



## CHAPTER I

### INTRODUCTION

The history of solid dosage forms dates back over a thousand years, and tablets have been in widespread use since the latter part of the nineteenth century and their popularity continues. The advantage of tablets include relative ease of handling and ingestion, convenience to the patient, generally good palatability, and therapeutic desirability resulting from precision of dosage, stability and acceptable bioavailability. Although the basic mechanical approach for their manufacture has remained the same, tablet technology has undergone great improvement. Efforts are continually being made to understand more clearly the physical characteristics of tablet compression and the factors affecting the availability of the drug from dosage after oral administration (Mendes and Roy, 1978).

In order for medicinal substances, with or without excipients, to be made into tablets with using available equipments, it is necessary that the materials, either in crystalline or powdered form, possess a number of physical characteristics. These characteristics include the ability to flow freely, cohesiveness and lubrication. Since most materials none or only some of these properties, method of tablet formulation and preparation have been developed to impart these desirable characteristics to the material which to be compressed into tablets.

In general, there are three methods for tablet preparation: wet granulation, dry granulation and direct compression. The most widely used and usual method of tablet preparation is wet granulation. The purpose of wet granulation is to enlarge the particle size of powder and obtain uniform particles which have free-flowing. It improves the cohesiveness, compressibility, prevents segregation, and reduces dust (King and Schwartz, 1985; Mendes and Roy, 1978).

The appearance, elegance and tablet properties are directly related to the granulation form which tablets are compressed. The quality of granulation is depended on the materials used, processing techniques and various equipments utilized. Of these factors mentioned above, none is more critical than the binders used in granulation. Tablets binders impart a cohesiveness

to the tablet formulation which ensure the tablet remaining intact after compression, as well as improving free-flowing qualities by the formulation of granules of desired size and hardness ( Sheth, Bandelin and Shangrew, 1980; Sumner, Thomson, Poole, and Grizzie, 1966). Because of the importance of binders in tablet preparation, numerous materials have been evaluated as tablet binders .

Currently, Ispaghula seed and husk , seed and seed husk of *Plantago ovata* in Family Plantaginaceae, are used as a safe laxative. Since Ispaghula husk has more mucilaginous content than the other *Plantago* plants and was reported to have both exhibited water absorbing ability, swelling properties and forming a stiff mucilage in the presence of water (William ,1989 ; Varo, Lynn and James, 1980; Smith, 1959). Moreover, many workers have reported that it may stand a bigger chance of utility in the pharmaceutical field. Thus, it is reasonable to assume that it may have some binding properties which can be used in tablet formulations .

## LITERATURE REVIEW

### Ispaghula Husk

Ispaghula (*Plantago ovata*, Isapgol) is a valuable crop of pharmaceutical utility. It is cultivated on a large scale in the north of Gujarat, particularly in Mehsana, Palanpur and Banskantha (Sharma and Koul,1986). In Thailand, *Plantago* plants are usually found in the north at altitude 1,000 m and commonly found in the open floor of dry evergreen forest. India is the largest producer and exporter of the Isapgol seeds and seed husk which are valued for their rich mucilaginous content. Currently Isapgol husk is used as a safe bulk laxative. It is also being used in the production of palatable laxative granules and a device named Isaptent, (tradename: Dilex-C<sup>®</sup>) which is used for the dilation of cervix in gynaecological operations and also for medicinal termination of pregnancy (Smith,1959 ; Sharma and Koul,1986).

The seeds of *P. psyllium* and *P. arenaria* are known in commerce as Spanish or French psyllium , while those of *P. ovata* are known as blonde psyllium, Ispaghula, spogel seeds or Indian plantago seeds . Seeds of *Plantago* plant are mucilaginous. In an endeavor to evaluate many species for mucilage content , seeds of many allies of *Plantago* plant have been compared with respect to size, weight, swelling factor and mucilage content. Sharma and Koul (1986) found that *Plantago ovata* seed has the maximum mucilage content, those studied and the domesticated *P. ovata* Forsk. seed lies in the quality and quantity of the mucilage in the superficial layers of the seed coat .

Some of the more important characteristics of these seeds are given in Table 1 ( Willium , 1989) .

