CHAPTER I

GENERAL BACKGROUND

INTRODUCTION

The terms , controlled release and sustained release are not new to many of us working in various disciplines of pharmaceutical research and development.

Controlled-release drug administration means not only prolonged duration of drug delivery, as in sustained-release and prolonged release , but also implies predictability and reproducibility of drug release kinetics.

The classification of controlled-release may be confusing. However, it can be classified by the concentration of drug in blood or tissues of the body into 3 types as shown in Figure 1 (Ballard and Nelson, 1975).

1. Sustained-release dosage forms:

This form has loading dose for therapeutic effect and residual drugs will be slowly relqased for prolonged pharmacological effect and longer than conventional dosage forms.

2. Prolonged-action dosage forms:

Release method was likely the first type, but the quantity of drugs in blood or tissues of the body was not necessary to be constant.

3. Repeat-action dosage forms:

After oral administration, these forms have repeated drug effect like multiple dosing regimen in interval times.

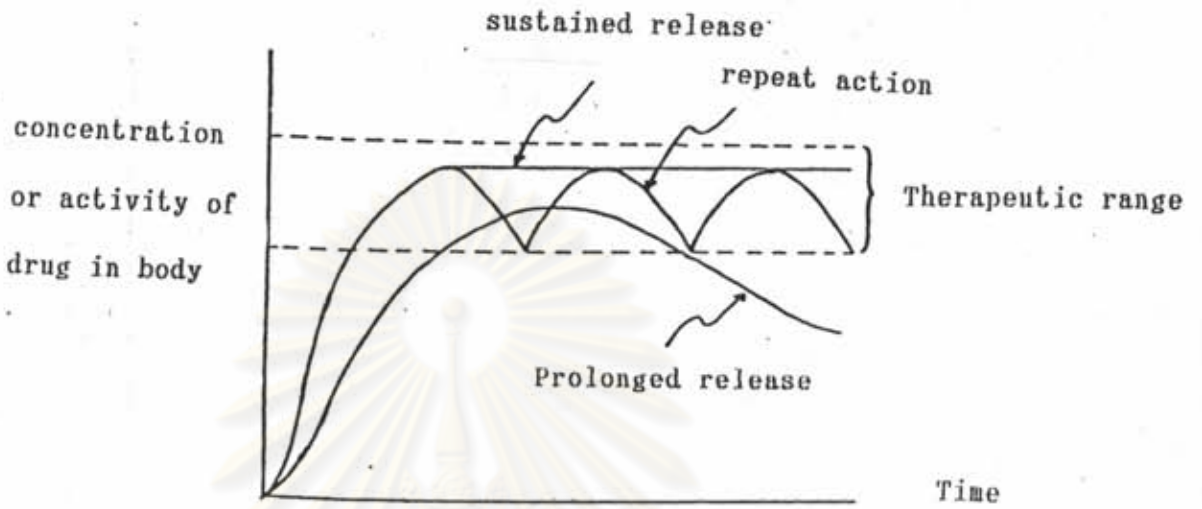


Figure 1 Relationship between drug concentration or activity and time

There are many different definitions of sustained release, but the simple definition of sustained release drug systems is any drug or dosage form modification that prolongs the therepeutic activity of the drug. Accordingly, a prodrug or analog modification of the drug that sustains drug activity, or blood drug levels, is viewed as a sustained-release system in the same sense as an alteration in the dosage form.

Sustained-release dosage forms are developed for a variety of reasons such as they may avoid patient compliance problems, reduce unexpected toxic effect due to high peak concentration and improve efficiency in treatment because of the less

fluctuations in drug level. Sustained release drug preparations are especially recommended when the drug has a relatively short half-life and needs steady plasma drug level to achieve desired therapeutic effects.

The two main approaches utilized in the design of the production of oral sustained-release dosage forms are :

(a) the introduction of a physical barrier preventing contact between the drug and the fluids of the digestive system, the effect of which is to reduce the rate of diffusion or leaching out of the drug from the dosage form.

(b) the addition of selected interactions to the formulation,such as ion-exchange resin (Gerald, Robert and Sunil, 1986)or complexants,which form weak chemical bonds with the drug.

The first type of products may be produced using widely different technologies. The main ones are based on (a) coating techniques b) embedding the drug in a wax (Bodmeier and Pearattakul, 1990) or polymer matrix (Huet de, Lapeyre and Cuine ,1989).

