



*Universita' degli Studi di Milano*



## *Corso di Laurea in Chimica e Tecnologia Farmaceutiche*

### *Fabbricazione Industriale dei Medicinali - 8 CFU*

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**FORME FARMACEUTICHE SOLIDE ORALI - Processo di Rivestimento**

# **COATING OF PHARMACEUTICAL SOLID-DOSAGE FORMS**

Carlo Vecchio

# INTRODUCTION

Benefits of tablet and granule coating include:

- Improved aesthetic quality
- Masking of unpleasant taste or odor
- Increasing the ease to swallow by the patient
- Facilitating handling, particularly in high-speed filling/packaging lines
- Improving product stability
- Modifying drug release characteristics.

# INTRODUCTION

Changes that have occurred in coating processes reflect a desire to:

- obtain a finished product of high and reproducible quality
- achieve processes in which the economics are maximized (process times and equipment utilization).

# INTRODUCTION

The major pharmaceutical coating techniques are :

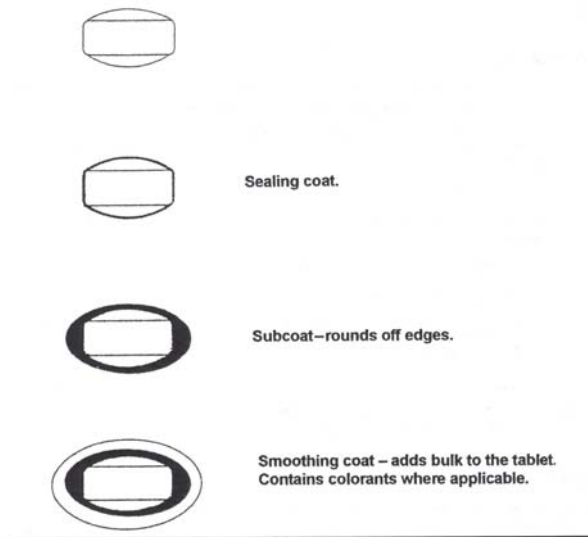
- Sugar Coating
- Film coating
- Microencapsulation
- Compression coating
- Dry coating
- Melting coating

and

- Dip coating
- Rotary die coating
- Electrostatic coating.

# INTRODUCTION

Figure 11.24 Stages of sugar coating.



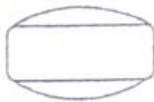
## Sugar Coating

It involves coating tablets with sucrose.

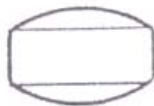
This is a highly skilled, multistep process that is very labour intensive.

The process involves applying a number of aqueous solutions of sucrose, together with additional components, which gradually build up into a smooth, aesthetically pleasant coat.

# INTRODUCTION



Cores as tablets



Film coated tablets

## Film coating

It involves the application of a polymer film to the surface of appropriate substrates such as:

- tablets,
- pellets,
- granules,
- capsules,
- powders, and
- crystals.

# INTRODUCTION

## Microencapsulation

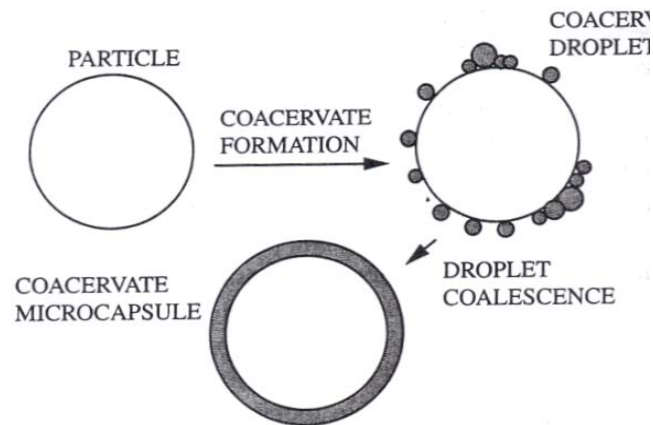
It involves the encapsulation of small particles of drug (a particle size range between 1 and 2000 microns), or solution of drug, in a polymer coat.

Microcapsules can be prepared by:

1. Coacervation (separation) of macromolecules around the core material, this being induced by temperature change, solvent change or addition of second macromolecule of appropriate physical properties
2. Interfacial polymerization of a monomer around the core material by inducing to polymerise at the interphase of a liquid dispersion
3. Physical methods such as pan coating, fluidized bed coating and spray drying coating.



# INTRODUCTION



**Fig. 2** Schematic diagram of the formation of a coacervate around a core material.

Coacervation is defined as the separation of colloidal systems into two liquid phases, one rich in colloid (i.e. the coacervate), and the other poor in colloid.

In simple coacervation the polymer is salted out by electrolytes such as sodium sulfate, or desolvated by the addition of a water miscible nonsolvent such as ethanol, or by an increase or decrease in temperature, pH, or ionic strength.

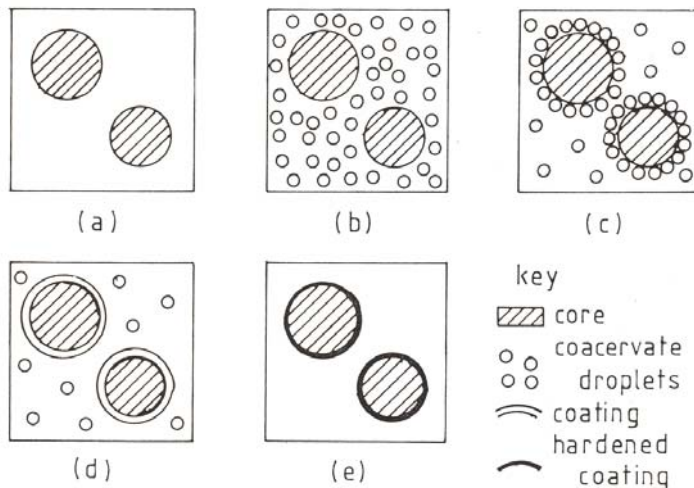
The liquid or solid to be encapsulated is dispersed in a solution of a macromolecule (gelatin and cellulose derivatives are the most widely used) in which it is immiscible.

A non-solvent, miscible with the continuous phase but a poor solvent for the polymer (es.  $\text{Na}_2\text{SO}_4$ ), under certain conditions will induce the polymer to form a coacervate (polymer-rich) layer around the dispersed phase.

This layer coating may then be treated to give a rigid coat (es. formaldehyde).

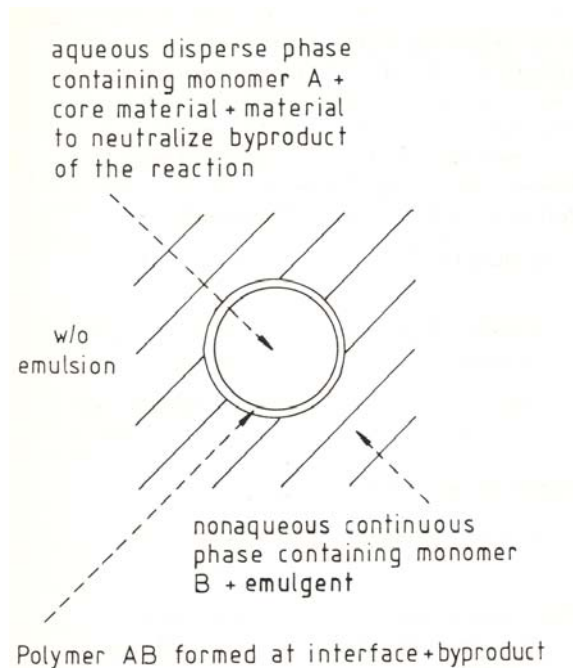
# INTRODUCTION

Typical steps in a coacervation method of microencapsulation:



- (a) Core particles dispersed in solution of polymer by agitation.
- (b) Coacervation visible as droplets of colloid-rich phase induced by one or more agents.
- (c) Deposition of coacervate droplets on surface of core particles.
- (d) Mergence of coacervate droplets to form the coating.
- (e) Shrinkage and crosslinking of the coating to rigidize it as necessary.

# INTRODUCTION



Interfacial polymerization involves the reaction of various monomers at the interface between two immiscible liquid phases to form a film polymer that encapsulated the dispersed phase.

Usually two reactive monomers are used, one dissolved in the aqueous disperse phase containing a solution or dispersion of the core material and the other dissolved after the emulsification step in the nonaqueous continuous phase .

The oil in water emulsion formed required the addition of a suitable emulgent as stabilizer.

# INTRODUCTION

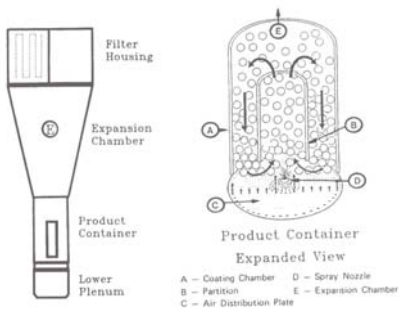
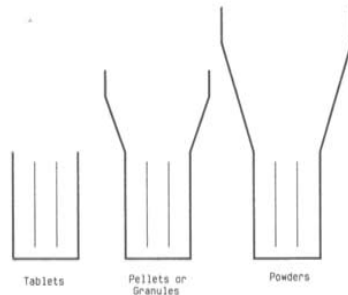


Fig. 12 Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

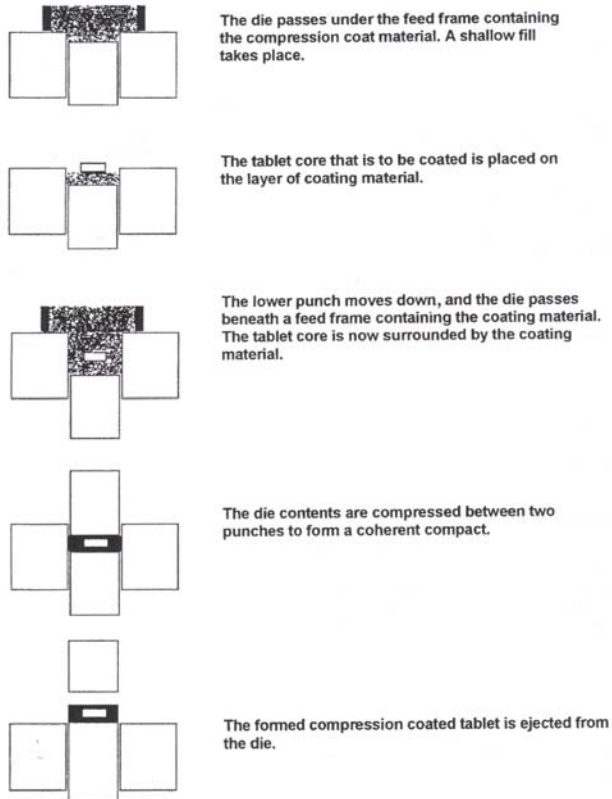
Physical methods such as:

- pan coating  
(for particles greater than 300-400  $\mu\text{m}$ ) ,
- fluidized bed coating  
(for particles greater than 50  $\mu\text{m}$ ) and
- spray drying coating.



# INTRODUCTION

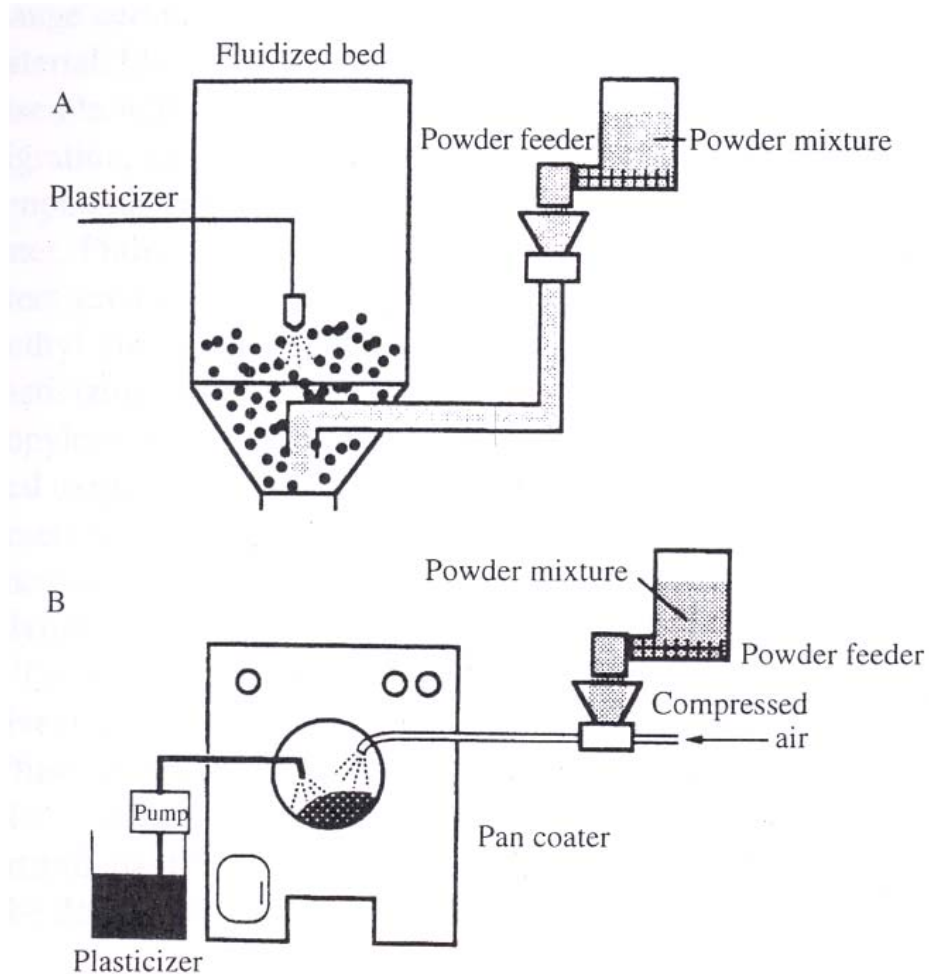
Figure 11.28 Schematic of the compression coating process.



## Compression coating

It involves producing a relatively soft tablet core containing drug substance and compressing a coating around it.

# INTRODUCTION



## Dry coating

It involves the application of a polymer powder spraying the liquid plasticizer to the surface of appropriate substrates

**Fig. 5** Schematic of the “dry coating” method: (A) fluidized bed apparatus; (B) pan coating apparatus.

# INTRODUCTION

## Melting coating

An alternative to the application of polymeric solutions or dispersions is to select a coating material that can be applied molten.