Table 1 Characteristics of the *Plantago* seeds from various species

	<i>P. psyllium</i>	<i>P. arenaria</i>	<i>P. ovata</i>
<b>Origin</b>	France , Spain , Cuba	Mediterranean Europe , Egypt	Pakistan , India
<b>Colour</b>	Glossy ; deep brown	Dull ; blackish - brown	Dull ; pinkish grey-brown
<b>Shape</b>	Boated-shaped ; outline elongated ovate	Boated-shaped ; outline elliptical	Boated-shaped ; outline ovate
<b>Length</b>	2.0 - 3.0 mm	2.0 - 2.5 mm	1.8 - 3.3 mm
<b>Weight of 100 seeds</b>	0.09 - 0.10 g	0.12 - 0.14 g	0.15 - 0.19 g

Ispaghula husk , the epidermis and the collapsed adjacent layers removed from dried ripe seeds of *Plantago ovata* Forsk .,in family Plantaginaceae as well as *Plantago afra* (*P. psyllium* ) and *P. indica* (*P. arenaria*). The US National Formulary includes the seeds of all three species under the name "Plantago Seed ". In the British Pharmaceutical Codex the seeds of the last two species are included as Psyllium BPC while those of *Plantago ovata* from the source of Ispaghula husk BPC (Willium,1989).

Ispaghula husk contains mucilage and hemicellulose. Two fractions have been separated form mucilage: one is soluble in cold water and the other in hot water giving a highly viscous solution which gels on cooling ( Willium , 1989 ; The British Pharmaceutical Codex 11<sup>th</sup> edition, 1979 ; Smith, 1959). On hydrolysis cold water fraction yields a polysaccharide composed of D-xylose (46%), L-arabinose (7%), and the aldouronic acid, 2-O- $\alpha$ -D-galactopyranosyluronic acid L-rhamnose (40%) and hot water extraction removes a xylan composed of D-xylose(80%) and L-arabinose(40%)(The British Pharmaceutical Codex 11<sup>th</sup> edition, 1979 ; Smith, 1959) .

Since Ispaghula husk was reported to form viscous and adhesive mucilage it was thought worthwhile to study the possibility of its utility in the fields of pharmaceutical formulation and in the other fields of pharmacy .

## The Possibility of Ispaghula Husk Use as Pharmaceutical Necessities

1. The possible use of Ispaghula Husk as a gel former. Mithal and Zacharias (1971) observed *Plantago ovata* seed husk to yield semi-solid gels with water at concentrations of 1.5% and above. Baveja and Gupta (1969) reported Ispaghula dispersions to be antithixotropic changing into thixotropic gel systems on storage. Mithal and Zacharias (1971) found that the gel prepared from *P. ovata* compared with those of sodium alginate, methyl cellulose, sodium carboxymethylcellulose and starch appeared to be superior in spreadability, penetration, washability etc. Hence, gel forming properties of seed husk may be used as a base for medicated jellies.

2. The possible use of Ispaghula Husk as a binding agent in the granulation materials for compressed tablets. Mithal and Bhutiani (1969) found that mucilage of Ispaghula husk powder 2% w/v prepared in cold water compared favorably with starch mucilage 10% w/v in its binding qualities but was inferior to 5% w/v methylcellulose and 15% w/v acacia mucilage. And mucilage of husk 1.5 % w/v in hot water possessed better binding properties than 10% w/v starch but was slightly inferior to the methylcellulose and acacia mucilages.

3. The possible use of Ispaghula Husk as a suspending agent in the formulation of dry powder mixtures for reconstitution. Beveja and Jindal (1979) studied the use of Ispaghula husk as suspending agent in erythromycin stearate, ampicillin trihydrate and tetracycline hydrochloride mixtures. The results showed that use of Tween 80 with suspending agents sodium alginate 1.5 - 1.75 %, or sterculia 1.0 - 1.2 %, or pectin 2.5 - 3.0% or sodium CMC 0.75 - 1.0 % or Ispaghula 1.75 - 2.0 % produced satisfactory rheological characteristics.

