreen tree grows to about thirty feet, producing low branches with oval leaves and pink-streaked yellow flowers on long spikes. Its greenish-gray fruit or apple is, in fact, a thickened stem. The true fruit is the cashew nut which hangs immediately below the fruit. It is encased in a red or yellow flesh. The gum exuded by the stem wards off ants and other insects. Cashew is a multi purpose tree of the Amazon that grows up to 15 m high. It has a thick and tortuous trunk with branches so winding that they frequently reach the ground. Cashew trees are often found growing wild on the drier sandy soils in the central plains of Brazil and are cultivated in many parts of the Amazon rainforest.

The cashew tree produces many resources and products. The bark and leaves of the tree are used medicinally, and the cashew nut has international appeal and market value as a food. Even the shell oil around the nut is used medicinally and has industrial applications in the plastics and resin industries for its phenol content. Then, there is the pseudo-fruit-a swollen peduncle that grows behind the real fruit that yields the cashew nut. The pseudo-fruit, a large pulpy and juicy part, have a fine sweet flavour and is commonly referred to as the "cashew fruit" or the "cashew apple." Fresh or frozen cashew fruit concentrate is as common a juice product in South American food stores as orange juice is in the United States. It is very perishable, however; therefore, no fresh cashew fruit is exported into the United States or Europe from South America.

The cashew nut is defined botanically as the fruit. It grows externally in its own kidney-shaped hard shell at the end of this pseudo-fruit, or peduncle. The nut kernel inside is covered with an inner shell, and between the two shells is a thick, caustic, and toxic oil called cardol. Cashew nuts must be cleaned to remove the cardol and then roasted or boiled to remove the toxins before they can be eaten.

1.2.6.1 CLIMATE, SOILS AND PROPAGATION

It requires a warm humid climate, with a minimum of 600 mm rainfall, but well distributed rainfall is more important. Cashew thrives under a wide range of temperatures from 15 to 40 degrees centigrade. Cashew does not grow well in areas subject to frost and cold waves. It is also drought resistant. It has a high degree of adaptability and can be raised on any soil free from rocky strata or hard pan and water stagnation. The best soils for cashew are deep friable, well drained sandy loam soils. Hilly slopes up to an elevation of 700 m above mean scale level can also be utilized for cashew cultivation. Cashew is commercially propagated by seed only. Vegetative propagation through air layering, side grafting, veneer grafting and epicotyls grafting is also possible. Planting material should be collected only from trees possessing all the desirable higher percentage of bisexual flowers, good fruit set, medium sized nut and high yielding capacity of 15-25 years old.

1.2.6.2 TRIBAL AND HERBAL MEDICINE USES

Native to the northeast coast of Brazil, cashew was domesticated long before the arrival of Europeans at the end of the fifteenth century. It was "discovered" by European traders and explorers and first recorded in 1578. It was taken from Brazil to India and East Africa, where it soon became naturalized. In sixteenth-century Brazil, cashew fruits and their juice were taken by Europeans to treat fever, sweeten breath, and "conserve the stomach."

The cashew tree and its nuts and fruit have been used for centuries by the indigenous tribes of the rainforest, and it is a common cultivated plant in their gardens. The Tijuana tribe in northwest Amazonia considers the fruit juice medicinal against influenza, and they brew a tea of leaves and bark to treat diarrhoea. The Wayãpi tribe in Guyana uses a bark tea as a diarrhoea remedy and colic remedy for infants. Tribes in Suriname use the toxic seed oil as an external worm medicine to kill butterflyfly larvae under the skin. In Brazil, a bark tea is used as a douche for vaginal discharge and as an astringent to stop bleeding after a tooth extraction. A wine made from the fruit is used for dysentery in other parts of the Amazon rainforest. The fruit juice and a bark tea are very common diarrhoea remedies throughout the Amazon today, used by *curanderos* and local people alike.

In Peruvian herbal medicine today, cashew leaf tea (called *casho*) is employed as a common diarrhoea remedy; a bark tea is used as an antiseptic vaginal douche; and the seeds are used for skin infections. In Brazilian herbal medicine, the fruit is taken for syphilis and as a diuretic, stimulant, and aphrodisiac. A leaf tea is prepared as a mouthwash and gargles for

mouth ulcers, tonsillitis, and throat problems and is used for washing wounds. An infusion and/or maceration of the bark is used to treat diabetes, weakness, muscular debility, urinary disorders, and asthma. The leaves and/or the bark is also used in Brazil for eczema, psoriasis, scrofula, dyspepsia, genital problems, and venereal diseases, as well as for impotence, bronchitis, cough, intestinal colic, leishmaniasis, and syphilis-related skin disorders. North American practitioners use cashew for diabetes, coughs, bronchitis, tonsillitis, intestinal colic, and diarrhoea, and as a general tonic (Rickson et. al. 1998; Orwa et. al., 2009).

1.2.6.3 PLANT CHEMICALS

In addition to being delicious, cashew fruit is a rich source of vitamins, minerals, and other essential nutrients. It has up to five times more vitamin C than oranges and contains a high amount of mineral salts. Volatile compounds present in the fruit include esters, terpenes, and carboxylic acids. The bark and leaves of cashew are a rich source of tannins, a group of plant chemicals with documented biological activity. These tannins, in a 1985 rat study, demonstrated anti-inflammatory and astringent effects, which may be why cashew is effective in treating diarrhoea. Anacardic acids are found in cashew, with their highest concentration is in the nutshells. Several clinical studies have shown that these chemicals curb the darkening effect of aging by inhibiting tyrosinase activity, and that they are toxic to certain cancer cells.

The main chemicals found in cashew are alanine, alpha-catechin, alpha-linolenic acid, anacardic acids, anacardol, antimony, arabinose, caprylic acid, cardanol, cardol, europium, folacin, gadoleic acid, gallic acid, ginkgol, glucuronic acid, glutamic acid, hafnium, hexanal, histidine, hydroxybenzoic acid, isoleucine, kaempferols, L-epicatechin, lauric acid, leucine, leucocyanidin, leucopelargonidine, limonene, linoleic acid, methylglucuronic acid, myristic acid, naringenin, oleic acid, oxalic acid, palmitic acid, palmitoleic acid, phenylalanine, phytosterols, proline, quercetin-glycoside, salicylic acid, samarium, scandium, serine, squalene, stearic acid, tannin, and trans-hex-2-enal tryptophan.

1.2.6.4 BIOLOGICAL ACTIVITIES AND CLINICAL RESEARCH

Cashew's antimicrobial properties were first documented in a 1982 *in vitro* study. In 1999, another study was published indicating it had good in vitro antibacterial activity against *E. coli* and *Pseudomonas*. Most recently, a 2001 study reported that a bark extract exhibited in

vitro antimicrobial activity against 13 of 15 microorganisms tested. In 1999, researchers reported that cashew fruit exhibited antibacterial activity against the Gram-negative bacterium *Helicobacter pylori*, which is now considered to cause acute gastritis and stomach ulcers. Its effectiveness against leishmanial ulcers also was documented in two clinical studies. Finally, two studies (one in mice and the other in rats) in 1989 and 1998 document the protective quality of a leaf extract against lab-induced diabetes, although the extract did not act as hypoglycaemic as some others, it did stabilize blood glucose levels near pre-test levels (Orwa et. al., 2009).

1.2.6.5 CURRENT PRACTICAL USES

The different products produced from this tree offer a wide range of applications. The fruit is used to make highly nutritive snacks and juices, and fruit extracts are now being used in body-care products. Because of its high amount of vitamin C and mineral salts, cashew fruit is used as a catalyst in the treatment of premature aging of the skin and to remineralize the skin. It is also an effective scalp conditioner and tonic and is often used in shampoos, lotions, and scalp creams for the conditioning activity of its proteins and mucilage. Cashew leaf or bark tea is still widely used throughout the tropics as an effective diarrhoea and colic remedy, considered gentle enough for children. .

Contraindications: Skin contact with various parts of the fresh plant (leaves, bark, fruit, fruit oil) may cause dermatitis and to produce an allergic response. Cashew nuts and fruits have also been documented to cause food allergy reactions.

Drug Interactions: None reported (de Paiva et. al, 2008).

1.2.7.0 CHEMICAL PROPERTIES OF CASHEW GUM

Cashew gum is a complex polysaccharide of high molecular mass, on hydrolysis it yields galactose and galacturonic acid. The variation in acid number is influenced not only by the source of the sample but also by its age. The sticky exudates from this tree darken and thicken rapidly on exposure to air. When applied as a vanish, provides remarkable protection, as is unchanged by acids, alkalis, alcohols or heat up to 70°C. The gum exudate from *Anacardium occidentale* contains galactose (61 %), arabinose (14 %), rhamnose (7 %), glucose (8 %) and glucuronic acid (5 %) in addition to small amounts (< 2 %) of each of mannose, xylose and 4-0 methylglucuronic acid. Contrary to earlier findings, the main

aldobiuronic acid present is 6-O-(β -D-glucopyranosyluronic acid)-D-galactose; smaller amounts of the 4-O-methyl analogue are also present. Mild acid hydrolysis showed only two galactobioses, 3-O- β -D-galactopyranosyl-D-galactose (major component) and 6-O- β -D-galactopyranosyl-D-galactose (minor component). Degraded gum A, prepared by controlled acid hydrolysis, contained galactose, glucose, and uronic acid. A Smith-degradation of degraded gum A gave degraded gum B, which contained only galactose. Sequential Smith-degradations of *Anacardium occidentale* gum, and methylation analyses of the gum and of its degradation products indicated a highly-branched galactan framework consisting of chains of β -(1–3)-linked D-galactose residues branched and interspersed with β -(1–6) linkages. Arabinose is present as end-groups or in short (1–2)-linked chains up to five units long. Glucose, rhamnose, mannose xylose, and uronic acid are all present as end-groups (Anderson et. al., 1974; De Paula et. al., 1995).

1.2.7.1 USES OF CASHEW GUM

Cashew gum is used primarily in industrial application for binding books, as adhesives for envelopes, label, stamps and posters. It is also used as an additive in the manufacture of chewing gum because of its thickening power. It is used as a jellying agent in canned food and jellies for fruit jam.

Other possible uses are as a binder, emulsifying and suspending agent in the pharmaceutical industry.

1.2.7.2 RESEARCH ADVANCEMENT ON POSSIBLE USES

The polysaccharide, combined with water soluble, branched 1 $\rightarrow$ 3 β galactose and with other oligosaccharides and proteins, exhibited high inhibitory activity (average 88% $p < 0.005$) against an implanted sarcoma 180 solid tumours in mice, characterizing an antitumor activity of the cashew gum (Mothe et. al, 2008). Kubo et. al. (1993) found out that, there are antitumour agents from cashew juice. Jiona et. al., (1991) also found out that, the nut shell oil of *Anacardium occidentale* has antibacterial properties.

Crude and purified cashew tree gums were tested for their antimicrobial activity against bacteria, yeast and fungi. Their use was also evaluated as a carbon source for microbial growth. Cashew gum presented only a weak activity against *Saccharomyces cerevisiae* and no activity was observed against all other microorganisms tested. The possibility that removal of anacardic acid present in the raw gum during purification may explain the negative results

obtained was discussed. When purified cashew tree gum was used as carbon source, only *Listeria monocytogenes*, *Saccharomyces cerevisiae* and *Kluyveromyces marxianus* did not grow after 5 days of incubation (Torquato et. al., 2004).

KNUST



1.2.8. 0 ORAL SOLID DOSAGE FORMS

Drug substances most frequently are administered orally by means of solid dosage forms such as tablets and capsules. In the manufacture of these dosage forms, other materials are required in addition to the active ingredient. Additives may also be included in the formulation to enhance physical appearance, improve stability etc. The supposedly inert ingredient as well as the production methods employed has been shown in some cases to influence the release of the drug substances. Therefore care must be taken in the selection and evaluation of additives and preparation methods to ensure that the physiological availability and the therapeutic efficacy of the active ingredient will not be diminished.

1.2.8.1 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). 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.

1.2.8.2 TYPES OF TABLETS

COMPRESSED TABLETS: These tablets are formed by compression and they contain no special coating. They are made from powdered, crystalline or granular materials alone or in combination with binders, disintegrants, lubricants and diluents

SUGAR COATED TABLETS: These are compressed tablets containing a sugar coating. Such coatings may be coloured and are beneficial in covering up drug substances possessing objectionable taste or odour and in protecting materials sensitive to oxidation.

FILM COATED TABLETS: These are compressed tablets which are covered with a thin layer or film of water soluble material. A number of polymeric materials with film coating properties may be used.

ENTERIC COATED TABLETS: These are compressed tablets coated with substances that

resist solution in the gastric fluid but disintegrate in the intestine. They are normally used for drugs that are inactivated or destroyed in the stomach, for those which irritate the mucosa or as a means of delayed release of the medication.

MULTIPLE COMPRESSED TABLETS: These are compressed tablets made by more than one compression cycle. Examples are layered tablets and press-coated tablets.

CONTROLLED RELEASED TABLET: Compressed tablets can be formulated to release the drug slowly over a prolonged period of time. These tablets can be categorised into three types;

Those which respond to some physiological condition to release the drug, such as enteric coating.

Those that release the drug in a relatively steady, controlled manner.

Those that combine combinations of mechanisms to release pulses of drugs such as repeat-action drugs.

EFFERVESCENT TABLETS: In addition to the drug substance, these contain Sodium bicarbonate and inorganic acid such as citric acid or tartaric acid. In the presence of water these additives react liberating carbon dioxide which act as a disintegrator and produces effervescence.

BUCCAL AND SUBLINGUAL TABLETS: These are small, oval tablets. Tablets intended for buccal administration by inserting it into the buccal pouch (Zografi et. al., 1990).

1.2.9.0 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.

- **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, manning, dry starch and powdered sugar.

- **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. 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.

- **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.

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

- **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.

- **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 for 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 croscarmellose and crospovidone. The method of addition of the disintegrant in the course of granulation is also of much importance.

1.2.9.1 TABLET CHARACTERISTICS

Tablets as a dosage form should meet certain specific requirements. The diameter, shape, thickness, accuracy of dosage, weight, hardness, stability, disintegration time and dissolution has to conform to certain parameters.

- **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 tableting machine. A tablet property related to hardness is friability. This parameter assess the ability of the tablet to withstand abrasion in packaging, handling and shipping.
- **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.
- **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 ordinary tablets and 60 minutes for coated tablet. This test does not apply to depot tablets, lozenges and chewable tablets.

- **Dissolution:** For certain tablets the monographs 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 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.
- **Stability:** The stability of the drug substances is investigated when developing the formulation. A suitable method of preparation must be chosen for the tableting 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.

1.2.9.2 METHODS OF PREPARATION OF TABLETS

1.2.9.2.1 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 solvents.

➤ Procedure of Wet Granulation

- Step 1: Weighing and Blending - the active ingredient, filler, disintegration agents, are weighed and mixed.
- Step 2: The wet granulate is prepared by adding the liquid binder/adhesive. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, and cellulose derivatives such as methyl cellulose.
- Step 3: Screening the damp mass into pellets or granules
- Step 4: Drying the granulation
- Step 5: Dry screening: After the granules are dried, pass through a screen of

smaller size than the one used for the wet mass to select granules of uniform size to allow even fill in the die cavity

- Step 6: Lubrication- A dry lubricant, anti adherent and glidant are added to the granules either by dusting over the spread-out granules or by blending with the granules. It reduces friction between the tablet and the walls of the die cavity. Anti adherent reduces sticking of the tablet to the die and punch.

1.2.9.2.2 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
- Tableting excipients with good flow characteristics and compressibility allow for direct compression of a variety of drugs.

1.2.9.3 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 as 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.

1.2.9.3.1 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

1.2.9.3.2 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_0 . 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 of fluff or poured bulk density, D_0 . 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_0 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.