Because there is nothing to be evaporated, processing times are comparatively short.

Many of the reasons for coating (improved stability, taste masking, sustained release) can be achieved with available relatively inexpensive materials (polyethylene glycol, partially vegetable hydrogenated oils, waxes) .

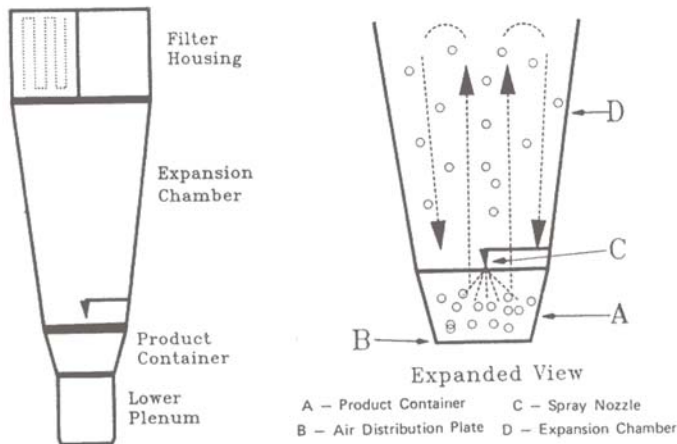


Fig. 11 Top spray coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

The top-spray fluidized-bed is used for melting coating

# INTRODUCTION

## Melting coating

The selection criteria for coating materials also include

- melting point,
- melting range, and
- viscosity (in a liquid state).

Typically, coatings should have a melting point of less than 85°C.

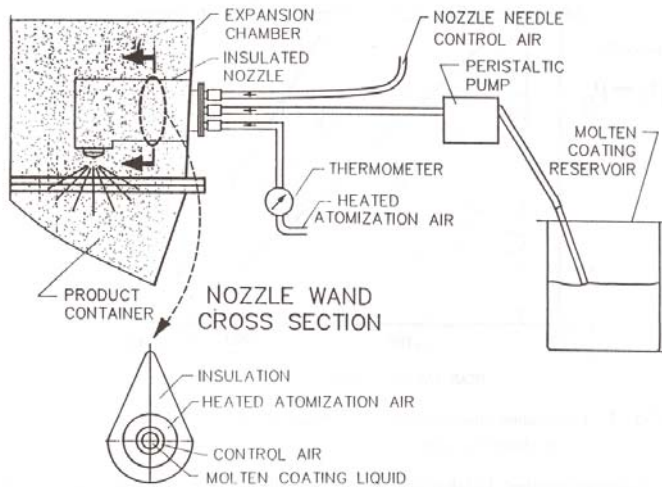


Fig. 2 Insulated nozzle and wand for top-spray hot-melt coating.

The liquid is maintained at a constant temperature during application, which is typically 40 to 60°C above its melting point.

Therefore, the liquid temperature may be as high as 140 to 150°C, which presents some challenges to equipment users concerning liquid storage and delivery to the spray nozzle, as well as operator safety during processing.

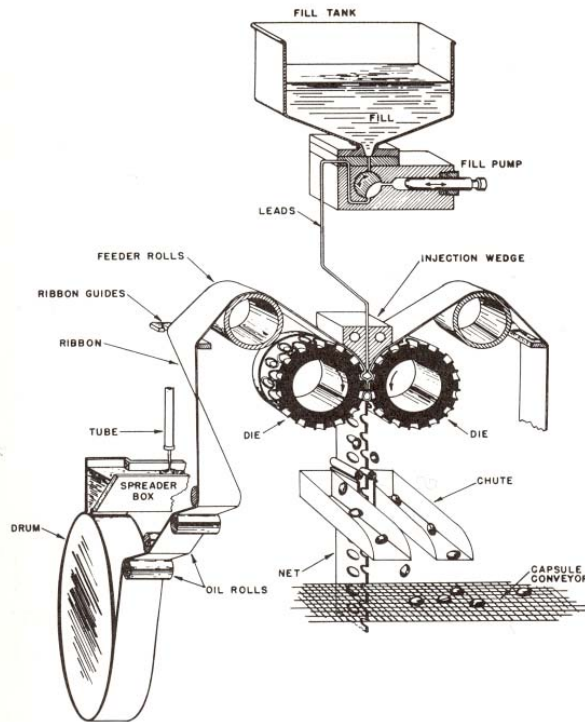


# INTRODUCTION

## Rotary die coating

It is used the same equipment of rotary die process for preparing the soft gelatin capsules.

The gelatin mass is substituted by coating liquid.



**FIG. 13-27.** Schematic drawing of rotary die process.  
(Courtesy of R.P. Scherer Corporation, Troy, MI.)

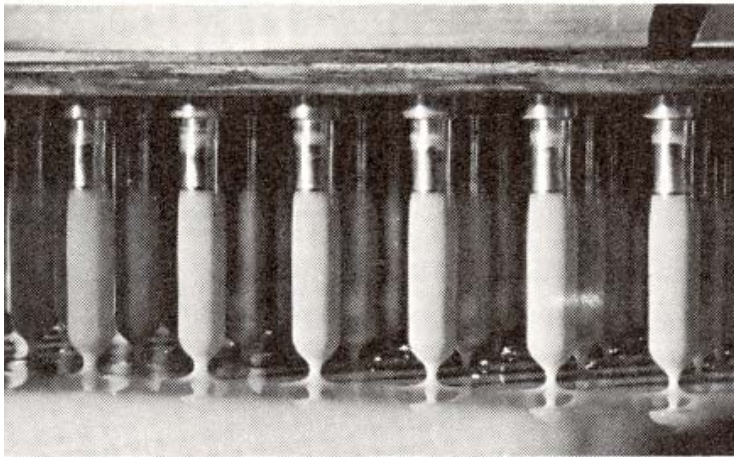
# INTRODUCTION

## Dip coating

It is applied to the tablet core by dipping them into the coating liquid.

The wet tablets are dried in a conventional manner in coating pans.

Alternate dipping and drying steps may be repeated several times to obtain the desired coating



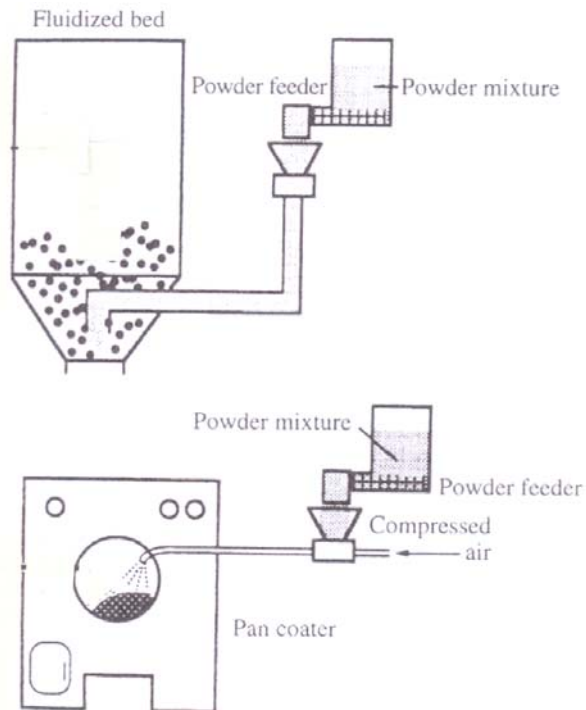
# INTRODUCTION

## Electrostatic coating

It is an efficient method of applying coating to conductive substrates.

A strong electrostatic charge is applied to the substrate.

The coating material containing conductive ionic species of opposite charge is sprayed onto charged substrate.



# INTRODUCTION

The lecture will focus on processes of sugar and film coating, and will discuss with respect to:

- Raw materials
- Application techniques
- Potential problems
- Available coating equipment.

# **SUGAR COATING**

## **Introduction**

Sugar coating has certain advantages over film coating:

- Raw materials are inexpensive and easily available
- Raw materials are widely accepted with few regulatory problems
- No complex equipment can be used
- Sugarcoated products are aesthetically pleasing and have wide consumer acceptability
- Process is generally not as critical as film coating and recovery procedures are possible.

# **SUGAR COATING**

## **Introduction**

Sugarcoating process does have some potential shortcomings:

- Increase of packaging and shipping costs (size and weight)
- Potential damage from mishandling because of brittleness
- Highly skilled coating operators to achieve of high aesthetically quality
- Difficult imprinting after final gloss step
- More difficult automation for the variety of procedures and formulations

# SUGAR COATING

## Introduction

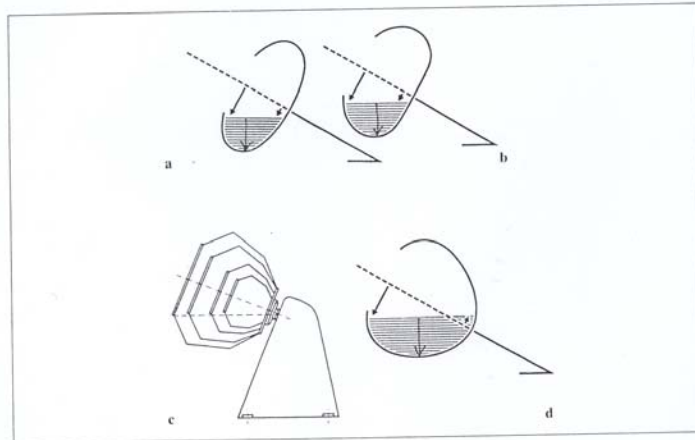


Fig. 7-12. Shapes of conventional coating pans  
(a) onion, (b) tulip, (c) polygon (in different sizes), (d) pear

Conventional coating pans are the spherical, hexagonal, or pear-shaped pans.

Drying is accomplished by ducting heated air into the opening.

An important modification to conventional coating pans is an angular coating pan that rotates on a horizontal axis, with access through openings in both the front and back (ducts for drying and exhausting air as well as the spray system).

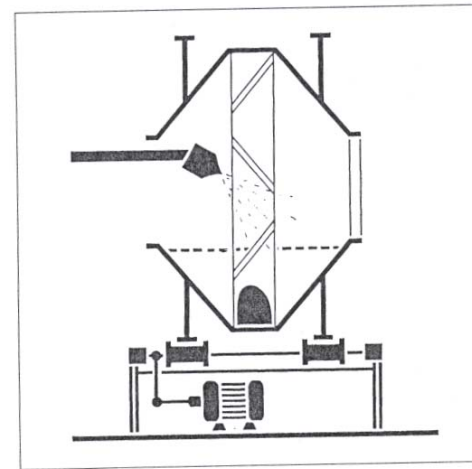


Fig. 7-13. Pan rotating on a horizontal axis (Pietro Pellegrini, Milan, Italy)

# Raw Materials Used in Sugar Coating

The major ingredient is sugar (sucrose), although this may be substituted by sorbitol.

A variety of additives may be incorporated:

- *Fillers* (Calcium carbonate, talc, titanium dioxide)
- *Colorants* (dyes, aluminum lakes, iron oxides, titanium dioxide)
- *Film former* (acacia, gelatin, cellulose derivatives)
- *Antiadhesives* (talc)
- *Flavors*
- *Surfactants* (as wetting agents and dispersion aids).



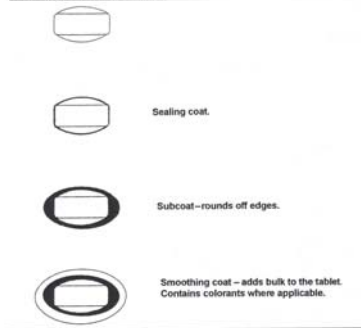
# Sugar Coating

A typical sugarcoating process involves five stages:

1. Sealing
2. Subcoating
3. Grossing
4. Color coating
5. Polishing.

# Sealing

Figure 11.24 Stages of sugar coating



The purpose of sealing is to offer the initial protection to the cores and to prevent the migration of ingredients from core to coating. Sealing is obtained by the application of a polymer-based coating to the surface of the tablet cores.

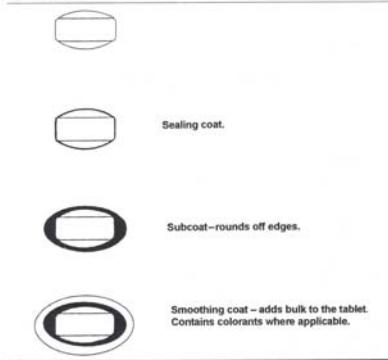
Polymers used are:

- *Shellac*
- *Zein*
- *Hydroxypropyl methylcellulose (HPMC)*
- *Polyvinyl acetate phthalate (PVAP)*
- *Cellulose acetate phthalate (CAP).*

They are dissolved in an appropriate organic solvent (at a 15-30% conc.).

# Subcoating

Figure 11.24 Stages of sugar coating.



Subcoating, the first major step of the sugar coating process, provides the means for rounding off the tablet edges and building up the core weight. Subcoating formulations contain high level of fillers such as:

- *talc*
- *calcium carbonate*
- *calcium sulphate*
- *kaolin and*
- *titanium dioxide.*

Auxiliary film former such as:

- *acacia*
- *gelatin*
- *cellulose derivatives*

may be included to improve the structural integrity of the coating.

# Tablet Shapes

The convex radius should be between 0.70 and 0.75 times the tablet diameter, and the band height between 0.07 and 0.12 times the tablet diameter

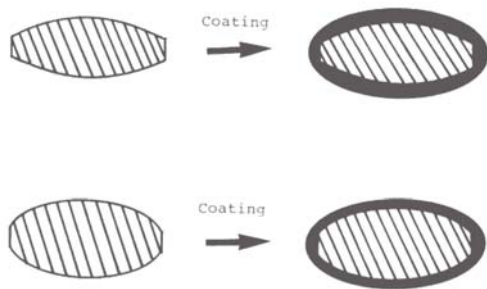


Figure 1 Schematic of examples of acceptable tablet-core shapes for sugar coating.

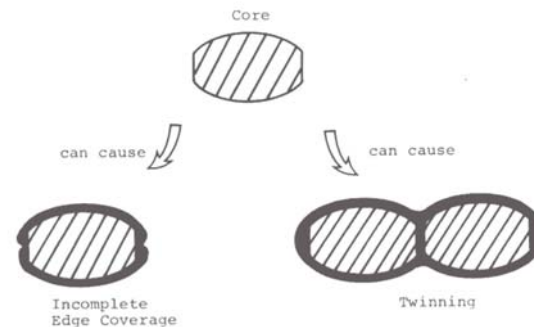


Figure 2 Schematic example of poor tablet core shape for sugar coating. (The twinning problem illustrated is more prevalent when using capsule-shaped tablets.)