4. The possible use of Ispaghula Husk as a sustaining agent in the formulation of sustained release tablets and capsules. In considering gel forming properties as a sustaining material, Singla and Singh (1990) found that the formulations which contained 5 % w/w and 0.5 % w/w of sustaining material from Ispaghula husk gave sustained release properties in tetracycline capsules and tablets, respectively.

## Type of Binders

The commonly used binders (Table 2) are hydrophilic polymers, which because of their properties as film formers and viscosity builders are used in pharmaceutical formulations for a number of different purposes. For example, povidone is utilized as a drug carrier, dispersing agent, viscosity builder, tablet binder and diluent, and coating agent (King and Schwartz, 1985; Mendes and Roy, 1978 ; Sheth et al., 1980).

In wet granulation method, aqueous binder solutions are preferred, unless nonaqueous solutions are necessary because of the properties of the drug substance and formulation. Thus, the drug may be sensitive to moisture with regard to its chemical stability. If the substance is readily soluble in water, granulation with aqueous binder solution gives rise to partial dissolution of the drug substance and subsequent crystallization or deposition during drying.

Binders are either sugars or polymeric materials. The latter fall into two categories, one is natural polymers such as starches and gum( including acacia and tragacanth) and the other is synthetic polymers such as polyvinylpyrrolidone (povidone), hydroxypropylcellulose (Klucel®) and methylcellulose (Methocel®). Binders of both types may be added dry to the powder mix, and the mixture wetted with granulating solvent or the binder may be added in solution form.

## The Purposes of Adding Binder in Tablet Formulation

The major reasons for adding binder are to:

1. Adhere the powder to each other so they can be formed into agglomerate, called granules.
2. Improve flow property of powder.
3. Insure the tablet remaining intact after compression by imparting cohesive quality to the powder.

These give materials to have suitable physical characteristics to be compressed.

4. Increase tablet hardness and reduce friability (King and Schwartz, 1985 ; Mendes and Roy, 1978 ; Sheth et al., 1980).

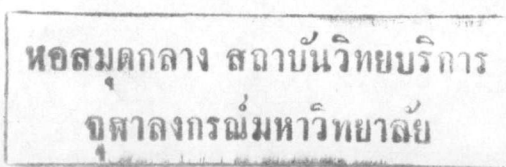


Table 2 Summaries of some commonly used binders with the usual concentration range of their application , together with the granulating solvent

Binder	Form used	Concentration % of Formula	Granulating Solvent
<b>Binder of Natural Origin</b>			
Sucrose	Solution	2 - 20	Water
Dextrose	Dry / Solution	5 - 10	Water
Starch	Warm paste	1 - 5	Water
Pregelatinized starch	Dry /Solution	5 - 10	Water
Acacia	Dry / Solution	5 - 20	Water
Gelatin	Warm Solution	1 - 5	Water
<b>Synthetic Binders</b>			
Polyvinyl pyrrolidone	Dry / Solution	0.5 - 5	Water, alcohol or hydroacohol
Methylcellulose	Solution paste	1 - 5	Water
Ethylcellulose	Solution	0.5 - 2	Alcohol
Hydroxypropyl methylcellulose	Solution paste	1 - 5	Water

### Binder Incorporation Methods

For preparing damp mass in wet granulation process , binders are added to provide agglomeration of powder materials . Binders could be added in either a solution or a dry form depending on the other ingredients in the formulation and the method of preparation ( King and Schwartz , 1985 ; Gunsel , Kanig and Shngrew , 1976) .

**1. Dry Incorporation Method .** Binders in dry form , diluents and drug are blended and then the mixtures are moistened with water or suitable solvents.

**2. Solution Incorporation Method .** Binders solutions are prepared as a paste or solution and added to premixed powder .

## Granule Formation in Wet Granulation

In wet granulation, binder solution is usually added to the powder mixture. The liquid play an influential role in the granulation process. Addition of a granulating liquid to a mass of powder may be characterized in a series of stages as described in Figure 1 by Newitt and Conway-Jones as follows (Marshall, 1985).

