COMPARATIVE STUDY OF THE DISINTEGRANT PROPERTIES OF MAIZE STARCH AND BAMBARA NUT STARCH ON METRONIDAZOLE TABLETS

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CERTIFICATION

This is to certify that this project work was carried out by **Ifeoma Chiamaka Okafor** in the Department of Pharmaceuticals and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin City

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DEDICATION

This work is dedicated to the Almighty God for His favour, protection and guidance throughout my stay in this great institution. It is also dedicated to my family for their love, care and support, during my academic pursuit in the University of Benin.

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ABSTRACT

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. They can be added extra-granularly, intra-granularly or both during tablet formation. A standard disintegrant used extensively for tablet formation is maize starch. There is a growing interest in locally sourced tablet excipients, hence the disintegrant property of indigenously sourced Bambara nut (*Vigna subterranea*) starch and its effect on metronidazole tablets is evaluated in this study

The purpose of the study is to compare the effect of the disintegrant properties of various concentrations of Bambara nut starch (*Vigna subterranea*) and maize starch BP on metronidazole tablets.

The starch from *Vigna subterranea* seeds was extracted and its disintegrant ability was compared to that of maize starch BP at concentrations of 10%, 15%, 20%, 25% in metronidazole-based tablets. All other parameters were kept constant during the formulation process. The organoleptic properties, bulk and tapped density and the chemical properties of the starch of *Vigna subterranea* was determined. The flow properties of the granules formed with both starches were determined and the metronidazole tablets were evaluated for weight uniformity, dimensions, tablet hardness, friability, disintegration and dissolution rates.

The metronidazole granules and tablets formulated with the starch from *Vigna subterranea* were comparable in granule flow properties, tablet weight, variation, hardness, friability. The study revealed that *Vigna subterranea* starch used as a disintegrant performed better with a shorter disintegration time than tablets formulated with the different concentrations of maize starch BP. It was discovered that 20% and 25% of the starches were not adequate for tablet formation due to their friability values of above 1%.

This study revealed that *Vigna subterranea* starch can be used as a disintegrant in the production of tablets of adequate pharmaceutical quality. It serves as an adequate disintegrant for metronidazole tablets

CHAPTER ONE

1.1 DEFINITION OF TABLETS

A tablet is a pharmaceutical dosage form. It consists of a combination of active substances and excipients usually in powdered form pressed or compacted from a powder into a solid dose. they may differ in size, shape, weight, hardness, thickness, disintegration, and dissolution characteristics and in other aspects, depending on their intended use and method of manufacture.

A compacted solid dosage form containing medication with or without excipients is known as a tablet. According to Indian pharmacopoeia, pharmaceutical tablets are solid flat or biconvex dishes prepared by compressing a drug or a mixture of drugs with or without diluents (Rudinic et al, 2005).

Due to their convenience, tablets are the most popular solid dosage form for pharmaceutical active substances. (Ghadiri et al 2018)

Tablets can also be defined as solid dosage forms containing medicinal substances with or without suitable diluents. Tablets can be given intravaginally, rectally, or sublingually.

1.2 Advantages of tablets over other dosage forms:

1. Unit dosage form (dosage accuracy)
2. Compactness of dosage
3. easy to swallow
4. Highly soluble
5. Flexibility of dosage form
6. Easy to prepare
7. economic for packaging, shipping and storage

8. They are easy to carry.

9. Some of the tablets are divided into halves and quarters by drawing lines during manufacture to facilitate breakage whenever a fractional dose is needed

10 Lighter and compact

11 Sustained release product is possible by enteric coating.

12 Suitable for large scale production

13 Objectionable odour and bitter taste can be masked by coating techniques

14 Unpleasant odor or taste of the drug can be masked by sugar coating or film coating.

15 Economically their cost of production is relatively low.

16 Sealed covering protects the tablet from atmospheric conditions e.g., light, air etc.

Disadvantages

1. Highly amorphous substances are very difficult to compress.
2. Poor wetting and dissolution cannot be placed in the form of tablets.
3. Objectionable odour, bitter tasting and humectants substances need special treatment for compression.
4. Due to their amorphous and low-density properties, some medicines defy compression into dense compacts. Irritants effects on the GI mucosa by some solids e.g. Aspirin problems
5. Possibility of bioavailability problems resulting from slow disintegration and dissolution
6. Patients with vomiting and diarrhea cannot take it or absorb it.
7. Tables are not suitable for children or old man because they cannot take it easily.

1.3 Tablet Class and Types

1 Tablet for oral ingestion:

a. Compressed Tablets are tablets made from crystalline or granular materials, alone or in combination with binders, disintegrant, lubricants and fillers. They are pharmaceutical tablet formed by subjecting dry granular powders to sufficient pressure to make the particles cohere and do not contain special coating. Compressed tablets represent a significant proportion of tablets that are clinically used to provide systemic administration of therapeutic agents either in an uncoated state (i.e., in their simplest form) or in a coated state.

b. Multiple compressed tablets tablets that have undergone more than one compression cycle. They are typically designed to separate physically or chemically incompatible components, induce repeat or prolong pharmacological activity, or all of the above.

- **Layered tablets** are made by compressing extra tablet granulation on top of a compressed tablet. This operation may be repeated several times to produce a multi-layered tablet.
- **Compression-coated tablets** are made by inserting a previously compressed tablet into a unique tablet machine and compressing an additional layer on top of it. By using this technique, a compacted tablet with separate layers of compatible substances may be maintained. It has all the advantages of the compressed tablet, such as: - sleeting, monogramming. speed of disintegration, etc. while keeping the benefits of sugar-coated tablets in terms of internal layer masking of the taste of medication.

c. **Repeat-action tablets** are one type of extended-release dosage form. They usually contain two single doses of medication, one for immediate release and one for delayed release.

They are layered tablets in which the outer layer gives an initial dose, quickly disintegrate in the stomach. Components that are soluble in intestinal solution but insoluble in gastric solution make up the inner layer.

d. **Delayed-action and enteric-coated tablets** are tablet coatings that resist solution in gastric fluid but disintegrate and release their medication in the intestines. Amongthe agents used to enteric-coat tablets are fats, fatty acids, waxes, shellac and cellulose acetate phthalate.

e. **Sugar-coated tablets** are coating that cover up medicinal possessing objectionable tastes and odours and protect sensitive medicinal subject to deterioration. Sugar-coated may be coated with a colored or an uncolored sugar. The procedure comprises polishing, sub coating, syrup coating (for smoothing and coloring), and seal coating (waterproofing).

Sugar-coated tablets may be 50 % larger and heavier than the usual tablet.

f. **Chocolate-coated tablets** Originally, chocolate was employed as a coloring agent; however, iron oxide that has a consistent color is now readily available and has mostly supplanted chocolate in this role.

g. **Film-coated tablets** have a thin layer or film of a water-soluble substance that imparts the same general qualities as sugar-coated tablets with the added benefit of requiring a significantly shorter amount of time for coating. For this, a variety of polymeric materials with film-coating capabilities are employed.

h. **Air suspension-coated tablets** Tablets coated with air suspension are inserted into a vertical cylinder that is supported by an air column that enters from the bottom of the cylinder. The coating solution is quickly applied to the suspended spinning solids as it enters the system. With the use of warm air blasts, rounding coats can be applied in under an hour.

i. **Chewable tablets** are made of mannitol that has been specifically colored and flavored to break down smoothly and quickly when chewed or allowed to dissolve in the oral cavity, creating a creamy base. For kids who typically take multivitamin tablets, this formulation is fantastic.

2 **Tablets used in the oral cavity**

a. **Buccal or sublingual tablets** are small, flat, oval tablets that are meant to be placed in the buccal pouch or under the tongue so that the active component can be absorbed directly via the mucosa.

b. **Dental cones, troches, and lozenges** all take time to dissolve in the mouth and largely work locally.

3 **Tablets used to prepare solutions**

a. **Effervescent tablets** Citric acid, tartaric acid, and sodium bicarbonate, as well as other substances with the ability to emit carbon dioxide gas when in contact with water, are compressed to form tablets.

b. **Dispensing tablets** are tablets that should not be given out as such because they contain very large and occasionally deadly amounts of the powerful medicine. They offer a manageable dosage of a powerful medication that can be easily mixed with powders, liquids, and other preparations at the dispensing counter.preparations at the dispensing counter.

c. **Hypodermic tablets** are tablets manufactured in a tablet triturate mold are called hypodermic tablets and are used to create hypodermic injection preparations. They must be totally and quickly soluble in the vehicle since they are prepared with the utmost cleanliness because it is how parenteral solutions are typically made on the spot.