# Subcoating

Two main approaches to the subcoating are :

- *lamination technique*
- *suspension subcoat formulation.*

Lamination process involves alternate application of binder solutions and dusting powder.

Suspension subcoating process results from combining the binder and powder formulations used in the traditional lamination technique.

Suspension subcoat technique reduces the complexity of the process.

*Less risk of sticking and twinning, automation of the process, less-experienced operators.*

# Subcoating

Tab. I - Formulation used in the lamination  
subcoating process

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<u>Binder solutions</u> , % w/w:		
Gelatin	3.3	8.0
Gum acacia	8.7	8.0
<u>Sucrose</u>	55.3	45.0
Distilled water	32.7	41.0
 <u>Dusting powders</u> , % w/w:		
Calcium carbonate	40.0	--
Titanium dioxide	5.0	1.0
Talc (asbestos free)	25.0	61.0
<u>Sucrose (powdered)</u>	28.0	38.0
Gum acacia	2.0	--

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# Subcoating

Tab. II - Suspension subcoating formulations

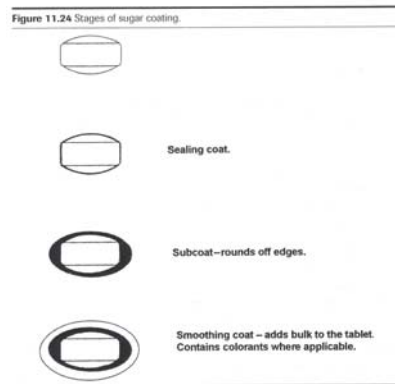
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Suspension components, % w/w

<i>Sucrose</i>	40.0	58.25
<i>Calcium carbonate</i>	20.0	18.45
Talc (asbestos free)	12.0	--
Titanium dioxide	1.0	1.00
Gum acacia	2.0	--
Gelatin (120 bloom)	--	0.01
Distilled water	25.0	22.29

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# Grossing or smoothing

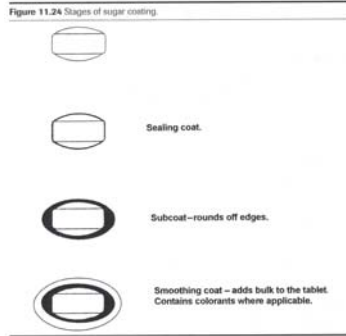


In order to manufacture a quality sugarcoated product, it is imperative that the surface of the coating be smooth and free of irregularities prior the application of the color coating.

Smoothing is usually achieved by application of a 70% sucrose syrup, often containing titanium dioxide as an opacifier/whitening agent.



# Color Coating



This is the most important step in the sugar coating process as it has immediate visual impact.

Use of appropriate colorants, which are:

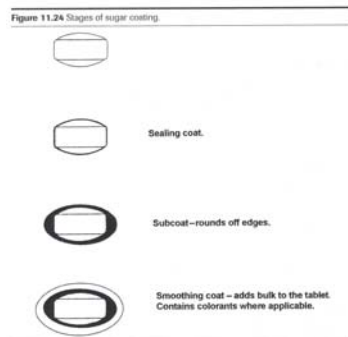
- dissolved (water soluble dye) or
  - dispersed (water insoluble pigments)
- in the coating syrup, allows achieving the desired color.

# Polishing (Glossing)

Since freshly coated-coated tablets are dull, it is necessary to polish them to achieve the typical gloss of finish sugarcoated tablets.

*Polishing systems include:*

- *Organic solvent-based solutions of wax (beeswax, carnauba wax)*
- *Alcoholic slurries wax*
- *Finely powdered mixture of dry waxes*
- *Pharmaceutical glazes (alcoholic solutions of various shellac).*



## Printing

This involves the application of a pharmaceutical branding ink to the coated tablet surface by means of a printing process known as offset rotogravure.

# APPLICATION TECHNIQUES

The basic application procedure involves three steps:

1. Application of an appropriate volume of coating liquid to a cascading bed of tablets
2. Distribution of the coating liquid across the surface of each tablet
3. Drying the coating liquid once uniform distribution is achieved.

# Sugar-coating liquid

In the past sugar-coating liquids were applied manually, now mechanical dosing techniques involve the use of spray guns or dosing “sparges” (see figure)

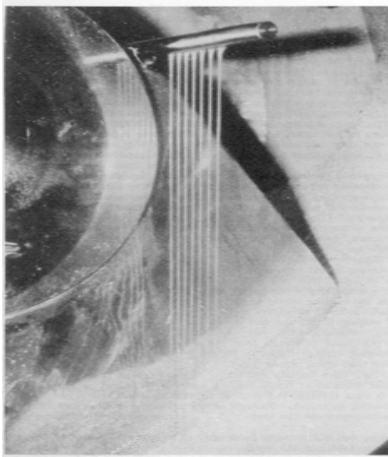


Figure 3 - Figure showing a dosing sparge for sugar coating.

Summarizing, since coating uniformity is achieved as the result of tablet-to-tablet transfer of liquid coating material, it not necessary for each tablet to pass through the zone of application.

# Sugar-coating liquid

Factors which influence coating uniformity in the sugar-coating process are that:

- the coating material remains fluid until it is spread across the surface of every tablet in the batch
- sufficient volume of coating liquid is applied to ensure that every tablet in the batch is capable of being wetted
- The coating pan exhibits good mixing characteristics, particularly so that dead spots are avoided.

# Problems in Sugar Coating

## ***Problems with tablets core robustness***

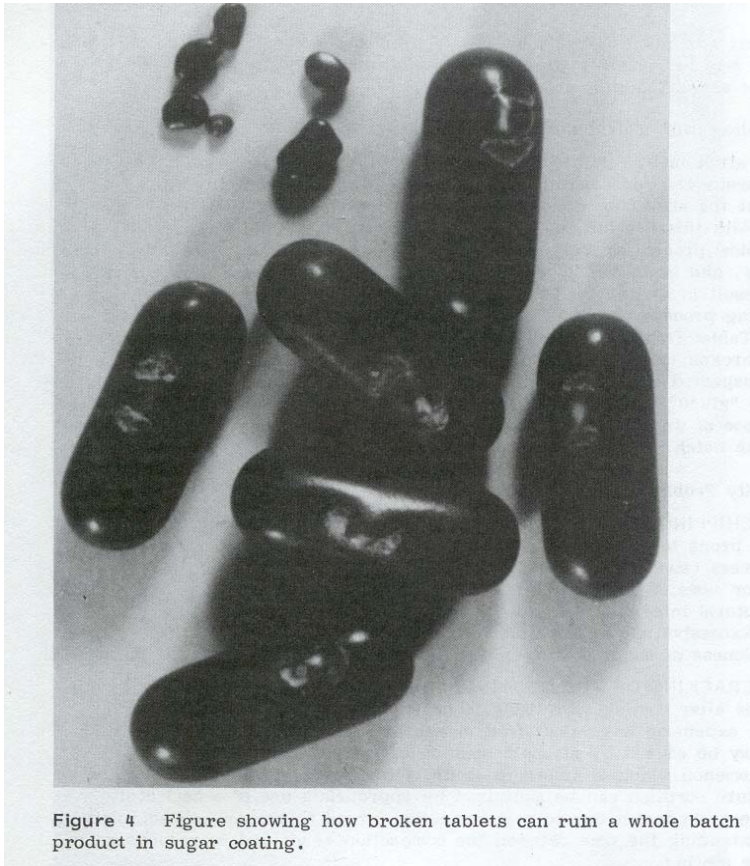
Tablet cores must be sufficiently robust to resist the stress to which they will be exposed during sugar coating.

Particular attention must be paid to important physical properties such as:

- hardness,
- friability and
- lamination tendency.

# Problems in Sugar Coating

## *Problems with tablets core robustness*



Tablet fragmentation is not only a problem due to broken tablets that will not be saleable.

But, broken fragments may become glued to the surface of undamaged tablets.

# Problems in Sugar Coating

## *Quality problems with finished tablets*

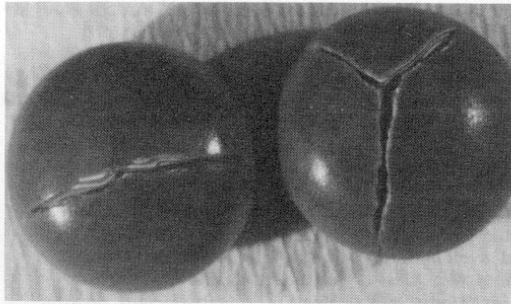


Figure 5 Sugar-coated tablets with cracked coating.

*Chipping* of coating (increased brittleness by excessive use of insoluble fillers and pigments or low amount of polymers, small addition of polymers).

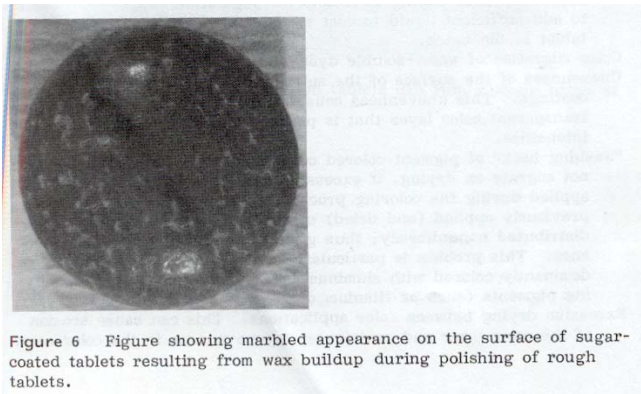
*Cracking* of the coating (expansion resulted from moisture absorption or caused by stress relaxation of the core after compaction).

*Non-drying* coatings (inability to dry when Level of inverted sugar is greater than 5%).



# Problems in Sugar Coating

## *Quality problems with finished tablets*



*Twinning or build-up of multiples* (stickiness during the beginning the drying; appropriate punch design minimizes the problem)

*Uneven color* (poor distribution of coating liquid, color migration, excessive drying between color applications)

*Blooming and sweating* (moderate and higher levels of moisture egress).

# FILM COATING

## Introduction

Film coating is a complex process that involves the application of thin (in the range of 20-200  $\mu\text{m}$ ) polymer-based coatings to an appropriate substrate (*tablets, pellets, granules, capsules, powders, and crystals*) under conditions that permit:

- Balance between (and control of) the coating liquid addition rate and drying process
- Uniformity of distribution of the coating liquid across the surface of product being coated
- Optimization of the quality (both visual and functional) of the final coated product.

# FILM COATING

## Introduction

Film coating almost always utilize a spray atomization technique.

In the spray process, coating liquid are finely atomized and delivered in droplets sufficiently fluid to wet the surface of the core being coated, spread out and coalesce to form film.

Because of the adhesive nature of partially dry droplets, it is necessary to dry instantaneously when they contact the surface of the substrate; otherwise sticking occur.

*There is a need to strike an appropriate balance between liquid application rate and drying process.*

# Simple schematic of film-coating process

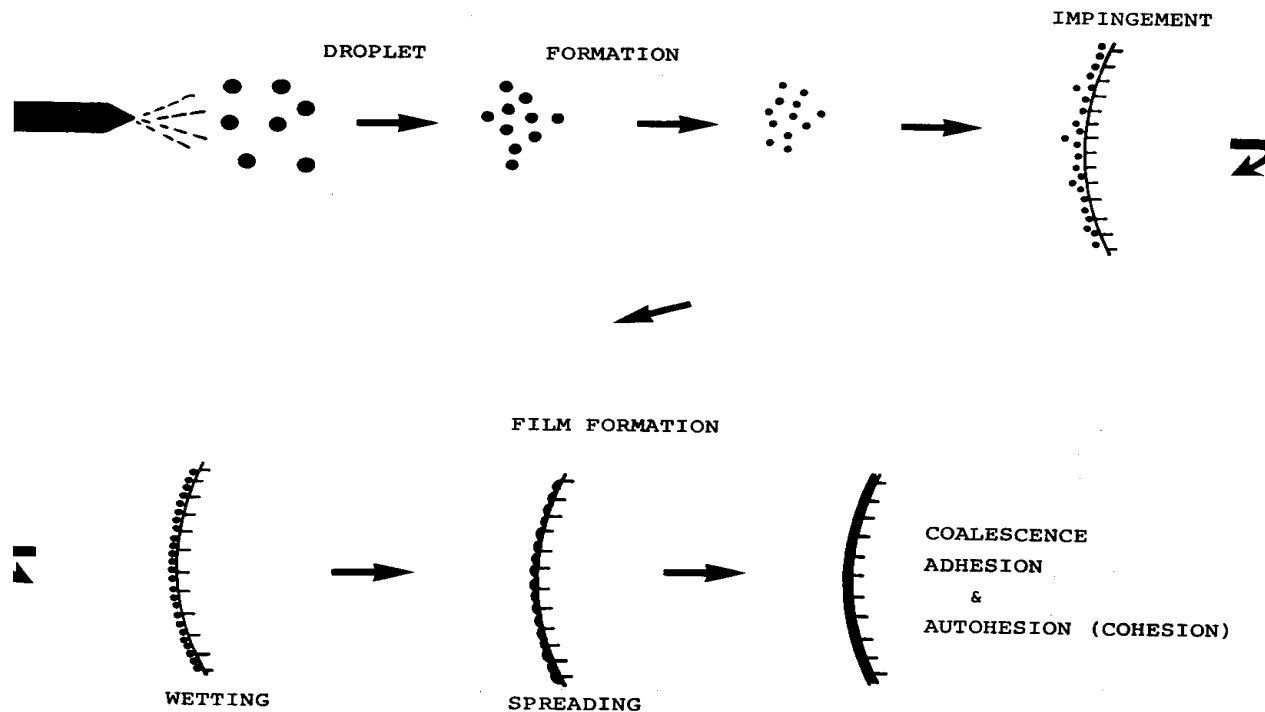


Figure 7 Schematic representation of the film-coating process.

