Overview of Film-Coating Technologies in the Pharmaceutical & Nutritional Industries

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Presentation Outline

- Introduction
- Thermodynamic issues
- Spray dynamic issues
- Understanding the impact of coating structure
- Understanding the impact of coating structure
## Film Coating of Pharmaceutical & Nutraceutical Products: Comparing Issues & Requirements

<table>
<thead>
<tr>
<th>Requirements &amp; Issues</th>
<th>Pharmaceutical Products</th>
<th>Nutraceutical Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aesthetic coatings</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Modified-release coatings</td>
<td>YES</td>
<td>POSSIBLY</td>
</tr>
<tr>
<td>Barrier coatings</td>
<td>YES</td>
<td>POSSIBLY</td>
</tr>
<tr>
<td>Coating of tablets</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Coating of multiparticulates</td>
<td>YES</td>
<td>POSSIBLY</td>
</tr>
<tr>
<td>Considerations for cost</td>
<td>MODERATE</td>
<td>HIGH</td>
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</table>
Film coating, especially the aqueous process, is a complex, critical process:

- Complexity is derived from the potentially large number of process variables that can impact the quality (in its broadest sense) of the final product.
- Criticality stems from the need to identify the key process variables, and ensure that they are appropriately controlled (an issue that speaks to the PAT initiatives that are now being promulgated).

While we may profess to be aware of these issues, it is interesting to note how rarely we truly understand this process.
Film Coating: Key Elements of the Process

Exhaust air:
Volume, temperature and humidity

Inlet air:
Volume, temperature and humidity

Spray Delivery

Tablet Motion

Flow Control

Pump Delivery
Film Coating: Gaining a Better Understanding of the Process

Although we may have a long way to go in gaining a better understanding, fortunately, there are many tools available today that facilitate this understanding, and these include computer-based programs that:

- Enable us to identify critical process variables in a systematic way through application of D.o.E.
- Analyze process thermodynamics, and facilitate technology transfer.
- Analyze spray dynamics.
- Model many aspects of the coating process (spray distribution, airflow, and heat transfer) using CFD.
- Make predictions with regard to uniformity of distribution of the coating material.
Key Objectives in Film Coating

Although film coatings are applied to pharmaceutical and nutritional products for a variety of reasons, the common thread that runs through all of our coating processes is the need to understand:

- Process thermodynamics.
- Spray dynamics.
- Factors that influence coating structure, and hence functionality.
- Factors that influence uniformity of distribution of the coating.
Film Coating: Thermodynamic Issues

In order to achieve quality, functional, and stability objectives, it is necessary to:

- Understand the interaction between the process air stream and the coating liquid.
- Ensure that an appropriate balance exists between:
  - the rate at which the coating liquid is delivered into the coating environment, and
  - the ability of the process air stream to remove the coating solvent.
Overview of the Drying Process

There are three key components of drying, namely:

- **Vaporization** of the coating solvent, which represents a phase transition, and
- **External Mass Transfer** of the coating solvent, involving diffusion of solvent from the boundary layer at the surface of the product (or droplet of coating liquid) into the process air stream.
- **Internal Mass Transfer** of the coating solvent, involving diffusion of solvent from within the core and coating to the surface of the product

A key consideration is the *effectiveness* of the drying process is, which will be governed predominantly by:

- Heat transfer.
- Latent heat of vaporization (for the solvent).
- The solvent concentration gradient between the surface of the product (or droplet of coating liquid) and bulk of the process air stream (which, in aqueous film coating, can be dramatically impacted by the humidity of the inlet air).
What Factors Affect the Drying Process?

Removal of coating solvent will depend upon:

- **Drying capacity of process air stream:**
  - Mass, or volume, of air.
  - Temperature of air.
  - Moisture content of air.

- **Surface area from which drying takes place:**
  - Droplet size (controlled by atomization air pressure and coating solution properties) of coating liquid, and ultimately the diffusion rate of water to the surface of the droplet as viscosity increases.
  - Tablet surface area (impacted by pan fill, tablet size and shape).

- **Rate at which solvent is introduced into the process:**
  - Spray rate.
  - Solvent content of coating liquid.
Side Vented Pan – Influence of Inlet Plenum Configuration on Airflow
Film Coating: the Need to Achieve a Balance

Film coating is a process where the extreme process conditions, namely those producing overwetting and those producing overdrying, create unacceptable results.

