Chapter I

General Background

1. Introduction

Tablet disintegration is a necessary first step to achieve rapid release of the active drugs. To accomplish this, a substance is added to the tablet granulation that will react when brought into contact with fluids causing the tablet to break apart such substances are termed disintegrants.

Disintegrants comprise a group of materials which on contact with aqueous environments, swell, hydrate, change in volume or position or react chemically to produce disruptive changes within tablets. This group of substances include various forms of starches, celluloses, certain algins, vegetable gums, clays in finely divided solids, ion-exchange resins and acid-base combinations (1). Later, a number of chemically modified derivatives of starches and celluloses including the synthetic polymers like cross-linked polyvinylpyrrolidone (2,3,4,5) have been introduced. Though various disintegrant materials are available to be selected, the search continues for other types of materials such as non fibrous attapulgite (6), xylan (7), Key-Jo Clay (8) and soy polysaccharide (9,10).

This study is also an attempt to investigate the new substance which may be used as tablet disintegrant. The material to be tested in this investigation is the fruitpulp of *Scaphium macropodum* Beumée which is the native plant found in the eastern area of the country. It was found that when soaking a fruit in water it could swell and absorb water many times of its weight without exhibiting mucous or gel formation. As the swelling of disintegrant is considerably important and it is the most widely accepted general mechanism of tablet disintegration (11). It is, therefore, of interest to assess the disintegration properties of the fruitpulp of *Scaphium macropodum* Beumée for its potential use as a disintegrating agent.

2. Objectives of the Study

The aims of this investigation are concerned with

a) the evaluation of disintegration properties of the fruitpulp of *Scaphium macropodum* Beumée in water soluble and water insoluble directly compressible tablet systems,

b) the comparative studies of disintegration properties of the fruitpulp of *Scaphium macropodum* Beumée with a selected number of commercial disintegrants,

c) the examinations of the physical properties of the fruitpulp of *Scaphium macropodum* Beumée in relation to disintegrating efficiency e.g., particle size distribution, bulk swelling, water uptake etc.,

d) the examination of the release rate of an active drug from the tablet system which employed the fruitpulp of *Scaphium macropodum* Beumée as a disintegrating agent.

3. *Scaphium macropodum* Beumee

Scaphium macropodum Beumée or *Sterculia lychnophora* Hance (Family Sterculiaceae) is found in Indo - China, Thailand, the Malay Peninsula, Sumatra, and Borneo.

The characteristic features of *Scaphium macropodum* Beumée can be described (12,13) as follows :

A big tree about 20-40 metres tall with reddish-brown hairs on the angular branches. The bark is rich rust-brown with gray lichen patch which turns flaking in oblong pieces. The inner bark is reddish-brown fibrous with prominent mosquito-net-like markings. Twigs possess prominent leaf scars. Leaves are about five inches long, simple, entire, ovate accuminate and glabrous on both surfaces. Leaf bases are shallowly heart-shaped (immature trees). Leaf stalks are slender about 3.7-15 centrimetres long. Infloescence appears as panicle covering with red hairs. The fruits are about an inch long, ovoid, and without a pedicle, the cicatrix left by the dark-brown, deeply-wrinkled fruit being very conspicuous and curiously oblique, with a kind of spur. The thin, dry epidermis being removed, reveals a dry black mesocarp, within which is the central seed, consisting of

the two shrunken cotyledons. The seeds are ellipsoid about 25x15 millimetres and glabrous.

The general uses of *Scaphium macropodum* Beumée as a drug can be found (13,14) as below :

The part used is the mucilaginous substance obtained from soaking the fruit in water. The medicinal use described from many sources gave practically identical applications. It is used to bring out the eruption of smallpox, to cure all fevers, phthisis, haemorrhage from the nose, stomach, bowels or bladder , to counteract poison, sunstroke, opthalmia, toothache, intestinal worms, haemorrhoids, dry cough, fever in the marrow, all sorts of ulcer, and it is difficult to enumerate all of its medicinal virtues.

