

**EVALUATION OF *DIGITARIA IBURUA* (FAMILY POACEAE)
STARCH AS A BINDER AND DISINTEGRANT IN A
MACRO-DOSE TABLET FORMULATION.**

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JUNE, 2009

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**DEPARTMENT OF PHARMACEUTICS AND
PHARMACEUTICAL MICROBIOLOGY,
FACULTY OF MEDICINE,
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JUNE, 2009

DECLARATION

I declare that the work in this thesis entitled “Evaluation of *Digitaria iburua* (Family Poaceae) Starch as Binder and Disintegrant in a Macro-dose Tablet Formulation” has been performed by me in the Department of Pharmaceutics and Pharmaceutical Microbiology under the supervision of Dr. H. Musa and Dr. P.G. Bhatia.

Information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this thesis was previously presented for another degree or diploma at any University.

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CERTIFICATION

This thesis entitled EVALUATION OF *DIGITARIA IBURUA* (FAMILY POACEAE) STARCH AS A BINDER AND DISINTEGRANT IN A MACRO-DOSE TABLET FORMULATION by Gambo Aishatu meets the regulation governing the award of degree of MASTER of SCIENCE of AHMADU BELLO UNIVERSITY, ZARIA, and is approved for its contribution to knowledge and literary presentation.

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DEDICATION

This thesis is dedicated to the sweet memory of my late Father, Alhaji Gambo Dauda, who made me what I am today. For this, I wish your gentle and humble soul an eternal rest in Aljanna Firdausi.

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I start in the name of Allah, Most Beneficent Most Merciful.

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ABBREVIATIONS

1. BPC - British Pharmaceutical Codex
2. BP - British Pharmacopoeia
3. U.S.P - United States Pharmacopeia
4. mg - Milli Gramme
5. mm - Milli Metre
6. KgF - Kilogram Force
7. MNm⁻² - Mega Newton Per Metre Square
8. w/w - Weight by Weight
9. pH - Hydrogen-Ion-Concentration
10. °C - Degree Centigrade (Celsius)
11. % - Percentage
12. g - Gramme
13. ml - Milli Litre
14. µm - Micro Metre
15. v/v - Volume by Volume
16. w/v - Weight by Volume
17. NS - Normal Solution
18. N - Normal

19.	r.p.m	-	Rounds (Revolutions) Per Minute
20.	QS	-	Sufficient Quantity
21.	Kg	-	Kiligramme
22.	NaOH	-	Sodium Hydroxide
23.	g/sec	-	Gramme Per Second
24.	°	-	Degree
25.	min	-	Minutes
26.	MGS	-	Mean Granule Size
27.	PGS	-	Pregelatinised Starch
28.	DI	-	<i>Digitaria iburua</i>
29.	MS	-	Maize Starch
30.	Fig.	-	Figure

ABSTRACT

The study aims at formulating Paracetamol tablets using *Digitaria iburua* (DI) starch as binder and disintegrant. *Digitaria iburua* starch was extracted from *Digitaria iburua* grains using wet milling and sieving method and thereafter purified. Pregelatinised *Digitaria iburua* starch (PGS DI) was also prepared. Paracetamol granules were produced by wet granulation method using these two starches as binders and disintegrants and the properties of the granules were compared with gelatin as binder and Maize starch as disintegrant. Properties of the granules and the resulting tablets were determined thereafter compressed into tablets on a single station tablet press. The percentage yield of the starch (DI) extracted was 62.20% w/w while that of (PGS DI) was 73.18% w/w. *Digitaria iburua* starch when compared with maize starch BP. as tablet binder showed similarity in the values of their moisture content, swelling power, Hausner ratio, tapped and bulk densities. However, there was superiority displayed in some properties such as flow rate, angle of repose and true density. Increasing the concentration of *Digitaria iburua* starch as tablet binder and disintegrant resulted in an increase in tablet thickness, a decrease in friability and an increase in disintegration time.

Compaction studies showed that DI starch and PGS when used as binder and disintegrant produced granules that compact by initial fragmentation followed by plastic deformation.

CHAPTER ONE

1.0 INTRODUCTION

1.1 GENERAL INTRODUCTION

Tablets are solid preparations, each containing a single dose of one or more active ingredients and are obtained by compressing uniform volumes of particles/granules intended for oral administration. Tablets are formulated to release the active ingredients in a way that will achieve the desired effect, and their quality is controlled by a number of standard tests which may include uniformity of weight and content, hardness, friability, disintegration and dissolution (B.P, 2002). Medicinal tablets are often stamped with symbols, letters, and numbers which enable them to be identified. Sizes of tablets to be swallowed range from a few millimeters to about a centimeter. Some tablets are in the shape of capsule, and are called "caplets".

There are several reasons for the popularity of tablets:

- (i) All tablets employ the oral route of administration, which is generally the most acceptable route.
- (ii) Tablets permit a high accuracy of dosage

- (iii) The dose of the active drug is contained in a relatively small volume. Thus a concentrated dosage form is produced, leading to ease of packaging, transport, storage and eventual administration.
- (iv) They are essentially water-free and hence loss of potency due to hydrolysis is minimised.
- (v) They are cost effective to manufacturers.
- (vi) Various types of tablets formulations are available that can monitor controlled drug release.

Tablets have some disadvantages, including

- (i) Some drugs such as insulin that are denatured by stomach acids cannot be made into tablets.
- (ii) Tablets could be difficult to swallow for old or young patients.
- (iii) Due to poor absorption and consequently low bioavailability of some drug, the injectables are preferred.

1.2 STATEMENT OF PROBLEM

Substances that are used to impart the desired characteristics to the active ingredient, during formulation are called excipients, of which, starch is a very important example. Starch is one of the earliest

excipients to be used for pharmaceutical dosage forms. Depending on the application, starch acts as a diluent, disintegrating agent or binder.

To proffer solution to the cost of importation of starch for tableting, researchers have evaluated local starches for use as pharmaceutical excipients.

Nasipuri, (1986) evaluated cassava starch (*Manihot utilissima*) as a tablet binder and disintegrant and found it to be as efficient as potato starch. In the same year, Cocoyam starch (*Colocasia esculenta*) was evaluated by Nasipuri as binder and disintegrant and found that the product is a suitable alternative to potato starch. Esezebo and Ambujam (1982) evaluated plantain (*Musa paradisiaca*) starch as tablet binder and disintegrant and compared it with maize starch as standard. They concluded that plantain starch has twice the binding and half the disintegrant property of maize starch.

Iwuagwu *et al*,(1986) studied African bitter yam (*Dioscorea dumetorum*) and white yam (*Dioscorea rotundata*) starches for their binding and disintegrating properties and compared them with potato starch. They found that white yam tuber starch have stronger binding property than potato and African bitter yam. However the disintegrant properties were more or less similar.

In 1987, Deshpande and co-workers studied the binding and disintegrating properties of starch extracted from sorghum (*S.bicolor*) and found that it was as good as maize starch. Akande, (1988) investigated pearl millet starch as tablet binder and disintegrant using maize starch as standard. He concluded that millet starch can be used as both binder and disintegrant. Garr,(1988) also found sorghum starch as useful as maize starch, in respect of binding and disintegrating characteristics. Similar studies on the effect of some local starches (fresh yam tuber, cassava and cocoyam) on the properties of granules and tablet formulation by Kunle (1988) concluded that these are adequate as binders and disintegrants.

Many local starches have been studied extensively but no work seems to have been reported on *Digitaria iburua* despite its abundance in Nigeria especially in Northern Nigeria.

1.3 SCOPE OF THE STUDY

Digitaria iburua starch is intended to be evaluated as tablet binder and disintegrant. The compactional behavior of various granules produced will also be investigated.

The study will be limited to the evaluation of the binding and disintegrant properties of *Digitaria iburua* starch in a macro-dose

tablet formulation. Tablet formulation containing Paracetamol 500mg as active ingredient will be used as the template.

1.4 OBJECTIVES OF THE STUDY

The aim of this research work is to formulate tablets using *Digitaria iburua* as tablet binder and disintegrant. It is proposed to achieve its aim by pursuing the following objectives.

- Procure *Digitaria iburua* grains from Sabongari market, Zaria, authenticate it and extract its starch using the wet milling and sieving method.
- Purify and characterize the physico-chemical properties of the starch using standard testing procedures such as microscopy, size distribution, solubility, iodine test, acid tests, etc.
- Produce pregelatinised starch from the *Digitaria iburua* starch and similarly characterize the physico-chemical properties stated above.
- Determine the flow characteristics and other properties such as moisture content, moisture sorption and swelling power of the two starches and compare them with those of Maize starch BP.
- Produce Paracetamol granules using the two starches as binder and disintegrant, and evaluate their granule properties such as flow, etc

- and compare with granules produced using gelatin as binder and Maize starch BP. as disintegrant.
- Compress the above Paracetamol granules into tablets and evaluate the effects of *Digitaria iburua* starch as binder and disintegrant on the properties of the resulting tablets such as weight, thickness, friability, disintegration, dissolution, etc.
 - Determine the effect of *Digitaria iburua* starch when used as tablet binder and disintegrant on the compaction behavior of the tablets using the Heckel equation.

1.5 JUSTIFICATION OF STUDY

Pharmaceutical raw materials should be cheap and readily available so as to have an overall availability and accessibility of the finished pharmaceutical dosage form to a large populace. The current Federal Government of Nigeria Policy, Vision 2020 for economic development makes it necessary for scientists to source for pharmaceutical raw materials locally. This is likely to conserve foreign exchange and also increase the income of local farmers.

Digitaria iburua with high starch content has not been exploited for pharmaceutical utilization despite its abundance in Nigeria especially in the northern part of the country.

1.6 LIMITATION OF THE STUDY

In this study, wet method of extraction is used; other extraction methods that might give higher starch yield could not be explored for lack of equipment and financial constraints.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 TABLETS AND TABLETTING

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or moulding methods (Musa,1999). The particles to be compressed consist of one or more active ingredients with or without auxillary substances such as diluents, binders, disintegrating agents, glidants, lubricants substances capable of modifying the behavior of the active ingredients in the digestive tract, authorized colouring matter and flavouring agents (B.P,1988)

2.2 EXCIPIENTS

Substances that are used to impart the desired characteristics to the active ingredient, during formulation are called excipients, of which, starch is a very important example. The most important property desired of an excipient, is that it must be pharmaceutically inert and also be compatible with the drug molecules (King,1980; French,1984). Other desirable properties include good flowability, compressibility, physical and chemical stability (French,1984). Unfortunately, no single substance has been found to possess all these

qualities in one, therefore a combination of excipients are often employed.

An excipient is an inactive substance used as a carrier for the active ingredients of a medication. In addition excipients can be used to aid the process by which a product is manufactured. At times, the active substances may not be easily administrable. They need to be put in some appropriate form. The active substance is then dissolved or mixed with an excipient. Excipients are also sometimes used to bulk up formulations involving very potent active ingredients, to allow for convenience and also for accuracy of dosage. Depending on the route of administration, and form of medication, appropriate excipients may be chosen.

Pharmaceutical codes require that all ingredients in drugs, as well as their chemical decomposition products are identified and guaranteed to be safe. For this reason, excipients are only used when absolutely necessary and in the smallest amounts possible.

2.2.1 Types of excipients

(a) Binders

Binders causes particles of drug and other excipients to cohere into a granular form. They are frequently of a polymeric

nature, either natural or synthetic and are normally used as aqueous solutions or dispersions or be mixed with the other dry ingredients. The choice of a suitable binder for a tablet formation requires extensive knowledge of the relative importance of binder properties for enhancing the strength of the tablet and also of the interactions between the various materials constituting a tablet (Mattsson, 2000). Examples of binders include glucose, gelatin, starch mucilage and polyvinyl pyrrolidone (PVP).

(b) Disintegrants

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. It is a paradox of tablet manufacture that considerable ingenuity is used to make individual particles form a coherent structure and yet further ingenuity is then often required to ensure the breakdown of that individual components after ingestion. This is achieved by the incorporation of a disintegrant. Although all disintegrants may not act by the same mechanism, their general role is to provide a hydro-philic network within the structure of the tablet through which water may diffuse (Lowenthal, 1972). Examples of disintegrants include starch,

cellulose, crosslinked polyvinyl pyrrolidone, sodium starch glycolate, sodium carboxymethyl cellulose.

(c) Fillers/Diluents

Fillers fill out the size of a tablet or capsule, making it practical to produce and convenient for the consumer to use. By increasing the bulk volume, the final product has the proper volume for patient handling.

A good filler must be inert, compatible with the other components of the formulation, non-hygroscopic, water soluble, relatively cheap, compactable, and preferably tasteless or pleasant tasting. By far the most common diluent used in tableting is lactose (Vromans, *et al* 1985). Examples of fillers include lactose, sucrose, glucose, mannitol, sorbitol, and, calcium carbonate.

(d) Lubricants

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and injection can occur with low friction between the mix and the die wall.

Common minerals like talc or silica, and fats, for example, vegetable stearin, magnesium stearate or stearic acid are the most frequently used lubricants in tablets.

(e) Flavors and Colors

Flavors and Colors are added to improve the taste and appearance of a formulation leading to increase in compliance. Their presence serves also as a means of identification by the manufacturer and also the patient.

(f) Glidants

Glidants are used to improve the flowability of the powder or granules or both into the die cavity. A most commonly used Glidant is talc. Another glidant of choice is finely divided silica.

(g) Preservatives

Some typical preservatives used in pharmaceutical formulations are:

- (i) Antioxidants like vitamin A, vitamin E, and vitamin C
- (ii) Amino acids cysteine and methionine.
- (iii) Citric acid and sodium citrate.

(iv) Synthetic preservatives like methyl paraben and propyl paraben.

(h) Sorbents

Sorbents are used for tablet/capsule moisture-proofing by limited fluid sorbing (taking up of a liquid or a gas either by adsorption or by absorption) in a dry state.

(i) Sweeteners

Sweeteners are added to make the ingredients more palatable, especially in chewable tablets. Sugar can be used to disguise unpleasant tastes.

(j) Coatings

Tablet coatings protect tablet ingredients from deterioration by moisture in the air, and, make large and unpleasant-tasting tablets easier to swallow. For most coated tablets, a cellulose (a plant fiber) film coating is used which is free of sugar and potential allergens. Occasionally, coating materials may comprise synthetic polymers, or other polysaccharides.

2.3 METHODS OF TABLETS PRODUCTION

Before it can be tableted, the particulate matter must possess the ability to

(i) flow uniformly and quickly into the die of the tablet press,

- (ii) cohere when subjected to a compressing force,
- (iii) ensure that the finished tablet will be ejected from the die of the press quickly and easily undamaged.

Few substances possess all three of these properties and hence few powders can be made directly into tablets without a preliminary treatment and the addition of one or more excipients. There are three principal methods of converting powder into a form suitable for tableting. These are direct compression, granulation, and precompression.

2.3.1 Wet Granulation

The wet granulation method of tablet production is essentially a process of size-enlargement, sticking particles of drug and excipient together using an adhesive to produce a granular product with improved flow properties and an increased ability to cohere under pressure.

(a) Mixing

The mixing stage ensures homogeneity of drug content. A blend of solid particles is produced such that when a sample is examined, the relative proportions of ingredients in that sample are the same as in the whole of the mixture. Unlike molecules in a liquid, solid particles

do not undergo spontaneous diffusion but remain in their relative positions; thus to bring about mixing of solid particles, work must be put into the system. The first step in the mixing process is to dilate the powder bed which in turn allows relative particle motion. As the mixing process proceeds, the mixture becomes progressively more random. In a random mixture there is an equal chance of any given particle being at a given point at any one time. The deviation of a given mixture from randomness is expressed as the index of mixing; this is the ratio between the calculated variation among samples taken from a random mixture of a given composition and the actual variation seen among samples from the same mixture (Staniforth, 1982; 1983). The degree of mixing normally increases with length of the mixing time, but under certain conditions, segregation may occur where the mixture shows a tendency to separate back into its components. Segregation is most common in mixtures which have marked variation in particle size between the components; differences in particle shape and density are further contributing factors. Segregation is particularly likely to occur if the motion of the mixing device is regular as patterns of particle movement may be established. It is therefore desirable that an irregular mixing motion is adopted.

Ordered mixing occurs when small particles of one component become lodged in surface irregularities of much larger particles of another component. Such mixtures cannot be considered random as the particles do not behave independently of each other. The concept of ordered mixing is particularly useful in the manufacture of tablets which contain potent materials with direct compression diluents.

(i) Mixing Equipment:

The underlying function of mixing equipment is to cause particles to move relative to one another. Free flowing materials are usually mixed in some form of rotating container, for example cube or Y-cone blenders, the function of which is to raise the powder bed until its angle of repose is exceeded and flow occurs. The asymmetry of their design imparts a lateral movement to the solid, as well as, a tumbling action. These mixers are often fitted with baffles that break up regular patterns of particle flow.

(b) Granulation

The purpose of the granulation stage is primarily to improve the flow properties of the mixture and also to improve its compression properties. Granulation may also prevent segregation of components of the powder mixture and reduce dust generation. Size enlargement

of the particles in the powder mixture can be achieved by one of two mechanisms:

- (i) use of an adhesive substance which sticks adjacent particles together or,
- (ii) particle dissolution in the granulating fluid, followed by bridge formation between adjacent particles on evaporation of the granulating fluid; this mechanism obviously depends on the solubility of the solid in the granulating fluid.

The rate of granule formation is a function of the amount of granulating fluid present, maximum granulation being achieved when all the pores in the powder bed are filled with liquid. To form granules, bonds must be formed between powder particles so that they adhere with sufficient strength to prevent breakdown (Newitt Conway-Jones (1958) and Capes (1965))

Granulation Apparatus:

The mixing of an adhesive and probably viscous liquid into a solid requires the application of a considerable shearing force.

Shearing and Planetary Mixers:

Powder is fed into the bowl of the mixer and the liquid is added with agitation. The moist material is then forced through a

sieve, often by means of oscillating bars. This process tends to be of long duration and results in high processing and equipment costs. The process has been improved by the introduction of high speed mixer/granulators, which have an agitator (usually mounted horizontally in the base of the mixer) and also a second chopping blade which rotates in the vertical plane. Thus mixing, massing, and granulation all take place in the same piece of apparatus; massing should take place rapidly and as there is a danger that the solid can be over massed. The granulation process is constantly monitored (for example by measuring the electrical power consumption of the impeller) (Leuenberger, 2000)

Fluid Bed Granulation:

A fluid, usually air, is passed into the powder bed from below. If the air velocity is sufficient, the particles become suspended in the air and move relative to one another; this is termed fluidization and gives effective mixing. Granulating liquid is sprayed over the particles, which become sticky and adhere on collision. Alternatively, they can be mixed with the other dry ingredients and water added to the mixture. Water itself can be used as a granulating agent with hydrophilic and water-soluble materials. Substances which react in the

presence of water may require the use of an anhydrous granulating fluid.

(c) Drying

After granulation, the product exists as a damp mass. It is sieved through a relatively coarse screen to produce wet granules, which must be dried. The drying process involves removal of liquid by the application of energy, usually heat energy, but occasionally microwave radiation is used. The relationship between a solid and water is important in a variety of situations. Many drug substances and excipients are susceptible to hydrolysis and hence the water content of pharmaceutical preparations is often a matter of concern. A drying stage is essential to the wet granulation process of tablet manufacture. Unless moisture is removed, the required flow properties will not be acquired. Furthermore many tablet formulations appear to have an optimal water content which is believed to be related to the porosity of the tablet when under its maximum compressive force

Drying Equipment:

The requirements for rapid drying can be summarized as a heat supply to increase the temperature, a system that allows the removal

of evaporated liquid from the atmosphere, and minimization of the distance over which the water must diffuse before evaporation.

For drying tablet granules, the drying equipment commonly used are tray driers, fluid bed driers and Microwave driers.

In case of tray driers, air (which is repeatedly heated) flows over a series of shelves on which the wet material is spread. The rate of evaporation is governed by the area available for heat transfer, the temperature difference between the wet solid and the drying air, and the thickness of the layers of wet material. Fluid bed driers offer a number of advantages. This includes,

1. In fluid bed driers, the solid is fluidized from below, but hot air is used. In effect, each particle is surrounded by a current of hot air and so rapid drying ensues.
2. The temperature of the bed can be precisely controlled and a free flowing product is obtained.
3. The same apparatus can be used for mixing, granulating, and drying and so handling costs are reduced.
4. During drying, each granule is dried individually preventing migration of solutes between neighbouring granules

However, the process is not free from disadvantages. The disadvantages of the fluid bed drier include:

- a. movement of particles in hot dry air can lead to the generation of static electricity with attendant risk of explosion, especially if inflammable liquids have been used in the granulation process.

A recent development in drying has been the use of microwaves. Microwaves are electromagnetic radiation in the wavelength range 10mm to 1m, although the wavelengths used for drying are limited to 122mm and 312mm (equivalent to frequencies of 2450MHz and 960 MHz) to avoid interference with radio and television transmissions. As microwaves fall on materials such as water, electrons resonate rapidly in sympathy with the radiation and these results in the generation of heat and the evaporation of water. Microwave driers usually operate under vacuum and this removes the water vapour.

Advantages of microwave drying include:

- a. There is rapid drying at low temperatures.
- b. The particle bed is stationary so inter-particle attrition may be avoided.
- c. Microwave driers can be combined with high speed granulators.

Disadvantages of microwave driers include:

- a. Transport of water to the drying surface will also involve the movement of any substance dissolved in the water.
- b. Migration of solutes can occur between neighbouring granules during drying. This can lead to non-uniform drug content and, if coloured substances such as dyes are involved, uneven coloration of the tablet surface.

2.3.2 Precompression

An alternative to the wet process for making a granular product is precompression, sometimes referred to as double compression or 'slugging'. In this, the lubricated components of the tablet are compressed and the resultant aggregate is broken down to a granular mass which is then recompressed. Precompression takes place in either a tablet press, or via a roller compactor. In the former case, the tablets will be poorly formed and of variable weight due to poor flow properties of the powder mixture. Though not widely used, this process is a useful alternative when neither direct compression nor wet granulation are feasible.

