CHAPTER I

INTRODUCTION

A number of nutritionally rich health foods such as yeast tablet, algal tablet, royal jelly tablet are available commercially. But tabletting properties of these nutritionally rich ingredients are rarely available in literature. Yeast extract in tablet form has not been found in literature. Only vacuum granular yeast extract was produced and claimed to be less hygroscopic than spray dried yeast extract ("Granulates Yeast Extracts," 1964).

Yeast extract powder from brewer's yeast has been developed locally (Chernchit, 1985). The material was a rich source of B-vitamins, amino acids, and trace elelments. Tabletting the yeast extract powder was attemped to diversify yeast extract product form and enhance application of yeast extract as a health food.

1.1 Yeast Extract

Yeast extract consists of the content of yeast cells that have their cell walls and other solid removed by filtration. Yeast extract powder is prepared under optimum conditions, clarified, and dried to a reddish yellow to brown powder, having a characteristics but not putrescent odor. Dissolving in water, it formed a yellow to brown solution and has a slightly acid reaction (United States Pharmacopeial Convention, 1990). Yeast extract powder produced by spray drying

process or vacuum drying process has hygroscopic property (Peppler, 1970, 1982).

Yeast extract can be produced by autolysis or hydrolysis or plasmolysis. Due to the difference in process condition of the yeast extract production, the product composition is markly varied. Besides, type and strain of yeast and the composition of yeast growth nutrient are also important factors that can cause the difference in yeast extract composition (Ferrer, 1954; Peppler, 1982; Pyke, 1958). Usually, yeast extract are widely used as condiments in the preparation of food. They are frequently used as nutritional additives in health-food formulations, baby foods, feed supplements, and enrichment of food and production media for microorganisms and other biological culture systems. Yeast extract is known to be a good source of B-vitamin (Ferrer, 1954; Peppler, 1982; Pyke, 1958) and it is a potential source of protein (Chernchit, 1985) and trace minerals (Peppler, 1982). Moreover, it consists of all essential amino acids (Ferrer, 1954).

There are a number of investigations about the positive effect of yeast extract in human when it is consumed for medicament. For example, it was found that autolyzed yeast extract showed no sign of poisoning when it was given to human patients. It affected acute peripheral symptoms of neuritis and given full relief in mild acute cases in a week treatment. Additionally, Infantile-beriberi symptoms were relieved rapidly (Saleeby, 1919).

Thompson and Ungley (1951) studied in pregnant women and the puerperium which were megaloblastic anemia patients. After they were given yeast extract, the reticulocyte and erythrocyte were found increasing.

Due to the nutritional component of yeast extract and its benefit for human body, production of the yeast extract can be developed for health food. Comparing with the food yeast which is producing and selling in markets in the form of powder and tablet, yeast extract component is similar to the food yeast (Ellison, 1973). In the case of food yeast, viable yeast may absorb vitamins as it passes through the gastrointestinal tract (Kingsley and Parson, 1947; Menegazzi and Ingledew, 1980). Besides, Tannenbaum et al. showed that digestibility of microbial protein is greater for cell contents than for whole cells. This may be due to microbial cell walls are not frequently digested by animals or humans gastric enzymes (Snyder, 1970). Therefore, human body would receive more useful components from the yeast extract than from the food yeast.

It is commonly notable that many yeast tablets have to be taken per day, as it is shown on the Brewer's yeast tablet label (produced by Greater Pharma Ltd.,Part.) and mentioned by Peppler (1970) that the usual dosage prescription for adult is 4 tablets, 3 times daily. So the concentrated yeast extract tablet would be a new product that will reduce the amount of tablet for daily consumption.

1.2 Manufacture of Tablet

In general, purposes of tablet making are for accuracy of dosage, easy transportation, minimized storage area and cost of transportation, convenient administration, and reduction of powder mixture segregation. Furthermore, for particular food product, another probable purpose is to maintain stability of chemical and physiological activity of ingredients.

1.2.1 Essential Properties of Compressible Material

Powder intended for tablet compression must possess three essential properties (Armstrong, 1988; Little and Mitchell, 1963) :

1.2.1.1 Ability to Flow Freely

This property is important for material transportation through feed shoes or hoppers into dies of a tabletting machine. Free flowing causes adequate filling of the dies and uniform particle packing to produce a consistent weight of tablet. If the powder formulation flows satisfactorily, equal die filling will produce tablet that unvary in weight, thickness, and hardness. Probability of tablet capping or laminating defects due to the air entrapping is also decreased since the uniformity of flow corresponds to the compression speed of the tabletting machine.

1.2.1.2 Ability to Form a Stable Compact Mass

Material needs the ability to form a stable compact mass wher pressure is applied or it can be said that the material

needs to have its binding property. Having this property, the compressed tablet do not break into pieces during packing, transporting, and before eating.

1.2.1.3 Lubricating Property

This property will minimize the abrasive deterioration, due to tablet enlargement during ejection, on punches and dies.

