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DEVELOPMENT OF A FLUIDIZED-BED COATER
FOR PHARMACEUTICAL APPLICATION

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งานนี้เป็นการพัฒนาเครื่องเคลือบผิวอนุภาคเพื่อใช้ในงานทางด้านเภสัชกรรม รวมไปถึงศึกษาตัวแปรกระบวนการ (ความเร็วอากาศที่ใช้ในการฟลูอิดไดซ์, อุณหภูมิของอากาศที่ใช้ในการฟลูอิดไดซ์) และชนิดของหัวฉีด (แบบไบนารีและแบบคลื่นเหนือเสียง) ที่มีต่อคุณสมบัติของฟิล์มเคลือบที่ได้ ได้แก่ ความหนาของฟิล์มเคลือบ, สัดส่วนน้ำหนักที่เพิ่มขึ้น, ร้อยละผลิตผล, ร้อยละการจับตัวกันของอนุภาค, ลักษณะรูปร่างของอนุภาคฟิล์มเคลือบ ที่วิเคราะห์โดยใช้ตะแกรงร่อนและกล้องจุลทรรศ์อิเล็กตรอนแบบส่องกราด สมบัติทางกายภาพของอนุภาคฟิล์มเคลือบ ได้แก่ ความหนาแน่นปรากฏขณะอัด, มุมกองขณะสงบ ที่วิเคราะห์โดยใช้เครื่องทดสอบสมบัติวัสดุผง และระยะเวลาในการละลายของอนุภาคฟิล์มเคลือบ

จากการศึกษาพบว่า เมื่อความเร็วอากาศและอุณหภูมิที่ใช้ในการฟลูอิดไดซ์เพิ่มขึ้น ทำให้สัดส่วนน้ำหนักที่เพิ่มขึ้น, เปอร์เซนต์ผลิตผล, มุมกองขณะสงบ, ความหนาของฟิล์มเคลือบ และความขรุขระของอนุภาคฟิล์มเคลือบมากขึ้น เนื่องจากความเร็วอากาศที่เพิ่มขึ้นทำให้อนุภาคในคอลัมน์เกิดการหมุนเวียนได้ดีขึ้น ในขณะที่อุณหภูมิที่สูงขึ้นจะทำให้ความชื้นภายในคอลัมน์ลดลง แต่ในทางกลับกันความหนาแน่นปรากฏขณะอัดและเปอร์เซนต์การจับตัวกันของอนุภาคลดลง อันเป็นผลมาจากความชื้นที่ลดลงและปริมาณฟิล์มเคลือบที่มาเกาะอนุภาคแกนกลางมากขึ้น เมื่อพิจารณาระยะเวลาในการละลายของอนุภาคฟิล์มเคลือบ พบว่าอุณหภูมิของอากาศที่ใช้มีผลเพียงเล็กน้อย ปรากฏการณ์ดังกล่าวข้างต้นพบในทั้งกรณีที่ใช้หัวฉีดแบบไบนารีและหัวฉีดแบบคลื่นเหนือเสียง เมื่อเปรียบเทียบสมบัติทางกายภาพของอนุภาคฟิล์มเคลือบที่ได้จากหัวฉีดทั้งสองพบว่ามีผลแตกต่างไม่มากนัก แต่การกระจายตัวของหยดสเปรย์ที่ได้จากหัวฉีดแบบคลื่นเหนือเสียงจะมีขนาดเล็กกว่าจากหัวฉีดแบบไบนารี

ภาควิชา........วิศวกรรมเคมี.........　　ลายมือชื่อนิสิต กิตติศักดิ์ ปึงสมบูรณ์ยิ่ง
สาขาวิชา.......วิศวกรรมเคมี.........　　ลายมือชื่ออาจารย์ที่ปรึกษา.................................
ปีการศึกษา........2544...............　　ลายมือชื่ออาจารย์ที่ปรึกษาร่วม..............................

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KEY WORD : FLUIDIZATION / FLUIDIZED-BED COATER / COATING

KITTISAK PHUENGSOMBOONYING: DEVELOPMENT OF A FLUIDIZED-BED COATER FOR PHARMACEUTICAL APPLICATION. THESIS ADVISOR: ASSOC. PROF. TAWATCHAI CHARINPANITKUL, D. Eng. THESIS COADVISOR : ASSIST. PROF. HATHAICHANOK VANISRI, Ph. D., 108 PP. ISBN 974-03-1269-1

Objective of this research is to develop fluidized bed coater for pharmaceutical industry. The investigation of influence of operating variables (fluidizing air velocity, fluidizing air temperature) and type of nozzle (binary and ultrasonic renonator) on coated particles properties, namely, film thickness, percent weight gain, percent yield, percent agglomerate, morphology, packed bulk density, angle of repose and dissolution time have been carried out.

From experimental results, it is found that when fluidizing air velocity and fluidizing air temperature are increased effect on percent weight gain, percent yield, angle of repose, film thickness and roughness of surface morphology increasing. Because higher air velocity produces good circulation of particles in the column, meanwhile increasing air temperature reduce moisture content in fluidized bed coater. While packed bulk density and percent agglomerate is decreased due to reducing moisture film coated and increasing film coated sticked the core particles. Considered from the solubility time of coated particles is found that fluidizing air temperature has little effect on the characteristic. The phenomena mentioned above are found in case of using binary and ultrasonic resonator. Comparison of physical property obtained from two nozzle has no difference, but droplet size distribution of ultrasonic resonator is smaller than producing from binary nozzle.

Department...Chemical Engineering... Student's signature.....kittisak Phuengsomboonying

Field of study.Chemical Engineering... Advisor's signature..............................

Academic year.......2001.................. Co-advisor's signature......H. Vanisri..........................

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NOMENCLATURE

bar	kg/cm^2
^oC	degree celcius (centrigrade)
m	meter
s	second
m/s	meter per second
e.g.	exampli gratia, for example
min	minute (s)
i.e.	id est, that is
ml	millilmeter (s)
PEG	polyethylene glycol
HPMC	hydroxypropyl methylcellulose
et al.	et alli, and others
SEM	scanning electron microscopy
w/w	weight by weight
μm	micrometer (s), micron (s)
%	percentage
o	degree
mm	millimeter (s)
mg	milligram (s)
cm^2	square centimeter (s)
PhEur	European Pharmacopoeia. 2nd edition
USPNF	US Pharmacopoeia combined with National Formulary
USP	The United States Pharmacopoeia
mg/ml	milligram (s) per milliliter (s)
g/cm^3	gram (s) per cubic centimeter (s)
g/l	gram (s) per liter (s)
nm	nanometer (s)
kHZ	kilohertz

NOMENCLATURE (CONTINUE)

ms	millisecond (s)
ρ	density
g/cc	gram (s) per cubic centimeter (s)
Dp	Particle diameter
bi	Binary
ul	Ultrasonic
N	newton
w/v	weight by volume
mPa.s	milliPascal second
kg/m^3	kilogram (s) per cubic meter (s)
kg/s^2	kilogram (s) per $(second)^2$

CHAPTER 1

INTRODUCTION

1.1 Background of particle coating

Fluidized-beds are use widely in several industries due to various advantages, which are, for example, good heat and mass transfer during the mixing of particle in the equipment. The application of fluidization could be found in many processes such as drying, coating and granulation etc.

Pharmaceutical raw materials are almost fine particle. Therefore, it results in difficult dosage forms production according to its poor flow properties. Fluidized bed is widely used for particle enlargement, sometimes called granulation, which helps improve flowability of powder. Moreover, it could be also employed for coated pharmaceutical dosage forms. The fluidized bed is well known for coating of a wide range of particle as a one-step, enclosed operation. This technique reduces material handling and processing times compared with other processes.

The objective of film coating depends on type of industries e.g. in ceramic industry, film coating made to strengthen of ceramic surface and made beautiful the finished product. For pharmaceutical industry use film coated to protect the active ingredients from against environmental hazards, light, air and for hiding bad taste odor or appearance. Today, coating technology widely used in controlled release dosage forms.

Nowadays, medicine in the pharmaceutical dosage form granule or pellet are generally used to treat patients. Hence the fluidized bed granulator and coater are very important equipment for producing such particulate matter in form of granule or pellets in pharmaceutical industry. Additionally, so far Thailand has imported such fluidized bed coater and granulator from the foreign countries. But there is very limited work of developing such equipment in Thailand.

In general, binary nozzles are used in typical fluidized bed for spray coating. Early practical application ultrasonic nozzles were used for combustion area. However, in recent years ultrasonic nozzle technology has found a variety of industrial and laboratory applications such as semiconductor processing, humidification and so on.

For that reason, this research preliminary develop fluidized bed coater equipped with the different nozzle types for regional pharmaceutical application as an alternatice to imported ones.

1.2 Objectives of the Present study

1. To construct a fluidized bed coater equipped with a binary or an ultrasonic resonator for pharmaceutical application.
2. To test the performance of the developed fluidized bed under various conditions by varying process variables to study their effect on properties of the coated particles.

1.3 Scope of study

1. To develop a fluidized bed coater which could be employed with two types of nozzles, which are binary and ultrasonic resonator.
2. To test-performance of the equipment.

   Investigation the process variables affecting to the properties of film coated onto non-pareil seed pellets, which was considered as the model drug. Aqueous Hydroxypropyl Methylcellulose (HPMC) was employed as film coating agent.

   The process variables consisted of:

   2.1 Fluidizing air velocity: 1.3, 1.7, 2.1 m/s

   2.2 Fluidizing air temperature: 50, 60, 70 °C

   2.3 Types of nozzle (Binary and Ultrasonic).
3. Properties of coated particles, to be investigated were

   3.1 Packed bulk density of coated particle

3.2 Morphology and surface of coated particle by using Scanning Electron Microscope (SEM)
3.3 Film thickness of coated particle
3.4 Dissolution of coated particle

1.4 Obtained benefit

1. Understand the principle of coating process using fluidized bed coater.
2. Understand how the mentioned factors affect the coating process using fluidized bed coater.
3. Gained know-how of selection of types of nozzle which could provide better quality of coating film from fluidized bed coater.

CHAPTER 2

LITERATURE REVIEW

Fluidized bed processing technology was first introduced into the pharmaceutical industry in appearance form fluidized bed dryer. The addition of spray nozzle allowed to the equipment to be extended to cover the wet granulation process. In the 1960s, Wurster develops fluidized bed coater equipped with coating chamber, inner partition (draft tube), air distribution plate and spray nozzle. Subsequently, **Scott M.W. et al. (1964)** preliminary studied and designed continuos fluidized bed granulation from the fluidized bed dryer by using material balance, energy balance, heat and mass transfer for their work. Then, in this chapter is review about the fluidized bed coater and ultrasonic application in the pharmaceutical industry.

Metha M. and Jones M. (1985) used scanning electron microscopy (SEM) to evaluate film coating applied to pellets, several different processing methods were used to apply the films, which were of both aqueous and organic-solvents types. For aqueous coating system, the equipments were used to apply coating included a conventional pan, a modified perforated pan, and fluidized bed. On organic coating system, pellets were coated in fluidized bed using three different methods: top-spray, bottom-spray and tangential-spray. Scanning electron micrographs of pellets revealed differences in the morphology of pellets that had been coated using the different techniques.

Reiland T. and Eber A. (1986) investigated effect of the formula and process variable on the surface of film coated tablets. The process variables studied included: spray distance, drying temperature, air cap and atomizing air pressure. Hydroxypropyl methylcellulose was used as aqueous film coating. A Taylor-Hobson Surtronic 3 surface roughness analyzer and attached parameter module were used to obtain surface roughness. For minimum surface roughness, was obtained from the largest annular orifice air cap at the shortest spray distance and lowest drying temperature used for spraying. Moreover, the increasing concentration of HPMC in coating solution increased slightly surface roughness.

Twitchell A., Hogen J. et al. (1987) study the effect of atomization conditions on the surface roughness of aqueous film-coated tablets. The concave placebo tablets are coated with aqueous solution of HPMC (concentration 9 or 12%w/w) in Accela-Cota. Sprays were applied at a rate 40 g/min by using pneumatic nozzle, which set to produce a normal flat spray or 10^{O} solid spray cone. After coating, surface roughness measurements were made with a Talysurf. They found both viscosities and spray shape pattern an increase in the atomizing air pressure result in a decrease in surface roughness and an increase tablet gloss.

Heinamaki J., Lehtola V. et al. (1994) investigate the effect of a molecular weight of Polyethylene glycols (PEG400, 1500 and 4000) on the moisture permeation and mechanical properties of free films hydroxypropyl methylcellulose (HPMC) prepared from aqueous solution. Three types of polyethylene glycols 10, 20 and 30% w/w of polymer weight were used as plasticizer. The free films were prepares by using pneumatic spray, which continuously fed at a flow rate 6 ml/min atomizing air pressure 1 bar and drying free films temperature was 55$\pm$5 ^{O}C. The permeability of films was determined using vial containing 2 g of $CaCl_2.2H_2O$, which sealed with a piece of film and closed tightly with a rubber ring and an aluminum hole cup. The mechanical and stress-strain properties of free films were determined using a Lloyd LRX instrument under conditions 22$\pm$1 ^{O}C and 40$\pm$5 % relative humidity. Films of thickness 75$\pm$5 μm were cut into 8*1.5 cm strips and were performed using 50 N load cell, initial gauge length of 60 cm speed 5 mm/min. They found moisture permeability of HPMC films; over the range of concentration tested, that property decreased with increasing molecular weight as a compared to unplasticized films. The mechanical strength of platicized HPMC films was general clearly lower than unplasticized films, and the value for applied force decreased as increasing concentration of plasticizer. The results suggest that use of PEGs as plasticizer in aqueous films is beneficial at concentrations of 10-20 % with respect to polymer weight.

Guo J. (1994) studied effect of plasticizer, polyethylene glycol (PEG600), on the sucrose permeability, void volume and morphology of cellulose acetate free films. The polymer solutions were prepared by dissolving cellulose acetate 4 %w/v, and the plasticizer level were prepared from 0 to 40% w/w. The sucrose permeability tests of free films polymer were performed in a standard diffusion cell at 25 ^{O}C. He was found sucrose permeability decreasing with increasing PEG600 to a minimum and increase dramatically when they were plasticized over 30%w/w. The decrease in sucrose permeability of free films could be interpreted by the antiplasticization effect. The dramatic increase of sucrose permeability of free film at high level could be explained by the formation of plasticizer channels. The void volume were calculated by determining the water content in the films, and used the scanning electron microscopy to study the morphology of free films. Both investigations supported the assumption that the plasticizer channels would be formed in the polymer that high concentration of plasticizer.

Govender T., et al. (1995) studied the influence of various formulation additives on the drug profiles of controlled release characteristics and surface morphology of salbutamol pellets. Salbutamol sulphate was coated which Eudragit$^{®}$ RS 30D and used triethyl citrate, polyethylene glycol 200 as a plasticizer; magnesium stearate as a lubricant. From the results of scanning electron microscopy and dissolution test, at higher concentrations in this study (12.5%) of triethyl citrate displayed uniform and continuous polymer film resulting in a slower release. If the plasticizer (triethyl citrate) maintained constant at 16.67% relative to the polymer content, drug release rates inversely proportional to the quantity of polymer coated onto the pellets. The percentage of salbutamol release per unit time increased dramatically with the incorporation of HPMC into the coating liquid. This effect attributed to its hydrophilic nature, which promoted the formation of pores and cracks on the polymer films. The addition of lubricant to the formulation retarded the release of salbutamol into the dissolution medium. As compared to polyethylene glycol 300 (PEG300) and triethyl citrate (12.5%) in the formulation, triethyl citrate retarded drug release to a greater extent and formed more homogeneous and compact polymer films.

Heng W., et al. (1996) reported the relationship between the percentage of aggregates formed during film coating of pellets in Wurster process and tack force, viscosity and cloud point of hydroxypropyl methylcellulose (HPMC) coated spheroids. They consisted of HPMC with and without additives. The additives are primarily divided into three groups i.e. plastizers, film formers and thickeners. The spheroids formed were sieved and batches of size fractions 0.85 – 1.18 mm were coated in bottom-spray. From the results of the various tests to correlation statistical treatment, it is shown that the percentage of aggregate is best associated linearly with tack force. Moreover, percentage of aggregate is also correlated to the viscosity of the coating formulations in a nonlinear manner. However, there is no strength indication showing that the percentage of aggregate is correlated with cloud point, mechanical strength, dissolution $T_{50\%,}$ value and initial release rate constant.

Honary S., Orafai S., et al. (2000) were designed to introduce a new and simple method to demonstrate the state of droplet distribution on the surface of a tablet. The apparatus, which is used to find the influence of plasticizer molecular weight on spreading droplet size of HPMC aqueous solutions, consists of three parts. The first part was the spray gun containing 100% of F12 as propellant. The second part was a polyamide sheet as a hydrophilic substrate and was held 40 cm from the spray gun perpendicular. The another part was the beam barrier, an aluminum plate (15*12*0.5 cm), was positioned between the gun and the sheet. Coating solutions (HPMC) with different grades, Methocel E5, E15 and E50, were sprayed on the sheet at room temperature. The droplet size distribution was analyzed by using light microscopy at least 300 circular droplets and /or the mean of two Martin diameters of noncircular droplet in the vertical and horizontal directions. They found that the higher polymer grade and the addition of plasticizer would increase in mobility and spreading properties of droplet on the substrate surface. The results obtained from this method show a better match to the real condition in the film-coating process than the other methods.

In the granulation, coating and spray-drying process, the atomization step is essential in order to control the physical properties of the product. In the pharmaceutical industry, three types of atomizers are commonly used: pneumatic, pressure and wheel. Nevertheless, in the present ultrasonic nozzle is widely used in other industries and sometimes applied to pharmaceutical application too.

Rodriguez L., et al. (1999) proposed preliminary evaluation of a new ultrasonic atomizer for spray-congealing processes. The preliminary results obtained in spray-drying technique using theophylline and fenbufen as model drugs and Cutina HR®, Compritol 888 ATO®, carnauba wax and stearic acid as excipients. Non-aggregate, spherical shaped microparticles and smooth surface were obtained with all the materials tested except stearic acid that seem imperfection. In vitro release of the drug depends on its solubility and on the excipient lipophilicity.

Levina M., Rubinstein M. et al. (2000) reviewed the application of ultrasound in pharmaceutical powder compression. Normally a tablet is formed by the compression of a powder mass between two punches within the confines of a die into a single unit. The compression of a powder is the compaction and consolidation of powder particles into a tablet specified strength. But all pharmaceutical materials do not undergo compaction and consolidation during tableting to produce coherent tablets. Poor compressibility of pharmaceutical powders is one of the main causes of tablet defect. These imperfections may be due to one or more of the following: low crushing strength, binding, stricking, filming, capping, lamination and cracking. High-intensity ultrasound improves the characteristics of the compression leading to optimize mechanical strength of the compacts without applying excessive compression force. Therefore, problems associated with high compression pressure may be overcome and tablets may be manufactured more economically and more consistently with ultrasound than by conventional pressure processes.

CHAPTER 3

FUNDAMENTALS

3.1 Fluidization

Fluidization is the operation by which fine solids are transformed into a fluidlike state through contact with a gas or liquid.

3.1.1 The Phenomenon of Fluidization

Pass a fluid upward through a bed of fine particles as shown in Fig. 3.1. At a low flow rate, fluid merely percolated through the void spaces between stationary particles. This is a fixed bed.

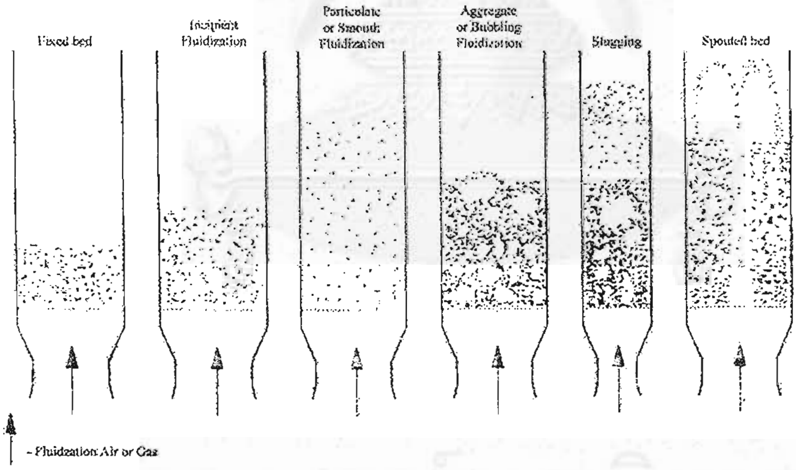

Figure 3.1 Characterization of Fluidized beds

(Redrawn from Fliudization Engineering, 1969)

With an increase in flow rate, particles move apart and a few are seen to vibrate and move about in restricted regions. This is the expanded bed.

At a still higher velocity, a point is reached when the particles are all just suspended in the upward flowing gas or liquid. At this point the fractional force between a particle and fluid counterbalances the weight of the particle, the vertical component of the compressive force between adjacent particles disappears, and the pressure drop through any section of the bed about equals the weight of fluid and particles in that section. The bed is considered to be just fluidized and is referred to as an incipiently fluidized bed or a bed at minimum fluidization.

In liquid-solid systems an increase in flow rate above minimum fluidization usually results in a smooth, progressive expansion of the bed. Gross flow instabilities are damped and remain small, and large-scale bubbling or heterogeneity is not observed under normal conditions. A bed such as this is called a particulately fluidized bed, a homogeneously fluidized bed, a smoothly fluidized bed, or simply a liquid fluidized bed.

Gas-solid systems generally behave in quite a different manner. With an increase in flow rate beyond minimum fluidization, large instabilities with bubbling and channeling of gas are observed. At higher flow rates agitation becomes more violent and movement of solids become more vigorous. In addition, the bed does not expand much beyond its volume at minimum fluidization. Such a bed is called an aggregative fluidized bed, a heterogeneously fluidized bed, a bubbling fluidized bed, or simply a gas fluidized bed. In a few rare cases liquid-solid systems will not fluidize smoothly and gas-solid systems will not bubble. At present such beds are only laboratory curiosities of theoretical interest.

Both gas and liquid fluidized beds are considered to be dense-phase fluidized beds as long as there is a fairly clearly defined upper limit or surface to the bed. However, at s sufficiently high fluid flow rate the terminal velocity of the solids is exceeded, the upper surface of the bed disappears, entrainment becomes appreciable, and solids are carried out of the bed with the fluid stream. In this state we have a disperse-, dilute-, or lean-phase fluidized bed with pneumatic transport of solids.

Consider briefly the quality of fluidization in a bubbling bed. Although the properties of solid and fluid alone will determine whether smooth or bubbling fluidization occurs, many factors influence the rate of solid mixing, the size of bubbles, and the extent of heterogeneity in the bed. These factors include bed geometry, gas flow rate, type of gas distributor, and vessel internals such as screens, baffles, and heat exchangers.

As an example consider slugging, a phenomenon strongly affected by the vessel geometry. Gas bubbles coalesce and grow as they rise, and in a deep enough bed they may eventually become large enough to spread across the vessel. Thereafter the portion of the bed above the bubble is pushed upward, as by a piston. Particles rain down from slug and it finally disintegrates. At about this time another slug forms and this unstable oscillatory motion is repeated. Slugging is usually undesirable since it increases the problems of entrainment and lowers the performance potential of the bed for both physical and chemical operations. Slugging is especially serious in long, narrow fluidized beds.

3.1.2 The Geldart Classification of Particles

A full classification of powders according to their behavior in fluidization is complex because their behavior depends on many particle properties. Geldart and co-worker have identified two parameters to classify powder for fluidization i.e. the particle size, the particle density. This classification, for fluidization by air ambient conditions, shows Fig. 3.2.

Powders in group A, sometimes referred to as slightly cohesive, (typically cracking catalysts), are size range 50 to 200 microns. This particles exhibit large bed expansion after minimum fluidization and before start of bubbling; the bubble size is limited.

Powders in group B (e.g. sand, pellets and granules) bubble at the minimum fluidization velocity and the bed expansion is small.

Group C (cohesive) is size range less than 20 microns. This group is difficult to fluidize at all, they exhibit a tendency to form channeling. The denser and larger the crystal are behave like group D. With group D the bed expansion is minimal, even less than for the group B. This group can form stable spouted beds if the gas is admitted only through a centrally-positioned hole. Moreover, the transition group AC, size range 20 to 50 microns, has been recognized as "semi-cohesive", between groups A and C.