The fruit is considered to be an economical emollient, an infusion is employed very satisfactorily to treat light bronchitis, the gum residue may be a constituent of poultices. A French pharmacist made "mictasol" from this and found it efficacious for certain maladies of the gentio-urinary system. In Cambodia, the mucilaginous infusion of the fruits is refreshing and somewhat laxative, the bark is utilized in recipes which are antidysenteric, hemostatic in metrorhagia, and diuretic. The jelly is sweetened and eaten, but its principal used is for domestic cooling, demulcent, and laxative remedies. The original chemical analysis showed approximately 59% bassorin.

4. Literature Review

A. General

Most tablets and capsules are ordinarily desired to be disintegrated after contacting with the gastric juice in the stomach. To achieve this goal, a disintegrating agent generally needs to be incorporated in the formulation. Ideally it should cause the tablet to disrupt not only into the granules from which it was compressed,but also into the powder particles from which the granulation was prepared (1). It is commonly used in tablet formulation to promote its dispersion in dissolution fluid (15).

There are two methods used for incorporating disintegrating agents in tablets. These methods are called external addition and internal addition. The most common method is the external addition method in which the disintegrant is added to the granulation with mixing just prior to compression. In the internal addition method, the disintegrant is mixed with other powders befor wetting the powder mixture with the granulation solution. Thus, the disintegrant is incoporated within the granules when this method is used, part of the disintegrant is added internally and part by external addition. This provides immediate disruption of the tablet into the previously compressed granules while the disintegrating agent within the granules produces further erosion of the granules to the original powder particles. Use of the two-step method usually

produces better and more complete disintegration than the usual method (1,16).

In regard to the suitability of a new product, the requirements placed on a tablet disintegrant should be clearly defined as poor-solubility, poor gel formation, good hydration capacity, good moulding and flow properties and no formation complex with drugs and other excipients (17). The disintegrants commonly used in tablet formulations are summarized in Table 1 (11,18,19,20).

B. Mechanism of Action of Disintegrants

The disintegration process can be devided into three phases; wetting of the tablet, penetration of fluid into the tablet and development of disintegration force (7).

Although many theories have been proposed to elucidate mechanisms of action of various tablet disintegrants, non has yet explained disintegrant activity for all of the effective disintegrants. It now seems obvious that no single mechanism of disintegrant action is applicable to all disintegrants. In some instances, a a combination of mechanism may be operative. Those mechanisms can be referenced by the physical and chemical properties of different disintegrants. The current thinking of mechanisms of action for disintegration agents are presented as follows (11,15,18,21,22,23):

Table 1 Commonly Used Modern Disintegrants

Category	Chemical Name	Tradname	Supplier
Starches	Corn starch	*	*
	Sodium starch glycolate	Explotab	Edward Mendell Co.Carmel,New York
		Primojel	Generichem Corp.,Little Falls,New Jersey
	Pregelatinized Starch	Starch 1500	Colorcon,Inc., West Point,Pennsylvania
Cellulose	Microcrystalline cellulose	Avicel	FMC Corp.,Philadelphia
	Carboxymethylcellulose(CMC)	*	*
	Croscarmellose	Ac-Di-Sol	FMC Corp.,Philadelphia
		CLD	Buckeye Cellulose Corp.,Memphis,TN.
	Sodium CMC(low substituted)	Nymcel	FMC Corp.,Philadelphia
	Calcium CMC	ECG	Laporte,Inc.,Hackensack, New Jersey
	Hydroxypropyl cellulose low substituted	L-HPC	Shin Etsu Chemical, Japan
Pyrrolidones	Crosspovidone	Polyplasdone XL	GAF Corp.,New York
		Kollidon CE5050	BASF Corp.,Parsippany,New Jersey
Alginate	Alginic acid,sodium alginate	Satialgine	Edward Mendell Co.,Carmel,New York
Clays	Magnesium aluminum silicate	Veegum	R.T.Vanderbilt Co.,Norwalk,Connecticut
Polysaccharides	Soy polysaccharide	Emcosoy	Edward Mendell Co.,Carmel, New York
Ion-exchange	Cation-exchange resin (Potassium polymethacrylate)	Amberite IRP-88	Lenning Chemical, London

* This material is available from several sources under a variety of trade names.