1.2.2 Physical Properties of Compressible Material

Physical properties of compressible material are nescessary informations for formulation development. Relationship between each physical property of material before compression and physical properties of compressed tablet were previously found as follows.

1.2.2.1 Surface Shape and Texture

For a given particle size, the more it is spherical, the better flow occurs. This is due to spherical shape particle has minimum interparticle contact (Ibralhim, Henry, and William, 1972). Whereas the irregular shape particle has high surface-to-volume ratio and poor flow property.

The rough-surface particle will have tendency to interlock than smooth-surface particle (Fassihi and Kanfer, 1986).

1.2.2.2 Particle Size

In general, fine particles with high surface to mass ratios are more cohesive than coarser particles which are influenced more by gravitation (Staniforth, 1988). The addition of appropriate amount of fine particles caused the increase in flow rate due to the smaller particles fitting within the voids between the larger particles. As a greater concentration of fines was added, the flow rate was decreased (Danish and Parrott, 1971).

For a given concentration, the reduction in diameter of fines related to flow rate in the same manner as increasing in the amount of fines (Danish and Parrott, 1971; Gold et al., 1968). Particles smaller than 100 μm. usually become cohesive, consequently, flow problem are likely to occur (Staniforth, 1988). The difficulty in particle flow due to the high amount of fines caused by interparticle friction (Nelson, 1955). More recently, Pilpel (1964) stated that the frictional and van de Waal's cohesive forces caused predominantly to the slower flow of fine particles, comparing to the other forces such as electrostatic, surface-tension, and mechanical forces caused by interlocking of particle irregularity.

Relationship between granule size and physical properties of tablet was found that as the granule size was reduced, the average tablet weight increased and the weight variation decreased (Kassem, Sakr, and Mesiha, 1972; Marks and Sciarra, 1968). Marks and Sciarra (1968) found no relation between granule size and tablet hardness and disintegration time. Some investigations showed different

way of the relation. Kassem et al. (1972) found that as granule size decreased, disintegration time increased and the coefficient of variation for disintegration time decreased. At constant pressure, smaller granule size gave harder tablet and decreased tablet friability (Sakr, El-Sabbagh, and Mesiha, 1973).

1.2.2.3 Particle Size Distribution

Narrow range of particle size distribution resulted in an improved flow rate (Ibralhim et al., 1971). Wide difference in particle size causes segregation due to large particle has greater mass that will firstly rolls down then results in weight variation (Lantz and Schwartz, 1990).

1.2.2.4 Moisture

Occasionally, poor flow may result from the presence of moisture which will increase cohesiveness of particles. The excessively adsorbed surface moisture films on the surface of particles cause the surface tension to occur (Staniforth, 1988).

1.2.2.5 Density and Compressibility

Bulk density and compressibility value are parameters which can indirectly indicate powder flow behavior in regard to powder cohesiveness. Peleg, Mannheim, and Passy (1973) found the relationship between bulk density and compressibility that in the case of noncohesive powders, when bulk density was slightly affected by the applied pressure which may be tapping or vibration during handle, the very low values of compressibility was a result. Applied pressure

mostly affected random voids left in a container beyond the powder occupation. In the case of cohesive powder, strong interparticle forces enable the open structure formation. The greater effect of applied pressure caused this structure collapse so high values of compressibility were obtained. Besides, the relationship between powder flow and percent of compressibility was developed by Carr (Staniforth 1988).

True density is also important. Dense particles are generally less cohesive than less dense particles of the same size and shape so the former flows freely (Staniforth, 1988).

1.2.2.6 Flowability

The flow rates of powder depend on many variables as mentioned in previous section. A higher weight variation is obtained with increasing compressibility index (Fassihi and Kanfer, 1986). Moreover, flow rate of particle increased when the diameter of orifice increased (Danish and Parrott, 1971).

1.2.3 Methods of Preparation

Few substances possess those essential properties without some preliminary treatment. To improve these three properties of the unsuitable material, the granulation procedure plays a useful role. The granulation can be divided into two major methods as follows (Gunsel and Kanig, 1976) :

1.2.3.1 Dry Methods

1.2.3.1.1 Direct Compression

This method is suitable for material having binding property and flowability.

1.2.3.1.2 Dry Granulation

Heat and/or moisture sensitive material is suitable for this method. Active ingredient and/or diluent used in formulation must have binding property.

1.2.3.2 Wet Methods

1.2.3.2.1 Wet Massing

It is the oldest method. Although it is the most labor-intensive, most expensive of the available methods, it has been widely used with versatility for variety of material.

1.2.3.2.2 Special Procedure

The special procedure are for example : fluidized bed granulation, spray drying, etc.

Steps in different methods of tablet manufacture are showed in Table 1-1.