# FILM COATING

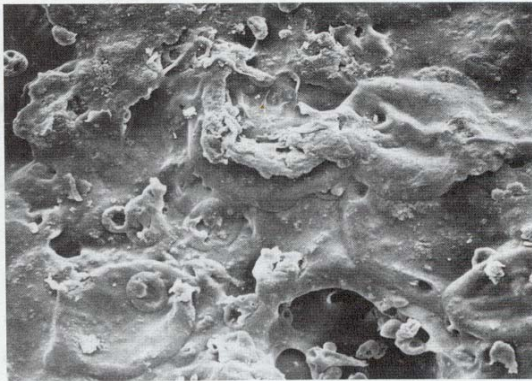
## Introduction

Because of the rapid drying during the application of film coatings, uniformity of distribution of the coating is controlled both by:

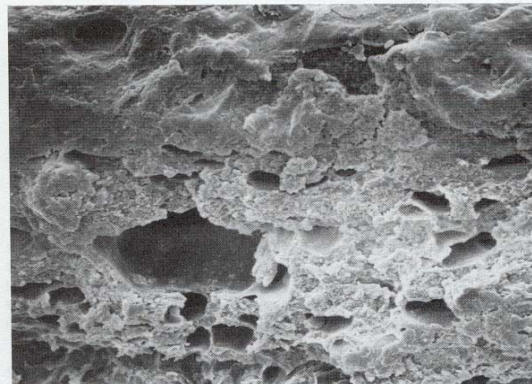
- uniformity of distribution of the coating liquid (*number of spray guns, types of spray patterns used, and fineness of atomization of coating liquid*) and
- uniformity of mixing (*controlled by pan speed, baffle design, tablet size and shape*) of the product being coated.

# Film coating structure

Most current film coating are considered to be continuous because the application of coating liquid continues uninterrupted. But, it is more appropriate to consider a discontinuous process since each core receives only a fraction of its total coating each time it passes through the spray zone.



(a)



(b)

Figure 8 Scanning electron micrographs of film-coated tablets to show heterogeneous film structure. (a) Surface view,  $\times 1000$  and (b) transverse section through coating,  $\times 1000$ .

*Film coatings are generally built up as a series of layers one upon another so that the final coating is structurally far from homogeneous.*

# FILM COATING

## Introduction

*Film coating* has supplanted *sugar coating* as the method of choice for coating of pharmaceutical solid dosage forms, even though many people consider the elegance of sugar-coated product to be superior than film-coated product.

# FILM COATING

## Introduction

The major advantages of the film coating include:

- Substantial reduction in quantity of coating applied (2-4% for film coating, compared with 50-100% for sugar coating)
- Faster processing times
- Improvement in process efficiency and output
- Greater flexibility in optimizing formulations as a result of the availability of a wide range of coating materials and systems
- A simplified process that facilitates automation
- Ability to be applied a wide range of pharmaceutical products.



# FILM COATING

## Introduction

Initially, organic solvents had to be used to help offset the deficiencies in drying capacity of coating equipment.

Then, significant improvements in processing equipment had facilitated the introduction of aqueous-based coating formulations solving the problems associated to:

- *flammability,*
  - *toxicity, and*
  - *environmental pollution hazards*
- of organic solvents .

# ***Type of Film Coating Used***

The applications for use of film coatings are quite diverse.

While such applications require some functionality of the coating formulation, it is not uncommon to see film coating described as

- either functional
- or non-functional (conventional).

Functionality relates specifically to an ability to modify drug release characteristics.

# ***Type of Film Coating Used***

Non-functional (conventional) film coating are typically reserved for situations in which it is necessary to improve the:

- product appearance,
- ease of swallowing,
- product stability,
- mechanical resistance

and for:

- taste masking.

# ***Type of Film Coating Used***

Functional film coatings are used when drug release characteristics need to be modified, and are represented by:

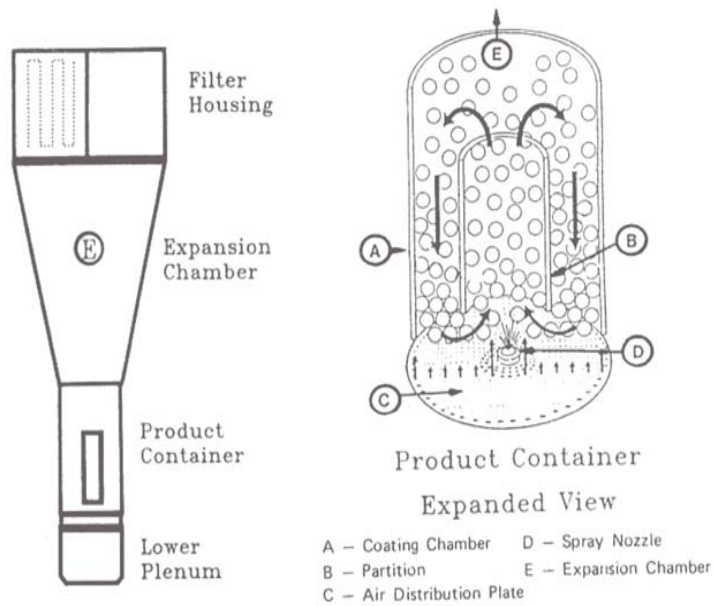
- Enteric (gastroresistant)
- Prolonged (or sustained) and
- Target

release coatings.

# FACTORS INFLUENCING THE QUALITY OF FILM COATING

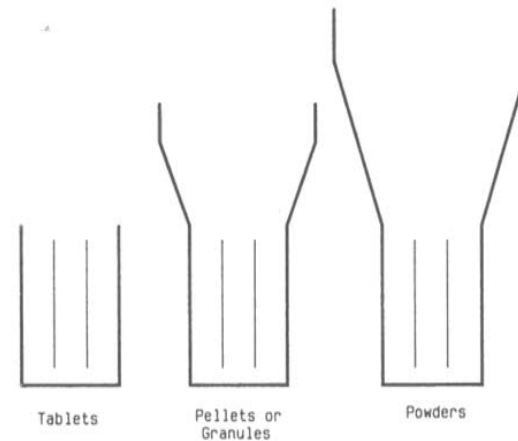
In order to understand the factors affecting the quality (both visual and functional) of the finished coated products, it needs to examine the factors the have an effect on:

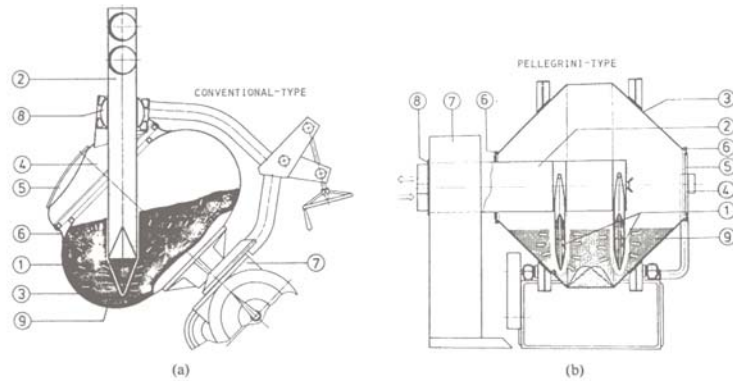
1. interaction between the core material (substrate) and the applied coating
2. the drying process
3. the uniformity of distribution of the coating.



**Fig. 12** Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

## Fluidized bed





- Key:
- 1. Immersion Sword
  - 2. Coaxial conduit
  - 3. Coating pan
  - 4. Pan cover
  - 5. Clear control cover
  - 6. Silicone seal
  - 7. Stand
  - 8. Coaxial conduit adjustment
  - 9. Coating bed

Fig 90-5. Schematic diagram of the immersed-sword apparatus for use in either (a) a conventional pan or (b) a Pellegrini pan.

## Pans

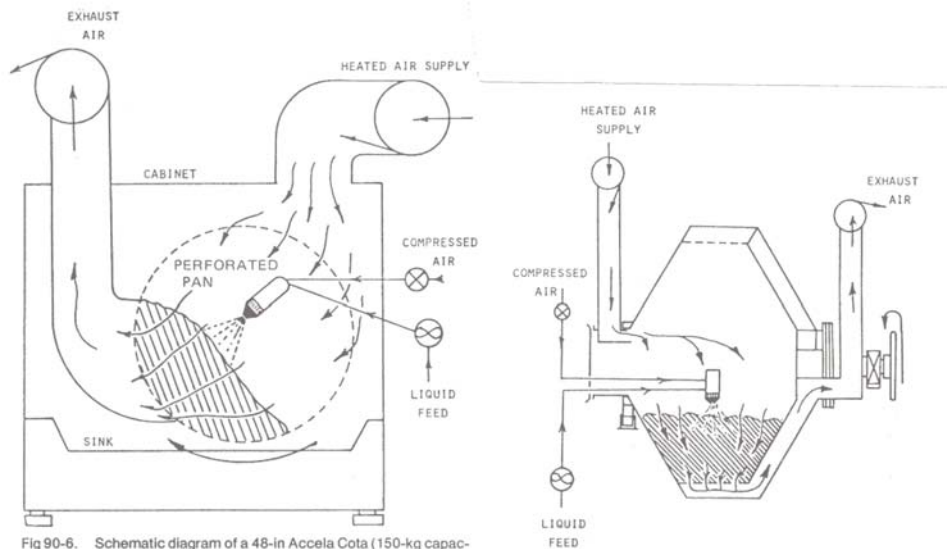
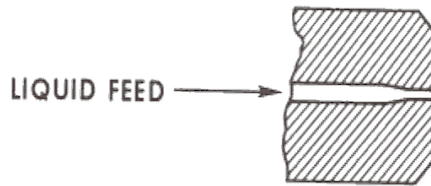


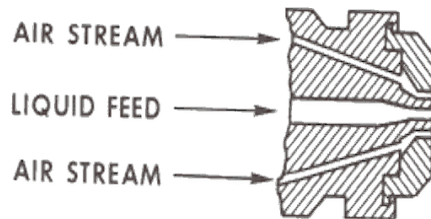
Fig 90-6. Schematic diagram of a 48-in Accela Cota (150-kg capacity).

Fig 90-7. Schematic diagram of the Hi-coater.

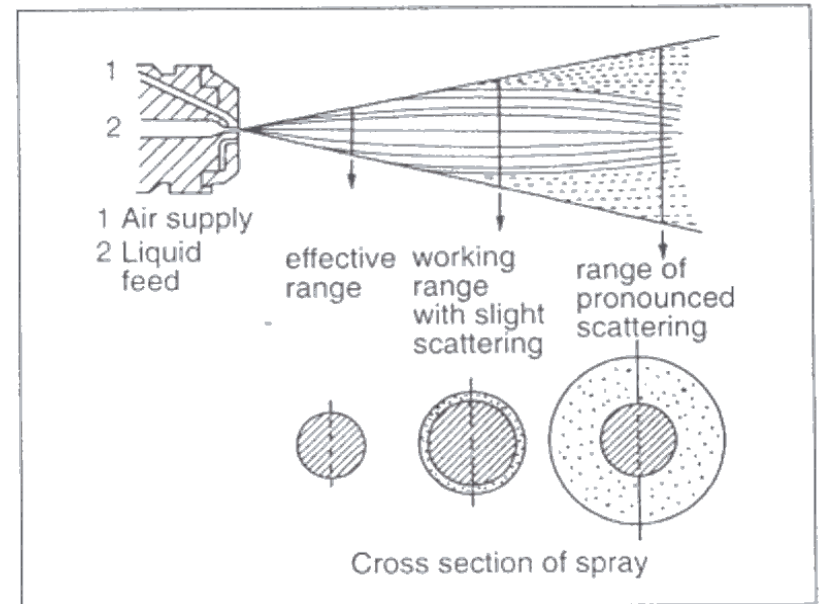
# Nozzles



**FIG. 12-14.** *Simplified diagram of a high-pressure, airless nozzle.*



**FIG. 12-15.** *Simplified diagram of a low-pressure, air-atomized nozzle.*



**Fig. 7-4.** Spray of an air nozzle



# FACTORS INFLUENCING THE QUALITY OF FILM COATING

Factors influencing interaction between substrate and coating are:

1. Tablet core
2. Coating liquid
3. Process drying.

# FACTORS INFLUENCING INTERACTION BETWEEN SUBSTRATE AND COATING

## **Tablet core**

*Ingredients* have influence on:

- wetting by coating liquid and
- adhesion of dry film.

*Porosity* has influence on:

- adhesion of dry film.

*Surface roughness* has influence on:

- wetting by coating liquid,
- spreading of coating liquid across surface and
- roughness of coating.

# FACTORS INFLUENCING INTERACTION BETWEEN SUBSTRATE AND COATING

## **Coating liquid**

*Solid content* has influence on

- roughness of dry coating and
- coating liquid viscosity.

*Viscosity* has influence on

- spreading of coating liquid across surface of substrate and
- coalescence of droplets of coating liquid into a continuous film.

*Surface tension* has influence on

- wetting of substrate surface by coating liquid,
- spreading of coating liquid across surface of substrate and
- coalescence of droplets of coating liquid into a continuous film.

# FACTORS INFLUENCING INTERACTION BETWEEN SUBSTRATE AND COATING

## **Process drying**

*Drying rate* has influence on

- viscosity of coating liquid at time of contact with surface of substrate and
- structure of dried coating.

*Heat* has influence on

- development of internal stress within film (and effect on adhesion and cohesion) and
- mechanical properties of coating (and effect on defects).

# FACTORS INFLUENCING THE QUALITY OF FILM COATING

Factors influencing the drying process:

1. Spray equipment
2. Drying conditions
3. Spray rate
4. Solid content of coating liquid.

# FACTORS INFLUENCING THE DRYING PROCESS

## **Spray equipment**

*Nozzle design* has influence on

- fineness of atomization of coating liquid (and thus evaporation rate of solvent/vehicle).

*Atomizing air* has influence on

- fineness of atomization of coating liquid (and thus evaporation rate of solvent/vehicle).

*Number of spray guns used* has influence on

- uniform distribution of coating liquid and
- avoidance of localized overwetting.

# FACTORS INFLUENCING THE DRYING PROCESS

## **Drying conditions**

*Air flow, temperature and humidity*  
have influence on:

- rate at which solvent /vehicle can be removed from the coating liquid and
- product temperature.

# FACTORS INFLUENCING THE DRYING PROCESS

## **Spray rate**

*Nozzle design, number of spray guns and pumping system*  
have influence on:

- rate at which solvent /vehicle needs to be removed from the coating liquid and
- product temperature.