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

$$\% \text{Compressibility} = (D_f - D_0 / D_f) \times 100$$

1.2.9.0 SUSPENSIONS

Suspensions may 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. 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.

Suspensions may be classified into three 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 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.

1.3.1.0 PROPERTIES OF SUSPENSIONS

- Suspension should possess good pourability leading to ease of removal of dose from container.
- They should have good organoleptic properties
- The particle size distribution should be uniform.
- 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.

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.

1.3.2.0 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.

1.3.3.0 INTERFACIAL PROPERTIES OF SUSPENSIONS

1.3.3.1 Flocculation

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.

1.3.3.1.1 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, tragacanth and silicates

1.3.4 QUALITY CONTROL TEST FOR SUSPENSIONS

1.3.4.1 Sedimentation volume

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

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

$$F = V_u / V_O \text{ ----- (A)}$$

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 (V_u) to the original volume of sediment (V_O) before settling.

Some time '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 than 1; 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

$$F_{\infty} = V_{\infty} / V_O$$

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.

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 preserve in 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.

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 also called 'cracking' or 'claying'. In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquid so supernatant appears cloudy whereby in flocculated suspension, even the smallest particles are involved in flocs, so the supernatant does not appear cloud

1.3.4.2 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. .

1.3.4.3 Particle size and size distribution

The freeze-thaw cycling technique used to assess suspension for stress testing for stability testing result in increase of particle growth and may indicate future state after long storage. 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 are 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.

1.3.4.4 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.

1.4.0 EMULSIONS

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. They stabilize the system by forming a thin film around the globules of the dispersed phase.

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 , etc. lotions and liniments.

1.4.1 Types of Emulsions

- Oil in water
- Water in oil
- Multiple emulsion
- Micro emulsions

1.4.2 METHODS FOR PREPARING EMULSIONS

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

1.4.2.1 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 water is added in small portions with constant agitation after each addition to produce the final volume.

1.4.2.2 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.

Table: 1 Proportions of Oil, Water and Gum required for formation of primary emulsion

PROPORTION			
TYPE	Oil	Water	Gum
Mineral oil	3	2	1
Fixed oil	4	2	1
Volatile oil	2	2	1

1.4.3.0 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.

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

$$V = \frac{2r^2 (d_1 - d_2) g}{9\hat{\eta}}$$

Where V = rate of creaming

R = radius of globules

d_1 = density of dispersed phase

d_2 = density of dispersion medium

g = gravitational constant

$\hat{\eta}$ = 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. Bigger is the size of the globules, more will be 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

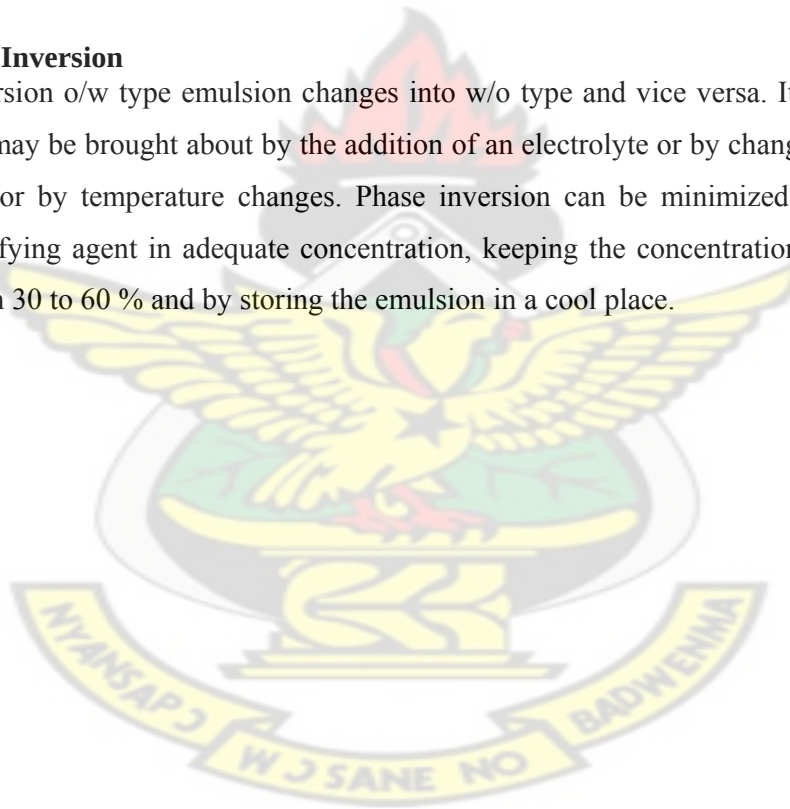
continuous phase, less will the problem of creaming. Therefore to avoid creaming in emulsions, the viscosity of the continuous phase should be increased by adding suitable viscosity enhancers like gum acacia, tragacanth etc.

1.4.3.2 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.

1.4.3.3 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.



CHAPTER TWO

MATERIALS AND METHODS

2.1.0 MATERIALS

Crude cashew gum was used for the study. The crude gum was obtained from the Ejura cashew plantation as natural exudates from the barks of the plant *Anacardium occidentale*, family, Anacardiaceae at Ejura in the Ashanti Region of Ghana. The plant was authenticated by the curator of the plantation. Other materials used include Metronidazole powder BP (Kinapharma Ltd., Kumasi) and Maize Starch (Tradewinds Chemist, Kumasi). Zinc oxide, Talc, Magnesium stearate, Lactose, Glycerine, Castor oil, Paraffin oil and peppermint oil were obtained from the chemical store of the Department of Pharmaceutics, KNUST, Kumasi.

2.1.1 REAGENTS

Concentrated hydrochloric acid was obtained from Phillip Harris plc (Shenstone, England). 96 % ethanol, diethyl ether, perchloric acid, distilled water and sodium benzoate 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.

2.1.2 EQUIPMENT AND APPARATUS

Trohm pH meter, Domestic lab blender, WA 210 Analytical balance, Cecil CE 8020 UV machine, Erweka Dissolution Apparatus, (type DT 6, GmbH Heusenstamm, Germany), SOTAX Friabilator (USP), AA- 6300 Shidmazu Atomic Emission Spectrophotometer (Shidmazu Corporation), Brookfeild Viscometer Model DV-I+, Retsch laboratory sieves, Electrolab Disintegrating Tester USP- ED-2L, Photometer (Jenway, United Kingdom) model PF P7, Dr. Schleuniger Pharmatron Model 5Y Tablet Tester, Sartorius Electrical Balance, Venier calliper, among others were the equipments and apparatus used.

2.2.0 PREPARATION AND PURIFICATION OF CASHEW GUM

The crude cashew gum was cleaned by removing the bark and other extraneous materials by hand picking, breaking and sieving. The gum was dried in an oven at 50°C for about 8 h until it became sufficiently brittle. The dried gum was then sorted into two grades, light coloured grade and dark coloured grade. The light coloured grade was selected for further processing by milling in a domestic blender into fine powder. The powdered gum was used in some of the subsequent test and analysis as crude cashew gum powder. To purify the gum 100 g of the crude gum powder was dissolved in 200 ml of distilled water and allowed to stand for 24 h with intermittent stirring as the gum was very soluble in water. Using a piece of calico the gum mucilage obtained was filtered by squeezing to remove any insoluble debris or impurities. The filtered mucilage was re-filtered to ensure that all debris was removed. The filtered mucilage was purified by precipitating the gum out with 96 % ethanol. About 350 ml of 96 % ethanol was used to precipitate 100 g of the gum, the precipitated gum was filtered and washed with 96 % ethanol and washed with di-ethyl ether and dried in the hot air oven at 50°C for about 8 h. The dried purified gum was milled and sieved through sieve number 80. The powdered gum was used in subsequent test and analysis as purified cashew gum.

2.3.0 EXAMINATION OF PHYSICAL PROPERTIES OF CASHEW GUM

2.3.1 MACROSCOPIC PROPERTIES OF CASHEW GUM

In evaluating the macroscopic properties of cashew gum, its form, shape, size, surface characteristics, colour and nature, fracture, odour and taste were observed.

2.3.2 MOISTURE CONTENT OF THE GUM

Two (2) grams of powdered crude cashew gum was weighed accurately into a porcelain crucible which had previously been dried to a constant weight. The gum was placed in a hot air oven and maintained at a temperature of 105°C. After 5 h, the gum was removed and cooled, after which it was placed in a desiccator for 30min. The weight of the crucible and the gum were recorded. The determination was done in triplicate. The moisture content or loss on drying was expressed as a percentage of the cashew gum sample. The entire process was repeated for purified cashew gum.

2.3.3 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 min, while shaking frequently, and filtered whilst hot through number 4 sintered glass filters. The residue was then washed with hot water and dried at 105 °C to constant weight. The weight of the insoluble matter was expressed as a percentage.

2.4.0 SPECTROPHOTOMETRIC ANALYSIS OF METALLIC ION CONTENT OF GUM

2.4.1 Wet Digestion of sample

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 ml (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 min 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.

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

One (1) ml of the digest was used to determine the content of Ca, Mg, Zn and Fe in the sample using the Perkin Elmer Precisely A Analyst 400 Atomic Absorption Spectrophotometer (AAA) 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.

2.4.3 Determination of Sodium (Na) and Potassium (K)

Two (2) ml 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.

2.5.0 ACIDITY OF CRUDE AND PURIFIED GUM MUCILAGE

Purified gum mucilage and crude gum mucilage were prepared with distilled water to a concentration of 2 % w/v. The pH of the samples were determined weekly for six weeks, using a standardized pH meter.

2.6.0 EFFECT OF STORAGE TEMPERATURE AND PRESERVATION ON pH OF PURIFIED GUM MUCILAGE

Samples of purified gum mucilage were prepared with distilled water to a concentration of 2 % w/v with and without a preservative (0.2 % sodium benzoate). The samples were then stored at room temperature, 50°C and in a refrigerator. The pH of the samples were determined weekly for six weeks, using a standardized pH meter.

2.7.0 DETERMINATION OF THE RHEOLOGICAL PROPERTIES OF GUM

2.7.1 EFFECT OF CONCENTRATION ON VISCOSITY OF GUM MUCILAGE

Mucilages of four different concentrations of acacia and cashew gum, namely: 5 % w/v, 10 % w/v, 20 % w/v, 30 % w/v, and 40 % w/v were prepared using distilled water. The viscosity of the samples was determined at shear rate of 1 rpm using a Brookfield viscometer (spindle number 2).

2.7.2 EFFECT OF TEMPERATURE ON VISCOSITY OF GUM MUCILAGE

40 % w/v of purified cashew gum mucilage was prepared in distilled water and the viscosity determined with a Brookfield viscometer at different shear rates at 25°C, 30°C, 45°C, 60°C and 80°C.

2.8.0 DETERMINATION OF MICROBIAL QUALITY OF CRUDE AND PURIFIED GUM

0.1 g of crude and purified cashew gum were dissolved separately in 10 ml of sterile water and 1ml of the mucilage was inoculated into a previously stabilised MacConkey agar, mannitol salt agar, cetrimide agar, sabouraud 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.

2.8.1 DETERMINATION OF ANTIMICROBIAL PROPERTY OF GUM

20 – 50 % w/v concentrations of the purified and crude cashew gum were prepared and the antimicrobial activity determined against *E. coli*, *Staph. aureus*, *Candida albicans*, *Klebsiella*, and *Pseudomonas aeruginosa* using the cup plate method. The plates were observed for any zones of inhibition after incubating for 48 hours. All experiments were duplicated.

2.9.0 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. Details of ratio of oil to water to gum used in finding an appropriate ratio for preparation of stable primary emulsions are shown in Tables 2.0-2.2

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. The weight of oil, water and gum that were used are shown in Tables 2.0 – 2.2.

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. The weight of oil, water and gum that were used are shown in Tables 2.1 – 2.3.

Sample calculation for the preparation of primary emulsion out of fixed oil using the ratio: 4:2:1 i.e. oil : water : gum.

Volume of emulsion to be prepared = 100ml

Total percentage of oil = 25%

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

Table 2.0

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 2.1

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 2.2

VOLATILE OIL

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

2.9.1 PREPARATION OF 100ml MINERAL OIL EMULSION WITH 25% 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.

2.9.2 STABILISATION OF EMULSION BY HOMOGENISATION

Emulsion prepared in 2.9.1 was transferred into a domestic blender and homogenised for 3 min. It was then transferred into plain bottles and covered.

2.9.3 STABILISATION OF EMULSION BY ADDITION OF A THICKENING AGENT

25 ml of mineral oil was measured and 10 g of gum of previously weighed 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 and the volume made up to 100ml added and homogenised. It was then transferred into a plain bottle covered and stored.

2.9.4 STABILISATION OF EMULSION BY REDUCING INTERFACIAL TENSION USING TWEEN 80

25 ml of mineral oil was measured and 10 g of gum of previously weighed gum was added and triturated. Different solutions of tween 80 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 80

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 100ml volume with water and homogenised and transferred into a plain bottle and tightly covered.

2.10.0 CASHEW GUM AS A SUSPENDING AGENT

The gum was investigated for its suspending ability by incorporating different concentrations of the gum in zinc oxide suspension. The suspending property of cashew gum was compared to that of a standard suspending agent, xanthan gum. The parameters evaluated were sedimentation profile, redispersion and rheological behaviour

2.10.1 PREPARATION OF ZINC OXIDE SUSPENSION WITH XANTHAN GUM

The zinc oxide was first sieved through sieve number 80. 20 g of the sieved zinc oxide was weighed into a clean mortar and levigated with 20 ml of glycerine. The specified amount of xanthan gum was weighed, added to the mixture and triturated to produce the suspension. A little amount of distilled water was added to make it pourable. It was then transferred into a 50 ml measuring cylinder and made up to volume. It was then tightly covered and labelled. Zinc oxide suspensions containing the following concentrations of xanthan gum were prepared: 0.1 % w/v, 0.2 % w/v, 0.3 % w/v, 0.4 % w/v and 0.5 % w/v. Each suspension was preserved with 0.2 % sodium benzoate.

2.10.2 PREPARATION OF ZINC OXIDE SUSPENSION WITH CASHEW GUM

The zinc oxide was first sieved through sieve number 80. 20 g of Zinc oxide was weighed into a clean mortar and levigated with 20 ml of glycerine. The specified amount of cashew gum was weighed, added to the mixture and triturated to produce a suspension. A little amount of distilled water was added to make it pourable. It was then transferred into a 50 ml measuring cylinder and made up to volume. It was the tightly covered and labelled. Zinc oxide suspensions containing the following concentrations of cashew gum were prepared: 0.1

% w/v, 0.2 % w/v, 0.3 % w/v, 0.4 % w/v, 0.5 % w/v, 1.0 % w/v, 2.0 % w/v, 3.0 % w/v and 4.0 % w/v. Each suspension was preserved with 0.2 % sodium benzoate.

2.10.3 SEDIMENTATION PARAMETERS

Sedimentation Volume: Each suspension (50 ml) was stored in a 50 ml-measuring cylinder for 42 days at room temperature. Observations were made at every hr for 6 hrs and then every 72hr for 42 days. The sedimentation volume, F (%), was then calculated using the following equation: $F = 100V_u/V_o$, where V_u is the ultimate volume of the sediment and V_o is the original volume of the suspension.

2.10.4 RHEOLOGY

The time required for each suspension sample to flow through a 10 ml pipette was determined and the apparent viscosity (η_{α} in mls^{-1}) was calculated using the equation: Flow rate = (η_{α} in mls^{-1}) = Volume of pipette (ml) /flow time/sec. The flow rates of the fresh and stored suspensions were determined.

2.10.5 REDISPERSIBILITY

A fixed volume of each suspension (50 ml) was kept in calibrated tubes which were stored at room temperature for 42 days undisturbed. After the storage period the suspensions were shaken vigorously to redistribute the sediment and the presence of deposits and cakes if any was recorded and the ease of redispersibility was assessed.