Table 1-1 Steps in Different Methods of Tablet Manufacture *

Wet Granulation	Dry Granulation	Direct Compression
1. Milling of drugs and excipients	1. Milling of drugs and excipients	1. Milling of drugs and excipients
2. Mixing of milled powders	2. Mixing of milled powders	2. Mixing of ingredients
3. Preparation of binder solution	3. Compression into large, hard tablets called slugs	3. Tablet compression
4. Mixing binder solution with powder mixture to form wet mass	4. Screening of slugs	
5. Coarse screening of wet mass using 6- to 12- mesh	5. Mixing with lubricant and disintegrating agent	
6. Drying moist granules	6. Tablet compression	
7. Screening dry granules with lubricant and disintegrant		
8. Mixing screened granules with lubricant and disintegrant		
9. Tablet compression		

* Bandelin, 1989

1.2.4 Tablet Excipients and their Roles on Physical Properties of Granules and Tablets

A tablet does not contain only the active ingredient but has to induce other substances which have specific function. Excipients which are normally incorporated into tablet formulations especially for wet granulation process are as follows (Bandelin, 1989; Peck, Baley, and Banker, 1989; Rubinstein, 1988) :

1.2.4.1 Diluents

Diluents are ideally inert substances which are generally added to make a reasonably sized tablet. Mufrod and Parrott (1990) found that with insoluble diluent such as calcium hydrogen phosphate tablet disintegration was approximately 6 - 7 times faster than with the soluble diluent such as lactose. The widely used diluents are lactose, calcium hydrogen phosphate, starch, etc.

1.2.4.2 Binders

Binders are substance that act as adhesive for powder binding to form granules. They also help granule binding during tablet compression. Common binding agents are starch, acacia, gelatin, polyvinylpyrrolidone (PVP or Kollidon®), hydroxypropylcellulose, etc.

1.2.4.3 Disintegrants

Disintegrants are added to facilitate the tablet breakup, thereby causing an increase in rapid release of active ingredient due to the surface area increase of tablet fragment. Commonly used tablet disintegrants are starch, sodium starch glycolate, etc.

1.2.4.4 Lubricants and Glidants

1.2.4.4.1 Lubricants

They used to ease the ejection of tablets from dies to prevent sticking of tablet to punches. The best lubricants are hydrophobic, but it may retard the disintegration time. The decrease in tablet hardness may also be affected by using high amount of the lubricants.

1.2.4.4.2 Glidants

They are materials that improve flow characteristics of granules by reducing interparticulate friction. So tablet weight uniformity directly depends on uniform die filling. Usual content of glidant for promoting flow is not more than 1%.

In general, materials that are good glidants are poor lubricants. (Table 1-2)

1.2.4.5 Adsorbents

Adsorbents, for example: magnesium carbonate, magnesium oxide, bentonite, colloidal silicon dioxide, etc., are capable of retaining large quantity of liquid without becoming wet. Silicon dioxide can hold up water to 50% of its weight.

1.2.5 Good Tablets

Finished tablets have to be evaluated for knowing their properties which describe the total quality of tablets or tablet formulation, according to its particular method of manufacture.

Table 1-2 Properties of Some Lubricants and Glidants*

Material	Usual Concentration (%)	Glidant Properties	Anti-adherent Properties	Lubricant Properties
Metallic stearate	≤ 1	Poor	Good	Excellent
Strearic acid	1-5	None	Poor	Good
Talcum	1-5	Good	Excellent	Poor
High melting point waxes	3-5	None	Poor	Excellent
Corn starch	5-10	Excellent	Excellent	Poor

* มนต์ชุลี นิติพน, 2525

An acceptable tablets have to be (Bandelin, 1989) ;

1.2.5.1 sufficiently strong and resisitant to shock and abrasion to withstand handling during packing, shipping, and before eating. This property is measured by hardness and friability test.

1.2.5.2 uniform in weight and active ingredient content of individual tablet. This is measured by weight variation test and content uniformity test.

1.2.5.3 good bioavailability of active ingredient. So disintegration and dissolution are measured. The bioavailability is complicated, thus, blood level measurement have to be done.

1.2.5.4 elegant in tablet appearance

1.2.5.5 stable and efficacious. All their function must be retained.

The resulting tablets must meet physical and biological standards describing detail about testing procedure and their regulations in the United States Pharmacopeia (USP).

1.3 Aging Studies

For further formulation development or stability study, the evaluation data of physical properties of tablets during aging will be useful. Factors affecting tablet stability are temperature, oxygen, moisture, and light.

1.4 Scope Note

There are needs to investigate physical properties of yeast extract powder and experimental development to apply excipients and granulation for yeast extract tablet forming. Then granules will be test for their physical properties prior to compression. The evaluation of physical properties of finished tablets at initial condition and during aging will be done. Besides, effects of excipients on yeast extract tablet properties will be evaluated.

1.5 Objectives of the Studies

The aims of this research are concerned with :

a) the characterization of physical properties of yeast extract powder
b) the investigation on effects of type and amount of excipients in yeast extract tablet production
c) the evaluation of physical properties of yeast extract granules and tablets
d) the effect of aging on physical properties of yeast extract tablets