1.4 Tablet-manufacturing methods:

A Direct compression

B Granulation

A) Direct compression: The procedure by which tablets are made directly from powder mixtures of API and acceptable excipients is referred to as "direct compression." The powder blend does not need to be pre-treated using a wet or dry granulation process.

It is the easiest to regulate and least expensive manufacturing choice because it requires the fewest manufacturing stages.

Direct compression production processes: Direct compression just requires a handful of steps:

• Drug and excipient milling

• Combining drugs with excipients

• Compression of tablet

B) Granulation: Granulation is a process that enlarges the size of tiny particles such that they become physically stronger and larger agglomerates. One of the most important unit operations in the manufacturing of pharmaceutical dosage forms, namely tablets and capsules, is this one. Small, coarse, or fine particles are transformed into granule-sized agglomerates during the granulation process. Due of the strict requirements for the formed granules' content uniformity and physicochemical properties, including granule size, bulk density, porosity, hardness, moisture (Shanmugam et al 2015)

1)Dry Granulation

2)Wet Granulation

1 **Dry granulation**: Slugging may be employed to create granules when tablet ingredients have sufficient inherent cohesive or binding qualities but are susceptible to moisture or cannot sustain high temperatures during drying. Dry granulation precompression or twofold compression are the terms used to describe this technique. Huge tablets are turned into slugs when slugging is employed because fine powders flow easier into large cavities. These

compressed slugs are then softly combined with lubricants before being crushed to produce tablets. The desired mesh screen is coarsely screened through these compressed slugs either manually or for large quantities using Fitzpatrick or similar comminuting mills. The alternative method involves utilizing a device like a Chilsonator to pre-compress the powder using pressure rolls.

Steps in Dry Granulation:

- Milling of drugs and excipients.
- Mixing of milled powders.
- Compression into large, hard tablets to make slugs
- Screening of slugs.
- Mixing with lubricant and disintegrating agent.
- Tablet compression.

Two main Dry Granulation processes:

- **Slugging process:** Granulation by slugging is the compression of dry powder used in tablet formation with a tablet press that has a die chamber with a large enough diameter to fill it quickly. It is not crucial that the slug is accurate or in good condition. Use only the amount of pressure required to compact the powder into even slugs. After slugs are created, they are milled and screened to the proper granule size before final compression.
- **Roller compaction:** A device known as a 'Chilsonator' can also be used to compact powder using pressure rolls. In contrast to a tablet machine, a chilsonator produces a compressed material in a steady, uninterrupted flow. From the hopper, which has a spiral auger to feed the powder into the compaction zone, the powder

is fed down between the rollers. The aggregates are screened or processed to create granules, just like slugs.

2. **Wet granulation**: The pharmaceutical industry's most popular agglomeration process is. moist granulation Granulation is the only step in the wet granulation process. Simply wet massing the powder mixture with a granulating liquid, wet sizing, and wet drying constitute the wet granulation process. Wet milling, wet sizing, and drying are the distinctive steps in the wet granulation process.

   Important steps involved in the Wet Granulation:

   - Mixing of the drug(s) and excipients.
   - Preparation of binder solution.
   - Mixing of binder solution with powder mixture to form wet mass.
   - Coarse screening of wet mass using a suitable sieve.
   - Drying of moist granules.
   - Screening of dry granules through a suitable sieve.
   - Mixing of screened granules with disintegrant, glidant and lubricant.

1.5. Properties of tablet

- Tablets should be classy products with distinct personalities that are devoid of flaws like chips, fractures, discolouration, and contamination.
- • Tablets need to be sturdy enough to survive the strains of shocks they will experience during production, packaging, shipping, and distribution.
- Tablets should be able to release the medication agent(s) in the body in a predictable and reproducible manner, and they should be physically stable enough to preserve their physical characteristics throughout time.
- Must maintain a reasonable level of chemical stability over time to prevent the therapeutic substance from changing.

- They should contain stated dose within permitted limits.
- They should be of suitable size for ease of administration and be free of foreign particles.

1.6 Evaluation of Tablets

Tablets are evaluated by a variety of methods.

1. **Analytical determination of tablet content:** Due to the need for specialist equipment, this is probably not going to be done. However, by weighing each tablet separately and calculating the percentage deviation from the planned amount, the weight fluctuation of the pills may be quantified. Each pill "must be not less than 90% and not more than 110% of the theoretically calculated weight for a unit," according to the USP 24/NF19 Supplement 1 guidelines.
2. **Tablet hardness**: Recently, it has become clear how important hardness is and how it relates to tablet dissolving and, maybe more importantly, how quickly drugs dissolve. The tablets must be durable enough to endure mechanical strain during shipping, packing, and consumer handling. There are a variety of manually operated tablet hardness testers available. The Strong Cobb, Pfizer, and Stokes hardness testers are a few examples of tools. The hardness increases with increasing compression pressure. (2007) Tanabe et al The measurement principle entails applying an increasing stress to the tablet until it fractures or breaks. The tablet's radial axis is where the load is exerted. However, hypodermic and chewable tablets are substantially softer (3 kg), and some extended-release tablets are much tougher (10-20 kg) than oral pills, which typically range in hardness from 4 to 8 or 10 kg.

   3.**Tabletdisintegration:**

   Commercially available dissolution and disintegration equipment is available. Most pharmacists won't have access to this machinery. However, a straightforward

disintegration device can be created. Start by holding a 10-mesh screen 2 inches above a 1000 ml beaker's bottom. The beaker should be placed on a magnetic stirring plate after being filled with 1000 ml of water, a stirring bar, and stirring rod. Stir quickly but steadily. Drop the tablets onto the mesh screen, then note how long it takes for them to break up. An acceptable disintegration time should be between 15 and 30 minutes (Marlk et al 2017), while the exact amount of time will vary depending on the product, the rate of stirring, etc.

4. **Tablet dissolution:** Determining the disintegration time is a helpful production control technique, however a tablet's disintegration does not necessarily mean that the medicine has dissolved. Even if a tablet disintegrates quickly, it may still be inaccessible to living things. The pace at which the drug dissolves from the tablet's main particles is crucial to drug absorption and, in many formulations, it is the rate-limiting phase. Therefore, a dissolving time rather than a disintegration test is a better indicator of a drug's availability from a tablet. Although this is a crucial characteristic to monitor, most pharmacies lack the tools required to carry out these kinds of testing.

1.7 PHARMACEUTICAL EXCIPIENTS

Often referred to as "bulking agents," "fillers," or "diluents," excipients are substances that are formulated alongside the active ingredient of a medication in order to bulk up formulations that contain potent active ingredients or to confer a therapeutic enhancement on the active ingredient in the final dosage form, such as facilitating drug absorption or solubility. Excipients can be helpful throughout the manufacturing process to facilitate the handling of the active substance in question, such as by improving powder flowability or non-stick characteristics, as well as to support in vitro stability, such as by preventing denaturation beyond the anticipated shelf life. The dosage form, mode of administration, active ingredient, and other variables all play a role in choosing the best excipients. Though

excipients were at one time considered to be "inactive" ingredients, they are now understood to be "a key determinant of dosage form performance" (Bhattacharyga et al 2006).

I. Antiadherents

By providing a non-stick surface, antiadherents lessen the adhesion between the powder (granules) and the punch faces, preventing adhering to tablet punches. Additionally, they are employed to prevent pills from sticking. Magnesium stearate is the most common

II. **Binders**

A tablet's constituent parts are bound together by binders. Binders give low active dosage tablets volume and guarantee that tablets and granules may be made with the necessary mechanical strength. Typically, binders are

a) Saccharine and their derivatives:

- Disaccharides: sucrose, lactose.
- Polysaccharides and their derivatives: starches, cellulose or modified cellulose such as microcrystalline cellulose and cellulose ethers such as hydroxypropyl cellulose (HPC).
- Sugar alcohols such as xylitol, sorbitol or maltitol.

b) Protein: gelatin;

- Synthetic polymers: polyvinylpyrrolidone (PVP), polyethylene glycol (PEG)

Binders are classified according to their application:

- Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose and polyethylene glycol.
- Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose, polyvinylpyrrolidone and polyethylene glycol.