2.11.0 TABLET FORMULATION

2.11.1 PREPARATION OF ACACIA MUCILAGE

10 g of acacia gum was weighed into a clean mortar and triturated. About 40 ml of distilled water was added bit by bit until uniform mucilage was formed. The mucilage was then transferred into a clean measuring cylinder and made up to volume with distilled water to produce 20 % w/v acacia mucilage. The mucilage was used as a binding agent for the preparation of granules.

2.11.2 PREPARATION OF CASHEW MUCILAGE

The cashew gum mucilage was prepared the same way as the acacia mucilage using different amounts of the gum to prepare 10 % w/v, 20 % w/v, 30 % w/v and 40 % w/v cashew gum mucilage.

2.11.3 PREPARATION OF GRANULES

6.4 g of maize starch was weighed and put in a clean mortar, 20 g of metronidazole was also weighed and added and mixed thoroughly. 49.6 g of lactose was also weighed and mixed thoroughly for uniformity. 20 % w/v acacia mucilage was added to the powder mix bit by bit until a damp mass which easily broke into lumps (not powder) when pressure was applied to it using the thumb was formed. The volume of binder solution used was recorded and the amount of binder used calculated as shown in Table 2.8 below. The damp mass was screened through sieve number 8 and the wet granules were dried at 60 °C for 1 hour in a hot air oven. The dried granules were screened through sieve number 20 and lubricated with 1.6 g of talc and 2.2 g of magnesium stearate. The lubricants and granules were hand mixed for 5 min after which the granules were put on a metallic tray and dried at 50 °C for 10 minutes. The same procedure was used to prepare different batches of granules with 10 % w/v, 20 % w/v, 30 % w/v and 40 % w/v cashew gum mucilage as binder. The different batches of granules produced were compressed into tablets using a lubricated single punch tableting machine. Each tablet of diameter 11 mm contained approximately 100 mg metronidazole which was prepared from about 400 mg of granules.

Table 2.3

General Formula for Metronidazole tablets

Ingredients	1 unit quantity/ mg	200 unit quantities/g
Metronidazole	100	20.00
Lactose	248	49.60
Maize starch	32	6.40
Acacia mucilage (16ml)	16	3.20
Talc	8	1.60
Magnesium Stearate	1	0.20

Table 2.4

Total volume of cashew gum mucilage used

Concentration %w/v	Volume used/ ml	Total weight used (g)	Binder in granules (% w/w)
10	20.00	2.00	2.50
20	18.00	3.60	4.40
30	17.00	5.10	6.20
40	16.00	6.40	7.60

2.12.0 BULK DENSITY MEASUREMENTS

About 30 g of granules was weighed and poured through a funnel into a 100 ml tarred 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 i.e. mass/V_o . The final density was also calculated as the final bulk density or equilibrium or tapped or consolidated bulk density, D_f i.e. mass/V_o . 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 $(D_f - D_o/D_f) \times 100\%$

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

2.13.0 QUALITY COMPLIANCE TESTS CARRIED OUT ON TABLETS

2.13.1 UNIFORMITY OF WEIGHT TEST

Twenty (20) tablets from each batch were randomly selected and weighed together; the tablets were then weighed individually. The tablet 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.

2.13.2 FRIABILITY TEST

A number of tablets of total weight greater than 6 g was weighed initially, W_o and dedusted. It was then placed in the drum of the friabilator and all the parameters set on the machine. The drum rotated and tumbled the tablets 100 times, after which the machine stopped automatically. The tablets were dedusted again and its final weight, W_f taken and the percentage weight loss calculated as $(W_o - W_f/W_o) \times 100$. The tablets were observed for cleavages, breakages and cracks.

2.13.3 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 machine. 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 needed 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.

2.13.4 DISINTEGRATION

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 ± 2 °C. The machine was put 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 was then recorded. This test was done in triplicate.

2.13.5 DISSOLUTION

2.13.5.1 CALIBRATION

Appropriate amounts of metronidazole powder was dissolved in 0.1 M HCl 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 278 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.

2.13.5.2 DISSOLUTION TESTING

900 mls of the dissolution medium (0.1N HCl) was placed in the six vessels of the Dissolution machine. The dissolution medium was equilibrated to 37 ± 0.5 °C, and the paddle speed set to 100 revolutions per minute. One dosage unit was placed in each of the vessels of the dissolution machine and operated at the specified rate. Extreme care was taken to exclude air bubbles from the surface of the dosage unit. At specified time intervals of 5 min, 10 min, 15 min , 30 min, 45 min and 60 min, 5 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. To replace the 5 ml sample withdrawn, 5 ml of fresh dissolution medium was added to the beaker from which the volume was withdrawn. The vessel was kept covered for the duration of the test and the temperature of the medium maintained at 37 ± 0.5 °C at all times. The withdrawn samples were filtered and diluted 10 times. The diluted filtrate were analysed by UV spectrophotometry at a wavelength of 278 nm using a 1cm cell and 0.1M HCl as blank solution.

Using the equation obtained from the calibration curve, the concentration of metronidazole in samples taken at time 5, 10,15,30,45 and 60 min were calculated and the percentage release values were then calculated. A plot of percentage drug release against time was established.

2.14.0 STATISTICAL ANALYSIS

Results obtained were analysed and graphs drawn using Microsoft Office Excel, Graph Pad prism and SPSS Base 10.0 for windows, SPSS Inc. (1999).



CHAPTER THREE

RESULTS AND CALCULATIONS

3.1.0 PURIFICATION OF CASHEW GUM

- **Calculation**

The percentage yield of purification process is given by:

Final weight of gum (after purification) x 100

Initial weight of gum (before purification)

Hence for cashew gum

Percentage yield = $\frac{78.54 \text{ g}}{100 \text{ g}} \times 100 = 78.54 \%$

3.2.0 PHYSICAL TEST ON CASHEW GUM

Table 3.1.0

Macroscopic properties of the gum

Property	Characteristic of gum
Colour	Glassy white, brown golden
Odour	Characteristic
Taste	Bland
Surface appearance	Somewhat smooth surface
Size	3-7cm in length, 2mm wide
Form and Shape	Thin long cylindrical tears, Round to ovoid short tears
Fractures	Some fractures with difficulty and the thin ones easily

Table 3.1.1

Insoluble matter and moisture content of cashew gum

Gum	Insoluble matter (%)	Moisture content (%)
Purified gum	0.280 ± 0.060	10.44 ± 0.16
Crude gum	0.350 ± 0.105	11.19 ± 0.52

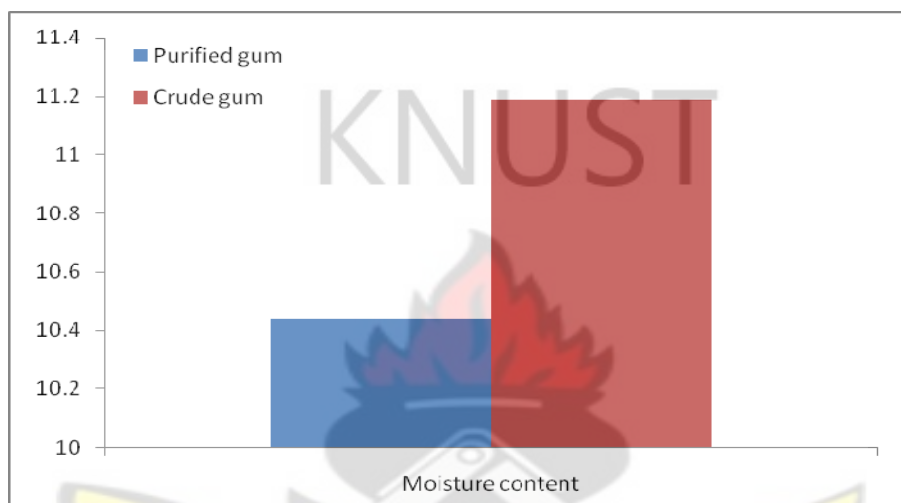


Fig3.1.1 Moisture content crude and purified Cashew gum

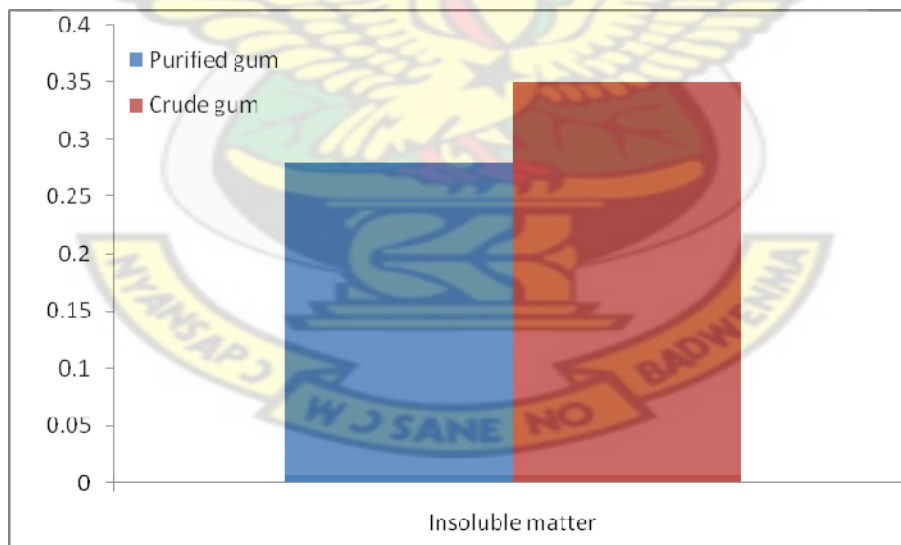


Fig3.1.2 Insoluble matter of crude and purified Cashew gum

3.3.0 CHEMICAL TEST ON CASHEW GUM

MINERAL ANALYSIS

Table 3.2.0

Metallic Ion Content of Cashew gum

Mineral/mg/kg	Crude gum	Purified gum
Iron	16.71±0.085	2.000±0.100
Calcium	883.5±0.361	662.4±0.372
Sodium	0.073±0.001	0.052± 0.001
Potassium	0.081±0.001	0.03 ±0.001
Zinc	8.337±0.031	4.14±0.012
Magnesium	54.44±0.062	50.69±0.030

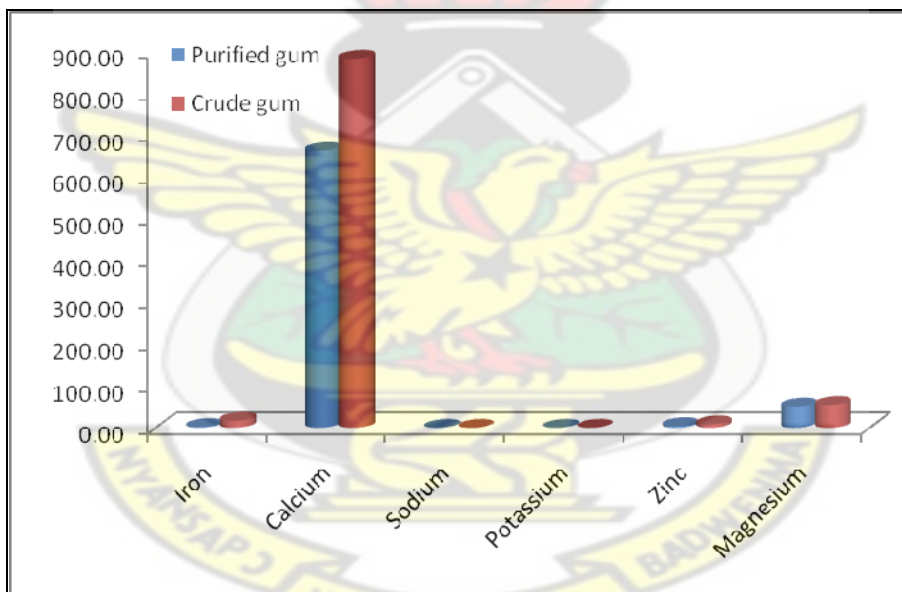


Fig 3.2 Metallic ion content of crude and purified gum

Table 3.2.1**pH of 2% crude gum with preservative**

Week	pH1	pH2	pH3	Mean pH
0	5.14	5.14	5.14	5.14 ± 0.000
1	5.64	5.68	5.71	5.68 ± 0.035
2	4.78	4.78	4.76	4.77 ± 0.012
3	4.79	4.78	4.80	4.79 ± 0.010
4	4.62	4.64	4.61	4.62 ± 0.015
5	4.92	4.93	4.95	4.93 ± 0.015

Table 3.2.2**pH of 2% crude gum without preservative**

Week	pH 1	pH 2	pH3	Mean pH
0	4.90	4.90	4.90	4.90 ± 0.000
1	5.23	5.25	5.31	5.26 ± 0.042
2	4.41	4.42	4.44	4.42 ± 0.015
3	4.42	4.39	4.44	4.42 ± 0.025
4	4.94	4.95	4.92	4.94 ± 0.015
5	4.64	4.63	4.62	4.63 ± 0.010

Table 3.2.3**pH of 2% purified gum with preservative at 25°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.40	5.40	5.40	5.40 ± 0.000
1	6.46	6.47	6.45	6.46 ± 0.010
2	4.00	4.01	3.99	4.00 ± 0.010
3	3.56	3.55	3.54	3.55 ± 0.010
4	3.48	3.46	3.47	3.47 ± 0.010
5	3.80	3.77	3.79	3.79 ± 0.015

Table 3.2.4**pH of 2% purified gum without preservative at 25°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.22	5.22	5.22	5.22 ± 0.000
1	5.43	5.42	5.44	5.43 ± 0.010
2	3.68	3.67	3.69	3.68 ± 0.010
3	3.64	3.66	3.65	3.65 ± 0.010
4	3.64	3.65	3.67	3.65 ± 0.015
5	3.66	3.66	3.65	3.66 ± 0.015

Table 3.2.5**pH of 2% Purified gum with preservative at 0-8°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.40	5.40	5.40	5.40 ± 0.000
1	5.38	5.39	5.40	5.39 ± 0.010
2	4.44	4.44	4.43	4.44 ± 0.006
3	4.43	4.46	4.45	4.45 ± 0.015
4	4.49	4.48	4.47	4.48 ± 0.010
5	4.55	4.54	4.56	4.55 ± 0.010

Table 3.2.6**pH of 2% purified gum without preservative at 0-8°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.22	5.22	5.22	5.22 ± 0.000
1	5.99	5.98	5.97	5.98 ± 0.010
2	4.94	4.92	4.93	4.93 ± 0.010
3	5.01	5.02	5.01	5.01 ± 0.006
4	5.03	5.02	5.04	5.03 ± 0.010
5	4.99	4.97	4.94	4.97 ± 0.025

Table 3.2.7**pH of 2% purified gum with preservative at 50°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.40	5.40	5.40	5.40 ± 0.000
1	5.58	5.56	5.49	5.54 ± 0.047
2	4.57	4.58	4.61	4.59 ± 0.021
3	4.64	4.62	4.73	4.66 ± 0.059
4	4.60	4.58	4.71	4.63 ± 0.070
5	4.65	4.65	4.63	4.64 ± 0.012

Table 3.2.8**pH of 2% purified gum without preservative at 50°C**

Week	pH 1	pH 2	pH3	Mean pH
0	5.22	5.22	5.22	5.22 ± 0.000
1	5.41	5.40	5.42	5.41 ± 0.010
2	4.39	4.42	4.45	4.42 ± 0.030
3	4.70	4.68	4.71	4.70 ± 0.015
4	4.58	4.55	4.58	4.57 ± 0.017
5	4.63	4.64	4.71	4.66 ± 0.044