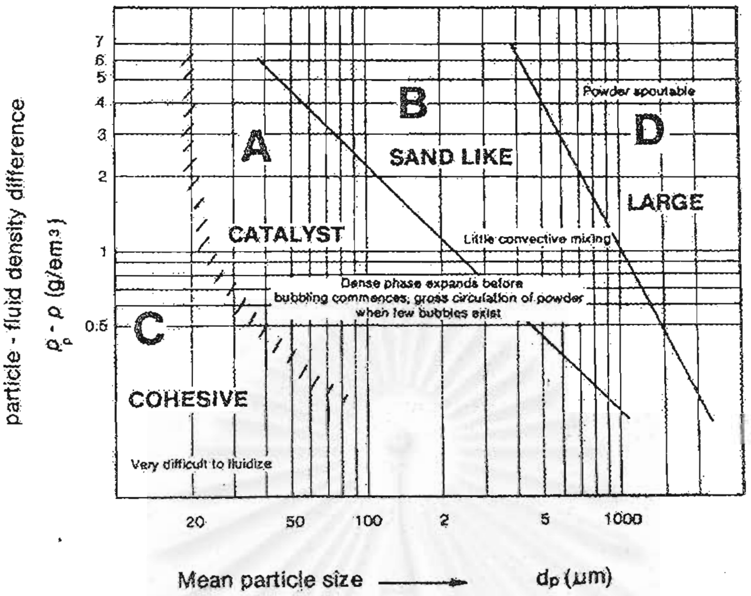

Figure 3.2 Diagram for classifying powders in fluidized bed

(Redrawn from Powder testing guide, 1987)

Group C (cohesive) is size range less than 20 microns. This group is difficult to fluidize at all, they exhibit a tendency to form channeling. The denser and larger the crystal are behave like group D. With group D the bed expansion is minimal, even less than for the group B. This group can form stable spouted beds if the gas is admitted only through a centrally-positioned hole. Moreover, the transition group AC, size range 20 to 50 microns, has been recognized as "semi-cohesive", between groups A and C.

The key fluidization properties of solids from the different groups appear in table 3.1.

Table 3.1 Summary of Group properties

	A	B	D
Most obvious Characteristic	Bubble-free range of fluidization	Starts bubbling at Minimum fluidization velocity	Coarse solids
Typical Pharmaceutical substrates	Microparticles	Pellets; granules; Light, small crystals	Tablets; capsules; Heavy, large crystals
1. Bed expansion	High	Moderate	Low
2. Deaeration rate	Slow, linear	Fast	Fast
3. Bubble properties	Splitting/recoalescence predominate Maximum size exists Large wake	No limit on size	No known upper Size Small wake
4. Solids mixing	High	Moderate	Low
5. Slug properties	Axisymmetric	Axisymmetric; Asymmetric	Horizontal voids, Solids slug, wall Slugs
6. Spouting	Not except in very shallow beds	Shallow beds only	Even in deep beds

3.2 Coating

3.2.1 Purpose of coating

The first coated pharmaceutical dosage forms were medication with sugar coatings for the purpose of masking unpleasant tastes and imparting a more elegant appearance. For a long time lasting gloss was therefore the major prerequisite. Nowadays there are other important reasons for pharmaceutical particle coating:

- protection of active ingredients against light, air and moisture
- increased mechanical stability during manufacture, packing and shipment
- protecting the active ingredients against the influence of digestive fluids
- ensuring their controlled release
- avoidance of side effect
- increasing drug safety by better identification

3.2.2 Types of coatings

Coatings materials usually consist of a mixture of substances. The matrix formers are responsible for the stability of the coating structure, and they also determine the coating process. Depending on the type of matrix former or binder used, three coating categories can be distinguished.

1. Coating with sucrose and other sugars: It permits application of copious amount of mass to the core and is widely used in the manufacture of pharmaceuticals and confectionery. Coating pans are the preferred type of equipment, belt coaters being the exception.

2. Hot melts: It also adds a considerable amount of mass while cooling is required for solidification of the coating on the core. They are mainly use for confectionery. The most important raw materials are fats, mostly cocoa fat and the sugar/alcohol mixture xylitol/sorbitol. The process is conducted in pans or on belts.

3. Film coatings: They require less material, forming thin membranes that largely follow the contours of the substrate, e.g. scores and engravings. The film formers affect the partly pH-dependent solubility and selective permeability of coatings. Coating pans and fluidized bed equipment are generally used for processing.

Film and sugar coatings differ substantially in thickness and therefore also in the necessary mass of coating material (table 3.2).

Table 3.2 Comparison between film and sugar coatings

	Sugar-coated tablets	Film-coated tablets
Coating thickness (mm)	0.2 - 0.5	0.05 – 0.03
Film former (mg/cm^3)		0.5 – 3
mg mass/cm^2	30 – 100	1 – 12

3.2.3 Fundamentals of film coating

Among these three coating methods, film coating has gained wider attention especially for application of controlled release. Uniformity of distribution of the film and evaporative efficiency to inhibit core penetration by solvents or water are common to the three types of fluidized bed processing: top-spray, bottom-spray, tangential-spray. However, each of the techniques has limitations, and they are by no means equivalent.

Application of a film to a solid is indeed very complex. A layer of coating does not occur during a single pass through the coating zone, but relies on many passes to produce complete coverage of the surface. Droplet formation, contact, spreading, coalescence, and evaporation, as illustrated in figure 3.3, are occurring almost simultaneously during the process.

The nozzles typically used in fluidized bed coating process are binary type nozzles: liquid is supplied at a low pressure and is sheared into droplets by air. Droplet size and distribution are more controlled with this type of nozzle than with a hydraulic nozzle, especially at low liquid flow rates. However, the air used for atomization also contributes to evaporation of the coating solvent. This evaporation results in increasing the droplet's viscosity, and it may inhibit spreading and coalescence upon contact with the core material. Another factor affecting droplet viscosity is the distance that the droplets travel through the primary evaporation media (the fluidization air) before impinging the core. This problem becomes more stressed with the use of organic solvents which evaporate much more quickly than water. Films whose visocity is very sensitive to changes in solids concentration

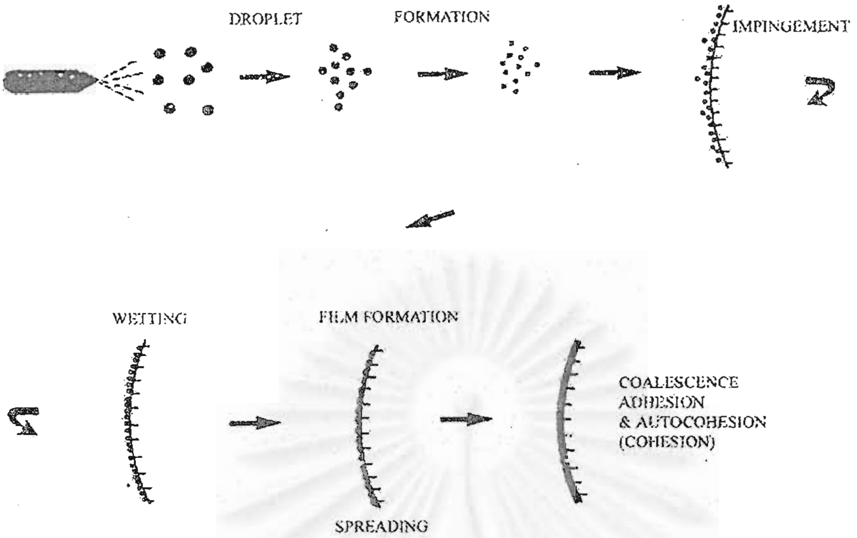

Figure 3.3 Schematic of the film-coating process

(Redrawn from Pharmaceutical dosage forms, 1990)

also give rise to such problem. In all three fluidized bed processes, the nozzle is positioned to minimize droplet travel distance.

3.2.4 Process variables

The rate of evaporation of the coating application media can significantly affect film formation in both aqueous and organic solvent systems. Fluidization air volumetric flow rate, temperature, and humidity are the three factors, which have strong influence on efficiency of coating process.

For organic solvents, low fluidization air temperature may be chosen to accommodate the solvent's low heat of evaporation. The danger in allowing absolute humidity to vary is that enthalpy, which determines evaporation rate, increases at a given dry bulb temperature as the absolute humidity increases. Additionally, if absolute humidity is high, evaporative cooling by the solvent in the coating zone may locally depress the air temperature below the dew point, causing condensation of water onto the substrate surface, as the film forming. If the film is incompatible with water, the coating would not perform as desired.

Consistency in absolute humidity is recommended, but removal of all moisture is not required. In fact, in many organic solvents coating processes, a quantity of moisture in the process air is usually helpful in dispelling static electricity, which develops after the surface of the particles is completely covered.

Coating uniformity is a result of the rapid cycling of particles or the number of times the particles are exposed to the spray. The rate at which the coating is applied (on a solids basis) is dependent on the solution concentration and the spray rate. However, the droplet size and spreading characteristics will be affected by the increased viscosity.

Spray rate is dependent on three factors: (1) capacity of air for the solvent being used; (2) the tackiness of the coating being applied; and (3) the speed with which the particles travel through the coating zone. The rate-limiting factor is generally the tackiness of the coating solution as it changes from a liquid to a solid. In the fluidized bed process, coating is applied to particles suspended in the air stream. However, particle-machine and particle-particle collisions do occur and have strong effect on the coating efficiency.

3.2.5 Factors affecting the quality of film coatings

Film coating is a process in which the results obtained are attributable to the complex interaction of numerous factors. In order to better understand those factors that influence the quality of the finished product, it is necessary to examine the factors that have an effect on the coating phenomena. These factors are interaction between the core material (substrate) and the applied coating, the drying process and the uniformity of distribution of substrate in the equipment during coating process. Some of these important factors are spray equipment, solid content of coating liquid and fluidizing air velocity etc.

3.2.6 Ingredients used in film coating

In general, film coating formulations consist of an extensive list of ingredients, including film formers, plasticizers, colorants, surfactants, flavors, glossing agents, and solvents. Nowadays, typical formulation contains polymer, plisticizer, colorant and solvent.

Film coatings consist mainly of polymer, which are applied to the core in the form of solutions or dispersions in which other excipients are dissolved or suspended. After drying the solvents or dispersing agents, the polymer and other excipients remain on the cores as a coherent, uniform film.

Pharmaceutical film coating formulations consist of organic solutions and aqueous dispersions. Film coating which use organic solvents produces good results but has a limitation due to its serious drawbacks such as associated flammability, toxicity, and environmental pollution hazard. However, this technique is still widely used and probably always have application where specialized polymers are used for coating.

1. Polymer

A polymer is a large molecule built up by the repeat of small, simple chemical units. The repeat unit of the polymer is usually equivalent to the monomer, or stating material from which the polymer is formed. In the majority of film coating formulations, the polymer is the major ingredient. Consequently, this material has the greatest impact on the final properties of the coating.

Polymers have various chemical types and grades. When selecting a polymer for film coating, it is thus necessary to define this material in terms of chemical structure, molecular weight, and molecular distribution because molecular weight characteristics of the polymer have a significant effect on coating properties. Nowadays, there are numerous commercially synthetic polymers, which have found wide range of usage in pharmaceutical formulations.

For aqueous-based coating systems, the polymers can be divided into essentially two classes: aqueous-soluble polymers and water-insoluble or pH-dependent soluble polymers.

The most commonly used aqueous-soluble polymers consist primarily of:

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The most commonly used aqueous-soluble polymers consist primarily of:

1.1 Acrylate copolymers: Eudragit E® (cationic copolymer based on dimethylaminoethyl methacrylate and other neutral methacrylate)

1.2 Cellulosic polymers: Carboxymethylcellulose sodium, Hydroxypropyl-cellulose, Hydroxypropyl methylcellulose, Methylcellulose, Methyl hydroxycellulose

Polyethylene glycols, Povidone

On the other hand, Enteric coatings constitute the major portion of the water-insoluble or pH-dependent polymers. These polymers can be solubilized by adjusting the pH of the coating solution, or they can be formulated to be suspended in the aqueous media and applied as insoluble polymer particles. The water-insoluble polymers are used when an enteric coating or a special controlled-release delivery system is desired. Some of the most common insoluble polymer candidates are: Methacrylic acid copolymer, Eudragit L and S®, Cellulose acetate phthalate, Hydroxypropyl methylcellulose phthalate, Polyvinyl acetate phthalate, Ethylcellulose.

Among these coating polymers, HPMC is one of the most widely employed coating materials and it is of interest in this work. Therefore information of HPMC will shortly introduced as follows,

Hydroxypropyl methylcellulose (HPMC)

PhEur: Methylhydroxypropylcellulosum

USPNF: Hydroxypropyl methylcellulose, Pharmacoat®, Methocel®

Type of HPMC for film coating: It is available in several grades, which vary in viscosity and extent of substitution. HPMC defined in the USP XXII specifies the substitution type by appending a four digits number to the nonproprietary name. The first two digits refer to the approximate percentage content of the methoxy group (OCH_3). The second two digits refer to the approximate percentage content of the hydroxypropoxy group ($OCH_2CHOHCH_3$). The substitution affects the solubility-temperature relationship.

The majority of HPMC used in pharmaceutical products is primarily used as a tablet binder, in film coating and as an extended release tablet matrix. Concentrations of between 2-

5% w/w may be used as a binder in either wet or dry granulation processes. HPMC 2910 of low-labeled viscosity (3-15 mPa.s) is commonly used in film coating.

Structure formula.

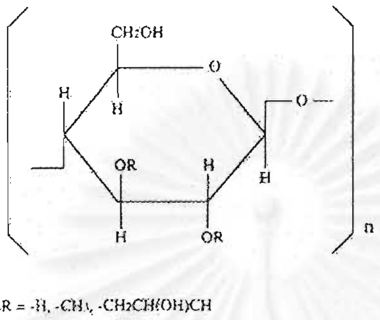


Figure 3.4 Hydroxypropyl methylcellulose

(Redrawn from Handbook of pharmaceutical excipients, 1994)

Properties of HPMC: HPMC is an odorless and tasteless, white or creamy-white colorless fibrous or granular powder.

Ash: 1.5-3.0% depending upon the grade.

Melting point: 190-200 °C

Moisture content: depending upon the initial moisture content and the temperature and relative humidity of the surrounding air.

Solubility: soluble in cold water, forming a viscous colloidal solution; practically insoluble in chroloform, ethanol (95%) and ether, but soluble in mixtures of ethanol and dichloromethane, and mixtures of methanol and dichloromethane.

Specific gravity: 1.26

2. Plasticizers

Plasticizers are usually high-boiling liquids – sometimes also polymeric substances – of low molecular weight that should disperse as homogeneously as possible in the film formers to be modified. By interacting with the film-forming polymer, they alter certain physical and mechanical properties by enhancing the mobility of the polymer chains. Plasticizers are added for reasons of processing technique and to achieve specific properties in use, e.g. to reduce the brittleness of the film former, to increase their flexibility, facilitate their distribution on the substrate and to improve film formation.

Plasticizers act by penetrating between the chains of the film-forming polymer, thereby reducing the interactions among the polymer chains in the film. The plasticizer molecule increase the flexibility of the polymer chain segments furthers apart of altering the average chain conformation through molecular effects. The glass temperature of the system decreases as a result of the increased segmental mobility, and the film becomes plastic in the temperature range for processing or use.

Plasticizers for pharmaceutical purpose must be

- colorless
- odorless
- non-volatile
- thermally stable
- water-resistant
- chemically resistant
- non-migrating in films
- physiological harmless

The effectiveness of plasticizers in the coating formulation depends on further factors, however, e.g. other excipients, solvent systems, application method etc.

In this work, PEG used as plasticizer in the coating formulation so physical properties of PEG is described below.

<ins>Polyetylene Glycol</ins> (PEG)

PhEur: Macrogolum 1000

USPNF: Polyethylene glycol

Formula: $HOCH_2(CH_2OCH_2)_mCH_2OH$

Where m represents the average number of oxyethylene groups.

Properties of PEG6000: PEG is available in the form of lumps, flakes or powders. PEG used as gloss enhancers, glidants and lubricants, plasticizer type 6000 also as a coating substance. PEG is soluble in water, hot alcohols and chlorinated hydrocarbons.

Molecular weight: 6000

Melting point: 55 – 63 °C

Density: 1.12 g/cm^3

Solubility in water at 25 °C: 1,900 mg/ml

3. Opaquants and Colorants

The colorant can be either solubilized in the solvent system of suspended as insoluble particles. Colorants are included in many films coating formulations to improve the appearance and visual identification of the coated product.

The most brilliant colorants are provided by certified Food, Drug and Cosmetic (FD&C) or Drug and Cosmetics (D&C) dyes and lakes. Lakes are prepared from dyes by precipitating the colorant with alumina or talc carriers. Lakes are water-insoluble and provide the most reproducible tablet colors.

Sunset Yellow. It is generally used as coloring agent for foods and drugs.

Formula: $C_{16}H_{10}N_2Na_2O_7S_2$

Structure:

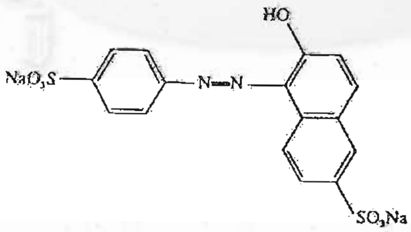


Figure 3.5 Sunset Yellow

(Redrawn from Handbook of pharmaceutical excipients, 1994)

Molecular weight: 452.4

Appearance: reddish yellow powder. Aqueous solutions are bright orange colored.

Solubility in water at 25 °C: 70 g/l, slightly soluble in ethanol, in soluble in vegetable oil.

Absorption maximum: 482 nm

Incompatibilities: poorly compatible with citric acid, saccharose solutions and saturated sodium bicarbonate solutions. Incompatible with ascorbic acid, gelatin and glucose.

3.2.7 Fluidization in the coating process

1. Top Spray Coating

The most significant characteristics of the top spray method is that the nozzle sprays countercurrently or down, into the fluidizing particles. The fluidization pattern is random and unrestricted. As a result, controlling the distance the droplets travel before contacting the substrate is impossible.

The top spray coating system is the least complicated of the three machines. It has the largest batch capacity, and downtime between batches can be only minutes. Its biggest disadvantage is that its applications are somewhat limited.

2. Wurster Bottom Spray Coating

This type is affected by the air distribution plate configuration and the partition height. The air distribution plate at the base of the coating chamber is divided into two sections. The open area of the plate, which is under the partition, is typically nearly fully open, allowing a high air volume and velocity to accelerate the substrate vertically past a spray nozzle that is mounted in the center of the orifice plate. On the other hand, the closed section is nessary for supporting the particle bed.

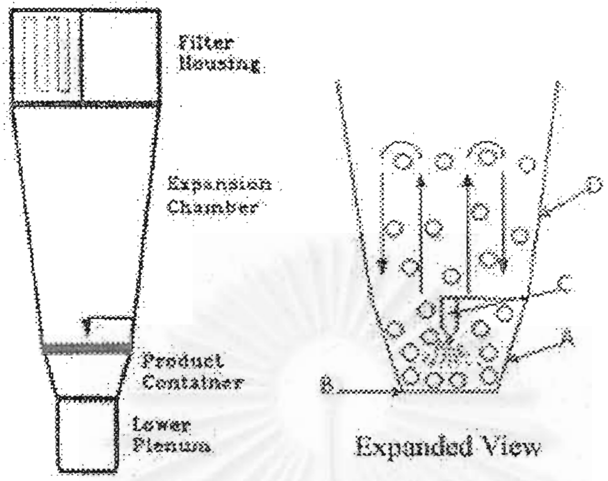


Figure 3.6 Top spray coater: (a) product container; (b) air distribution plate (c) spray nozzle; (d) expansion chamber.

A second key process variable in Wurster processing is the height that the partition sits above the orifice plate. In general, the smaller the particles, the smaller the gap must be. This gap controls the rate of the substrate flow into the spray zone.

The Wurster system has the widest application range of both water and organic solvents. The primary disadvantages of this system are that it is somewhat complicated, it is the tallest of the three types of fluidized bed machines, and the nozzles are inaccessible during the processing.

3. Tangential Spray Coating

The rotary or tangential spray system, also an immersed-nozzle, concurrent-spray technique, appears to offer film characteristics similar to the Wurster system. This systems can be used with both water and organic solvents. The significance in this equipment is that the substrate is placed into the product container and put into motion by the rotor disc, which is adjusted by spinning at high speed to impart significant energy into the bed. The disc, which is typically smooth, may be configured with a variety of surfaces from grooves to a multi-pyramid type of waffle plate. The gap at its perimeter is set small to allow a high velocity but low flow of air. Inlet air temperature is maintained at or near ambient.

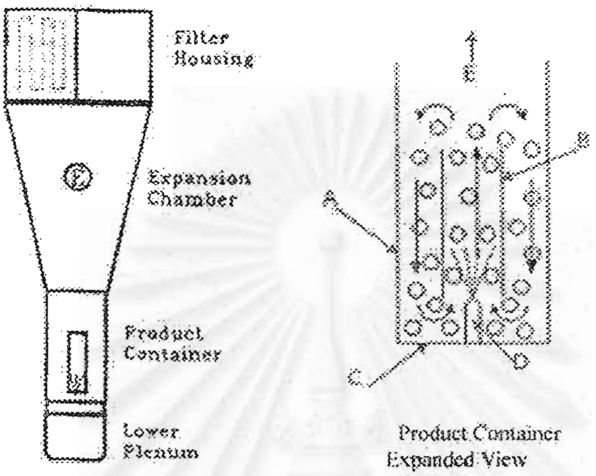


Figure 3.7 Wurster bottom spray coater: (a) coating chamber; (b) partition; (c) air distribution plate; (d) Spray nozzle; (e) expansion chamber.

The process variables unique to the rotor system primarily involve disc slit width, disc configuration, and rotation speed. The volume of the fluidization air is controlled independently by adjusting the slit width.

Different from the Wurster system, the rotary tangential spraying system has a relatively wide application range, is the shortest machine in height of the three, and allows nozzle access during processing. It has the capability to produce high dose pellets and apply coating for all types of release. Its primary disadvantage is that it exerts the greatest mechanical stress of the three methods and, thus, is discouraged for use with friable substrates.

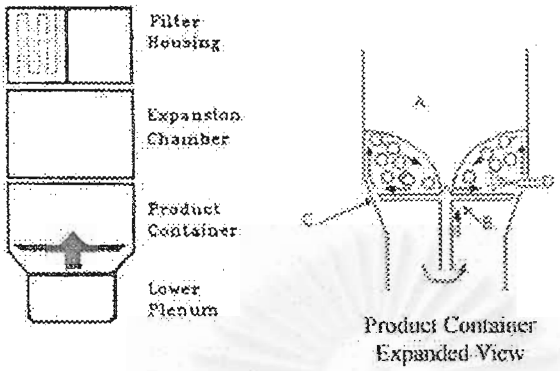


Figure 3.8 Tangential spray coater: (a) produce chamber; (b) variable speed disc; (c) disc gap or slit; (d) spray nozzle.

3.2.8 Problems in film coatings

Various problems occur during the coating process can be attributed to an improper coating formulation or processing condition. Some of problems are discuss below.

1. Defective coatings

Defective coatings are caused by poor quality of the cores and/or inadequate formulations, application or lack of process control.

2. Cracks in the film along edges

They are caused by too much internal stress, owing to differences in the thermal expansion of film and core. Cracks may also be the result of swelling of the core during the coating operation.

3. Chipping

If the film does not adhere properly to the substrate surface, or its solids content too high, or it is too brittle foe want of plasticizer, this may lead to chipping. The problem can only be eliminated by total revision and optimization of the formulation for core and/or coating.

4. Blistering

If drying of spraying is performed at high speed, solvent may be retained in the film, which evaporates on post-drying and may then form blisters in the film. Normally this problem can be solved by lowering the inlet air temperature and reducing the spray rate. Moreover, blisters may also form between film and core if the adhesion of the film is inadequate.

5. Bridging

This is the phenomenon where the film fails to follow the contours of the core particles over break lines of engravings and settles in these without adherence the substrate.

The bridging forces in the film exceed the interfacial forces between film and core. This problem can be eliminated either by changing the tablet surface or by adding plasticizer.

6. Picking

If the film surface contains substances that are not molecularly dispersed and start to melt at the core bed temperature of the film-coating process (e.g. stearic acid, PEG) these substances may interfere with the film-forming polymers and produce holes in the film surface. This can be prevented either by replacing these substances or by lowering the core bed temperature.

Holes and defects in the film may also be caused by too rapid spraying at too low a temperature. As a result, tablets stick together and tear off fragments of each other's film coating during drying.

7. Embedded particles

Particles broken off from the cores are embedded in the film during spraying. This may happen if the cores lack mechanical stability.

8. Dull surfaces

This happens most frequently if the droplets start to dry before reaching the cores. In this case they are too viscous to form a smooth film.

Improvement can be achieved by lowering the inlet air temperature and reducing the atomizing air quantity or pressure. Other remedial measures are additions of the substances that enhance film formation e.g. plasticizers or extra solvents.

9. Roughness

Roughness within the film is caused spray droplet. It may also be the result of porous cores, a very high concentration or relative molar mass of the film-forming pigments too large in number of size and excessive film thickness.

10. Orange Peel effect

The caused are too rapid drying or spraying, film layers that are too thick, or insufficient droplet coalescence. Orange peel may also form when small droplet dry before reaching the substrate surface or before they are able to coalesce.

Orange peel can be avoided by adjusting the spray rate and inlet air temperature.

11. Twinning

The core stick permanently together. Possible reasons are excessive spraying, a very tablet shape or very high bands.

3.3 ATOMIZATION

Sprays may be produced in various ways. There are several basic processes associated with all methods of atomization, such as the hydraulics of the flow with in the atomizer, which governs the turbulence properties of the emerging liquid stream, the development of the jet or sheet and growth of small disturbances, which lead to disintegration into filaments and then droplet.