# FACTORS INFLUENCING THE DRYING PROCESS

## **Solid content of coating liquid**

*Concentration of coating liquid*  
has influence on

- quantity of solvent /vehicle that must be removed from the coating\_liquid.

## FACTORS INFLUENCING THE QUALITY OF FILM COATING

Factors influencing uniformity of distribution of coating are:

- Spray equipment
- Drying conditions
- Spray rate
- Solid content of coating liquid
- Pan speed or fluidizing air velocity
- Baffles (in coating pans).

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

## **Spray equipment**

*Nozzle design* has influence on

- fineness of atomization of coating liquid and
- area over which coating liquid is applied.

*Atomizing air* has influence on

- fineness of atomization of coating liquid.

*Number of spray guns* has influence on

- area over coating liquid is applied and length of coating process.

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

## **Drying conditions**

*Air flow, temperature and humidity*  
have influence on

- efficiency of drying process  
(i.e., amount of coating that ends up on core material).

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

## **Spray rate**

*Spray rate* has influence on

- length of coating process,
- amount of coating liquid that deposited on substrate at each pass through spray zone and
- amount of coating that is lost during process.

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

## **Solids content of coating liquid**

*Solids content of coating liquid*

has influence on:

- length of coating process,
- amount of coating liquid that deposited on substrate at each pass through spray zone and
- smoothness of dried coating.

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

## **Pan speed or fluidizing air velocity**

*Pan speed or fluidizing air velocity*

has influence on

- uniformity of mixing,
- amount of coating liquid that deposited on substrate at each pass through spray zone

and

- loss of coating due to attrition effects.

# FACTORS INFLUENCING UNIFORMITY OF DISTRIBUTION OF COATING

**Baffles** (in coating pan)

*Baffles* (in coating pan)  
has influence on

- uniformity of mixing.



# Mechanism of Film Formation for Film- Coating Systems

Pharmaceutical film-coating formulations consist of:

- solutions of polymers (and other additives) in organic solvents or in water
- aqueous polymeric dispersions (commonly called latices or pseudolatices).

Coating process involves the conversion of a liquid into a “dry solid”.

*Polymers used in film coating are amorphous.*

## ***A practical definition***

A “dry film” is one that resist blocking when two coated surface are brought into contact, for 2 seconds, under a pressure of 14 kPa.

Such resistance occurs when the viscosity exceeds  $10^7 \text{ Pa} \times \text{s}$ .

A viscosity conducive to a such blocking occurs when a coating is exposed to temperature conditions are about 20°C above glass transition temperature ( $T_g$ ).

## ***A practical definition***

Since pharmaceutical coatings process may now employed

- polymeric solutions (organic-solvent or aqueous) or
- aqueous polymeric dispersions,

the *formulator and process engineer* must be very aware of how such coating forms films in order to be sure that formulation additives and process conditions are employed to achieve consistent quality results.

# FORMULATION OF FILMS FROM POLYMERIC SOLUTIONS

The film-forming process, and internal structure of final dried coating, will depend upon the *rate of solvent evaporation*.

Rate of solvent evaporation will be controlled by the *latent heat of vaporization* of solvent and *drying conditions* provided in the process.

# FORMULATION OF FILMS FROM POLYMERIC SOLUTIONS

Film formation generally comprises:

- Initial rapid evaporation of solvent from atomized droplets of coating liquid, causing an increase in polymer concentration (and, hence, viscosity) and contraction in volume of the droplets
- Further loss of solvent from the film (this is, coalescing on the surface of the dosage form) at slower rate which is now controlled by the rate of diffusion of solvent through the polymer matrix
- Immobilization of the polymer molecules at the “solidification point”
- Further gradual solvent loss from the film at a very much reduced rate.

# FORMULATION OF FILMS FROM POLYMERIC SOLUTIONS

*Solvent loss* from the film coating will be continuous but at ever-decreasing rate.

*Solvent loss* from the polymer matrix is governed by *amount of space* between the polymer molecules (*usually termed the free volume*).

As solvent loss progresses, *glass-transition temperature* of the polymer film *increases* and the free volume *decreases*.

Ultimately, free volume becomes so small that the total removal of solvent from the coating becomes almost impossible.

# FORMULATION OF FILMS FROM POLYMERIC SOLUTIONS

Indeed, total solvent removal requires heating the film to a temperature significantly above the *glass-transition temperature* of the solvent-free polymer.

Solvent loss (*from the coating*) that occurs beyond the solidification point creates shrinkage stresses that contribute to the internal stress within the coating.

*Cracking formation can occur when internal stress exceeds the tensile strength.*

# FORMATION OF FILMS FROM AQUEOUS POLYMERIC DISPERSIONS

Film formation from *aqueous dispersions* requires the coalescence of polymer particles into a continuous film.

Drying of such a system is rapid, whereas coalescence can be a much slower process.

This process is very sensitive to process conditions used during film coating.

*The actual mechanism is quite complex and many competing theories exist.*



## Definitions of Latexes

Aqueous dispersions are dispersed substances in the dispersing agent, water.

When the dispersed phase is built up by polymers, they are called polymeric dispersion.

The term *latex* is used for colloidal polymer dispersions. It comes from the caoutchouc latex, which is called *natural latex*.

*Generally, colloidal dispersions are systems in which particles are extremely small, below about 1 micron in diameter.*

## Definitions of Latexes

The analogous synthetic product produced *by emulsion polymerization* (monomers emulsified in water, then polymerization by adding initiators) called *synthetic latex*.

The product prepared *by direct emulsification* of polymers in water is called *artificial latex*.

The term *pseudolatex* is used for dispersions that are prepared by emulsification of organic polymer solutions in water followed by the elimination of the organic solvents (spray drying).

## The Physicochemical Specifications of Latexes

The *particle size* is the most important specification of a latex and is between *10 and 1000 nm* (1 micron).

The upper limit, near 1 micron, is imposed by thermal convection and the Brownian movement of the particles.

Both together must be so high that the sedimentation velocity of the particles is overcompensated and no sedimentation occurs over a very long period of time.

## The Physicochemical Specifications of Latexes

This means that sedimentation occurs at a rate of less than 1 mm/24 h calculated from the Stokes equation.

La velocità di una particella che sedimenta in un fluido (velocità di settling) si può descrivere con la legge di Stokes:

$$d = \sqrt{18\eta h / (\rho - \rho_0) g t} \quad \text{dove:}$$

$d$  è il diametro medio delle particelle,  
 $\eta$  è la viscosità del mezzo,  
 $h$  è la distanza di caduta nel tempo  $t$ ,  
 $\rho$  è la densità delle particelle,  
 $\rho_0$  è la densità del mezzo disperdente,  
 $g$  è l'accelerazione di gravità

The lower limit (near 10 nm) is defined such that the latex will give a light-scattering effect resulting in *a milky appearance*.

Systems of smaller particle sizes are called *microemulsions* or *colloidal solutions*.

They are nearly clear but exhibit the Tyndall effect when a light beam is shown through them.

## The Physicochemical Specifications of Latexes

Latexes are characterized by low viscosity even when they have a high solids content.

Some dispersions used in drug formulations contain significant amounts of particles 1-3 microns or more in diameter and form sediments after a few hours.

Nevertheless they form acceptable films when applied with stirring.

So the term dispersion includes all fine particulate systems that contain around or near 1 micron and are able to form coating layers under the conditions of application.

## The Physicochemical Specifications of Latexes

The term *minimum film-forming temperature* (MFT) is used for that temperature above which a continuous film is formed under distinct drying conditions of the dispersion.

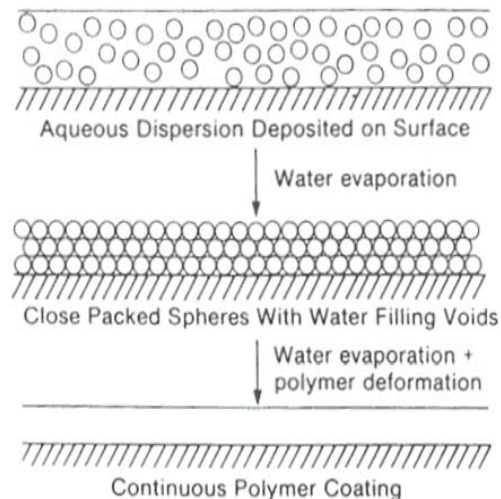
The *white point* (WP) is defined as the temperature below which no film and only a white powdery mass is formed.

The white point is normally some degrees below the MFT.

Film formation of polymer dispersion is correlated to the glass transition temperature ( $T_g$ ) of the polymer.

A method used for the determination of  $T_g$  is the differential scanning calorimetry (DSC).

A film-forming polymer latex is deposited from an aqueous colloidal dispersion of discrete polymer spheres. Individual submicron-size spheres, *each containing hundreds of polymer chains*, coalesce into a continuous film as the aqueous phase evaporates.



**Fig. 5** Film formation from pseudolatex. (From Ref. 7)

Figure 5 represents a latex dispersion consistent of spheres that are suspended and separated by electrostatic repulsion.

As water evaporates, interfacial tension between water and polymer pushes particles into point contact in a close-packed ordered array.

A strong driving force is necessary to overcome repulsive forces, deform the particles, and cause the spheres to fuse, resulting in complete coalescence.

*Capillarity* caused by the high interfacial surface tension of water provides the *driving force* to fuse the particles, and *plasticizer inclusion* in the dispersion swells and softens the polymer spheres, facilitating coalescence and reducing minimum film formation temperatures.

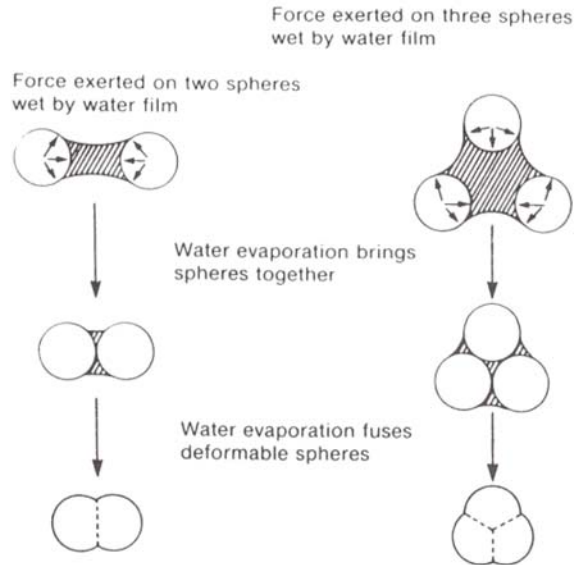


Fig. 6 Particle coalescence during the evaporative phase.

Figure 6 examines the forces exerted on spherical particles as evaporation proceeds.

The polymer spheres are pulled closer together as a result of surface tension (water-air interfacial tension) and capillarity as the surrounding water film constricts.

According to Voyutskii, an interdiffusion of polymer chains (autohesion) is the final step in the formation of integral homogeneous latex films.



# FORMATION OF FILMS FROM AQUEOUS POLYMERIC DISPERSIONS

In simplified terms, film formation process from aqueous polymeric dispersions involves:

- Rapid evaporation of water
- Development of pressures (associated with capillary forces within the structure) that overcome repulsive forces and cause deformation of the polymer particles
- Gradual coalescence as a results of viscous flow and movement of molecules across the interfaces.

# FORMATION OF FILMS FROM AQUEOUS POLYMERIC DISPERSIONS

This process of film formation is very sensitive to the process conditions used during film coating.

Aqueous dispersions must be processed at the temperatures in excess of the glass-transition temperature of the plasticized polymer ( $10^{\circ}\text{C}$  above the MFT).

A curing step or thermal treatment is used to accelerate the coalescence of the polymer particle prior the long term storage ( $45^{\circ}\text{C}$  for 8-12 hours or  $70^{\circ}\text{C}$  for 1 hour).

# Ingredients used in film coating

Film-coating formulation consisted of a extensive list of ingredients, including:

- film formers,
- plasticizers,
- colorants,
- surfactants,
- flavors,
- glossing agents, and
- solvents.

# Ingredients used in film coating

POLYMERS are not well-defined entities with differing chemical types having different grades.

It is necessary to define this material in terms of chemical structure, molecular weight and molecular weight (*cellulosics, vinyls, glycols, acrylics, fats and waxes, silicone elastomers*).

**Table 11** Polymers Used in Conventional Film-Coating Formulations

Class	Examples
1. Cellulosics	Hydroxypropyl methylcellulose Hydroxypropylcellulose Hydroxyethylcellulose Methylhydroxyethylcellulose Methylcellulose Ethylcellulose Sodium carboxymethylcellulose
2. Vinyls	Polyvinyl pyrrolidone
3. Glycols	Polyethylene glycols
4. Acrylics	Dimethylaminoethyl methacrylate-methylacrylate acid ester copolymer Ethylacrylate-methylmethacrylate copolymer

**Table 13** Examples of Enteric-Coating Polymers

Polymer	Comments
Cellulose acetate phthalate (CAP)	Subject to hydrolysis (high) <sup>b</sup>
Cellulose acetate trimellitate (CAT)	Subject to hydrolysis <sup>b</sup>
Polyvinyl acetate phthalate (PVAP)	Subject to hydrolysis (low) <sup>b</sup>
Hydroxypropyl methylcellulose phthalate (HP)	Subject to hydrolysis (medium) <sup>b</sup>
Hydroxypropyl methylcellulose acetate succinate (HPMCAS)	Subject to hydrolysis (low) <sup>b</sup>
Poly (ME-EA) 1:1 <sup>a</sup>	—
Poly (MA-MMA) 1:1 <sup>a</sup>	Relatively high dissolution pH
Poly (MA-MMA) 1:2 <sup>a</sup>	Relatively high dissolution pH

<sup>a</sup>MA, methacrylic acid; EA, ethylacrylate; MMA, methyl methacrylate.

<sup>b</sup>When exposed to conditions of elevated temperature and humidity.