1. water uptake
2. swelling
3. deformation
4. particle repulsion theory
5. disintegration force
6. heat of wetting
7. porosity and capillary action

Water Uptake

Water uptake has been implicated as an important mechanism of action for tablet disintegrants. The process called wicking was the ability of particle to draw up water into the porous network of a tablet being essential for effective disintegration. The rate of water uptake is of critical importance for a number of tablet disintegrants(11).

It has been stated that substances that absorb about 20 % water and are insoluble in water are good disintegrants e.g., alginic acid, calcium alginate, methylcellulose, and various starches. Those that absorb about 40% water and are soluble in water increase disintegration time, e.g., a carboxyvinyl polymer, sodium carboxymethylcellulose, sodium alginate, while those that absorb water poorly reportedly are poor disintegrants, e.g., ethyl cellulose (21).

Ganderton and Fraser (24) showed for lactose tablets that the addition of starch, can give a marked

increase in water penetration, as was shown for lactose tablets.

The excipients used in the formulation some aid penetration others impede the process. Wan and Heng (25) found that polysorbate 80 and sodium lauryl sulfate enhanced water uptake due to improve the wettability of the tablet interior facilitating liquid access in tablets containing microcrystalline cellulose.

Kornblum and Stoopak (4) observed that cross-linked polyvinylpyrrolidone swells very little, although it takes water up into its network quite rapidly. They concluded that the mechanism of action for disintegrant is wicking.

Rudnic, Kanig and Rhodes (26) observed that as molecular structure of sodium starch glycolate was altered to improve water uptake, disintegrant efficiency also improved. It was found that proper combination of carboxymethylation and degree of crosslinking of potato starch enabled the production of sodium starch glycolates with optimal disintegration properties, and also enhanced disintegrating effciency by purification (27).

Gissinger and A.Stamm (28) evaluated cross-linked carboxymethylcellulose in comparision with other disintegrants used in direct compression and compression after wet granulation. The results showed superior

properties of cross-linked carboxymethylcellulose comparing with a low substituted carboxymethylcellulose, the former swells much more and faster. It has high water-uptake and so showed an excellent property of rapid disintegration of tablets.

Wan and Choong (29) studied water penetration behaviours reflected disintegration and dissolution behaviour of phenacetin tablets formulated with starch, PVP and magnesium stearate. The absorption of water by starch was primary mechanism involved in the penetration of water into tablets. Even if the pores in the tablets aid water penetration it was of secondary importance. Increasing PVP concentration resulted in a stronger binding of granules in the tablets, consequently this prevented further swelling of the starch which in turn prevented further uptake water by starch.

An extremely strong effect on volumetric water uptake and penetrate can be seen when disintegration is presented in the tablet formulation (19,30,31). Gissinger and Stamm (19) showed that disintegrant powders such as sodium starch glycolate and hydroxypropylcellulose could take up water more than ten times of their own weights. They also showed that the rate of water uptake made from tablet containing dicalcium phosphate dihydrate and different disintegrants depended on the types of the disintegrants.

It was found that compressional force has strongly affected on the penetration rate. The compressional force increases with an decrease in penetration rate (32,33). This effect was mainly due to decrease porosity when increasing compressional force.

Swelling

Swelling is the most widely accepted general mechanism of action for tablet disintegrants. Primarily, this is because almost all disintegrants swell to some extent and swelling has been reported quite universally in the literature (11).

Starch swelling was claimed to be dependent upon the rate of the amylose and amylopectin content, and their molecular structure, the amylopection expands and amylose gives osmotic pressure. Defatted corn starch swelled more freely and caused it to swell 44% (21,22,30,34). Tablets made with low pressure have high porosity and, hence, too much space. When starch swells, no pressure is exerted so disintegration is slow. Medium pressure allows just enough space so that when the starch swells, it exerts pressure on the granules to cause disintegration. High pressure, producing low porosity, decrease the ability of fluid to enter, so disintegration is again slow. This would seem to indicate there is an optimum compression force for tablet disintegration (21).