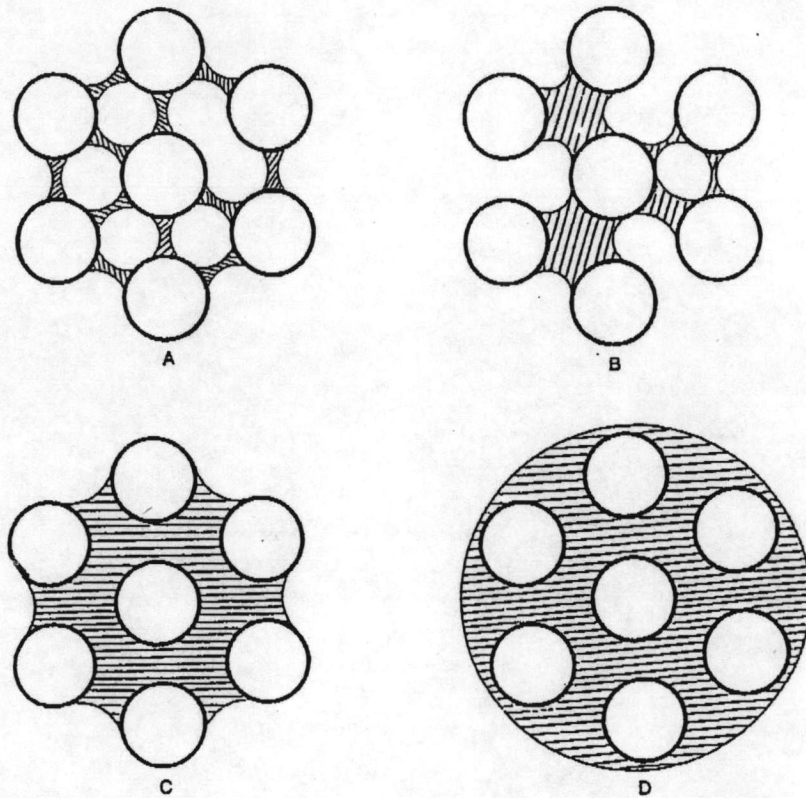
**1. Pendular State** At the initial stage, the powder are wetted with the granulating liquid. The liquid films will be formed on the surface and may combine to produce discrete liquid bridges at points of contact (Figure 1-A). The surface tension and negative capillary pressure in such bridge provide the cohesive force. In this state, the granules have comparatively low mechanical strength.

**2. Funicular State** As the amount of granulating liquid increases, several bridges of granules also further increase (Figure 1-B).

**3. Capillary State** Eventually as more liquid is added and the mass is kneaded to bring particles into closer proximity, the void space within the granule are entirely eliminate (Figure 1-C). At this point, bonding is effected by interfacial forces at the granule surface by a negative capillary pressure throughout the interior liquid filled space. The maximum strength of the granules is obtained in this state. Consequently, optimization of granulation process ensuring that this state has been achieved.

**4. Droplet State** Further addition of granulation liquid result in droplet formation (Figure 1-D). The particles are still held together with surface tension but without intragranular forces; such structures are weaker.

During drying, solid bridges of soluble materials (eg. drug, diluent and binder etc) will be formed in the granule. It may crystallize or precipitate out. This process results in the increasing in granule strength.



**Figure 1** Stage in the Development of Moist Granules as the Proportion of Liquid is increased in Wet Granulation Process

key : A is Pendular State  
B is Funicular State  
C is Capillary State  
D is Droplet State



## Processing Variables in Wet Granulation .

Many of processing variables in wet granulation, i.e., concentration of binder in the paste (Nelson, Arndt and Busse, 1957; Sakr, Kasem, Aziz and Shalaby, 1972; Davies and Gloor, 1972 ; Chalmers and Elworthy, 1976 ; Jacob and Plein, 1968 ; Shubair and Dingwall, 1976 ; Stanley-Wood and Shubair, 1979) , volume of binder solution (Chalmers and Elworthy , 1976 ; Shubair and Dingwall, 1977), temperature of binder solution (Shubair and Dingwall, 1976) , viscosity of binder solution ( Davies and Gloor, 1972 ; Chalmers and Elworthy, 1976; Stanley-wood and Shubair, 1979; Shubair and Dingwall, 1976, 1977; Hill, P.M., 1976; Davies and Gloor, 1973; Tiamraj and Dingwall, 1978), kneading time (Tiamraj and Dingwall, 1978; Zoglio, Huber, Kohne, Chan and Carstensen, 1976 ; Ganderton and Hunter, 1971 ; Chalmers and Elworthy, 1976 ; Opakunle and Spring, 1976; Hunter and Ganderton, 1972) and granulating vehicle (Wells and Walker, 1983; Selkirk, 1976) affect the granule characteristics .

