



Particle coating: From conventional to advanced

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ABSTRACT

Powder particle coating is the most important technique in pharmaceutical industry. It has constantly being refined and modified since last four decades. There are numerous applications of coating, including drug layering, modified release coating, physical and chemical protection, aesthetic purposes, taste masking, and enhanced identification of drugs. Various coating techniques from conventional pan coating to laser assisted solvent free techniques have been highlighted with its unique credentials.

1. Introduction

Particle coating to alter the surface properties and/or functionality of fine particles or powders is very important to many industries^[1, 2]. The modern coating technique has developed over the years from the use of sugar to provide a pleasant taste and attractive appearance to tablets which were unpleasant to swallow due to their bitterness. There are, of course, many forms of coating which have a special function (such as enteric coating to delay the release of the drug until it reaches the intestine)^[3]. Powder materials designed to have specific properties are called Engineered or Designed Particulates. Basically there are three types of particles. 1. Coated particles (discrete and film coatings), 2. Designer particles having a specific size, shape or morphology and 3. Composite particles (nano-composites, granulated particles)^[4].

When a thin layer of a substance is placed around a core particle it is called coating of the particle. Coating may be applied to a wide range of oral solid dosage form, including tablets, capsules, multiparticulate systems and drug crystals. When coating composition is applied to a batch of

tablets in a coating pan, the tablet surfaces become covered with a tacky polymeric film. Before the tablet surface dries, the applied coating changes from a sticky liquid to tacky semisolid and eventually to a nonsticky dry surface. The entire coating process is conducted in a series of mechanically operated acorn-shaped coating pans of galvanized iron stainless steel or copper. The smaller pans are used for experimental, developmental, and pilot plant operations, the larger pans for industrial production^[5].

- The first reference to tablet film coating appeared in 1930 but it was not until 1954 that Abbott Laboratories produced the first commercially available film-coated tablet. This was made possible by the development of a wide variety of materials—for example, the cellulose derivatives. Then comes fluidized bed-coating column based on the Wurster principle^[6]. There was also a belief that the lower viscosity grades produced weaker films which would not meet the formulation requirement for stability and patient acceptability. However, there is now a very significant move towards aqueous film coating for the following reasons^[7]:
 - The cost of organic solvents has escalated.

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- A number of regulatory authorities have banned chlorinated hydrocarbons altogether because of environmental pollution.
- The development of improved coating pans and spraying systems has enabled these more difficult coating materials to be applied.
- Flameproof equipment is not required. This reduces capital outlay and a less hazardous working environment is provided for the operator.
- Solvent recovery systems are not required resulting in less capital outlay.

1.1 The rational of particle coating^[8]

- To modify the drug release profile, e.g. enteric coating, sustained release coating, osmotic pumps, etc.
- Improve appearance
- Facilitate identification
- Facilitate swallowing
- Mask taste and odor
- Protect the core from external environmental factor like O₂, humidity, light etc.
- Obtain easier product handling
- To separate incompatible substances by using the coat to contain one of them or to coat a pellet this was previously compressed into a core.
- The coated tablet is packed on a high-speed packaging unit. The coating reduces friction and increases the production rate.

1.2 Types of particle coating

There are basically two types of Particle coating finds Pharmaceutical Applications. Some new innovations are made which are described later in this article.

- 1) Wet Particle Coating
- 2) Dry Particle Coating

1) Wet particle coating (WPC)

At present, the commercially used technology for coating solid dosage forms is the liquid coating technologies which incorporate any kind of solvent in coating. Generally, a mixture of polymers, pigments and excipients is dissolved in an appropriate organic solvent (for water insoluble polymers) or water (water soluble polymers) to form a solution, or dispersed in water to form dispersion, and sprayed onto the dosage forms and dried by continuously

providing heat until a dry and smooth film coating film is formed. A typical liquid coating process is carried out in a rotary pan coater for larger size solid dosages such as tablets, or in a fluidized bed coater for smaller size dosage forms such as pellets, pills, granules etc. WPC solution may be volatile and toxic which needs consideration. Apart from that it requires post treatment and waste processing which subsequently increase the cost^[9].