A multiple-unit type of dosage form such as pellets or granules, compared to single-unit type such as tablets, is less influenced by variations in the gastric emptying rate and overall gastrointestinal transit time and therefore has more reproducible absorption behavior. The advantages of multiple-unit dosage form product over single-unit dosage forms have been demonstrated by several workers.

The coating of particulates such as powders, granules, pellets and tablets to produce controlled-release dosage form is

becoming increasingly popular, mainly as a result of recent advances in fluidized-bed process.

The term fluidized-bed has been defined in a number of ways; most simply, when a solid is "fluidized" in a process, it show in its behavior many of the physical characteristics of a liquid (Donbrow and Friedman , 1978)

In pharmaceutical production, fluidization methods are utilized in stages of drying, granulation and coating. As a coating technique, its main advantages over the pan-coating method are as follows :

(a) irregular particles may be coated directly

(b) loss of material is small

(c) the process may be automated and does not require learning the "art" of coating.

(d) it is very rapid.

This present work was a study of the preparation of sustained release beads by the fluidized-bed coating techniques which considered the concept of dispersing model drug into a film coated on non-drug beads. The general concept of sustained release beads is to use the combination of drug and the other ingredient to form pellet, and coating with film former to form sustained release characteristics.

Propranolol has been selected as the active drug to be investigated. It has both of these specifications ; its half-life is approximately 3-4 hrs. and the therapeutic range at constant condition in plasma is 20-50 μg/ml.

Dose of propranolol is varied, depending on the type and state of disease. In general the usual initial dose is 10-40 mg, three to four times a day.

Various dosage forms of propranolol hydrochloride are available, included :

Film coated tablets	10, 20, 40 and 80 mg
Sustain release capsules	80 and 160 mg
Injection	1 mg/ml.

Sustain release capsules of propranolol hydrochloride in Thailand have been marketed in the name of Inderal LA 80 and Inderal LA which are composed of propranolol 80 mg and 160 mg, respectively, and both are manufactured by ICI. Inderal LA 80 and Inderal LA capsules contain the following inactive ingredients: cellulose, ethylcellulose, gelatin capsules, HPMC, titanium dioxide, D & C Red No.28 and FD & C Blue No.1 which were manufactured by mixing inactive ingredients and drugs in process of pelletization for spheroidal pellets. After that, mixing with colorants and filling of the pellets in hard gelation capsules took place.

The beads to be used in this study were sucrose crystal and pellets were prepared by extrusion and spheronization method.

Ethylcellulose (EC) was selected tobe a coating film former because it is probably the most widely used water insoluble polymer for film coating ; giving a satisfactory control of the drug release pattern as well as inexpensive and easy to prepare into a coating solution (Porter, 1989).

OBJECTIVES

On the basis of the rationale mentioned above, the objectives of this research are

1. To develop sustained release beads of propranolol hydrochloride by coating the mixture of the drug and EC on non-pareil seed using fluidized bed techniques.

2. To study the release characteritics of the coated beads and the effect of type and content of plasticizer incorporated in the coating formulas on the release behaviors.

3. To evaluate the fundamental physical properties of the coated beads.

4. To compare the effects of sucrose crystal and spherical pellets used as the coating core on physical property and release characteristic of the coated beads.

5. To develop the sustained release product of propranolol hydrochloride using this technical concept to have the amount of drug release comparable to the requirements specified in the US pharmacopoeia.

Literature Reviews

1. Propranolol hydrochloride in sustained release

Sustained release dosage forms are of great interest for the formulation of an oral drug containing an active ingredient with short half-life in plasma and narrow therapeutic range. They offer a way to reduce the number of administration. In recent years , many drug entities has been developed into sustained release products. Propranolol is one of the drug candidate prepared in such dosage forms.

Propranolol, (+)-1-Isopropylamino-3-(1-naphthyloxy) propan-2-ol hydrochloride. Its structural formular is given in Figure 2 along with its molecular weight, It is a white or off-white, odourless or almost odourless, crystalline powder with a bitter taste. It is commercially available as hydrochloride salt. It is soluble 1 in 20 of water and of alcohol, slightly soluble in chloroform and practically insoluble in ether.

In aqueous solution, propranolol decomposes with oxidation of the isopropylamine side-chain, accompained by a reduction in pH and discoloration of the solution. Its solution most stable at pH 3 and decompose rapidly in alkali medium.

Das and Kenneth (1987) reported stability of propranolol hydrochloride extemporanous suspension and solution which compounded from propranolol tablet and injection, respectively. Both of dosage form, content of propranolol hydrochloride almost equal the initial content which not significant after kept in room temperature at least 238 days because pH of suspension

and solution was in pH range 2.8-4.0 which provided maximum stability of propranolol hydrochloride.