**Table 15** Examples of Coating Materials Used in Sustained-Release Film-Coating Formulations

Coating material	Membrane characteristics
Fats and waxes (e.g., beeswax, carnauba wax, cetyl alcohol, cetylstearyl alcohol)	Permeable and erodible
Shellac	Permeable and soluble (at high pH)
Zein	Permeable and soluble (at high pH)
Ethylcellulose	Permeable
Cellulose esters (e.g., acetate)	Semipermeable
Silicone elastomers	Permeable (when PEG added)
Acrylic esters	Permeable

Table 4-1. Chemical structure and specifications of cellulose derivatives

<div style="display: flex; align-items: center; justify-content: space-between;"> <div style="flex: 1;"> </div> <div style="flex: 2;"> <p>R¹, ² or ³ ether radical:</p> <div style="display: flex; justify-content: space-between;"> <div> <math>-\text{CH}_3</math>  <math>-\text{CH}_2\text{COOH}</math>  <math>-\text{CH}_2-\text{CH}_2-\text{OH}</math> </div> <div> <math>-\text{C}_2\text{H}_5</math>  <math>-\text{CH}_2\text{COONa}</math>  <math>-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_3</math> </div> </div> <p>ester radical: <math>-\text{CO}-\text{CH}_3</math></p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> </div> <div style="text-align: center;"> </div> </div> </div> </div>							
Products	OR	Substitution (mole)**			Substituents (%)		
Methylcellulose (MC) (Methocel®)	$-\text{O}-\text{CH}_3$	1.5-2.0			high	28.0-32.0	
					medium	23.0-28.0	
					double	22.0-26.0	
Hydroxypropyl methylcellulose (Pharmacoat) (HPMC) Type 2910 USP/NF	$-\text{O}-\text{CH}_3$ $-\text{O}-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_3$	1.8				27.0-30.0	
		0.25				7.0-12.0	
Cellulose acetate	$-\text{O}-\text{CO}-\text{CH}_3$	1.2				21.5-26.0	
phthalate (CAP)	$-\text{O}-\text{CO}-\text{C}_6\text{H}_4-\text{COOH}$	0.5				30.0-36.0	
Hydroxypropyl methylcellulose phthalate (HPMCP)	$-\text{OCH}_3$	a*	b*		a*	b*	
	$-\text{O}-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_3$	1.6	1.6		18.0-22.0	20.0-24.0	
	$-\text{O}-\text{CO}-\text{C}_6\text{H}_4-\text{COOH}$	0.2	0.2		5.0- 9.0	6.0-10.0	
		0.5	0.3		27.0-35.0	21.0-27.0	
Hydroxypropyl methylcellulose acetate succinate (HPMCAS)	$-\text{OCH}_3$	c*	d*	e*	c*	d*	e*
	$-\text{OCH}_2-\text{CH}(\text{OH})-\text{CH}_3$	2.0	2.0	2.0	20-24	21-25	22-26
	$-\text{O}-\text{CO}-\text{CH}_3$	0.25	0.25	0.3	5- 9	5- 9	6-10
	$-\text{O}-\text{CO}-\text{CH}_2-\text{CH}_2-\text{COOH}$	0.3	0.4	0.5	5- 9	7-11	10-14
		0.4	0.3	0.1	14-18	10-14	4- 8

Polymers or  
film forming  
agents

Cellulose  
derivatives

**Table 2** Methacrylic Acid and Methacrylic Ester Copolymers

Methacrylic acid copolymers								
$\left[ \begin{array}{c} \text{CH}_3 \\   \\ -\text{CH}_2-\text{C}- \\   \\ \text{C}=\text{O} \\   \\ \text{OH} \end{array} \right]_{n_1} \quad \cdots \quad \left[ \begin{array}{c} \text{R}_1 \\   \\ -\text{CH}_2-\text{C}- \\   \\ \text{C}=\text{O} \\   \\ \text{OR}_2 \end{array} \right]_{n_2}$								
Scientific name	$n_1:n_2$	MW	USP/NF type	$\text{R}_1$	$\text{R}_2$	Behavior in digestive juices	Eudragit type	Marketed form
Poly(methacrylic acid, ethyl acrylate)	1:1	250,000	C	H	$\text{C}_2\text{H}_5$	Soluble, pH > 5.5	{ L 30D L 100-55	30% aqueous dispersion powder
Poly(methacrylic acid, methyl methacrylate)	1:1	135,000	A	$\text{CH}_3$	$\text{CH}_3$	Soluble, pH > 6.0	L 100	Powder
Poly(methacrylic acid, methyl methacrylate)	1:2	135,000	B	$\text{CH}_3$	$\text{CH}_3$	Soluble, pH > 7.0	S 100	Powder
Methacrylate ester copolymers								
$\left[ \begin{array}{c} \text{H} \\   \\ -\text{CH}_2-\text{C}- \\   \\ \text{C}=\text{O} \\   \\ \text{OC}_2\text{H}_5 \end{array} \right]_{n_1} \quad \cdots \quad \left[ \begin{array}{c} \text{CH}_3 \\   \\ -\text{CH}_2-\text{C}- \\   \\ \text{C}=\text{O} \\   \\ \text{OCH}_3 \end{array} \right]_{n_2} \quad \cdots \quad \left[ \begin{array}{c} \text{CH}_3 \\   \\ -\text{CH}_2-\text{C}- \\   \\ \text{C}=\text{O} \\   \\ \text{OR} \end{array} \right]_{n_3}$								
Scientific name	$n_1:n_2:n_3$	MW				Behavior in digestive juices	Eudragit type	Marketed form
Poly(ethyl acrylate, methyl methacrylate)	2:1	800,000				Insoluble films of medium permeability	NE 30D	30% aqueous dispersion
Poly(ethyl acrylate, methyl methacrylate) trimethylammonioethyl methacrylate chloride	1:2:0.2	150,000				Insoluble films of high permeability	{ RL 30D RL 100	30% aqueous dispersion Granules
R: $\text{CH}_2-\text{CH}_2-\text{N}^+(\text{CH}_3)_3\text{Cl}^-$								
Poly(ethyl acrylate, methyl methacrylate) trimethylammonioethyl methacrylate chloride R: $\text{CH}_2-\text{CH}_2-\text{N}^+(\text{CH}_3)_3\text{Cl}^-$	1:2:0.1	150,000				Insoluble films of low permeability	{ RS 30D RS 100	30% aqueous dispersion Granules

Source: Ref. 47.

Polymers or film forming agents

Methacrylic copolymers

Table 14 Examples of Aqueous Enteric-Coating Systems

Product	Form	Polymer	Comments
Eudragit L 30 D	Latex dispersion	Poly (ME-EA) 1:1 <sup>a</sup>	System essentially contains only the polymer
Eudragit L-100-55	Spray-dried latex	Poly (ME-EA) 1:1 <sup>a</sup>	Requires dispersing in water with addition of alkali System only contains polymer
HP-F	Dry powder	HP	Requires dispersing in water System only contains polymer
Coateric	Dry powder	PVAP	Complete system Requires dispersing in water with addition of ammonia
Aquateric	Spray-dried pseudolatex	CAP	System essentially contains only polymer Requires dispersing in water
HPMCAS	Dry powder	HPMCAS	System contains only polymer Requires dispersing in water
CAP	Dry powder	CAP	System contains only polymer Requires dissolving in water with aid of alkali (ammonia)
CAT	Dry powder	CAT	System contains only polymer Requires dissolving in water with aid of alkali (ammonia)

<sup>a</sup>MA, methacrylic acid; EA, ethacrylic acid.

Aqueous  
polymeric  
dispersions for  
gastroresistant  
release film  
coating



**Table 16** Examples of Aqueous Polymeric Dispersions for Sustained-Release Film Coating

Material	Polymer	Comments
1. Surelease	Ethylcellulose	Aqueous polymeric dispersion contains requisite plasticizers  Addition of lake colorants should be avoided because of alkalinity of dispersion
2. Aquacoat	Ethylcellulose	Pseudolatex dispersion  Requires addition of plasticizers to facilitate film coalescence
3. Eudragit NE 30 D	Poly(ethylacrylate-methyl methacrylate) 2:1	Latex dispersion  No plasticizers required unless improved film flexibility is desired
4. Eudragit RL 30 D	Poly(ethylacrylate-methyl methacrylate)triethyl ammonioethyl methacrylate chloride 1:2:0.2	Aqueous polymeric dispersion  No plasticizers required unless improved film flexibility is desired
5. Eudragit RS 30 D	Poly(ethylacrylate-methyl methacrylate)triethyl ammonioethyl methacrylate chloride 1:2:0.1	Aqueous polymeric dispersion  No plasticizers required unless improved film flexibility is desired
6. —	Silicone elastomer	Requires addition of PEG

Aqueous polymeric dispersions for sustained (prolonged) release film coating

# Ingredients used in film coating

PLATICIZERS reduces the glass-transition temperature of amorphous polymers and impart flexibility.

They affect the inter-molecular bonding between polymer chains.

The basic requirements of a plasticizer are the

- permanence and
- compatibility.

Table 12 Common Plasticizers Used in Conventional Film Coating

Class	Examples
1. Polyhydric alcohols	Propylene glycol Glycerol Polyethylene glycols
2. Acetate esters	Glyceryl triacetate (Triacetin) Triethyl citrate Acetyl triethyl citrate
3. Phthalate esters	Diethylphthalate
4. Glycerides	Acetylated monoglycerides
5. Oils	Castor oil Mineral oil

## Plasticizers

# Ingredients used in film coating

COLORANTS are included to improve the appearance and visual identification of the coated product.

They are:

- water-soluble dyes complexes with hydrates alumina, known as lakes (sunset yellow, tartrazine, erythrosine),
- inorganic pigments (titanium dioxide, iron oxide yellow, red and black, talc) and
- natural colorant (riboflavin, carmine, anthocyanins)

# Ingredients used in film coating

SOLVENTS must be chosen with careful attention (water, alcohols, esters, ketones, chlorinated hydrocarbons).

Solubility, viscosity, rate of solution and volatility are the main factors.

Optimal polymer solution will yield the maximum polymer chain extension, producing films having the greatest cohesive strength and thus the best mechanical properties

Table 10 Common Solvents Used in Film Coating

Class	Examples
1. Water	—
2. Alcohols	Methanol Ethanol Isopropanol
3. Esters	Ethyl acetate Ethyl lactate
4. Ketones	Acetone
5. Chlorinated hydrocarbons	Methylene chloride 1:1:1 Trichloroethane

Solvents  
or  
vehicles

# CONVENTIONAL FILM COATINGS

The greatest application of films coatings is to improve product appearance, stability and ease of ingestion of the dosage form, but not alter drug release.

The selection is often based on factors that:

- affect the mechanical properties (tensile strength, elasticity and adhesion) of coating,
- allow the smoothest, glossiest coatings to be obtained and
- produce coatings that ready dissolve in the gastrointestinal tract.

Conventional film coating is the area of aqueous technology.

*Polymers (hydroxypropyl methylcellulose, acrylate copolymers), plasticizers (polyethylene glycols, triethyl citrate) and colorants (iron oxides, titanium dioxide) are the main ingredients.*

# CONVENTIONAL FILM COATING FORMULATIONS

## Basic cellulosic formula

	% w/w	Function
HPMC 5 mPa s	7.5	Polymer
PEG 400	0.8	Plasticizer
Iron oxide yellow	0.6	Pigment/opacifier
Titanium dioxide	3.1	Pigment/opacifier
Purified water	88.0	Polymer solvent and coating medium vehicle
Total	100.0	

## High opacity formula

	% w/w
HPMC 5 mPa s	6.9
PEG 400	0.7
Iron oxide red	4.4
Purified water	88.0
Total	100.0

## Alternative colour formula

	% w/w
HPMC 5 mPa s	7.5
PEG 400	0.8
Indigo carmine lake	0.4
Titanium dioxide	3.3
Purified water	88.0
Total	100.0

Basic and alternative aqueous cellulose formulation for conventional film coating



# CONVENTIONAL FILM COATING FORMULATIONS

## Typical aqueous acrylic formula (Lehmann, 1989b)

<i>Pigment suspension 30%</i>	<i>% w/w</i>	<i>Function</i>
Talc	15.0	Anti-tack agent
Titanium dioxide	8.0	Pigment/opacifier
Quinoline yellow lake	4.0	Pigment/opacifier
Antifoam emulsion	0.1	Process aid
PEG 6000	3.0	Stabilizer
Water	69.9	Vehicle
Total	100.0	

<i>Final formulation</i>	<i>% w/w</i>	<i>Function</i>
Eudragit RL30D (as 30% w/w dispersion)	5.5	Polymer
Pigment suspension (as 30 % w/w)	16.4	
Citroflex 2	1.1	Plasticizer
Water	77.0	Vehicle
Total	100.0	

Basic and alternative aqueous acrylic formulation for conventional film coating

# MODIFIED-RELEASE FILM COATINGS

Film coating techniques can be effectively used to modify the release of active ingredient.

USP recognizes two types of modified-release dosage form:

1. Extended release: one that permits at least a twofold reduction in dosing frequency as compared to the situation in which the drug is presented as a conventional dosage form (called also sustained- or controlled- or prolonged-release)
2. Delayed release: One that releases the active ingredient at some time other than promptly after administration (an enteric-coated product).

# Enteric Film Coating

Enteric coatings are those which remain intact in the stomach, but break down readily once the dosage form reaches the small intestine.

The prime uses of such coatings are to:

- maintain the activity of drug that unstable when exposed to gastric milieu (e.g., erythromycin and pancreatin)
- minimize either nausea or bleeding that occurs with those drugs that irritate the gastric mucosa (e.g., aspirin and certain steroid)
- target the drug delivery.

# Enteric Film Coating

Examples of enteric coating polymers are

- *cellulose acetate phthalate,*
- *polyvinyl acetate phthalate,*
- *hydroxypropyl methylcellulose phthalate,*
- *methacrylic acid-acrylate copolymers.*

The important factors that can influence the behavior of enteric coatings include:

- the nature of the drug in the dosage form
- the quantity of coating applied
- the presence of imperfections in the coating
- the dissolution pH of the polymer used in the coating
- the effect of in vitro test conditions.

*Enteric-coated pellets or granules can give greater reproducibility than enteric-coated tablets.*

# Sustained-Release, or Controlled Release, Film Coatings

Drug release from such sustained-release products is moderated by the film coating which acts as a membrane that allows infusion of GI fluids and the outward diffusion of dissolved drug.

Examples of coating polymers used in sustained release formulations are

- *ethylcellulose,*
- *cellulose acetate,*
- *acrylic esters,*
- *fats and waxes,*
- *silicone elastomers.*

# **Sustained-Release, or Controlled Release, Film Coatings**

Pharmaceutical forms used as a substrates for sustained release may be classified as:

- Tablets
- Capsules
- Multiparticulates.