Wet particle coating techniques

1.2.1 Microencapsulation

Microencapsulation is a versatile and very precise coating technique used to encapsulate individual drug particles^[10]. This technique efficiently and uniformly coats drug particles (droplets if the drug is in liquid form) with polymeric membranes of varying degrees of porosity using coacervation/phase separation processes. Although the word capsule implies a core and shell structure, the term microcapsules admits not only membrane enclosed particles or droplets but also dispersion in solid matrix lacking a distinctive external wall phase as well as intermediate types^[11]. The size range (2 to 2000 µm approximately) distinguishes them from the smaller nanoparticles or nanocapsules^[12]. These processes result in individual particles of a drug substance being enveloped into a membrane. Microcapsulated particles can be incorporated into different dosage forms including fast melt tablets, sachets, sprinkles and reconstitutable and temporary suspensions. It is a new formulation concept for creams, ointments, aerosols, etc. **Table 1** provide the information regarding the microencapsulation processes and their applications. Mechanical methods used for microencapsulation utilize the special equipments for their own. The microcapsules produced result from mechanical procedures rather than from a well-defined physical or chemical phenomenon. The most commonly employed mechanical methods for the preparation of microcapsules and microspheres^[13] are; (1) Multiorifice-centrifugal process, (2) Air suspension coating (wurster), (3) Vacuum coating, (4) Spray drying, (5) Spray congealing, (6) Pan coating, (7) Rotary fluidized bed granulator, and (8) Spheronization.

Table 1: Microencapsulation processes and their applications^[14]

Process	Applicable core material	Approx. Particle size (μm)
Air Suspension	Solids	35-5000
Coacervation phase separation	Solids & Liquids	2-5000
Multi orifice Centrifugal	Solids & Liquids	1-5000
Pan Coating	Solids	600-5000
Solvent Evaporation	Solids & Liquids	5-5000
Spray Drying and Congealing	Solids & Liquids	600

a) Coacervation– Phase separation process (Simple)^[15, 16]

This process consists of three steps that are carried out under continuous agitation:

- (i) Formation of three immiscible chemical phases
- (ii) Deposition of the coating
- (iii) Rigidization of the coating

Coacervation: Phase separation process applicable for solids and liquids with particle size ranges from 2- 5000 μ .

Step I: Formation of three immiscible chemical phases

It involves three immiscible chemical phases which are

- (i) Liquid manufacturing vehicle phase
- (ii) Core material phase and
- (iii) Coating material phase.

To form the three phases, firstly core material is dispersed in a solution of the coating polymer. The solvent for the polymer is the liquid manufacturing vehicle phase in most of the cases. The coating material phase, an immiscible

polymer in a liquid state, is formed by utilizing one of the methods of phase separation coacervation, that is:

- By changing the temperature of the polymer solution.
- By adding a salt
- By adding a non-solvent
- By adding incompatible polymer to the polymer solution
- By inducing a polymer-polymer interaction.

Step II: Deposition of the coating

This process consists of depositing the liquid polymer coating upon the core material accomplished by controlled physical mixing of the coating material and the core material in the manufacturing vehicle. Deposition of the liquid polymer coating around the core material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid vehicle phase. This adsorption phenomenon results in effective coating.

Step III: Rigidization of the coating

Rigidization of coating is done by thermal, cross-linking or desolvation techniques to form self-sustaining microcapsules.