III Coatings

The components in tablets are shielded from deterioration by airborne moisture by coatings, which also make swallowing larger or bad-tasting pills simpler. The majority of coated pills use a sugar- and allergen-free cellulose ether hydroxypropyl methylcellulose (HPMC) film coating. Other coating materials, such as synthetic polymers, shellac, the protein zein from corn, or other polysaccharides, are occasionally utilized. Gelatin coats the capsules. Drug release is regulated by enterics, which also define where in the digestive tract it will occur. Fatty acids, waxes, shellac, polymers, and plant fibers are some examples of the materials utilized for enteric coatings.

IV. Colours

To enhance a formulation's appearance, colors are added. Color uniformity is crucial since it makes it simple to identify a drug. Additionally, colors frequently enhance the aesthetic feel and look of pharmaceuticals; frequently, titanium oxide is employed as a coloring ingredient to create popular opaque colors as well as azo dyes for other hues. A patient is more likely to stick to their schedule and therapy goals with an increase in these organoleptic qualities will also result in a better outcome for the patient, especially children.

V. Disintegrants

The tablet disintegrates in the digestive tract, releasing the active components for absorption when the disintegrants expand and dissolve when wet.

They make sure that the pill quickly dissolves when it comes into touch with water. Examples of disintegrants include:

·Crosslinked polymers: crosslinked polyvinylpyrrolidone (crospovidone), crosslinked sodium carboxymethyl cellulose (croscarmellose sodium).

The modified starch sodium starch glycolate.

VI. Flavors

Flavors can be used to cover up unpleasant-tasting active components and increase patient willingness of finishing a drug course. Flavorings might be artificial or natural (like fruit extract) (Mills et al 2012). For instance, to enhance:

- a bitter product - mint, cherry or anise may be used
- a salty product - peach, apricot or liquorice may be used
- a sour product - raspberry or liquorice may be used
- an excessively sweet product - vanilla may be used

VII. Glidants:

Glidants are used to encourage powder flow by lowering cohesion and interparticle friction. These cannot lessen the friction between the die walls, hence they are employed in conjunction with lubricants. Talc, fumed silica, and magnesium carbonate are other examples.

VIII. Lubricants

Lubricants stop materials from sticking to the tablet presses or capsule filling equipment and clumping together. Additionally, lubricants make sure that there is minimal friction between the solid and the die wall during tablet production and ejection.

The most often used lubricants in tablets or hard gelatin capsules are typically common minerals like talc or silica, as well as fats like vegetable stearin, magnesium stearate, or stearic acid. Lubricants are substances that are sparingly added to tablet and capsule formulations to enhance specific processing traits.

There are three functions identified with lubricants as follows:

- True lubricant role:

  To lessen wear on punches and dies and friction at the point where a tablet's surface meets a die wall during ejection.

- Anti-adherent role:

- Avoid adhering to punch faces or lubricants in the case of encapsulation. Avoid clinging to tamping pins, machine dosators, etc.
- Glidant role:

  Reduce inter particulate friction to improve product flow.

IX. Preservatives

Some typical preservatives used in pharmaceutical formulations are

- Antioxidants like vitamin A, vitamin E, vitamin, retinyl palmitate, and selenium
- The amino acids cysteine and methionine
- Citric acid and sodium citrate
- Synthetic preservatives like the parabens: methyl paraben and propyl paraben.

X. Sorbents

By restricted fluid sorbing (the taking up of a liquid or a gas either by adsorption or absorption) in a dry state, sorbents are used to moisture-proof tablets and capsules. Desiccants, for instance, absorb water and dry out (desiccate) the items around them.

XI. Sweeteners

Sweeteners are added to liquids like cough syrup and chewable tablets like antacid to make the components more pleasant. To cover up bad tastes or odors, add sugar.

1.8 QUALITY CONTROL OF TABLETS:

The majority of businesses already enforce Good Manufacturing Practices, thus it is important to follow the prescribed laws for drug production. Some of these standards have strict guidelines for microbiological control and contaminant management, such as removing dust from tableting machines. In order to ensure that the patient receives a product that contains the necessary amount of the drug substance in a form that allows the drug to exert its full therapeutic action, a number of pharmacopoeia tests have been developed and are described in the official books as the minimum standards to which

tablets must adhere. These pharmacopeia tests, which are also known as official tests, comprise the following:

- Uniformity of weight
- Uniformity of content
- Disintegration test
- Dissolution test

In addition to these official tests, there exist several unofficial tests which are also used by individual manufacturers to guarantee that the tablets are the same from one production lot to the next. These "in-house" tests have standards that are set by the manufacturer themselves to meet their specific quality assurance needs and they include:

- Hardness test
- Friability tests
- Thickness uniformity
- Tensile strength determination etc.

These tests are described below.

Disintegration Test: This test determines if the tablets dissolve when submerged in the necessary liquid medium under the specified experimental circumstances. According to the BP (2013), the disintegration chamber consists of a glass tube closed at one end by a 2mm aperture steel mesh and six of such chambers are usually arranged around a central pole. A tablet is placed in each tube thus the BP recommendation of six tablets per batch can be conveniently carried out.

The tubes are raised and lowered in a water bath at a constant frequency so that at the highest point, the mesh remains below the surface of the liquid medium. The standard requires that all six tablets dissolve within the allotted time frame. Depending on the kind of tablet, the time restriction varies. Standard uncoated tablets are 15minutes; film coated tablets is

30minutes and other coated tablets is 60minutes. In each case, the disintegrating medium is water maintained at a temperature of 37oc except in cases of noncompliance (of other tablets other than film-coated) where the disintegration medium is changed to 0.1m hydrochloric acid and tested on a further six tablets. When there are no remnants on the test apparatus's screen other than bits of undissolved tablet coating, disintegration has been said to have occurred. If any additional residue is left, it should be a mushy mass without a discernibly solid, unmoistened center.

Dissolution test: This assay, which provides the most direct correlation to the potential in vivo effect of the drug that enters solution as a function of time, is arguably the most significant. The tablet is dissolved by placing it in a chamber that has the necessary dissolution media in a flowing form. The forced convection sink approach is this. Three techniques—the basket, paddle, and flow cell apparatus—are suggested by the BP. The official monograph provides a thorough discussion of all the different ways. In the BP (2003), a sample is taken out of the dissolving fluid after a predetermined amount of time (often 45 minutes) and is then analyzed as per the instructions in the monograph. Unless otherwise specified, the tablet should dissolve to at least 70% of its stated content. Drugs' pharmacological action is significantly influenced by how they dissolve. In fact, it has been shown that many medications' in vitro dissolution rates and their bioavailability are directly related; this link is known as the in vitro-in vivo correlation, or IVIVC38. Depending on how they are made, solid dose forms may or may not dissolve after being swallowed and interacting with gastrointestinal fluid.

The kinetics of dissolution plays a crucial role in determining a drug's bioavailability. According to (Levy 45) and a few other researchers, the rate of dissolution affects how quickly certain medications build up in the bloodstream. This led to the realization that in-vitro dissolution kinetics offers helpful knowledge on the accessibility of medications and

their subsequent in-vivo therapeutic effects. As a result, dissolving tests for one capsule and twelve tablet formulations were added to the USP XVIII (1970) and NF XIII (1970) monographs. Dissolution tests for digoxin tablets were added to the British Pharmacopoeia in 1975 (as an amendment to BP 1973). The dissolving requirements for various medications are specified in the various pharmacopoeias. Dissolution testing apparatus has been designed in a number of ways, from basic beakers with stirrers to sophisticated systems with lipid phases and lipid barriers that aim to replicate the biological environment. The physicochemical characteristics of the dosage form play a significant role in the apparatus that should be employed.

Weight uniformity: During the tableting process, there will inevitably be variances; nevertheless, as long as they stay within the parameters specified in the official monographs, they are okay. A homogeneity of weight test must be performed on all tablets when the active ingredient makes up the majority of the dose form. A total of 20 tablets are chosen for the test, and according to B.P. (1993), only two of the individual weights can differ from the average weight by more than the % deviation stated in the table below, and none can deviate by more than twice that percentage.