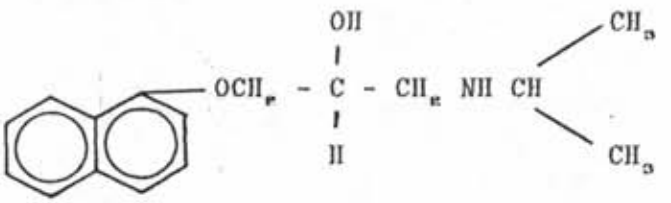
The study by Henry (1986) reported the stability of propranolol solution heated at pH 2 and 6 but at pH 8.5, it was found that the drug degraded and changed to strawcolors. This report supports the degradation of propranolol hydrochloride in alkali medium as previously mentioned.

Propranolol hydrochloride has pharmacological action similar to those of other β-blocker for treatment hypertension, cardiac arrythmias , angina pectoris , propylaxis after recovery from myocardial infraction , treatment symtomatic condition from hyperthyroidism and propylaxis the headache from migrain.

Propranolol hydrochloride is almost completely absorbed after oral administration. Dosage is 20 mg to 2 gm daily in divided doses. Peak plasma concentration is achieved at approximately two hours in fasting patient. It is highly bound to plasma proteins about 85-95% but it has short plasma half-life 3-4 hrs. (Evan, 1973) and rapidly hepatic metabolism after oral administration, therefore; it needs several times (3-4 times) by oral regimen.

Propranolol has narrow therapeutic range at constant condition in plasma 20-50 μg/ml.(Niebergall, Sugita and Schnaare, 1974). The apparent volume of distribution 182 liters are larger than volume of total water in body (52 liters) (approximately 50 liters in 70 kg body weight), it means drug is highly deposit or bound to tissue. The clearance is 637 ml/min result in rapidly excretion. (Lee and Robinson , 1978)

Isopropylamine side-chain



$C_{16}H_{21}NO_2$ .HCl

MW. 295.8

Figure 2 : Structural formula of propranolol hydrochloride

2. Materials used in coating formulations

Film former

Ethylcellulose (EC)

It is a tasteless, free flowing, white to light tan powder. The various type of ethylcellulose are not affected by water. Ethycellulose is insoluble in water, glycerin and propylene glycol,but soluble in varying degrees in certain organic solvents, depending upon the ethoxyl content. The addition of 10-20% of a lower aliphatic alcohol to solvents , such as ketones, esters and hydrocarbons, can improve the solubility. The solubility data of ethylcellulose was listed in Table 1.

Table 1 Solubility of ethylcellulose in various solvents

Solvent	Solubility (g/ml)	
	A	B
Water (25 °C)	< 0.001	0.010
Water (37 °C)	< 0.001	0.012
Alcohol (25 °C)	0.053	0.015
Alcohol (37 °C)	0.066	0.025
Propylene glycol (25 °C)	0.025	0.025
Propylene glycol (37 °C)	0.025	0.025
Hexane (25 °C)	< 0.002	< 0.002
Hexane (37 °C)	< 0.006	< 0.006

Supplier : A. Hercules Ltd.

B. Dow chemical Co.

Ethylcellulose is the ethyl ether of cellulose and contains between 44.0 and 51.0 percent of ethoxy groups ($-OC_2H_5$). Ethylcellulose is prepared by reacting ethyl chloride with alkali cellulose (obtained by treating crude cellulose with an alkaline solution, as expressed by the following type reaction:

$$RONa + C_2H_5Cl \longrightarrow ROC_2H_5 + NaCl$$

; R represents the cellulose radical

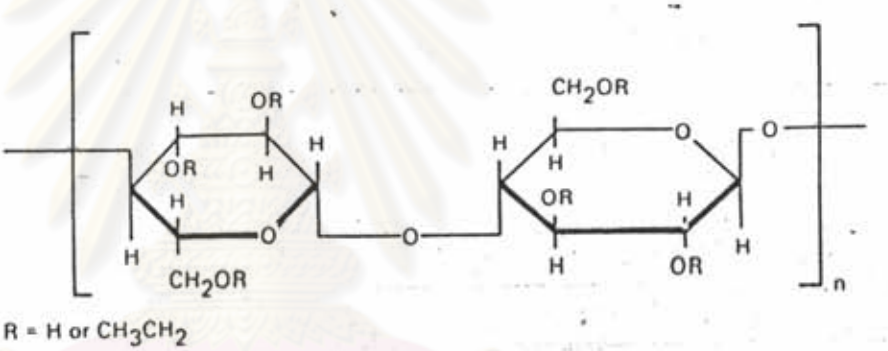


Figure 3 : Structural formula of ethylcellulose (ethoxy content 48-49.5 %)

The structures of ethylcellulose was shown in Figure 3 where it can be seen that each anhydroglucose unit of cellulose (position 1, 2, 3) has three reactive hydroxyl groups that can be ethoxylated.