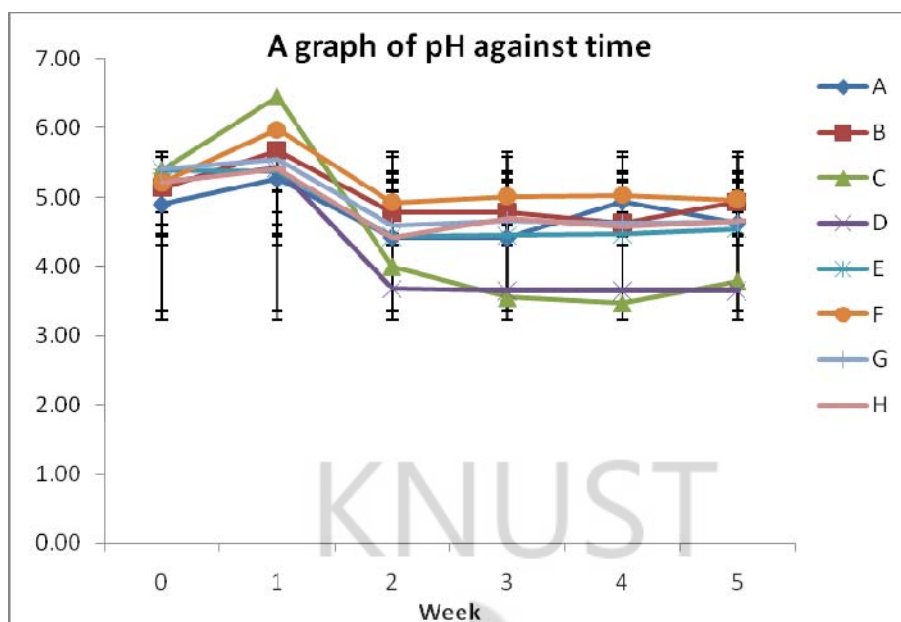


Fig.3.3 Relationship between pH of 2% crude and purified gum mucilage and storage time

- A- 2%w/v Crude gum with preservative stored at room temperature
- B- 2%w/v Crude gum without preservative stored at room temperature
- C- 2% Purified gum with preservative stored at room temperature
- D- 2% Purified gum without preservative stored at room temperature
- E- 2% Purified gum with preservative stored at 0-8°C
- F- 2% Purified gum without preservative stored at 0-8°C
- G- 2% Purified gum with preservative stored at 50°C
- H- 2% Purified gum without preservative stored at 50°C

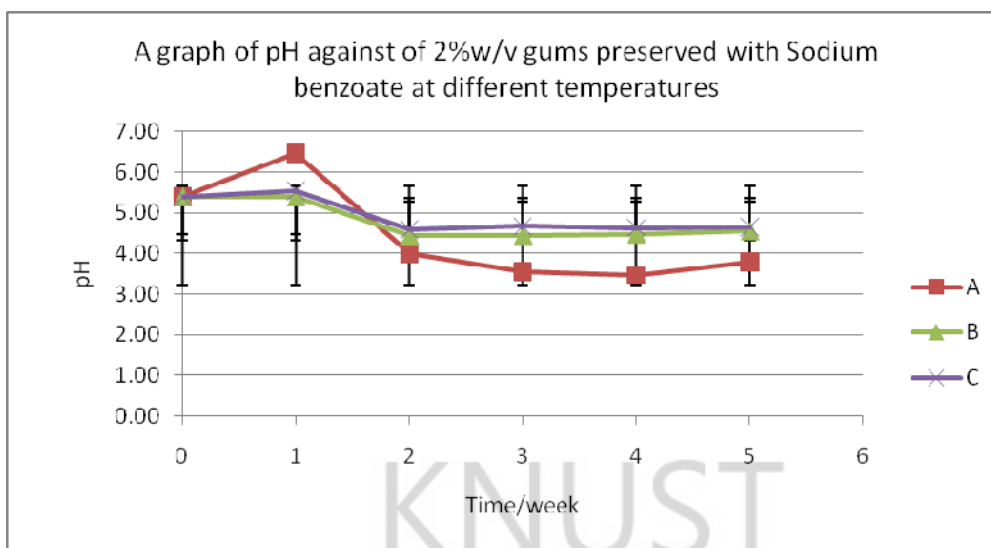


Fig. 3.3.1 Relationship between pH of preserved 2% crude and purified gum mucilage and storage time

- A- 2% Purified gum with preservative stored at room temperature
- B- 2% Purified gum with preservative stored at 0-8°C
- C- 2% Purified gum with preservative stored at 50°C

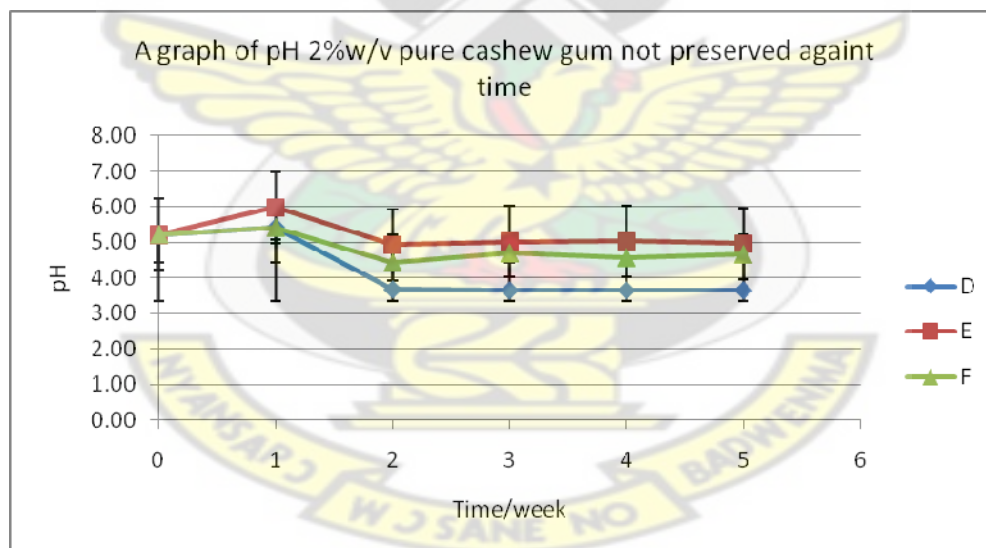


Fig. 3.3.2 Relationship between pH of unpreserved 2% purified gum mucilage and storage temperature

- D- 2% Purified gum without preservative stored at room temperature
- E- 2% Purified gum without preservative stored 0-8°C
- F- 2% Purified gum without preservative stored 50°C

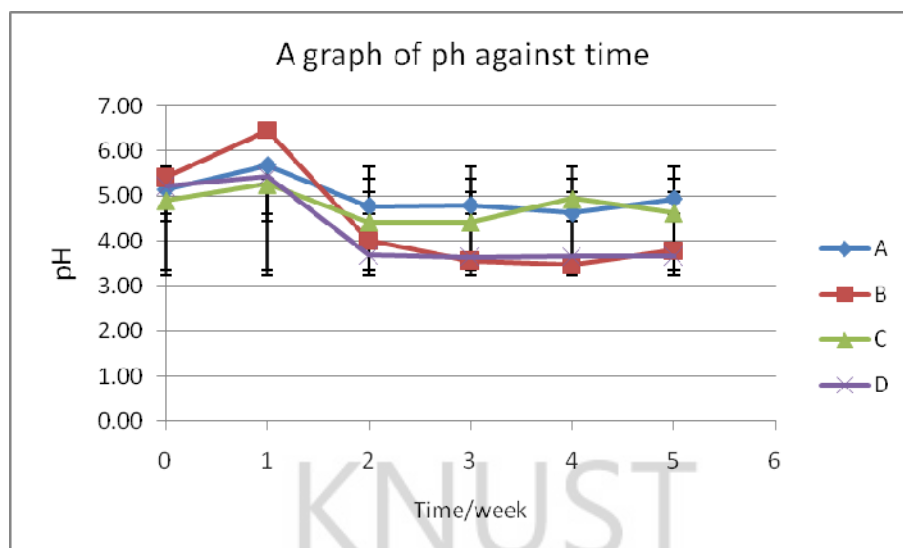
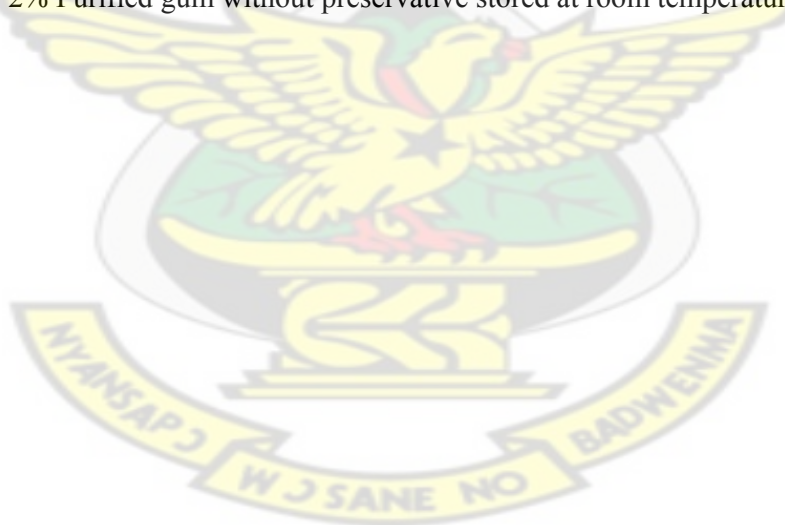


Fig 3.3.3 Relationship between pH of preserved and unpreserved 2% purified and crude gum mucilage and storage time

- A- 2% Crude gum with preservative stored at room temperature
- B- 2% Purified gum with preservative stored at room temperature
- C- 2% Crude gum without preservative stored at room temperature
- D- 2% Purified gum without preservative stored at room temperature



3.4.0 MICROBIAL TEST ON CRUDE AND PURIFIED GUM

Table 3.3.0

Microbial quality of crude gum

Selective culture medium	Results	Inference
MacConkey Agar	White colonies present No reddish colonies seen	Non Lactose fermenting coliforms present, No <i>E.coli</i>
Mannitol Salt Agar	No growth observed	Presumptive pathogenic staphylococci absent
Bismuth Sulphite Agar	Black zones with rabbit eye colonies with metallic sheen observed	Salmonella present
Cetrimide Agar	No greenish pigmented colonies seen	Pseudomonas absent
Sabauraud Agar+ Streptomycin	White to creamish growth observed	Fungi present

Table 3.3.1

Microbial quality of purified gum

Selective culture medium	Results	Inference
Mac Conkey Agar	White colonies present No reddish colonies seen	Non Lactose fermenting coliforms present, No <i>E.coli</i>
Mannitol Salt Agar	No growth observed	Presumptive pathogenic staphylococci absent
Bismuth Sulphite Agar	No Black zones with rabbit eye colonies with metallic sheen observed	Salmonella absent
Cetrimide Agar	No greenish pigmented colonies seen	Pseudomonas absent
Sabauraud Agar+ Streptomycin	White to creamish growth observed	Fungi present

Table 3.3.2

Antimicrobial activity of crude cashew gum

Organism	Concentration of gum %w/v			
	20.00%	30.00%	40.00%	50.00%
<i>E. coli</i>	+	+	+	+
<i>Pseudomonas aureginosa</i>	+	+	+	-
<i>Staph. Aureus</i>	+	+	+	+
<i>Klebsiella</i>	+	+	+	+
<i>Candida albicans</i>	+	+	+	+

Table 3.3.3

Antimicrobial activity of purified cashew gum

Organism	Concentration of gum %w/v			
	20.00%	30.00%	40.00%	50.00%
<i>E. coli</i>	+	+	+	+
<i>Pseudomonas aureginosa</i>	+	+	+	+
<i>Staph. Aureus</i>	+	+	+	+
<i>Klebsiella</i>	+	+	+	+
<i>Candida albicans</i>	+	+	+	+

+ - Growth of organism on the whole plate. i.e. no zone of inhibition present

- - Growth of organism on the plate. i.e. but zone of inhibition present

3.5.0 RHEOLOGICAL TEST

Table 3.4.0

The effect of concentration on the viscosity of cashew and acacia gum mucilage

Concentration of gum %w/v	Viscosity of Cashew gum/ cp	Viscosity of Acacia gum/cp
5	25.2	54.3
10	60.20	165.0
15	92.40	288.4
20	154.3	306.3
30	221.3	414.1
40	316.3	764.3

Table 3.4.1

The effect of temperature on the viscosity of cashew gum

Temperature/°C	Viscosity/cp
25	309.4
30	312.4
45	300.1
60	198.4
80	*101.4

*But gelling start at the surface

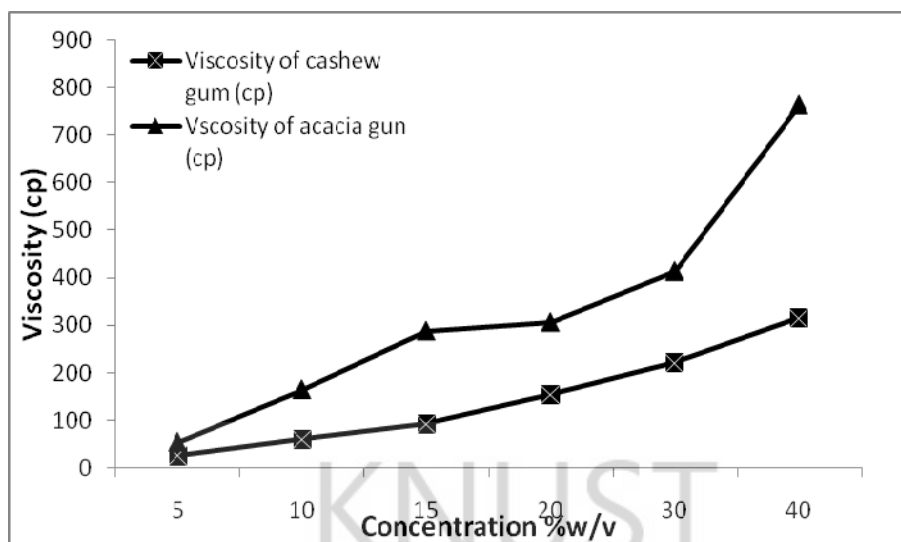


Fig. 3.4.0 Relationship between viscosity and concentration of gum mucilage

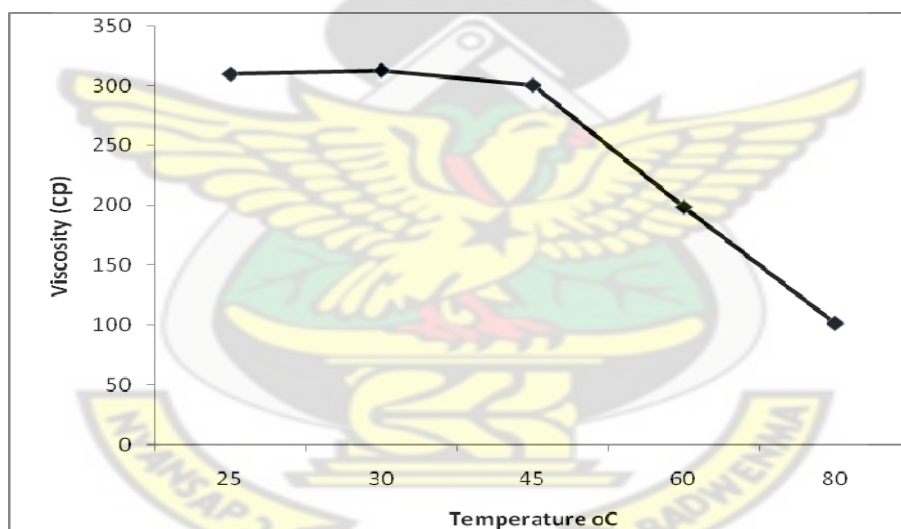


Fig. 3.4.1 Relationship between the viscosity and temperature of gum mucilage

3.6.0 EMULSIONS

Table 3.5.0

Stability ratio of primary emulsion prepared with a Fixed oil

Oil	Water	Gum	Result
4	2	1	Cracked
3	2	1	Cracked
4	2	1.5	Formed not stable
3	1	2	Gum hardened on addition of water
5	2	1	Cracked
2	3	2	Cracked
3	1.5	1	Formed and stable