3.3.1 Atomizers

Atomization is often accomplished by discharging the liquid at high velocity into a relatively slow-moving stream of air or gas. Notable examples include the various forms of pressure nozzles and also rotary nozzles that eject the liquid at high velocity from the periphery of a rotating cup or disk. An alternative approach is to expose a relatively slow-moving liquid to a high-velocity airstream. Types of atomizers classify by operating condition.

1. Pressure nozzles. Pressure atomizers rely on the conversion of pressure in kinetic energy to achieve a high relative velocity between the liquid and the surrounding gas. They include simplex nozzle, wide-range and fan spray nozzle.

1.1 Simplex nozzles. (Pressure-swirl)

A circular outlet orifice is preceeded by a swirl chamber into which liquid flows through a number of tangential holes or slots. The swirling liquid creates a core of air or gas that swirl chamber. Finest atomization occurs at high delivery pressures and wide spray angles. There are two basic types of simplex nozzle.

1.1.1 Solid-cone spray. The spray is comprised of droplets that are distributed fairly throughout its volume. The main drawback of this type is relatively coarse atomization, the droplets at the center of the spray being larger than near the periphery.

1.1.2 Hollow-cone spray. The drops are concentrated at the outer edge of a conical spray pattern. The nozzles provide better atomization and their radial liquid distribution is also preferred for many industrials purpose.

Figure 3.9 shows spray produced by pressure-swirl nozzle and pattern of spray in this type depended on air pressure (shown in figure 3.10).

1.2 Wide-range Nozzles.

The nozzles provide good atomization over the entire operating range of liquid flow rates without resorting to impractical levels of pump pressure. The most types are described below.

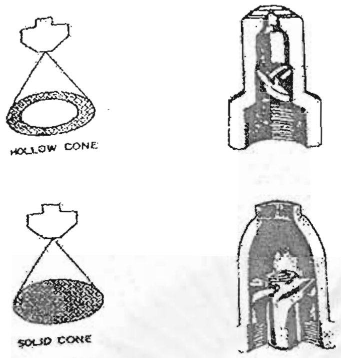


Figure 3.9 Solid cone spray and Hollow cone spray pressure nozzle

(Redrawn from Atomization and sprays, 1989)

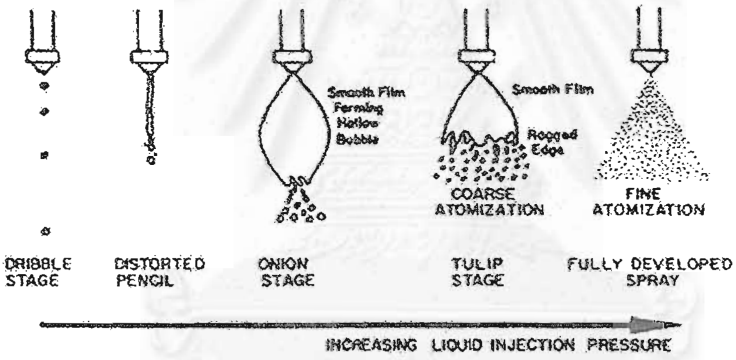


Figure 3.10 Spray development with increase in liquid injection pressure

(Redrawn from Atomization and sprays, 1989)

1.2.2 Duplex. A drawback of all types of pressure nozzles is that the liquid flow rate is proportional to the square root of the injection pressure differential. In practice, this limits the flow range of simplex nozzles to about 10:1. The duplex nozzle overcomes this limitation by feeding the swirl chamber through two sets of distributor slots (figure 3.11). At low flow rates all the liquid to be atomized flow into the swirl chamber through the primary slots. At some predetermined pressure level a valve opens and admits liquid into the swirl chamber through the secondary slots. Duplex nozzle allow good atomization to be achieved over a range of liquid flow rates of about 40:1 without the need to resort to excessively high delivery pressure.

1.2.3 Dual orifice. Diagram of dual orifice is shown in figure 3.12. This is similar to the duplex nozzle except that two separate swirl chambers are provided, one for the primary flow and the other for the secondary flow. The two swirl chambers are housed concentrically within a single nozzle body to form a "nozzle within a nozzle". Dual-orifice nozzles offer more flexibility than duplex nozzles.

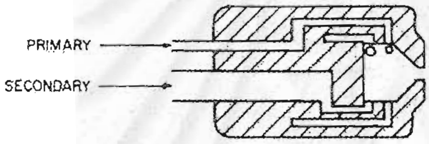


Figure 3.11 Duplex nozzle

(Redrawn from Atomization and sprays, 1989)

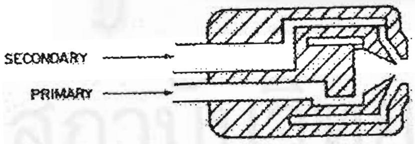


Figure 3.12 Dual orifice nozzle

(Redrawn from Atomization and sprays, 1989)

1.3 Fan spray nozzles.

These nozzles are used in the coating industry, in some small annular gas turbine combustors, and in other special applications. Arranging for a round liquid jet to impinge on a curved surface forms the spray. This arrangement produces a wide, flat relatively coarse spray pattern containing a fairly uniform distribution of droplets (figure 3.13). The nominal spray pattern is 120° or more, depending on size. It is the most widely used type fan spray nozzle, producing a narrow elliptical spray pattern with tapered edges that provide uniform distribution when overlapped. Excellent atomization and patterns can be obtained with viscous and non-Newtonian materials.

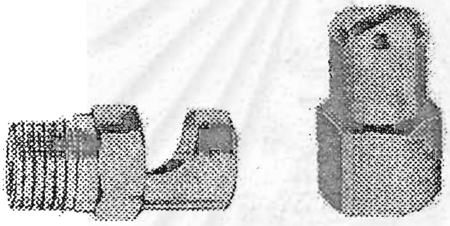


Figure 3.13 Fan spray nozzle

(Redrawn from Atomization and sprays, 1989)

2 <u>Rotary nozzles</u>. Liquid is fed into rotating surface, where it spreads out fairly uniformly under the action of centrifugal force. The rotating surface may take the form of a flat disk, vaned disk, cup or slotted wheel. The nozzles have been to atomize successfully liquids varying widely in viscosity. An important asset is that the thickness and uniformity of the liquid sheet can readily be controlled by regulating the liquid flow rate and the rotational speed.

Generally, it is found that atomization quality is improved by

1. Increase in rotational speed.
2. Decrease in liquid flow rate.
3. Decrease in liquid viscosity.
4. Serration of the outer edge.

Moreover, to obtain a uniform film thickness, and hence a more uniform droplet size, the following conditions should be met

1. The centrifugal force should be large in comparison to the gravitational force.
2. Cup rotation should be vibrationless.
3. Liquid flow rate should be constant.
4. Cup surfaces should be smooth.

The main drawback of the flat disk nozzle is that slippage occurs between the liquid and the disk, especially at high rotational speeds (figure 3.14). In consequence, the

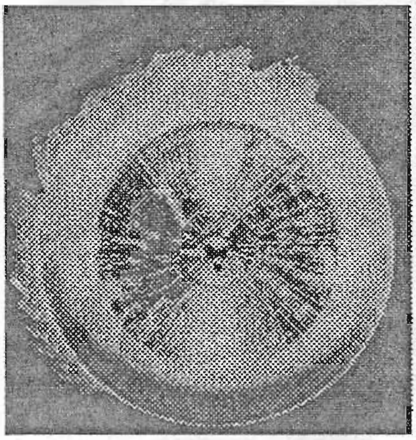
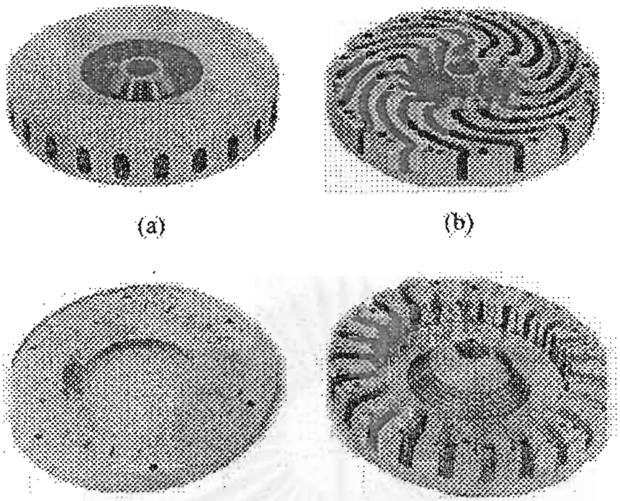


Figure 3.14 The liquid slide from the rotary disk nozzle

(Redrawn from Atomization and sprays, 1989)



(a) (b)

(c)

Figure 3.15 Type of rotary nozzle: (a) Straight vanes; (b) Curved vanes; (c) Wear-resistant vanes (inserts)

(Redrawn from Atomization and sprays, 1989)

liquid is ejected from the edge of the disk at a velocity much lower than the disk peripheral speed. This problem is overcome in commercial nozzles by the use of radial vanes (figure 3.15).

3 Air-assist nozzles. In this type of nozzle the liquid is exposed to a stream of air or stream flowing at high velocity. This type of nozzle categorizes two types: internal mixing, external mixing (figure 3.16 and 3.17).

3.1 Internal-mixing.

In this type, the spray cone angle is a minimum for maximum airflow, and the spray widens as the airflow is reduced. This type of atomizer is very suitable for highly viscous liquids, and good atomization can be obtained to very low liquid flow rates.

3.2 External-mixing.

External-mixing types can be designed to give a constant spray angle at all liquid flow rates, and they have the advantage that there is no danger of liquid finding its way into the airline. However, their utilization of air is less efficient, and consequently their power requirements are higher.

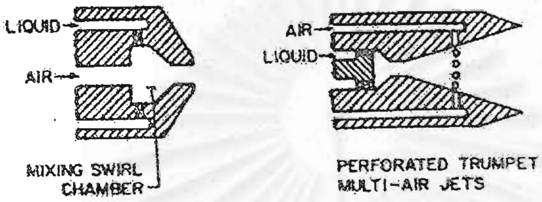


Figure 3.16 Internal-Mixing

(Redrawn from Atomization and sprays, 1989)

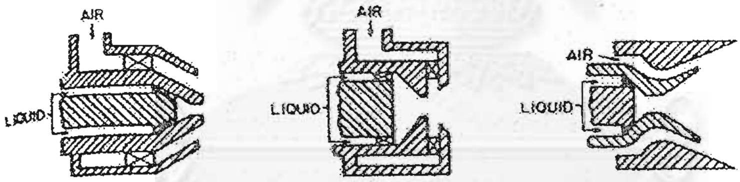


Figure 3.17 External-Mixing

(Redrawn from Atomization and sprays, 1989)

4 Airblast nozzles. In principle, the airblast nozzle functions in exactly the same manner as the air-assist nozzle. The main difference between the two systems lies in the quantity of air employed and its atomizing velocity, which is usually around 120 m/s.

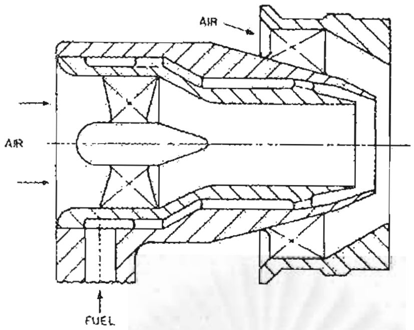


Figure 3.18 Airblast nozzle

(Redrawn from Atomization and sprays, 1989)

5 Electrostatic nozzles. A basic requirement for atomizing any liquid is to make some area of its surface unstable. The surface will then rupture into filaments, which subsequently disintegrate into droplets. In electrical atomization, the energy causing the surface to disrupt comes from the mutual repulsion of like charges that have accumulated on the surface. An electric pressure is created that tends to expand the surface area. This pressure is opposed by surface tension forces, which tend to contact or minimize surface area. When the electrical pressure exceeds the surface tension forces, the surface becomes unstable and droplet formation begins. Droplet size is a function of the electrical pressure, the liquid flow rate, and the physical and the electrical properties of the liquid.

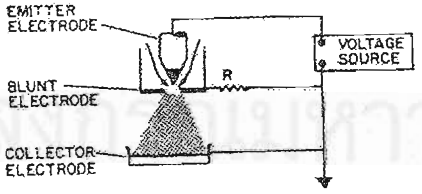


Figure 3.19 Electrostasitc nozzle

(Redrawn from Atomization and sprays, 1989)

6 Ultrasonic nozzles. This type of nozzle categorizes two types: ultrasonic resonator, ultrasonic piezoelectric.

6.1 Ultrasonic resonator.

This nozzle produces ultrasound wave from a resonator. The liquid and air are ejected from the different orifice. The liquid is deliveryed through an orifice into the nozzle outlet channel, where a high velocity air streams provides a shearing force to break up the liquid. Then, the air stream carrying the drop collides with a resonator placed in front of the nozzle outlet channel that generates a field of high frequency, ultrasonic sound waves. The echo of the sound wave makes a shock wave at the gap between orifice nozzle and the resonator. The exposure of the liquid to this field causes the drops to break up into an even finer spray.

6.2 Ultrasonic piezoelectric.

The liquid to be atomized is fed through or over a transducer and horn, which vibrates at ultrasonic frequencies (beyond the audible range i.e. 20 kHz-100kHz) to produce the short wavelengths necessary for fine atomization. The system requires a high-frequency electrical input, two piezoelectric transducers, and a stepped horn. The concept is well suited for applications that require very fine atomization and a low spray velocity.

A most useful attribute of the ultrasonic nozzle is its low spray velocity. This makes it an easy matter to entrain the spray in a moving stream and convey the droplets in a controlled manner as a uniform mist. This is especially important in coating applications and in such process as humidification, product moisturizing, and spray drying.

Another asset of the ultrasonic nozzle is its ability to provide very fine atomization at the extremely low flow rates required for pharmaceutical (nebulizers, term in medicine) and lubrication processes.

Ultrasonic nozzle is shown in figure 3.20 and 3.21. Figure 3.22 depicts the amplitude of a standing wave.

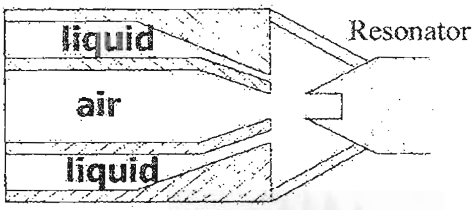


Figure 3.20 Ultrasonic resonator

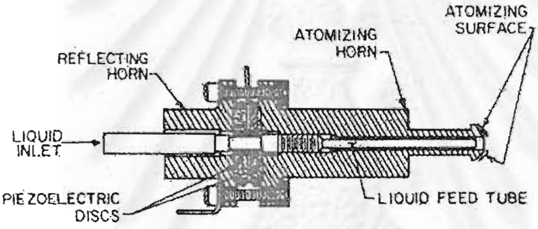


Figure 3.21 Ultrasonic piezoeletric

(Redrawn from Atomization and sprays, 1989)

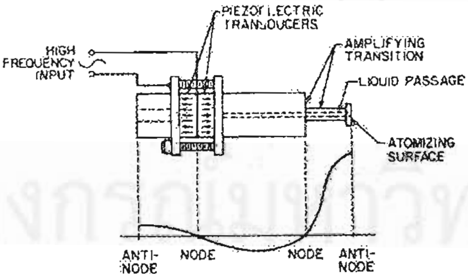


Figure 3.22 Standing wave pattern in ultrasonic nozzle

(Redrawn from Atomization and sprays, 1989)

The relative merits of various types of nozzles are listed in table 3.3.

Table 3.3 Relative merits of various types of nozzles

Type	Description	Advantages	Drawbacks
Pressure nozzle	Simplex	1. Simple, cheap 2. Wide spray angle (up to 180°)	1. Needs high supply Pressures 2. Cone angle varies with pressure differential and ambient gas density
	Duplex	Same as simplex, plus good atomization over a very wide range of liquid flow rate	Spray angle narrows as liquid flow rate is Increased
	Dual orifice	1. Good atomization 2. Turndown ratio as High as 50:1 3.Relatively constant spray angle	1.Atomization poor in transition range 2.Complexity in design 3.Susceptibility of small passages to blockage
Rotary	Rotary cup	Capable of handing slurries	May require air blast around periphery

Table 3.3 (continue)

Air assist	Internal mixing	1.Good atomization 2.Large passages prevent clogging 3.Can atomize high-viscosity liquids	1.Liquid can back up in air line 2.Reqkuires auxiliary metering device 3.Needs external source of high pressure air or steam
	External mixing	Same as internal mixing, plus construction prevents backing up of liquid into the air line	1.Needs external source of air or stream 2.Does not permit high liquid/air ratios
Airblast	Plain Jet	1.Good atomization 2.Simple, cheap	1.Narrow spray angle 2.Atomizig performance inferior to prefilming airblast
Electrostatic		Very fine atomization	Cannot handle high flow rates
Ultrasonic		1.Very fine atomization 2.Low spray velocity	Cannot handle high flow rates

3.3.2 Measurement of droplet size distribution

The various methods employed in droplet size measurement may be grouped conveniently into three broad categories.

1. Mechanical
    - Droplet collection on slides or in cells
    - Moltern-wax and frozen-droplet techniques
    - Cascade impactors
2. Electrical
    - Charge-wire and hot-wire techniques
3. Optical
    - Imaging – photography, holography
    - Nonimaging – single-particle counters, light scattering, Malvern particle Analyzer

1.Mechanical Methods

These usually involve the capture of a sample of the spray on a solid surface or in a cell containing a special liquid. The drops are then observed, or photographed, with the aid of a microscope. The method is fairly simple and has many variations.

1.1 Collection of droplets on slides

With this technique a solid surface, usually a glass slide, is covered with a suit able coating, which must be of very fine grain structure to make distinct the impression created by very small droplets. A very fine grain structure may be obtained by burning a kerosene-soaked wick under the glass to produce a thin coating of soot, or by burning a magnesium ribbon to deposit a thin layer of magnesiumoxide.

After the slide is exposed to the spray, the sizes of the droplet impressions are measures, sometimes by means of a microscope fitted with traversing scale, but more usually with an image analyzer computer. These sizes are then converted to actual droplets sized using correction factor. The problem's this method consist of 3 factors:

- Fraction of the slide area should be covered by droplets. If too many droplets are collected, the probability of error due to overlap is high and droplet counting become tedious. On the other hand, if too few droplets are collected, the sample may not be representative of the spray.

- Other important considerations are droplet evaporation and collection efficiency. The lifetime of small droplets is extremely short. For example, a water droplet that is 10 μm in diameter has lifetime of about 1 s in a 90% relative humidity atmosphere. Thus, evaporation effects are very significant in the measurement of fine spray. Collection efficiency is especially important with airblast nozzles, owing to the flow field created around the collecting surface. The large droplets have enough inertia to hit the surface, but the small droplets tend to follow the streamlines. For these reasons, droplet size data for airblast nozzles obtained by direct droplet collection tend to indicate larger than actual size.

- The collection of droplets on coated slides is the determination of the correction factor by which the diameter of the flattened droplet must be multiplied to obtain the original diameter of the spherical volume. Its value depends on liquid properties, notably surface tension, and on the nature of the coating employed. For example, with oil droplets the correction factor is around 0.5 for a clean glass surface and 0.86 for an magnesium-coated slide.

1.2 Collection of droplets on cells

An improvement on the coated-slide technique is one in which the droplets are caught on a target where they are held suspended while they are counted and measurement. This method use the target microscope slides coated with a special liquid in which the droplet would not dissolve but would remain stable and suspended. An alternative approach is to collect the droplets in a cell containing a suitable immersion liquid. This method has three advantages over collection on a slide: (1) the droplets remain almost perfectly spherical, (2) evaporation is prevented, and (3) provided on splitting of the droplet occurs on hitting the immersion liquid, the true sizes of the droplets are obtained and can be measured directly. The method cannot be applied satisfactorily to coarse sprays due to the risk of disintegration of the largest droplets on impact with the immersion liquid. The problem of droplet breakup can be alleviated to some extent by choosing immersion liquids of low viscosity and surface tension. After droplet settling at the bottom of the cell, the droplets are photographed at high magnification. The magnified droplet images are then processed and the final computer determines mean and median droplet diameters.

1.3 Molten wax technique

The basic idea is that paraffin wax, when heated to a suitable temperature above its melting point, has physical properties close to those of aviation kerosene (density 780 kg/m^3; surface tension, 0.027 kg/s^2; kinematic viscosity, 1.5x10^{-6} m^2/s). The molten wax is ejected into the atmosphere of a large pressure vessel, where the droplets rapidly cool and solidify. The sample is then subjected to a sieving operation in which the wax droplets are separated into size groups. Each size group is weighed to obtain the volume (or mass) fraction in each size range. Thus the cumulative volume distribution and mass median diameter are measured directly without the large expenditure of time and personal associated with the sizing and counting of multitudinous individual droplets. Furthermore, the number of droplets in a sample runs into millions, so clearly the technique does not suffer from a sample size that is too small to be statistically accurate.

One serious disadvantage of the hot wax technique is the limited choice of materials that can be used conveniently. If the properties of any given liquid are different from those of the simulant, it is necessary to establish the effect of these properties (notably surface tension and viscosity) on the atomization process. Other drawbacks of the method are the practical problems associated with preheating the wax and the error incurred because of change on the physical properties of the wax droplet as it rapidly cools after leaving the atomizer, so that the processes of formation and secondary recombination may not be accurately reproduced.

1.4 Droplet freeze technique

A natural extension of the molten wax technique is to solidify the droplets by freezing as soon as they emerge from the nozzle. In an early investigation, Longwell developed a technique for collecting the liquid droplets from a fuel spray into an alcohol bath kept at approximately the temperature of dry ice, which was cold enough to freeze the droplets into solids spheres. The droplets were then sieved while still frozen to separate them into different size groups. The method is unsuitable for kerosene, fuel oils, and water, which clearly represents a serious disadvantage-especially coupled with a minimum measurable droplet size of 53 μm.

2. Electrical Methods

Electrical methods generally rely on the detection and analysis of electronic pulses produced by droplets for calculating size distributions.

2.1 Charged wire technique

This technique operates on the principle that when a droplet impinges on an electrically charged wire it removes an amount of charge that depends on its size. This allows droplet sizes to be obtained by converting the charge transfer into a measurable voltage pulse.

2.2 Hot wire technique

When a liquid droplet becomes attached to a heated wire it causes local cooling of the wire as it evaporates. This phenomenon can be used to obtain the sizes and concentrations of liquid droplets present in a gas stream. Essentially, the device employed is a constant-temperature hot wire amemometer. When no droplets are present, the electrical resistance of the wire is high and sensibly uniform along its length. When a droplet attaches to the wire, local cooling by the droplet reduces the resistance in proportion to the droplet size. The reduction in resistance is manifested as a voltage droplet across the wire supports. The constant-current electrical energy supplied to the subsequently evaporates the droplet, leaving the device ready to receive another droplet. The entire process takes place within a time of 2 ms, depending on the droplet size.

3. Optical methods

Optical methods can be broadly divided into two types:

- Imaging such as photography, holography
- Nonimaging such as single-particle counters, light scattering, Malvern particle analyzer, Phase/Doppler particle analyzer

Imaging methods have the advantage of allowing the droplets to be seen as they exist at the point and time where knowledge of their size requires. Another advantage is that errors that might arise from coalescence or evaporation of droplets after sampling are eliminated.

Nonimaging methods can be subdivided into two classes-those that count and size individual droplets, one at a time, and those that measure a large number of droplets simultaneously. For accurate results it is important to know both droplet size and velocity, and some nonimaging instrument can provide both sets of information (figure 3.22).

Nonimaging employed is based on the diffraction of a parallel beam of monochromatic light by a moving droplet spray. When a parallel beam of light interacts with a droplet, a diffraction is formed in which some of the light diffracted by and amount depending on the size of the droplet.

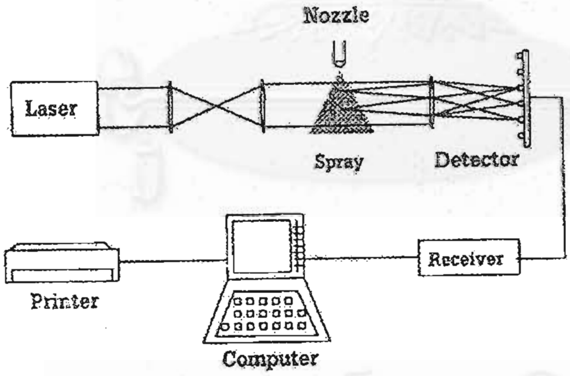


Figure 3.23 Laser diffracttion

3.3.3 Factors influencing the measurement results of droplet size distribution

All measuring techniques, whether simple or sophisticated, are susceptible to various errors and ambiguities, the nature and importance of which depend on the particular method employed. However, a number of potential sources of error in droplet size measurement are common to almost all methods. They include the method of sampling (spatial or temporal), sample size, drop saturation, droplet evaporation, droplet coalescence, and sampling location.

1. Spatial and Temporal Sampling

Two types of sampling are employed to determine droplet size distribution. One is spatial sampling, which describes the observation or measurement of droplets contained within volume during such short intervals of time that contents of the volume do not change during any single observation. The second type is temporal sampling, which describes the observation or measurement of droplet pass through a fix area during a specific time interval.