List and Muazzam (35,37) concluded from their studies of several disintegrants that swelling pressure within the tablet is a primary factor responsible for disintegration. Swelling pressure (36), however, cannot be determined by volume dilation. They concluded that good disintegrants are excipients that have high swelling pressure but a limited degree of gel formation in the presence of water, because the barrier that forms prevents water from penetrating into the tablets, which in turn prevents further swelling. In all cases, they found that cross-linked natural or synthetic products with limited swelling and gel formation such as Ac-Di-Sol$^{(R)}$ and Polyplasdone XL$^{(R)}$ were superior to the different natural starches, Nymcel$^{(R)}$ type, and microcrystalline cellulose.

The bigger particles of disintegrants gave higher values of swelling force with that shorter disintegration time than the smaller particles of the same constitution (37). The reason is the bigger particles can fill the empty space better as with the tightness of the comprimates, therefore have a greater swelling pressure.

It is interesting to note that the swelling of some disintegrant particles is dependent upon pH (22,38,39). Shangraw and co-workers (22) reported that with macroscopic method by observing the sedimentation volumes of anionic cross-linked starches such as Explotab$^{(R)}$ and Primojel$^{(R)}$

and celluloses such as Ac-Di-Sol(R) (croscarmellose type A) and CLD-2(R) (croscarmellose type B) are significantly altered in acidic media while Polyplasdone XL(R) and Starch 1500(R) remained unchanged. A microscopic study was also carried out qualitatively and the results were in the same rank order as that observed macroscopically.

Mitrevej and Hollenbeck (40) using photomicrographic technique studied hydration of disintegrants by prolonged exposing at high humidities. They concluded that the super disintegrants functioned effectively because of their remarkable ability to absorb water and to swell.

Bolhuis and coworkers (41) found that the action mechanism of modern disintegrants, with particular regard to the influence of lubricants on the disintegration process of a formulation based on dicalcium phosphate dihydrate and containing different disintegrants. They concluded that the swelling capacity of disintegrating agents plays a dominant role in the process of disintegration when a hydrophobic lubricant is incorporated in the tablet whereas the swelling capacity of the disintegrating agent is of minor importance when no hydrophobic vehicle is present.

The results of the investigation indicate that the swelling is the governing factor regarding the kinetics of the disintegration process because it is linked both to water penetration and force development (42). The role of

the swelling materials is to make pore walls hydrophilic, providing enough swelling force to produce interparticle bond disruption.

Deformation

Plastic deformation of starch grains under high pressure has been reported by a number of investigations (19,30,43). Hess (43) with using scanning electron micrographs reported that disintegrant particles deform during the compression. The deformed particles were shown to relase to their original shapes when exposed to moisture.

Potato starch was found to plastically deform under pressure, but the individual grain could still be recognized. Corn and waxy maise starches also plastically deformed when compressed and degree of deformation increased with increasing pressure (21,44). It was asserted that the 5-10% melting that occured at grain contact points was also directly proportional to pressure. The contact point dissolved in water causing tablet break-up. It was stated that compression force decreased grain stability, resulting in energy rich grains being formed, so that no more energy was required for swelling to occur (21). The deformed starch grains are "energy rich" and this energy may be released when the grains are exposed to water thus breaking the tablet apart (21).

Vadas, Down and Miller (45) discovered that tablets containing sodium carboxymethylcellulose derivatives tended to increase disintegration efficiency with increasing compressional force at all pH values. This may be strongly indicated that the importance of deformation due to compression as the mechanism of action of sodium carboxymethyl cellulose derivatives.

Particle Repulsion Theory

Another theory of tablet disintegration attempts to explain the swelling of tablets made with "nonswellable starch". Guyot-Hermann and Ringard (38) proposed a particle/particle repulsion theory based upon the observation that particles that do not seem to swell may still disintegrate tablets. They explained that the destruction of the cohesion forces between the constitutive elements of the tablet under the action of water may be described as follows : a) the creation of a repulsive force when the elements of the tablet enter into contact with water, b) a simple annihilation of the hydrogen bonds or of the capillary cohesion forces.

Fox et al. (46) found that disintegration of microcrystalline cellulose tablets was due to entrance of water into the tablet matrix by means of capillaries and subsequent breaking of hydrogen bonds between adjacent bundles of microcrystalline cellulose.