Table 3.5.1

Stability ratio of primary emulsion prepared with a Mineral oil

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

Table 3.5.2**Stability ratio of primary emulsion prepared with a Volatile oil**

Oil	Water	Gum	Result
2	2	1	Cracked
5	4	5	Cracked
1	1	1	Formed, less stable
3	2	2.5	Formed, less stable

3.6.1 STABILISATION OF EMULSION**STABILISATION BY HOMOGENISATION**

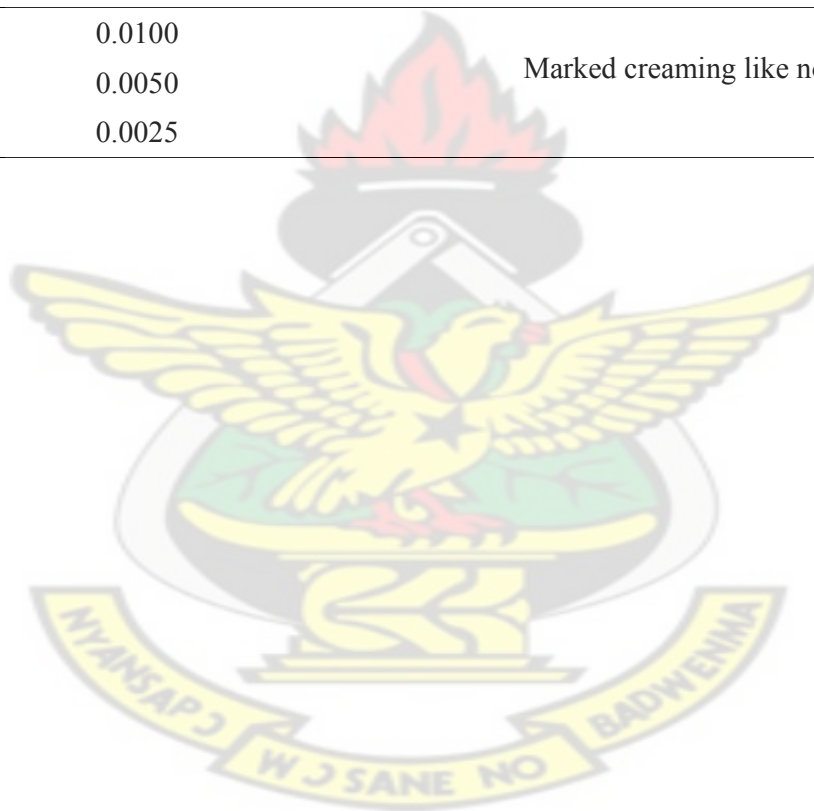
All emulsions exhibited creaming

Table 3.5.3**Stabilisation with xanthan gum + homogenisation**

Concentration of xanthan gum (% w/v)	Results
0.025	Creaming
0.050	Creaming
0.075	Creaming
0.100	Creaming
0.200	Marked Creaming
0.300	Marked Creaming
0.400	Marked Creaming
0.500	Marked Creaming

Table 3.5.4**Stabilisation by reducing interfacial tension with Tween 80**

Concentration of Tween 80 (% w/v)	Results
0.050	Three layers, marked creaming, gum thrown out of solution as emulsifying agent
0.025	
0.024	
0.022	
0.018	
0.015	Reduced creaming, gum not thrown out
0.0125	
0.0100	
0.0050	Marked creaming like no Tween
0.0025	



3.7.0 SUSPENSIONS

Table 3.6.0

Flow time for fresh and stored xanthan gum suspension

Concentration %w/v	Freshly prepared xanthan gum suspension	Stored xanthan gum suspension
0.10	9.5±0.26	10.77± 0.12
0.20	9.4±0.36	24.33±0.06
0.30	9.83± 0.06	41.77±0.59
0.40	10.17±0.15	79.00±1.00
0.50	11.3±0.10	141 ±6.00

Table 3.6.1

Apparent viscosity of freshly prepared and stored xanthan gum suspension

Concentration %w/v	Apparent viscosity of freshly prepared xanthan gum suspension/mlss ⁻¹	Apparent viscosity of Stored xanthan gum suspension/mlss ⁻¹
0.10	1.053	0.929
0.20	1.064	0.411
0.30	1.017	0.239
0.40	0.984	0.127
0.50	0.885	0.071

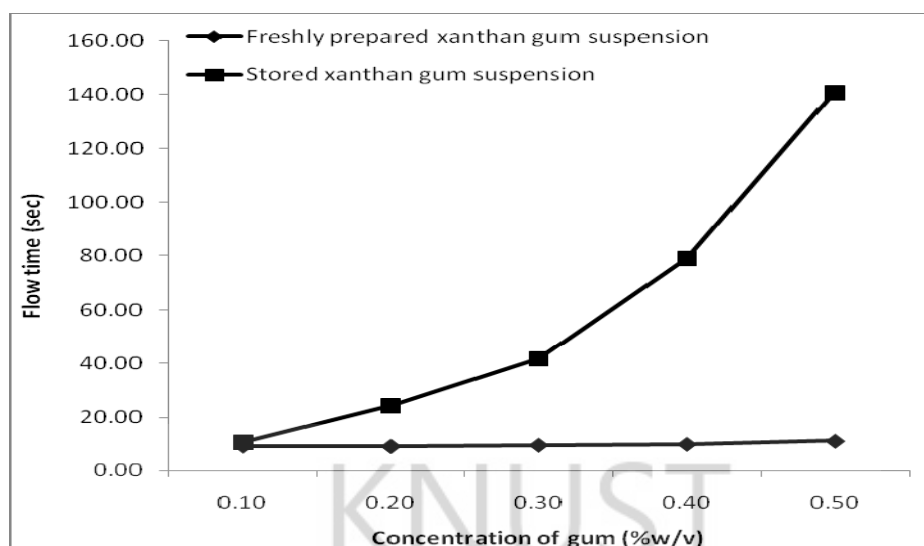


Fig. 3.5.0 Relationship between flow time of freshly prepared and stored xanthan gum suspensions and concentration of gum used

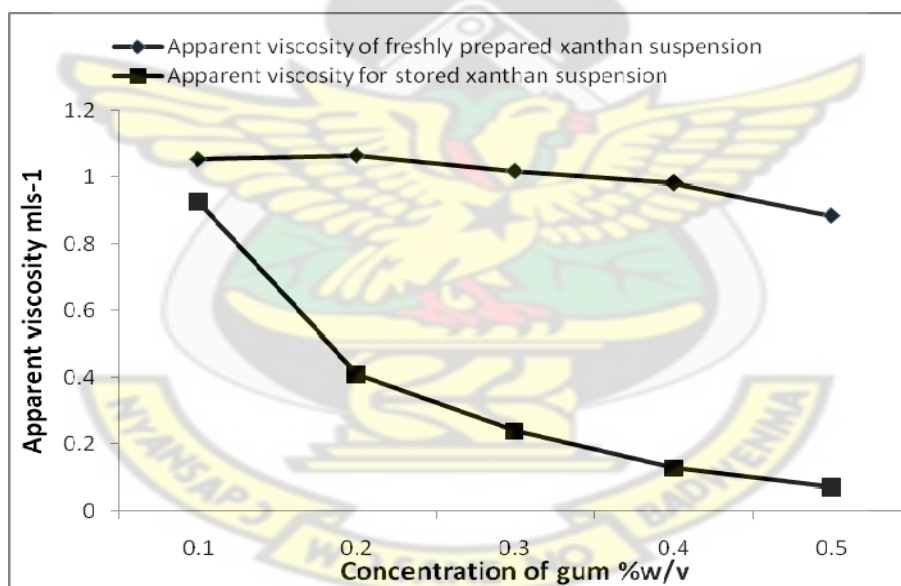


Fig. 3.5.1 Relationship between the apparent viscosity of freshly prepared xanthan gum suspensions and concentration of gum used

Table 3.6.2**Flow time of freshly prepared and stored cashew gum suspension**

Concentration %w/v	Freshly prepared cashew gum suspension	Stored cashew gum suspension
0.10	7.90±0.08	8.23±0.25
0.20	8.67± 0.23	8.17±0.12
0.30	8.38±0.37	8.37±0.15
0.40	8.34±0.16	7.87±0.15
0.50	8.25 ±0.15	7.77±0.06
1.00	8.48±0.06	8.45±0.16
2.00	8.29±0.07	8.21±0.02
3.00	8.68±0.18	8.73±0.02
4.00	8.53±0.54	8.94±0.05

Table 3.6.3**Apparent viscosity of freshly prepared and stored cashew gum suspension**

Concentration %w/v	Apparent viscosity of freshly prepared cashew gum suspension/mls ⁻¹	Apparent viscosity of Stored cashew gum suspension/ mls ⁻¹
0.10	1.266	1.215
0.20	1.154	1.224
0.30	1.193	1.195
0.40	1.199	1.271
0.50	1.212	1.288
1.00	1.179	1.183
2.00	1.206	1.218
3.00	1.152	1.145
4.00	1.172	1.119

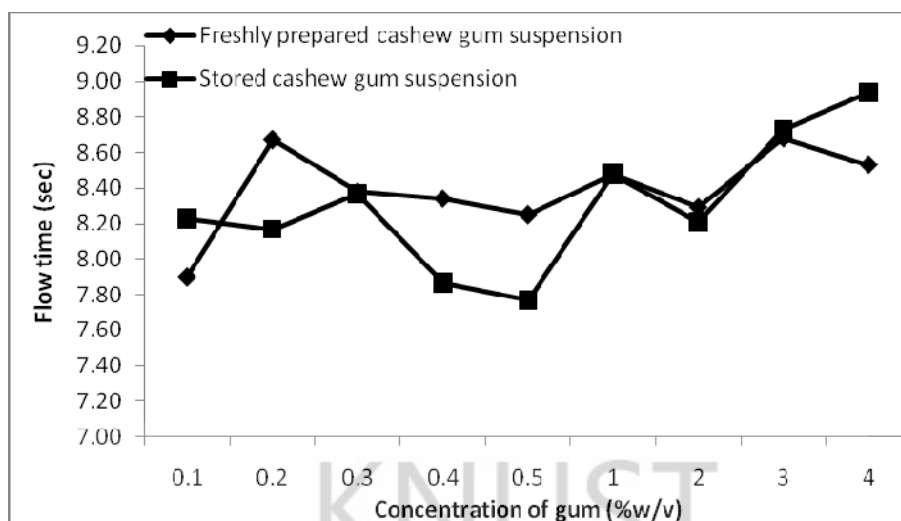


Fig. 3.5.2 Relationship between the flow time of freshly and stored cashew gum suspensions and concentration of gum used

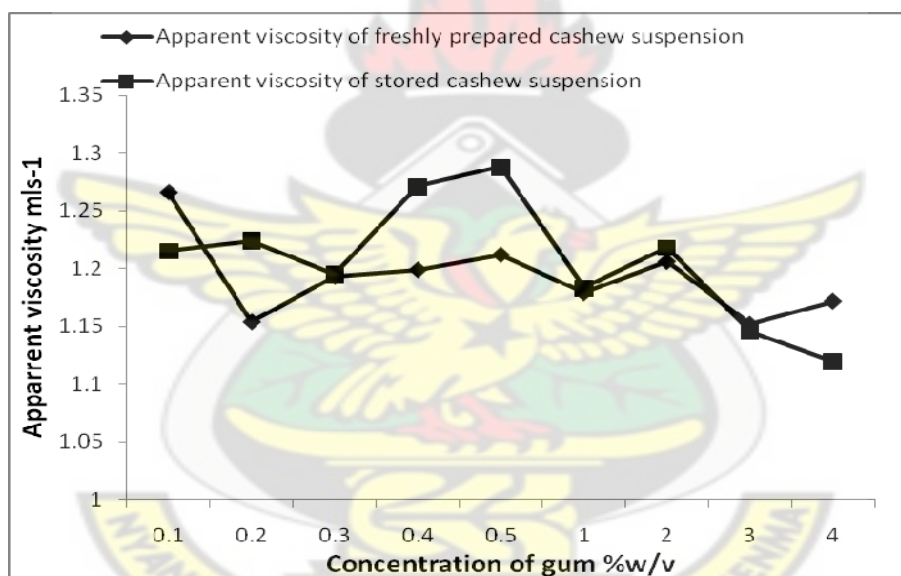


Fig. 3.5.3 Relationship between the apparent viscosity of freshly and stored cashew gum suspensions and concentration of gum used.

Table 3.6.4

Control- suspension with no gum

Control	Flow time
Fresh suspension without gum	7.88
Stored suspension without gum	7.87

Table 3.6.5**Apparent viscosity of freshly prepared and stored suspension without gum**

Apparent viscosity of freshly prepared suspension without gum/mls ⁻¹	Apparent viscosity of Stored suspension without gum /mls ⁻¹
1.269	1.271

Table 3.6.6**Relationship between concentration of xanthan gum and Sedimentation volume of xanthan gum suspension over 6hrs**

CONC/ DAY	X0.1/ml	X 0.2/ml	X 0.3/ml	X 0.4/ml	X 0.5/ml
0	100	100	100	100	100
1	76	80	80	84	90
2	62	66	76	84	90
3	58	64	70	80	84
4	54	60	67	74	78
5	50	58	64	68	74
6	46	54	50	64	70

Table 3.6.7**Relationship between concentration of cashew gum and Sedimentation volume of cashew gum suspension over 6 hours**

Conc/ day	C 0.1/ml	C 0.2/ml	C 0.3/ml	C 0.4/ml	C 0.5/ml	C 1/ml	C 2/ml	C 3/ml	C 4/ml	NG/ml
0	100	100	100	100	100	100	100	100	100	100
1	44	48	50	53	55	61.5	63	66	68	48
2	34	40	42	45	48	56.5	58	61	62	43
3	31	34	36	38	41	48	50	54	56	34
4	28	30	34	33	36	40	47	49	50	34
5	26	26	26	28	29	31	30	33	34	34
6	24	23	24	24	24	26	26	30	34	34

Table 3.6.8**Sedimentation volume of xanthan gum suspension over 42 days**

Conc./ day	X0.1/ml	X 0.2/ml	X 0.3/ml	X 0.4/ml	X 0.5/ml
0	100.0	100.0	100.0	100.0	100.0
3	42.0	48.0	54.0	56.0	58.0
6	42.0	48.0	54.0	56.0	58.0
9	42.0	48.0	54.0	55.0	58.0
12	42.0	48.0	54.0	55.0	58.0
15	42.0	48.0	54.0	55.0	58.0
18	42.0	48.0	54.0	55.0	58.0
21	42.0	48.0	54.0	55.0	58.0
24	42.0	48.0	54.0	55.0	58.0
27	42.0	48.0	54.0	55.0	58.0
30	42.0	48.0	54.0	55.0	58.0
33	42.0	48.0	54.0	55.0	58.0
36	42.0	48.0	54.0	55.0	58.0
39	42.0	48.0	54.0	55.0	58.0
42	42.0	48.0	54.0	55.0	58.0