Seager (1977) suggested that the binder distribution within the granules was determined by the method of manufacture . The binder distribution affected the granule structure , compression characteristics of the granule and tablet characteristics ( Seager, Burt, Ryder, Rue, Murray, Beal and Warrack, 1979; Seager, Burt, Ryder, Rue, 1980, 1981). In wet granulation, the distribution of binder was governed by the kneading step ( Zoglio et al., 1976 ; Dingwall and Ismail, 1977; Carstensen, Lai, Flickner, Huber and Zoglio, 1976). Dingwall and Ismail (1977) found that, in general, less binder (paste) was distributed to the larger bead for the granulation of glass beads. The binder distribution was fairly regular with povidone and gelatin granulations but was rather irregular with methocel and starch paste. Zoglio et al. (1976) and Carstensen et al. (1976) stated that the following steps consecutively occurred in kneading:

- a ) an excessive wetting , which is localized ,
- b ) distribution of the paste ,
- c ) formation of an equilibrium granule , and
- d ) in the case of a soluble binder, excipient, or active ingredient, excessive dissolution of material into the liquid, densification (decrease in porosity), and an increase in particle size, caused by further kneading .

The drug distribution was also altered with kneading time (Ojile, Macfarlane and Selkirk, 1982). In general, prolonged kneading time may cause the granules to be more consolidated in structure and a large amount of water soluble excipient to dissolve in the granulating fluid. These two factors resulted in the increases in drying time and disintegration time, and a decrease

in drug dissolution (Zoglio et al.,1976;Ganderton and Hunter,1971; Chalmers and Elworthy ,1976).

Many workers have reported that the viscosity of binder solution affected the granule and tablet properties (Davies and Gloor , 1972 ,1973 ; Chalmers and Elworthy ,1976; Stanley-Wood and Shubair, 1979 ; Shubair and Dingwall ,1976,1977 ; Hill, P.M.,1976 ; Tiamraj and Dingwall ,1978) The viscosity of binder solution has widely been known that it can affect the distribution of binder in granulated material . The higher viscosity of binder solution is , the less binder solution becomes . Viscosity of binder solution is virtually influenced by temperature. Shubair and Dingwall (1976) found that the release of erythosine from tablet was affected by the temperature of potato starch mucilage. Increase in temperature of kneading also increases the disintegration time and hardness of tablets ( Pipel and Esezobo ,1977).

The amount of vehicle used in granulation process was also important regarding the distribution of paste as responsible for particle size of the granules ( Selkirk,1976). The granulating vehicle played a significant role on wettability and drug solubility of the granulated powder. Greater wettability improved granule growth. Moreover, greater drug solubility produced larger granule with tighter distribution ( Zoglio et al.,1976).

### **Effect of Binder Incorporation Methods .**

Binder are mostly used in the solution form. It has been stated that incorporating binder in solution form is more effective in reaching and wetting each of particles within the mass of powders ( King and Schwartz, 1985). Since powders differ with respect to the ease which they can be wetted and it is often possible to gain effective binding with a lower concentration of binder, it is preferable to incorporate the binding agent in solution form ( Sheth et al., 1980 ; King and Schwartz, 1985). Generally the admixture of dry binder requires a higher concentration in formulation than when it is added as a binder solution, probably because of incomplete dissolution of the binder and effect of local high viscosities that oppose the distribution of the binder as previously described. In general, the method gives rise to smaller granule size and a high content of larger lumps .

Little work has been done on investigating the effect of binder incorporation methods on granule and tablet properties. Shubair and Dingwall (1976, 1977) studied the incorporation of binders in the forms of diluted solution as well as concentrated solution which followed by addition of

fluid. The result showed that these binder addition technique obviously affected the tablet hardness, disintegration time and dissolution time.