Content Uniformity: Tablets that contain less than 2mg or less than 2%w/w and to whom the weight uniformity test does not apply must go through this test, under the B.P., unless justified or approved. This is done to make sure that each tablet contains the right amount of the active ingredient. It is especially useful for powerful medications, where a uniform tablet weight may not be enough to highlight potential, potentially large variations in the amount of the active ingredient. This test also aids in providing insight into the homogeneity of the powder mixture before compression.

Hardness: The property, often known as the crushing strength, measures how well the tablet can withstand breaking or crushing under a compressive stress that is applied in opposite directions. To quantify this burden, a variety of instruments have been developed. For instance, the Monsanto hardness tester, which holds the tablet between two sets of moveable and fixed jaws. By twisting the compression screw and measuring the load needed to crush or fracture the tablet from the scale, the force delivered to the edge is steadily raised. Many of these tests are performed each batch, and the mean is calculated, because errors may occur as a result of changes in tablet diameter and the rate at which the compression plunger is cranked. For the majority of tablets, a minimum crushing strength of 4 kg is adequate.

Friability test: The abrasion test is another name for this. Given that it also pertains to the tablet's mechanical strength, this may be seen as a variant of the hardness test. This test determines the tablet's resistance to the three problems that could significantly reduce the weight of the tablet: chipping, abrasion, and crumbling (i.e., the creation of particles). It shows the likelihood of edge damage that would happen if tablets were handled during shipping, storing, and dispensing. The tablets are subjected to a consistent tumbling motion for the duration of the test, and the weight changes—typically expressed as a % of the different weights—are then calculated. The most popular abrasion tester is the Roche friabrilator. The recommended upper limit for effective tablets is 1% or less.

1.9 PHYSIOCHEMICAL PROPERTIES OF THE MATERIALS USED IN THIS WORK

Metronidazole Powder

Figure 1.1: Structure of Metronidazole

Structure of Metronidazole

An antibiotic called metronidazole is used to treat a range of infections. It functions by preventing the development of specific bacteria and parasites. Only specific bacterial and parasite illnesses are treated by this antibiotic. Viral infections cannot be treated with it (such as common cold, flu). Certain stomach/intestinal ulcers brought on by a bacterium can also be treated with metronidazole in combination with other drugs (H. pylori).

Table 1.1: Physic Chemical Properties of Metronidazole

Chemical Properties of Metronidazole	
	Metronidazole is a 5-nitroimidazole derivative.
Chemical Formula	C6 H9 N3 O3
Properties	
Physical Properties	White to pale yellow crystalline powder. Mp 158–160° C. Protect from light. Saturated aqueous solution has a pH of 5.8
Molecular Weight	171.155
Solubility	The solubility of metronidazole at 20°C (g/100 ml) is: Water (1.0); ethanol (0.5); ether (<0.05); and chloroform (<0.05). It is soluble in dilute acids.

Maize starch B.P: It is made from the Zea mays L. caryopsis. It is odorless and tasteless, a very fine white powder that may be slightly yellowish and creaks when squeezed between fingertips. Granules with fissures or uneven edges are extremely rare to find. The granules are polyhedral, measuring 2 to 3 um, or spherical, measuring 25 to 32 um. The 2–5 rayed cleft or distinct hollow that makes up the central helium is present. No striations are concentrically spaced.

Like all other types of starch, maize starch is insoluble in both cold water and alcohol. A translucent, yellowish jelly is produced after being boiled in boiling water that is around 20 times its weight for a short period of time. Although its aqueous suspension is inert to litmus, iodine causes it to assume a distinctive purple-blue or deep blue color. In the pharmaceutical sector, maize starch is used for a wide range of purposes, such as tablet filler or diluents, disintegrants, and absorbents in dusting powders. It serves as a binding agent when present in mucilage at a concentration of 5–10%.

Magnesium stearate: This is an extremely thin, odorless white powder that may also contain very little stearic acid particles. It is hydrophobic because it is almost insoluble in water, ethanol absolute, and ether. It is frequently used in tablet manufacturing as a lubricant and is

thought to be superior to talc in this regard. It can be added as a powder directly to the tablet formulation or as an aqueous solution dispersed in 1% chloroform to lubricate the die and punch surfaces just prior to compression. When the chloroform evaporates, a tiny layer of the powder is left on the surface, serving as the lubricant.

Talc: This metamorphic mineral is produced when magnesium minerals like serpentine, pyroxene, and olivine undergo metamorphism in the presence of carbon dioxide and water. In pharmaceutical goods, such as tableting, it serves as a glidant. Talc typically appears as foliated to fibrous masses; monoclinic crystals are so uncommon as to be practically unheard of. It doesn't dissolve in water, although it does a little bit in diluted mineral acids. Its hues range from white to grey to green, and its specific gravity is between 2.5 and 2.8. It feels very oily.

1.11 *Vigna Subterranea* (Bambara Nut)

Figure 1.2: Bambara Groundnut (*Vigna subterranean*) Seeds

A member of the Fabaceae family, *Vigna subterranea* is also known as Bambara groundnut, Bambara nut, Bambara bean, Congo goober, earth pea, ground-bean, or hog-peanut. The plant is of West African origin. Similar to groundnut, vigna subterranea ripens its pods underground. They can be dried and then eaten fresh or cooked after being ground to form puddings. When using grains directly, the starch output was higher (about 45%) than when using flours (18-41%) (Oyeyinka et al 2016)

In many regions of Central and West Africa, where it is mostly grown by women for the support of their families, bambara groundnut (Vigna subterranea) is an important source of proteins. The protein level of bambara groundnuts is on par with or higher than that of other legumes, making them an excellent addition to diets based on cereal. Nutritionally speaking, bambara groundnut includes 3.4% ash, 0.098% calcium, 0.007%, 6.1% fat, 53.1% carbs, 19.7% protein, and 6.1% fiber. Protein, starch, and sugar contents of flour ranged from 15.6 to 19.6%, 47.8 to 52.0%, and 1.9 to 5%, respectively. Iron (Mubaiwa 2018). Additionally, the amount of lysine is rather large whereas the amounts of methionine and calcium are low. Despite having a high nutritious value, bambara groundnut is hardly ever used outside of its native regions. However, bambara is not thought of as a lucrative cash crop but rather as a snack or meal supplement. The absence of processing methods has been connected to an increase in the hard-to-cook fault in the nuts and a decrease in production, which are two factors that limit the use of bambara groundnut. This bean is frequently prepared and consumed as is in Central Africa, or it is frequently used to make the beloved koki, a dish made of legumes.

The range of the particle size distribution was found to be 0.10 to 0.15.

Origin and Cultivation

The warm tropical regions of Sub-Saharan Africa are where the Bambara groundnut is grown and is native to West Africa. The bambara nut thrives anywhere groundnut (peanut) grows,

which is why it is widely distributed starting in Kwara state and extending throughout northern Nigeria and northern Ghana.

Importance

The third-most significant grain legume in semi-arid Africa is the bambara groundnut. It can thrive on marginal soils where other leguminous crops cannot since it is tolerant of high temperatures.

It is reported an antimicrobial activity (Udeh et al 2020) against

- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*
- *Eschericha coli*
- *Bacillus cereus*
- *Candida albicans*
- *Aspergillus niger* (mold)

The red hull had the highest quantities of chlorogenic and ellagic acid among tannic compounds, whereas the brown hull had the highest concentrations of rutin and myricetin among flavonoids.

Distribution

Vigna subterranea is farmed in dry tropical Africa and is native to West Africa (Nigeria, Cameroon, Central African Republic, and Chad). Zimbabwe is the production hub of Southern Africa. Although it can also be found in tropical regions of America, Asia, and Australia, the extent of its cultivation outside of Africa is currently essentially nonexistent.

Vigna subterranea may thrive in hot, dry, marginal soils up to 2000 meters above sea level. Unlike most crops, it can continue to grow in challenging conditions (sorghum, maize and peanuts)

Environmental impact

Like other legume plants, *Vigna subterranea* makes an excellent rotation crop and soil fertilizer. No more fertilizer is necessary. Typically, it is interplanted with vegetables, other pulses like cowpea and groundnut, root and tuber crops, and cereals like maize, sorghum, and pearl millet.