X 0.1/ml = Volume of sediment of 0.1% xanthan gum

X 0.2/ml = Volume of sediment of 0.2% xanthan gum

X 0.3/ml = Volume of sediment of 0.3% xanthan gum

X 0.4/ml = Volume of sediment of 0.4% xanthan gum

X 0.5/ml = Volume of sediment of 0.5% xanthan gum

Table3.6.9**Sedimentation of cashew gum suspension over 42 days**

Conc./ day	C 0.1/ml	C 0.2/ml	C 0.3/ml	C 0.4/ml	C 0.5/ml	C 1/ml	C 2/ml	C 3/ml	C 4/ml	NG/ml
0	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
3	20.00	21.00	20.00	20.00	20.00	20.00	22.00	26.00	30.00	34.00
6	20.00	21.00	20.00	20.00	20.00	20.00	21.00	26.00	30.00	34.00
9	20.00	21.00	19.00	19.00	19.00	20.00	21.00	26.00	30.00	34.00
12	20.00	21.00	19.00	19.00	19.00	19.00	21.00	25.00	29.00	34.00
15	20.00	21.00	19.00	19.00	18.00	19.00	21.00	25.00	29.00	34.00
18	23.00	21.00	19.00	18.00	18.00	19.00	21.00	25.00	29.00	34.00
21	20.00	21.00	19.00	18.00	18.00	19.00	21.00	25.00	29.00	34.00
24	20.00	21.00	19.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00
27	20.00	21.00	18.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00
33	20.00	21.00	18.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00
36	20.00	21.00	18.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00
39	20.00	21.00	18.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00
42	20.00	21.00	18.00	18.00	18.00	19.00	21.00	25.00	28.00	34.00

C 0.1/ml = Volume of sediment of 0.1% cashew gum

C 0.2/ml = Volume of sediment of 0.2% cashew gum

C 0.3/ml = Volume of sediment of 0.3% cashew gum

C 0.4/ml = Volume of sediment of 0.4% cashew gum

C 0.5/ml = Volume of sediment of 0.5% cashew gum

C 1/ml = Volume of sediment of 1% cashew gum

C 2/ml = Volume of sediment of 2% cashew gum

C 3/ml = Volume of sediment of 3% cashew gum

C 4/ml = Volume of sediment of 4% cashew gum

CNG/ml = Volume of sediment of NO gum

Table 3.6.10**Redispersibility of xanthan gum suspension**

Concentration (% w/v)	Xanthan gum suspension
0.10	Easily redisperses on shaking
0.20	Easily redisperses on shaking
0.30	Redisperse on vigorous shaking
0.40	Redisperse on vigorous shaking
0.50	Redisperse on vigorous shaking

Table 3.6.11**Redispersibility of cashew gum suspension**

Concentration (% w/v)	Cashew gum suspension
0.10	Easily redispersed
0.20	Easily redispersed
0.30	Easily redispersed
0.40	Easily redispersed
0.50	Easily redispersed
1.00	Easily redispersed
2.00	Easily redispersed
3.00	Cake formed, redispersed on vigorous shaking
4.00	Cake formed redispersed on vigorous shaking



Fig. 3.5.4 Sedimentation volume of xanthan gum suspension before redispersion



Fig. 3.5.5 Sedimentation volume of xanthan gum suspension after redispersion



Fig. 3.5.6 Sedimentation volume of cashew gum suspension before redispersion as compared to suspension without gum



Fig.3.5.7 Cashew gum suspension three days after redispersion

3.8.0 FORMULATION OF METRONIDAZOLE TABLETS

Table 3.7.0

Bulk density measurements on granules

Granules	Weight of granules(g)	Initial Volume/ml(V_o)	Tapped Volume(V_f)
20% Acacia	30.20	52.50	46.00
10% Cashew	30.20	52.00	40.00
20% Cashew	30.20	52.00	46.50
30% Cashew	30.20	50.50	46.00
40% Cashew	30.10	51.00	46.00

Table 3.7.1

Bulk density measurements on granules

Granules	Bulk Density (D_o)	Tapped Density (D_f)	Hausner's ratio	% Compressibility
20% Acacia	0.575	0.657	1.143	12.481
10% Cashew	0.581	0.755	1.299	23.046
20% Cashew	0.581	0.692	1.191	16.040
30% Cashew	0.598	0.657	1.099	8.980
40% Cashew	0.590	0.654	1.108	9.786

Formulation of 100 mg Metronidazole tablets

Tablet weight = 400 mg

Number of Tablets = 200

Practical yield = 158

3.8.1 QUALITY TEST CARRIED ON TABLETS

3.8.1.1 UNIFORMITY OF WEIGHT

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

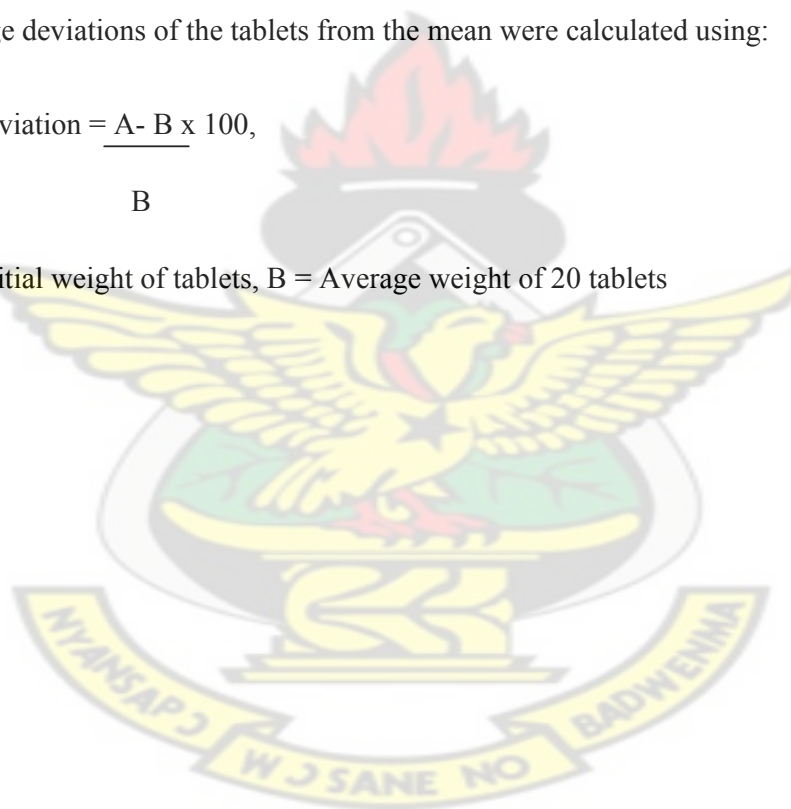


Table 3.8.0**Uniformity of weight of Metronidazole tablets formulated with 20% Acacia gum mucilage**

Tablet no.	Tablet weight(Ag)	(A-B)g	(A-B)g/B)	Percentage deviation
1	0.421	0.003	0.007	0.718
2	0.417	-0.001	-0.002	-0.239
3	0.416	-0.002	-0.005	-0.478
4	0.417	-0.001	-0.002	-0.239
5	0.418	0.000	0.000	0.000
6	0.416	-0.002	-0.005	-0.478
7	0.416	-0.002	-0.005	-0.478
8	0.415	-0.003	-0.007	-0.718
9	0.411	-0.007	-0.017	-1.675
10	0.411	-0.007	-0.017	-1.675
11	0.422	0.004	0.010	0.957
12	0.419	0.001	0.002	0.239
13	0.420	0.002	0.005	0.478
14	0.420	0.002	0.005	0.478
15	0.421	0.003	0.007	0.718
16	0.415	-0.003	-0.007	-0.718
17	0.416	-0.002	-0.005	-0.478
18	0.419	0.001	0.002	0.239
19	0.422	0.004	0.010	0.957
20	0.418	0.000	0.000	0.000
Total			8.350	
Average			0.418	
Stdev			0.0032	

Table 3.8.1**Uniformity of weight of Metronidazole tablets formulated with 10% Cashew gum mucilage**

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.428	0.001	0.002	0.234
2	0.429	0.002	0.005	0.468
3	0.426	-0.001	-0.002	-0.234
4	0.431	0.004	0.009	0.937
5	0.427	0.000	0.000	0.000
6	0.419	-0.008	-0.019	-1.874
7	0.421	-0.006	-0.014	-1.405
8	0.431	0.004	0.009	0.937
9	0.421	-0.006	-0.014	-1.405
10	0.431	0.004	0.009	0.937
11	0.424	-0.003	-0.007	-0.703
12	0.424	-0.003	-0.007	-0.703
13	0.425	-0.002	-0.005	-0.468
14	0.433	0.006	0.014	1.405
15	0.432	0.005	0.012	1.171
16	0.431	0.004	0.009	0.937
17	0.428	0.001	0.002	0.234
18	0.426	-0.001	-0.002	-0.234
19	0.431	0.004	0.009	0.937
20	0.422	-0.005	-0.012	-1.171
Total			8.538g	
Average			0.427g	
Stdev			0.0042	

Table 3.8.2**Uniformity of weight of Metronidazole tablets formulated with 20% Cashew gum mucilage**

Tablet no.	Tablet weight(A)g	(A- B)g	(A- B)g/B	Percentage deviation
1	0.425	0.008	0.019	1.918
2	0.420	0.003	0.007	0.719
3	0.420	0.003	0.007	0.719
4	0.412	-0.005	-0.012	-1.199
5	0.417	0.000	0.000	0.000
6	0.418	0.001	0.002	0.240
7	0.417	0.000	0.000	0.000
8	0.416	-0.001	-0.002	-0.240
9	0.424	0.007	0.017	1.679
10	0.418	0.001	0.002	0.240
11	0.414	-0.003	-0.007	-0.719
12	0.408	-0.009	-0.022	-2.158
13	0.411	-0.006	-0.014	-1.439
14	0.407	-0.010	-0.024	-2.398
15	0.414	-0.003	-0.007	-0.719
16	0.419	0.002	0.005	0.480
17	0.424	0.007	0.017	1.679
18	0.421	0.004	0.010	0.959
19	0.416	-0.001	-0.002	-0.240
20	0.417	0.000	0.000	0.000
Total			8.338g	
Average			0.417g	
Stdev			0.0049	

Table 3.8.3**Uniformity of weight of Metronidazole tablets formulated with 30% Cashew gum mucilage**

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.403	-0.012	-0.029	-2.892
2	0.409	-0.006	-0.014	-1.446
3	0.414	-0.001	-0.002	-0.241
4	0.410	-0.005	-0.012	-1.205
5	0.421	0.006	0.014	1.446
6	0.416	0.001	0.002	0.241
7	0.414	-0.001	-0.002	-0.241
8	0.412	-0.003	-0.007	-0.723
9	0.414	-0.001	-0.002	-0.241
10	0.417	0.002	0.005	0.482
11	0.407	-0.008	-0.019	-1.928
12	0.414	-0.001	-0.002	-0.241
13	0.406	-0.009	-0.022	-2.169
14	0.415	0.000	0.000	0.000
15	0.419	0.004	0.010	0.964
16	0.418	0.003	0.007	0.723
17	0.418	0.003	0.007	0.723
18	0.424	0.009	0.022	2.169
19	0.420	0.005	0.012	1.205
20	0.423	0.008	0.019	1.928
Total			8.294g	
Average			0.415g	
Stdev			0.0056	

Table 3.8.4**Uniformity of weight of Metronidazole tablets formulated with 40% Cashew gum mucilage**

Tablet no.	Tablet weight(Ag)	(A- B)g	(A- B)g/B	Percentage deviation
1	0.420	0.003	0.007	0.719
2	0.420	0.003	0.007	0.719
3	0.418	0.001	0.002	0.240
4	0.418	0.001	0.002	0.240
5	0.418	0.001	0.002	0.240
6	0.417	0.000	0.000	0.000
7	0.415	-0.002	-0.005	-0.480
8	0.421	0.004	0.010	0.959
9	0.415	-0.002	-0.005	-0.480
10	0.416	-0.001	-0.002	-0.240
11	0.417	0.000	0.000	0.000
12	0.407	-0.010	-0.024	-2.398
13	0.415	-0.002	-0.005	-0.480
14	0.418	0.001	0.002	0.240
15	0.415	-0.002	-0.005	-0.480
16	0.414	-0.003	-0.007	-0.719
17	0.415	-0.002	-0.005	-0.480
18	0.418	0.001	0.002	0.240
19	0.419	0.002	0.005	0.480
20	0.420	0.003	0.007	0.719
Total			8.336g	
Average			0.419g	
Stdev			0.0031	

3.8.2 FRIABILITY

Table 3.8.5

FRIABILITY TEST						
GUM CONCENTRATION	INITIAL WEIGHT(g)	FINAL WEIGHT(g)	LOSS(g)	LOSS/INITAL WEIGHT	% LOSS	AVE.% LOSS
20% ACACIA	7.120	7.071	0.049	0.007	0.688	0.664
	7.340	7.293	0.047	0.006	0.640	
10% CASHEW	7.421	7.276	0.145	0.020	1.954	1.560
	7.369	7.283	0.086	0.012	1.167	
20% CASHEW	7.453	7.337	0.116	0.016	1.556	1.428
	7.459	7.362	0.097	0.013	1.300	
30% CASHEW	7.483	7.412	0.071	0.009	0.949	0.870
	7.456	7.397	0.059	0.008	0.791	
40% CASHEW	7.582	7.541	0.041	0.005	0.541	0.534
	7.585	7.545	0.040	0.005	0.527	

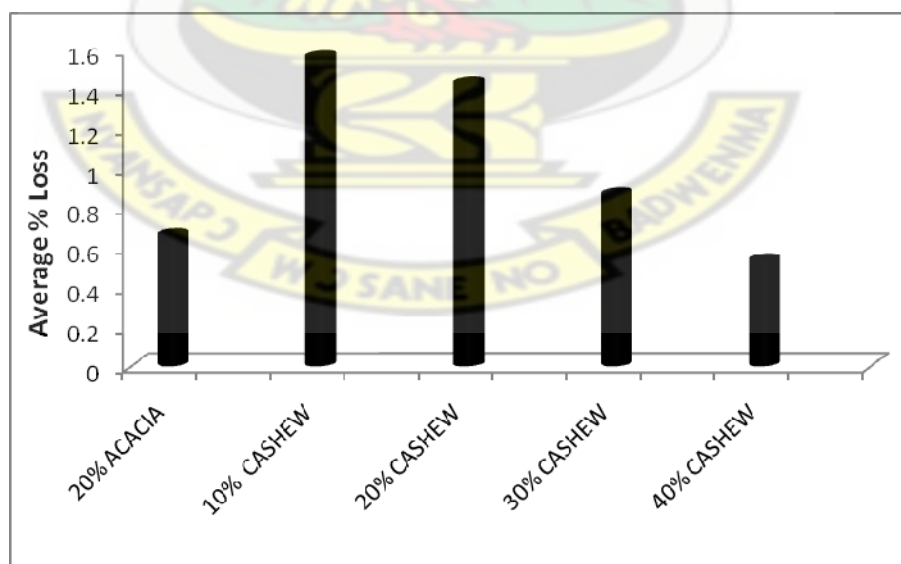


Fig. 3.6 Relationship between gum concentration and friability of tablets

3.8.3 HARDNESS

Table 3.8.6

Effect of gum concentration on hardness of metronidazole tablet formulations

Type of formulation	Mean force applied(kg)
20% Acacia	5.00 ± 0.47
10% Cashew	3.37 ± 0.53
20% Cashew	4.96 ± 1.15
30% Cashew	4.65 ± 0.49
40% Cashew	6.58 ± 0.61