Reier and Shangraw (47) postulated that microcrystalline cellulose tablets were a special form of cellulose fiber in which the individual crystallities were held together largely by hydrogen bonding. Tablet disintegration is merely the breaking of the intercrystallite bonds by the disintegrating medium.

Disintegration Force

The development of a disintegration force inside the tablet, capable of weakening and breaking interparticle bonds, due to the liquid/solid contact depends on a proper wetting of the material and occur according to saturation kinetics (48,49).

It is necessary that the liquid penetration into the tablet activates the development of a force capable of separating the particles (48).

Colombo et al. (48,49) divided the mechanisms by which the disintegrating force develops depend on the group of the following manner:

a) the pressure exerted by the air entrapped in pore structures due to a hydrodynamic process or the heat of wetting

b) the swelling of the disintegrating agent

c) the repulsion among particles caused by the contact between solid and liquid.

Caramella et al. (50) observed that, in tablets made of water insoluble and/or hydrophobic materials, a correlation existed between disintegration time and disintegrating force development kinetics indicated that the prevailing role in the disintegration process was played by active mechanisms. Therefore, the highly hydrophilic and strongly swelling disintegrants were to be preferred for capable of developing its maximum swelling force, besides drawing water inside the compact. On the other hand, the lack of such a correlation in tablets made of hydrophilic, water-soluble materials indicated that passive mechanisms (such as dissolution or hydrogen bond annihilation) were also involved in the disintegration process and may prevail over active mechanisms. Therefore, the disintegrant, when needed, assisted in the drawing of water inside the compact, but was not always able to develop its maximum swelling force. This suggested that limited swelling disintegrants should work as well as, and even better than, strongly swelling materials.

Heat of Wetting

The heat generated by the wetting of the ingredients that occurs when the tablet is immersed in a fluid has been suggested as a method of tablet disintegration. The heat presumably caused the air in the tablet to expand pushing the tablet apart (21). Matsumaru (51,52) calculated the heat of immersion of water using the BET method and stated

that it was an important factor in tablet disintegrant because the decrease in this heat due to compression agreed with the fact that disintegration times increased i.e. aluminium silicate tablet. It was also (11) observed that starch granules exhibited slight exothermic properties when wetted and purposted that this was the cause of localized stress resulting from capillary air expansion. However this explanation is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents. List and Muazzam (53) found that exothermic reactions upon wetting were not universal for all disintegrants and that when significant heat of wetting is generated, there is not always a corresponding decrease in disintegration time.

Porosity and Capillary Action

The effect of porosity is difficult to interpret because of the effect of pressure, materials, method of measurement and types of pores(21). Porosity generally decreases with the increase in compression pressure (54,55), and the penetration of fluid into the tablets may be related to the mean pore diameter or porosity (54,56).

Water can penetrate or wick into the tablet either as a result of capillary or by sorption. Curlin (57). suggested that the disintegrating action of starch in tablets was due to capillary action rather than swelling

because the spherical shape of the starch increase the porosity of the tablet. Owing to its low compressibility starch enhances pore formation and thus facilities wicking (24).

Pernetration of fluid into tablets is affected by the interfacial tension of liquid-solid boundary, contact angle, pore-size distribution, geometry of the pore surface, viscosity of the liquid, and electrostatic charges. Surfactants may selectively increase liquid penetration into tablets but their effect may be delayed because of a slow rate of solution (21).

C. Method for Studying Disintegration Properties .

The number of tablet disintegrants available is continually on the increase, therefore the suitable methods of testing a new product evaluation should be required.

Over the past years, a variety of investigators have introduced a number of test methods. Some methods possess as follows :

1. Moisture Sorption

Sorption of a disintegrant can be studied by two independent methods 1) sorption from aqueous phase and 2) sorption from the vapour phase. The former method is usually employed to evaluate the disintegration property of disintegrants while the latter can give more information on the behavior of disintegrants in the environment encountered in every day life in addition to the surface area and monolayer capacity of the disintegrants.

The method can be examined in the form of powders and in compressed tablets under constant relative humidity and constant temperature conditions in desiccators containing water or saturated salt solutions in their reserviors. Tablets or powder were sampled periodically as a function of time and the amount of water absorbed was calculated from the weight difference (58,59,60,61,).