Ethnomedical Uses of Bambara Nut:

Eating Bambara nuts offers a variety of health advantages. Eating this unusual snack food can assist with everything from alleviating minor aches and pains to aiding in the management of diabetes.

Bambara nuts have the following health advantages:

1. **It is high in nutrients loss:**

   It is a powerhouse of nutrients and minerals, including:

   • Magnesium–Magnesium helps to boost one's metabolism in order to burn more calories throughout the day, adding weight loss.

   • Manganese–Manganese helps to regulate one blood sugar and insulin levels, which are both important in managing hunger and preventing overeating.

2. **It can help lower blood sugar.**

   A good plant protein source that lowers the risk of heart disease and type 2 diabetes is the bambara nut. This protein with high lysine helps to reduce cholesterol, this nut contains healthy unsaturated fat.

3. **It improves cardiovascular function.**

   Bambara nuts are top of the list of healthy snack foods that can prevent heart disease. This is because of the high fiber content of Bambara nuts, which helps to reduce

cholesterol levels in your body. In addition, Bambara nuts can also help reduce inflammation and improve blood vessel function. Dietary fiber in BGN decreases blood pressure and serum cholesterol and protects against cardiovascular diseases Tan.W. et al(2021)

4. **It is a rich antioxidant**

   Bambara nut is a legume, it's low in fat and high in protein, also it's richness in antioxidants and amino acids, which is protective against cancerous cells.

5. **It helps to boost the body's immune system.**

   Bambara nut boost's the immune system.

   It provides the body with a rich source of immune-boosting nutrients, including vitamins C and D, folate, selenium, niacin, and zinc.

6. **It enhances digestion and reduces inflammation**

   Bambara nut is good for the gut because it contains prebiotic (a type of fiber that feeds the normal flora of the digestive system).

7. **It is good for bone health and malnourishment**

   Bambara Nut aids in maintaining strong bones due to its high content of vita It's also a great source of nutrients for people who are malnourished. The high protein content protects young children from suffering kwashiorkor (protein deficiency and is also a good choice for those who are looking for a reliable source of iron to treat or prevent anemia and iron deficiency (Atoyebi et al 2017)

1.12 AIMS AND OBJECTIVES OF THE STUDY

With the growing interest in locally sourced tableting excipients, the need to test the properties of locally sourced plant products have arisen. This study is an extension of a previous test on the characteristics of the starch of *Vigna subterranea*, which has been

evaluated and shown to be a conventional excipient used as a binder and disintegrant in the formulation of tablets. (Bambara nut) as a disintegrant since it is known that the presence of a disintegrant can affect some mechanical properties of the tablet.

The objectives are:

To evaluate the disintegrant properties of *Vigna subterranea* starch

To compare the disintegrant properties of *Vigna subterranea* starch and maize starch at different concentrations

To formulate metronidazole tablets and evaluate the effect of these disintegrants on the tablet

CHAPTER TWO

MATERIALS AND METHOD:

2.1 MATERIALS:

The materials used in the study include:

- Metronidazole Powder (William Ransom and Son Limited Nitchin Hertfordshire, England). Metronidazole is the active ingredient used in the formulation.
- Dried bambara nuts which were sourced from Ringroad market, Benin city, Edo state,
- Maize starch USP (William Ransom and Son Limited Nitchin Hertfordshire, England).
- Talc (William Ransom and Son Limited Nitchin Hertfordshire, England).
- Magnesium Stearate (William Ransom and Son Limited Nitchin Hertfordshire England).
- Hydrochloric Acid

while the metronidazole, maize starch and other chemicals were obtained from Pyrex Laboratory Supply Company Benin City Nigeria.

Equipment Used:

- Single punch tableting machine-Type F3, Manesty Machines, Liverpool, UK.
- OHAUS Scout Pro Weighing Balance
- Hot air oven- kottermann, Germany
- Tablet disintegration apparatus -MK IV, Manesty Machines, Liverpool, England.
- ENKAMP dissolution apparatus - England
- Hardness tester - Monsanto chemical, Liverpool, England

- Roche Friabilator - Erweka, Apparatebau, GmBH, Germany.

2.2 METHODS

2.2.1. Extraction of Bambara nut starch:

All the stones and dirt were removed from the Bambara nut and about 5kg of the seeds were soaked overnight and ground. It was pulverized with a grinding mill and the shaft was sieved out to obtain a fine powdery form. After mixing the powder with enough water, it was strained through a muslin cloth, and the liquid that was obtained was stored. The process was repeated until all the liquid has been removed from the Bambara nut flour. It was then kept in a storage container. The suspension obtained was allowed to stand for a day. The starch split out and fell to the bottom as the container stood, and the supernatant layer was gently decanted. The starch sediment was rinsed with enough water, agitated, and allowed to settle for two hours in order to remove any water soluble contaminants. The starch was left after the supernatant layer was removed and dried in the oven.

2.2.2 Characteristics of The Starch Powders Used In The Study

The following tests were carried out for maize starch and *Vigna subterranea* starch

Organoleptic Properties:

The powder's characteristics, including taste, odor, and color, were identified and recorded.

Chemical Test:

A 5ml starch suspension was prepared 3 drops of 0.01M iodine solution was added to the suspension and the colour change was recorded.

Solubility Of the Powder:

100mg of the starch was added to 2ml of cold water in a test-tube, shaken and its solubility was recorded.

Bulk Density:

20g of the starch was gently poured into a 100ml graduated cylinder. The volume of the starch was recorded and used in the calculation of the bulk density.

Tapped Density:

20g of the starch was gently poured into a 100ml graduated cylinder and tapped 100 times gently on a wooden platform to a constant volume. The volume of the starch was recorded and used in the calculation of the bulk density.

Swelling Capacity:

In a 100ml measuring cylinder, the tapped volume of 10g of the starch was determined (V1). It was then initially dissolved in 85ml of distilled water before being reconstituted to volume with additional water. After standing for 24 hours, the sediment's volume was calculated (V2). The equation below was used to calculate the swelling capacity..

Swelling capacity = $V_1 - V_2$ …..(1)

2.2.3 Preparation of Maize Starch Mucilage

10% concentration of maize starch mucilage as starch binder was prepared by mixing 2g maize starch powder in 20ml of water and stirring until properly dispersed. The volume was made up to 100ml by adding hot water with continuous stirring in order to form the mucilage. It was then used while still slightly warm.

2.2.4 Preparation of Metronidazole granules

A total of 9 batches of granules were made, four batches each for the tablets to be made with varying concentrations of maize starch and starch from *Vigna subterranean* (Bambara nut starch). The wet granulation method was used to prepare the granules.

Each batch was prepared by thoroughly combining the appropriate quantity of metronidazole with half of the weighed amount of disintegrant. 10% w/v maize starch mucilage is gradually added in the required amount to the powder mixture. The moist mixture was passed through a

1.7 mm sieve before being dried for 10 minutes in a hot air oven (Gallenkamp UK) set to 50°C. To uniformize the granule size, the dry coarse granules were subsequently pressed through a 710um mesh. The granules' flow characteristics were then established.

2.2.5 Determination of Flow Properties

a) Angle of Repose

The approach involving a fixed funnel and a free-standing cone was used to calculate the angle of repose (a). The tip of a funnel was clamped 3 cm above a sheet of graph paper that was laid out horizontally on a level table. The granules were slowly poured through the funnel until the apex of the cone that was created just touched the funnel tip. The height of the heap was measured. The equation is used to compute the tangent of the angle of repose and the mean diameters of the bases of the granules' cones:

$Tan\emptyset = 2h/d$ …. (1)

Where h is the height of the heap of granules and d is the diameter of the base of the heap of powder.

b) Bulk and Tap Densities

A 100 ml clean, dry measuring cylinder was filled with 20g of each of the grains. Each granule's volume without tapping is measured as V0, and the volume after being gently tapped 100 times on a hardwood platform is measured as V100.

Using the bulk and tapped volumes, the bulk and tap densities are determined as the weight to volume ratio of the granules.

$$\text{Bulk density} = \frac{Weight\ of\ granules}{V0} \quad \ldots. (2)$$

$$\text{Tapped density} = \frac{Weight\ of\ granules}{V100} \quad \ldots.(3)$$

c) Hausner Ratio

This is determined by dividing the samples' tap density by their bulk density.

$$\text{Hausner's ratio} = \frac{Tapped\ density}{Bulk\ density} \quad \ldots.(4)$$

d) Compressibility Index or Carr index (C%)

This is calculated by inputing the data gotten from the bulk and tap densities into the equation below

Compressibility = $\frac{(Tapped\ density - bulk\ density)}{Tapped\ density}$ x 100% …. (5)

e) Flow Rate

The flow rate of the granules was determined was determined by dividing the weight of the granules used in the determination of the angle of repose by the time taken for all the granules to fall under the influence of gravity.