2. Sample Size

Although a spray contains a far larger proportion of small droplets than large ones, it is the few large droplets that predominate in determining the average droplet diameter of the spray. As Lewis et al. Have pointed out, the presence or absence of one large droplet in a sample of 1,000 droplets may affect the average diameter of the sample by as much as 100%.

To achieve a reasonably accurate estimate of spray quality, it is necessary to measurement about 5,500 droplets. The accuracy of the mean diameter obtained for various sample sizes, as estimated by Bowen and Davies for 95% confidence limit.

Table 3.4 Influence of sample size on accuracy of drop size measurements

No. droplets in sample	Accuracy (%)
500	±17
1,500	±10
5,500	±5
35,000	±2

3. Saturation

This occurs when the droplet flux or population exceeds the capability of the sizing instrument or method. The problem is most evident when droplets are collected on coated slides or in immiscible solvents. If the sample too large, the probability of error due to overlapping of droplets (or their impressions) is high. Saturation is also encountered in optical systems.

4. Evaporation

As the lifetime of small droplets is extremely short, evaporation effect is very important in the measurement of fine spray. Whether evaporate leads to an increase and decrease in mean droplet size depends on the initial droplet size distribution. For a monodisperse spray, evaporation always reduces the mean droplet size, but if the spray contains a wide range of droplet sizes initially, then evaporation may produce an increase in mass median diameter (MMD).

5. Coalescence

The collision of droplet sometimes results in droplet coalescence. Whether or not, the collision of two droplets leads to coalescence depend on the diameter of the droplets, their relative velocity, and collision angle. It also depends on the number density of the spray and the time available for collisions. Thus coalescence is most likely to occur in dense sprays when sampled at large distances from the atomizer.

6. Sampling Location

It is possible to sample the entire spray or, at least, a representative portion of it. In other methods the data are drawn from a very small volume, typically around 1 mm^3. With such methods the acquisition of sufficient data to characterize the total spray could prove tedious and time consuming.

Most pressure-swril nozzles produce a hollow cone spray in which the largest drops, due to their higher inertia, are located at outer periphery. In fan spays also, the largest droplets are usually found at the outer edges of the spray pattern. For such sprays local measurements of droplet size distribution could clearly be misleading, but it should also noted that even instruments that measure a line-of-sight average through the complete spray are not immune to errors from this source.

CHAPTER 4

EXPERIMENT APPARATUS AND PROCEDURE

4.1 Materials

1. Core particles - Non-pareil seeds (size range 850 – 1,180 μm, $\rho = 1.6$ g/cm^3)
2. Film former - Metochel E5 (hydroxypropyl methylcellulose, HPMC)
3. Plasticizer - Polyethylene glycol 6000
4. Colorant - Yellow sunset Lake
5. Solvent - Distilled water

Others - Grease
- Glass slide

4.2 Equipments

Figure 4.1 shows the experimental setup used in this work. The fluidized bed coater, which is made up of acrylic (Ekasilp Bangkok Co., Ltd.), equipped with bag filter (made from Polyester 25 μm, Golden Filtech Cooperation Co., Ltd.), at the upper section of the equipment in order to prevent entrainment of particles, whose size is smaller than 50 micrometer. At the top of air distributor set a draft tube column (inside diameter 5.4 mm., height 12 cm). The fluidizing air was drawn from the blower (model DBR-010-1A, Paisan Machinery) (shown in figure 4.2) and heated by the heater (model PMB075U240 and PMB150U240, Utility Electric Co., Ltd.) located at the bottom of air distributor. The thermocouple (model JB-10 type CA (K), Sang Chai Meter Co., Ltd.) and the controller temperature (model Digicon type DD-6, Sang Chai Meter Co., Ltd.) are used to control the fluidizing air temperature in the range studied.

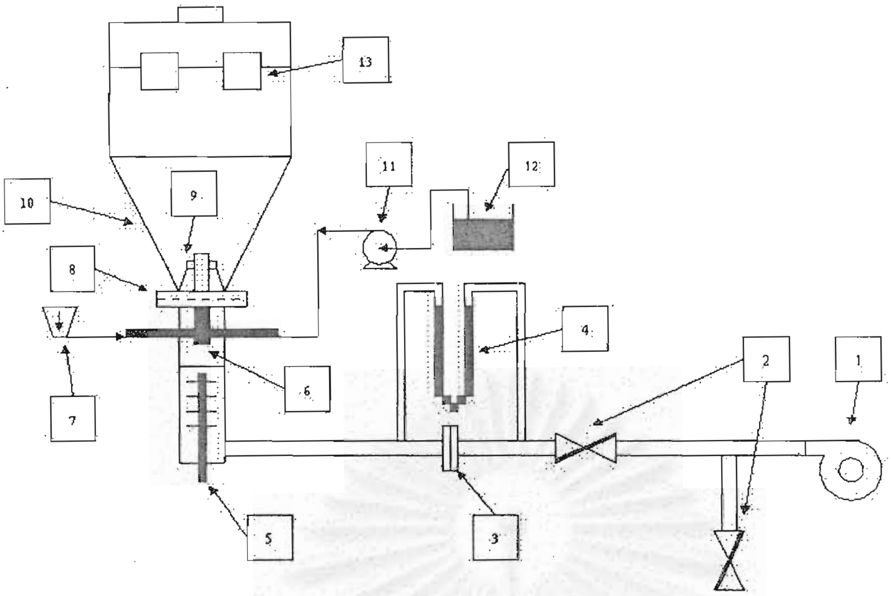


Figure 4.1 Schematic diagram of the fluidized bed coater developed in this work.

1) Blower 2) Ball Valve 3) Orifice plate 4) Manometer 5) Heater 6) Nozzle

7) Air compressor 8) Distributor Plate 9) Draft tube 10) Fluidized bed

Chamber 11) Peristaltic pump 12) Coating solution 13) Bag filter

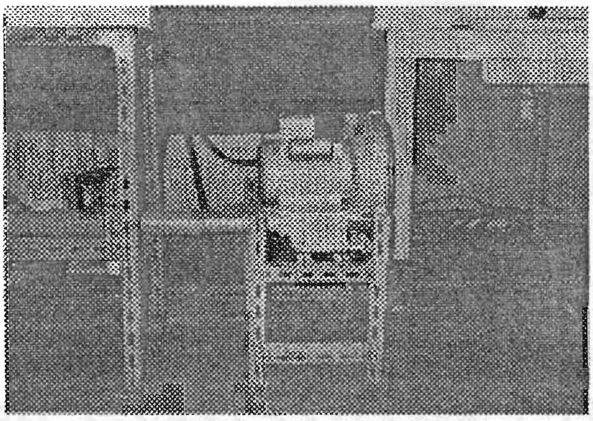


Figure 4.2 Blower

Hot Plate & Magnetic Stirrer

The equipment (model Fish Erband, Fisher Scientific, USA.), as shown in figure 4.3, used to prepare coating solution and to stir continuous the solution while feeding solution to the nozzle.

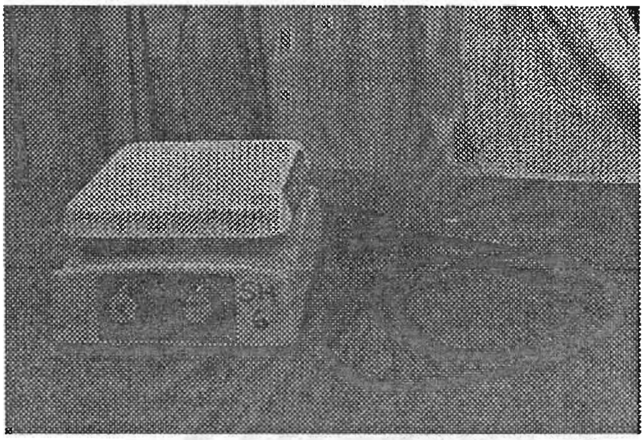


Figure 4.3 Hot plate & magnetic stirrer

Peristaltic Pump

This pump head (model 7554-95, Cole-Parmer Instrument Co., Ltd.), figure 4.4, combined with a MasterFlex L/S drive to control constant flow rate. The high performance precision tubing, series number 6429 model L/S 15, is selected to transport solution. Additionally, digital interrupter timer (model Digicon type PIR-43, Sang Chai Meter Co., Ltd.), as illustrated in figure 4.5, control spraying rate.

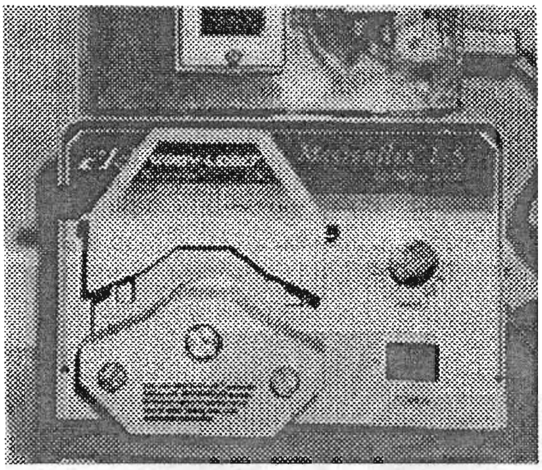


Figure 4.4 Peristaltic pump

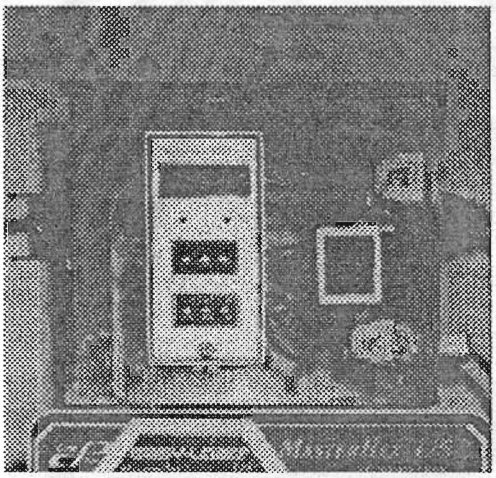


Figure 4.5 Digital interrupter timer

Nozzles

In this work compares types nozzle, i.e. binary and ultrasonic resonator, effect on the coated particles. Binary nozzle, figure 4.6, (model Wide-Angle round spray, Pawin Engineering Co., Ltd.) body type 1/8J equips with fluid cap No. 40100 and air cap No. 120. Spray angle is 13.5 degree when used atomizing air pressure 2 bar. The other type, an ultrasonic resonator, as shown in figure 4.7, made from stainless steel. Spray angle of ultrasonic nozzle at atomizing air pressure 2 bar is 18.1 degree. Air employed to nozzles is supplied from air compressor (Model SVP-202, Swan Pneumatic Corporation Ltd.), figure 4.8.

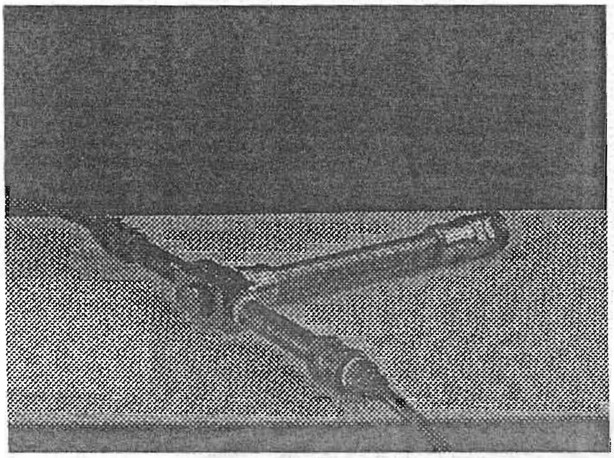


Figure 4.6 Binary nozzle

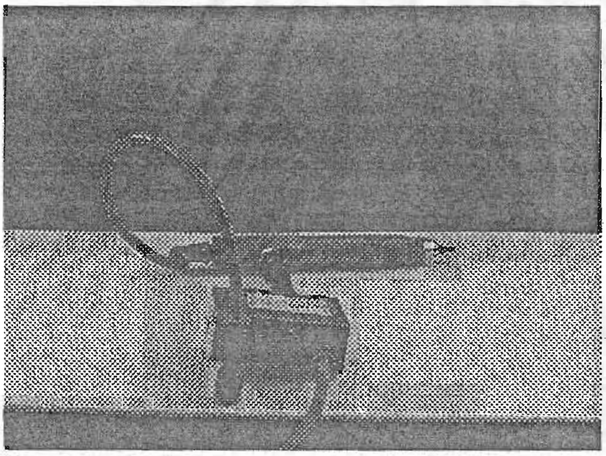


Figure 4.7 Ultrasonic resonator

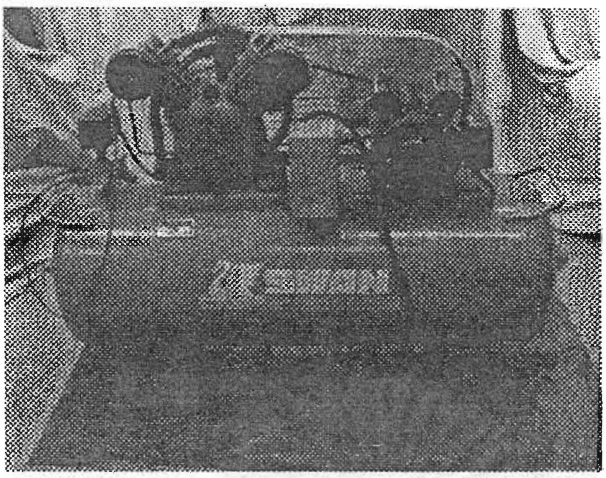


Figure 4.8 Air compressor

The moisture content of coated particles is reduced by hot air oven (model UM400, Memmert, Germany) before to find percent agglomerate from the vibration shaker and sieve screen (Ratch, Type Vibro, West-Germany), shown in figure 4.9. The morphology and powder characteristic of the coated particles are observed by using scanning electron micscope (model JSK-6400 LV, Jeol Ltd., Japan), Powder Characteristic Tester (model PT-N, Hosokava Micron) (figure 4.10).

The Optical microscope (model BH-2, Olympus) used to find spray droplet size distribution with mechanical techniques.

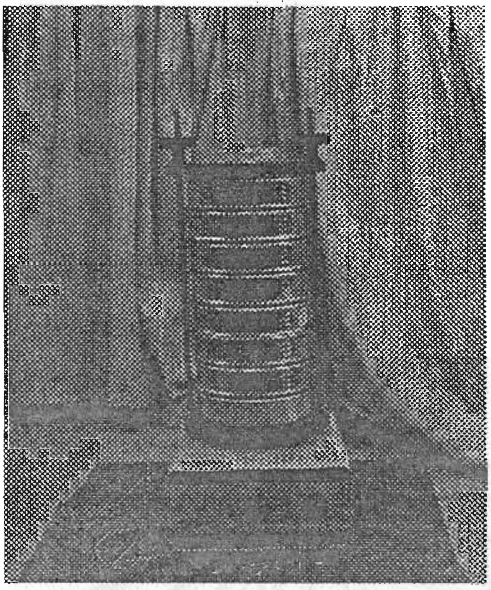


Figure 4.9 Sieve shaker and sieve screen

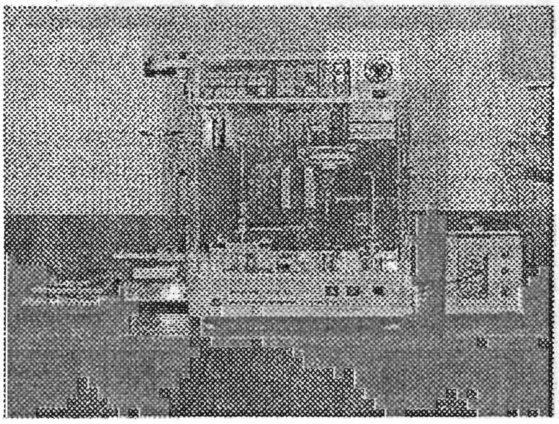


Figure 4.10 Powder characteristic tester

4.3 Condition in the experimental

This work study affect of process variables i.e. fluidizing air velocity, fluidizing air temperature and type of nozzle to physical properties of coated particles such as percentage of weight gain, surface morphology etc. by using other equipment.

Fluidizing air velocity

The range of fluidizing air velocity was selected from trial and error. The minimum of fluidizing air velocity in the range can move core particles, Non-pareil seeds, upward through the draft tube, sometimes called Wurster column, which is positioned at the center of column. Besides, in order to prevent the particles strike the bag filter on the top of column, the fluidizing air velocity was not more than. Thus, the range of fluidizing air velocity in this study was 1.3, 1.7 and 2.1 m/s respectively.

Fluidizing air temperature

Because of the fluidized bed coater made from acrylic, which withstand temperature above 85 ^{o}C, then maximum the fluidizing air temperature not over 85 ^{o}C too. The minimum fluidizing air temperature for film coating of HPMC was nearly 50 ^{o}C. The optimum range of fluidizing air temperature in this studied was 50, 60 and 70 ^{o}C respectively.

Pressure air atomization

For purpose of comparison with the type of nozzle that used to spray film coating were selected 2 bars for atomization droplet spray coating. Because atomization ultrasonic resonator could operated at 2 bars.

The other conditions in this work were fixed:

- film coating is hydroxypropyl methylcellulose
- concentration of film coated is 5 %w/w
- solvent is distilled water amount 150 ml
- feed rate of coating solution is 10 ml/min
- timer to spray film coated on 7 s. and off 20 s.
- drying time in fluidized bed after the coating process about 10 minutes
- height of draft tube column (coating zone) equal 12 cm.
- height of draft tube column from the air distributor equal 0.8 cm.
- height of spray nozzle from the air distributor is 5 cm.

4.4 Experimental procedure

1. Preparation of coating solution.

The composition of coating solution is presented in table 4.1.

Table 4.1 Composition of coating solution

Ingredients	% w/w
Polymer (Methocel E5, hydroxypropyl methylcellulose, HPMC)	5
Plasticizer (polyethylene glycol 6000)	1.6
Lake (yellow sunset lake)	0.6
Distilled water	100

- Dissolve plasticizer and lake in distilled water (about half of total amount coating solution, 75 milliliters).
- The solution was heated to 60 °C and stirred until the solution is homogeneously.
- Added the polymer into the solution.
- The solution should be moderate agitation during mix the solution and heated the solution to 70 °C.
- When HPMC dissolve ready, cold distilled water is added to produce the required volume.
- A clear solution is obtained after cooling within a day on standing at room temperature.

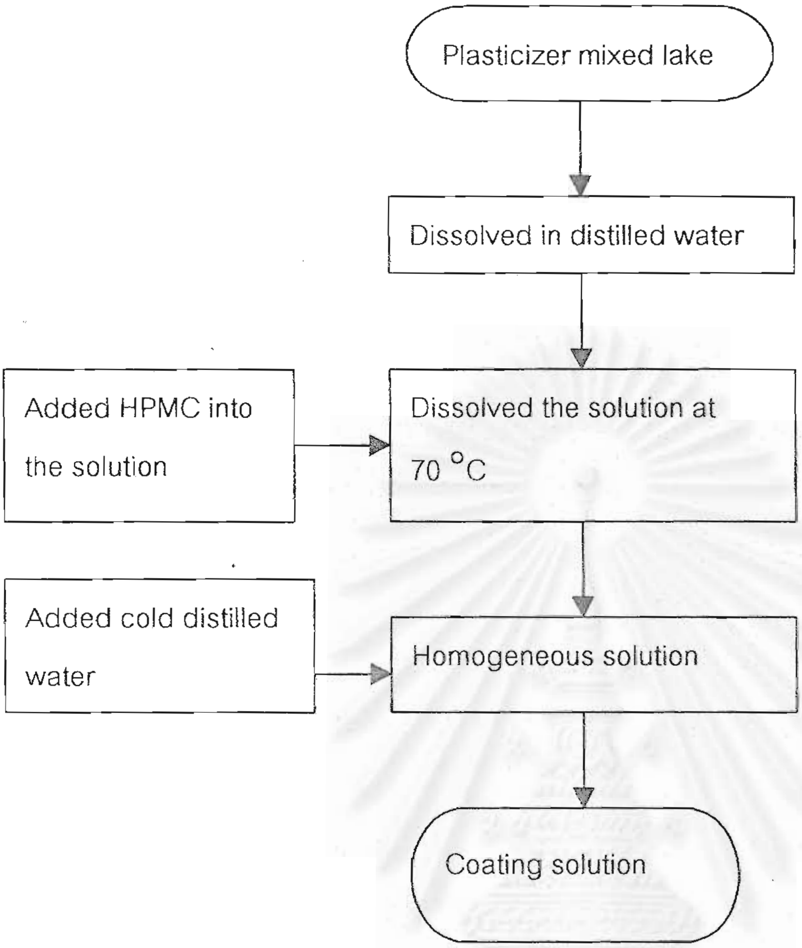


Figure 4.11 Flow chart of preparation of coating solution

2. Preparation of coated particles.

- Known weight of Non-pareil seeds (150 grams) were transferred into the fluidized-bed coater.
- Turned on the switch air blower and controlled constant fluidizing air velocity at set point.
- Turned on the switch temperature controller and set fluidizing air temperature.
- Turned on peristaltic pump and set feed flow rate of the coating solution to the nozzle at 10 milliliters per minutes.
- Turned on the air compressor and opened pressure valve at 2 bars.
- When the air temperature and velocity move to set point set the interrupter timer that is sprayed coating solution for on 7 seconds and stopped 20 seconds. The spraying cycle is repeated until all of coating solution is used up.
- After the coating process, the coated particles were dried in coating chamber at the same temperature and air flow about 10 minutes.

Remark During the coating operation, the coating solution was stirred continuously to prevent sedimentation of the insoluble particles.

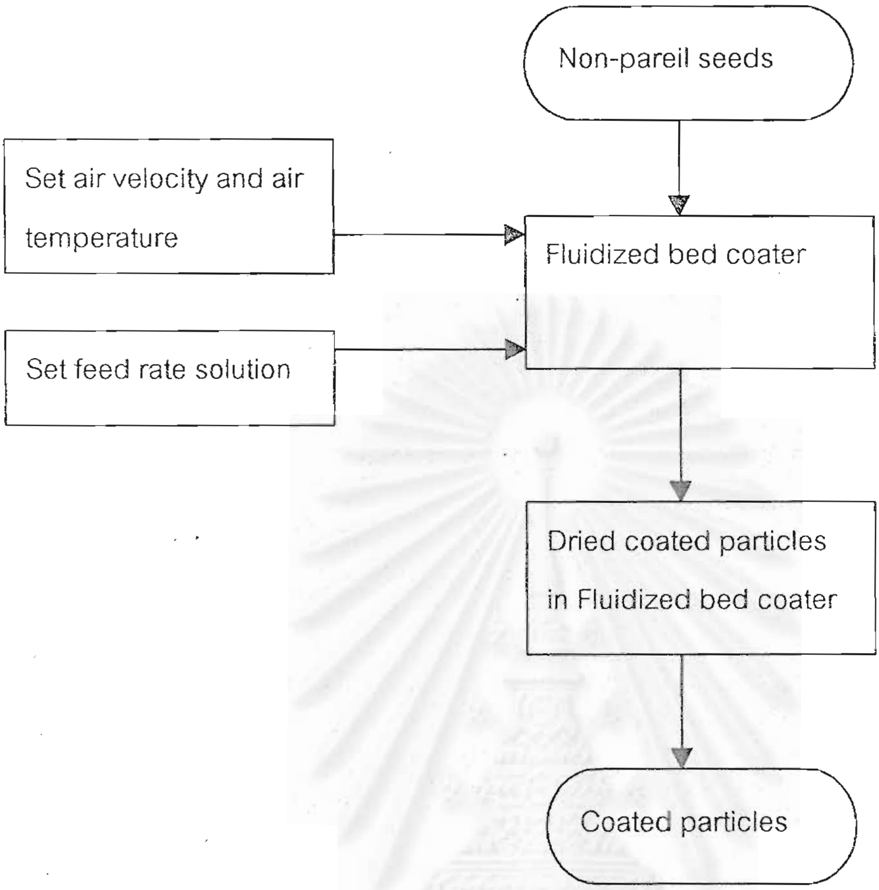


Figure 4.12 Flow chart of preparation of coated particles

3. Coated particles characterization.

3.1 Morphology.

The shape and the surface characteristics of the coated particles were evaluated by scanning electron microscope (SEM). The coated particles were cut with scalpel for cross-section observation. All samples were coated with gold by using an ion sputter coater under the vacuum. The film thickness and surface topography of coated particle s were examined.

3.2 Percentage of weight gain and percent yield of coated particles.

After the coating process, the coated particles were weighted. Percentage of weight gain and yield of coated particle were given by

$$\%\text{ weight gain} = \frac{\text{weight of coated particles - weight of uncoated particles}}{\text{weight of uncoated particles}} \times 100$$

$$\%\text{ yield} = \frac{\text{weight of particles after coating}}{\text{total weight of materials in the formulation}} \times 100$$

3.3 Coated particles size analysis.

The agglomerate of coated particles is screened out by using a vibrate shaker and standard sieve screens of 850 and 1,180 micrometers.