The rate and amount of moisture sorption change upon various properties of disintegrants. Khan and Rhodes (60) observed the water sorption by four disintegrants as a function of time in powder and when incorporated in calcium phosphate dihydrate tablets. They also demonstrated that the disintegrants with the highest water sorption were generally the most effective in most tablet systems.

Kornblum and Stoopak (4) comparing between cross - linked PVP, alginic acid and starch. They postulated that crosslinked PVP showed significantly greater moisture sorption than either of the others which appeared responsible for its tablet disintegration property.

2. Hydration Capacity

Hydration capacity is the capable of water actually wetting the material which reveals about the same liquid-solid interactions or swelling power. This parameter can be employed as a guideline for the selection of new materials as potential tablet disintegrants (4). Kornblum and Stoopak (4) described a method of determining the hydration capacity of cross-linked polyvinylpyrrolidone in comparison with starch and alginic acid with this method the amount of water taken on by one gram of disintegrant after shaking, centrifuging and decanting is determined. The advantage of this method is that it can be carried out quickly and easily whilst being very reproducible.

3. Swelling of Particles

3.1 Microscopic Method

3.1.1 By Modrzejewski and Wochna (62)

A grain of the examined substance was placed on a microscopic slide, covered with a cover-glass and a small drop of water was cautiously added by means of a pipette which caused the swelling of the grain. The surface of the swollen grains contour was photomicrographically determined on the screen of the microscope the increase in volume being calculated from it. The volume of the sphere was calculated as below :

$$V = (4/3)\pi r^3$$

The radius of the sphere was calculated from the surface of the cross-section measured from the following equation :

$$r = \sqrt{s/4\pi}$$

3.1.2 By Beukelaer, Ooteghem and Ludwig(63)

The diameters of the "dry" particles and the swollen particles were measured on a suspension in paraffin oil and simulated gastric fluid, respectively. Microphotographs of the suspensions are brought on the digitizer pad of a Kontron MOP-AMO 2 apparatus, the diameter of particles were calculated.

3.1.3 By Mitrevej and Hollenbeck (40)

A dry sample was sealed in the stage chamber on the microscope and after maintaining the sample for 24 hr at 0% RH, a photograph was taken. The sample was then exposed to 100% RH for 24 hr and a photograph was taken again. The swelling ratio was calculated by particle dimension at 100% RH versus dry particle dimension at 0% RH.

3.1.4 By Caramella et al. (64)

Samples of monodispersed materials were prepared in various solvents and photomicrographs of a suitable number of microscopic fields, depending on the magnification employed, were taken. The projected dimensions of the particles were averaged on a suitable number of idividual measurements. The volume increase of particles changing from an inert to a swelling medium was expressed as the ratio between the mean particle volume swelling medium and the mean particle volume diameter in the inert medium (swelling index).

3.1.5 By Wan and Prasad (65)

A representative sample of the powder was obtained by intermittent sampling of a following stream of powder. The sample so obtained was subdivided into portions suitable for microscopic observation. The powder was spread uniformally in a thin layer on a microscope slide and cover slip was placed on it. Special

care was taken to ensure that particle agglomerate formation was avoided. Hydration of the powder was under taken by introducing water in sufficient quantity below the cover slip using a microsyringe. Timing was carried out from the moment water was introduced. The swelling phenomena was observed on the video monitor and recorded. The field of vision was not changed once swelling of particles was initiated. An arrangement of light bulbs around the microscope ensured that the temperature of the immediate surrounding air was maintained at 37 $\pm$ 1^{o}C.

3.2 **Coulter Counter Method** (64)

The coulter counter method is proved to be applicable to many kinds of materials and media, although with some limitations, especially for materials containing highly hydrophilic ionizable moieties. The method is rapid, satisfactorily accurate and reproducible and seems to be useful especially for materials which swell to a limited extent, which can be hardly evaluated by optical microscopy.