The structure as shown for ethylcellulose has all three hydroxyl groups ethoxylated , and consequently is said to have a degree of subsitution (D.S.) of 3.0. In practice, the D.S. may vary, depending on end use of the polymer.

Typically , ethylcellulose used in pharmaceutical film coating has an ethoxyl content of 48.0 to 49.5 percent, and a D.S. of 2.41 to 2.51 this specification conforms to the Ethocel standard premium product supplied by Dow Chemical and Ethylcellulose N. Series supplied by Hercules.

As with most film-coating polymers, ethylcellulose is available as various grades of different molecular weights, each grade being represented by a viscosity number as determined by measuring the viscosity (ASTM D 914) of a 5% solution of the polymer in an 80:20 toluene/ethanol solvent mixture.(Stuart ,1989) .

Ethylcellulose is probably the most widely-used water insoluble polymer in film coating and has good film-forming properties that enable tough, flexible coating to be produced.

Ethylcellulose has many characteristics that allow the formulator a lot of flexibility in optimizing formulations, including :

(a) availability in a wide range of viscosity (or molecular weight) grades.

(b) solubility in a variety of organic solvents (and organic-solvent mixtures)

(c) miscibility with various water-soluble material the permit the permeability characteristics of resultant films to be readily changed.

Generally, formation of coating from polymer solution in organic solvents involves conversion of a viscous liquid into a visco-elastic solid. Simply, this process involves :

1. Rapid evaporation of solvent (typically from the surface of droplets created by a spray-atomization techniques), causing on increase in polymer concentration in the solution and concentration in volume of the coating liquid.

2. Further loss of solvent after the solvent has diffused to the surface of the coating. Concentration of the polymer in the coating increases to the point where the polymer molecules ultimately become immobilized (that so called solidification point).

3. Additional loss of solvent(beyond the solidification point) resulting from the slow diffusion of residual solvent through the "dry" coating. Such solvent loss is very much time-dependent, and ultimately causes shrinkage stresses to develop within the coating.

From a structural standpoint, the quality of the final dried coating is very much determined by :

1. The initial interaction between the polymer and the solvent.

Maximum interaction between the polymer and solvent (often determined by cohesive energy densities, or solubility parameters), typically results in maximum chain extension of the polymer such that interaction between the polymer chains in the resultant dried coating will also be high, (yielding a film with good mechanical properties).

2. The volatility of the solvent system used.

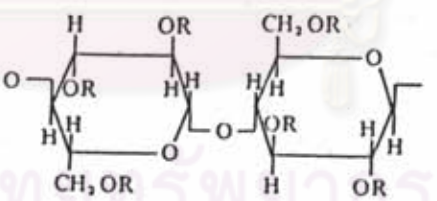
Volatility of the solvent will play a large part in

determining the tendency of the polymer-solution to partially "spray dry" during application, resulting in the formulation of a very porous coating.

Hydroxypropylmethylcellulose (HPMC)

HPMC also has been used in this experiment in order to modify the release of the drugs from the coating film.

HPMC appears as an odourless, tasteless white or creamy-white fibrous or granular power. It is water soluble and stable in the presence of heat, light, air and moisture, and its films are flexible, tolerate the presence of colorants and other additives, and are resistant to abrasion. The structural formular of HPMC was shown in Figure 4.



R= H-, CH_3- or $CH_3CH(OH)CH_2$-

Figure 4 : Structural formula of HPMC

Plastizicer

In general, plasticizer is used in coating formulation in order to increase flexibility of the film. But in this research

plasticizer was used for decreasing permeability of the film and subsequent retarding drug release.

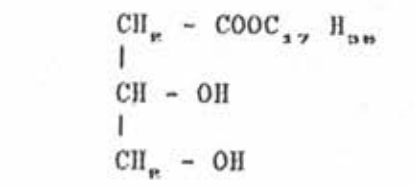
Plasticizers with low water solubility are generally recommended for controlled drug release. High proportion of plasticizer may result in seed agglomeration, sticking, and poor fluidization problems caused by excessive softening of the polymer film.