3.4 Flowability of coated particles.

The coated particles were dried overnight in hot air oven at 50 ^{o}C.

- Angle of repose.

The angle of repose of the coated particles was measured using a Powder characteristic tester. A sieve is used to screen out particles larger than 1,180 micrometers. Each sample was determined in triplicate and the results averaged.

- Packed bulk density.

The packed bulk density of coated particles were determined using a Powder characteristic tester. A sieve is used to screen out particles larger than 1,180 micrometers. Each sample was determined in triplicate and the results averaged.

3.5 Dissolution time of coated particles.

The coated particles were dried overnight at 50 °C before testing dissolution time. Coated particles 1.50 grams were dissolved in distilled water 150 milliliters at 28 °C. After the particles were dissolved ready recorded time. Each sample was measured in triplicate and the results averaged.

CHAPTER 5

RESULTS AND DISCUSSION

In order to investigate the effects of adjusting variables on the properties of coated particles, many experiment had been performed intentionally. The core particles employed in this work were glucose non-pareil seed particles with the nominal size ranged from 850 – 1,180 μm. The coating agent was a mixture of Polyethylene glycol and Methocel E5, hydropropyl methycellulose (HPMC) with distilled water (conc. was fixed at 5 % w/w). The characteristics of the coated particles, which were taken into consideration, were the coating film thickness, weight gain, bulk density and morphology. Moreover time period required for the complete dissolution of coated particles was also measured and then discussed by considering its dependence upon other coated particle characteristics.

5.1 Film Thickness

5.1.1. Effect of fluidizing air velocity

The experimental result indicating the film thickness of the coated particles obtained from coating by using two different nozzles, which are ultrasonic resonator and binary nozzle, revealed that an increment of the fluidizing air velocity could provide thicker coated film (figure 5.1 and 5.2). This could be attributed that the increase in the fluidizing air velocity could give rise to higher evaporation rate of coating droplets, as well as providing good circulation of particles inside the chamber. Thus, the coating droplets could impinge and spread on the surface of particles much easier. This could provide a large film thickness of coated particles.

5.1.2. Effect of fluidizing air temperature

As also illustrated in figure 5.1 and 5.2, the increase in the fluidizing air temperature, regardless of types of nozzles, had exhibited an effect on the thickness of the coated particles. The higher temperature could result in the higher rate of evaporate of solvent

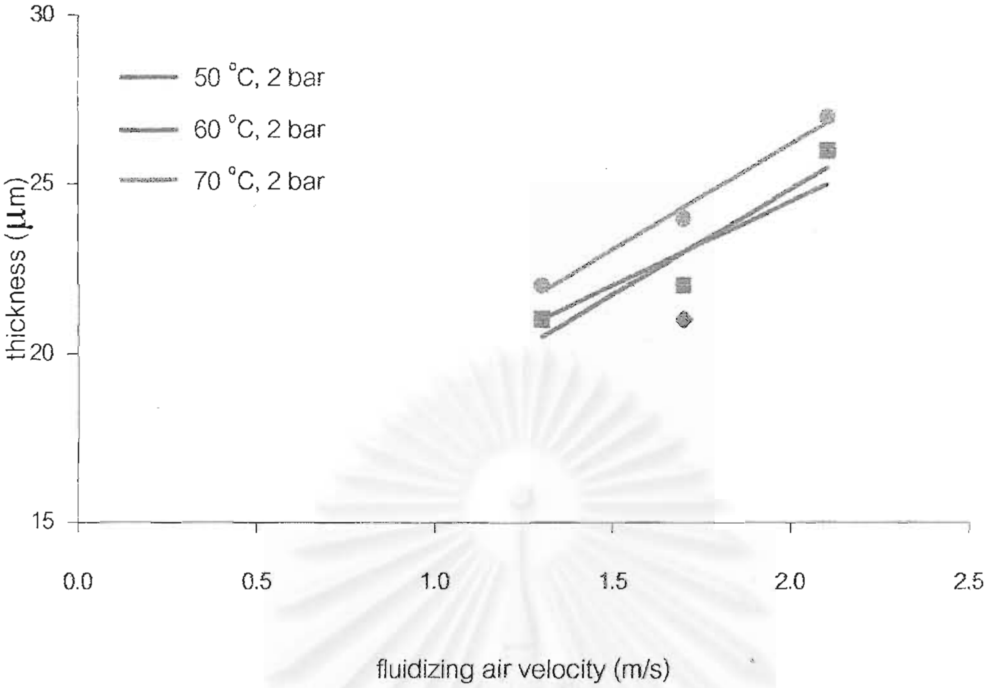


Figure 5.1 Film thickness of coated particles using ultrasonic resonator under various coating conditions

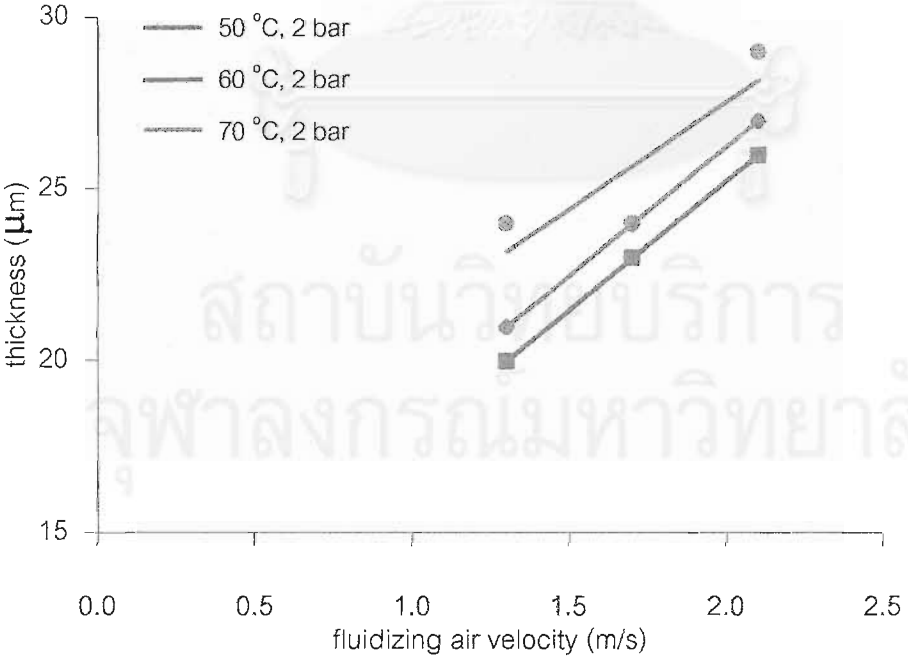


Figure 5.2 Film thickness of coated particles using binary nozzle under various coating conditions

prevent in the coating agent, which spread out over the surface of the coated particles. The faster evaporation could allow the more efficient coating process then resulted in the thicker coating film.

5.2 Percentage of weight gain

5.2.1. Effect of fluidizing air velocity

The percentage of the weight gain of the coated particles obtained from the usage of an ultrasonic resonator and binary nozzles in coating process, is shown in figure 5.3 and 5.4, respectively. Higher air velocity could lead to the increasing percentage of the weight gain. Nevertheless, at fluidizing air velocity higher than 1.7 m/s, with the same fluidizing air temperature, it was found that there was no significant change in the particle weight gain. This may be attributed to two factors: loss of coating droplets and the promoted attrition of coated particles due to higher fluidizing air velocity. The similar results were also reported by Phattanathong(1999).

5.2.1 Effect of fluidizing air temperature

The effects of the fluidizing air temperature on the percentage of the weight gain of the coated particles were shown in figure 5.3 and 5.4. The particle weight gain was slightly declined with an increase in the air temperature regardless of the types of the nozzles. This effect could be attributed to the reason that the fluidizing air temperature could reduce the moisture content of the coated particles. Therefore the weight of the coated particles at higher temperature were less than the products obtained at lower temperature.

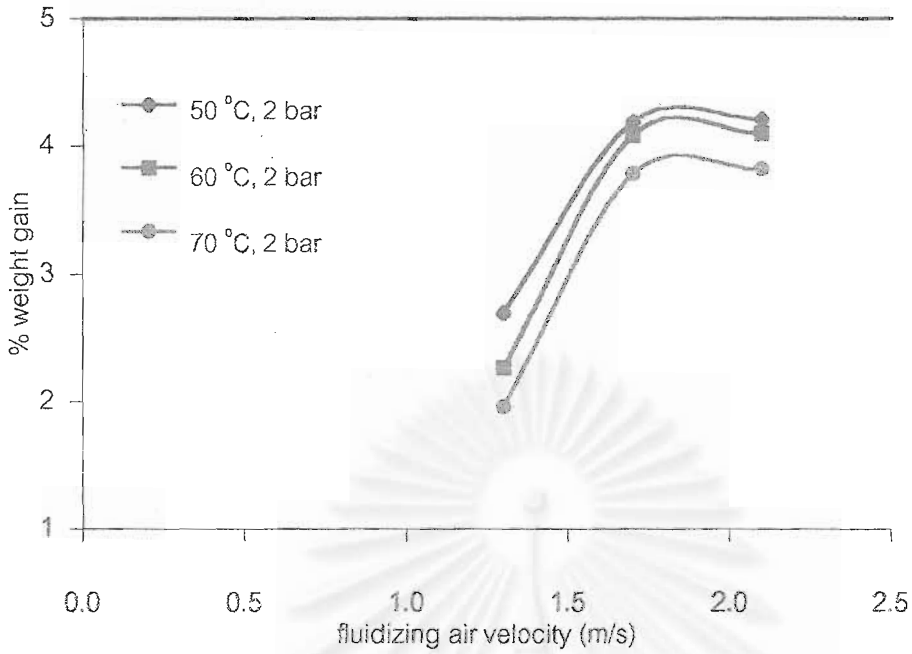


Figure 5.3 % weight gain of coated particles obtained by using ultrasonic resonator under various coating conditions

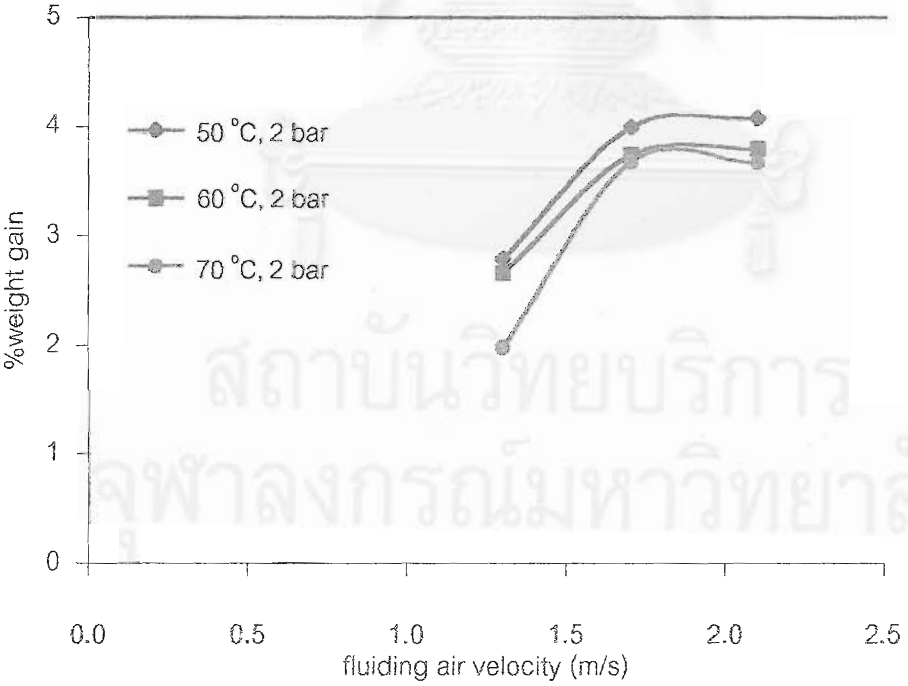


Figure 5.4 % weight gain of coated particles obtained by using binary nozzle under various coating conditions

5.3 Yield of coated particle

5.3.1 Effect of fluidizing air velocity

The production yield of the coated particles obtained by using ultrasonic resonator and binary nozzle is shown in figure 5.5 and 5.6. Regardless of the coating conditions, the yield of the coated particles was formed to become more than 97 percent with respect to total raw materials used in the coating. These results were similar to those of the percentage of the weight gain. Therefore it could be explained with the similar reasons to that for the percentage of the weight gain.

5.3.2 Effect of fluidizing air temperature

The effects of the fluidizing velocity on the production yield of the coated particles, which were obtained by using two type nozzles, are shown in figure 5.5 and 5.6, respectively. As could be seen, the results are the same as that of the effects on the weight gain. Moreover, it could be clearly seen think the equipment developed in this work could provide the very high yield of the coated particles production. The yield obtained in every experiment was higher than 97 percent.

5.4 Percentage of agglomeration

5.4.1 Effect of fluidizing air velocity

Regardless of the types of the nozzles increasing the fluidizing air velocity could reduce the percentage of agglomeration of coated particles (figure 5.7 and 5.8). It should be noted higher air velocity could provide more rigorous movement of particles in the fluidized bed coater and in turn resulted in more attrition of coated particles. Hence, the faster fluidizing air velocity could result in less percentage of agglomeration.

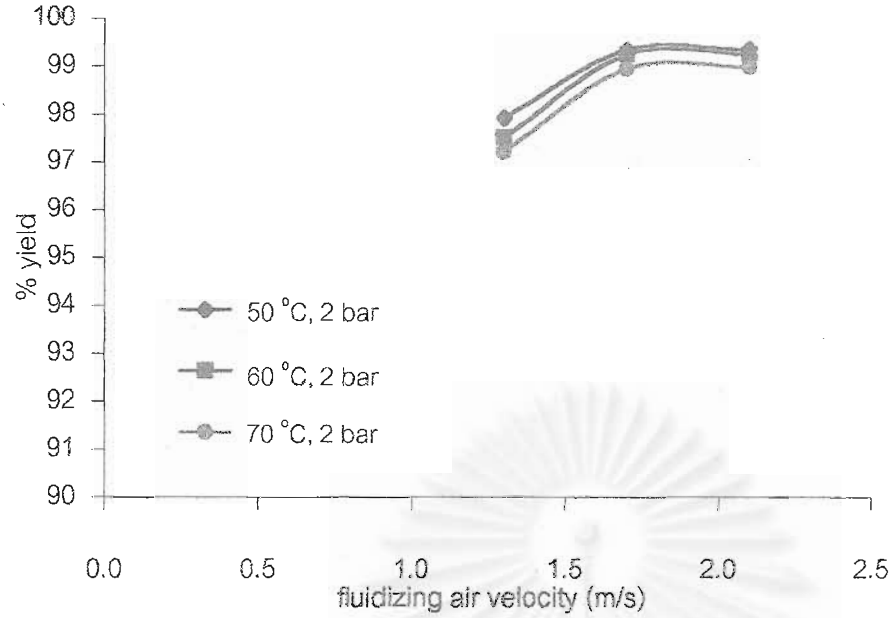


Figure 5.5 % yield of coated particles obtained by using ultrasonic resonator under various coating conditions

Figure 5.6 % yield of coated particles obtained by using binary nozzle under various coating conditions

5.4.2 Effect of fluidizing air temperature

Figure 5.7 and 5.8 also displayed the effect of the fluidizing air temperature which exhibited on the percentage of the agglomeration of coated particles. During the coating process, sprayed droplet could impinged the non-pareil seeds and spreaded out over the surface of the seeds. Rapidly evaporating, droplets on the particle surface could become dry quickly than even the coated particles got collisions with other particles in the fluidized bed coater, they would not undergo the agglomeration process.

5.5 Morphology

5.5.1 Effect of fluidizing air velocity

First, the non-pareil seeds were examined their morphology using a scanning electron microscope at different magnifications. The shape and surface topography of the uncoated particles are illustrated in figure 5.9. The uncoated seeds exhibited smooth surface, and spherical shape. The cross section of uncoated particle was also observed.

The SEM micrographs of the coated particles produce by using ultrasonic resonator and binary nozzle are shown in figure 5.10 – 5.11 and 5.12 – 5.13, respectively. When compared to the SEM micrographs of the uncoated particles it was found that the coated particles had comparatively rougher surface but still occupied the same shape. The microscopic view of the coated particles exhibited rougher surface especially for lower fluidizing air velocity. The cross section of the coated particles likewise displayed obvious stratified layers of the coating film.

Additionally, the surface morphology of the uncoated particles compared with that of the coated particles exhibited another distinct difference. The coated particles obtained from using two different nozzle exhibited orange-peel like surface (figure 5.10(b); 5.11(b); 5.12(b); 5.13(b)). However, the Orange-peel like surface is one defection of the coated particles inevitably obtained when using HPMC polymer (Nagai T.et.al, 1997).

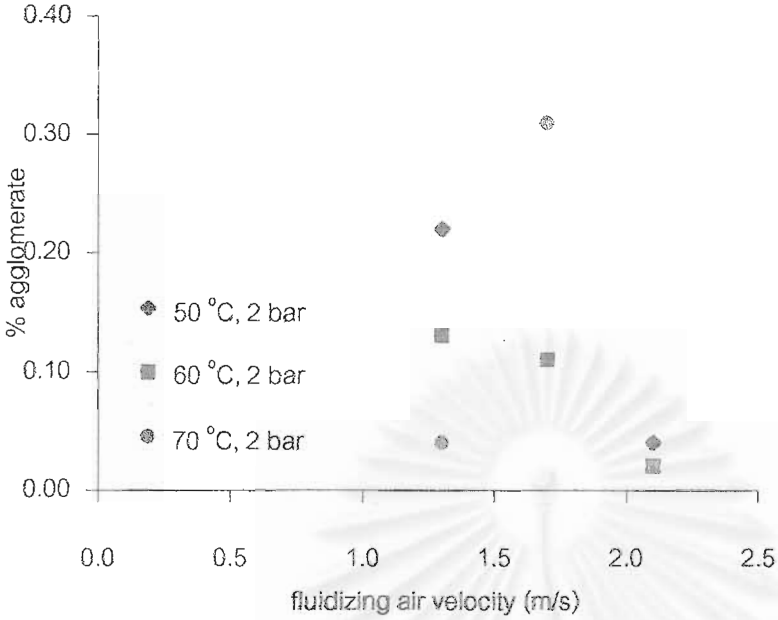


Figure 5.7 % agglomerate of coated particles obtained by using ultrasonic resonator under various coating conditions

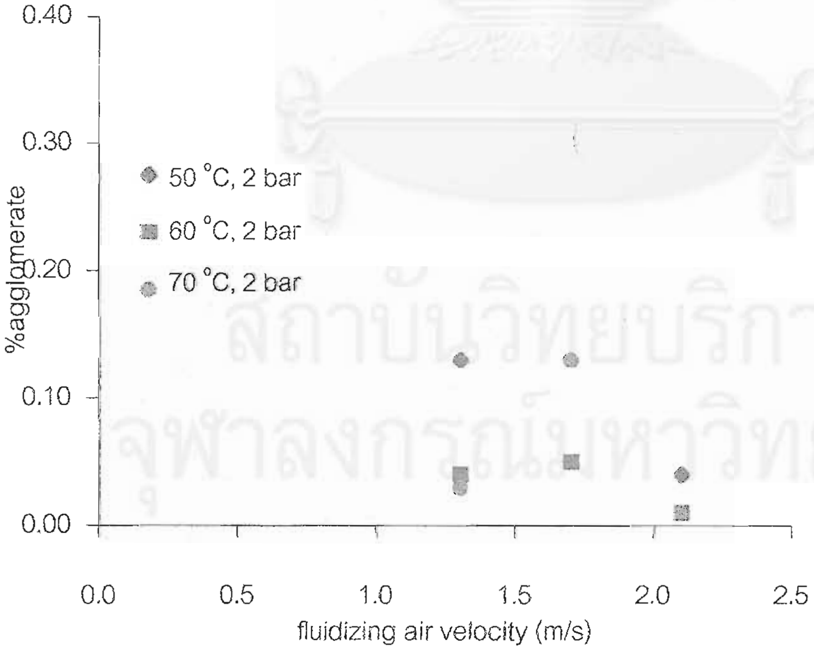


Figure 5.8 % agglomerate of coated particles obtained by using binary nozzle under various coating conditions

5.5.2 Effect of the fluidizing air temperature

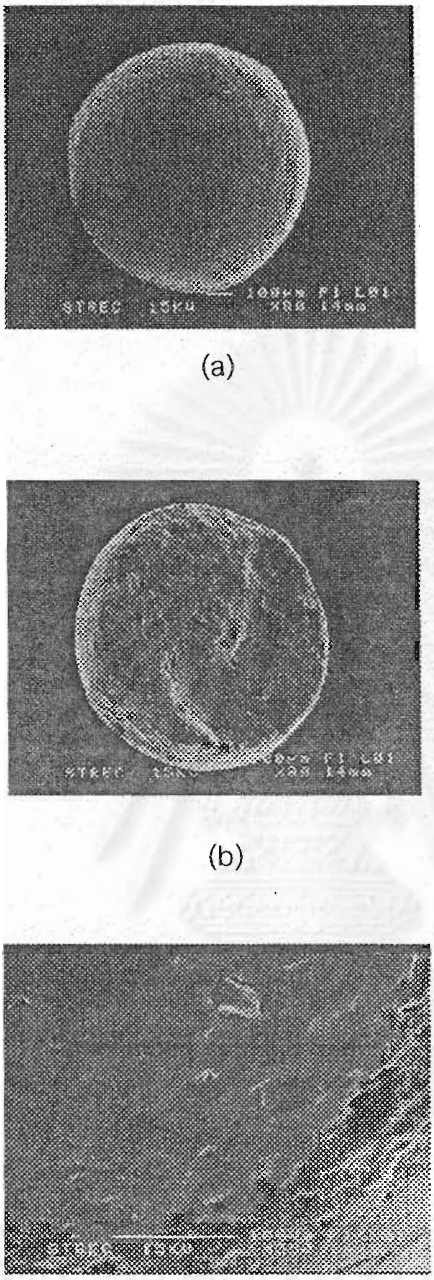
The effect of the fluidizing air temperature on the coated particle was shown in figure 5.14 to 5.17. With comparisons of SEM micrographs of the uncoated particle and coated particles, it is found that the coated particles had much rougher surface than that of the uncoated. The cross section of the coated particle exhibited a distinct boundary between the coating film and the core. The similar characteristics were observed by Mehta and Jones (1985).

At the magnification of 350 (figure 5.14(b); 5.15 (b); 5.16 (b); 5.17 (b)), the pictures present the orange-peel like surface. There was no distinct difference in the surface topography of the coated particles obtained by different types of nozzle.

5.6 Packed bulk density

5.6.1 Effect of fluidizing air velocity

Figure 5.18 and 5.19 present the relation between packed bulk density of coated particles with the fluidizing air velocity. Regardless of the air velocity (1.3 to 2.1 m/s), it was found that the packed bulk density of the coated particles became less than that of the uncoated particles. Furthermore, the packed bulk density became lower with the higher air velocity. This could be implied as the results of the increasing thickness of the coating film with respect to the increase in the fluidizing air velocities, which was already mentioned above. When considering the density of the polymer (HPMC) and the non-pareil seeds, it is known that the density of the polymer (1.037 g/cm^3) is lower than that of the non-pareil seed (1.83 g/cm^3). Hence, the thicker the coating film, the lower the bulk density of the coated particles could obtained.