Flow rate = $\frac{Weight\ of\ granules}{Time\ taken}$ ….(6)

2.2.6 Preparation of Metronidazole Tablets

Table 2.1: Formular for The Preparation of Metronidazole Tablets

INGREDIENTS	QUANTITIES/TABLET	QUANTITIES/BATCH
Metronidazole	400mg	20000mg
Disintegrant	10%, 15%, 20%, 25%$^{W}/_{W}$	10%, 15%, 20%, 25%$^{W}/_{W}$
Binder mucilage	10%$^{W}/_{v}$ Maize starch	10%$^{W}/_{v}$ Maize starch
Magnesium stearate	1%$^{W}/_{W}$	1%$^{W}/_{W}$
Talc	1%$^{W}/_{W}$	1%$^{W}/_{W}$

The granules were mixed with the required amount of talc and magnesium stearate and the other half of the disintegrant.

The granules mixed for each batch were compressed into whole tablets using a manually operated rotary press (Manesty Machine Liverpool). The machine was set at an arbitrary compression pressure of 27kpa for all the tablets.

9 batches of 50 tablets were prepared using maize starch as binder and different percentages of maize starch and bambara nut starch as the disintegrant and are shown below.

Table 2.2 The Various Concentration Of Disintegrant In The Batches Of Metronizole

BATCHES	**Concentration of Disintegrant**
Batch 1	Contains 0% Disintegrant
Batch 2	Contains 10%w/w Maize Starch as Disintegrant
Batch 3	Contains 15% w/w Maize Starch as Disintegrant
Batch 4	Contains 20% w/w Maize Starch as Disintegrant
Batch 5	Contains 25% w/w Maize Starch as Disintegrant
Batch 6	Contains 10% w/w Bambara nut Starch as Disintegrant
Batch 7	Contains 15% w/w Bambara nut Starch as Disintegrant
Batch 8	Contains 20% w/w Bambara nut Starch as Disintegrant
Batch 9	Contains 25% w/w Bambara nut Starch as Disintegrant

2.3 EVALUATION OF THE TABLETS

The tablets were stored in an airtight container to allow elastic recovery and hardening for 24 hours before tests were carried out.

A) Uniformity of weight test

This was determined by using an electronic weighing balance. 5 randomly chosen tablets from each batch were weighed, and the mean weight was computed.

B) Crushing strength determination

Using a portable hardness tester, the tablets' hardness was determined (Mosanto Type). Each batch of 10 tablets was evaluated independently, and the mean hardness was computed.

C) Friability test

From each batch, 5 tablets were randomly selected and weighed. Their weight was recorded as initial weight W_1, the tablets were then placed in a friabilator (Eweka TA Germany). They were subjected to rolling and repeated shocks resulting from fall in the apparatus. After a given time (5mins) at 25rpm, the tablets were removed and reweighed W_2. The friability was calculated using the formular below

Formular $= \frac{W1-W2}{W1} \times 100$

Where W_1 = initial weight of the sample before friability and W_2 = weight of samples after friability test.

A maximum weight loss (obtained from a single test or from the mean of three tests) of not more than 1.0% is regarded by USP, IP, and BP as acceptable for the majority of products. The maximum allowed weight reduction should be between 0.8% and 1%.

D) Disintegration test

Distilled water kept at 37°C was used as the disintegration medium in the BP disintegration device (MK4, Manesty machine). 6 tablets were taken randomly from each batch and used in

the determination. A tablet was placed in each of the tube closed at the lowered end by a wire mesh. The test tubes were caused to move up and down in the disintegration medium so that the tablets were constantly agitated. Once all of the tablet particles had passed through the mesh, the process of disintegration was considered complete, and the time was noted.

E) Dissolution test

on the various tablet batches. In the apparatus's vessel, 1000ml of the dissolution media (0.1M HCl), free of air, was added. The dissolving medium was kept at 37 ±1°C. Before the paddle started to rotate, the tablet was allowed to reach the bottom of the vessel. The tablet was kept horizontal by a wire helix to prevent it from sinking to the bottom of the vessel.

At intervals of 5 minutes, 10 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 1:30 minutes, and 2 hours, 10 ml of the dissolution media were removed using a pipette, and the solution's absorbance was measured using a UV spectrophotometer at a wavelength of 277 nm. The percentage of drug released at these time intervals was determined.

2.3.2 Standard Calibration Curve

The standard calibration curve of metronidazole powder was obtained by doing a serial dilution with 100mg of the metronidazole powder in 100ml of the dissolution medium (0.1M HCL), to obtain a stock solution of 1mg/ml. Further dilution was carried out with a dilution of 10 and the absorbance was read from a UV spectrophotometer at 277nm wavelength.

2.3.3 Statistical Analysis

The results from the evaluation of the tablets were subjected to the student's t-test at a 5% level of significance using IBM SPSS statistics, p values < 0.05 were considered statistically significant. The results were reported as mean ±standard deviation

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 Organoleptic Properties of Bambara Nut (*Vigna Subterranea*) Starch

The physical properties of the starch evaluated in this study is shown in Table 1. The starch powder of *Vigna subterranea* was light brown, odourless and tasteless. It had a rough texture, while the maize starch had a white colour, it was odourless and tasteless with a smooth texture. The starch of *Vigna subterranea* had a higher bulk density, which is indicative of larger particles and a higher porosity than the maize starch, this property enhances disintegration. The swelling value of Bambara nut starch was 2.14 as opposed to that of maize starch which was 1.13. Swelling is as a result of the penetration of a solvent into the network of particles leading to volume change and a large volume force which breaks the tablet apart hence disintegration(Adjei et al 2017) Water uptake and swelling are important functions of disintegrants and *Vigna subterrenea* starch had a higher swelling capacity than maize starch. This indicates that Bambara nut starch has properties of a good disintegrant.

Starch Identification test

On reaction with iodine both starches produced a blue-black colouration, indicating the presence of starch.

Table 3.1: Physical Properties Of *Vigna subteranea* Starch

Tests	**Bambara Nut Starch**	**Maize Starch**
Appearance	Light Brown	White
Taste	Tasteless	Tasteless
Odour	Odourlesss	Odourless
Texture	Rough	Rough
Solubility	Insoluble in cold water	Insoluble in cold water
Chemical test with iodine	Positive test (starch confirmed)	Positive test (starch confirmed)
Bulk density(g/cm^3)	0.58	0.41
Tapped density(g/cm^3)	0.65	0.46
Swelling capacity	2.18	1.31

3.2 Flow Properties of The Granules:

The physicochemical properties have shown a direct relationship between the concentration of the disintegrant and the flow properties. As the disintegrant concentration increased, the flow properties improved. There was a decrease in the angle of repose, tapped density, Carr's index and Hausner's ratio and an increase in the flow rate of the granules with increase with the concentration of the disintegrants.

It has been determined that a good granule flow rate is essential for effective tableting. The flow characteristics of granules can be evaluated using the Hauser's and Carr's index. Values of the Hausner's ratio higher than 1.26 indicate poor flow characteristics. Good flow property is indicated by a Carr's index value of less than or equal to 16%, whereas a poor flow is indicated by a number more than 23%.

From the results obtained, the granules with the disintegrants have good flow properties with Hausner ratio values lower than 1.26 and within the range of 1.11 – 1.18. The Carr's index of the granules falls with the range of 12% – 16%, which is also an indication of good flow properties.

Another way to evaluate the flow characteristics of granules is to measure their angle of repose. The angle of repose of the granules used for the experiment's tablets had angles of repose between 25 and 30 degrees. Generally speaking, granules with angles of repose greater than 50 degrees have unsatisfactory flow properties, while those with angles of repose between 25 and 30 degrees have good flow rates.

Table 3 shows the granules' flow characteristics.