2.4 COMPRESSION AND COMPACTION STUDIES

Compression is defined as the process of applying pressure to a material. Compaction can be defined as the series of events that take place following the application of pressure to a powder bed in a die cavity until a compact mass is ejected from the die cavity. In the compaction process, particles are brought sufficiently close together so that the bonding forces between them are large enough to produce a strong compact.

The consolidation process is closely associated with the compression process which describes the resultant increase in mechanical strength due to particle rearrangement and slippage, plastic deformation or fragmentation and particle-particle bonding. The compaction of powders therefore, consists of compression and consolidation processes.

2.4.1 Sequence of events in compaction of powders:

Granules enhance compactability of the tablet material. They are porous and contain both inter and intragranular pores. The sequence of events that take place during compaction is as follows:

Transition and particle rearrangement

Under pressure, particles get rearranged in such a way that the smaller ones fill the void created by the larger particles. This leads to closer packing and a decrease in relative volume, thereby increasing the density of the powder bed. The shape of the particle influences such a rearrangement.

Deformation at the point of contact

Increase in the applied pressure is likely to lead to deformation of particles at the point of contact. The type of deformation that occurs depends on the nature of particle being compressed. The deformation can either be elastic or plastic in nature.

Fragmentation

This is the breaking of the particles into smaller parts, especially bigger granules. When the applied pressure is high, particles crack and the new cracks expose fresh surfaces which yields potential bonding areas.

Bonding between the particles

This is the permanent attachment of particles to each other resulting from close proximity; the closer the distance between the two particles the higher the attachment.

Deformation of solid body

As the applied pressure is increased, the bonded solids consolidate. The deformation can either be elastic or plastic; the ability of formulated powder to form a satisfactory tablet depends on its plastic deformation during compression and elastic recovery during ejection (decompression).

Decompression

This is the series of subsidiary events that occur after applied pressure is removed from the upper punch. As the upper punch is removed from the die cavity, the residual pressure confines the tablet. The ability or otherwise to produce an intact tablet depends on the pressure exerted by elastic rebound and the associated deformation process during decompression/ejection.

Ejection

This is the process by which compressed tablet is removed from the die as the lower punch rises and pushes the tablet upward. There is continuous residual die wall pressure and considerable energy may be expended due to die wall friction. When the tablet is removed from the die wall and lateral pressure is removed, the tablet undergoes

plastic recovery with an increase in volume of that portion of the tablet removed from the die.

2.4.2 Deformation of Powder upon application pressure

Force is being transmitted through the interparticulate points of contact with the application of an external force to a powder bed. These force applied will result to stress which will be developed at these points of contact and local deformation of the material follows.

The ability of a powdered material to undergo plastic deformation during compaction is essential for ensuring adequacy of good crushing strength of compact after tableting. This attribute is commonly investigated by measuring stress relaxation in particulate material when compressed in a die at predetermined pressure and held at constant strain for a specific period of time (Malamataris *et al*, 1984).

When a powder is subjected to a compressive force, the overall bulk of the powder decreases with force exponentially, after the initial consolidation stage, where particles undergo rearrangement. A powder is considered to be undergoing deformation when there is further decrease in porosity which results if the elastic limit is exceeded. This deformation will either be elastic, plastic or

destructive (Fig. 2.1) depending upon the rate of application of the external force, the magnitude of the force, the duration of the locally induced stress and the physical properties of the material (Wray, 1992).

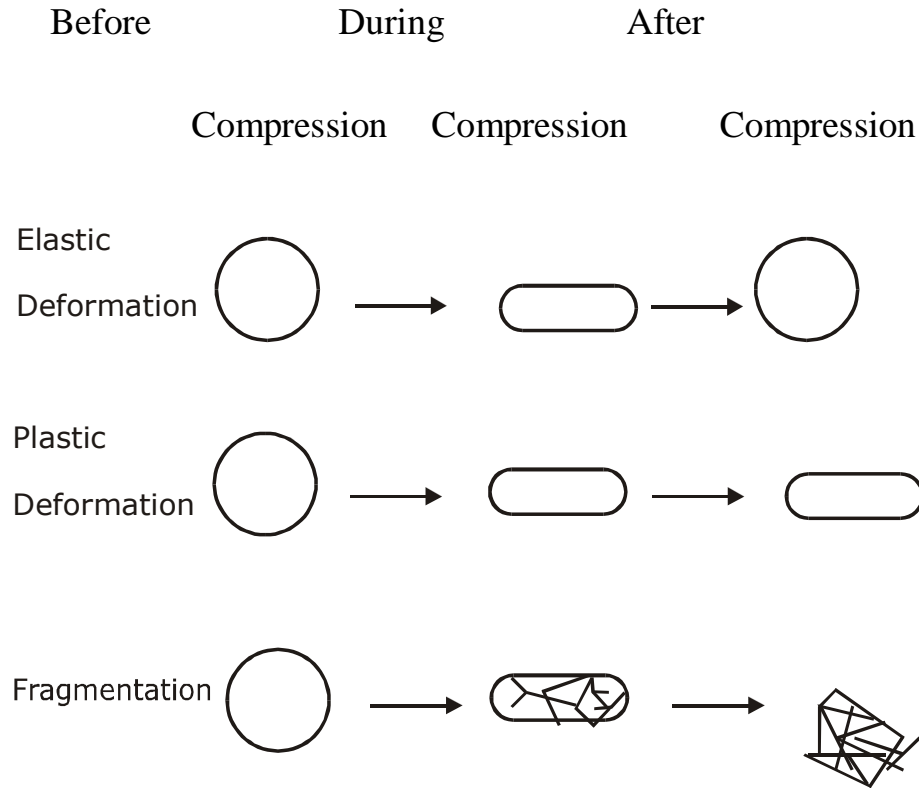


Fig 2.1 Schematic diagram illustrating the processes that take place during compression (Adapted from Ragnarsson, 1996)

The point at which the system undergoes an instantaneous and totally irreversible response to an applied force have been defined by Rippie and Danielson (1981) as the stage at which a material yields plastically. Newtonian flow is considered to occur between this stage and plastic deformation where the strain rate is directly proportional to the applied stress.

The total energy (E_1) applied at the irreversible stage has been described and quantified mathematically, as stated in equation 1 (De Blaey and Polderman, 1970; Durr *et al*, 1972; Parrott, 1990)

$$E_1 = E_1 + E_2 + E_3 \quad \dots\dots\dots\text{Eqn.1}$$

Where:-

E_1 is the work lost in the form of friction,

E_2 is the net energy spent in the formation of the tablet, and

E_3 is the elastic deformation energy

The physico-chemical nature of the material will be expected to affect the influence of E_2 and E_3 on any compaction mechanism.

2.4.3 Factors Affecting Compaction and Consolidation of Powders

The factors which affect compaction and consolidation processes may be classified according to material, process and environmental factors. The identification and quantification of such factors with effects on compaction is of great importance during manufacture where the production of uniform product is essential, and to enable the control of such factors. Among the important process variables affecting the compaction and consolidation of powders includes:

- a. Compression speed
- b. Compaction force.

2.4.4 Compaction Characteristics of Pharmaceutical Powders

Various workers (Seeling and Wulff, 1946; Train, 1954; Huffine and Bonilla, 1962) have described the sequence of events during compaction, to consist of:

- a. Filling and particle rearrangements
- b. Deformation at points of contact
- c. Fracture of particles (fragmentations)

d. Bonding

These stages are sequential, but in practice, they usually overlap each other and at least one of them may be absent under certain conditions. The significance of the phases depends to a large extent on the plasticity of the powder used (Seeling and Wulff, 1946).

2.5 POWDER COMPRESSION EQUATION

Many researchers have carried out studies on compaction characteristics of pharmaceutical powders with many equations and expressions reported (Train, 1956; Heckel, 1961; Cooper and Eaton, 1962; Kawakita and Ludde, 1970; Pilpel, 1973). However, York and Pilpel, (1973) as well as Kurup and Pilpel, (1978) have also concluded that the Heckel equation appears to be the most sensitive in distinguishing the various processes for certain soft pharmaceutical materials and also for describing the compaction properties of powders (Sune and Grant, 2001; Oladapo *et al*, 2006; Odeku, 2005). The Heckel equation analyses the ability of granules to undergo volume reduction, i.e compressibility.

The Heckel equation which relates the relative density D of a powder bed during compression to the applied pressure P ,

provides information on the mechanism of powder consolidation during compact formation by the equation

$$\ln (1/1-D) = kP + A \dots \dots \dots (2)$$

Where

D is the relative density at applied pressure P; K and A are constants.

The Heckel plot is a plot of $\ln (1/1-D)$ against applied pressure P in Newton per meter square NM^{-2} . It shows the mode of consolidation, fragmentation, plastic or elastic deformation or a mixture of any of processes mentioned above.

The slope of the plot k is the reciprocal of the mean yield pressure P_y that is an important compressibility index which is the force required to attain plastic deformation. From the intercept A, which is a function of the original compact volume, and represents two stages of consolidation:- one due to the initial relative density of the powder and the other due to densification by particle rearrangement. From the value of A, the relative density D_A , can be calculated using equation 3 as described by Roberts and Rowe, (1986).

$$D_A = 1 - e^{-A} \dots \dots \dots (3)$$

The relative density of powder at the point when the applied pressure is equal to zero is D_0 which is used to describe the initial rearrangement phase of densification as a result of die filling with high value indicating very dense packing (Itiola, 1991). D_B describes the phase of rearrangement at low pressure, the extent of which depends on the theoretical point of densification at which particle deformation begins, and is expressed as:

$$D_B = D_A - D_0 \dots \dots \dots (4)$$

These stages are sequential, but in practice, they usually overlap each other and at least one of them may be absent under certain conditions.

Based on the Heckel's equation, various researchers have identified three types of power compression behavior, namely type A, B and C (Hersey and Rees, 1971; York and Pilpel, 1973). With type A behaviour, a linear relationship is observed at all applied pressures indicating densification apparently only by plastic deformation. Sodium chloride is an example of a material with such behaviour. For type B behaviour, there is an initial region, usually curved, followed by a linear region. The initial region represents brittle fracture or particle fragmentation followed by plastic flow or deformation. This is

usual with hard, brittle materials, such as lactose (Armstrong and Lowudes, 1984) which requires initial consolidation by fragmentation to form consistent (denser) packing. Type A curves usually exhibit a steeper final slope than type B, indicating a lower mean yield pressure value. In practice, hard brittle materials are more difficult to compress than soft yielding ones because fragmentation with subsequent percolation of fragment is less efficient than void filling by plastic deformation.

Type C behaviour, which was proposed by York and Pilpel (1973) while studying the compression of fatty acids and lactose-fatty acid mixture is believed to be due to the absence of a rearrangement phase and densification is due to plastic deformation and asperity melting. The type C materials do not exhibit the curved region but rise linearly and then flattens out as the packing fraction approaches unity.

2.6 QUALITY CONTROL AND MEASUREMENT OF TABLET PROPERTIES

Tablets are subjected to a number of test procedures, some of which are pharmacopoeial.

2.6.1 Pharmacopoeial Tests

The British Pharmacopoeia 2007 contains standards and test methods for the following tablet properties:

- (i) uniformity of weight
- (ii) content of active ingredient
- (iii) uniformity of content
- (iv) disintegration
- (v) dissolution

The first three standards are designed to control the amount of active material in the tablet and the last two control the ability of that drug to be released from the tablets.

2.6.1.1 Uniformity of weight test

In the uniformity of weight test, 20 tablets taken from a batch are individually weighed and the mean calculated. Not more than two tablets are permitted to deviate from the mean by more than 10% average weight of tablet of 80mg or less, 7.5% deviation for tablets

more than 80mg but less than 250mg and 5% deviation for 250mg tablet weight or more.

2.6.1.2 *The content of active ingredient*

This is determined from a sample of 20 tablets, by crushing the tablets and subjecting an aliquot of the resultant powder to the stipulated assay procedure. The result of the assay gives the average drug content of the 20 tablets but gives non indication of the variation of drug content among the individual tablets. Gross variation would be excluded by the uniformity of weight test only if the drug comprises the bulk of the tablet; this would be true of relatively non-potent drugs which do not require dilution before tableting. Content variation among tablets of high potency drugs, in which most of the tablet mass will be diluent, cannot be picked up by a combination of these two tests. In such cases, the uniformity of content must be established by individual tablet assays. Ten tablets are assayed by the specified method. The preparation being examined fails to comply if more than one tablet is outside the range of 85% to 115% of the average value or if any tablet is outside the range of 75% to 125% of the average. If one tablet is outside the 85% to 115% range, then a further set of 20 tablets is assayed and no more tablets outside this

range should be found. To comply with the standards of the British Pharmacopoeia, the uniformity of content test must be applied to all tablets which have a drug content of less than 2mg or when the active ingredient comprises less than 2% of the total tablet weight.

The United States Pharmacopoeia XXII (22nd Revision, 1990) adopts a somewhat different approach. It permits uniformity to be demonstrated by either weight variation or content uniformity, but accepts that weight variation is not an adequate test when the active substance is a minor component of the tablet formulation. Hence weight variation can only be used when there is 50mg or more of active ingredient present which comprises at least 50% of the weight of the dosage form. A sample of 30 tablets is randomly selected. Ten are weighed and the average calculated. From the results of the assay, the content of active ingredient is calculated, assuming homogeneous distribution of the drug among the tablets.

Content uniformity is also established using a random sample of 30 tablets. Ten are assayed and the mean content and relative standard deviation (RSD) calculated. If one tablet is outside the range 85% to 115% of the claimed content but within the range 75% to 125%, or the RSD is greater than 6% or both, the remaining 20 tablets

are assayed. No further tablets outside the 85% to 115% range may be present, but an RSD of not greater than 7.8% is now permitted.

2.6.1.3 *Tablet Disintegration Test*

Until recently, the only pharmacopoeial standard relating to the release of drug from a tablet was a simple tablet disintegration test. One tablet is placed in each of six tubes of specified dimensions, each tube being closed at the lower end by a screen of 2mm nominal aperture. The tubes are raised and lowered in a bath of fluid maintained at 37°. The fluid is water unless otherwise specified and for most tablets the permitted disintegration time is 15 minutes. Tablets are said to have disintegrated if no fragment (other than fragments of coating) remains on the screen or, if particles remain, they are soft without an unwetted core.

The above test is applied to tablets which are designed to disintegrate in the gastro-intestinal tract. If this is not the case, the test may be modified. For example, dispersible tablets must disintegrate in water at 19° to 21° within three minutes, and effervescent tablets must disintegrate in 200ml of non-agitated cold water at 15° to 25° within five minutes.

2.6.1.4 *Dissolution Test*

Although tablet disintegration is monitored by this test, a drug must be in solution before it can be absorbed from the gastrointestinal tract. It therefore follows that a tablet may meet disintegration standards yet be therapeutically inactive. Hence where there may be problems in dissolving the active ingredient, the tablet is subjected to a dissolution test. The British Pharmacopoeia 1993 permits three types of apparatus, the 'rotating basket', the 'paddle', and the 'flow-through cell' methods; the precise form of the test, including the medium to be used, is specified in the relevant monograph. In general, acidic media are used with basic drugs, alkaline media with acidic drugs and water for non-ionising molecules. Unless otherwise specified, a sample is removed from the dissolution fluid after 45 minutes and analysed. The most common standard is that 70% of the stated amount of drug must be in solution after this time has elapsed. The approach of the United States Pharmacopoeia to disintegration and dissolution is slightly different, although the apparatus used is virtually identical. In the disintegration test, six tablets are used, and if after the specified time one or two have not disintegrated, another 12 are tested. Not less than 16 of the

18 should disintegrate fully. In the dissolution test, the relevant monograph specifies details of the apparatus and test fluid.

2.6.2 *Non-pharmacopoeial Tests*

A wide variety of non-pharmacopoeial tests are applied to tablets, both as in-process controls and as part of quality assurance programmes. Thus individual tablet weights, thicknesses, and diameters are often routinely and automatically measured.

2.6.2.1 *Crushing strength*

Mechanical strength measurements are also important. The most common is that of crushing strength; this is the compressional force which, when applied diametrically to the tablet, just causes it to fracture. A number of commercial instruments are available (CT40, Erweka, Monsanto, Pfizer, Strong Cobb, Schleuniger) which work on similar principles. A moving plunger presses on the edge of the tablet, which is held either vertically or horizontally, and the applied force is measured by a transducer. It has been shown that the rate at which force is applied can affect the measured value of the crushing strength, and so more accurate results are obtained if the force is applied at a uniform rate by mechanical or electromechanical means rather than manually.

2.6.2.2 *Tablet hardness*

Another variant is to calculate the tablet hardness in which the movement of the plunger as well as the applied force is measured. The hardness is the area under the curve of a plot of force against plunger movement.

2.6.2.3 *Friability test*

Although the crushing strength is a useful measurement which can be obtained easily, it could be argued that a tablet is more likely to be subjected to a large number of smaller impacts, during coating, packaging and transportation. Therefore, tablets may be subjected to friability tests which measure the resistance of the tablet to abrasion. Tablets are subjected to a standardized level of agitation for a given time, and friability is expressed as percentage loss in weight.

2.7 STARCH AS TABLET EXCIPIENT

Starch is one of the earliest excipients to be used for pharmaceutical dosage forms. Depending on the application, starch acts as a diluent, disintegrating agent or binder. Starches are the major polysaccharide food reserve of seeds, stems and roots of plants, with definite chemical structures and composition. The starch polymer consists of D-glucose units linked together through (1 4) bonds to

form a linear component called amylose and in addition (1-6) branch points. The branched form of amylose is called amylopectin. Amylose and amylopectin are the major chemical components of starch granules. Generally, amyloses have good structural properties because they pack closely to form strong, rigid and insoluble material unlike amylopectins which are readily soluble in aqueous systems, thus giving good thickening properties (King, 1980). The proportion of amylose in starch depends on its botanical source and this may vary from 10% to 30% (Gilliard, (1987). Starches with low amylose content have better pharmaceutical uses.

Starch in its pure form is a white, amorphous, relatively tasteless solid, odourless and insoluble in cold water and in organic solvents such as ethanol, ether and acetone. Starch is hygroscopic and absorbs water when equilibrated under normal atmospheric condition until the amount present is 10-17% (Akande,1988; Kunle,1988).

Official starches available, recommended by British Pharmacopocia 2002 for pharmaceutical industries are:-

- i maize starch obtained from caryopsis of *zea mays L.*
- ii. Rice starch obtained from caryopsis of *oryza sativa L.*
- iii. Wheat starch obtained from caryopsis of *triticum aestivum,*

L(T.vulgare)

- iv. Potato starch obtained from tuber of *solanum tuberosum L.*
- v. Tapioca starch obtained from *mainhot utilissima.*

2.7.1 Extraction of starch

The art of starch extraction has been known for several centuries. The Greek scientist, Dioscoride, (1st Century BC) described starch as a substance employed for medicine and use at home. The credit for manufacture of starch goes to the Romans and other Europeans. The process they practiced remained the same until the middle of 19th Century. The wet technique of maize starch extraction was developed at the end of the 19th Century mainly in the USA while potato starch was developed in Europe. The wet method involves washing and steeping the cereal for a specified period usually 24 hours. The steeped grain is crushed and sodium hydroxide solution is added to separate starch and protein. The starch is then sedimented and the sediment dried.

Presently starch extraction is a subject of extensive research and several new methods have been developed, some of which are described below:

2.7.1.1 Microbial softening technique.

Here microorganisms (bacteria and yeast) are used for the extraction. Eyini *et al* (2005) reported on efficiency of starch extraction from the tubers of *Dioscorea alata* (starch between 64-91%) through microbial softening technique and found that the bacterial isolates were comparatively more efficient.

2.7.1.2 Enzymatic starch extraction

The ordinary wet method used for starch extraction, which includes tuber crushing, sieving, sedimentation, and drying, leads to starch losses of up to 20% and also involves high energy inputs, use of large quantity of water, and expensive machinery. The use of commercial cell wall degrading enzymes to release starch from cassava roots to enhance recovery has been investigated (Kallabinski & Balagopalan, 2005). The use of the enzyme combination (pectinases and cellulases) for starch recovery from ground cassava samples resulted in an increase of 21.49% yield when used on fresh cassava chips compared with a maximum extractable starch by mechanical method.

2.7.1.3 Use of microfluidiser

This involves the use of a machine to physically split apart the starch-protein agglomerates. The extraction process is done without steeping in sodium hydroxide which is corrosive. A single pass through this piece of equipment yields many small, individual particles of starch and protein homogeneously dispersed in a watery matrix. The starch and protein components can then be separated by traditional density-based separation processes.

2.8 *Digitaria iburua* (Family - Poaceae)

The grain, being investigated, is known by various names as indicated below:

English: hungry rice, hungry koos, hungry millet, Fonio,
fundi millet

French: fonto, petit mil

Fulani: Sereme, foinye, fonye, fundenyo

Bambara: fini

Nigeria: iburu (*Digitaria iburua*), Hausa: Aburo

Senegal: eboniaye, efoleb, findi, fundi

The Gambia: findo

Togo: afio-warun, lamba

Hausa: iburu or iboru.

Digitaria iburua is also called Black Fonio. It is grown in Northern Nigerian States, Zaria, the Jos-Bauchi-Plateau regions as well as the Northern regions of Togo and Benin (Harlan, 1993; Jideani, 1999). It is reportedly also cultivated in Zaire and some other equatorial locations. In a sample of black fonio, a protein content of 11.8% was recorded. It is more difficult to dehusk with the traditional pestle and mortar as compared with white fonio.