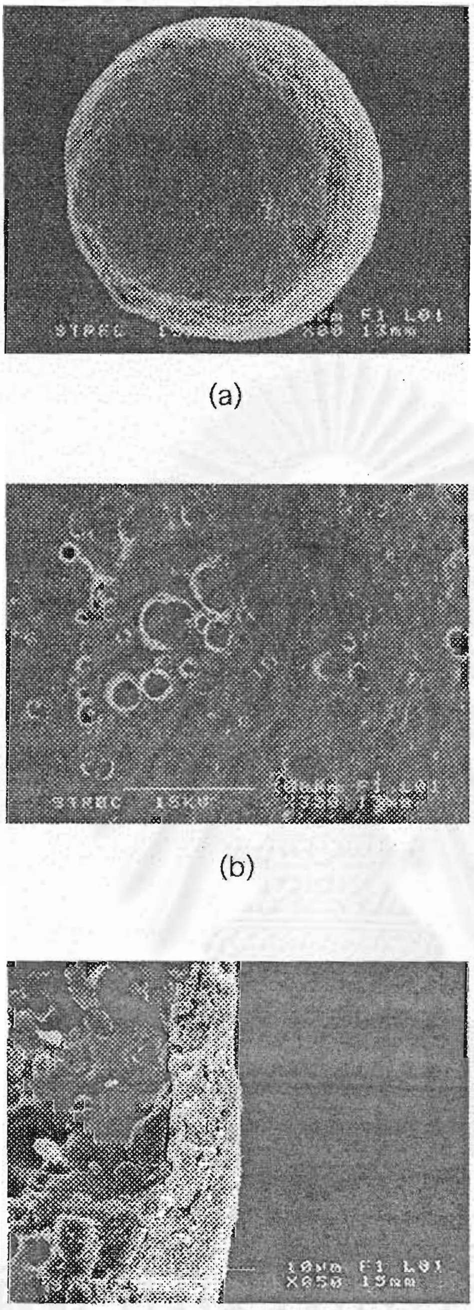


(a)

(b)

(c)

Figure 5.9 Morphology of Non-pareil seed (a) x80 (b) cross section x80 (c) x350

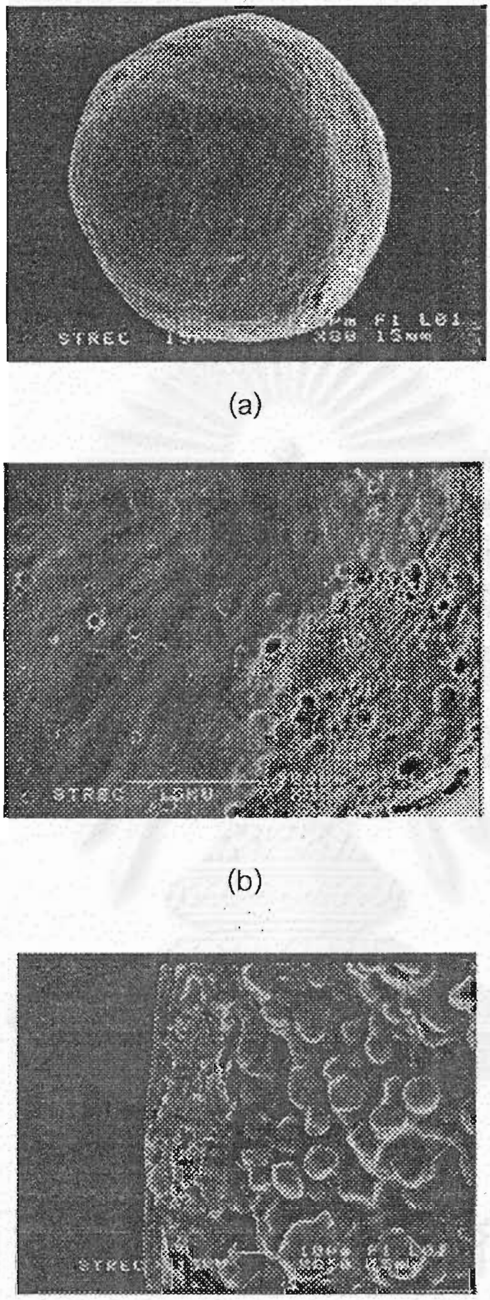


(a)

(b)

(c)

Figure 5.10 Morphology of coated particles using ultrasonic resonator at 1.3 m/s, 60 °C, 2 bar (a) x80 (b) x350 (c) cross section x850



(a)

(b)

(c)

Figure 5.11 Morphology of coated particles using ultrasonic resonator at 1.7 m/s, 60 °C, 2 bar (a) x80 (b) x350 (c) cross section x850

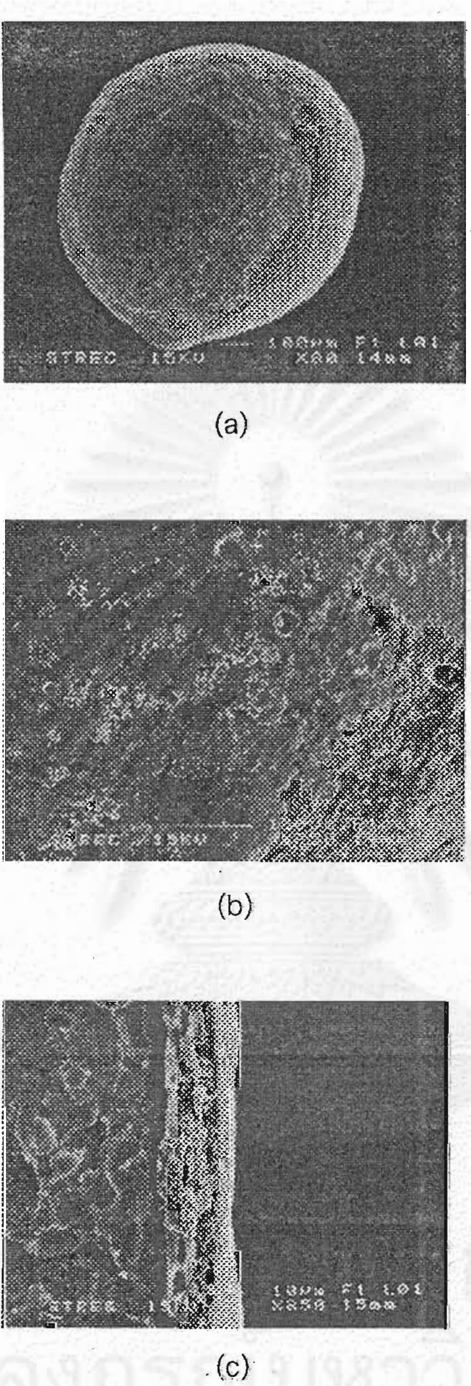


Figure 5.12 Morphology of coated particle using binary nozzle at 1.3 m/s, 60 °C, 2 bar (a) x80 (b) x350 (c) cross section x850

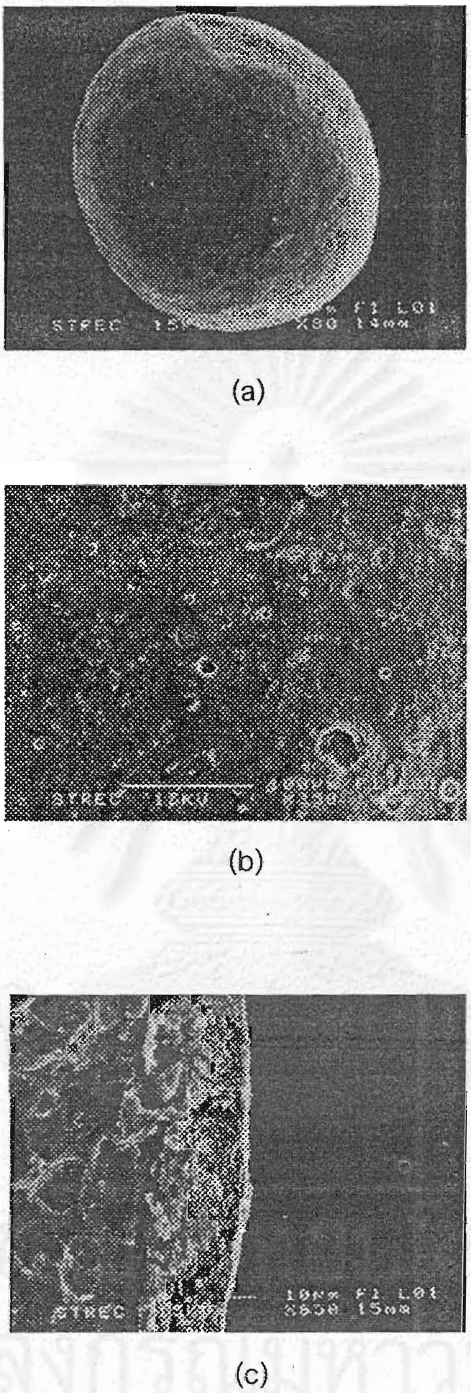
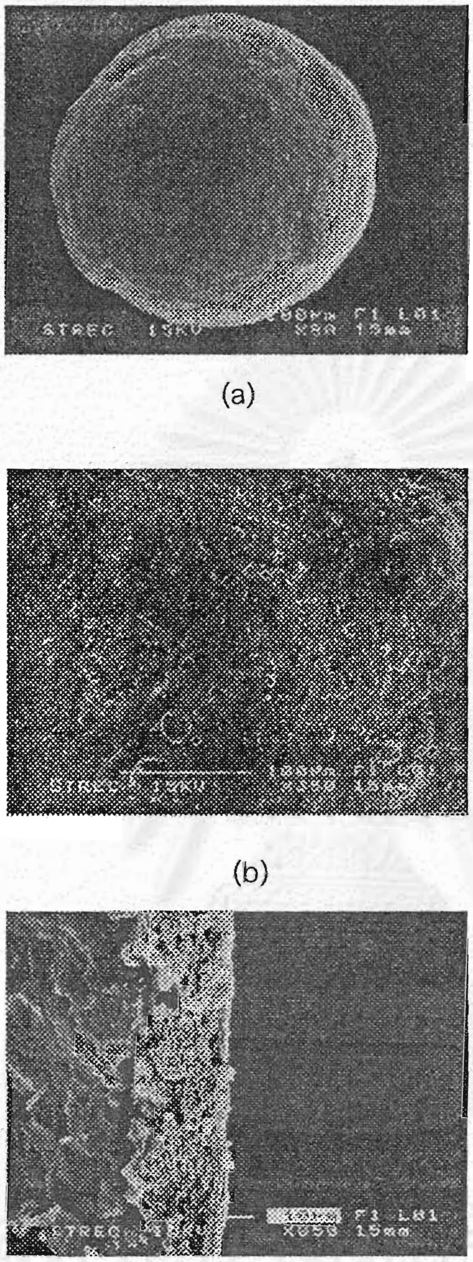


Figure 5.13 Morphology of coated particles using binary nozzle at 1.7 m/s, 60 °C, 2 bar (a) x80 (b) x350 (c) cross section x850



(a)

(b)

(c)

Figure 5.14 Morphology of coated particles using ultrasonic resonator at 2.1 m/s, 60 °C, 2 bar (a) x80 (b) x350 (c) cross section x850

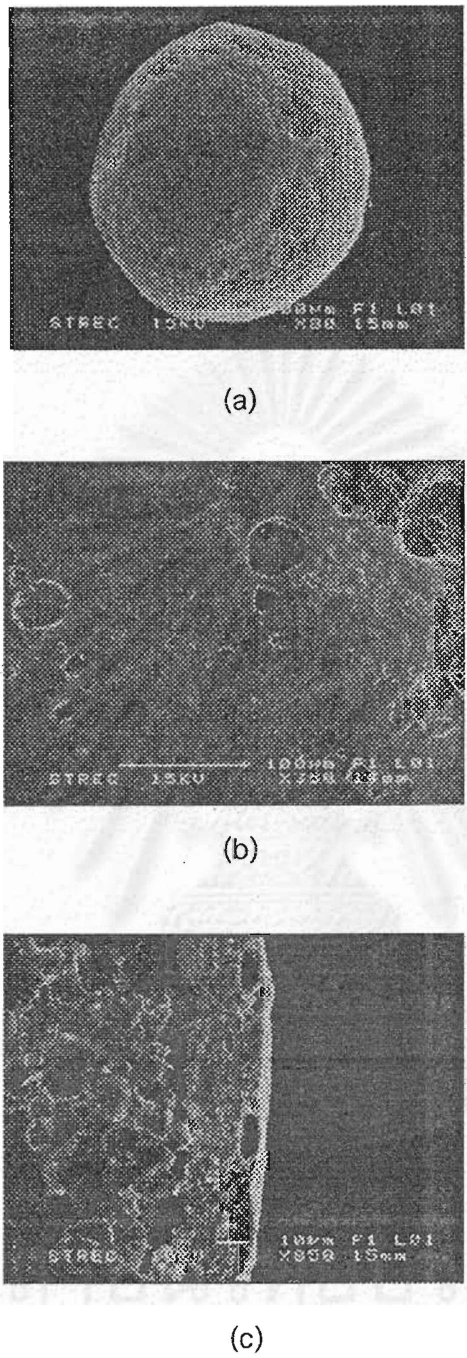


Figure 5.15 Morphology of coated particles using ultrasonic resonator at 2.1 m/s, 70 °C, 2 bar (a) x80 (b) x350 (c) cross section x850

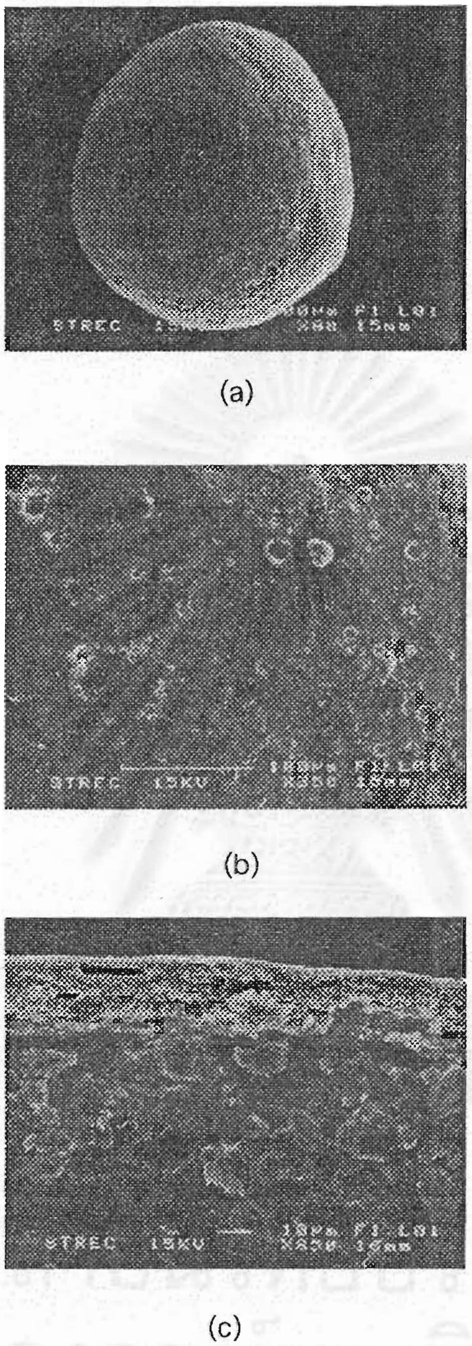


Figure 5.16 Morphology of coated particles using binary nozzle at 2.1 m/s, 60 °C, 2 bar
(a) x80 (b) x350 (c) cross section x850

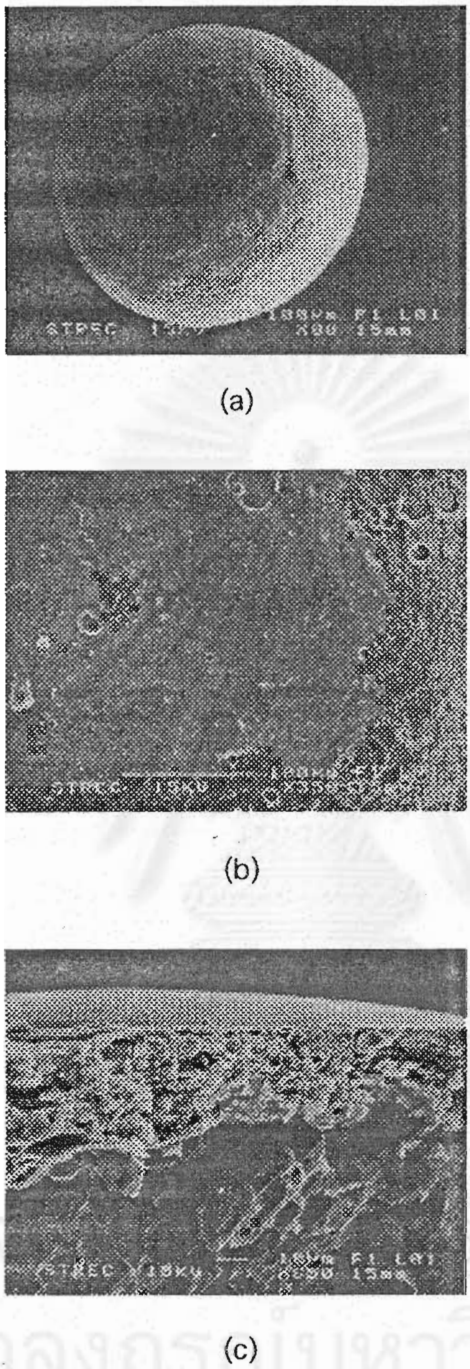


Figure 5.17 Morphology of coated particles using binary nozzle at 2.1 m/s, 70 °C, 2 bar

(a) x80 (b) x350 (c) cross section x850

5.6.2 Effect of fluidizing air temperature

Figure 5.18 and 5.19 also illustrated the effect of air temperature on the packed bulk density of the coated particles. It was found that the increase in the fluidizing air temperature could result in the increasing packed bulk density. This results reveals that the fluidizing air temperature could help get rid of the residual moisture content in the coated particles. Consequently, weight of particles, after coating process, per unit volume increased and affected on packed bulk density of particles too.

5.7 Angle of repose

5.7.1 Effect of fluidizing air velocity

The effect on the air velocity on the angle of repose on the coated particles is shown in figure 5.20 and 5.21. Higher air velocity led to an increase in the angle of repose of the coated particles. It is known that the angle of repose depends on the particles size, size distribution and morphology (Seko et al, 1993; Fonner et al, 1966; Nelson 1955). The higher air velocity could provide better circulation of particles inside the coating chamber then it increased chance of the particles strike the sprayed droplets. Moreover, the rough surface of the coated particles was also expected to exert an influence on the angle of repose. From the results, it is confirmed that the angle of repose of coated particles with an increment of air velocity. It means that the coated particles obtained became higher at higher air velocity will exhibit the worse flowability.

5.7.2 Effect of fluidizing air temperature

Figure 5.20 and 5.21 also present the effect of the air temperature on the angle of repose. The angle of the coated particles was sharply due to the coating effect when compared with that of the uncoated seeds. This effect was dependent on the fluidizing air temperature which contributed a higher evaporation rate of the coating droplets. Rapidly evaporating droplets required less time for being dry and depositing on the surface of the

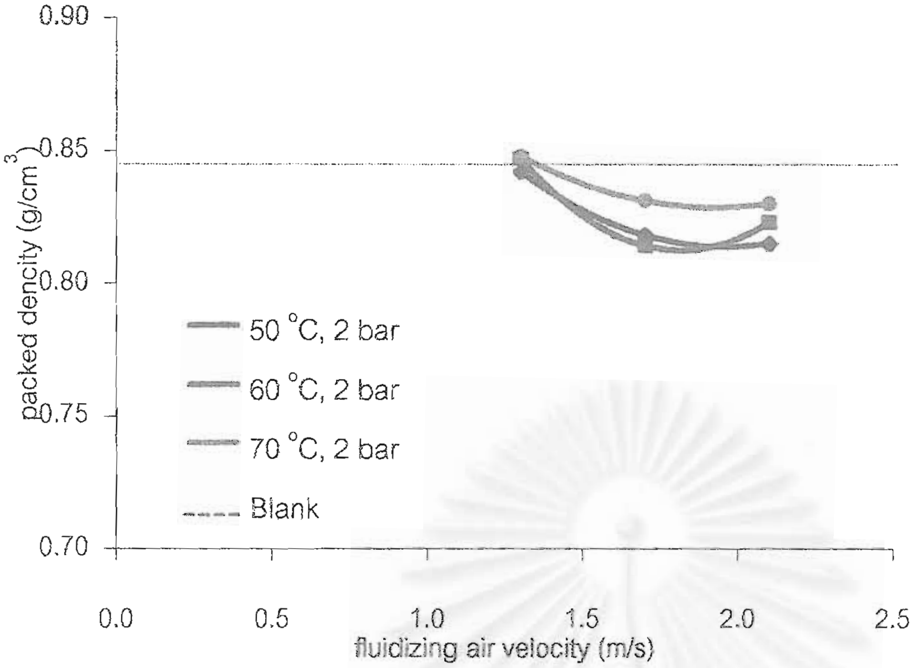


Figure 5.18 Packed bulk density of coated particles obtained by using ultrasonic resonator under various coating conditions

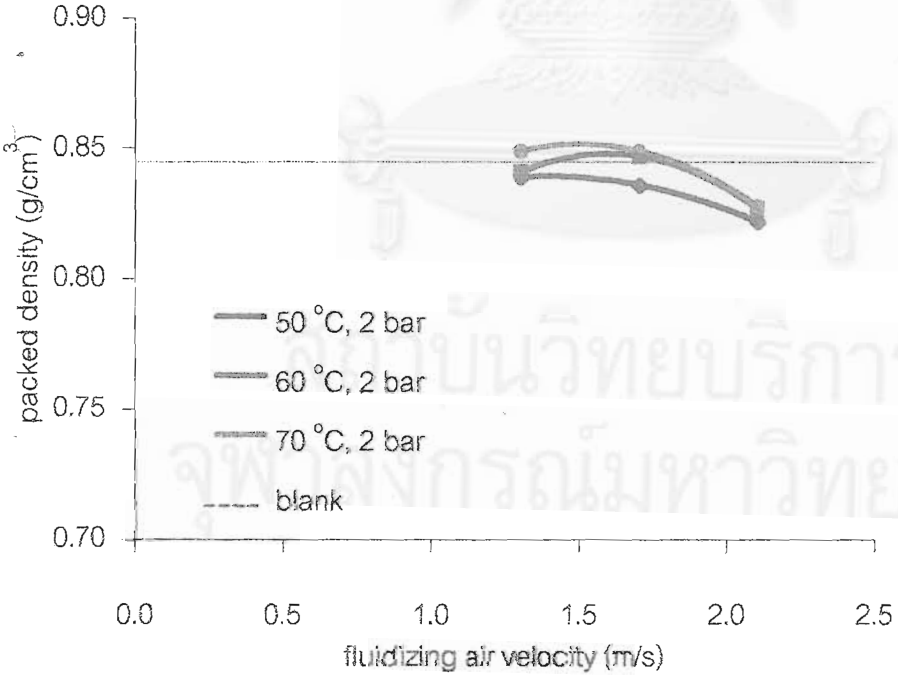


Figure 5.19 Packed bulk density of coated particles obtained by using binary nozzle under various coating conditions

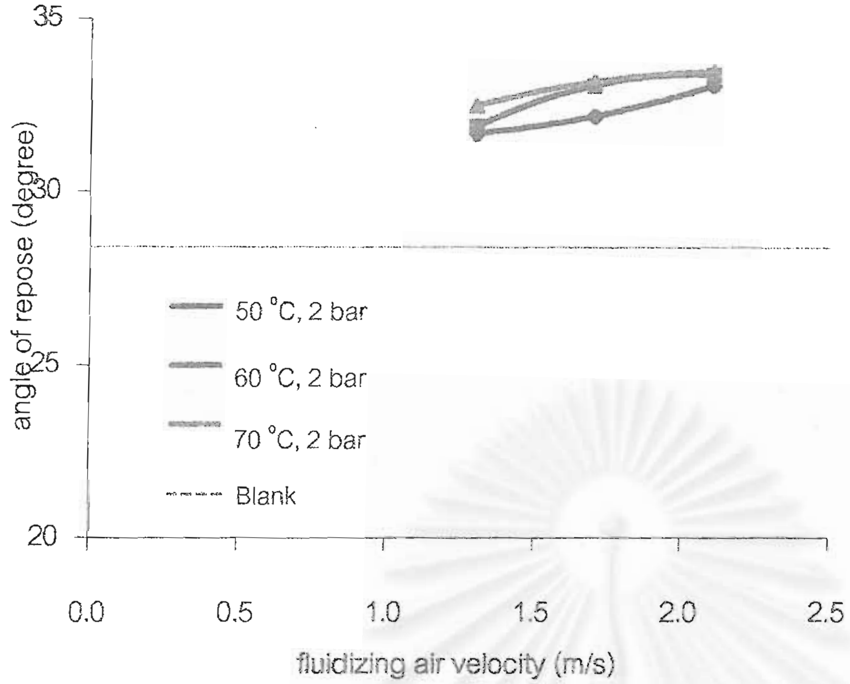


Figure 5.20 Angle of repose of coated particles obtained by using ultrasonic resonator under various coating conditions

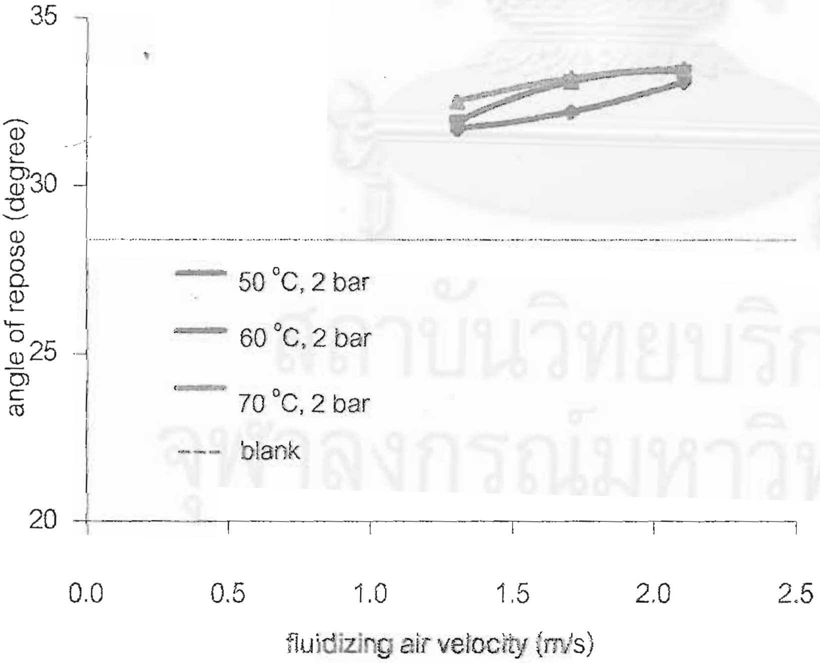


Figure 5.21 Angle of repose of coated particles obtained by using binary nozzle under various coating conditions

core particles, resulting in thicker film. As could be seen from the figures, the coating surface was rougher than that of the uncoated. Therefore the friction force acting on the surface of the coated particles should be supposed to be higher. Hence, it is reasonable to conclude that the angle of repose would become higher with an increase in the fluidizing air temperature.