An accurately weighed quantity of powder (2.00 to 10.00 mg) was dispersed in a 200-400 ml electrolyte volume. The number of particle size distribution of all the particles contained in an appropriate volume of the sample (2 to 100 ml) was determined. The volume of the sample analyzed was metered by the manometric method or by weighing the amount of sample passed through the orifice. Total particulate volume (V_{tot}) was calculated with the formula :

$$V_{tot} = (\pi/6).K.\sum_{i=1}^{i=16} \Delta n_i \bar{V}_i (S/s)$$

Where K is the volume calibration constant determined for each electrolyte and aperture using standard materials; Δn_i is the total particles count in channel i corrected for background, $\bar{V}_i$ is the mean volume (arbitrary) of channel i, s is the volume of the sample analyzed, S is the total electrolyte volume.

The percent volume increase of material in swelling media was calculated as follows :

$$\% \text{ volume increase} = \left(\frac{V_{tot}}{V_{true}} - 1\right) \times 100$$

Where V_{true} was calculated from the true density of the sample.

3.3 Macroscopic Method (22)

Two-percent aqueous dispersions of samples were prepared in water and dilute hydrochloric acid (1:100) in 100-ml graduated cylinders with stoppers, were shaken periodically, and were allowed to stand overnight. The sediments were read and compared.

3.4 Centrifugal Method (62)

This method is based on the measurement of changes in the volume of the material examined. The measurement was performed in 10-ml centrifuge tubes graduated to 0.1 ml. The first sample of the examined material was thoroughly mixed with water, while the second

one with rapeseed oil. Both the samples were next subjected to centrifugation for twenty minutes at 2,000 r.p.m.. The sample mixed with water swelled during this period and occupied a larger volume than the other one suspended in oil. From the difference in the resulting volumes, the percentage value of the swelling power could be calculated. This method may be employed for testing the swelling power of all the disintegrating agents insoluble in water.

3.5 Measurement of Bulk Swelling of Tablet Disintegrants by Rudnic et al. (66)

A sample of 500 mg of each disintegrant was packed in the graduated glass which was placed upon the moist glass filter plate, and the swelling volume of the powder due to the intake of water was observed at predetermined time intervals. Distilled water was used as a test media. The apparatus was shown in Figure 1. The bulk swelling of tablet disintegrant, V_b, was estimated as a percent of orignal volume using as follows :

$$V_b = ((h_t - h_o)/ho) \ 100$$

where h_o is the original height of powder bed and h_t is the height of powder bed at time t.

3.6 Measurement of Swelling of Tablet of Pure Disintegrants by Gissinger and Stamm (19)

Gissinger and Stamm evaluated the swelling of tablets of pure disintegrants prepared by direct compression. The linear inductive transducer was in contact