2.8.1 *Plant Description*

Black fonio is taller than white fonio and may reach 1.4m in height. It has 2-11 subdigitate racemes up to 13cm long. Its spikelets is in threes, or clustered at each node. Its fertile spikelets is pedicelled; 3-5 in the cluster. Pedicels are unequal; pubescent, hairy at tip., elliptic-lanceolate, acute, 2mm long, barren valve 7-nerved; fertile floret darkening late.

Racemes: 4 -10, digitates, the lowest usually below the others nearly 15cm long.

Leaf: pale green leaf, blades broadly linear tapered from near the base up to 30cm long and 1cm broad, with long hairs at the base.

Grain: ellipsioid, slightly compressed from the back, very tightly enclosed by the delicate pale to dark dull brown husks.

Scutellum: elliptic, not quite reaching to the middle of the grain.

Digitaria iburua is grown along with millet (Hutchinson and Dalziel, 1937)

Table 2.1: Nutritional Composition of *Digitaria iburua* (Danladi,*et al.*,(2003)

Main Components	Amount	Essential Amino Acids	Amount
Moisture (%)	10	Cystine (mg)	2.5
Food energy (Kc)	367	Isoleucine (mg)	4.0
Protein (g)	9.0	Leusine (mg)	10.5
Carbohydrate (g)	75	Lysine (mg)	2.5
Fat (g)	1.8	Methionine (mg)	4.5
Fiber (g)	3.3	Phenylalanine (mg)	5.7
Ash (g)	3.4	Threonine (mg)	3.7
Thiamin (mg)	0.47	Tryptophan (mg)	1.6
Ribofloavin (mg)	0.10	Tyrosine (mg)	3.5
Niacin (mg)	1.9	Valine (mg)	5.5
Calcium (mg)	4.4		
Iron (mg)	8.5		

Uses

Fonio grain is used in a variety of ways. For instance.

1. It is made into porridge and couscous to make breads, popped and brewed for beer.
2. It has been described as a good substitute for semolina-the wheat product used to make spaghetti and other pastas.
3. In the Hausa region of Nigeria and Benin, people prepare a couscous (wusu-wusu) out of both types of fonio.

4. In northern Togo, the Lambas brew a famous beer (tchapalo) from white fonio.
5. In Southern Togo, the Akposso and Akebou people prepare fonio with beans in a dish that is reserved for special occasions.
6. The straw is commonly chopped and mixed with clay for building houses or outer surfaces of wells to make it stronger.
7. The straw is also burned as fire-wood to provide heat for cooking or ash for potash.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 MATERIALS USED

1. Sample of *Digitaria iburua* grains was purchased from Sabon Gari market, Zaria, Nigeria.
2. Paracetamol powder: May and Baker Ltd Dagenham, England.
3. Maize Starch: May and Baker Ltd, Dagenham, England.
4. Gelatin: May and Baker Ltd, Dagenham, England.
5. Talc: BDH Chem. Ltd. Poole, England.
6. Magnesium Stearate: BDH Chem. Ltd. Poole, England.

3.1.1 Equipment Used

1. Top loading balance weighing machine, Metler Instrument, England.
2. Carver hydraulic hand press, model C, Carver Inc, U.S.A
3. Digital pH Meter, Blue Line, England.
4. Blender, model HR1757, Philips cucina Japan
5. Oven, size B.S three, Gallenkamp, England
6. Set of sieves
7. Test Sieve Shaker, EFL IK II, Endecotts, Germany
8. Flowabilty Tester, Type GDT, Erweka, Germany

9. Tablet Press, Erweka AR 400, Germany
10. Micrometer Screw Gauge, Moore and Wright, England
11. Monsanto Hardness Tester, Manesty machines, England
12. Friabilator, Type T.A 3R, Erweka, Germany
13. Disintegration machine, Erweka, Germany
14. Dissolution apparatus, model DGN-A Type multi purpose drug test device, China
15. Vernier caliper, Moore and Wright, England
16. Water bath, Type I M 840 Gallenkamp, England
17. Hot plate, Type 6B – 8547E Gallenkamp, England
18. Binocular Microscope, Type PM 7 / 202681, Japan

3.2 COLLECTION OF *Digitaria iburua* GRAIN.

A sample of *Digitaria iburua* grains was purchased from Sabongari Market, Zaria. It was identified in the Herbarium of Department of Biological Sciences, Ahmadu Bello university, Zaria, Nigeria and assigned Voucher no: 2787

3.3 EXTRACTION OF *Digitaria iburua* STARCH

A sample of *Digitaria iburua* grains, weighing 2kg was cleaned, washed and soaked in water for 24 hrs. The mass was milled to get a slurry and sufficient quantity of water was added to the pulp

and then passed through a sieve of size 50 μ m. The mixture was centrifuged to remove all proteins. The starch was allowed to settle and 0.1N sodium hydroxide was added. Excess sodium hydroxide was removed by repeated washing with distilled water. The starch was then poured into an aluminum tray and placed in an oven set at 40°C for 48 hrs until completely dried. Sieving through mesh 90 μ m was finally carried out.

3.4 PREPARATION OF PREGELATINISED *Digitaria iburua* STARCH (PGS)

Some *Digitaria iburua* starch powder weighing 400g was put in a beaker. A small quantity of cold water was added to make it into a suspension. Boiled water was then added to make up to 5 liters and heated on a hot plate with continuous stirring until a translucent paste was formed. The paste was poured on a tray and dried in an oven set at 40°C to obtain dried pregelatinised starch.

Table 3.1: Formula for tablets of Paracetamol containing *Digitaria iburua* starch and Gelatin as binders.

Composition	Quantities per tablet	Quantities for 200 tablets
Paracetamol	500mg	100g
Maize starch (Internal Disintegrant)	60mg	12g
Gelatin/ <i>Digitaria iburua</i> starch (binder)	x%	Qs
Dried maize starch (Exodisintegrant)	7.8% w/w	7.8% w/w
Magnesium stearate (Lubricants)	0.2% w/w	0.2% w/w
Talc (Glidant)	2% w/w	2% w/w

Concentrations of binders used were 0,2,5,7,10 & 12 % w/v

Table 3.2: Formula for tablets of Paracetamol containing *Digitaria iburua* starch and Maize Starch BP. as disintegrants.

Composition	Quantities per tablet	Quantities for 200 tablets
Paracetamol	500mg	100g
Maize starch / <i>Digitaria iburua</i> starch (Internal Disintegrant)	x%	
Gelatin (Binder)	5% w/v	Qs
Dried maize starch/ <i>Digitaria iburua</i> starch (Exodisintegrant)	7.8% w/w	7.8% w/w
Magnesium stearate (Lubricant)	0.2% w/w	0.2% w/w
Talc (Glidant)	2% w/w	2% w/w

Concentrations of disintegrants used were 0,2,5,7,10 & 12 % w/v

Table 3.3: Formula for tablets of Paracetamol using Pregelatinised *Digitaria iburua* starch and Maize Starch BP. as disintegrants.

Composition	Quantities Per tablet	Quantities for 200 tablets
Paracetamol	500mg	100g
PGS <i>Digitaria iburua</i> /Maize Starch BP.(Internal disintegrant)	x%	
Gelatin (Binder solution)	5% w/v	Qs
Dried maize starch <i>/Digitaria iburua</i> starch (Exodisintegrant)	7.8% w/w	7.8 w/w
Magnesium stearate (Lubricant)	0.2% w/w	0.2% w/w
Talc (Glidant)	2% w/w	2% w/w

Concentration of disintegrant used were 2,7 & 12 % w/v

3.5 COMPARATIVE EVALUATION OF *Digitaria iburua* STARCH, AND ITS PREGELATINISED FORM WITH MAIZE STARCH BP (2002)

The following investigations were carried out:

3.5.1 *Determination of percentage yield*

The percentage yield of *Digitaria iburua* starch was determined from the weight of grains used (W_0) and the weight of the final starch obtained (from the procedure) (W_1). For the pregelatinised starch, quantities of *Digitaria iburua* starch powder used and the pregelatinised starch obtained were also denoted as W_0 and W_1 respectively. Percentage yield (Y) was calculated using the equation:

$$Y = W_1/W_0 \cdot 100 \dots\dots\dots(5)$$

3.5.2 *Solubility test:*

One gram of *Digitaria iburua* starch was weighed and poured into four beakers respectively containing 1ml, 10ml, 1L and 10L of distilled water at 25°C and stirred. The solubility was observed. Same procedure was repeated using 65% alcohol as a solvent. The procedure were repeated for pregelatinised starch.

3.5.3 Iodine test:

Using BP (2002) starch identification test, 15ml of water in a beaker was poured into one gram of *Digitaria iburua* starch. The beaker was put on a hot plate to boil until mucilage was obtained. It was allowed to cool. A few drops of 0.1N Iodine solution was added to 1ml of the mucilage and the colour changes recorded.

3.5.4 Acidity test:

Ten grams of *Digitaria iburua* starch was added to 96%v/v alcohol which was previously neutralized using 2 drops phenolphthalein solution as indicator. The mixture was shaken for an hour using an automated beaker shaker, filtered and 50ml of the filtrate titrated with 0.1N NaOH solution. The quantity of NaOH solution used for neutralization was recorded. The procedure was repeated for PGS.

3.5.5 Determination of pH:

Ten grams of *Digitaria iburua* starch was weighed into 15ml distilled water and properly mixed. The mixture was poured into boiling distilled water to make up 100ml of slurry. The slurry was allowed to cool. Using a pH meter, model EIL 7055, Kent, the pH of the slurry was measured. The procedure was repeated for PGS.

3.5.6 *Determination of starch hygroscoy*

Two grams of DI starch was placed in an evaporating dish and exposed to the atmosphere in an open space in the laboratory for 24 hours. Any weight gain was observed and recorded every 6 hrs. The percentage weight gain was calculated.

3.5.7 *Determination of moisture content of starch*

Three grams of DI starch was weighed into an evaporating dish and placed in an oven set at 105°C. The starch was weighed periodically until constant weight was attained. The test was repeated and the mean of three readings recorded using the formula

$$MC = W_0 - W_1 / W_0 \% w/w \dots\dots\dots (6)$$

Where MC is the moisture content; W_0 an, W_1 are initial and final weights of the sample respectively. The procedure was repeated for PGS.

3.5.8 *Microscopic examination of starch*

Small quantity of DI starch in glycerol was mounted on a microscope. The sizes of the starch particles were measured and their shapes observed and photographed.

3.5.9 Determination of flow properties of starch

- i. *Angle of repose:* A funnel was mounted on a laboratory stand at a height of 10cm from the table-top. 50g of *Digitaria iburua* starch was poured into the funnel with the tip closed with a plug. The plug was removed and the starch was allowed to flow, the height and diameter of the starch heap were measured. The same procedure was done for PGS. The angle of repose, θ , given by the following equation was calculated.

$$\theta = \tan^{-1}(h/r) \dots \dots \dots (7)$$

Where h is height of conical powder heap and r is the radius of the circular base.

- ii. *Flow rate:* using Erweka Flow meter, 50g each, of the individual starches was allowed to pass through its orifice and the time taken was recorded. Mean of three readings was taken as the flow time of the starches, from which flow rate was calculated.

3.5.10 Determination of Starch Density

- i. *Bulk density:* 20g each, of individual starches (or granules) was poured through a short-stemmed glass funnel into a 200ml graduated glass cylinder and the volume occupied by the

starch/granules was read .The bulk density was calculated from the equation below:

$$\text{Bulk density} = \frac{\text{mass of the starch/granule}}{\text{volume of the starch/granule}} \dots\dots\dots(8)$$

- ii. *Tapped density:* 20g *Digitaria iburua* starch powder was put in a graduated cylinder. It was dropped on a bench 50 times from a height of about 20mm and the respective volumes recorded. The same procedure was done for PGS powder and the tapped densities were calculated using the equation

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}} \text{ g/ml} \dots\dots(9)$$

- iii. *Carr's Index:* The difference between the tapped and bulk densities divided by the tapped density was calculated and ratio expressed as a percentage.

$$\text{Carrs Index} = \frac{\text{Bulk density}-\text{Tapped density}}{\text{Tapped density}} \dots\dots\dots(10)$$

- iv. *Hausner ratio:* (the ratio of tapped density to bulk density) was calculated for all the starches.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \dots\dots\dots(11)$$

- v. *Determination of Starch true density:* The specific gravity bottle method was adopted,using xylene as displacement fluid. The bottle

was cleaned and filled with xylene, all spilled over liquid (xylene) was wiped off with an absorbent cloth. The weight of the bottle filled with xylene was noted as (a). Thereafter the bottle was emptied and cleaned, 2g of starch was weighed into the specific gravity bottle and the weight of the starch powder was noted as (w). The specific gravity bottle containing the starch was almost filled with xylene, stirred with glass rod and allowed to stand for 10 minutes for air bubbles to be removed. The bottle was then carefully filled with xylene and the final weight of the bottle was noted as (b). starch true density was then calculated as

$$\ell = w/[(a+w)-b]S \dots\dots\dots(12)$$

Where ℓ is the particle density of starch and S is the specific gravity of xylene = 0.86

3.5.11 Determination of swelling power.

Digitaria iburua starch granules were prepared with water as binding agent. The wet mass was passed through 1.7mm wire mesh, which was dried in an oven set at 40°C. Compaction using 12.5mm size punch and die set, the granules were compressed into tablets. Weights and dimensions of the tablets were recorded. Two tablets each were placed in a desiccator at 98% relative humidity at room

temperature for five days. The weight and volume of the two tablets were determined after five days. The difference between the initial and final volume was calculated and expressed as a percentage swelling power of the starches. The procedure was repeated and the mean of the two was taken as the swelling power. The swelling power, S, is given by the equation:

$$S = \frac{V_1 - V_0}{V_0} \times 100 \quad (13)$$

Where V_0 and V_1 are initial and final volumes of the tablet respectively.

The same procedure was repeated using PGS.

3.5.12 Determination of moisture sorption capacity

10g of individual starches was spread evenly in Petri dishes. The Petri dish was placed in a desiccator with 98% relative humidity at room temperature. The samples were periodically weighed until a constant weight was attained. The percentage increase in weight was calculated and taken as the moisture sorption capacity. The above procedure was repeated thrice and the average/mean of the readings recorded.

3.5.13 Sieve analysis of starch powders

50g of the powders was weighed and put in the uppermost sieve of a set of sieves arranged in decreasing mesh sizes. The sieves were then mounted on a sieve shaker and shaken for 10mins. The powders retained on each sieve after 10mins was weighed and recorded.

3.6 PREPARATION OF PARACETAMOL GRANULES

Using the techniques of wet granulation method of massing and screening, paracetamol granules were prepared based on Table 3.1 on page 53 using different concentrations of gelatin and *Digitaria iburua* starch as binders, and Tables 3.2 and 3.3 on pages 54 and 55 using different concentrations of maize starch BP., *Digitaria iburua* starch and its pregelatinized form as disintegrants.

The procedure used in the granules formulation includes:

- (i) Weighing: appropriate amounts of all the ingredients as shown in the formulae above with the exception of the exodisintegrants/ lubricants/ glidants were weighed for different batches of the formulae.
- (ii) Mixing: The ingredient weighted were then mixed in a pestle and mortar using doubling up technique.

(iii) Addition of Binder Solution:- According to the formular, gelatin and *Digitaria iburua* starch were used at different concentrations as binders for preparing granules of Paracetamol.

a.) Gelatin binder solution was prepared as follows:

Based on the composition of the paracetamol tablet formulation, appropriate amounts of gelatin was weighed on a top-loading balance. The gelatin was then put into a clean glass beaker and a known volume of distilled water added to make a solution. Further quantity of water (60⁰C) was added. The beaker was put on a hot plate and the mixture was stirred until the gelatin was dissolved.

(b) *Digitaria iburua* starch binder solution was prepared as follows:

Suspensions of different concentrations of *Digitaria iburua* starch powder was made, to which known volumes of hot water was added and brought to boiling until a translucent paste was obtained.

- (iv) Small quantities of the binder solution of gelatin and *digitaria iburua* starch were respectively added gradually to the different powder mixtures until moist mass was formed.
- (v) Wet screening: The moistened mass was then passed through a sieve size of 1.7 μ m using a spatula to get wet granules.
- (vi) Drying: The wet granules were dried in a hot air oven (Gallenhamp) set at 40°C.
- (vi) Dry screening: The dried granules were passed through a sieve size of 1.6 μ m size ;(oversized granules were size reduced.)

3.6.1 Analysis of paracetamol granules:-

The following tests were carried out on the granules: sieve analysis, moisture content, angle of repose, bulk and tapped densities, Carrs index and Hausner ratio.

The same procedures were repeated as earlier described on for powdered starch on page 56.

3.6.2 Addition of Exo-excipients to paracetamol granules:

The exo-excipients were added to the granules according to formular shown in Tables 3.1,3.2 and 3.3 in pages 53-55 as shown earlier. Mixing of the granules was done using an automated mixer.

3.7 COMPRESSION OF GRANULES

After the addition of the exo-disintegrant, lubricants and glidants, the granules were mixed gently using an automated tumble mixer and compressed into tablets in an Erweka single station tableting machine using different compressional pressures (244.43MNm⁻² to 611.075MNm⁻² determined from a preliminary investigation).

After the tablets were produced, they were kept in dessicator for 24 hours for elastic recovery and drying. The following Quality control tests were carried out on the batch of tablets that gave the best formed tablets.

3.8 QUALITY CONTROL TESTS

3.8.1 Official tests (Pharmacopoeial Tests)

a. Uniformity of Weight of Tablets:

The individual weight of 20 tablets from each batch produced at different compression pressures was determined using a top loading balance. The mean weights and variations were computed.

b. Thickness of Tablets:

Using micrometer screw gauge, the thickness of all of 20 tablets from each batch produced at varying compression pressures was recorded and the mean thickness calculated.

c. Disintegration Time:

Using the Disintegration Test Apparatus, one tablet was placed in the basket in which a mesh is situated. The water bath of the apparatus was thermostatically set at 37⁰C. The time at which the tablet had completely passed through the mesh was recorded using a stop clock. The same procedure was repeated six times and the time recorded.

d. Dissolution Test:

Six litres of 0.1N HCl was prepared by weighing 21.9g of HCl made up to 6000 mls with distilled water. The dissolution machine was set and the thermostat was adjusted to 37⁰C. The chambers were washed and one litre of 0.1N HCl prepared was poured into each basket which is situated in the dissolution machine and each basket was suspended into the chamber containing 0.1N HCl and a tablet was placed at each basket.

Samples from each chamber were taken at 15, 30, 45 and 60 minutes, filtered using a filter paper and drained in a test tube.

The absorbance of each sample at wavelength of 243nm was measured using a UV spectrometer from which the amount of drug dissolved at the specified time was recorded.

3.8.2 Un-official Tests

a. Friability Test:

Using Erweka friabilator, 20 tablets were weighed and put inside the friabilator chamber. It was set at 25 revolutions per minute for 4 minutes. Thereafter, the tablets were dusted and weighed again and the difference in weight was calculated as the percentage loss.

b. Determination of tablet packing fraction:

Tablet packing fraction was determined for all the batches of tablet produced using the following equation:

$$\text{Packing fraction (Pf)} = \frac{\text{Bulk density of tablets (D}_B\text{)}}{\text{Particle density(Dt)}} \dots\dots\dots(14)$$

$$\text{And } D_B = \frac{4W}{\pi d^2 h} \text{ gcm} \dots\dots\dots(15)$$

Where h = thickness of tablets (cm)

W = weight of tablet (g)

d = Diameter of tablet (cm)

c. Determination of tablet porosity:

Porosity of the tablets was calculated from the formula given below:

$$\text{Tablet porosity} = 1 - \text{Packing fraction (Pf)} \dots \dots \dots (16)$$

That is $1 - \frac{\text{Bulk Density of tablets}}{\text{Particle Density of tablet (Dt)}}$

$$= 1 - \frac{4W}{\pi d^2 h / Dt} \dots \dots \dots (17)$$

Where h = thickness of tablets(cm)

W = weight of tablet (g)

d = Diameter of tablet (cm)

e. Crushing Strength Test:

One tablet was put in between a Monsanto tablet hardness tester. The tablet was crushed and the force required to crush the paracetamol tablet was recorded. The same procedure was repeated. Average of 10 readings was taken and the forces recorded.

3.9 COMPACTION STUDIES ON PARACETAMOL GRANULES CONTAINING *DIGITARIA IBURUA* AS TABLET BINDER AND DISINTEGRANT.

Tablets were produced from lubricated granules by compressing them for 1 minute with predetermined loads (100, 200, 300, 400, 500, 600 and 700 MNm⁻²) in a Carver hydraulic hand press using flat faced punch of 10.5mm diameter. Before each compression, the die and the punches were lubricated with a 2% w/v dispersion of magnesium stearate in ethanol. After ejection, the tablets were stored over silica gel in a dessicator for 24 hours to allow for elastic recovery and hardening. This was to prevent false low yield pressure values.

The diameters and thickness of the tablets were determine using a micrometer screw gauge having a sensitivity of 0.01mm; Monsanto hardness tester was used to determine the tablet crushing strength and the tablets weights were determined using a top loading metler balance. In each case, the average of five readings was taken.

Using the Heckel equation (Heckel, 1961a), a graph of $\ln(1/1-D)$ versus compression pressure (P) was plotted. The yield pressure (P_y), which is a measure of the ability of the material to deform plastically, was determined from the slope of the linear region

of the graph and the intercept A, was recorded. From the value of A, the relative density, (D_A) that describes the densification of the materials due to particle deformation and interparticle bonding was obtained (Roberts and Rowe, 1986).

The forces required to fracture tablets by diametrical compression were determined using a Monsanto hardness tester.

CHAPTER FOUR

4.0 RESULTS

4.1 PHYSICO-CHEMICAL PROPERTIES OF *DIGITARIA IBURUA* STARCH, PREGELATINISED *DIGITARIA IBURUA* STARCH AND MAIZE STARCH BP.

Table 4.1 shows the results of the various physico-chemical tests such as solubility, acidity, iodine and percentage yield carried out on the three starches (DI, PGS DI and MS BP.). Morphological structures of the three starches is also shown.