Multiparticulates systems have the advantages such as:

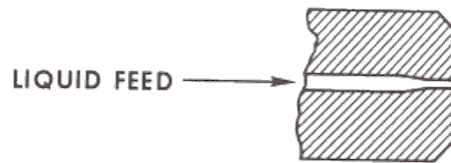
- minimization of risk of dose dumping (should membrane rupture) and
- optimization of GI transit.

# APPLICATION TECHNIQUES IN FILM COATING

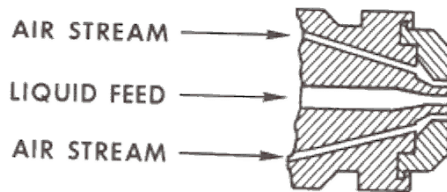
Film coating liquids can be applied by:

- manual ladling techniques  
*not practised today*
- means of spray atomization  
*more controlled and reproducible.*

# APPLICATION TECHNIQUES IN FILM COATING



**FIG. 12-14.** *Simplified diagram of a high-pressure, airless nozzle.*



**FIG. 12-15.** *Simplified diagram of a low-pressure, air-atomized nozzle.*

Three basic types of spray atomization processes:

1. Airless spray techniques (high delivery rate, organic solvent-based coating liquids)
2. Air-spray techniques (small-scale process, aqueous-coating systems)
3. Ultrasonic spray techniques (experimental for limitation due to the rheology of coating liquids).



# PROBLEMS IN FILM COATING

- The interaction between a film coating and the substrate is extremely complex.
- Core characteristics (porosity, surface rugosity and surface energy) can hinder or enhance the wetting.
- Liquid characteristics (viscosity, density and surface tension) can influence the initial wetting.
- Process conditions have a good deal of importance on the coating.

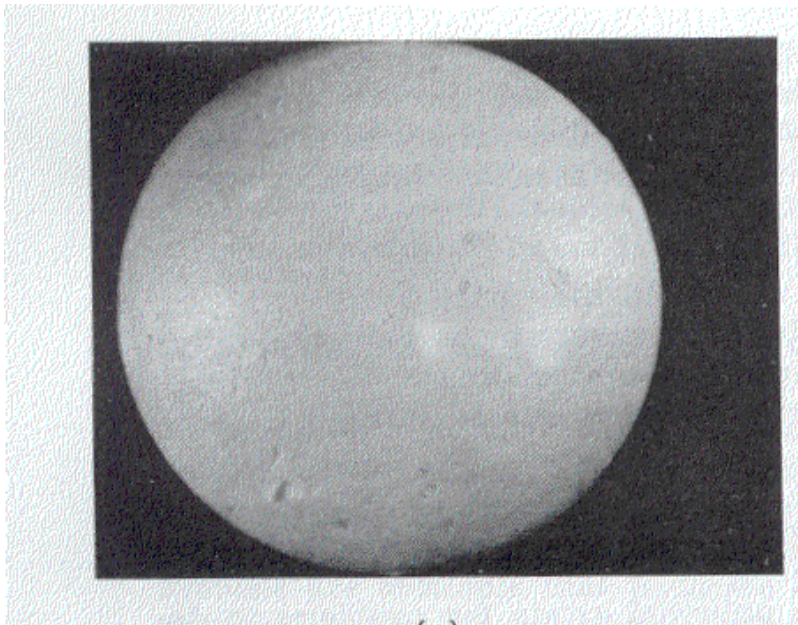
# PROBLEMS IN FILM COATING

The interaction between coating and substrate is also influenced by stresses that form within coating:

- shrinkage phenomena that develops as the coating dries
- expansion/contraction of both coating and substrate as they are subjected to heating and cooling cycles in the process
- other core-expansion factors (such as swelling due to moisture absorption)

These factors can affect the integrity of the film and the adhesion of the film to the substrate.

# PROBLEMS IN FILM COATING

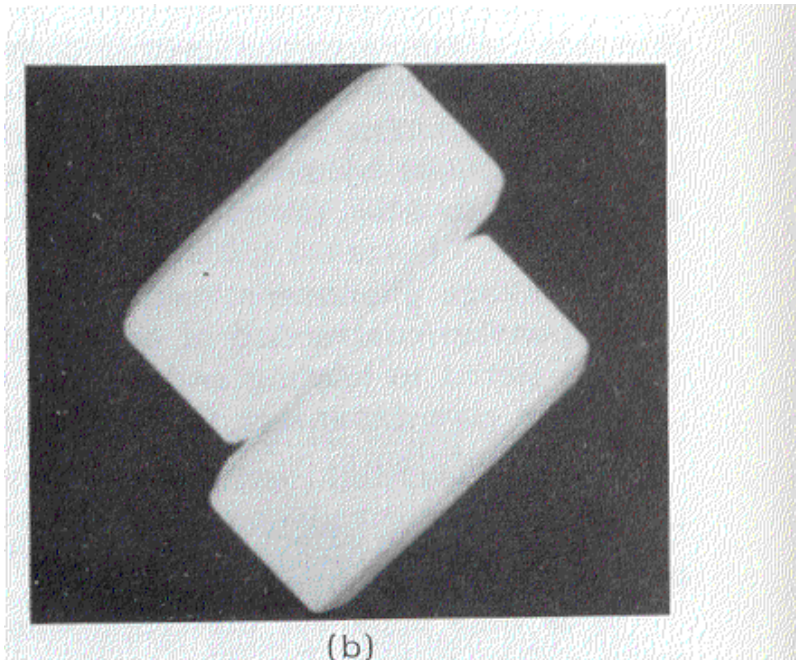


## Picking

when the coating on two adjacent tablets is not sufficient dry before contact between them occurs.

*Overwetting for excessive spray rate or insufficient number of spray guns or blocking of one nozzle.*

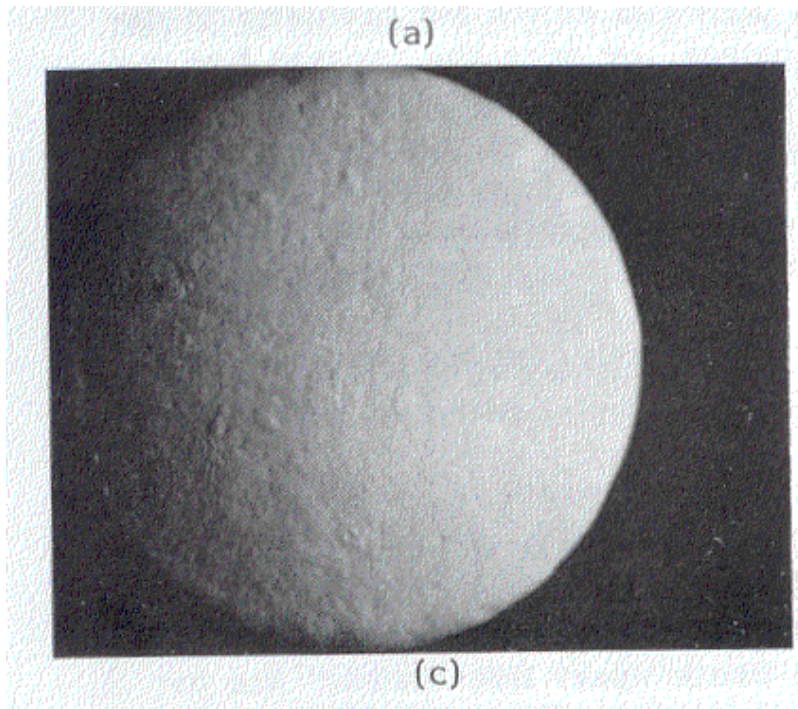
# PROBLEMS IN FILM COATING



## **Twinning**

In extremely tacky cases, tablets with flat faces or flat edges (as with capsule-shape tablets that have thick walls) may become permanently glued together so that twinning occurs.

# PROBLEMS IN FILM COATING

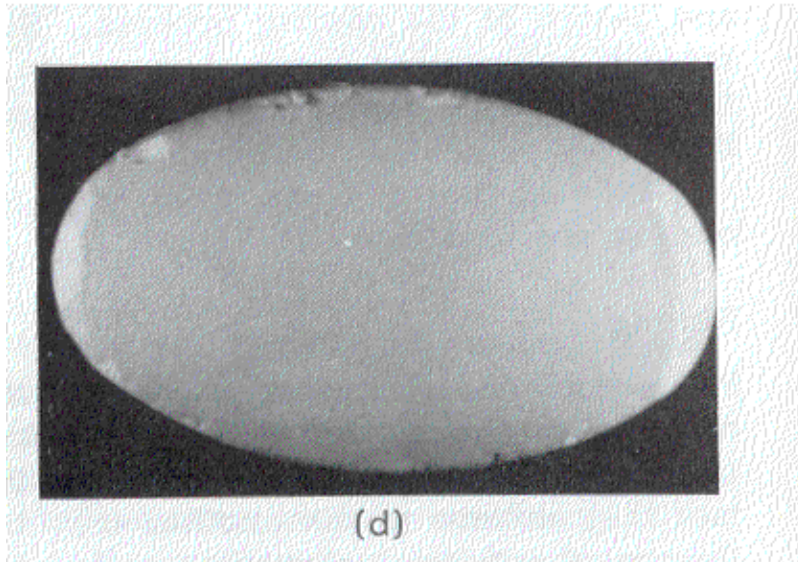


## ***Orange Peel (Roughness)***

when the droplets of coating liquid dry very soon after they make contact with the surface of the product being coated.

*Low spray rate with excessive drying conditions and use of excessive atomizing air pressure with drying of droplets.*

# PROBLEMS IN FILM COATING



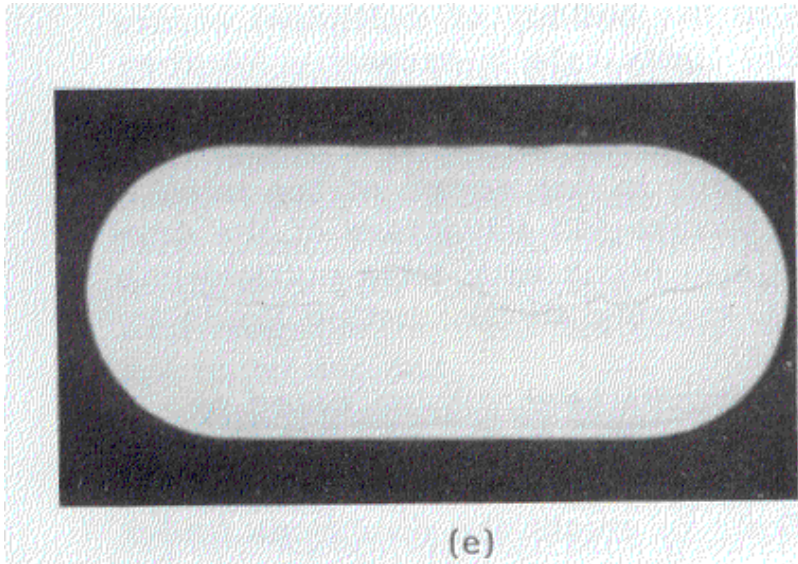
## ***Edge Wear (Chipping)***

results because tablets edges are exposed most to these attrition effects.

*Tablet cores with high friability, worn tablet punches, initial lamination with edge-erosion and brittle film coating with insufficient protection to tablet edges.*



# PROBLEMS IN FILM COATING



## *Film Cracking*

occurs when the internal stress (that develops within the coating on drying) exceeds the tensile strength of that coating.

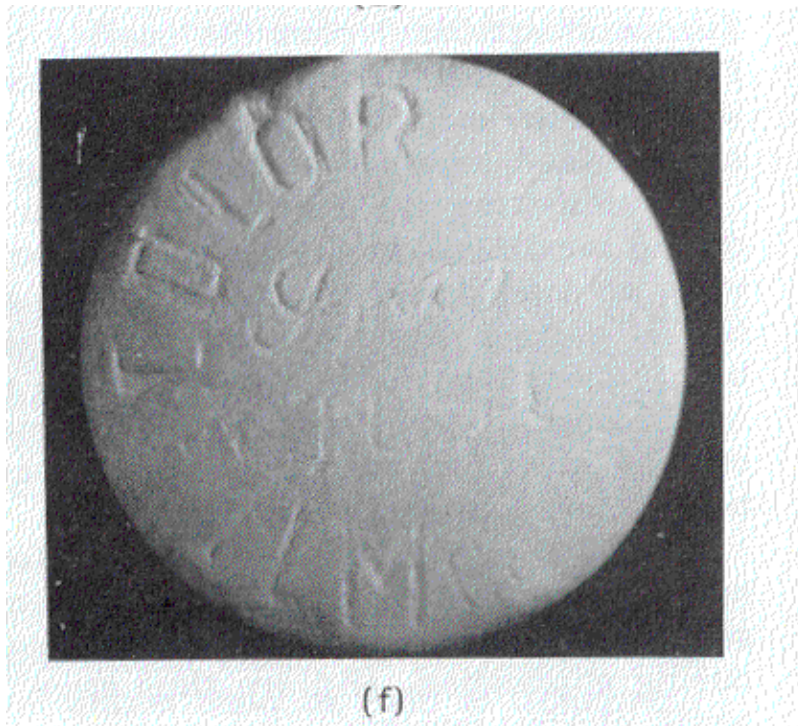
*Increase in polymer molecular weight and/or use plasticizers.*

# PROBLEMS IN FILM COATING

## ***Bridging of Logos (Intagliations)***

occurs when a component internal stress becomes sufficient high so as to cause partial or complete detachment of the coating in the region of the logo.

*Improving film adhesion and /or reducing stress within the film.*

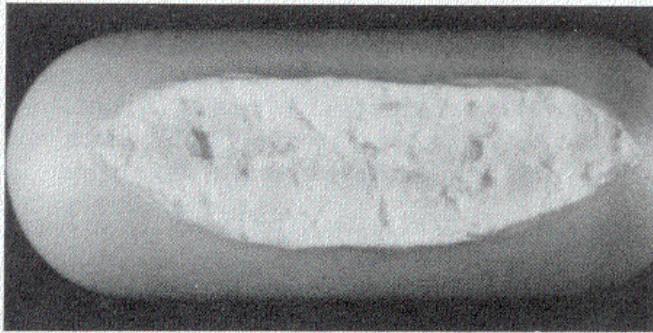




# PROBLEMS IN FILM COATING

## *Film Peeling*

occurs when the coating peel back from the surface of the substrate for cohesive failure.