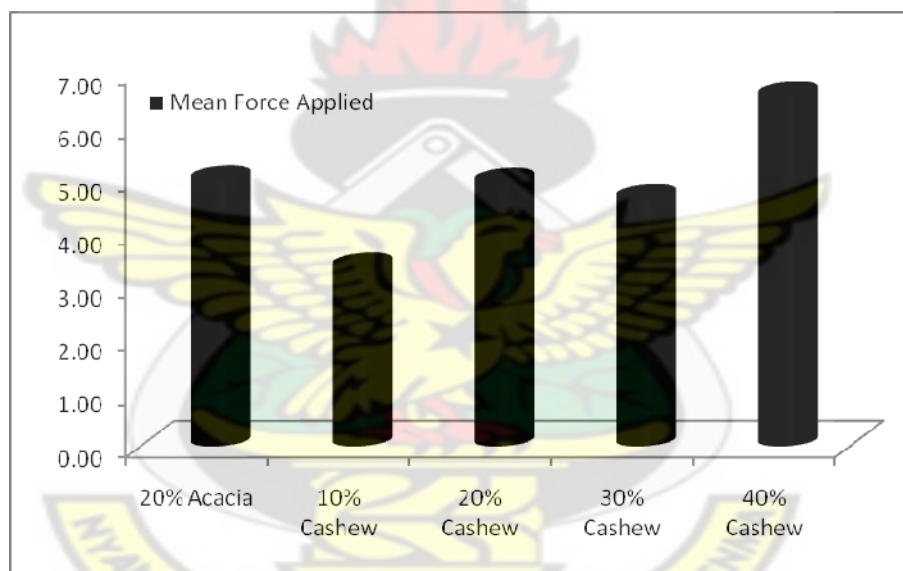


Fig.3.7 Relationship between gum concentration and tablet hardness

3.8.4 DISINTEGRATION

Table 3.8.7

Effect of gum concentration on Disintegration time of Metronidazole Formulations

Gum concentration	Disintegration Time			
	T1/ min	T2/ min	T3/ min	Tave/ min
20% Acacia	9.53	9.48	10.01	9.67 ± 0.293
10% Cashew	0.90	0.97	1.02	0.96 ± 0.060
20% Cashew	1.28	1.23	1.36	1.29 ± 0.066
30% Cashew	4.02	4.11	4.38	4.17 ± 0.187
40% Cashew	11.54	10.48	11.52	11.18 ± 0.606

3.8.5 DISSOLUTION PROFILE OF METRONIDAZOLE TABLETS FORMULATED WITH DIFFERENT GUM CONCENTRATIONS

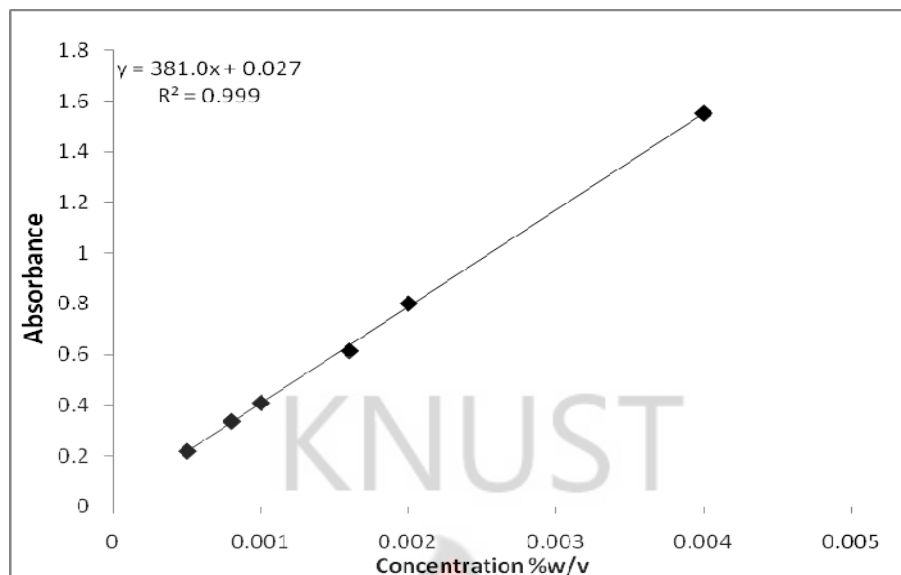
Table 3.8.8

Absorbance of pure metronidazole in 0.1M HCl

Blank used: 0.1M HCl

Concentration %w/v	Absorbance
0.0005	0.219 ± 0.04
0.0008	0.337 ± 0.026
0.0010	0.410 ± 0.017
0.0016	0.615 ± 0.011
0.0020	0.802 ± 0.034
0.0040	1.552 ± 0.015

Fig. 3.8 Calibration curve of pure metronidazole powder (in 0.1M HCl)



Calculation of concentration of Metronidazole

From the calibration curve the equation of the graph of pure metronidazole powder dissolved in 0.1M HCl :

$$y = 381.0x + 0.027$$

where y = absorbance, and x = concentration

$$\text{Hence } x = \frac{y - 0.027}{381.0}$$

Thus for a tablet having an absorbance of 0.186

Its concentration, $x = \frac{0.186 - 0.027}{381.0}$

$$X = 0.00042$$

$$4.2 \times 10^{-4} \text{ w/v}$$

Multiplying 'x' by the dilution factor of 10 gives the concentration of drug dissolved.

$$4.20 \times 10^{-4} \times 10 = 4.2 \times 10^{-3} \% \text{w/v}$$

$4.2 \times 10^{-3} \% \text{w/v}$ was contained in 1ml of solution taken

Calculation of percentage release

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

100mg of Metronidazole in 900ml of solution

Total concentration = 0.01111%w/v

Then, % release = $(0.0042/0.01111) \times 100$

= 37.65%

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

DRUG RELEASE PROFILES

Table 3.8.9

Drug release profile of tablets formulated with 20% Acacia gum mucilage

Time/ min	Mean absorbance	Concentration %w/v	Concentration x Dilution factor	Percentage release
5	0.18600	0.00042	0.00417	37.56
10	0.32700	0.00079	0.00787	70.87
15	0.41700	0.00102	0.01024	92.14
30	0.41700	0.00102	0.01024	92.14
45	0.42300	0.00104	0.01039	93.55
60	0.43400	0.00107	0.01068	96.15

Table 3.8.10

Drug release profile of tablets formulated with 10% Cashew gum mucilage

Time/ min	Mean absorbance	Concentration %w/v	Concentration x Dilution factor	Percentage release
5	0.4470	0.00110	0.01102	99.22
10	0.4520	0.00112	0.01115	100.40
15	0.4630	0.00114	0.01144	103.00
30	0.4580	0.00113	0.01131	101.82
45	0.4620	0.00114	0.01142	102.77
60	0.4650	0.00115	0.01150	103.47

Table 3.8.11**Drug release profile of tablets formulated with 20% Cashew gum mucilage**

Time/ min	Mean absorbance	Concentration %w/v	Concentration x Dilution factor	Percentage release
5	0.4230	0.00104	0.01039	93.55
10	0.4180	0.00103	0.01026	92.37
15	0.4270	0.00105	0.01050	94.50
30	0.4290	0.00106	0.01055	94.97
45	0.4400	0.00108	0.01084	97.57
60	0.4480	0.00110	0.01105	99.46

Table 3.8.12**Drug release profile of tablets formulated 30% Cashew gum mucilage**

Time/ min	Mean absorbance	Concentration %w/v	Concentration x Dilution factor	Percentage release
5	0.4200	0.00103	0.01031	92.84
10	0.4300	0.00106	0.01058	95.21
15	0.4360	0.00107	0.01073	96.62
30	0.4320	0.00106	0.01063	95.68
45	0.4260	0.00105	0.01047	94.26
60	0.4280	0.00105	0.01052	94.73

Table 3.8.13

Drug release profile of tablets formulated with 40% Cashew gum mucilage

Time/ min	Mean absorbance	Concentration %w/v	Concentration x Dilution factor	Percentage release
5	0.2470	0.00058	0.00577	51.97
10	0.4000	0.00098	0.00979	88.12
15	0.4260	0.00105	0.01047	94.26
30	0.4310	0.00106	0.01060	95.44
45	0.4280	0.00105	0.01052	94.73
60	0.4350	0.00107	0.01071	96.39

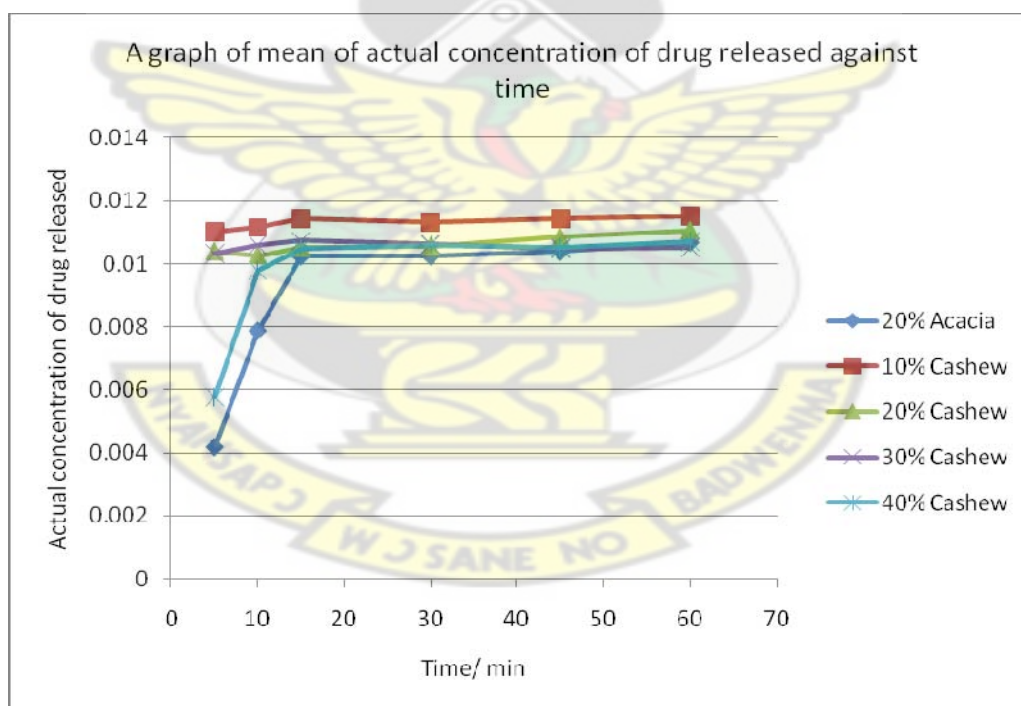


Fig 3.9 Relationship between actual concentration of drug released and time

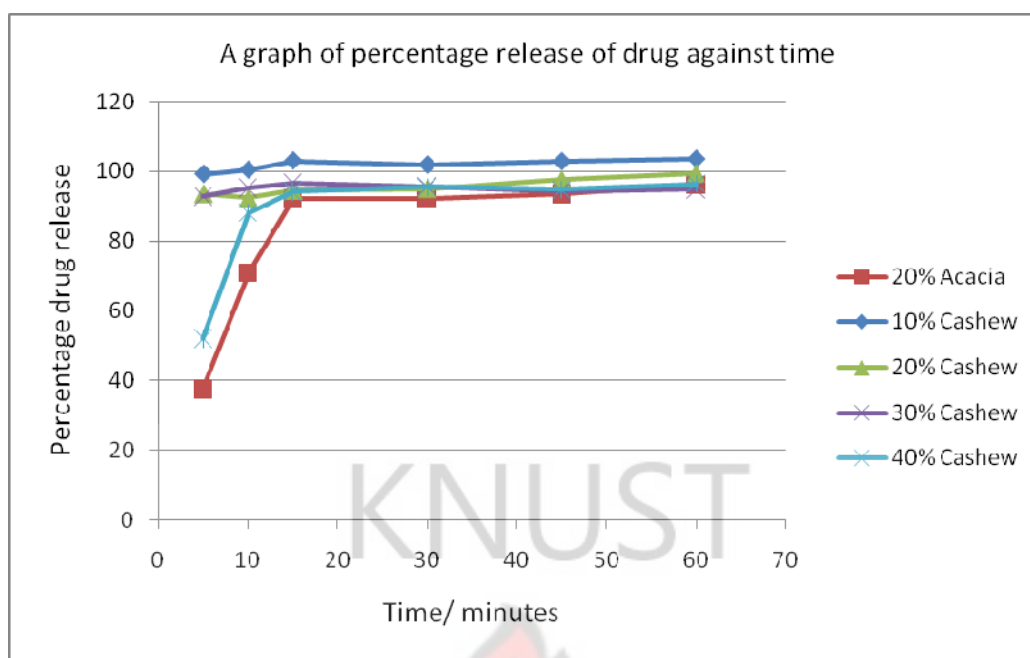
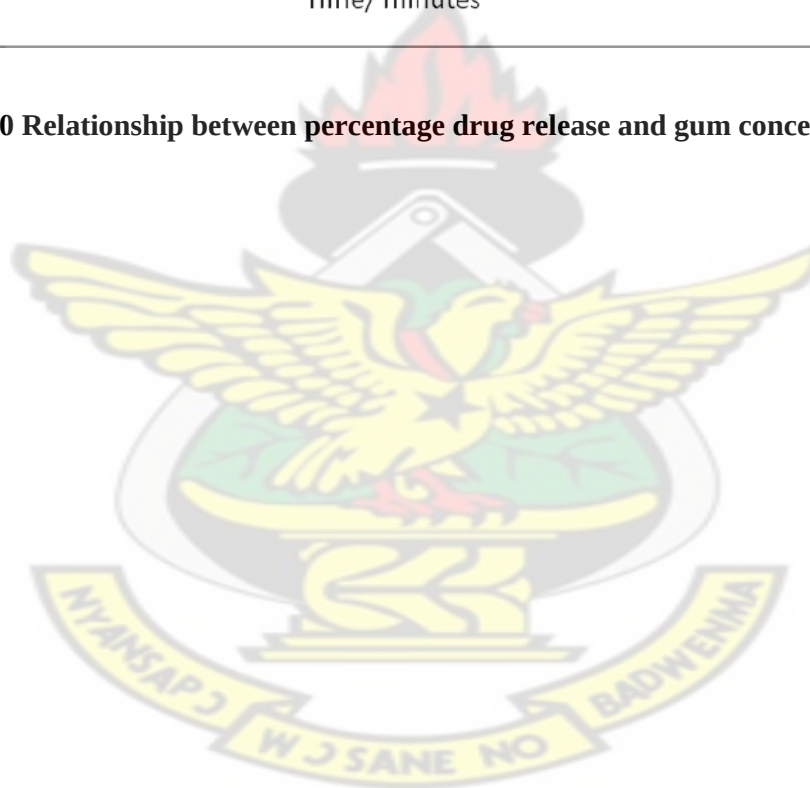


Fig 3.10 Relationship between percentage drug release and gum concentration



CHAPTER FOUR

DISCUSSION AND CONCLUSION

4.1.0 DISCUSSION

- **Macroscopic properties of cashew gum**

The macroscopic properties of cashew gum are shown in Table 3.1.0. Cashew gum occurred as thin long cylindrical, or round to ovoid tears. Its colour ranged from glassy white to golden brown. The colour of the gum is normally dependant on how long it has remained on the bark of the tree. Gums stuck to tree barks for long have a lot of tannins which tend to influence their colour (Smith and Montgomery, 1959). The thick gums fractures with much difficulty whilst the thin one fractures rather easily. The odour of the gum was somewhat characteristic but not that strong, but its use in formulation did not affect the odour of the formulation. The taste of the gum is bland and makes it suitable for pharmaceutical use.

- **Moisture content and insoluble matter of cashew gum**

From Table 3.1.1, the amount of moisture found in the purified and crude gum were 10.44 % and 11.19 % respectively. The difference between the moisture content of the purified and crude gums can be attributed to the purification and drying process of the crude gum. The moisture content calculated, complied with the required standard set in the U.S.P (2002) as 15 % w/w and in the B.P (2008) as 15 % w/w.

Fig 3.1.1 shows that the purified form of the gum had a relatively low insoluble matter compared to the crude form. The purification process and the method employed certainly removed most of the impurities in the crude gum. The gum was dissolved, filtered and reprecipitated so the purified gum will have less impurity as compared to the crude gum. Crude cashew gum had 0.35 % of insoluble matter present. Though this value falls within the B.P limits (0.5 % w/w) and U.S.P limit (0.5 % w/w), comparing it to that of the purified gum which was 0.28 % w/w, the percentage of insoluble matter in the crude was high. This implies that, improving upon the process of harvesting and cleaning of the gums would result in decreased levels of impurity and contamination.