The physico-chemical properties of DI starch and PGS DI were in most cases similar, and comparable with those of MS BP. DI starch was observed to be a white, odourless, polygonal powder which creaks when passed through the fingers. PGS DI starch however, appeared as a light brown, odourless, round (spherical) powder with fibres that cling to surfaces. The reference Maize starch BP. also appeared as a white, odourless, polyhedral powder.

The two test starches (DI and PGS DI) starches and the reference starch (Maize starch BP.) were all insoluble in water and 65% ethanol. All the three starches were positive to iodine test.

Higher percentage yield was obtained with the PGS DI starch (73.18%) compared with the DI starch (62.20%).

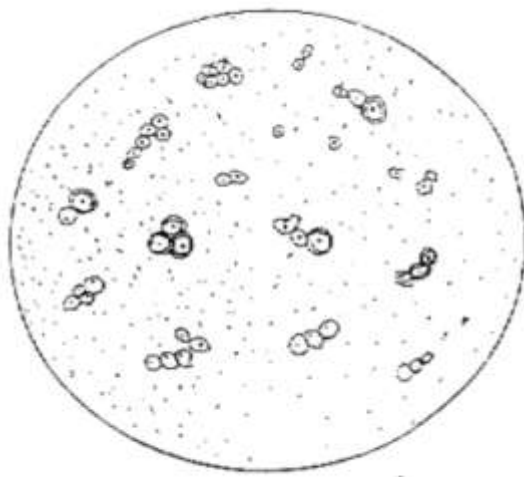
4.2 FLOW PROPERTIES, MOISTURE CONTENT AND OTHER PROPERTIES OF *DIGITARIA IBURUA*, PREGELATINISED *DIGITARIA IBURUA* AND MAIZE STARCH BP.

Table 4.2 shows the performance of the three starches (DI, PGS DI and MS BP.) when evaluated on the various indices of flow, moisture content, moisture sorption capacity and swelling power.

It is observed that DI starch has better flow properties compared with MS BP. as evident by its higher flow rate, lower Carr's index and Hausner ratio. Generally, the values for PGS DI in most of the parameters of flow determination were lower than those of DI starch. The moisture contents of the three starches were close, in the order of DI<PGS<MS. The swelling properties were also similar, lowest for PGS DI and highest for DI starch.

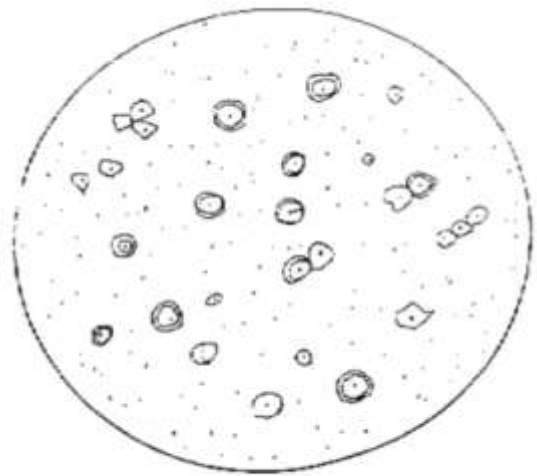
Table 4.1: Physico-chemical Properties of *Digitaria iburua* starch Pregelatinised *Digitaria iburua* Starch compared with Maize Starch BP.

Parameters	DI	PGS DI	MS BP.(May & Baker)
Percentage Yield	62.20	73.18	-
Colour	White	Light Brown	White
Shape	Polygonal	Round	Polyhedral
Iodine Test	+	+	+
Acid test (vol. needed for neutralization)	0.1ml	0.23ml	1.8ml
Water Solubility	Insoluble	Insoluble	Insoluble
65% Ethanol	Insoluble	Insoluble	Insoluble



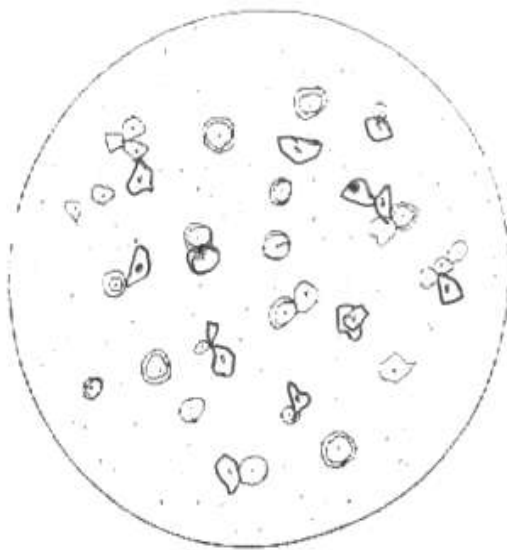
Digitaria iburua

starch



Maize

starch BP



PGS DI

Figure 4.1: The morphological structure of particles of *Digitaria iburua* starch, PGS and Maize starch B.P

Table 4.2: Flow Properties, Moisture Content and some other properties of DI Starch and PGS DI compared with MS B.P.

Parameters	DI Starch	DI PGS	MS B.P
True Density (g/ml)	2.08	1.50	1.48
Bulk Density (g/ml)	0.44	0.71	0.52
Tapped Density (g/ml)	0.59	0.86	0.76
Carrs Index(%)	24.4	17.8	31.60
Hausner ratio	1.34	1.22	1.46
Flow rate (g/sec)	0.59	0.51	0.54
Angle of Repose(°)	25.60	21.30	35.96
Moisture			
Content(%w/w)	11.33	11.75	12.10
Moisture Sorption (%)	10.50	8.00	14.84
Swelling Power (%)	22.50	21.03	21.07

4.3 PROPERTIES OF PARACETAMOL GRANULES USING DIFFERENT CONCENTRATIONS OF *DIGITARIA IBURUA* STARCH, PREGELATINISED *DIGITARIA IBURUA* STARCH, GELATIN AND MAIZE STARCH BP. AS BINDERS AND DISINTEGRANTS

The effect of using different concentration of DI starch as binder on paracetamol granules compared with a gelatin (as reference) is presented in Table 4.3.

As shown in this table, use of DI starch as binder, increased the flow rates, decreased the angles of repose, Hausner ratio and Carr's index of the paracetamol granules, in similar patterns with granules formulated with gelatin as binder. Generally, 2% w/v binder concentration of DI starch produced greatest improvement in the flow parameters.

The effect of using DI starch as disintegrant on the properties of paracetamol granules, compared with maize starch BP. is shown in Table 4.4. As shown in the table, as the concentration of DI as disintegrant was increased, there was an increase in flow rate up to 7% w/v. Angle of repose was highest at DI concentration of 10% w/v. There was no significant difference in moisture content. Generally,

values for Carrs index and Hausner ratio of the granules increased when the concentration of *Digitaria iburua* starch used as disintegrant, was increased from 0% to 12%.

The effect of using PGS DI starch as disintegrant on the properties of paracetamol granules, is shown in Table 4.5. As the concentration of DI PGS used as disintegrant was increased, the flow rate of the granules decreased, while the values for the angle of repose, Carr's index and Hausner ratio increased. The moisture content of the granules initially decreased when PGS DI disintegrant concentration was increased from 2% to 7% w/v and remained constant with further increase in disintegrant concentrations.

Table 4.3: Properties of Paracetamol granules using different concentrations of *Digitaria iburua* starch and Gelatin as binders.

Binders and Concentrations (% w/v)												
Properties of granules	<i>Digitaria iburua</i> Starch						Gelatin					
	0	2	5	7	10	12	0	2	5	7	10	12
Flow rate (g/secs)	1.52	4.25	3.28	3.88	3.34	3.62	1.52	4.13	3.57	4.17	4.27	3.64
Moisture contents (%)	2.00	3.00	3.00	2.00	3.00	3.00	2.00	3.00	4.00	2.00	3.00	2.00
Angle of repose(⁰)	28.20	20.32	19.40	22.50	20.04	21.45	28.00	21.32	18.52	20.20	20.66	20.30
Bulk densities (g/ml)	0.405	0.400	0.410	0.434	0.405	0.410	0.496	0.402	0.429	0.408	0.408	0.389
Tapped densities (g/ml)	0.5	0.476	0.5	0.508	0.508	0.5	0.684	0.508	0.491	0.487	0.49	0.476
Carrs index (g/ml)	19.0	15.96	18.0	14.56	20.2	18.0	28.36	20.86	13.44	16.22	16.73	18.27
Hausner ratio	1.23	1.19	1.21	1.17	1.25	1.21	1.37	1.26	1.15	1.19	1.20	1.22

Table 4.4: Properties of Paracetamol granules using different concentrations of *Digitaria iburua* starch and maize starch B.P as disintegrant.

Disintegrants and Concentrations (% w/w)												
Properties of granules	<i>Digitaria iburua</i> Starch						Maize starch BP					
	0	2	5	7	10	12	0	2	5	7	10	12
Flow rate (g/secs)	3.73	3.62	3.98	5.63	4.00	3.82	3.73	3.79	3.56	3.78	3.69	3.65
Moisture contents (%)	3.00	2.50	3.00	3.00	3.00	2.00	3.00	2.00	3.00	2.00	2.00	3.00
Angle of repose (o)	20.32	20.15	21.60	21.60	20.85	22.57	20.32	24.16	22.93	22.73	21.43	22.93
Bulk densities (g/ml)	0.405	0.410	0.4	0.389	0.394	0.384	0.434	0.434	0.394	0.416	0.410	0.410
Tapped densities (g/ml)	0.483	0.5	0.483	0.483	0.468	0.476	0.483	0.508	0.508	0.468	0.5	0.517
Carrs index (g/ml)	16.14	18.00	17.18	19.46	15.81	19.32	16.14	14.56	22.44	11.11	18.00	20.69
Hausner ratio	1.19	1.21	1.20	1.24	1.18	1.23	1.19	1.17	1.28	1.12	1.21	1.26

Table 4.5: Properties of Paracetamol granules using different concentrations of Pregelatinised *Digitaria iburua* starch as disintegrants.

Properties of granules	Disintegrants concentrations		
	% w/w		
	2 %	7 %	12 %
Flow rate (g/Secs)	9.58	9.34	8.40
Moisture contents %	3.00	2.00	2.00
Angle of repose	10.8	25.78	26.80
Bulk densities g/m	0.434	0.408	0.405
Tapped densities g/m	0.5	0.495	0.512
Carr's index (g/m)	13.2	17.57	20.89
Hausner ratio	1.152	1.213	1.264

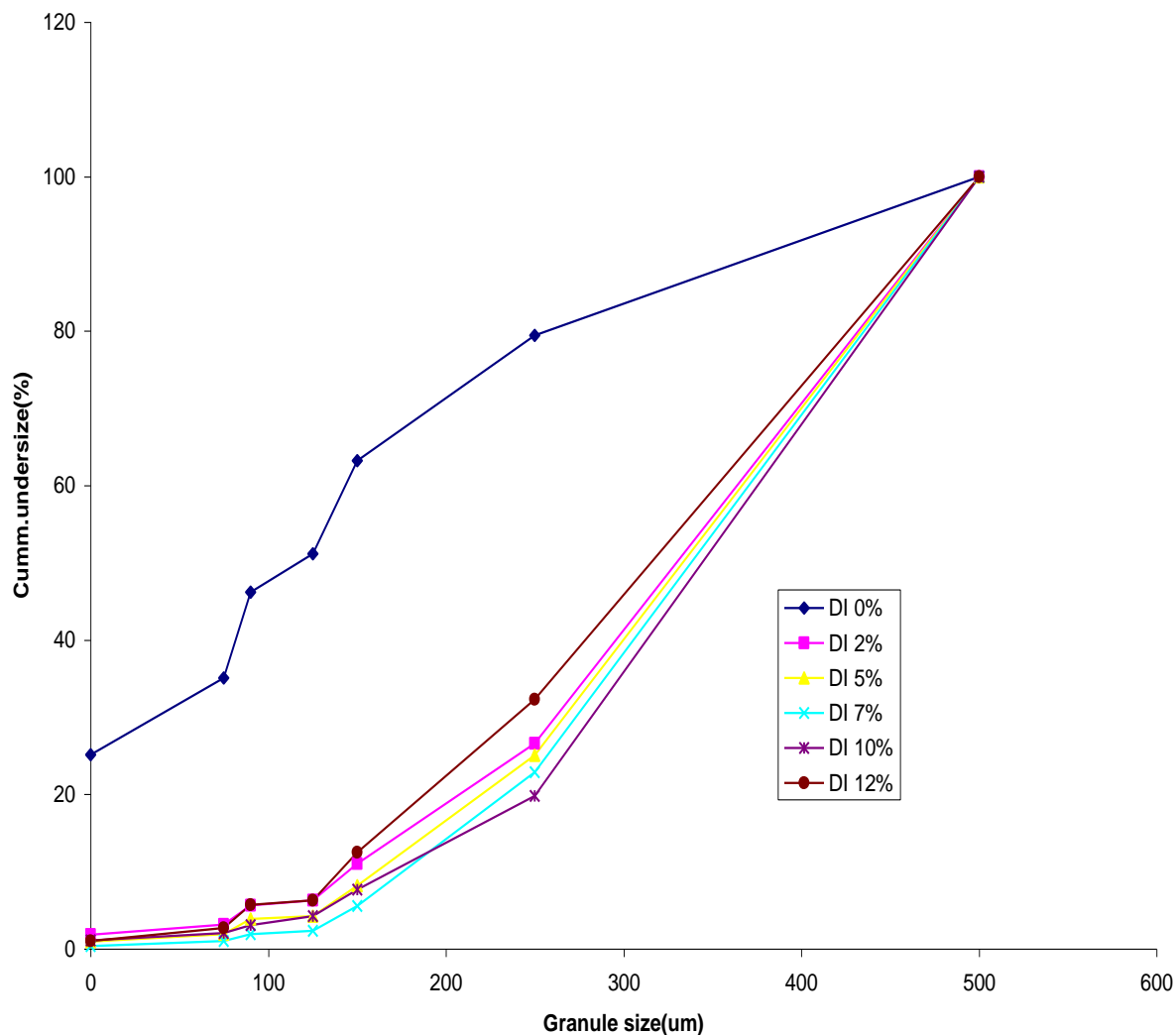


Fig.4.2: Size distribution of granules produced with *Digitaria iburua* starch as binder in paracetamol tablet formulation.

The granules size distribution of paracetamol tablet formulation prepared with different concentration of DI starch is presented in Figure 4.2. As shown in this figure (Fig.4.2), as the binder concentration increased, proportions of larger granules in the formulation increased.

4.4 PROPERTIES OF PARACETAMOL TABLETS FORMULATED WITH *DIGITARIA IBURUA* STARCH, PREGELATINISED *DIGITARIA IBURUA* STARCH, GELATIN AND MAIZE STARCH BP. AS BINDERS AND DISINTEGRANTS.

Tablet properties of paracetamol using different concentrations of DI starch compared with gelatin as binders is presented in Table 4.6a and 4.6b while those using DI and PGS DI starch compared with MS BP. are shown in Table 4.7a and 4.7b.

Data presented in Table 4.6a showed that as the concentration of DI starch used as binder increased, there was generally an increase in tablet thickness, disintegration time and crushing strength, while average tablet weight and friability values decreased. The pattern was similar with gelatin as binder, but in general with corresponding lower values with exception in the disintegration time.

As shown in Table 4.7a, as the concentration of DI used a disintegrant from 0 to 2% was increased, there was an initial increase in tablet thickness follow by a decrease and thereafter an increased with further increase in disintegrant. With PGS DI, the tablet thickness decreased with increased disntegrant concentration. The

values for tablet friability was decreased with increase in disintegrant concentration for the three starches investigated. There was an increase in the values for crushing strength as the concentration of PGS DI as disintegrant was increased. Generally, the corresponding values obtained for the reference disintegrant (MS BP.) in the various parameters such as friability, disintegration time and crushing strength were lower.

Although all the tablets dissolved within 25mins, the dissolution time was found to increase with increasing binder concentration whereas it decrease as disintegrant concentration was increased.

Table 4.6a The effects of different binder types and concentrations on properties of Paracetamol tablets.

Binder (%w/w)	Conc	Tablet Properties					
		Tablet thickness (mm)		Tablet weight variation(mg)		Tablet friability (% w/w)	
		DI	GEL	DI	GEL	DI	GEL
(0%)		5.73	5.73	0.677±(0.02)	0.677±(0.02)	0.9	0.9
(2%)		5.8	5.11	0.666±(0.02)	0.615±(0.022)	0.82	0.70
(5%)		5.86	5.41	0.655±(0.033)	0.624±(0.218)	0.69	0.64
(7%)		5.88	5.29	0.636±(0.032)	0.605±(0.021)	0.42	0.48
(10%)		5.98	5.57	0.625±(0.025)	0.613±(0.025)	0.25	0.23
(12%)		5.25	5.67	0.608 ±(0.03)	0.610 ±(0.027)	0.17	0.12

Table 4.6b The effects of different binder types and concentrations on properties of Paracetamol tablets.

(Cont)

Binder Conc (%w/w)	Tablet properties					
	Disintegration Time (sec)		Crushing Strength (KgF)		Dissolution Time (min)	
	DI	GEL	DI	GEL	DI	GEL
(0%)	32	32	4.17	4.17	0	4.00
(2%)	43	44.6	4.07	10.25	10.00	10.00
(5%)	69	78.6	8.17	8.25	11.00	12.00
(7%)	32	83.6	8.17	5.92	11.50	14.00
(10%)	95	97.3	8.07	6.25	12.00	15.00
(12%)	38	106.6	6.12	5.60	13.00	16.00

Table 4.7a: The effects of different types and concentrations of disintegrants on properties of Paracetamol tablets

Disint. Cont. (% w/v)	Tablet properties								
	Tablet thickness (mm)			Tablet weight variation(mg)			Tablet friability (% w/w)		
	DI	MS	PGS	DI	MS	PGS	DI	MS	PGS
(0%)	5.46	5.46		0.608±(0.359)	0.608 ±(0.359)		0.87	0.87	
(2%)	5.58	5.74	5.40	0.617±(0.047)	0.643±(0.033)	0.598±(0.023)	0.79	0.75	0.98
(5%)	5.21	5.83		0.604±(0.025)	0.671 ±(0.031)		0.64	0.60	
(7%)	5.23	5.73	5.17	0.637±(0.034)	0.637 ±(0.035)	0.588±(0.021)	0.59	0.52	0.86
(10%)	5.75	5.95		0.656±(0.034)	0.659 ±(0.034)		0.46	0.43	
(12%)	5.67	5.7	5.11	0.620±(0.038)	0.639 ±(0.034)	0.580±(0.023)	0.16	0.21	0.68

Table 4.7b: The effects of different types and concentrations of disintegrants on properties of Paracetamol tablets (cont)

Disint. Conc (%w/w)	Tablet Properties								
	Disintegration time (secs)			Crushing strength(kgf)			Dissolution Time (min)		
	DI	MS	PGS	DI	MS	PGS	DI	MS	PGS
(0%)	56.0	56.0		6.62	6.62		44.0	44.0	
(2%)	49.6	68.0	36.83	4.9	6.1	4.17	20.0	22.0	20.0
(5%)	48.3	59.3		5.15	8.95		15.0	15.0	
(7%)	8.0	68.6	97.20	11.8	6.15	6.35	13.0	14.0	7.0
(10%)	64.0	80.3		5.42	7.5		7.0	10.0	
(12%)	64.6	66.3	83.66	6.47	7.72	10.70	8.0	9.0	3.0

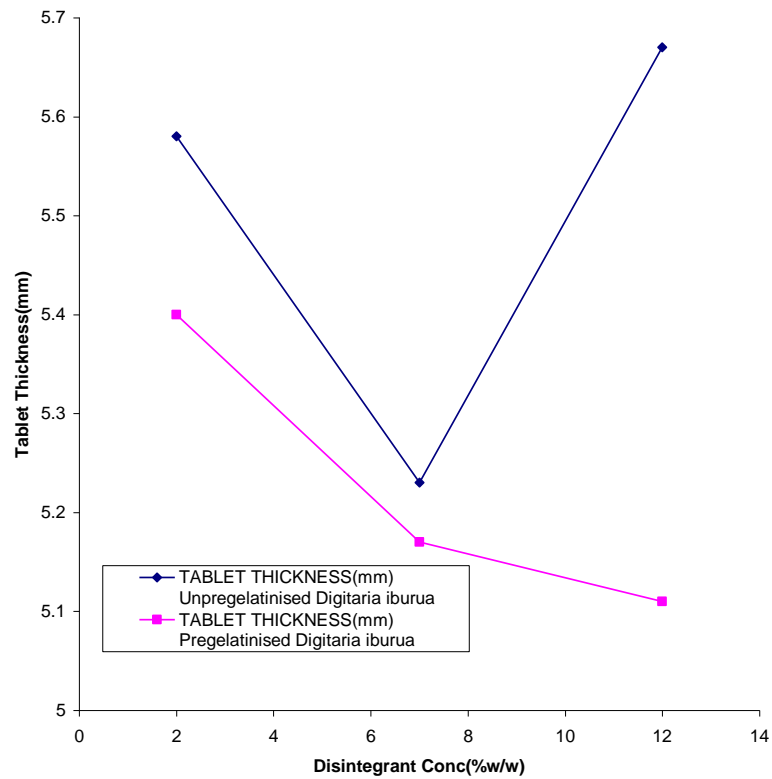


Fig.4.3: Plots of Tablet Thickness (mm) against disintegrant concentration (%w/w) in paracetamol tablets formulated using *Digitaria iburua* and pregelatinised *Digitaria iburua* starches as disintegrants.

As shown in figure 4.3, with further increase in PGS DI disintegrant concentration, there was decrease in tablet thickness.