The plasticizer used in the film coating process might be divided into 3 groups such as organic ester, vegetable oil & glycerides and polyols. For example, glyceralmonostearate, castor oil and polyethylene glycol 4000 representative for each group, respectively and are generally employed in several concentrations as follows :

Glycerylmonostearate

Glycerylmonostearate appears as a white to cream-colored, wax-like solid in the form of beads, flakes or powder. It is waxy to the touch and has a slight fally odour and taste.

It is practically insoluble in water, but readily dispersible in hot water the aid of an anionic or cationic agent, and also soluble in hot alcohol, ether, chloroform, benzene, hot acetone, mineral oil and fixed oils. It is incompatible with acidic substances. The structural formular of glycerylmonostearate was shown in Figure 5



$C_{20}H_{40}O_4$

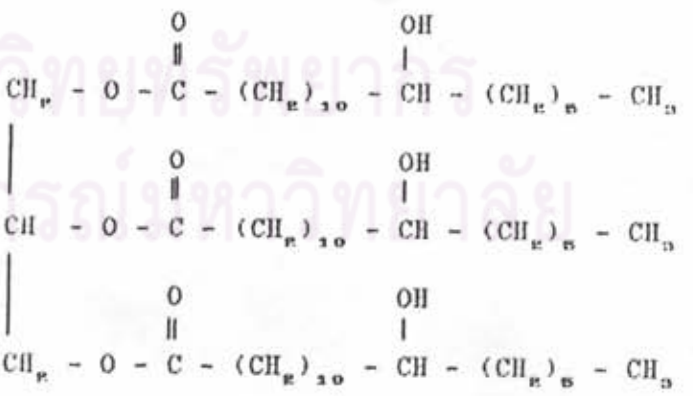
MW. 358.57

Figure 5 : Structural formula of glycerylmonostearate

Castor oil

Castor oil appears as a nearly colourless or slightly yellow transparent viscid oil with a slight odour and taste. It is soluble 1 in 2.5 of alcohol, miscible with dehydrated alcohol, chloroform, ether, carbon disulphide, and glacial acetic acid, slightly soluble in petroleum spirit, but insoluble in water.

Castor oil is prepared from the seeds of Ricinus Communis (Euphorbiaceae), containing about 80 % of the triglycerides of ricinoleic acid. The structural formula of castor oil was shown in Figure 6.



$C_{57}O_9H_{110}$

MW = 934 (approximately)

Figure 6 : Structural formula of castor oil

Polyethylene Glycol (macrogol) (PEG_n)

Polyethylene glycol divided in 2 form

1. Liquid PEG_n (Grades 200-600)
2. Solid PEG_n (Grades > 1000)

PEG was polymer between ethylene oxide and water. Liquid form appears as clearly, colouless, slight odour, dissolve with water, ethyl alcohol and other glycols. Solid form appears as white or creamy, dissolve in water and ethyl alcohol melting point 40-60 °C depend .on molecular weight. Special characteristic of PEG was lipid like substances but dissolve in water. The structural formula of PEG was shown in Figure 7.

$$HOCH_2 (CH_2OCH_2)_n CH_2 OH$$

Figure 7 : General formula of PEG_n

Solvent

Ethanol (Ethyl alcohol)

It appaers as a clear, colorless mobile and volatile liquid with a slight characteristic odor. It has a burning taste and absorbs water rapidly from air. It has specific gravity 0.7904 -0.7935 (at 20 °C), melting point 114.1 °C and boiling point 78.5 °C.

In acidic solution, ethanol may react vigorously

with oxidizing material. Its mixtures with alkali may darken in color due to the reaction with residual aldehydes in alcohol. Organic salts or acacia may be precipitated from aqueous solution or dispersion.

Chloroform (Trichloromethane)

It appears as a highly refractive, nonflammable, heavy, very volatile, sweet-tasting liquid with characteristic odor. It has melting point -63.5 °C and boiling point 61-62 °C.

Its dissolve in about 200 part of water and miscible with alcohol. Pure chloroform is light sensitive and reagent chloroform usually contains 0.75% ethanol as stabilizer.

Methylene Chloride (Dichloromethane)

It appears as a clear, colorless, mobile and volatile liquid with chloroform-like odor. It has specific gravity 1.318-1.322, melting point -95 °C and boiling point 39.5 -40.5 °C. Its soluble in about 50 parts of water and miscible with alcohol and ether. It vapour is not explosive when mixed with air.

3. Film coating equipment

Coating equipment has derived from two basic principles such as the traditional pan coaters and the fluidized bed. In this study, it was concentrated only on the fluidized bed machines.