Das and Jarowski (1979a, 1979b, 1979c) studied the effect of granulation methods on granule and tablet properties. The wet granulation and microgranulation methods, stated in their papers, were similar to those used for incorporating binder in a solution and a dry form. However, the process variables of these two methods described by the authors were not same. The microgranulation was found to produce narrower distribution and smaller average particle size of sulfadiazine and dexamethasone granules than those produced by the wet granulation (Das and Jarowski, 1979a). The sulfadiazine tablets prepared by microgranulation disintegrated more rapidly than those prepared by wet granulation while it was insignificant difference in dexamethasone tablets (Das and Jarowski, 1979b). The microgranulation also produced the better weight and content uniformity (Das and Jarowski, 1979b). The higher dissolution rates were found in both dexamethasone and sulfadiazine tablets prepared by the microgranulation technique (Das and Jarowski, 1979c).

### **Effect of Binders on Granule Properties**

#### **Effect on Granule Size and Granule Size Distribution.**

The granulation of lactose and boric acid was studied by Opakunle and Spring (1976), the results of which showed that greater mean granule size was obtained when the volume of polyvinyl pyrrolidone (PVP) solution was increased. Chalmers and Elworthy (1976) studied the effect of binder on granule size of oxytetracycline granulations prepared by using an oscillating granulator. It was found that the average granule size increased with (a) increasing the PVP concentration using a constant volume of granulating solution, (b) increasing the volume of granulating solution at a fixed PVP concentration, and (c) increasing the volume of granulating solution while decreasing the PVP concentration to give the same amount of PVP in each granulation. Similar results were also obtained in fluid bed granulation of lactose using PVP, acacia and hydroxypropyl cellulose as binders (Davies and Gloor, 1972).

### **Effect on Bulk Density, Tapped Density and Compressibility of Granule**

King and Schwartz (1985) revealed that the increasing in the average granule size at higher binder level yielded a lower bulk density. Stanley-wood and Shubair (1979) found that as the concentration of starch paste increased to 10 % w/w, bulk density, tapped density and percent compressibility tended to increase. But the results were converse when the concentration was over 10 % w/w. Harwood and Pilpel (1968) investigated the effect of size and shape on bulk density and tapped density of granules. As granule size increased, bulk density was found to decrease. These attributed to the fact that smaller granules were able to form a closer, more intimate packing than those larger granules.

### **Effect on Granule Strength and Granule Friability .**

Many reports showed that an increase in amount of binder in the granulation resulted in the granules of greater strength ( Davies and Gloor, 1972 ; Hunter and Ganderton, 1972 ,1973 ;Ganderton and Selkirk,1970 ; Harwood and Pilpel, 1968 ; Jaiyeoba and Spring ,1980) .

In lactose and sucrose granulations using water as the granulating fluid, granule strength was found to increase as the amount of water used to granulate was increased (Ganderton and Selkirk, 1970). Similar results were reported for lactose granulation (Hunter and Ganderton, 1972; Rue et al.,1980).

However, with calcium phosphate granulations, granule strength went through maxima as the amount of water used in granulating was increased (Fonner, Anderson and Banker , 1981) .

At a constant binder concentration in the formula, dilution of the binder solution could increase granule strength or reduce granule friability ( Davies and Gloor, 1973 ; Hill, 1976). This was found true for a lactose granulation prepared in a fluid bed dryer using gelatin as a binder, as well as a lactose granulation using starch paste and produced on conventional granulating equipment .

### **Effect on Granule Flow Rate .**

Davies and Gloor (1972) reported that increasing the formula weight of binder was found to decrease flow rate for the four binders tested ; gelatin, acacia, PVP, and hydroxypropyl cellulose. They concluded that the decreased flow rate was a result of the increase in average granule size that occurred as a formula weight of binder was increased. Marks and

Sciarra (1968); Gold, Duvall, Palermo, and Seater (1968); as well as Harwood and Pilpel (1968) also found that the flow rate was inversely proportional to average granule size.

#### **Effect on Percent Fine of Granule .**

Granule flowability and tablet uniformity were significantly effected by amount of fine particles. The optimum amount of percent fine lead to a maximum flow rate (Marshall, 1985). From comparative data of Agrawal and Prakasan (1988) showed that granules prepared from PVP as compared with starch and acacia have the minimum percent fine, low compressibility and the best flow rate.