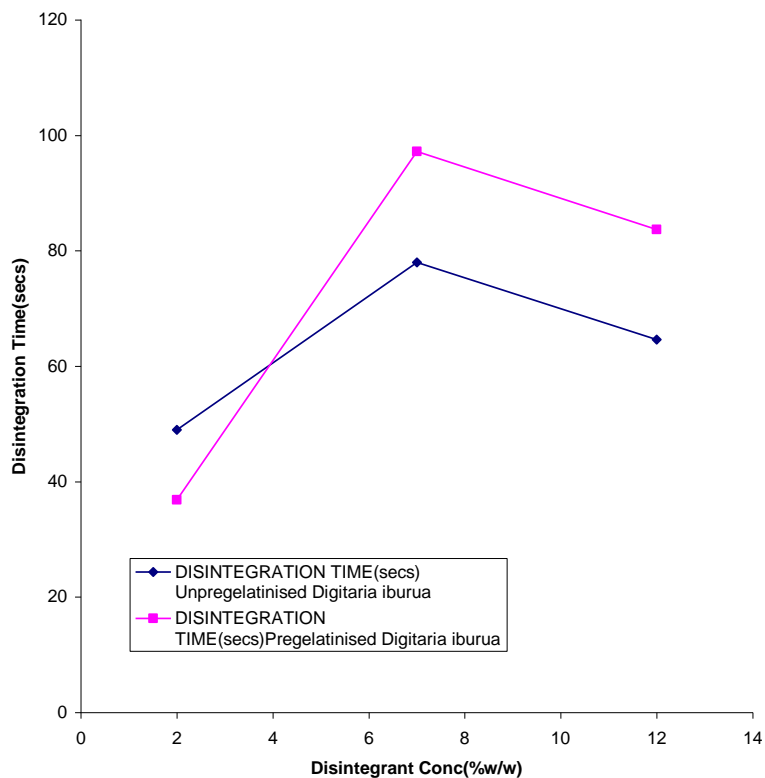


Fig.4.4: Plot of Disintegration Time (secs) against Disintegrant concentration (%w/w) in paracetamol tablets formulated using *Digitaria iburua* and pregelatinised *Digitaria iburua* starches as disintegrants.

As shown in figure 4.4, the disintegration time for both DI and PGS DI as disintegrant increased after which further increase in starch concentration decreased the disintegration time.

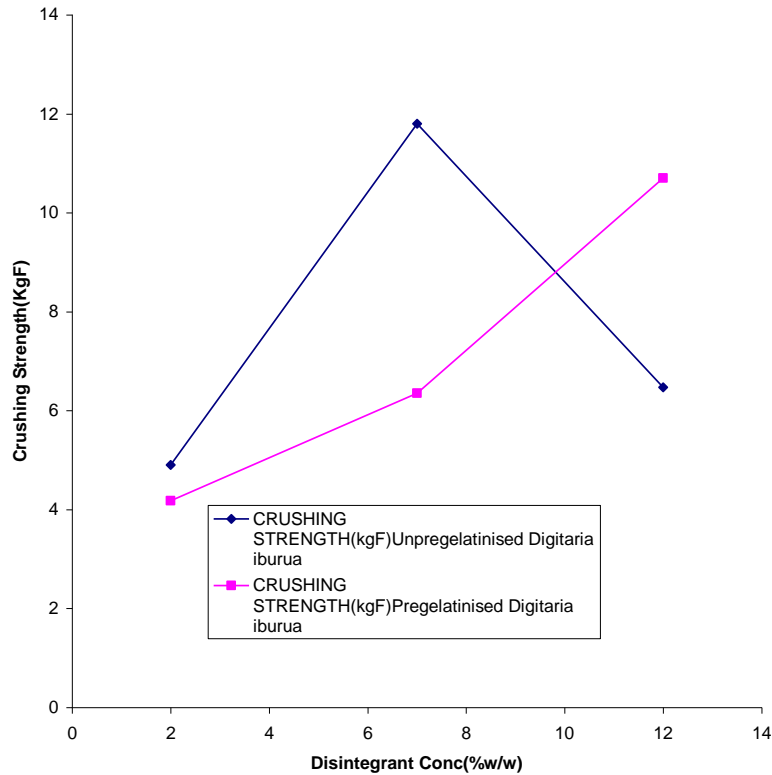


Fig.4.5: Graph of Crushing Strength (KgF) against Disintegrant concentration (%w/w) in paracetamol tablets formulated using *Digitaria iburua* and pregelatinised *Digitaria iburua* starches as disintegrants.

The plots represented in Fig.4.5 describes the behavior of tablets formulated with both starch powders analysed on the crushing strength of the tablets. There was an increase in crushing strength with initial addition of disintegrant. Values of crushing strength for PGS DI kept increasing with increase in disintegrant concentration.

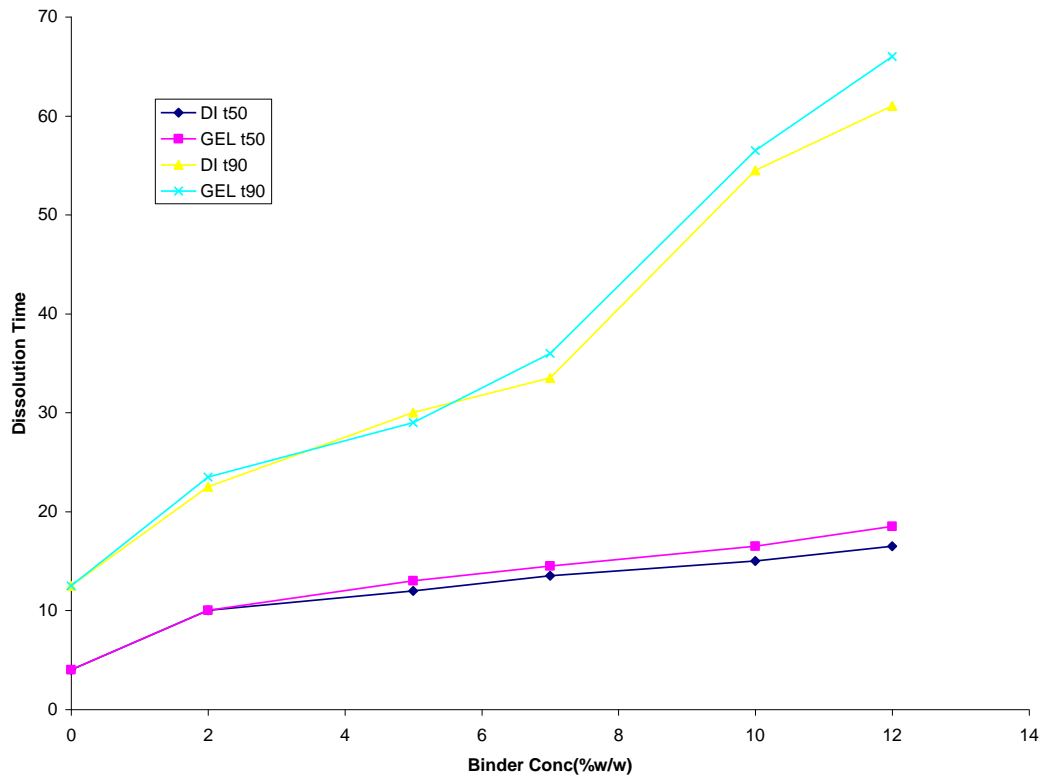


Fig.4.6: Effect of binder type and concentrations on Dissolution Time of paracetamol Tablets produced.

As shown in fig 4.6, the dissolution time for DI as binder was increased with increasing binder concentration.

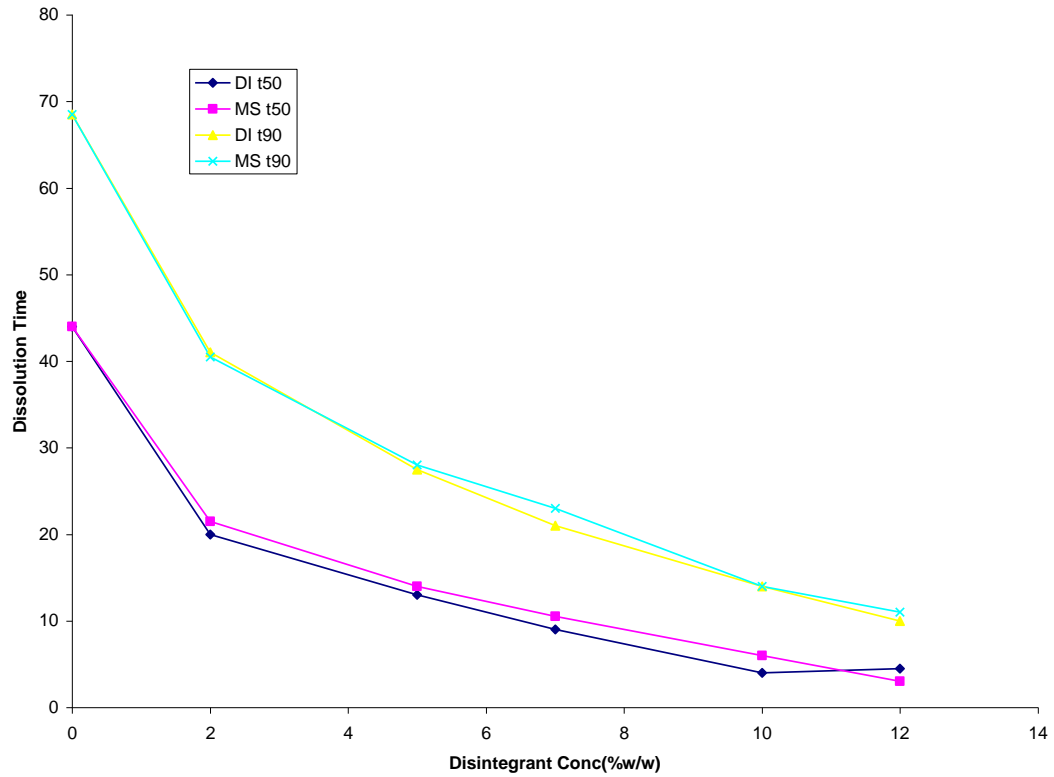


Fig.4.7: Effect of disintegrant type and concentrations on Dissolution Time of paracetamol Tablets produced.

As shown in fig. 4.7, there was a decrease in dissolution time with increasing disintegrant concentration.

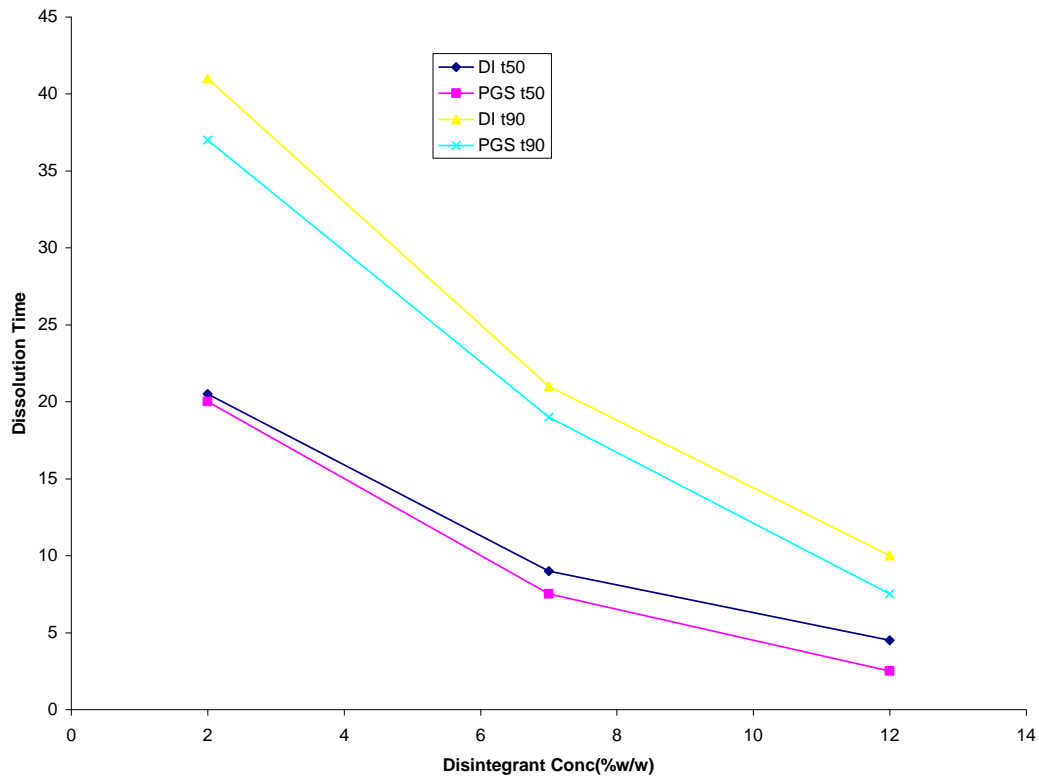


Fig.4.8: Shows effect of disintegrant type and concentrations on Dissolution Time of paracetamol Tablets produced.

As shown in fig.4.8, DI and PGS DI starch at the three concentrations analysed was found to decrease the dissolution time.

4.5 COMPACTION BEHAVIOUR OF PARACETAMOL GRANULES CONTAINING *DIGITARIA IBURUA* STARCH, PREGELATINISED *DIGITARIA IBURUA* STARCH, GELATIN AND MAIZE STARCH BP. AS BINDERS AND DISINTEGRANTS

Compaction behaviour of paracetamol using different concentrations of DI starch compared with gelatin as binders is presented in Table 4.8 while those using DI and PGS DI starch compared with MS BP. are shown in Table 4.9.

As shown in Table 4.8, the mean yield pressure (P_y) decreased while values for the initial rearrangement phase (D_0) increased as the concentration of DI as binder was increased from 0% to 12% w/v. There was a decrease in the relative density of particles during the initial states of compression (D_B) at 0% to 5% DI concentration after which it increased.

As shown in Table 4.9, The initial rearrangement phase of densification as a result of die filling (D_0) was found to increase as the concentration of all three starches analysed was increased from 0% to 12%. There was an initial increase in mean yield pressure (P_y) for DI from 0% to 5% with DI starch. Table 4.9 shows D_A values ranking

in order 7% > 0% > 2% > 10% > 12% > 5% disintegrant concentration. At 7% MS concentration, there was highest compaction with values of 0.71845 and 5% MS concentration gave the least compaction with values of 0.37484. The D_o value increases with increase in MS as disintegrant. The increase is due to change in particle sizes of granules.

The D_A value ranks in the order 7% > 0% > 2% > 10% > 12% > 5% disintegrant concentration.

Table 4.8: The Heckel constants for different compacts containing different concentrations of binders in paracetamol tablets

		Heckel Constants			
Binder type	Binder conc%w/w	Py (MNm⁻²)	D_A	D₀	D_B (D_A-D₀)
DI	0.0	454.545	0.944	0.218	0.726
	2.0	243.902	0.324	0.229	0.095
	5.0	232.558	0.250	0.243	0.007
	7.0	78.125	0.952	0.257	0.695
	10.0	93.457	0.912	0.264	0.648
	12.0	153.846	0.665	0.271	0.394
GELATIN	0.0	59.171	0.970	0.218	0.752
	2.0	454.545	0.944	0.213	0.731
	5.0	107.526	0.838	0.221	0.617
	7.0	238.095	0.245	0.223	0.022
	10.0	188.679	0.538	0.249	0.289
	12.0	178.571	0.496	0.264	0.232

Key: (D₀) = initial rearrangement phase of densification.

(D_A) = relative density at mean yield pressure.

(D_B) = phase of rearrangement at low pressure.

(Py) = mean yield pressure.

Table 4.9: The Heckel constants for different compacts containing different concentrations of disintegrants in paracetamol tablets.

Heckel constants					
Disintegrant type	Disintegrant conc % w/v	Py (MNm⁻²)	D_A	D_o	D_B (D_A-D_o)
DI	0.0	169.491	0.470	0.246	0.224
	2.0	185.185	0.487	0.249	0.238
	5.0	217.391	0.375	0.253	0.122
	7.0	138.888	0.711	0.257	0.454
	10.0	1428.571	0.557	0.283	0.274
	12.0	178.571	0.545	0.295	0.250
MS	0.0	169.491	0.470	0.218	0.224
	2.0	1000.00	0.432	0.218	0.214
	5.0	192.307	0.374	0.233	0.141
	7.0	123.456	0.718	0.241	0.477
	10.0	217.391	0.428	0.257	0.171
	12.0	204.081	0.409	0.266	0.143
PGS	2.0	2000.000	0.839	0.233	0.606
	7.0	250.000	0.266	0.245	0.021
	12.0	909.090	0.787	0.273	0.514

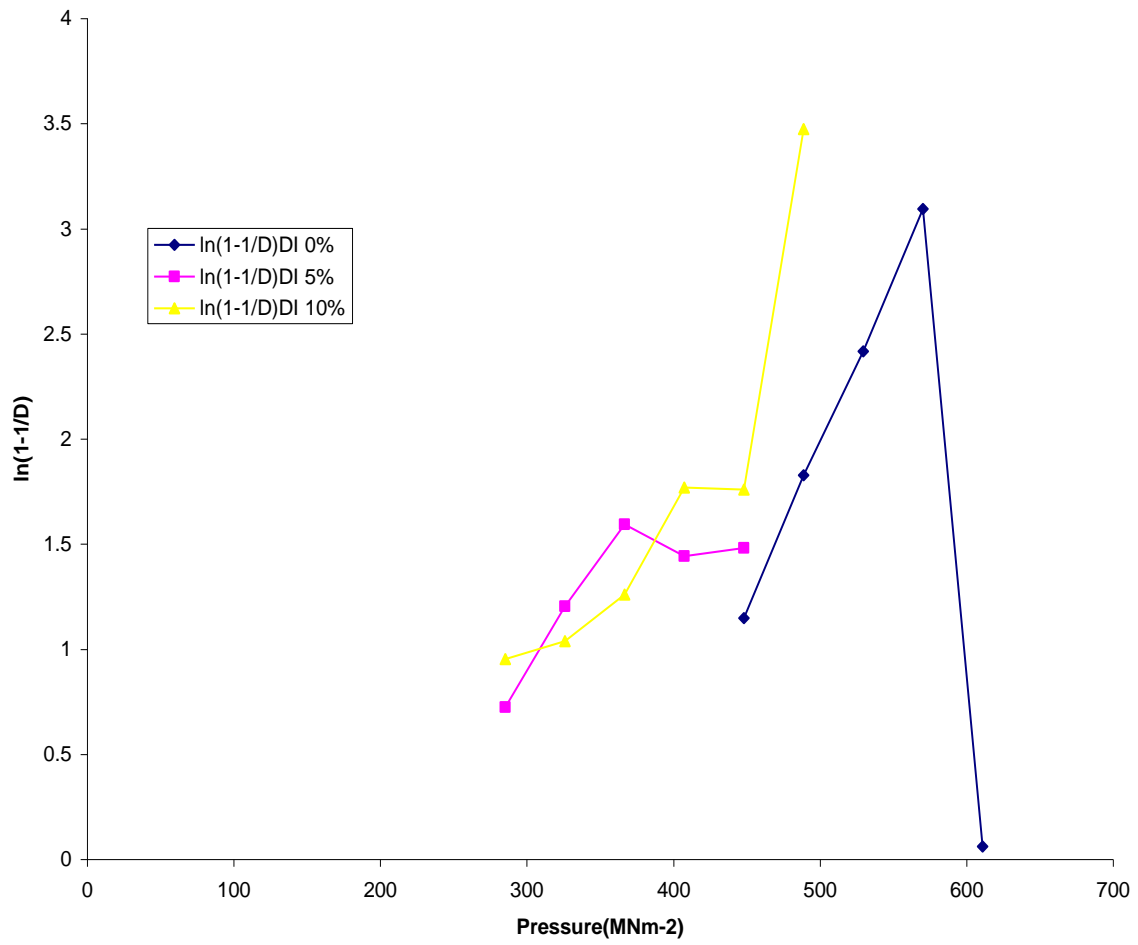


Fig 4.9: Heckel plots for paracetamol compacts with *Digitaria iburua* starch as binder.

Generally, all the Heckel plots of compacts prepared with different concentrations of *Digitaria iburua* starch as binder have two discernable phases: an initial linear region representing brittle fracture followed by plastic flow or deformation. The plots showed compacts of granules having higher densification when they contain 10% w/w *Digitaria iburua* starch as binder.

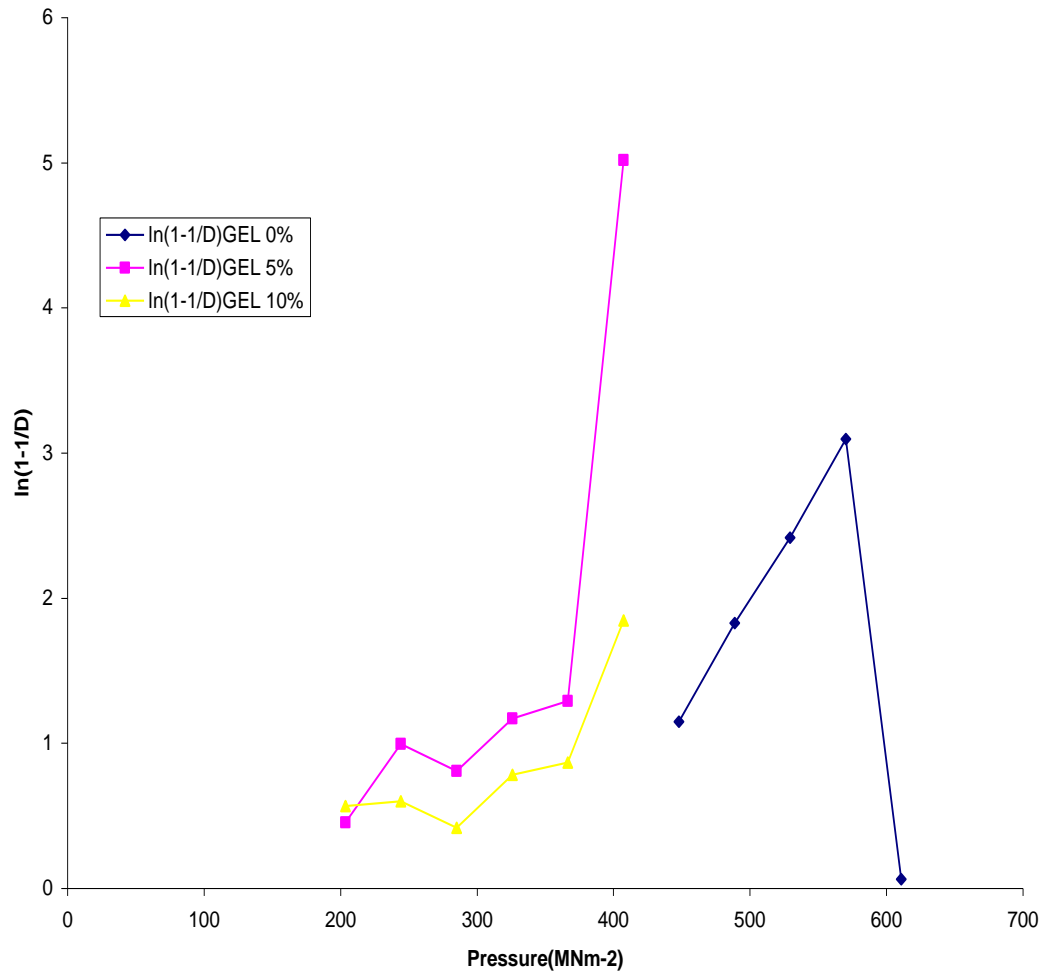


Fig 4.10: Heckel plots for paracetamol compacts with gelatin as binder.