The fluidized bed is well known for its drying

efficiency, as it has been used for drying and granulating for many years. It has ability to apply virtually to any type of coating system (solution, suspension, emulsion, latex and hot melt) to a wide range of particle sizes coating can be applied to fluidized particle by a variety of techniques such as top spray, bottom spray and tangentially.

2.1 Top spray method

The conventional top spray method (Figure 8) has been used for more than a decade for coating. It evolved from the fluidized bed drugs commercialized more than 30 years ago.

The substrate is placed in the product container (A), which is typically an unbaffled, inverted, truncated cone with a fine retention screen and an air or gas distribution plate (B), at its base. Preconditioned air is drawn through the distribution plate (B) and into the product. As the volume of air is increased, the bed no longer remains static but becomes fluidized in the air system.

The particles are accelerated from the product container part the nozzle (C), which sprays the coating liquid countercurrently onto the randomly fluidized particles. The coated particles travel through this coating "Zone" into the expansion chamber (D) which is wider in diameter than the base of the product container ; this result in a decreasing air velocity that allows decelaration of the particles to below entrainment velocity. The particle fall back into the product container and continue cycling throughout the duration of the process.

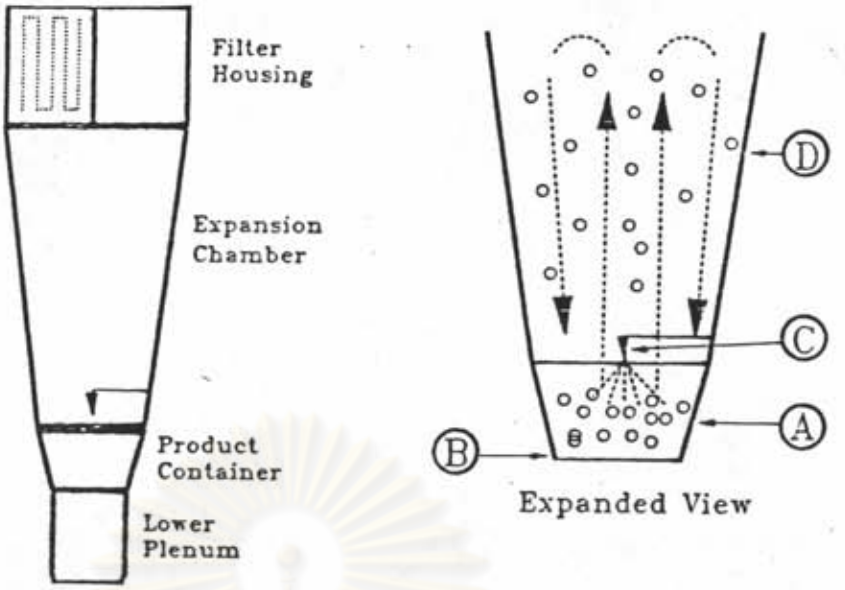


Figure 8 Top Spray Coater : (A) Product Container ; (B) Air Distribution Plate ; (C) Spray Nozzle ; (D) Expansion Chamber (Swarbrick and Boylan, 1988.)

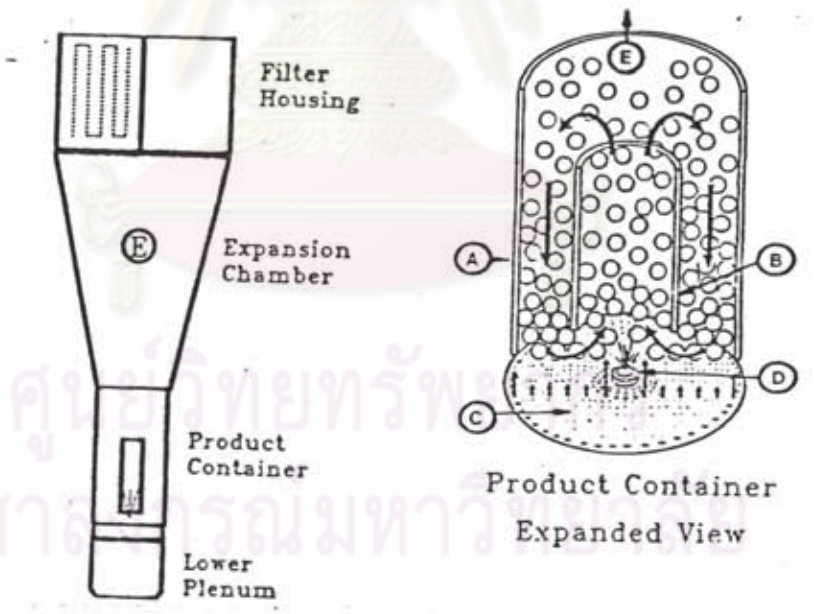


Figure 9 Wurster Bottom Spray Coater : (A) Coating Chamber ; (B) Partition ; (C) Air Distribution Plate ; (D) Spray Nozzle ; (E) Expantion Chamber (Swarbrick and Boylan, 1988.)