5.8 Dissolution time

5.8.1 Effect of fluidizing air velocity

Figure 5.22 and 5.23 show the results of the dissolution time of the uncoated particles and the coated particles obtained by using two different nozzles. As mentioned above, increasing the fluidizing air velocity gave rise to an increase in the film thickness. Thus, the thicker film helped retard the dissolution time of the non-pareil seeds dissolved in the distilled water. The release rate of coated particles with HPMC was in agreement with the result of Govender et al. (1995).

5.8.2 Effect of fluidizing air temperature

Figure 5.22 and 5.23 also displayed the effect of the fluidizing air temperature on the dissolution time. The experimental results reveal than fluidizing air temperature has less effect on the dissolution of coated particles.

5.9 Comparison nozzle type on coated particles' properties

5.9.1 Film thickness

When comparing the film thickness of the coated particles obtained by using the ultrasonic resonator with that of the binary nozzle under various coating conditions, it was found that the thickness of coating film obtained from the binary nozzle is somehow thicker than that of the ultrasonic resonator. This result could be implied that the size distribution of

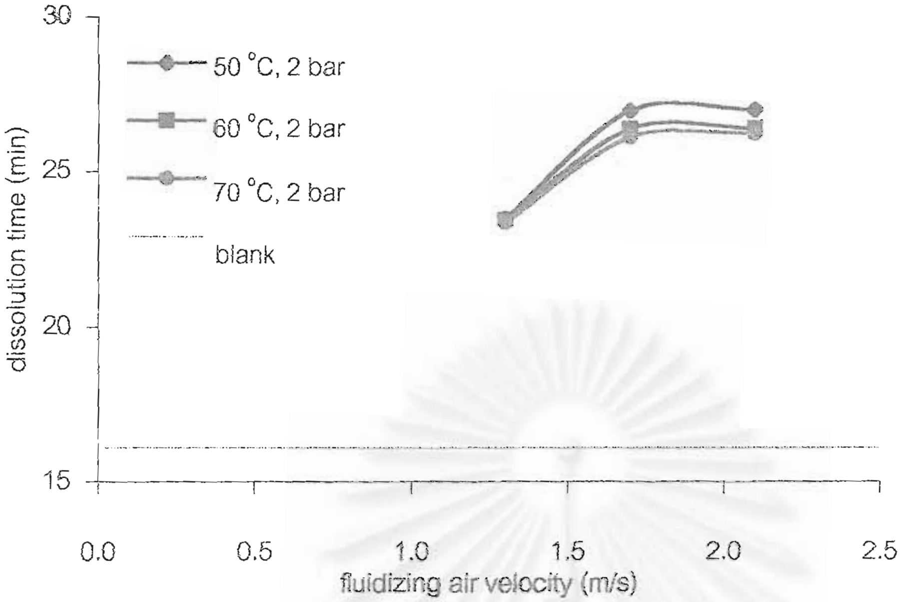


Figure 5.22 Dissolution time of coated particles obtained by using ultrasonic resonator under various coating conditions

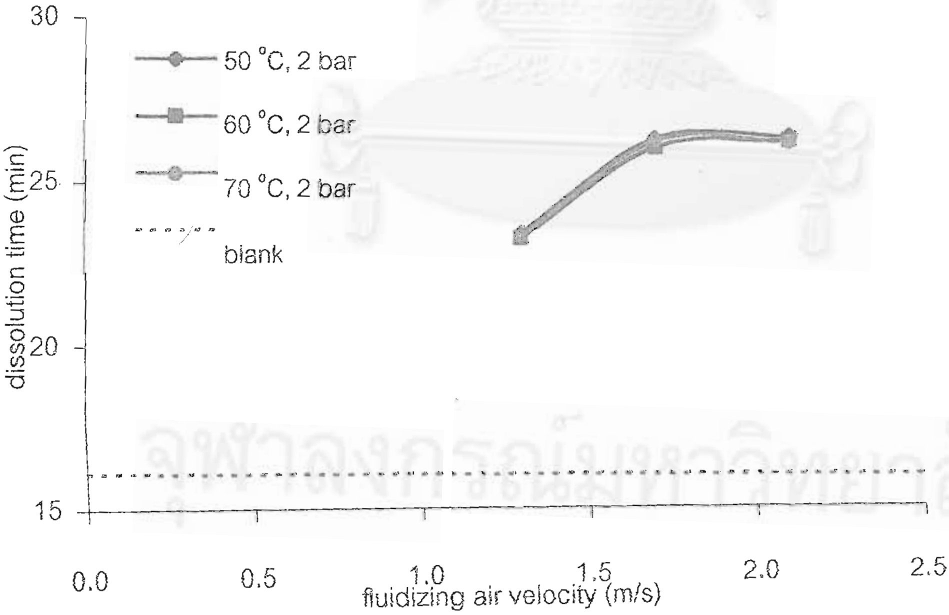


Figure 5.23 Dissolution time of coated particles obtained by using binary nozzle under various coating conditions

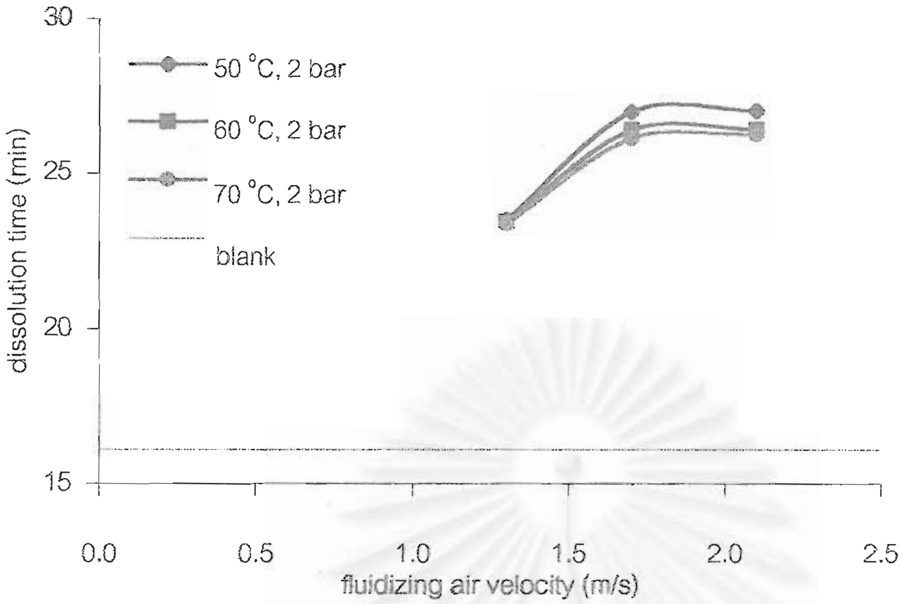


Figure 5.22 Dissolution time of coated particles obtained by using ultrasonic resonator under various coating conditions

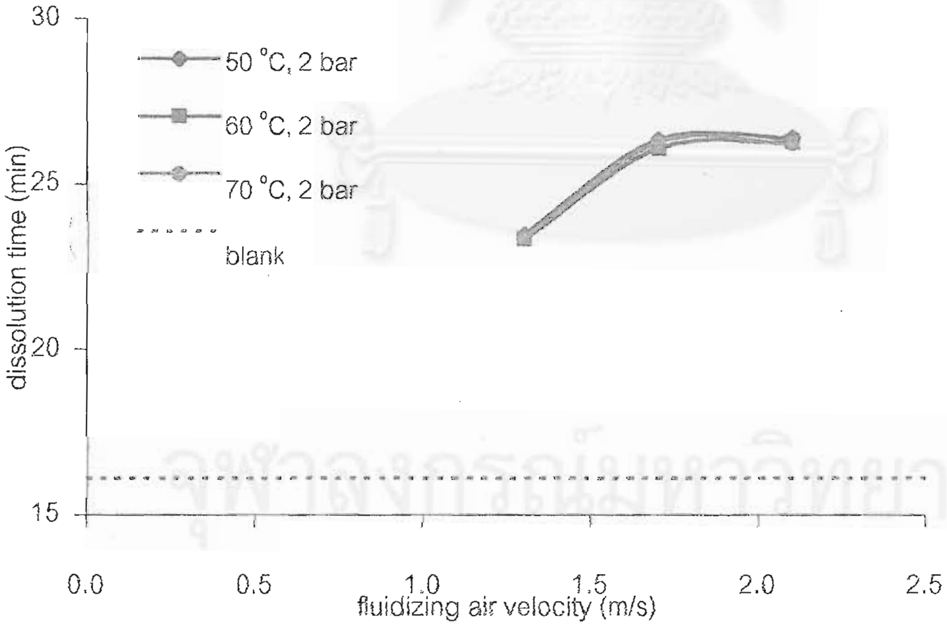


Figure 5.23 Dissolution time of coated particles obtained by using binary nozzle under various coating conditions

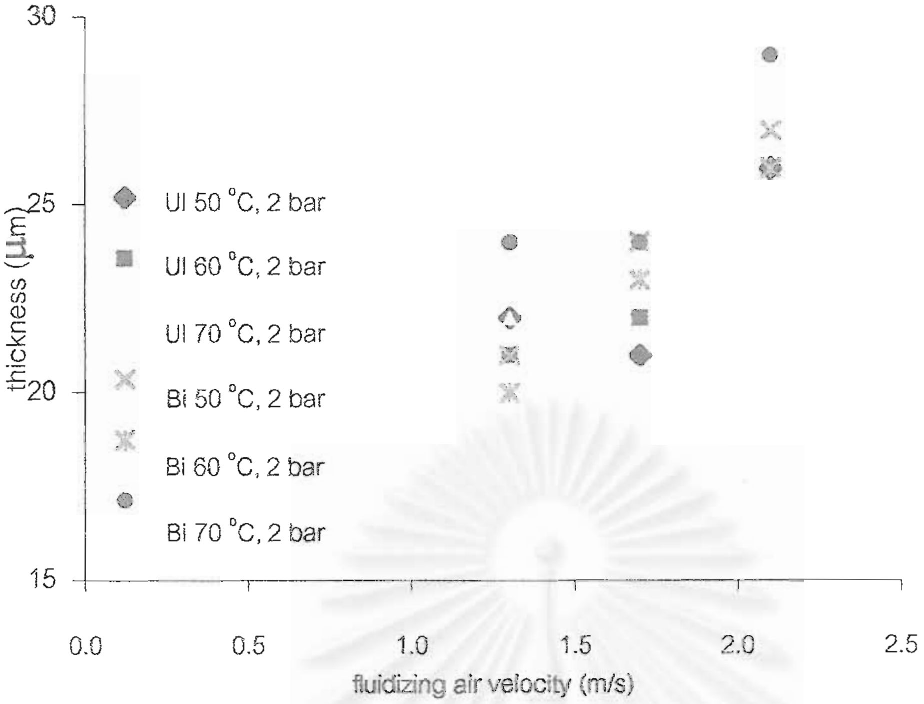


Figure 5.24 Comparison of film thickness of coated particles obtained by using ultrasonic resonator and binary nozzle under the various coating conditions

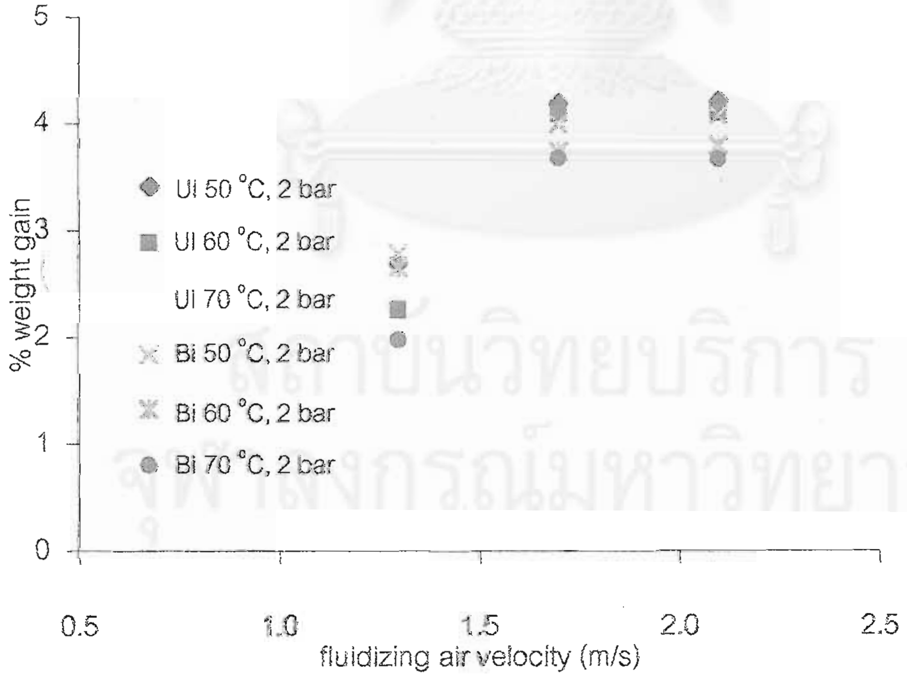


Figure 5.25 Comparison of % weight gain of coated particles obtained by using ultrasonic resonator and binary nozzle under various coating conditions

droplets produced by two nozzles (appendix b) were different. Geometric mean diameter of the sprayed droplets obtained from ultrasonic resonator was smaller than that of the binary nozzle. Consequently, the sprayed droplet obtained from the binary nozzle could be evaporated more slowly, resulting in less lose of the droplet. Moreover, the pressure exerted from the ultrasonic resonator was higher than that of the binary nozzle. It led to the higher degree of share at the surface of the coated particles.

5.9.2 Percentage of the weight gain and the production yield

Figure 5.25 and 5.26 show the result of comparison of the weight gain percentage and the production yield which were obtained by using two different nozzle types. It was found that there was no difference in both characteristics under the same coating conditions regardless of the nozzle types. It could be clearly understood that the core particles have average size range of 850 – 1,180 μm, as well as the same amount of coating solution (150 ml), therefore the coated product should be supposed to be the same.

5.9.3 Packed bulk density

As shown in figure 5.27, interestingly, it was found that the coated particles obtained by using the binary nozzle has somehow higher packed bulk density than that of the ultrasonic resonator. In fact, it was supposed that the binary nozzle could give rise to the thicker coating film, therefore it should result in the less dense particles. These results must required further investigation.

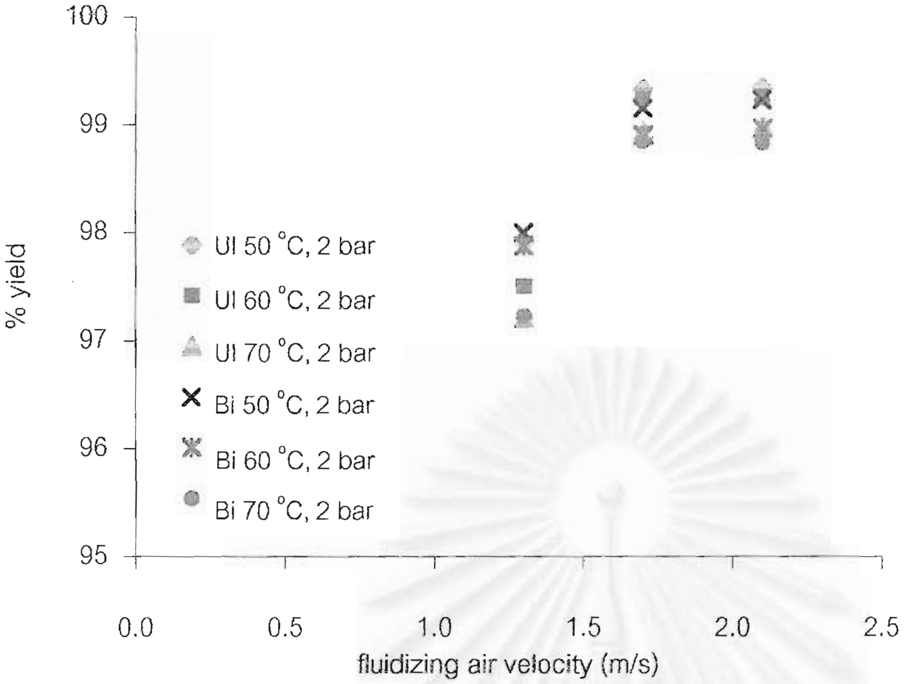


Figure 5.26 Comparison of % yield of coated particles obtained by using ultrasonic resonator and binary nozzle under various coating conditions

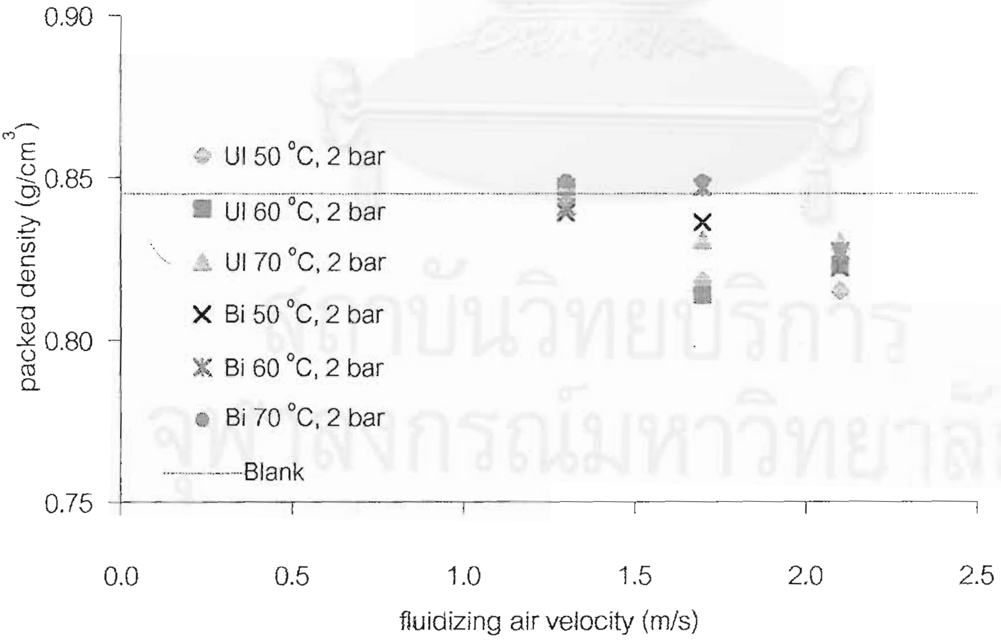


Figure 5.27 Comparison of packed bulk density of coated particles obtained by using ultrasonic resonator and binary nozzle under various coating conditions

CHAPTER 6

CONCLUSIONS

6.1 Concluding remarks

The effects of major operating variables, which were fluidizing air velocity (1.3 – 2.1 m/s) and air temperature (50 – 70 °C) on the characteristics of the coated particles obtained by using two different types of nozzles were investigated. The characteristics of the coated particles include the coating film thickness, the percentage of the weight gain, the percentage of the yield, the percentage of the agglomerate, the surface morphology, the angle of repose, the packed bulk density and dissolution time. From the experimental results, it could be concluded as follows,

1. Fluidizing air velocity has significant effect on all the properties studied.
2. Fluidizing air temperature also has tangible influence on every characteristics except the dissolution time.
3. After coating process, the thickness of the coating film on the coated particles became higher but no influence on average size of finished product was detected.
4. Two different types of nozzles used in this work exhibited different influence on the properties of the coated particles due to the difference of size distribution of the droplets produced by each nozzle.
5. The ultrasonic resonator employed in this work could produce droplet with size distribution narrow than that of the binary nozzle.

5.2 Recommendation for future work

1. Using ultrasonic nozzle equipped with piezoelectric transducer for coating process instead of ultrasonic equipped with resonator would help reduce effect of atomizing air pressure.
2. Humidity in the fluidized bed coater should be controlled the moisture content of particles.

3. Equip an exhausted duct at the top of the equipment in order to prevent the particles strike the bag filter and assist to evaporation of spray droplet.
4. The model drug should be changed to observe control release characteristics.
5. Comparison of the mechanical properties of free films obtained from ultrasonic resonator and binary nozzles should be further investigated.

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APPENDICES

APPENDIX A

Calibration Curve

The fluidizing air velocity versus height of water difference in difference orifice diameters is presented in table A.1 and A.2 respectively. The calibration curve obtained by pressure drop between orifice that shown in height of water difference in manometer are depicted in Figures 1, 2 and 3, respectively.

Table A.1 Height of water difference in orifice diameter 20 mm.

Height of water Difference in Manometer (cm)	Fluidizing air velocity (m/s)					
	No 1	No 2	No 3	No 4	No 5	Average.
3	0.5	0.4	0.4	0.5	0.4	0.4
6	0.9	0.9	0.9	0.9	1.0	0.9
7.5	1.1	1.1	1.0	1.1	1.2	1.1
13	1.5	1.5	1.5	1.5	1.5	1.5
15	1.7	1.7	1.7	1.7	1.7	1.7
18	2.1	2.1	2.1	2.1	2.1	2.1
22	2.4	2.4	2.4	2.4	2.5	2.4

Fluidizing air velocity is measured at room temperature (≈ 30 ^{o}C)

Table A.2 Height of water difference in orifice diameter 27 mm.

Height of water Difference in Manometer (cm)	Fluidizing air velocity (m/s)					
	No 1	No 2	No 3	No 4	No 5	Average.
2	2.1	2.1	2.0	2.1	2.1	2.1
3	2.4	2.5	2.5	2.5	2.5	2.5
5	3.2	3.3	3.2	3.2	3.2	3.2
8	4.3	4.3	4.3	4.3	4.3	4.3
12	5.0	5.1	5.0	5.0	5.0	5.0
14	5.2	5.3	5.2	5.2	5.2	5.2
15	5.4	5.4	5.3	5.3	5.4	5.4

Fluidizing air velocity is measured at room temperature ($\approx 30\,^{o}C$)

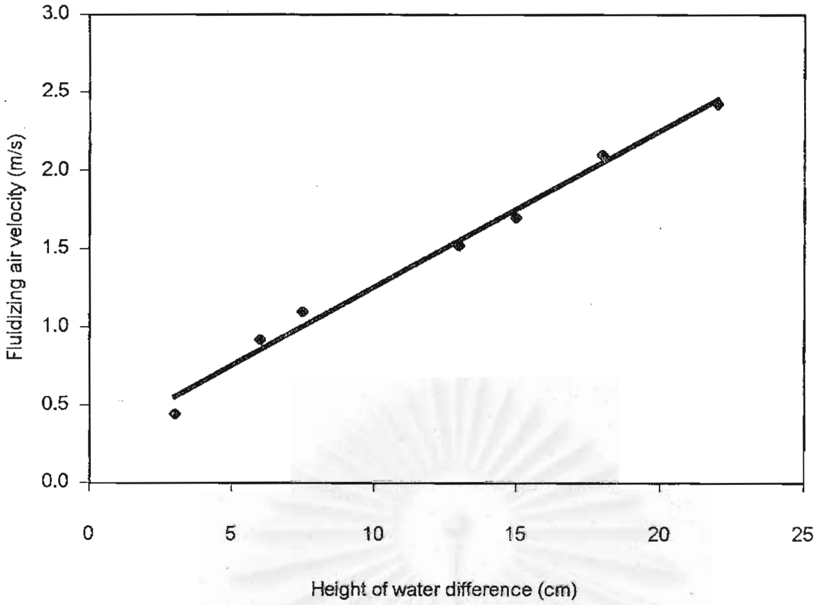


Figure 1 Calibration curve of orifice diameter 20 millimeters

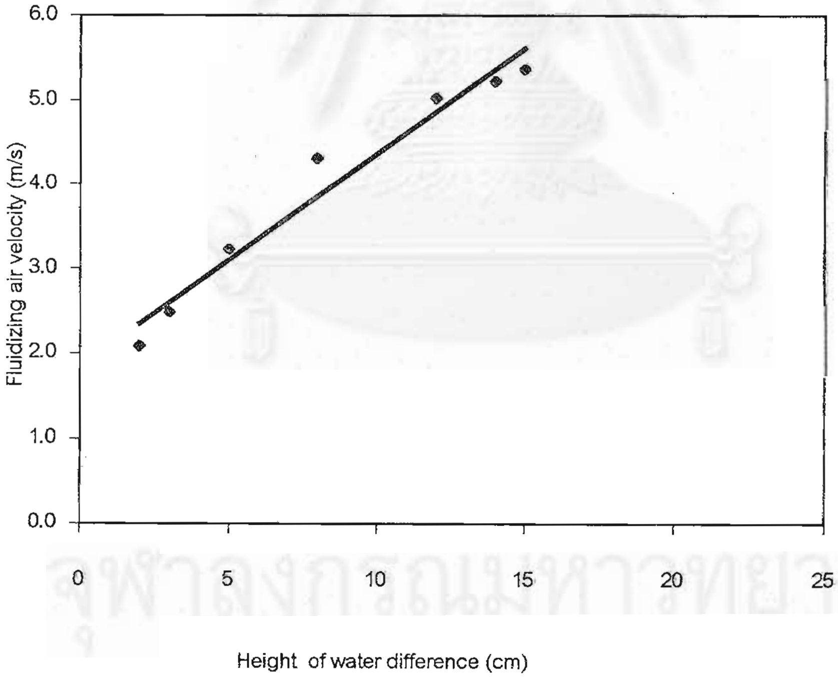


Figure 2 Calibration curve of orifice diameter 27 millimeters

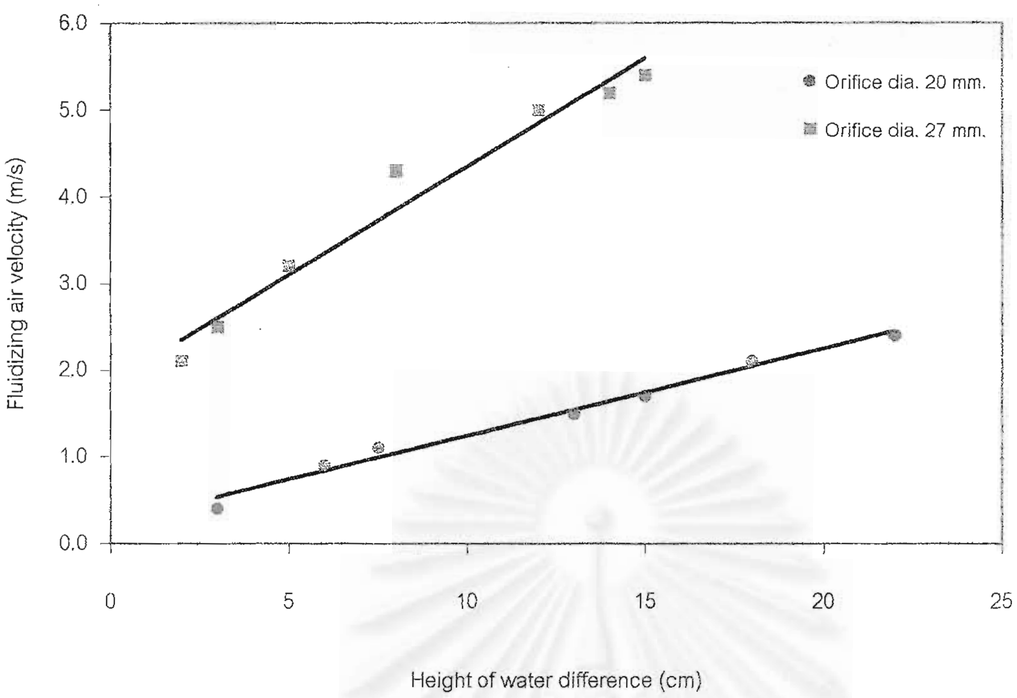


Figure 3 Calibration curve of orifice diameter 20 and 27 millimeters

APPENDIX B

B1. Spray droplet size distribution.