Generally, all the Heckel plots of compacts containing gelatin as binder at different concentrations displayed similar behavior. They have two discernable phases: an initial phase of linearity followed by a plastic deformation with decreasing compaction pressure. There was a decrease in granules densification with increase in gelatin concentration. The compacts of granules containing 5% w/w gelatin have higher densification while compacts containing gelatin of 7%w/w to 12%w/w concentration have lower densification.

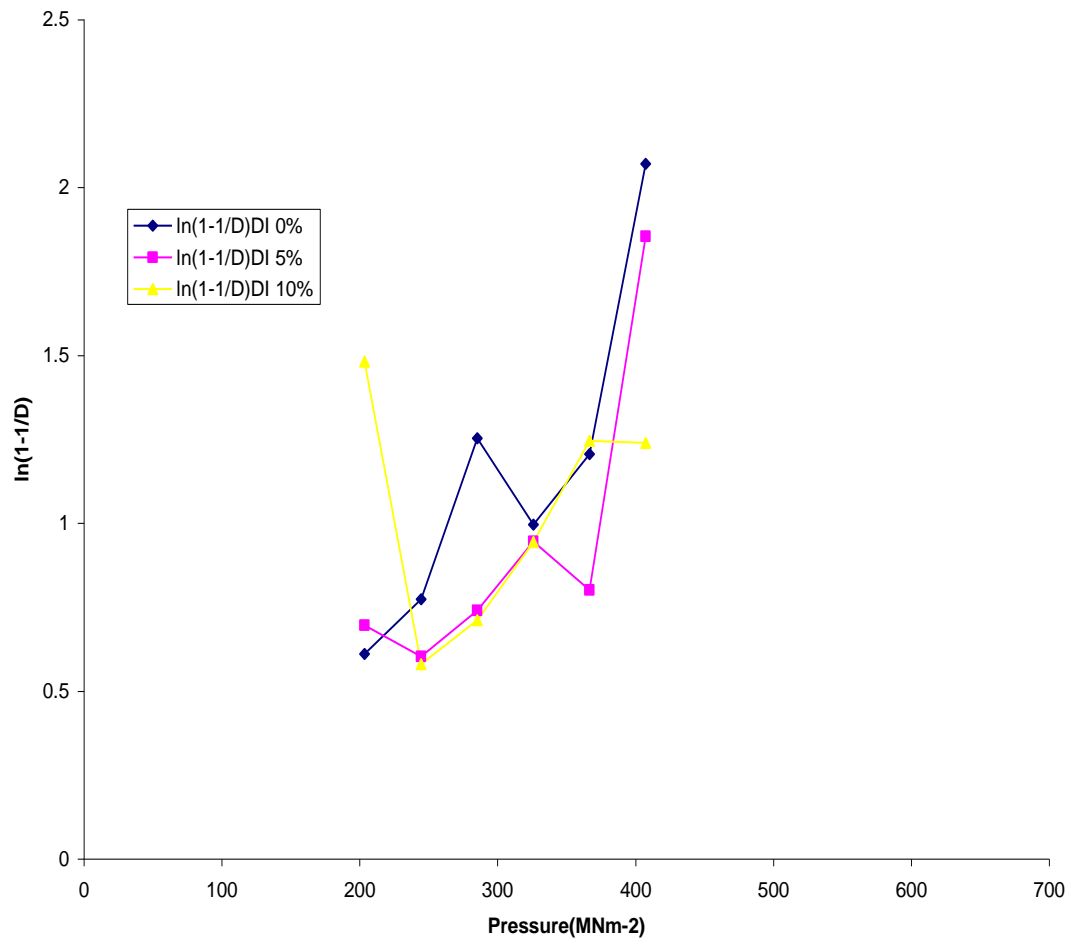


Fig.4.11: Heckel plots for paracetamol compacts with different concentrations of *Digitaria iburua* starch as disintegrant.

All the plots for compacts of granules having *Digitaria iburua* starch as disintegrant also displayed two compression phases of brittle fracture followed by plastic deformation. Generally, the linearity and deformation occurred at almost the same compressional pressure of 400MNm^{-2} and 360MNm^{-2} respectively.

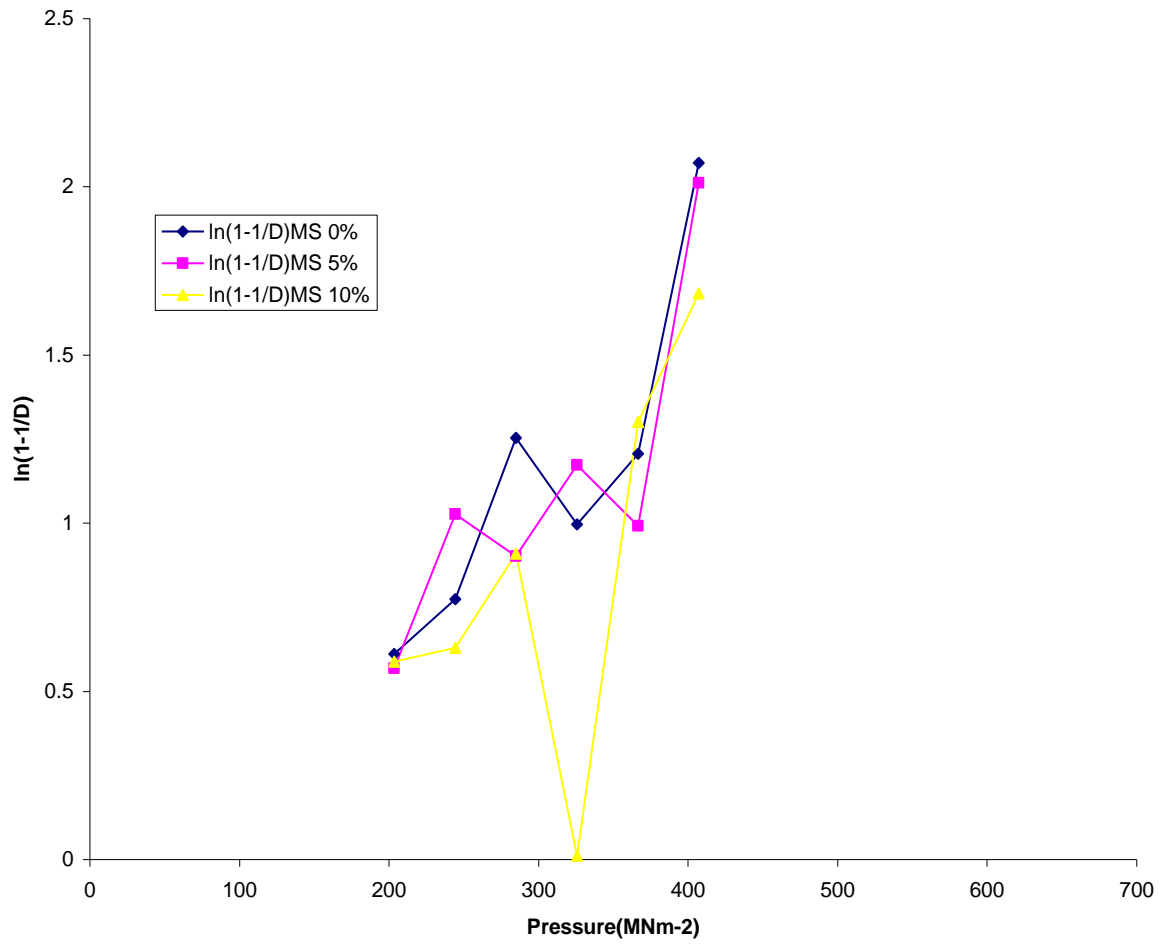


Fig.4.12: Heckel plots for paracetamol compacts prepared with different concentrations of maize starch as disintegrant.

The Heckel plots for compacts of granules having maize starch as disintegrant also displayed two phases: initial region representing brittle fracture or particle fragmentation followed by plastic flow or deformation as the disintegrant concentration was increased. Granules having 7%w/w maize starch displayed the highest compactibility.

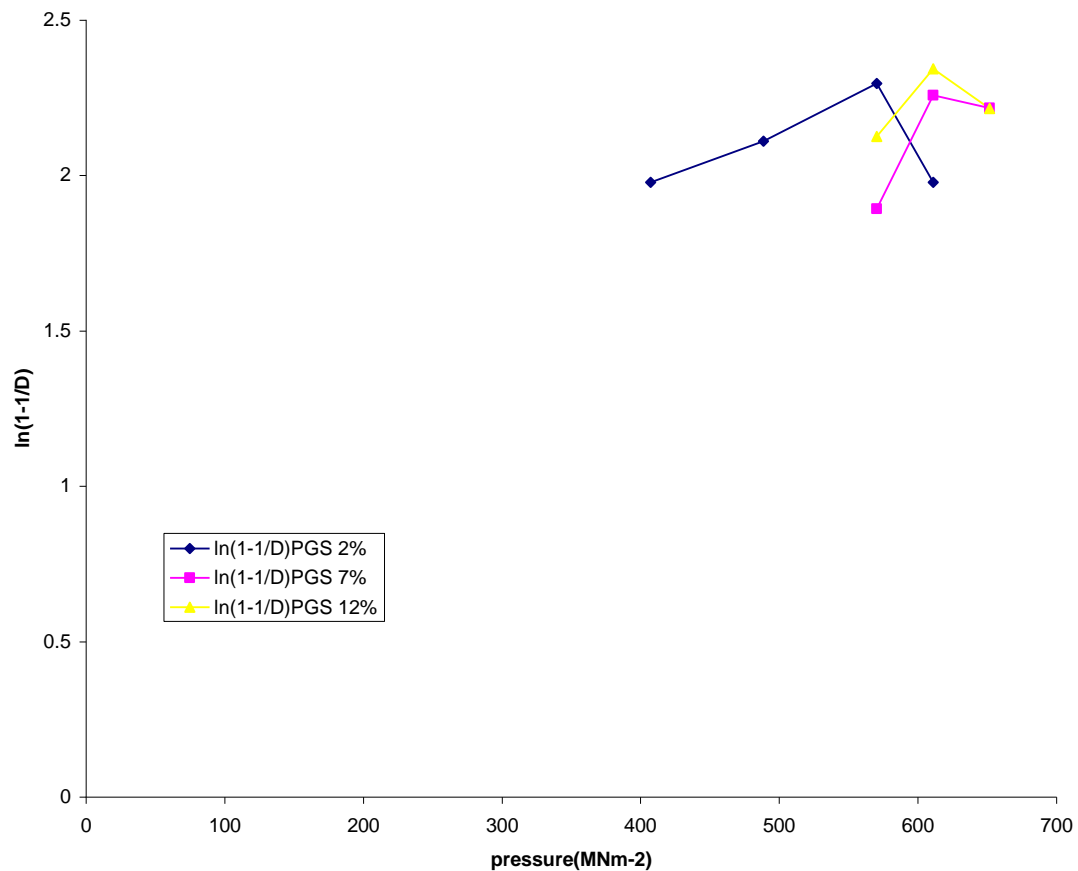


Fig.4.13: Heckel plots for paracetamol compacts prepared with different concentrations of pregelatinised *Digitaria iburua* starch as disintegrant.

Pregelatinised *Digitaria iburua* starch as disintegrant gave plots of similar compression behavior with two phases. All the three plots showed granules of high densification at the three disintegrant concentrations analysed

CHAPTER FIVE

5.0 DISCUSSION

5.1 PHYSICO-CHEMICAL PROPERTIES OF *DIGITARIA IBURUA* AND PREGELATINISED *DIGITARIA IBURUA* STARCHES.

The percentage yield of starch powder extracted from the grains of *digitaria iburua* was 62.20%w/w while the yield obtained from pregelatinising the starch was 73.18%w. The differences in the yield may be as a result of the processes involved in extracting pure DI starch powder from the grain. Pregelatinization of starch involves heating the starch suspension in water to a temperature lower than gelatinization temperature.

Thus, gelatinization brings about a partial rupture of the organized structure of starch to form a granular substance. Gelatinisation distrupts the crystalline lattice structure of starch completely to produce an amorphous form (Musa et al, 2004).

The results of the identification tests on the starches conforms to the specification in the official monograph (B.P,2002)

As shown by the values of the densities, PGS had the highest value. Bulk and tapped densities give indications on how well the starch powders will compress to make a tablet since the smaller the particle size, the more the resistance to powder flow; this is because of adhesion between the particles of powders (Carr, 1999). PGS starch gave the highest bulk and tapped densities which means that PGS will produce tablets with good compressibility. This probably could be due to the fact that the particles of PGS have been denatured giving the starch powder the thin fibre-like appearance which could be responsible for the closer packing of the particles.

Also both the Carr's index and Hausner ratio tells the percentage compressibility of a starch powder. The moisture content of the starch powders ranks in the order MS>PGS>DI. This ranking could imply that the particle of DI starch may have smaller pore sizes which traps lesser amounts of water resulting to the least moisture content. The swelling power ranks in the order DI>MS>PGS. The higher value of swelling power of DI indicates give good disintegrating properties. The Moisture sorption is a parameter for indicating how sensitive a powder is to atmospheric moisture and also indicates its physical stability when formulated into tablet. The

moisture sorption ranks in the order MS>DI>PGS. The least value for PGS could be due to the rupture of the organized structure of the starch particles into a disorganized amorphous form (Musa *et al*, 2004)

5.2 EFFECTS OF *DIGITARIA IBURUA* AND PREGELATINISED *DIGITARIA IBURUA* STARCHES AS BINDER AND DISINTEGRANT ON PROPERTIES OF PARACETAMOL GRANULES

The particle size distribution of granules containing DI starch as binder at varying concentrations was analysed. Statistically, there was no significant difference between any batch amongst the six batches at $p>0.05$.

The flow rate of the granules was found to increase with an increase in concentration of binder with DI observed to have the highest flow rate at 2%w/w binder concentration. This is because, as the concentration of binder is increased, a greater number of binding bridges are formed within the granules leading to increase in particle size of the granules. As a result, there is decrease in the attractive forces of cohesion and friction within the particles of the granules leading to increase in flow rate (Musa, 2002). As the binder

concentration was increased, there was only a slight change in bulk densities which means that increasing the concentration of binder does not have much influence on the bulk densities of the two granules.

The moisture content for the granules produced with DI and gelatin as binder were generally similar so the operational forces in the mechanism of granulation might be expected to be similar (Kristenten, 1984). Initially, there was a rise in moisture in granules containing DI starch and gelatin granules after which it then decreased as the binder concentration was increased. This decrease could be explained as follows; as the initial increase in binder concentration added did not increase the particle size of the granule which then causes a decrease in the moisture content

Carr's index describes the percentage compressibility of the granules. As the binder concentration of the granules was increased up to 10%, there was an increase in Carr's index. These could be due to the fact that at 10% concentration, enough binding bridges have been formed giving densier granules. The Hausner ratio (i.e the ratio of tapped density to bulk density) also explains the degree of densification of the granules. It gives a measure of the ability of a material to be reduced in volume under pressure. As the binder

concentration was increased, there was an initial decrease in Hausner ratio. It then rose at binder concentration of 10% which may be due to the fact that at 10% concentration the binder has greater effect on the compressibility of the granules.

Angle of Repose also explains the flowability of granules. Granules with large angle of repose has low flowability (up to 50%). As the binder concentration was increased angle of repose generally decreased which means better flowability of granules of both starch powders. At binder concentration of 7%, the angle of repose increased which means it has reached its maximum concentration after which any addition had little or no constructive effect on the angle of repose.

Tapped density explains the density of the powder after packing. Tapped density gives an idea of how well it will compact to make tablet. As the binder concentration was increased, the granules size increases meaning formation of more voids in between the granules, thereby decreasing the tapped density

The results shown in Tables 4.4 and 4.5 (i.e pages 79 and 80) indicates that as the disintegrant concentration was increased i.e. from 0% to 12%, the flow rate at 7% was at its highest. For MS BP. as disintegrant, the flow rate of the granules ranks in the order

2% > 7% > 0% > 10% > 12% > 5%. At 2% MS concentration the flow rate was at its highest. For PGS as disintegrant, the flow rate of the granules ranks 2% > 7% > 12%. These decrease in flow rate with increase in PGS concentration could be due to the fact that the shapes of the particle has been denatured. Moisture contents for DI and MS is relatively the same.

Angle of repose was increased in the order of 10% > 5% & 7% > 12% > 0% > 2% disintegrant concentration. At 10% DI concentration gave granules with the highest Angle of repose. At 2%, granules with the least and best angle of repose were produced. The higher the angle of repose, the slower the flow rates. There was also an increase in angle of repose of granules formulated with MS BP as disintegrant. For PGS as disintegrant, the angle of repose ranks in the order 12% . 7% > 2%. This means that increasing the concentration of PGS as disintegrant decreases the flowability of the granules.

The bulk densities is in the order DI 2% . > 0% > 5% > 10% > 7% > 12% disintegrant concentration. Also for maize starch, 2% concentration gave the highest bulk density which means it will give better compressibility when making tablets. Also at 2% PGS concentration the bulk density was at its highest.

Both the Carrs index and Hausner ratio which expressed the percentage compressibility of the granules increases in the order 7% > 12% > 2% > 5% > 0% > 10% disintegrant concentration. At 7% DI disintegrant concentration it showed the highest compressibility index. This is because higher density granules compact better. Also both the Carrs index and Hausner ratio increased as the concentration of PGS as disintegrant was increased.

Statistical analysis of all the properties analysed shows no significant differences at $p = 0.05$

5.3 EFFECT OF *DIGITARIA IBURUA* AND PREGELATINISED *DIGITARIA IBURUA* STARCHES AS BINDERS AND DISINTEGRANT ON PROPERTIES OF PARACETAMOL TABLETS

The result shown in table 4.6a indicates that as you increase the binder concentration for DI starch, the tablet thickness remain the same up to a concentration 7%, above which there was a slight increase followed by a decrease. This increase in tablet hardness with increase in binder concentrations is as a result of increase in strength of forces that bind the particles together (Vander Waals forces) as

well as mechanical interlocking .As the concentration of gelatin was increased, there was a decrease in tablet hardness at 2%.

The results shown in table 4.6a indicates an increase in the concentration of DI starch and Gelatin as binder causes a marked decrease in tablet friability. These means that the binders increased the binding bridges in between the granules thereby giving additional bonds which makes the tablets stronger which in turn decreases its friability.

Table 4.6b also shows that as the concentration of DI starch and gelatin was increased as binder there was an increase in Disintegration time for DI. This could be due to increase in granules interparticulate forces with increase in binder which then increased the hardness of the tablet making it harder up to a maximum concentration of 5% above which it decreased remarkably for DI. In case of gelatin as binder, disintegration time kept increasing as the concentration of binder was increased which means that as you increase the binder concentration stronger granules were obtained which in turn produce stronger tablets with higher disintegration time.

Table 4.6b also shows that there was an increase in crushing strength of tablets with an increase in the concentration of gelatin as binder. This increase in crushing strength corresponds to the decrease in tablet friability of gelatin. In case of DI as the binder concentration was increased, there was an initial decrease in crushing strength of the tablets meaning that the binder added at concentration of 2% acted as a disintegrant above which crushing strength increased resulting in harder tablets as supported by several authors (Esezebo, 1986; Odusote and Nusipuri, 1987; Kunle, 1988; Garr, 1988 and Akande, 1988). This increase in crushing strength might be as a result of increase in bonds formed within the tablets because the strength of the inter particulate bonds and the number of bonds depends on the concentration of binder used.

According to official limit set out in B.P 2002 for compressed tablet, the tablet should release 75% of the active content in less than 30mins. Although all the tablets dissolved within 20mins, the dissolution was found to increase with increasing the binder concentration.

Table 4.7a shows that as the disintegrant concentration was increased there was an initial rise in friability for both starches. There

was then a decline in values of friability between disintegrant concentration of 2% and 5%. This decline has been explained by Esezobo, (1986), as arising from the fact that small proportion of the starch added as disintegrant gets wetted in the process of granulation, thereby acting as a binder. For PGS, friability decreases at all concentration making the tablets harder. This could be explained that, PGS when added acted more as a binder than a disintegrant.