2.2 Bottom-spray coating (Wurster Process)

The Wurster process was invented by Dr. Dale Wurster (Figure 9). The machine employs a cylindrical product container with a perforated plate. Inside the container is a second cylinder (coating partition), which is raised slightly above the perforated plate. Centered in the plate below this partition is a spray nozzle used to dispense the coating solution. The perforated plate is designed with large holes in the area under the coating partition and smaller holes in the remainder of the plates, except for one ring of large holes at the perimeter. This design allows the substrate particles to be pneumatically transported upware through the coating partition, and downward outside this partition Material passing through the coating partition receives a layer of coating material,dries in the expansion chamber, and fall back in a semifluidized state. Material circulates rapidly in this fraction and recieves a layer of coating on each pass through the coating partition.

2.3 Tangential spray (Rotary Fluidized Bed coating)

A relatively new approach to coating is referred to as tangential coater (Figure 10). Originally conceived for high-density fluid bed granulation, this technique is being used to produce high dose pellets by applying a layer of drug particles to same type of materials. The controlled release coating can subsequently be applied.

The product container consists of an unbaffled cylindrical chamber (A) with a solid, variable-speed disc (B) at

Figure 10 Rotor Tangential Spray Coater : (A) Product Chamber ; (B) Variable-speed Disc ; (C) Disc Gap or Slit; (D) Spray Nozzle (Swarbrick and Boylan, 1988.)

its base. The disc and chamber are constructed such that during the process a gap (C) exist at the perimeter of the disc through which preconditioned air is drawn. During fluidization, three forces combine to provide a pattern best described as a spiraling helix. Centrifugal forces causes the product to move toward the wall of the chamber, air velocity through the gap provides acceleration upward, and gravity cascades the product inward and toward the disc once again, beneath the surface of the rapidly tumbling bed, a nozzle (D) is positioned to spray the coating liquid tangentially to and concurrently with the flow of particles. The particle cycling time of this technique is very rapids; hence, the films are uniform in thickness.

Each approach has its adventages and disadventages, depending on:

- Batch size of product being coated
- Functionalily of the final coating
- Type of coating formulation being applied (eg. solutions, polymeric dispersions hot melts)
- Flexibility with regard to the variety of types of coating that need to be applied in one piece of equipment.

Olsen and Mehta (1988) have described how the quantities of an orgnic solvent based ethylcellulose formulation that need to be applied to achieve the same end result differed widely when comparing the top spray method with the Wurster process. However, when using aqueous polymeric dispersion; differences in performance between the three types of coating process may not be as significant.

The efficiency of the coating processes controlled by three factors eg. temperature, concentration of the coating solution and spray pressure.

The coating efficiency of the apparatus was examined on the basis of the following criteria:

a) non-blockage of the spray nozzle

b) non-aggregation of the beads

c) homogeneity of the coating in each batch of beads

d) identify of coating in repeated batchs

The first two factors the last two are most conveniently measured by means of drug release experiments performed on the coated granules.

The coating morphology and dissolution characteristics can be effected by the variables of the fluid-bed process such as :

1. Spray rate

The primary objective of particle coating is to envelop each particle with sufficient coating material to acheieve the desired functions. To accomplish this, the size of the coating droplets must be kept small relative to the size of the particle that is to be coated. The liquid spray rate affected the degree of wetting and droplet size. Although increasing the liquid spray rate increases the droplets size, this also allow for a reduction in the processing time that is necessary.

The spray rate factor also will be determined by the size of the particle of the substance, the viscosity and nature of the liquid to be sprayed, and the temperature of the product.

Although it is possible to reduce the processing time by increasing the spray rate to its maximum level which does not cause agglomeration.

In addition, the atomizing air pressure that is selected might determine the spray rate in term of the size of the droplets.

2. Atomization air pressure

The majority of the nozzles that are used in fluid-bed processor are binary. That is, the liquid is supplied at a low pressure and it atomized into droplets by air. As mentioned previously, it is necessary to minimize agglomeration and to provide uniform film characteristics. In general, the higher the atomization air pressure, the smaller the size of the droplets at any given spray rate.