### **Effect of Binders on Tablet Properties**

#### **Effect on Tablet Strength and Friability .**

Generally, increasing the amount of binder used results in an increase in tablet strength and a decrease in tablet friability. With the uses of sodium alginate, acacia and gelatin as binders in lactose tablets, Sakr et al.(1972) reported that the hardness of tablet increased and the friability decreased as the binder concentration was increased. Jarosz and Parrott (1983) showed that tablet tensile strength increased with an increase in granule strength.

Nelson, Arndt and Busse (1957) found that the sugar-like binders, e.g. sucrose, dextrose and raffinose, showed maxima in hardness versus concentration curve, while increasing the concentration of gum-like binder, e.g. gelatin, acacia, and tragacanth, in the formulation resulted in an increase in tablet hardness but at a lesser extent.

Chalmers and Elworthy (1976) reported that the increases in binder concentration and volume of binder solution of PVP, the increase in breaking load of oxytetracycline tablets. Tensile strength of oxytetracycline tablets was also found to increase with the gelatin content (Esezobo and Pipel, 1976).

The result obtained by Hill (1976) showed that the granulation compressibility (hardness-pressure profile) of lactose tablets improved with starch paste dilution at a given starch concentration.

### **Effect on Tablet Disintegration .**

It has long been recognized that binder possessed an influence on tablet disintegration . Sakr and Elsabbagh (1973) found that disintegration time increased with an increase in percentage of acacia in nicotinic acid tablets while sodium alginate did not significantly affect the disintegration time. Disintegration times of oxytetracycline tablets, wet granulated with PVP, were found to increase with the increases in the concentration and volume of binder solution (Chalmers and Elworthy ,1976). Similar results were also obtained in oxytetracycline tablets granulated with gelatin (Chalmers and Elworthy, 1976) .

Davies and Gloor (1972) studied the effects of various binders and their concentrations on disintegration time of lactose tablets . Similar results were obtained in that all types of binders used in the study, i.e., PVP, gelatin, acacia and hydroxypropyl cellulose, caused an increase in disintegration time as their concentrations in the tablets increased .

### **Effect on Tablet Dissolution .**

Chalmers and Elworthy (1976) reported that tablet formulation containing PVP as the binder exhibited a decreased dissolution rate as concentration of PVP in the binder solution increased. However , for the same amount of PVP , the volume of granulating solution had little effect on the dissolution characteristics . Esezobo, Zubair, and Pipel (1989) indicated that T 50% of paracetamol tablets was increased as percent amount of binder , such as PVP , Tapioca increased .

The dissolution rates of erythrosine from lactose-based tablets granulated with starch mucilage and those nicotinic acid tablets formulated with sodium alginate were found to decrease with the increases in their binder concentration (Shubair and Dingwall,1976 ; Sakr and Elsabbagh,1973). Jacob and Plein (1968) also found that the increase in binder concentration resulted in a decrease in the dissolution rate of phenobarbital tablets using acacia , gelatin , ethyl cellulose and hydroxyethyl cellulose as binders . The increase in gelatin content in oxytetracycline tablet also delayed their dissolution (Esezobo and Pipel, 1976 ) .

### Purpose of the Study

The purpose of the study is to evaluate binding property of Ispaghula husk, seed husk of *Plantago ovata*, as the new binding agent in wet granulation process comparing with binders from natural origin; corn starch, pregelatinized starch, gelatin and synthetic binders; hydroxypropyl cellulose, polyvinylpyrrolidone which are commonly used in manufacture.

In this study, binding property of Ispaghula husk was evaluated with granules and tablets physical characteristics such as granule size distribution, density, flowability, granule friability, tablet strength, weight variation, porosity, disintegration and dissolution prepared by each binder.

Paracetamol and nicotinamide were selected as model drugs due to the former has slightly water solubility and poor compressibility, the latter is water soluble.

In addition, binder index ( $\emptyset_b$  index) which is a parameter integrating four important tablet characteristics including tensile strength, porosity, median dissolution time and percent friability is presented. So a higher " $\emptyset_b$  index" can infer better physical properties of tablets.