Table 4.7b shows that increase in the disintegrant concentration brought an initial decrease in crushing strength for both starches. This decrease can be explained in terms of tablet getting saturated with moisture. That is, the disintegrant acting as wetting agent. There was an increase in crushing strength as the disintegrant concentration was increased from 2% to 4%. The increase in crushing strength with increasing disintegrant concentration has been explained by Esezobo, 1986. The disintegrant added gets wetted in the process of granulation thereby acting as a binder thus increasing the crushing strength up to an optimum concentration of 10% after which the starch stopped acting as binder. For PGS, the crushing strength kept increasing in all concentrations. This means that PGS added acted more as a binder

than disintegrant thereby making more harder tablets with higher crushing strength.

Table 4.7b shows that as the concentration of disintegrant was increased there was a decrease in disintegration time for DI starch up to concentration beyond which it then increases with further increase in disintegrant concentrations. The presence of more starch particles could have resulted in the formation of more chains in the pore channel and enlargement of these pores which allows water to enter the tablet more easily and cause tablet rupture more easily (Lowenthal *et al*,1973) For MS BP., there was an initial increase in Disintegration time as the concentration of disintegrant was increased. For PGS there was an initial increase in disintegration time up to 7% concentration. The results for the tablet disintegration time for both MS BP. and PGS corresponds with the results of Friability and Crushing strength of both starches.

Although all the tablets formulated with DI and PGS DI starch as disintegrant dissolved within 25mins, dissolution was found to decrease with increasing disintegrant concentration.

Statistical analysis of all the properties analysed shows no significant differences at $p = 0.05$

5.4 EFFECT OF *DIGITARIA IBURUA* AND PREGELATINISED *DIGITARIA IBURUA* STARCHES AS BINDERS AND DISINTEGRANT ON COMPACTION BEHAVIOUR OF PARACETAMOL TABLETS.

The Heckel plots for various formulations were illustrated in Figures 4.2,4.3,4.4,4.5 and 4.6 and the Heckel constants were presented on Tables 4.8 and 4.9 respectively.

The Heckels equation evaluates the ability of granules to undergo volume reduction, that is, compressibility.

The plots of *Digitaria iburua* starch and gelatin as binder all conforms to type B compaction characteristics. This result is not unexpected as like lactose which is known to be a hard and brittle substance, thus requiring initial fragmentation before plastic deformation (Armstrong and Lowudes, 1984). On discussion of results of Heckel constants on table 4.8, the P_y value, which is the mean yield pressure decrease as the concentration of DI and Gelatin as binder were increased. A high value indicates plastic deformation at relatively low pressure and that deformation occurs faster. D_A is the relative density of the granules when compression has just started, that is at mean yield pressure. For granules prepared with DI starch as

binder, the D_A value ranks in the order 7% > 0% > 10% > 12% > 2% > 5% binder concentration.

A high D_A value indicates dense packing in pre-compression stage with granules at 5% DI starch concentration having poor compact and 7% DI starch concentration giving a more compacted granules. Shape of granules and also density are implicated in variation in compaction characteristics (Itiola, 1991).

The D_o values which describe the die filling stage for granules is indicative of the relative density at zero pressure that is, the packing fraction of the granules. The ranking order of D_o is 12% > 10% > 7% > 5% > 2% > 0% binder concentration. The value of D_o increases with the increase in the concentration of binder (Musa, 2002).

The D_B value, which is the relative density of the granules when compression has just been achieved is indicative of the densification due to rearrangement of particles during the initial stage of compaction. The higher the D_B value, the better the compressibility. The value of D_B increases in the following order: 0% > 7% > 10% > 12% > 2% > 5% binder concentration. The ranging order was as

above based on the granules size. Shape of the granules is an important determining factor (Itiola, 1991, Isimi, 2001).

In case of gelatin as binder at varying concentrations, the D_A value increases in order 0% > 2% > 5% > 10% > 12% > 7% binder concentration. There was a general decrease in D_A value as the concentration of gelatin was increased. In case of D_o values for gelatin, there was found to be an increase as the concentration of gelatin was increased from 0% to 12%. The increase in D_o values is related to the increase in granule mass with increasing binder concentration (Musa, 2002). D_B value was observed to decrease with increase in binder concentration.

The plots of *Digitaria iburua* starch and PGS as disintegrant all conforms to type B compaction characteristics as like lactose which is known to be a hard and brittle substance, thus requiring initial fragmentation before plastic deformation (Armstrong and Lowudes, 1984).

For granules prepared with DI starch as disintegrant, the relative density of the compact that is D_A ranks in the order 7% > 10% > 12% > 2% > 0% > 5% disintegrant concentration. There was highest

compaction at 7% disintegrant concentration and the least compaction occurred at 5%.

In case of PGS as disintegrant, the D_A values ranks in order 2% >12% >7% PGS concentrations. The D_O value which is the relative density at zero pressure increases, in this case, as the concentration of disintegrant was increased. Granules with higher D_O value indicate higher density.

A high value of D_O indicates a very dense packing while a low D_O value shows that the packing is loose (Kunle 1997). Granules prepared with PGS as disintegrant show also an increase in D_O value with increase in PGS concentration. D_B value which is the phase of rearrangement at low pressure when the deformation has just begun ranks in order 7% >10% >12% >2% >0% >5% of DI starch concentration as disintegrant indicating the rearrangement was highest with DI starch at 7% concentration. For PGS the deformation increases in order 2% > 12% >7% disintegrant concentration.

CHAPTER SIX

6.0 SUMMARY, CONCLUSION AND RECOMMENDATION.

Digitaria iburua starch conforms with BP specification for pharmaceutical starch.

Physicochemical properties of *Digitaria iburua* starch and PGS DI starch showed that the two starches appears better than Maize starch BP. in terms of flow rate, moisture content, true density and swelling power. PGS starch also displayed superiority in terms of moisture sorption, tapped and bulk densities and angle of repose.

Increasing the binder concentration of *Digitaria iburua* starch in granules generally improved its flow properties and compressibility index (bulk and tapped density, Carrs index and Hausner ratio). Also increase in the disintegrant concentration of *Digitaria iburua* starch cause increase in the flow rate, angle of repose and moisture content of the resulting granules. Pregelatinised *Digitaria iburua* starch produced paracetamol granules of good compressibility index.

In general, increasing the concentration of *Digitaria iburua* starch as binder and disintegrant gave paracetamol tablets of good friability, crushing strength and disintegration time. Pregelatinised *Digitaria iburua* starch also improved the tableting properties of

Paracetamol tablets. Paracetamol tablets had properties within B.P specification.

Digitaria iburua starch when used at 7%w/w to 10%w/w concentration as binder and disintegrant is recommended in the formulation of 500mg Paracetamol tablet. Pregelatinised *Digitaria iburua* starch is useful in producing good quality paracetamol tablet when used as disintegrants at 2,7 and 10%w/v.

Compaction studies show that native *Digitaria iburua* starch and Pregelatinised *Digitaria iburua* starch when used as binder and disintegrant produce granules that compact by initial fragmentation, followed by plastic deformation.

In view of the results of this study, the following recommendations are suggested:

- Evaluation of DI and PGS starches as binders and disintegrants in low dose tablet formulation.

- Evaluation of DI and PGS starches as diluents in tablet formulations.

- The gelling properties and use of DI and PGS in enhancing viscosities of suspensions should also be investigated.

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APPENDIX

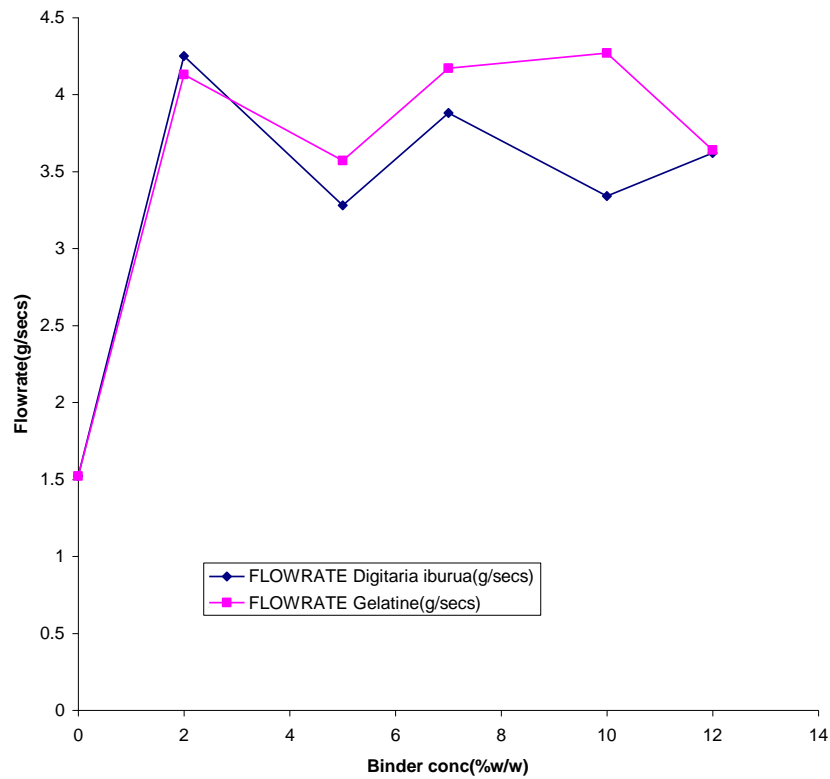


Fig 4.14: Plots of Flowrate(g/sec) against Binder concentration(%w/w) in paracetamol granules formulated from *Digitaria iburua* starch and Gelatin as binder.

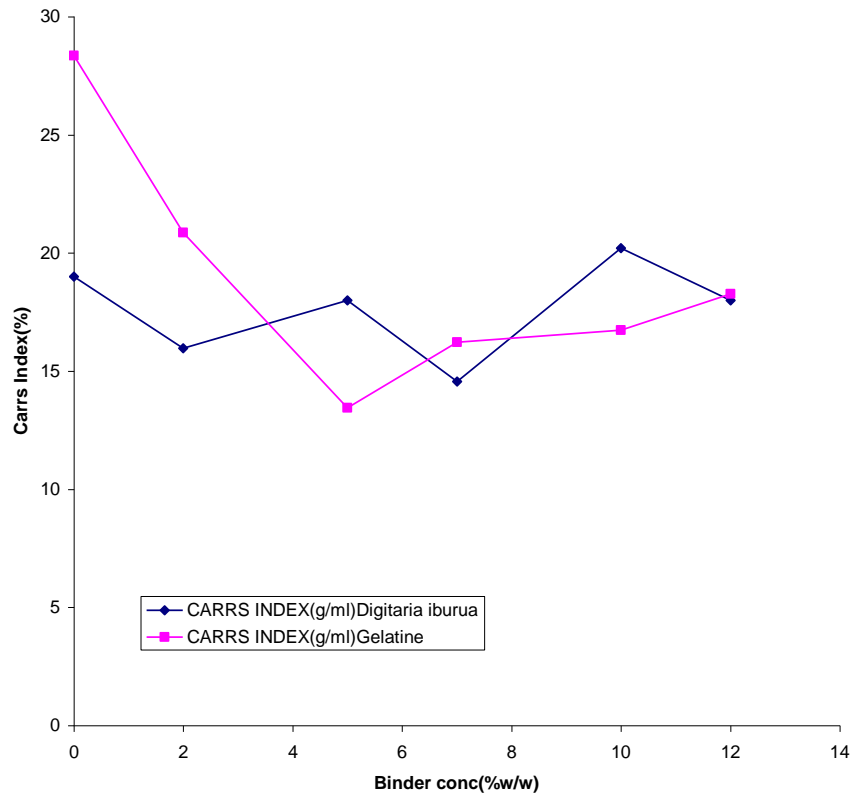


Fig.4.15: Plots of Carrs Index (%) against Binder concentration (%w/w) in paracetamol granules formulated from *Digitaria iburua* starch and Gelatin as binder.

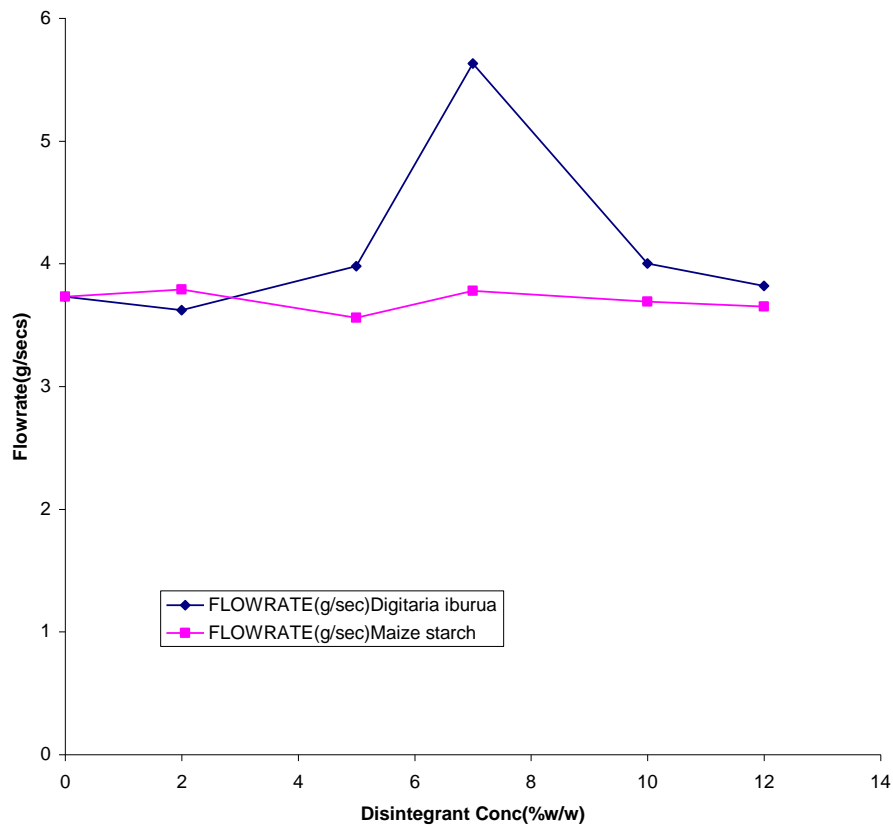


Fig.4.16: Plots of Flowrate(g/sec) against Disintegrant concentration (%w/w) in paracetamol granules formulated from *Digitaria iburua* starch and Maize starch as disintegrant.

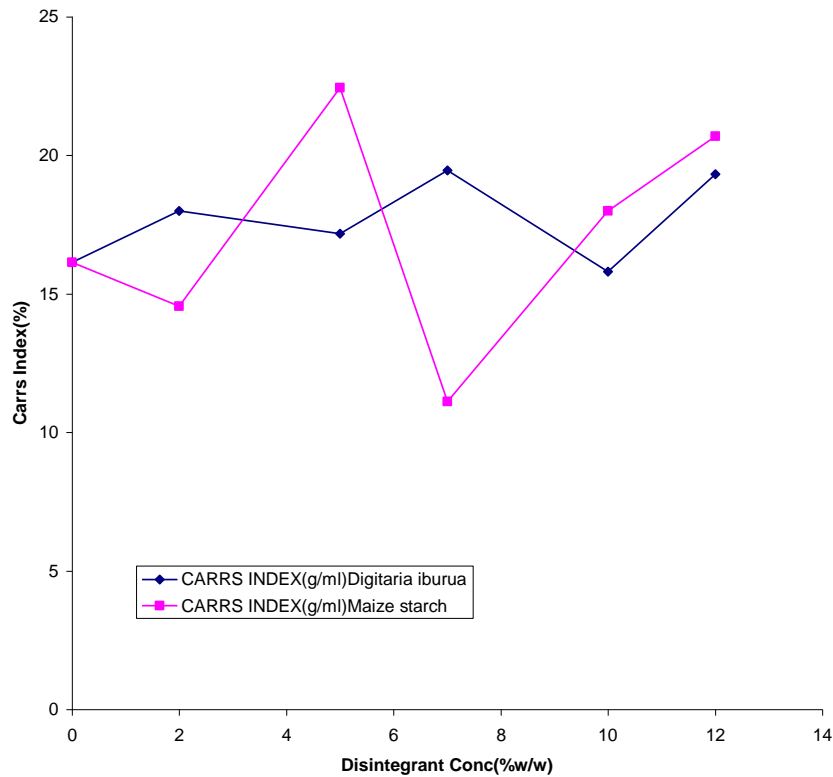


Fig.4.17: Plots of Carrs Index (%) against Disintegrant concentration (%w/w) in paracetamol granules formulated from *Digitaria iburua* starch and Maize starch as disintegrant.

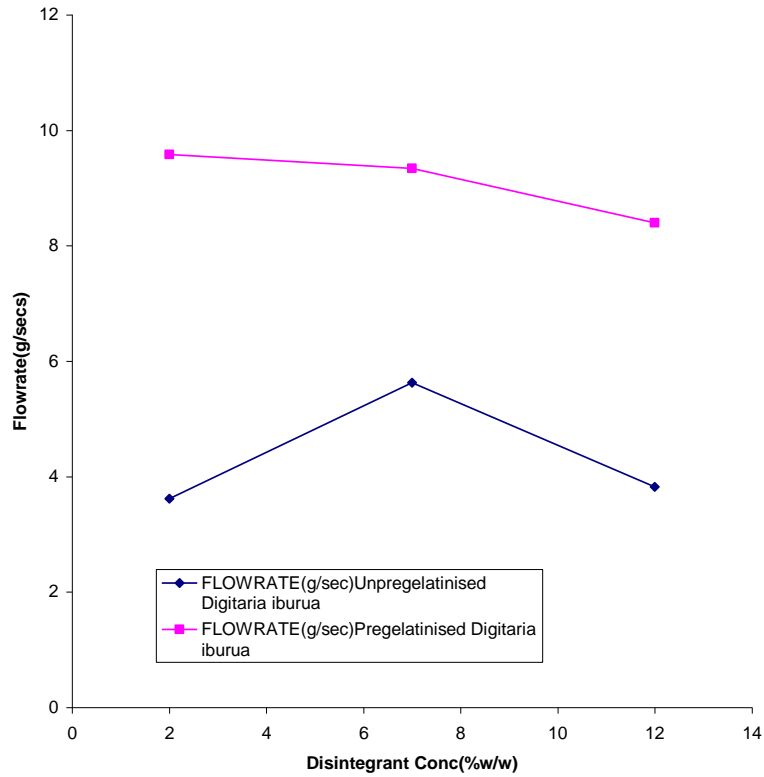


Fig.4.18: Plots of Flowrate(g/sec) against Disintegrant concentration (%w/w) in paracetamol granules formulated from pregelatinised and Unpregelatinised *Digitaria iburua* starch and as disintegrant.

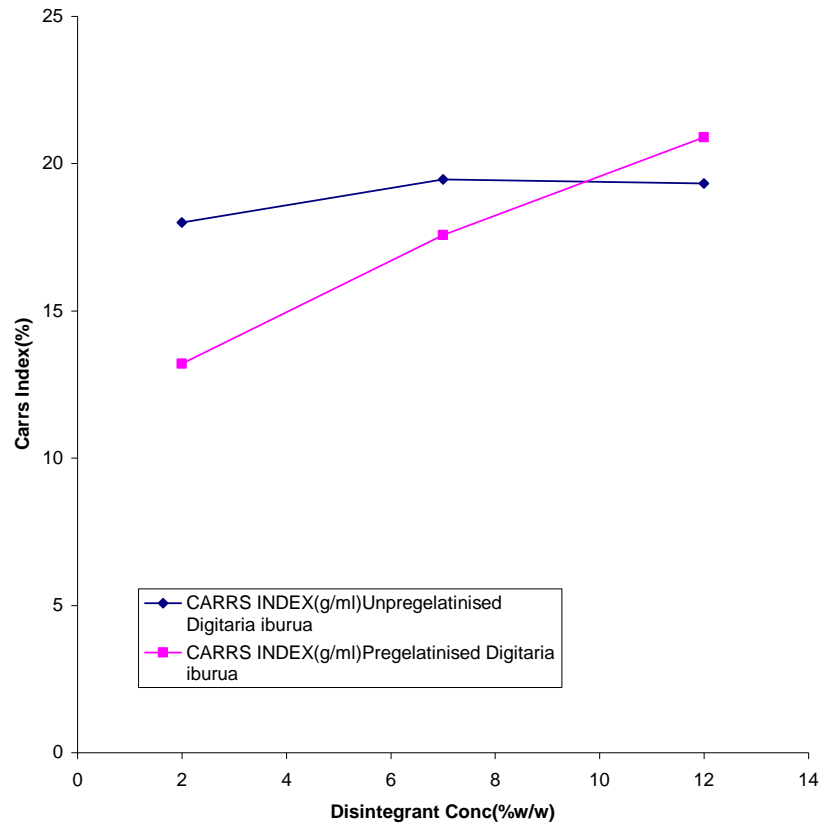


Fig.4.19: Plots of Carrs Index (%) against Disintegrant concentration(% w/w) in paracetamol granules formulated from pregelatinised and Unpregelatinised *Digitaria iburua* starch and as disintegrant.