Overwetting creates:
- Visual defects such as picking and sticking, twinning, swelling and cracking (due to moisture absorption be core), and rough tablets due to film rubbing.
- Stability problems when the drug is moisture sensitive.
- Drug release problems relating to premature swelling of disintegrants and drug leaching from the core during spray application.

Overdrying causes problems relating to:
- Creation of rough tablets due to partial spray drying of the coating material.
- Low process efficiencies due to spray drying.
- Unpredictable drug release characteristics due to potential sintering of tablet cores (or melting of ingredients therein), or creation of porous film coats that do not possess anticipated membrane characteristics.
- Stability problems when the drug is thermolabile.
Assessing Process Thermodynamics

![Thermodynamics calculation interface](image)

- **Inlet Air Flow Rate**: 8884.4 SCFM
- **Temperature**: 51.2 °C
- **Relative Humidity**: 6.21%
- **Process Air Flow Rate**: 34.78%
- **Dew Point Temperature**: 4.0 °C
- **Absolute Humidity**: 0.51% kg/kg dry
- **Relative Humidity**: 0.81%
- **Moisture Content**: 34.78%
- **Spray Rate/Solids Content**: 800.0 g/min
- **Solids Content (wt%)**: 15.0%
- **Process Air Flow Rate**: 4861.4 SCFM
- **% of Lower Explosion Limit**: 0%
Film Coating: Spray Dynamic Issues

The dynamics of the spraying process can have a profound effect on the quality of the final product, including:

- **Appearance**
  - Glossiness of the applied coating.
  - Roughness of the applied coating.
  - Existence of defects (including “picking”, “orange peel”, “chipping and edgewear”, and “infilling of logos”).
  - Color uniformity.

- **Functionality**
  - Uniformity of distribution of the coating material.
  - Porosity of the coating (which influences film permeability).
  - Solvent penetration into the core (and hence drug leaching and product stability).
Spray Dynamics: A Poorly Understood Issue?

Some general comments:

- Determination of appropriate spray dynamics is a critical issue during process development.
- Spray dynamics are, perhaps, the one area of the process that is least understood, and often receives scant attention.
- The concept that “a spray gun is just a spray gun” often prevails.
Spray Dynamics: Fundamental Concerns

Basically:
- No two spray guns are exactly alike, especially if supplied by different vendors.
- When reassembling a spray gun after, for example, cleaning, the dynamics of that gun may well change unless extreme care is taken.
- Spray gun dynamics can change through wear and misuse.

These issues may well mean that differences can occur, between spray guns, in terms of:
- Droplet size, and size distribution.
- Droplet velocity (which can influence dynamic wetting and spreading, and overspray).
- Relative “wetness” of droplets as they arrive at the surface of the product being coated.
Examples of Differences in Spray Gun Dynamics

Fixed Settings:
- Atomizing air pressure: 30.0 psi
- Pattern air pressure: 27.5 psi
- Spray rate: 82.5 g min\(^{-1}\)

A. Schlick 930-33 Spray Gun

B. Spraying Systems VAU Spray Gun
Film Coating: Issues Relating to Coating Structure

- Generally, those process factors that play a role in both process thermodynamics and spray dynamics are likely to have a great influence on film structure, and hence functional performance of the applied coating.

- This issue takes on greater importance when considering film coatings that are either intended to modify drug release characteristics, or play a significant part in improving product stability by acting as an environmental barrier coating.
Examples of Coating Structural Issues

Good Film

Poor Film
Coating uniformity is influenced by:

- The amount of coating picked up while the tablet is in the spray zone.
  
  \textit{Factors:} spray rate; tablet speed through spray zone; solids content of coating liquid; distribution of coating liquid by spray guns; coating process efficiency.

- Tablet orientation in the spray zone.
  
  \textit{Factors:} pan speed; tablet mixing.

- The number of times that a tablet passes through the spray zone during the coating process.
  
  \textit{Factors:} spray rate; solids content of coating liquid; pan speed; amount of coating being applied.
Why Is Coating Uniformity Important?

Coating uniformity will affect:

- Tablet appearance (particularly tablet-to-tablet color variability).
- Bridging of intagulations (logos), where variable coating distribution can result in variable logo clarity particularly for tablets where bridging problems are borderline.
- Drug-release characteristics when coating modified-release products.
- Processing time and costs.
Predicting Coating Uniformity