Table 3.2: Physiochemical Properties of The Metronidazole Granules

Starch	Disintegration Concentration ($\%\frac{w}{w}$)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (°)	Hausner's Ratio	Angle of Repose (%)	Flow Rate (g/s)
Maize	25	0.54	0.60	10	1.11	26	3.48
	20	0.57	0.64	11	1.12	27	3.42
	15	0.55	0.63	12.6	1.14	28	3.35
	10	0.56	0.65	14	1.16	29	3.15
	0	0.55	0.67	17	1.20	30	3.10
Vigna subterranea	10	0.53	0.64	16	1.18	30	3.13
	15	0.56	0.65	14	1.16	26	3.21
	20	0.52	0.60	13	1.15	27	3.45
	25	0.48	0.55	12	1.14	25	3.78

3.3 EVALUATION OF PHYSICOCHEMICAL PROPERTIES OF METRONIDAZOLE TABLETS FORMULATED

The physicochemical properties of the prepared metronidazole tablets were represented in table 3 and 4

3.3.1 Effect of the disintegrants on weight uniformity

According to the result from the table 3 and 4, the weight of the tablets varied with varying concentrations of the disintegrant. The weight uniformity test on the tablets revealed no appreciable variation in weight ($p>0.05$) amongst tablets made with equivalent concentrations of the disintegrant. The weight variation in the tablets with different concentrations of the disintegrant, was due to the difference of the varying weight of the disintegrant in these batches containing 10%, 15%, 20%, 25% percent of the maize starch and *Vigna subterranea* starch

3.3.2 Effect of the disintegrants on the hardness of the tablets

The official hardness range specified in BP/USP required to break a standard compressed tablet is a pressure not less than 4kg.

The hardness test values (Crushing strength) of the tablets ranged from 4kg - 9kg which is an acceptable limit (David et al 2014) There was no significant difference ($p>0.05$) within the groups of metronidazole tablets containing similar concentrations of the disintegrants.

The crushing strength of the tablets decreased as the concentration of both the maize starch and the bambara nut starch of the disintegrant increased.

The comparable hardness values obtained with different concentrations of the starches used, could be attributed to the fixed amount of binder used. Tablet hardness is majorly attributed to the binder used in tablet formation.

3.3.3 Effect of the disintegrants on the friability of the tablets

As shown in the tables 3.3 and 3.4, as the amount of the disintegrant increased, the friability value increased.

Some of the tablets did not meet the British Pharmacopoeia's requirement for a 1% maximum loss of tablets tested during a friability test.

The similar friability values obtained with similar concentrations of the starches used, could be attributed to the fixed amount of binder used.

The friability values of the tablets with disintegrant of 10% and 15% of both maize and bambara nut starch were less than 1%, which was acceptable, compared to the tablets with 20% and 25% of the disintegrants, which had values above 1% (Baltimore et al 2013)

3.3.4 Effect of the disintegrants on the disintegration rate of the tablets

From the results displayed in table 3.3 and 3.4, there was a reduction in the rate of disintegration with increase in disintegrant concentration. There was significant difference within the groups of metronidazole tablets containing similar concentrations of the different disintegrants.

The tablets made with the *Vigna subterranean* starch (bambara nut starch) had shorter disintegration time compared to the tablets with the same concentration of maize starch disintegrant.

The starch of *Vigna subterranea* absorbed more moisture than maize starch. This could be attributed to a more adequate formation of hydrophilic networks by *Vigna subterranea* starch particles and an indication of larger grain sizes and pore sizes, which trap moisture more efficiently than the maize starch, leading to higher moisture content and the faster rate of disintegration of the tablets formulated with this starch.

High moisture content is required for optimal disintegration and dissolution of the tablets.

These results could also suggest that the inter-particle bonds between the drug excipients and metronidazole is stronger in the tablets made with maize starch disintegrant than tablets made with Bambara nut starch disintegrant.

Table 3.3 Properties of Tablets Formed With Maize Starch Disintegrant

Concentration Of Disintegrant	Mean weight (g)	Mean hardness (kg/cm^2)	Mean friability (%)	Mean disintegration time (secs)
0% Maize Starch	0.405±0.002	9.00±0.521	0.613	96±8.650
10% Maize Starch	0.450 ±0.001	8.50±0.712	0.741	86±9.405
15% Maize Starch	0.467 ±0.002	8.100±0.831	0.867	76±7.567
20% Maize Starch	0.501±0.001	7.200±0.632	1.432	64±8.790
25% Maize Starch	0.521±0.002	5.100±0.734	1.921	52±7.201

Table 3.4 Properties Of Tablets Formed with *Vigna subterranea* Starch

Concentration Of Disintegrant	Mean weight (g)	Mean hardness (kg/cm^2)	Mean friability (%)	Mean disintegration time (secs)
10% Vigna ***subterranea***	0.451 ±0.002	8.300±0.810	0.662	71 ± 7.033
15% Vigna ***subterranea***	0.467±0.001	7.20±0.933	0.843	62±8.034
20% Vigna ***subterranea***	0.500±0.001	6.10±0.785	1.354	54±6.087
25% Vigna ***subterranea***	0.520±0.002	4.10 ±0.840	2.263	45±4.801

3.4 Dissolution Test Result

A systematic approach for determining the rate of drug release from a dosage form is the tablet dissolution test. It supports the enhancement of therapeutic efficacy during product development and stability evaluation.

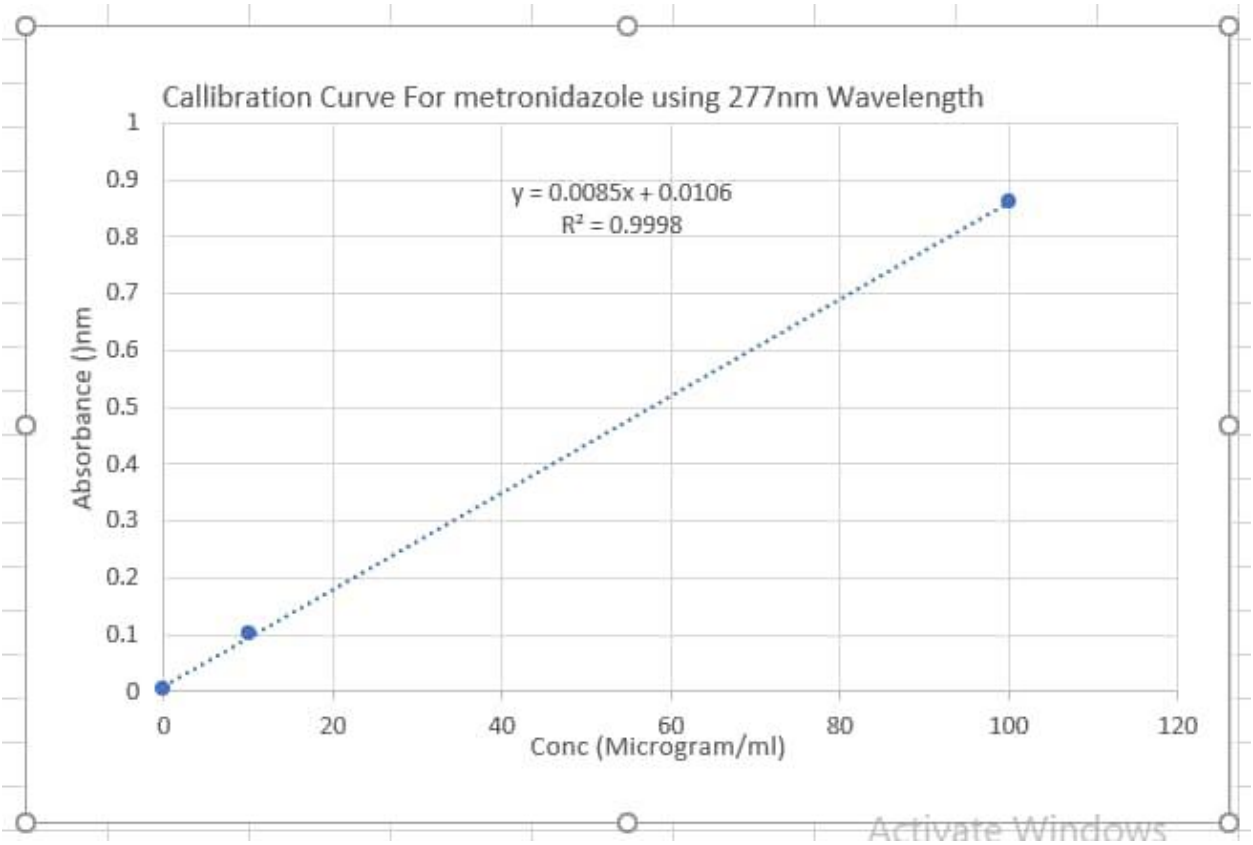

Figure 3.1: Standard calibration for dissolution test

3.4.1 Effect of the disintegrants on the dissolution of the tablets

From the results obtained from the tablet dissolution test, it was observed that the higher the concentration of the disintegrant, the higher the percentage of drug release. This is possibly because disintegrants help break down tablets into smaller pieces, which helps release drug particles from the matrix of the tablet and increases the surface area available for future dissolution.