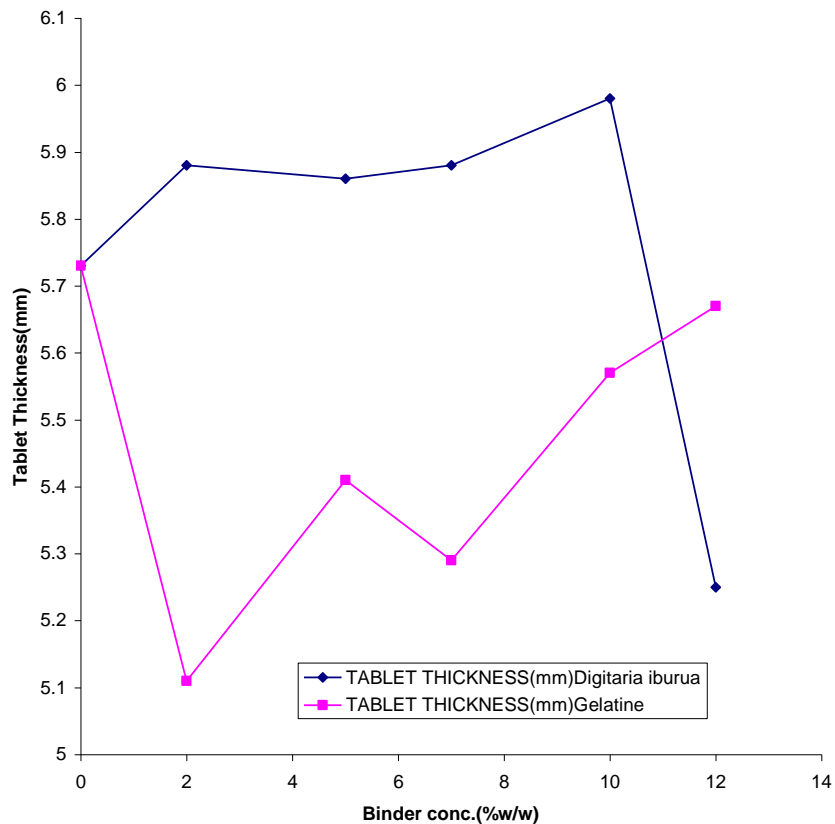


Fig.4.20: Plots of Tablet Thickness (mm) against Binder concentration (%w/w) in paracetamol tablets formulated from *Digitaria iburua* starch and Gelatin as binder.

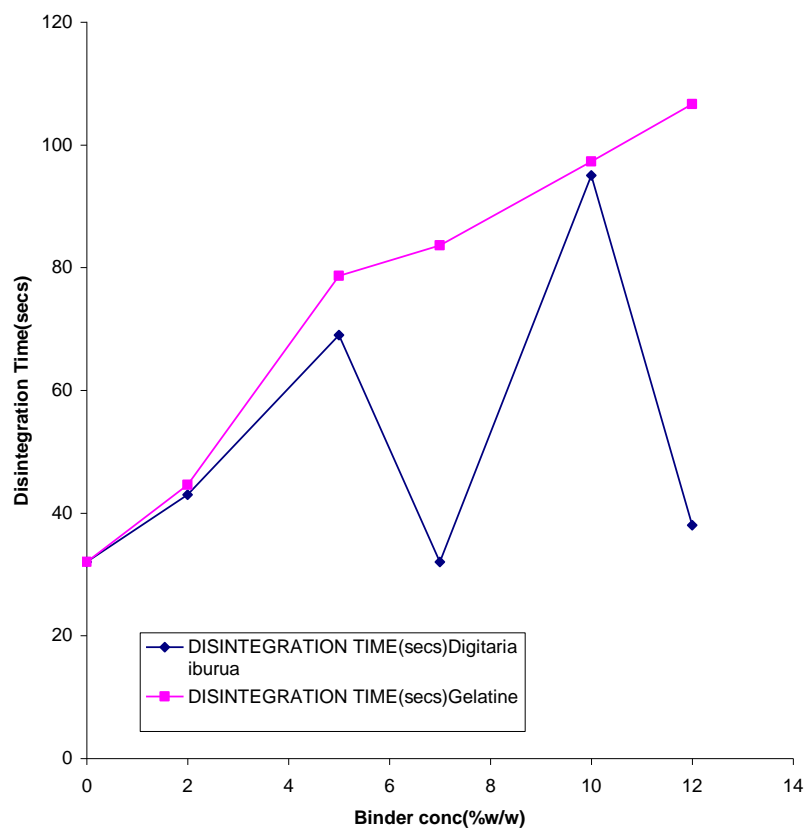


Fig.4.21 Plots of Disintegration Time (secs) against Binder concentration (%w/w) in paracetamol tablets formulated from *Digitaria iburua* starch and Gelatin as binder.

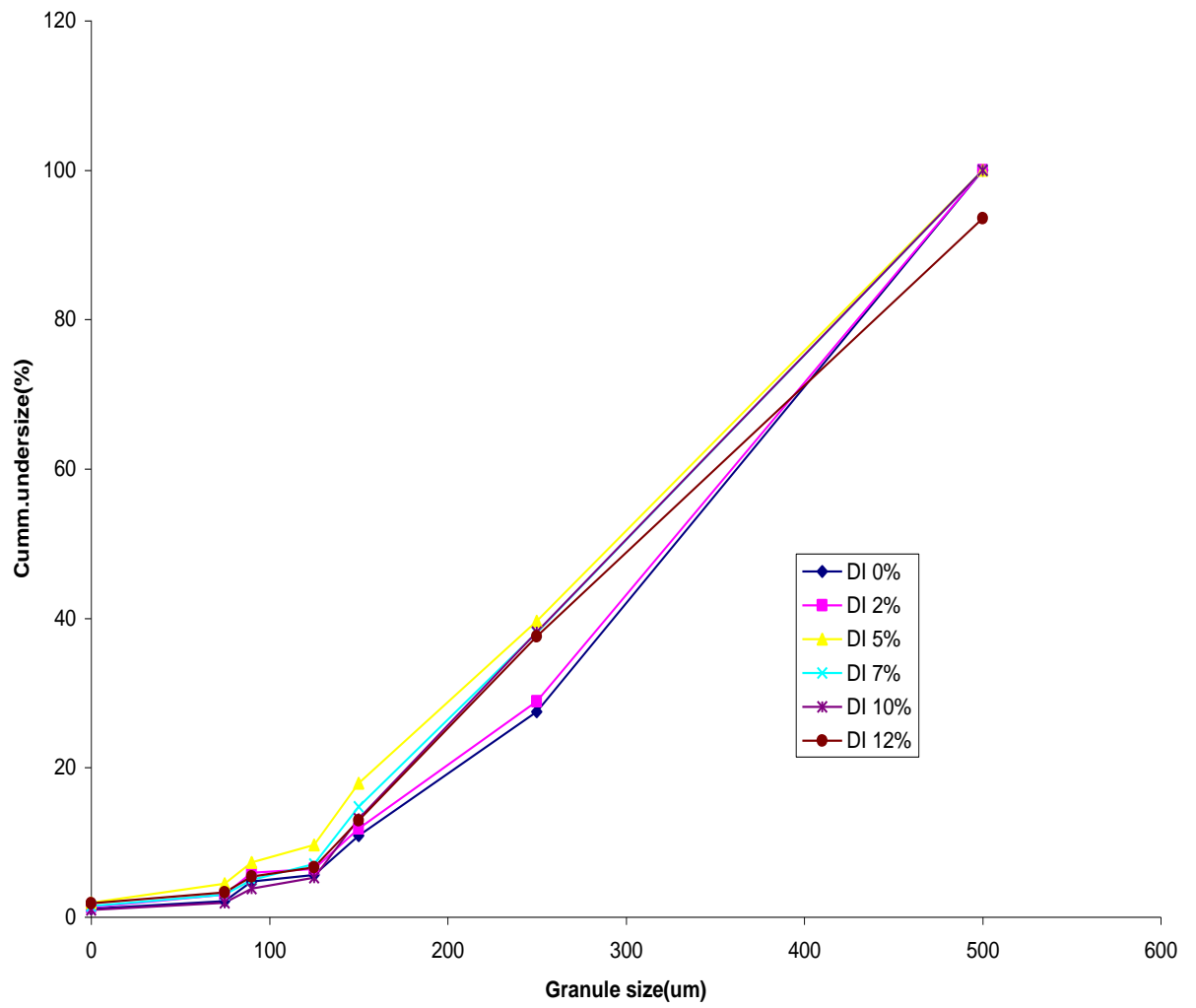


Fig.4.22: Size distribution of granules produced with *Digitaria iburua* as disintegrant in paracetamol tablet formulation.

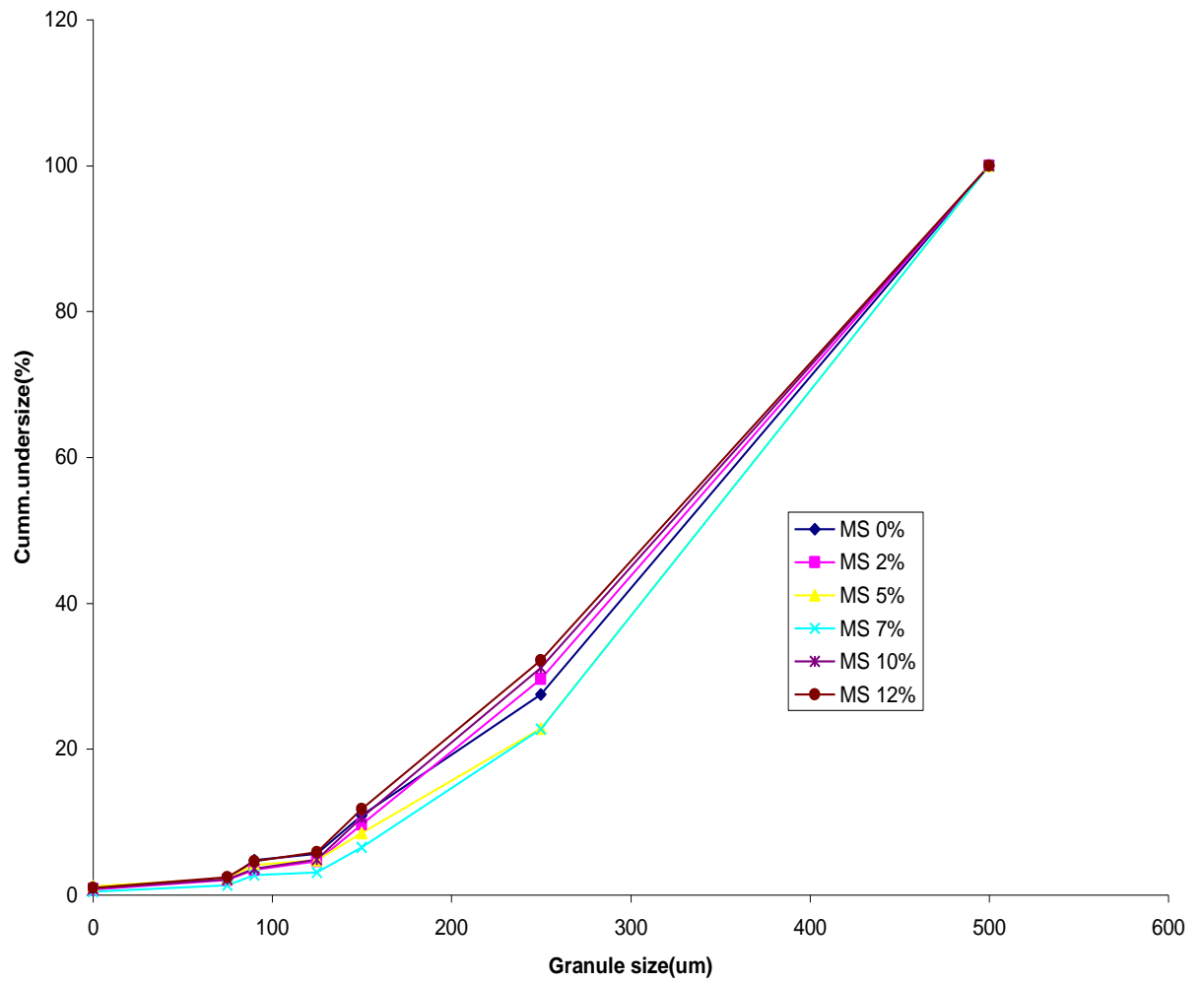


Fig.4.23: Size distribution of granules produced with maize starch as disintegrant in paracetamol tablet formulation

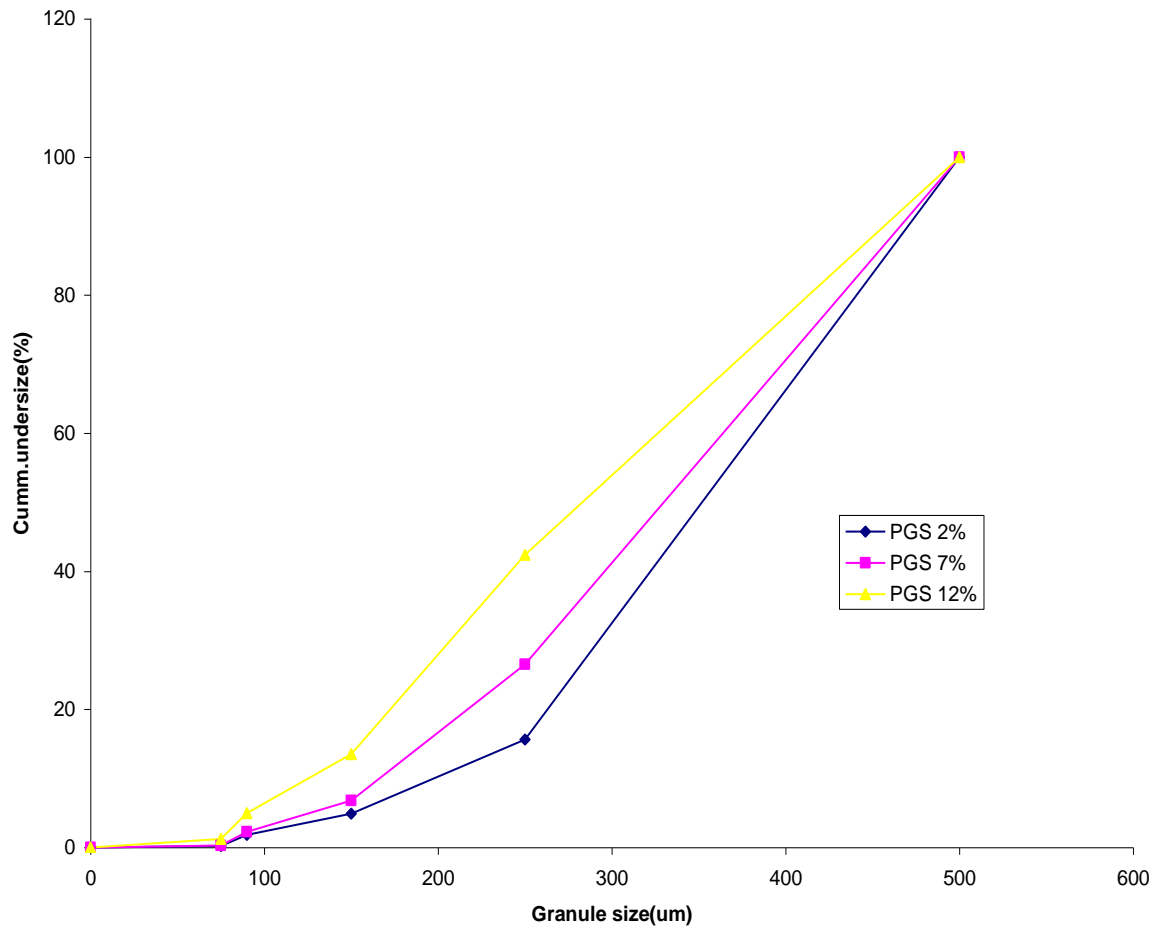


Fig.4.24: Size distribution of granules produced with pregelatinised *Digitaria iburua* starch as disintegrant in paracetamol tablet formulation

Appendix 1.00: Size distribution of granules with DI as binder.

SIEVE SIZES(um)	DI 0%	DI 2%	DI 5%	DI 7%	DI 10%	DI 12%
500	100	99.96	99.96	99.96	99.96	99.96
250	79.46	26.61	25.08	22.89	19.8	32.33
150	63.22	11	8.19	5.55	7.64	12.53
125	51.17	6.3	4.21	2.33	4.24	6.32
90	46.22	5.65	3.85	1.93	3.06	5.71
75	35.1	3.13	1.92	1	2.07	2.74
0	25.17	1.83	0.95	0.36	1.08	1.01

Appendix 2.00: Size distribution of granules with GEL as binder.

SIEVE SIZES(um)	GEL 0%	GEL 2%	GEL 5%	GEL 7%	GEL 10%	GEL 12%
500	100	99.95	99.97	99.96	99.98	99.97
250	79.46	46.46	22.91	26.86	39.29	23.24
150	63.22	21.61	3.72	9.1	17.87	7.65
125	51.17	10.45	1.2	2.31	9.46	3.56
90	46.22	7.61	0.82	1.32	6.69	2.34
75	35.1	4.18	0.44	0.78	2.12	1.26
0	25.17	1.66	0.18	0.36	0.94	0.48

Appendix 3.00: Size distribution of granules with DI as disintegrant

SIEVE SIZES(um)	DI 0%	DI 2%	DI 5%	DI 7%	DI 10%	DI 12%
500	99.96	99.97	99.96	99.96	99.96	93.55
250	27.45	28.86	39.61	38.07	38.17	37.55
150	10.87	11.85	17.89	14.76	13.13	12.91
125	5.61	6.41	9.64	7.1	5.23	6.65
90	4.73	5.93	7.29	4.99	3.79	5.43
75	2.14	3.02	4.44	3	1.92	3.28
0	1.08	1.32	1.93	1.46	0.94	1.8

Appendix.400: Size distribution of granules with MS as disintegrant

SIEVE SIZES(um)	MS 0%	MS 2%	MS 5%	MS 7%	MS 10%	MS 12%
500	99.96	99.96	99.96	99.96	99.97	99.96
250	27.45	29.58	22.79	22.7	31.11	32.12
150	10.87	9.65	8.47	6.52	10.57	11.73
125	5.61	4.58	4.78	3.06	4.83	5.81
90	4.73	3.42	4.08	2.72	3.6	4.58
75	2.14	2.02	2.3	1.3	2.11	2.43
0	1.08	0.74	1.18	0.44	0.88	0.92

Appendix.5.00: Size distribution of granules with PGS as disintegrant.

SIEVE SIZES(um)	PGS 2%	PGS 7%	PGS 12%
500	99.97	99.99	99.98
250	15.65	26.51	42.36
150	4.87	6.81	13.52
90	1.81	2.29	4.99
75	0.2	0.3	1.23
0	0	0	0

Appendix.6.00: Size distribution of native DI powder.

SIEVE SIZES(um)	DI POWDER
250	99.97
150	96.43
125	70.41
90	60.25
75	43.99
0	33.31

Appendix 7.00: Heckels plot values for granules with DI as binder.

PRESSURE (MNm ⁻²)	ln(1-1/D)DI 0%	ln(1-1/D)DI 2%	ln(1-1/D)DI 5%	ln(1- 1/D)DI 7%	ln(1-1/D)DI 10%	ln(1-1/D)DI 12%
244.43						0.5458
285.168			0.7242	0.8718	0.9527	0.8067
325.907			1.2032	0.8915	1.0385	0.9609
366.645		2.1374	1.5927	1.4812	1.2588	1.2114
407.383		1.6625	1.442	1.9952	1.7674	1.5079
448.122	1.1477	2.2396	1.4812	3.0584	1.758	1.9322
488.86	1.8269	2.4981		3.1183	3.4747	
529.598	2.4161					
570.337	3.0933					
611.075	0.0604					

Appendix 8.00: Heckels plot values for granules with GEL as binder.

PRESSURE (MNm ⁻²)	ln(1-1/D) GEL 0%	ln(1-1/D) GEL 2%	ln(1-1/D) GEL 5%	ln(1-1/D) GEL 7%	ln(1-1/D) GEL 10%	ln(1-1/D) GEL 12%
203.691			0.4549	0.5765	0.5668	0.5606
244.43		0.7216	0.9955	0.6483	0.5998	0.6102
285.168		0.8488	0.808	1.1398	0.4157	0.9439
325.907		1.0552	1.1708	0.8919	0.7811	0.8412
366.645		1.1429	1.2915	1.2006	0.8649	1.6554
407.383		1.9984	5.0176	1.4812	1.8458	1.5528
448.122	1.1477	2.672				
488.86	1.8269					
529.598	2.4161					
570.337	3.0933					
611.075	0.0604					

Appendix 9.00: Heckels plot values for granules with DI as disintegrant

PRESSURE (MNm ⁻²)	ln(1-1/D)DI 0%	ln(1-1/D)DI 2%	ln(1-1/D)DI 5%	ln(1- 1/D)DI 7%	ln(1-1/D)DI 10%	ln(1-1/D)DI 12%
203.691	0.6102	0.424	0.696	0.4727	1.4812	0.3914
244.43	0.7736	0.6375	0.6035	0.5077	0.5804	0.7862
285.168	1.2525	0.8195	0.7405	0.6746	0.7106	0.5621
325.907	0.9955	1.2051	0.9459	0.8218	0.944	0.913
366.645	1.2061	1.2406	0.8005	1.0236	1.2456	1.239
407.383	2.0707	1.5182	1.8539	2.1782	1.2388	1.6467
448.122						
488.86						
529.598						
570.337						
611.075						

Appendix 10.00: Heckels plot values for granules with MS as disintegrant

PRESSURE (MNm ⁻²)	ln(1-1/D) MS 0%	ln(1-1/D) MS 2%	ln(1-1/D) MS 5%	ln(1-1/D) MS 7%	ln(1-1/D) MS 10%	ln(1-1/D) MS 12%
203.691	0.6102	0.7107	0.5682	0.5182	0.5883	0.5799
244.43	0.7736	0.7957	1.0261	0.841	0.6288	0.6325
285.168	1.2525	0.8182	0.901	1.1506	0.9089	0.6996
325.907	0.9955	1.0627	1.1728	0.9365	0.0113	1.028
366.645	1.2061	1.1059	0.9913	1.1974	1.3007	1.3394
407.383	2.0707	0.7639	2.0108	2.6676	1.6831	1.4769
448.122						
488.86						
529.598						
570.337						
611.075						

**Appendix 11.00: Heckels plot values for granules with PGS as
disintegrant**

PRESSURE (MNm ⁻²)	ln(1-1/D) PGS 2%	ln(1-1/D) PGS 7%	ln(1-1/D) PGS 12%
407.383	1.9771		
488.86	2.1098		
570.337	2.2967	1.8928	2.125
611.075	1.9771	2.2575	2.3434
651.814		2.2171	2.2157