Atomization pressure affects the spraying pattern and droplet size. Excessive high atomization pressure may result in the loss of coating materials and breakage or attrition of the substrates. Excessive low atomization pressure may overwet the core and cause side wall bonding.

3. Inlet-air temperature

The fluidization air temperature is a key variable in the coating process. A low fluidization air temperature might lead to a problem commonly known as the weather effect. In a coating process that uses one or more organic solvents to apply a film, a low fluidization air temperature is often used because of the low heat of vaporization of the solvent. A problem might arise when the dew point of the fluidzation air is allowed to vary as changes in the season occur.

The method to avoid the weather effect it is necessary either to control the dew point of the air or to raise the temperature of the fluidization air. If possible, it is preferable to use a much higher fluidization air temperature because this tend to minimize the weather effect. However, a very high inlet-air temperature can cause spray drying of droplets. Also, if the product remains too dry and hence is subject to attrition, the product yield decrease. With certain thermoplastic polymeric systems a very high inlet-air temperature can also cause agglomeration: The most desirable setting for the inlet-air temperature is one that allows for equilibrium between the application of the solvent as a liquid and its subsequent evaporation so that the film forms properly. For this reason, the heats of vaporization of any solvents that are present in the coating system must be taken into consideration when selecting the inlet-air temperature.

The optimization of temperature of the product may be based on the properties of the substrate and the coating. It is not unusual to find that the inlet-air temperature must be altered to arrive at similar product temperature in different equipment.

4. Fluidization air volume

An air-volume indicator should be used to monitor airflow. Although an adjustable damper typically is used to control the fluidization air volume occlusion of the outlet-air filter or of the product bowl screen can cause resistance to airflow, and this might not be noticed unless the processor is equipped with an air-volume indicator. Because changes in air volume affect the fluidization pattern as well as heat exchange that is, evaporation of the solvent and drying of the product such changes might also affect the film formation process and consequently the performance of the finished product.

5. Batch size

Batch size is a vairiable that infrequently requires attention or adjustment. To determine batch sizes, the bulk density of the substrate is multiplied by the working volume of the processor, as shown in the following examples.

For top-spray coating in conventional granulators, maximum and minimum batch sizes are determined using the following equations:

$$S_{max} = V \times 0.8 \times BD$$

$$S_{min} = V \times 0.5 \times BD$$

where

S = batch size

V = volume of the container

BD = bulk density of the substrate

For bottom-spray coating in Wurster columns, the batch size for coating particles is calculated as follows:

$$S_{max} = (\pi R_1^2 H - N\pi R_p^2 H) \times BD$$

$$S_{min} = 1/2\ (\pi R_1^2 H - N\pi R_p^2 H) \times BD$$

where

R_1 = radius of the chamber

R_p = radius of the partition

N = number of partitions

H = length of the partition

The batch size for coating tablets when using the bottom-spray coating process is calculated using the following formula:

$$S = (\pi R_1^2 H - 1/2\ N\pi R_p^2 H) \times BD$$

For tangential spray coating in rotary fluid-bed granulators, maximum and minimum batch sizes are determined as follows:

$$S_{max} = V \times 0.8 \times BD$$

$$S_{min} = V \times 0.2 \times BD$$

6. Type of equipment

Ideally, the type of fluid-bed equipment to be used should be selected during the product development phase, several factors must be considered. For example, the length of the expension chamber is related to the type of product to be coated-whether powders, granules, pellets or tablets. Because the position of the outlet temperature probe varies in different type and sizes of equipment.

7. Nozzle height

In a conventional top-spray fluid-bed coater, it is possible to minimize the size of the coating zone - the region through which droplets must travel - by positioning the nozzle at the shortest possible distance from the static bed. This maximizes the concentration of partides in the coating zone.

8. Drying time

The effect of drying time on the performance of the end product is more critical when latex or pseudolatex films are applied for controlled release. This is because the rate and degree of coalescence depend not only on the temperature of the drying air but also on the length of the drying phase.

While many similarities exist for equipment supplied by the various vendors, opportunities for differentiation exist with :

- Clamping system (compressed air or hydraulic)
- Explosion protection
- Filter-bag assemblies
- Heating units (conventional stream or electric)
- Specialized designs, with taller expansion chambers that facilitate appropriate deceleration when coating small particles.

Sugar-coating liquids typically have solid content in excess of 70% (w/w) and subsequently can be extremely viscous. In contrast, this study used film-coating liquid which rarely contained greater than 20% non-volatile materials (which typically fall in the range of 5-15%).