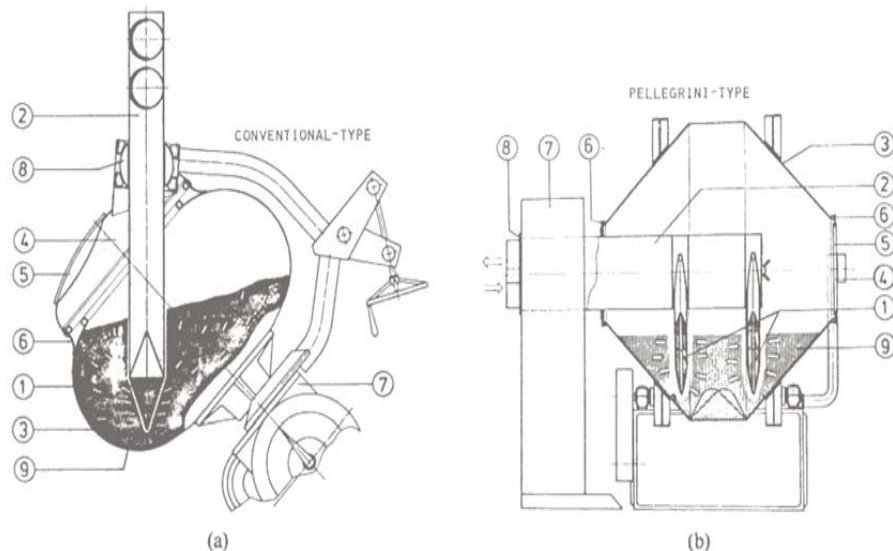
(g)

# COATING EQUIPMENT

Coating equipment includes:

- pan coating
- fluid bed coating columns
- air-handling equipment (including heat exchangers)
- coating liquid holding tanks ( including mixers)
- metering/delivery equipment (e.g. spray guns)
- liquid application systems
- control systems.
- monitoring systems
- effluent treatment systems (e.g. dust collectors, solvent recovery equipment).

# COATING PANS



- Key:
1. Immersion Sword
  2. Coaxial conduit
  3. Coating pan
  4. Pan cover
  5. Clear control cover
  6. Silicone seal
  7. Stand
  8. Coaxial conduit adjustment
  9. Coating bed

- Conventional coating pans (confectionery pans, glatt immersed swords)
- Modified conventional coating pans (Pellegrini, Pellegrini GS)

Fig 90-5. Schematic diagram of the immersed-sword apparatus for use in either (a) a conventional pan or (b) a Pellegrini pan.

# COATING PANS

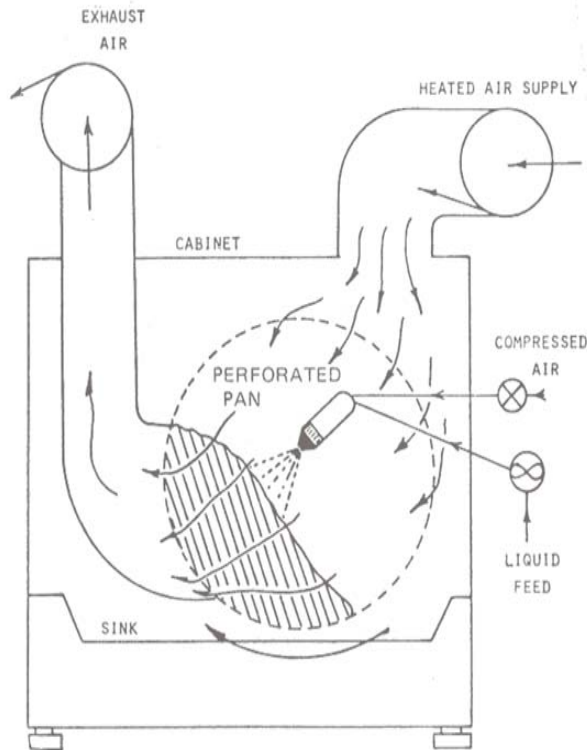


Fig 90-6. Schematic diagram of a 48-in Accela Cota (150-kg capacity).

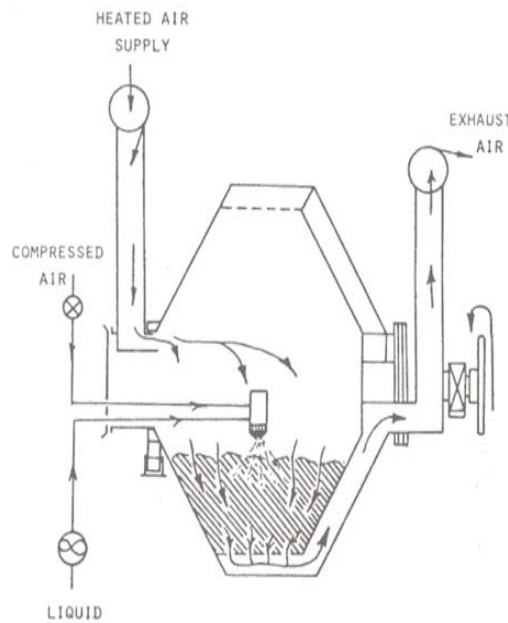


Fig 90-7. Schematic diagram of the Hi-coater.

- - Side vented coating pans (Accela-Cota,
- Hi-coater, Driacoater,
- Glatt Pan Coating Equipment, Huttling Butterfly Pan,
- Dumoulin IDA.X)

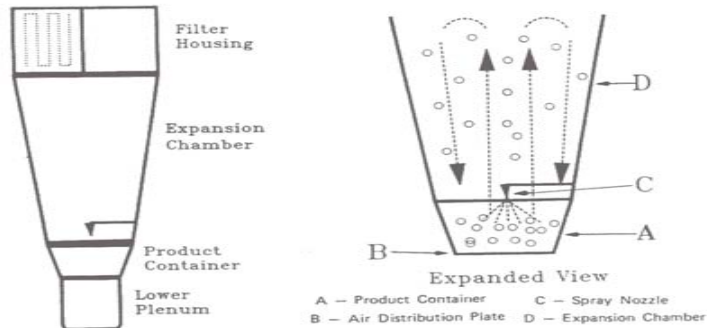


Fig. 11 Top spray coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

To meet these needs, three basic approaches have evolved:

1. *Top spray* (essentially similar to that used for granulation process)

2. *Bottom spray* (e.g., the Wurster process)

3. *Tangential spray* (or rotor process), which has developed from that used to prepare spheronized granulates.

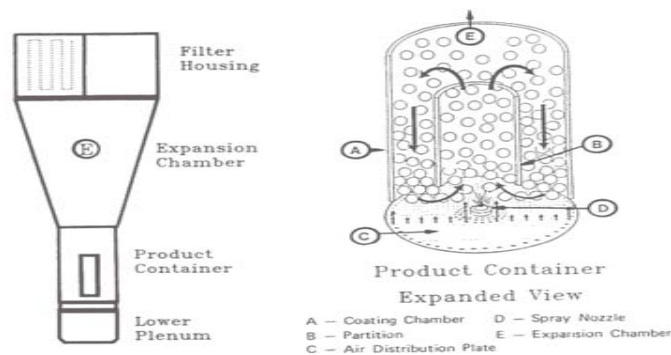


Fig. 12 Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

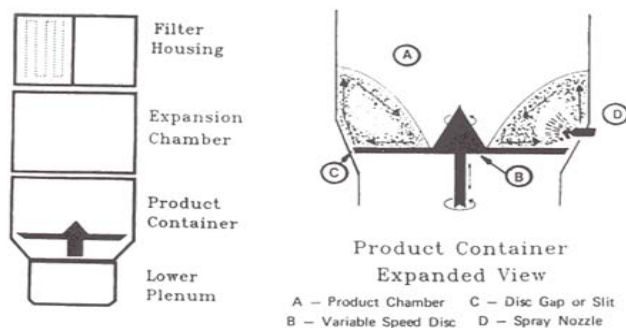


Fig. 20 Rotor tangential spray coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

# Fluidized beds

The fluid-bed process or air suspension process has also apply to the coating of pharmaceutical dosage forms

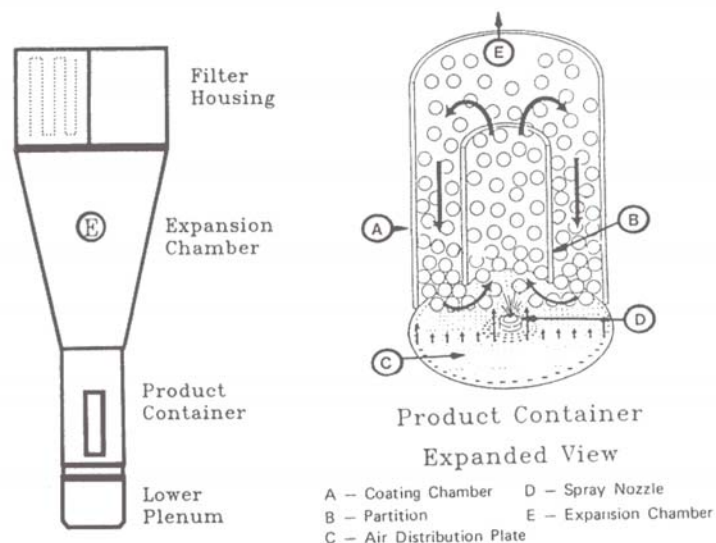


Fig. 12 Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

*Special equipment is the Wurster fluid bed, which salient features consist of:*

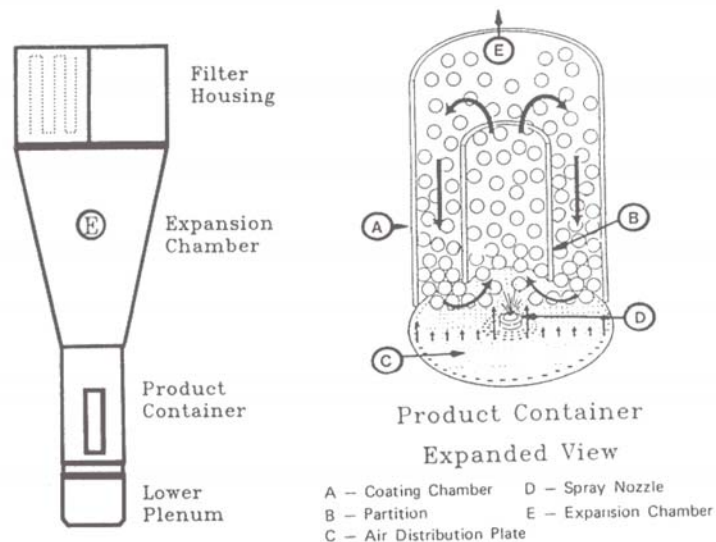
- coating chamber
- inner partition (diameter is 50% that of the coating chamber)
- air-distribution plate (larger diameter holes in the central portion than those of periphery)
- spray nozzle located at the center of the air-distribution plate.

# Fluidized beds

Fluid air causes the product being coated to accelerated rapidly up through the inner portion (which defines the spray zone).

Deceleration occurs in the region of the expansion chamber, causing the product to drop back into region confined by the walls of chamber and the insert.

The product moves quickly down to the bottom where cycle begins again.



**Fig. 12** Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

# Fluidized beds

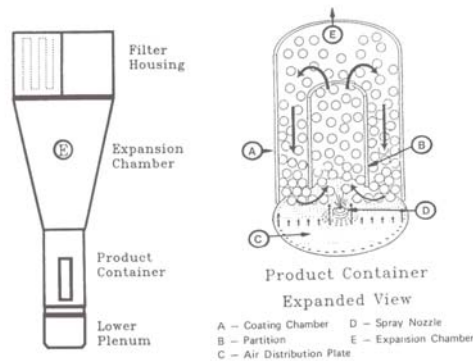


Fig. 12 Bottom spray (Wurster) coater. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)

The need to ensure that all product is uniformly coated imposes the multiple 9" inserts.

*The product coated in the Wurster process is typically characterized by uniform distribution of coating and high gloss; the process exhibits excellent drying characteristics.*

Longer expansion chambers is used to coat small particles (materials as fine as 50 microns).

Batch sizes from 0.5 to 500Kg)

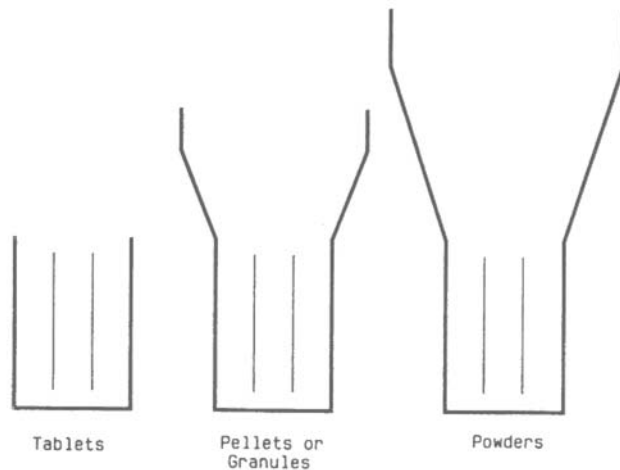


Fig. 17 Expansion chambers for Wurster columns. (Courtesy of Glatt Air Techniques, Inc., Ramsey, New Jersey.)



# **AUTOMATED COATED PROCEDURES**

## **Introduction**

The benefits to be derived from a well-automated process are:

- Independence from operator judgment
- Achievement of consistent product quality
- Achievement of a full optimized process with greater potential for minimizing processing times
- production of hard-copy documentation.

The automation involves activities:

1. Timing and sequencing
2. Measuring and controlling appropriate processing parameters (electromechanical, pneumatic and electronic).

# Automation of Film Coating

Film coating is simpler, but more critical process to automate.

*Independent variables* that need to be measured and controlled include:

- Drying air volume
- Drying air temperature
- Drying air humidity
- Pan speed
- Spray rate
- Atomizing air pressure/volume
- Pattern air pressure /volume

*Dependent variables* that need to be monitored are:

- Tablet bed temperature
- Exhaust air temperature
- Exhaust air humidity
- Tablet bed moisture

# Automation of Film Coating

***For example***, exhaust air temperature may be kept under control by maintaining an appropriate balance between inlet air volume, temperature and humidity, and spray rate.

Keeping inlet air humidity constant by a dehumidification is extremely expensive ( a typical 48" Accela Cota coating batch of tablets in 90 min requires about 5000 m<sup>3</sup> of conditioned air)

Compensation by adjusting one or more of :

- air volume
- inlet air temperature
- spray-rate.