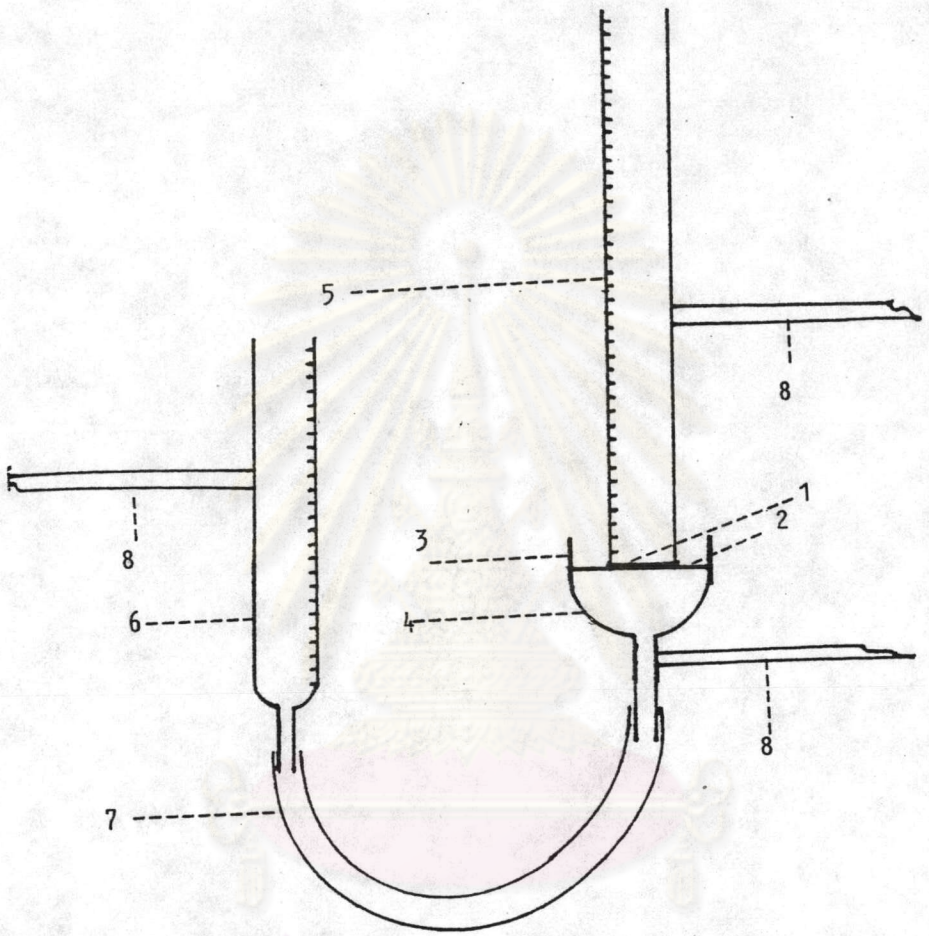

Figure 1 Diagramatic Representation of Apparatus for Measurement of Swelling Rate (Reference 66)

1	Sample	2	Filter Paper
3	Glass Filter Plate	4	Funnel
5	Graduated Cylinder	6	Graduated Pipette
7	Rubber Tubing	8	Clamps

with the tablets and connected with a recorder which was recorded in a function of time. The swelling measured is given in percent change in thickness in comparison with the initial thickness of the tablet.

3.7 Measurement of Tablet Swelling Force by Gould and Tan (67)

A tablet was loaded into the perspex die and the punch inserted; both punch and tablet exactly fitting the die. This was placed on a sintered polypropylene disc of 17 mm diameter, and then loaded on the gauze disc located centrally on a perspex annular ring contained in a perspex beaker on the lower platen of a calibrated tensile strength apparatus. The lower platen of the apparatus was then raised to a force of 0.023 kg to ensure contact between the top of the punch and the upper platen. Water was then introduced quickly and uniformly into the beaker and the resultant swelling force phenomenon followed using a chart recorder.

4. Water Uptake

The penetration rate of a liquid into a porous structure depends on the balance between capillary and opposing viscous forces, there is a linear relationship between the square of volumetric uptake (V) and the time (t) as given by Washburn's equation as below (31,68,69):

$$V^2 = \frac{2\ m\gamma\cos\theta}{k_o \cdot \eta} \cdot t$$

where m is the hydraulic pore radius, γ is the surface tension of the penetrating liquid, θ is the contact angle between liquid and solid within the pores, η is the liquid viscosity, and k_o is the constant depending on pore shape.

This equation indicated that water penetration in pharmaceutical tablets is determined by controlling factors like porosity, pore size and contact angle of liquid with the pore wall. However, this equation cannot be applied when the tablet structure changes during the penetration process.

5. Disingration Time

Disintegration time is one of the important physical parameters to evaluate the disintegration of compressed tablets. Besides it depending on a number of many factors such as fillers, active ingredients, lubricants, binders, manufacturing procedures, equipments and compression pressure, disintegration time also can be used and combined with other parameters for comparing disintegrant efficacy.

6. Dissolution of Tablets

Dissolution is the most commonly used to assess the equivalence of dosage forms. Because only disintegration test was never meant to serve as an indicator of the degree that the drug content might be absorbed by the body or even as an index to extent it was presented to the body in a form "available" for absorption (15).

It was the fact that disintegration could not distinguish between rapid and slow dissolving granules. Tablets that disintegrated in fine particles had faster dissolution rates than those that disintegrated into large clumps. The formation of fine particles was not depended on disintegration time, so it was suggested that particle size should be determined after disintegration to ensure product effectiveness (15).

Dissolution rate is also used properly as a control device to ensure process and batch-to-bach consistency for a particular formulation of a particular manufacturer and as a screening tool in formulation development (70).