Every tablet produced met the British Pharmacopoeia requirement that, after 30 minutes of dissolution, at least 70% of the medicine should be in solution.

The dissolution test results show that disintegration is crucial to dissolution because it determines the surface area of contact between the active ingredient in the tablet and the liquid. Disintegration breaks the tablet down into its constituents in other to release the drug into solution. The greater the concentration of disintegrant, the greater the percentage drug release with greater release from the tablets made with the Bambara nut starch

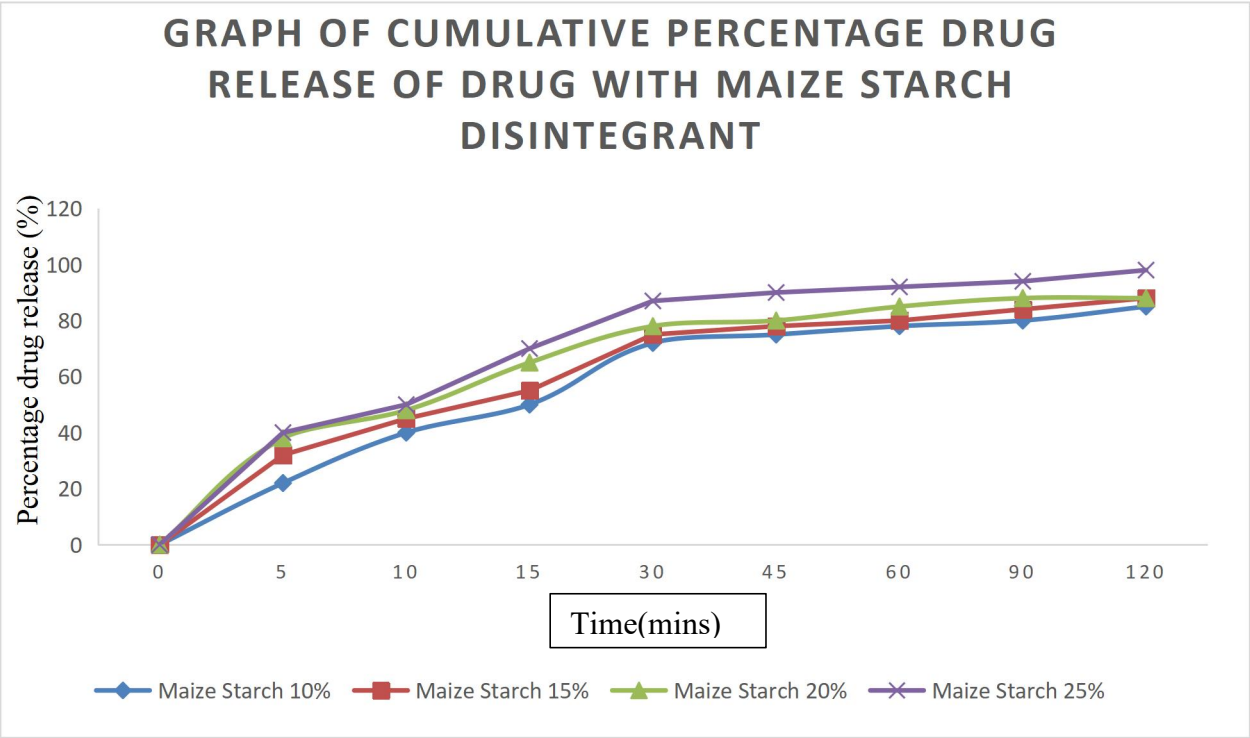

Figure 3.2: Table of Percentage Drug Release of Tablets with Varying Percentages of Maize Starch Disintegrant

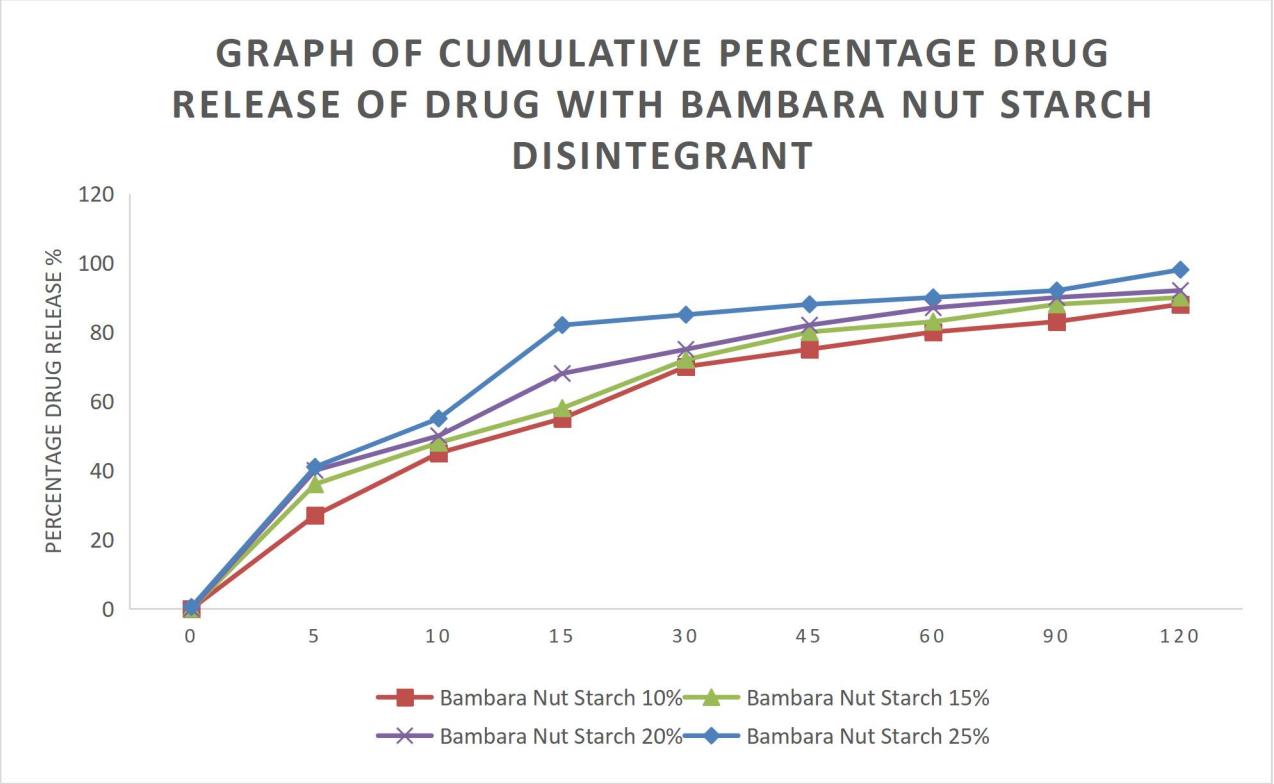

Figure 3.3: Table of Percentage Drug Release of Tablets with Varying Percentages of *Vigna subterranea* Starch Disintegrant

Figure 3.4 Image Of Formulated Metronidazole tablets

CHAPTER FOUR

4.0 CONCLUSION

As a disintegrant, *Vigna subterranea* it gave similar values with maize starch BP for the parameters tested, however it gave a shorter disintegration time than tablets made with the maize starch disintegrant at all concentrations.

From the experiment, the efficient concentrations of Bambara nut starch as a disintegrant in metronidazole tablets was 10% and 15%.

Therefore, at optimum concentration, starch from *Vigna subterranean* can be used as an adequate substitute for maize starch as a disintegrant for metronidazole tablet formulation.

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