Type Nozzle	: Ultrasonic with resonator
Flow rate of liquid coating	: 10 milliliters per minute
Liquid coating	: Hydroxypropyl methylcellulose (HPMC)
Concentration of liquid coating	: 5 % weight by ratio
Atomizing air pressure	: 2 bars
No droplets in sample	: 817 droplets

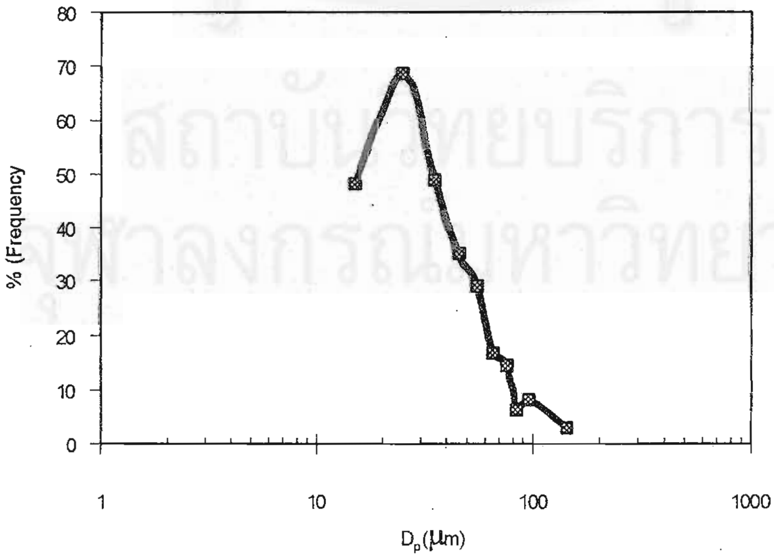
Interval, µm	Midpoint, d_i	no. (n)	n_i (%)	% Cumulative	$d_i \times n_i$	$d_{mean} - d_i$	$(d_{mean} - d_i)^2 \times n_i$	$\log d_i$	$n_i \log d_i$	$\log d_{mean} - \log d_i$	$(\log d_{mean} - \log d_i)^2 \times n_i$
0 – 10	5	31	3.79	3.79	18.97	25.88	2,540.42	0.699	2.652	0.791	2.372
10 – 20	15	271	33.17	36.96	495.55	15.88	8,359.55	1.176	39.011	0.314	3.260
20 – 30	25	227	27.78	64.74	694.61	5.88	959.05	1.398	38.841	0.092	0.233
30 – 40	35	115	14,08	78.82	492.66	-4.12	239.49	1.544	21.734	-0.054	0.042
40 – 50	45	64	7.83	86.65	352.51	-14.12	1,562.88	1.653	12.951	-0.164	0.210
50 – 60	55	43	5.26	91.91	289.47	-24.12	3,063.20	1.740	9.160	-0.251	0.331
60 – 70	65	21	2.57	94.48	167.07	-34.12	2,993.22	1.813	4.660	-0.323	0.269
70 – 80	75	16	1.96	96.44	146.88	-44.12	3,812.99	1.875	3.672	-0.385	0.291
80 – 90	85	6	0.73	97.17	62.42	-54.12	2,151.41	1.929	1,417	-0.440	0.142
90 – 100	95	7	0.86	98.03	81.40	-64.12	3,523.13	1.978	1.695	-0.488	0.204
100 – 190	145	16	1.96	100.00	283.97	-114.12	25,506.94	2.161	4.233	-0.672	0.884
	Total	817	100.00		3,087.52		54,712.27		140.025		8.238

Geometric mean diameter = 25.133 µm

Geometric standard deviation = 1.943

Arithmetic mean diameter = 30.875 µm

Arithmetic standard deviation = 23.508



Type Nozzle : Binary

Flow rate of liquid coating : 10 milliliters per minute

Liquid coating : Hydroxypropyl methylcellulose (HPMC)

Concentration of liquid coating : 5 % weight by ratio

Atomizing air pressure : 2 bars

No droplets in sample : 820 droplets

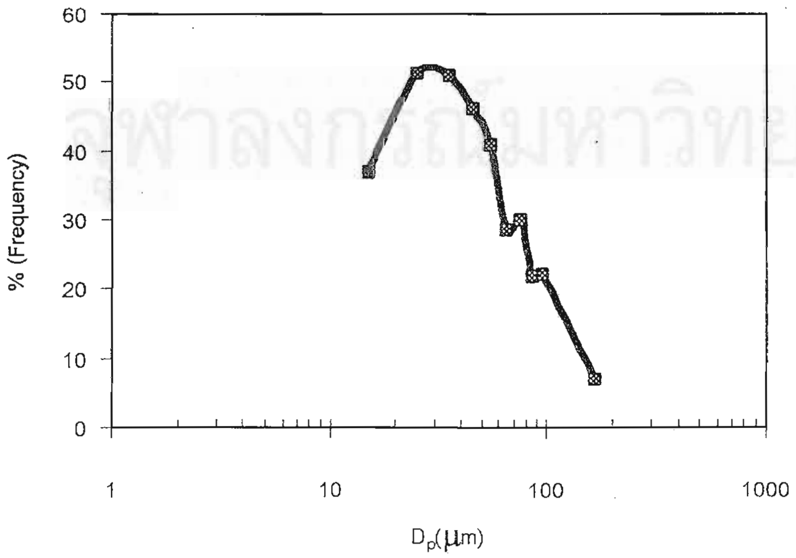
Interval, μm	Midpoint, d_i	no. (n)	n_i (%)	% Cumulative	$d_i \times n_i$	$d_{mean} - d_i$	$(d_{mean} - d_i)^2 \times n_i$	log d_i	n_i log d_i	log d_{mean} – log d_i	(log d_{mean} – log $d_i)^2 \times n_i$
0 – 10	5	18	2.20	2.20	10.98	37.68	3,117.08	0.699	1.534	0.931	1.904
10 – 20	15	211	25.73	27.93	385.98	27.68	19,719.35	1.176	30.263	0.454	5.308
20 – 30	25	170	20.73	48.66	518.29	17.68	6,482.51	1.398	28.982	0.232	1.119
30 – 40	35	120	14.63	63.29	512.20	7.68	863.82	1.544	22.596	0.086	0.109
40 – 50	45	84	10.24	73.54	460.98	-2.32	55.00	1.653	16.935	-0.023	0.005
50 – 60	55	61	7.44	80.98	409.15	-12.32	1,128.58	1.740	12.947	-0.110	0.090
60 – 70	65	36	4.39	85.37	285.37	-22.32	2,186.57	1.813	7.959	-0.183	0.146
70 – 80	75	33	4.02	89.39	301.83	-32.32	4,203.05	1.875	7.546	-0.245	0.241
80 – 90	85	21	2.56	91.95	217.68	-42.32	4,586.03	1.929	4.941	-0.299	0.229
90 – 100	95	19	2.32	94.27	220.12	-52.32	6,342.01	1.978	4.583	-0.347	0.280
100 – 230	165	47	5.73	100.00	945.73	-122.32	85,754.75	2.217	12.710	-0.587	1.977
	Total	820	100.00		4,268.29		134,438.73		150.996		11.408

Geometric mean diameter = 32.356 μm

Geometric standard deviation = 2.185

Arithmetic mean diameter = 42.683 μm

Arithmetic standard deviation = 36.851



APPENDIX C

C1.1 Experimental results of coated particles by using ultrasonic nozzle.

Properties	Uncoated particles	Fluidizing air velocity / Fluidizing air temperature / Atomizing air pressure (m/s, °C, bar)								
		1.3/ 50/ 2	1.3/ 60/ 2	1.3/ 70/ 2	1.7/ 50/ 2	1.7/ 60/ 2	1.7/ 70/ 2	2.1/ 50/ 2	2.1/ 60/ 2	2.1/ 70/ 2
Film thickness (μm)	-	22	21	22	21	22	24	26	26	27
% Weight gain	-	2.69	2.26	1.96	4.19	4.09	3.78	4.21	4.10	3.82
% Yield	-	97.91	97.51	97.21	99.34	99.25	98.95	99.35	99.26	98.99
% Agglomerate	-	0.22	0.13	0.04	1.78	0.11	0.31	0.04	0.02	0.02
Packed bulk density (g/ cm^3)	0.845	0.842	0.847	0.848	0.818	0.814	0.831	0.815	0.823	0.830
Angle of repose (degree)	28.4	31.7	31.9	32.5	32.2	33.1	33.2	33.1	33.4	33.5
Solubility time (minute)	16.11	23.51	23.49	23.40	27.00	26.41	26.14	27.04	26.44	26.28

C1.2 Experimental results of coated particles by using binary nozzle.

Properties	Uncoated particles	Fluidizing air velocity / Fluidizing air temperature / Atomizing air pressure (m/s, °C, bar)								
		1.3/ 50/ 2	1.3/ 60/ 2	1.3/ 70/ 2	1.7/ 50/ 2	1.7/ 60/ 2	1.7/ 70/ 2	2.1/ 50/ 2	2.1/ 60/ 2	2.1/ 70/ 2
Film thickness (μm)	-	21	20	24	24	23	24	27	26	29
% Weight gain	-	2.79	2.66	1.98	4.00	3.74	3.68	4.08	3.80	3.67
% Yield	-	98.00	97.88	97.23	99.16	98.91	98.85	99.24	98.97	98.84
% Agglomerate	-	0.13	0.04	0.03	0.87	0.05	0.13	0.04	0.01	0.01
Packed bulk density (g/ cm^3)	0.845	0.839	0.841	0.849	0.836	0.847	0.849	0.822	0.827	0.828
Angle of repose (degree)	28.4	30.3	30.6	31.4	30.6	31.4	31.9	31.0	31.9	32.4
Solubility time (minute)	16.11	23.47	23.35	23.38	26.36	26.10	26.27	26.41	26.28	26.25

APPENDIX D

Data of BET surface area analysis for coated pellets, which were obtained from the experiments.

<u>Remark</u> : SAMPLE I.D. = nozzle type under operating conditions velocity, temperature, pressure (m/s, °C, bar)

```
                      MICROMERITICS INSTRUMENT CORPORATION
                                 FlowSorb 2300

                            BET SURFACE AREA ANALYSIS
                              REPORT DATE: 01/14/45

SAMPLE I.D.: Non-pareil seed: Blank                       ADSORBATE:  Nitrogen
SAMPLE WEIGHT:  2.2244 g                        BAROMETRIC PRESSURE:  760 mmHg
MOL. CROSS-SECTIONAL AREA: 0.162 nm^2           SATURATION PRESSURE:  775 mmHg
AMBIENT TEMPERATURE:  22.00 C

         EXPERIMENTAL DATA       VOL ADSORBED        X=P/Po       Y=X/[(1-X)V]
           (%)       (VOL)      (cm^3/g AT STP)

          5.000      0.03            0.01           0.0490         4.13094
         12.000      0.05            0.02           0.1177         6.41136
         18.000      0.06            0.02           0.1765         8.58682
         24.000      0.07            0.03           0.2354         %10.56865

         BET SURFACE AREA:       0.12   +/-  0.00 m^2/g
         SLOPE:                 34.7656 +/-  0.5033
         INTERCEPT:              2.3958 +/-  0.0807
         C:                     15.51
         Vm:                     0.03 cm^3/g
         CORRELATION COEFFICIENT 0.9998

         +-------------------------------------------------------------------+
10.56865-|                                                               *   |
         |                                                                   |
         |                                                                   |
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         |                                                                   |
         |                                                                   |
         |                               *                                   |
     X   |                                                                   |
Y= ----- |                                                                   |
  (1-X)V |                                                                   |
         |            *                                                      |
         |                                                                   |
         |                                                                   |
         |                                                                   |
         |                                                                   |
         |                                                                   |
         |                                                                   |
       0-+-------------------------------------------------------------------+
         0                              X=P/Po                              0.25
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                      MICROMERITICS INSTRUMENT CORPORATION
                                 FlowSorb 2300

                            BET SURFACE AREA ANALYSIS
                              REPORT DATE: 02/05/45

SAMPLE I.D.: ul 1.3 70 2                                   ADSORBATE:  Nitrogen
SAMPLE WEIGHT:  0.5506 g                       BAROMETRIC PRESSURE:  760 mmHg
MOL. CROSS-SECTIONAL AREA: 0.162 nm^2          SATURATION PRESSURE:  775 mmHg
AMBIENT TEMPERATURE:  22.00 C

        EXPERIMENTAL DATA       VOL ADSORBED        X=P/Po        Y=X/[(1-X)V]
          (%)        (VOL)    (cm^3/g AT STP)

         5.000       0.03           0.05          0.0490          1.02252
        12.000       0.05           0.08          0.1177          1.58699
        18.000       0.06           0.10          0.1765          2.12547
        24.000       0.07           0.12          0.2354          2.61603

        BET SURFACE AREA:          0.47   +/-   0.01 m^2/g
        SLOPE:                     8.6054 +/-   0.1243
        INTERCEPT:                 0.5930 +/-   0.0199
        C:                        15.51
        Vm:                        0.11 cm^3/g
        CORRELATION COEFFICIENT    0.9998
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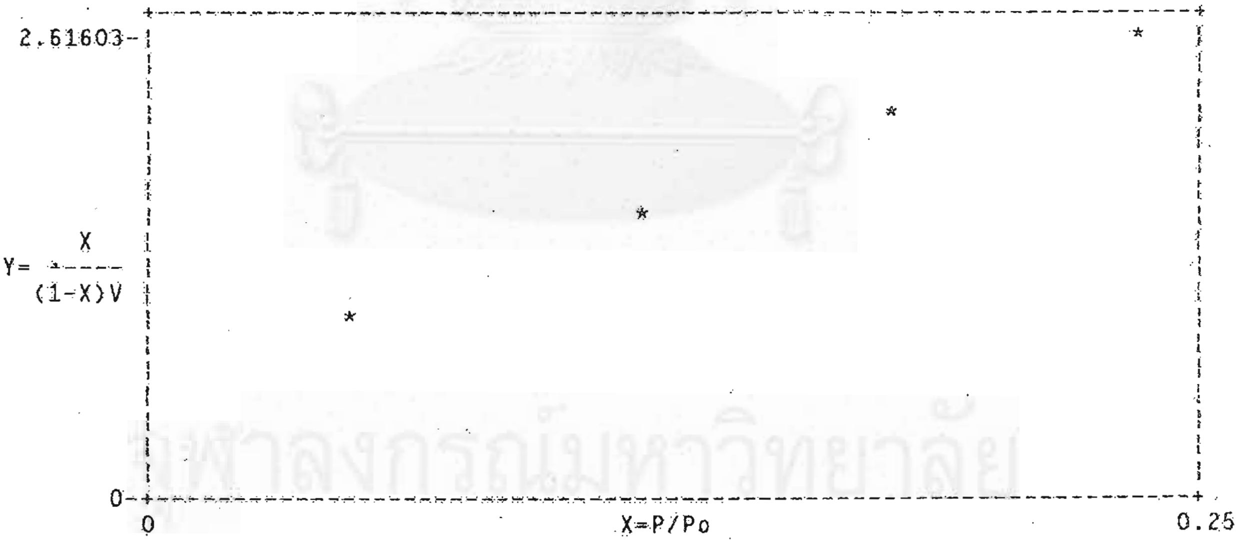

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                  MICROMERITICS INSTRUMENT CORPORATION
                             FlowSorb 2300

                       BET SURFACE AREA ANALYSIS
                         REPORT DATE: 02/05/45

SAMPLE I.D.: ul 1.7 50 2                              ADSORBATE:  Nitrogen
SAMPLE WEIGHT:  0.6804 g                    BAROMETRIC PRESSURE:  760 mmHg
MOL. CROSS-SECTIONAL AREA: 0.162 nm^2       SATURATION PRESSURE:  775 mmHg
AMBIENT TEMPERATURE:  22.00 C

         EXPERIMENTAL DATA       VOL ADSORBED        X=P/Po        Y=X/[(1-X)V]
           (%)        (VOL)    (cm^3/g AT STP)

          5.000        0.05          0.07             0.0490          0.75814
         12.000        0.07          0.10             0.1177          1.40079
         18.000        0.08          0.11             0.1765          1.96990
         24.000        0.09          0.12             0.2354          2.51435

         BET SURFACE AREA:         0.45   +/-  0.00 m^2/g
         SLOPE:                    9.4487 +/-  0.0523
         INTERCEPT:                0.2941 +/-  0.0084
         C:                       33.13
         Vm:                       0.10 cm^3/g
         CORRELATION COEFFICIENT 1.0000

        +--------------------------------------------------------------------+
2.51435-|                                                               *    |
        |                                                                    |
        |                                                                    |
        |                                                                    |
        |                                               *                    |
        |                                                                    |
        |                                                                    |
        |                                                                    |
    X   |                               *                                    |
Y= -----|                                                                    |
 (1-X)V |                                                                    |
        |                                                                    |
        |                                                                    |
        |            *                                                       |
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        |                                                                    |
        |                                                                    |
      0-+--------------------------------------------------------------------+
        0                              X=P/Po                             0.25
```

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                    MICROMERITICS INSTRUMENT CORPORATION
                               FlowSorb 2300

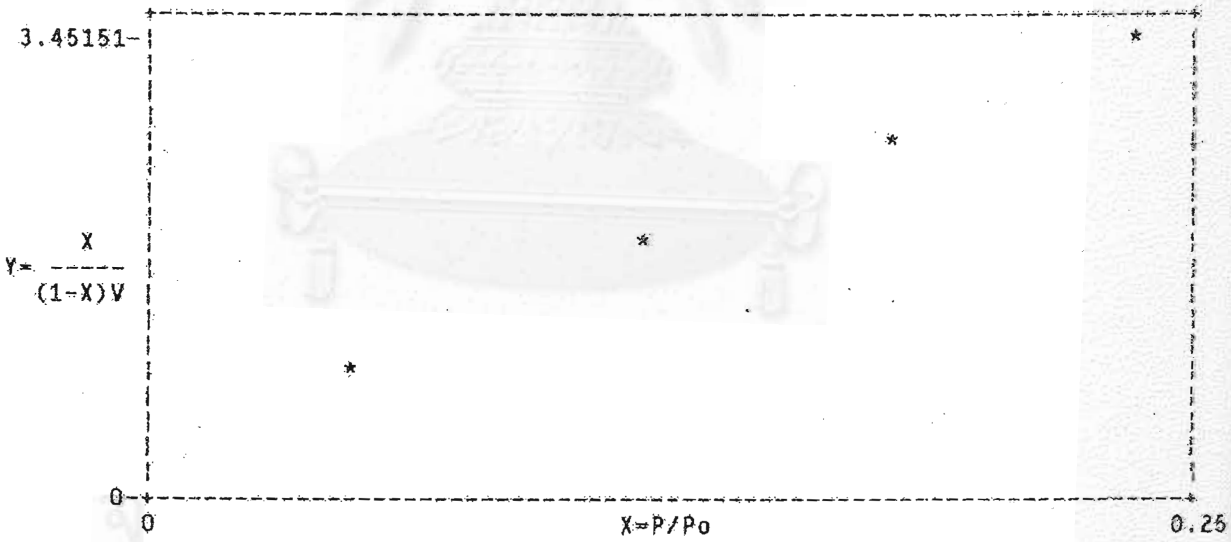
                          BET SURFACE AREA ANALYSIS
                          REPORT DATE: 01/14/45

SAMPLE I.D.: bi 1.3 70 2                           ADSORBATE:  Nitrogen
SAMPLE WEIGHT:   1.8680 g               BAROMETRIC PRESSURE:  760 mmHg
MOL. CROSS-SECTIONAL AREA: 0.162 nm^2   SATURATION PRESSURE:  775 mmHg
AMBIENT TEMPERATURE:  22.00 C

      EXPERIMENTAL DATA      VOL ADSORBED          X=P/Po       Y=X/[(1-X)V]
        (%)        (VOL)    (cm^3/g AT STP)

       5.000        0.10          0.05              0.0490         1.04072
      12.000        0.14          0.07              0.1177         1.92290
      18.000        0.16          0.08              0.1765         2.70413
      24.000        0.18          0.09              0.2354         3.45151

      BET SURFACE AREA:          0.33    +/-   0.00 m^2/g
      SLOPE:                    12.9705 +/-   0.0713
      INTERCEPT:                 0.4037 +/-   0.0114
      C:                        33.13
      Vm:                        0.07 cm^3/g
      CORRELATION COEFFICIENT 1.0000
```



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                         MICROMERITICS INSTRUMENT CORPORATION
                                   FlowSorb 2300

                              BET SURFACE AREA ANALYSIS
                                REPORT DATE: 02/05/45

SAMPLE I.D.: bi 1.7 50 2                                    ADSORBATE:  Nitrogen
SAMPLE WEIGHT:  0.8392 g                          BAROMETRIC PRESSURE:  760 mmHg
MOL. CROSS-SECTIONAL AREA: 0.162 nm^2             SATURATION PRESSURE:  775 mmHg
AMBIENT TEMPERATURE:  22.00 C

        EXPERIMENTAL DATA         VOL ADSORBED          X=P/Po          Y=X/[(1-X)V]
          (%)        (VOL)       (cm^3/g AT STP)

         5.000       0.06             0.07              0.0490             0.77924
        12.000       0.08             0.09              0.1177             1.51176
        18.000       0.09             0.10              0.1765             2.15970
        24.000       0.10             0.11              0.2354             2.79107

        BET SURFACE AREA:          0.39    +/-   0.00 m^2/g
        SLOPE:                    10.8164 +/-   0.0444
        INTERCEPT:                 0.2459 +/-   0.0071
        C:                        44.99
        Vm:                        0.09 cm^3/g
        CORRELATION COEFFICIENT 1.0000
```

VITA

Mr.Kittisak Phuengsomboonying was born on 29th March 1974 in Bangkok, Thailand. He finished his high school from Debsirin school in 1992. After that, he studied in the major of Chemical Industry in Faculty of Science at King Mongkut Institute's Technology. After graduation, he worked for a while as Technical sale person at Loxley Co., Ltd. before entering the Master program of Chemical Engineering at Chulalongkorn University in 1998. In 2002, he got his Master degree by carrying out a research work focusing on development of fluidized-bed coater with two types of spraying nozzles.