- **Mineral content of crude and purified gum**

Table 3.2 shows the metallic ion content of the purified and crude cashew gum. Very high levels of certain metals when ingested can be poisonous. Determination of the metallic ion content of the Cashew gums revealed that, both the crude and the purified forms of the gum

contained varying amounts of metallic ions. But looking at Fig. 3.2, it shows some level of difference in the metallic ion content of the purified and the crude gum. The metallic ion content of the purified gum was less than that of the crude gum. This can be attributed to the purification process. From Table 3.2 and Fig. 3.2, the dominant ion in both samples was Calcium, followed by Magnesium and then Iron. The levels of Sodium, Potassium and Zinc were very low.

- **Acidity of gum**

As seen in Tables 3.2.1 - 3.2.8, the pH of 2 % w/v crude and purified gums mucilage was acidic. The acidic nature of the gums could be attributed to the presence of the acidic functional group of sugar units in the gum. The crude gum was more acidic than the purified gum, this can be accounted for the fact that, crude gum contains anacardic acid and this acid is removed by purification (Torquato, et al. 2004). The gum being acidic can easily partition into aqueous or oily phases, thus acting as an emulsifying agent. The gums that were preserved with 0.1 % w/v sodium benzoate generally showed a higher pH than the unpreserved gums. The pH of sodium benzoate solution was high so that accounts for the pH difference between the preserved and unpreserved gum mucilages. The gum solutions were preserved to prevent possible microbial degradation and thus improve the stability of the samples. Generally, the extent of pH changes in both preserved gums and unpreserved gum mucilage was not all that prominent. The pH changes observed in the preserved gum mucilage may be due to chemical decomposition and less of microbial decomposition. The pH changes of the gum mucilage stored at 25°C was faster than in the mucilage stored in the fridge and at 50°C though the pH changes observed in samples stored in the fridge was less drastic. This also implies that, the temperature of storage had effect on the stability of the gum mucilage. Generally all the mucilage showed a slow decline in pH over the six weeks storage period.

- **Viscosity of Gums**

Looking at Tables 3.4.0 and 3.4.1 and Figs. 3.4.1 and 3.4.2, the viscosities of gum mucilages changed with concentration and temperature. At all concentrations, the viscosity of cashew gum was less than that of acacia gums. The viscosity of gums is also affected by the nature and treatment of the gum such as purification and age at which the gum was picked (Smith and Montgomery, 1959). The viscosity of cashew gum increased with concentration and decreased with increasing temperature, which is consistent with observations made by Gyedu- Akoto et al, 2008. There was thinning of the gum mucilage as the temperature

increased. An interesting observation made as the gum mucilage was heated at 80°C was the formation of a gel at the surface. This can be attributed to the evaporation of water at that high temperature from the gum mucilage and hence the eventual gelling of the mucilage.

- **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 Tables 3.3.0 and 3.3.1, It can be observed that, both purified gum and crude gum did not have *E.coli*, *Pseudomonas aeruginosa* or pathogenic Staphylococci. However, Salmonella specie was found in the crude gum but not the purified gum. Both gums had fungi present but fungal growth was scanty on the purified gum plate but profuse growth 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 cashew gum. The purified gum is therefore more likely to meet the criteria for microbial quality of pharmaceutical excipients than the crude gum.

- **Antimicrobial property of gum**

Crude and purified cashew tree gums at high concentrations were tested for their antimicrobial activity against bacteria, and fungi. Cashew gum presented no activity on the studied organisms. One study by Torquato et al. (2004) showed that cashew gum presented only a weak activity against *Saccharomyces cerevisiae* and no activity was observed against all other microorganisms tested. These researchers attributed the low antimicrobial activity of the purified cashew gum studied to the possible removal of anacardic acid present in the raw gum during purification. However, in the present study no antimicrobial activity was observed for both the crude and purified cashew gum. This implies that anacardic acid may not be present in adequate amounts even in the crude gum to elicit any antimicrobial action.

- **Preparation of emulsions**

Gums are normally used as emulsifying agents. Cashew gum was investigated for its emulsifying property. Different ratios of oil, water and gum were used for the preparation of primary emulsion out of fixed oil, mineral oil and volatile oil. The mineral oil used was paraffin oil, the fixed oil was castor oil and the volatile oil used was peppermint oil. From Tables 3.5.0 - 3.5.2, the ratio of oil to water to gum for the preparation of stable primary emulsions, determined for fixed oil was 3:1.5:1, for mineral oil was 5:3:2 and that of volatile

oil was 3:2:2.5. Different ratios were studied and the above recorded values were the ratios that gave very stable primary emulsions. It was observed that if the ratio of gum was more than that of the oil, once water was added in an attempt to form the primary emulsion, the gum was thrown out of the oil.

Of all the ratios investigated for volatile oil, primary emulsion formation was a problem. The stable ratio determined even broke down on standing for a short time. The wet gum method worked well for the preparation of the primary emulsion from fixed oil and volatile oil and the dry gum method worked well for primary emulsions prepared from mineral oil.

- **Stabilisation of Emulsion**

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 the emulsions continued to exhibit creaming. On addition of the thickening agent, there was marked creaming, even greater than emulsions prepared without a thickening agent.

When the interfacial tension was modified with Tween 80 an interesting observation was made. Different concentrations of Tween 80 ranging from 0.0025 - 0.050 % v/v were investigated. At concentrations between 0.018 - 0.050 % v/v, three layers were seen in the bottle- water, creamed layer and gum at the bottom. The gum was thrown out as an emulsifying agent; this implies that Tween 80 took over the emulsifying activity of the gum.

For Tween 80 at concentrations of 0.0125 – 0.015 % v/v, there was reduced creaming and the gum was not thrown out. But at concentrations below 0.0125 % v/v, there was marked creaming as if no Tween had been added. This implies that, there is a critical concentration of Tween 80 that can be used to reduce creaming in this kind of emulsion.

Emulsions can therefore be prepared with cashew gum and the rate of creaming can be reduced by the addition of a very low concentration of Tween 80 (0.015 – 0.0125 % v/v).

- **Gum as suspending agent**

Cashew gum was also investigated as a suspending agent. A lot of gums are available as suspending agents. The suspending ability of cashew gum was assessed in comparison to that of xanthan gum at the same concentration and ten times concentrations. Xanthan was found to be a better suspending agent than that of cashew gum. The parameters that were assessed were flow time, apparent viscosity of fresh and stored suspensions, the rate of sedimentation over time and ease of redispersibility.

Rheology: Different concentrations of xanthan gum suspension and cashew gum were prepared according Table 2.6 and 2.7, and their flow times and apparent viscosities were determined as a function of their viscosity. From Table 3.6.6 it was observed that, the flow time of the freshly prepared xanthan gum suspension increased gradually as the concentration of gum increased. The time frame was between 9.5sec to 11.30 sec for 0.1% gum concentration to 0.5% gum concentration and the apparent viscosity from Table 3.6.8 did not differ much for the concentrations. From Table 3.6.7, it can be observed that, the flow time of freshly prepared cashew gum suspensions did not differ much as the concentration of gum increased. The gum concentration does not affect the viscosity much, unlike xanthan gum.

From Tables 3.66 and 3.67 it can also be observed that the sedimentation volume measured over six hours decreased with time as the concentration of the gums increased. Sedimentation in the xanthan gum suspensions was slower than that of cashew gum suspensions.

On storage for about 42 days and redispersed, the flow time were changed drastically for xanthan gum suspensions and a little or no change for cashew gum suspensions. Looking at Table 3.6.8, there was increase in the flow time of xanthan gum suspensions as the concentration increased. For example, from Table 3.6.8, for 0.3% xanthan suspension that is freshly prepared the flow time was 9.83 second but after storage had a flow time of 42.0 seconds. That shows a marked increase in viscosity of the suspension. Some gums are well hydrated with time and their suspending ability increased with time and this can be seen characteristically with xanthan.

For cashew gum suspension, there was not much change in the flow time and apparent viscosity of both the stored and the freshly prepared suspension. This implies that, the viscosity does not change with time. Its flow time was comparable with that of suspension without any gum as seen in Table3.6.9.

Volume of sediment: The volume of sediment was recorded for the first 6hrs and in every three days. For all the suspensions, the final volume of sediment was reached by the 12th day. There was no practical change in the volume of sediment till the 42nd day. The volume of sediment for xanthan gum suspension was always higher than that of cashew gum suspension, those of cashew and xanthan gum at the same concentration and concentrations of cashew gum suspensions ten times that of xanthan gum. Before redispersion, the supernatant was clear as seen in Fig. 3.5.6, for cashew gum suspension, but that of xanthan was cloudier as seen in Fig. 3.5.4

There was tighter packing in the cashew gum suspensions as seen in Fig. 3.5.6. and that led to caking of the sediment at higher concentrations of the gum when used as suspending agent.

After storage and redispersion of xanthan 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 xanthan gum increases with time. With the redispersion of cashew gum suspension, there was not much change in the rate of sedimentation, but the marked observation was that, some particles were still suspended as seen in Fig.3.5.7, but that was still not comparable to that of xanthan gum

Ease of Redispersion: Concentration of cashew gum suspension between 0.1 %w/v and 2 %w/v were easily redispersed, but the higher concentrations i.e. those above 2 % were done with much difficulty. Some of the measuring cylinders turned upside down had the caked remaining up. This can be attributed to tighter packing of the particles. With xanthan gum only the 5 % concentration dispersed with a little difficulty. The addition of deflocculating agent may reduce the tight packing nature of the cashew gum. But xanthan gum had a better suspending ability than cashew gum.

- **Bulk density measurements on Metronidazole granules**

The Hausner ratio and the Carr index or % compressibility, which are measures of interparticle friction and the potential powder arch or bridge strength and stability, respectively, have been widely used to estimate the flow properties of powders and extrapolated to that of granules. According to Wells (1988), a Hausner ratio value of less than 1.20 is indicative of good flowability of the material, whereas a value of 1.5 or higher suggests a poor flow display by the material. The Carr index is also called "percent compressibility." According to Carr (1965), a value between 5 and 15, 12 and 16, 18 and 21, and 23 and 28 indicates excellent, good, fair, and poor flow properties of the material,

respectively. The Hausner ratio and Carr's index values listed in Table 3.7.1 indicates that all the formulations had good flow properties except 10% cashew granules with a high compressibility index of 23% and a Hausner's ratio of 1.299, which is just a little above 1.2 which indicates good flow. This may be attributed to the concentration of gum, because it was noticed during formulation, granules of 10% cashew had quite an amount of fines as compared to the formulations.

- **Quality control test on metronidazole tablets**

The uniformity of weight test carried out on tablets prepared with different concentrations of the gum showed that all the formulated tablets had uniform weight. This is indicative of the good flow properties of the granules. 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 a tablet of weight greater than 250mg 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 3.7.0 - 3.7.4, none of the tablets failed the uniformity of weight test. Tablets produced had weights ranging from 418 ± 3.2 mg for 20 % Acacia mucilage tablets, 427 ± 4.2 mg for 10 % Cashew gum mucilage tablets, 417 ± 4.9 mg for 20 % Cashew gum mucilage tablets, 415 ± 5.6 mg for 30 % Cashew gum mucilage tablets and 419 ± 3.1 mg for 40 % Cashew gum mucilage tablets. Tablets that were produced had a diameter of 11 mm. Tablets produced from 10 % cashew were slightly weightier, and this can be attributed to may be the flow properties of granules.

Table 3.8.5 shows the friability of the different batches of tablets. The maximum permitted loss in weight of a batch of tablets subjected to friability testing is 1 % (British Pharmacopoeia, 2009). This parameter assesses the ability of the tablet to withstand stress and abrasion associated with handling, packaging and transportation and how readily the tablets will chip. This property of the tablet is affected by the nature and amount of binder used. Binders impart the cohesive nature of the particle in the tablets.

Tablets produced from 40 % cashew gum mucilage were least friable whilst those produced from 10 % and 20 % cashew gum were more friable. Tablets produced from 10 % and 20 % cashew gum mucilage failed the friability. Those produce from 20 % Acacia gum, which was being used as a standard passed the test. From Fig. 3.6 it can be inferred that the friability of tablets decreased as the concentration of cashew gum mucilage increased.

Tablets produced from 20 % acacia gum mucilage, 30 % cashew gum mucilage and 40 % cashew gum mucilage passed the hardness test, whilst 10 % and 20 % cashew gum mucilage failed the hardness test. Under normal circumstances, pressure variation on the tableting machine leads to difference in hardness, but in this production case, all parameters were set equally on the compression machine due to the comparative nature of this study, so it can be inferred that the nature and concentration of the gum used in tablet preparation affected the hardness of the tablets.

Results of disintegration test in Table 3.8.7 shows that all the tablets produced disintegrated within the stipulated time of 15 min for uncoated tablets (British Pharmacopoeia, 2008) though there were variations depending on gum concentration. Tablets containing 40 % cashew gum mucilage showed the highest disintegration time of averagely 11.18 min, whilst 10 % cashew showed the least of averagely 0.96 min. As the concentration of cashew gum mucilage increased, the disintegration time also increased. This implies that, the amount of binder has an influence on the disintegration time, because in all the different batches of tablets that were produced, the amount of maize starch used as disintegrant was maintained at 8 % w/w. When individual powder particles are strongly bound to each other by the binder, more time will be needed to break the particles apart. For this reason the higher the concentration of gum used the higher the disintegration time of the resultant tablets.

Dissolution profile of tablets

According to the USP (2008), 85 % of the contents of metronidazole tablets should be released in aqueous media in 45 min. Since metronidazole is an anti protozoal agent, a fast release will be expected for effective parasitemia reduction and clearance.

From the calibration curve, Fig.3.8, it was observed that the r^2 value was 0.999 which is indicative of good linearity of the calibration curve and made the subsequent determinations from calibration curve valid.

From Tables 3.8.9 - 3.8.13 and Figs. 3.9 and 3.10, it can be ascertained that, all the batches of tablets passed the dissolution test. By 15 min more than 90 % release was seen in all the batches. Fast releases were seen in tablets with low concentrations of the gum. Drug release from tablets produced from 10 % w/v cashew gum mucilage was higher and above 100 %, truly reflecting from the weights of tablets produced in that batch, because the maximum set

was 420mg and the average weight there was 427 mg. All the same it fell within the B.P range of acceptable drug content, i.e. between 95 – 105 %.

Comparing the properties of the cashew gum tablets produced above to the standard used which was acacia gum tablets, it can be inferred that, tablets produced from 30 % and 40 % cashew gum had comparable parameters to that of 20 % acacia gum and therefore, cashew gum at these concentrations can be successfully employed as a binding agent.

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4.2.0 CONCLUSION

The following conclusions can be drawn from the study:

- Cashew gum can be purified to achieve a good yield
- That cashew gum can be used as an emulsifying agent with its creaming reduced by addition of very low concentrations of Tween 80
- Suspensions produced from high concentrations of the gum caked on standing, so low concentrations may be used, whilst adding a deflocculating agent. On the whole, cashew gum did not present itself as a good suspending agent.
- Xanthan gum appear to be a better suspending agent than cashew gum, since its suspending ability increased with time
- Cashew gum can be employed as an effective binding agent in tablets at concentrations of 30 – 40 % w/v.
- Cashew gum therefore finds many applications in the field of pharmacy.

4.3.0 RECOMMENDATIONS

- Further work should be done on using the gum as a potential film coating agent.
- Formulation of matrix tablets using the gum can also be attempted.
- More assessment should be done on drug – gum interaction.
- Purified gum has a brownish colour so more research can be conducted into decolourisation of the gum.

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4.5.0 APPENDIX – PREPARATION OF TEST SOLUTION

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 20 %w/v mucilage – 20 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 a uniform mucilage was formed.

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