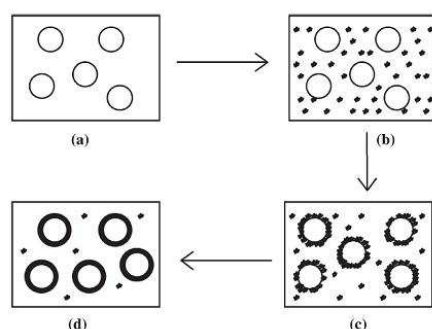


Figure 1: Schematic representation of the coacervation process. (a) Core material dispersion in solution of shell polymer; (b) separation of coacervate from solution; (c) coating of core material by microdroplets of coacervate; (d) coalescence of coacervate to form Microcapsules

b) Aqueous-phase separation, coacervation (Complex)
[17, 18]

Complex coacervation, in contrast to simple coacervation, requires at least two hydrophilic colloids in the continuous phase of the fluid system. The complex coacervation is principally a pH dependant process. The acidic or basic nature of the system is manipulated to produce microcapsules. Above a certain critical pH value, the system depending upon its acidic or basic nature may

produce microcapsules. Below that pH value they will not form. Usually complex coacervation deals with the system containing more than one colloid. This type of procedure allows the application of the well-known phenomenon whereby two oppositely charged colloids discharge with each other to produce a coacervate, as is shown in the following general-type reaction:

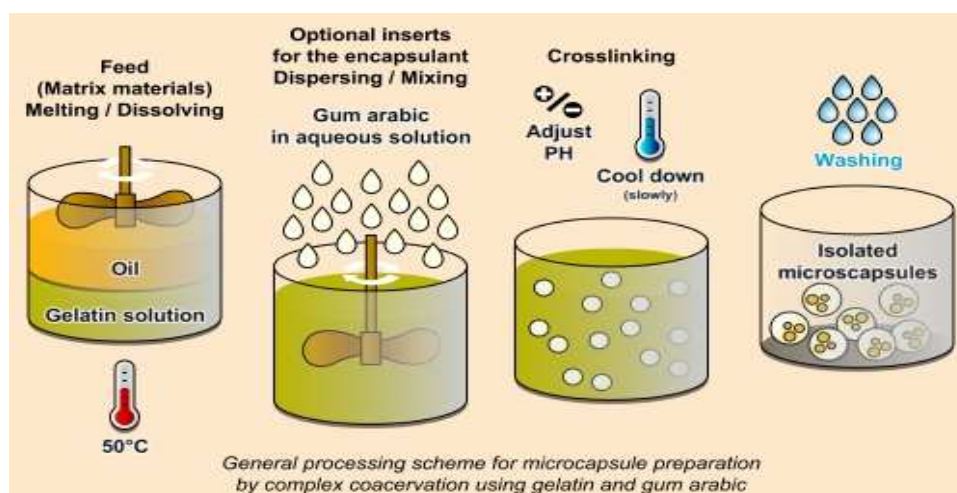
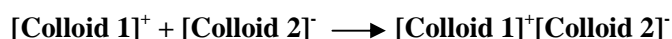


Figure 2: Complex Coacervation Process

c) Nonaqueous-phase separation^[17]

Phase separation can be induced in organic solvent systems as well as aqueous systems. Again, the suspended particle may be either a solid or an immiscible liquid. Thus, for dispersed liquids, emulsions of the W/O type are employed in contrast to the more conventional coacervation method in which O/W-type emulsions are used. Obviously, water-soluble solids can also be included either by suspending them in the organic solvent or by dissolving them in the internal phase of the W/O-type emulsion.

d) Spray drying and spray congealing^[19]

Spray drying and spray congealing processes are similar, both involves the dispersion of core material in a liquefied coating substance and spraying or introducing the core-coating mixture into some environmental condition, whereby relatively rapid solidification of the coating is

affected. Both processes are applicable for solids and liquids. Particle size ranges from 5 to 600 μ.

I. Spray drying

In this method involves the dispersion of core material into coating solution (core material must be insoluble in coating solution). Then spraying the mixture as atomized spray into air stream. The air is usually heated, which provides the latent heat of vaporization required to remove the solvent from the coating material, resulting in the formation of microencapsulated product.

II. Spray congealing

General process and conditions are same as spray drying except that the core material is dispersed into a coating solution melts rather than a coating solution. Microencapsulation is accomplished by spraying the hot mixture into a cool air stream.

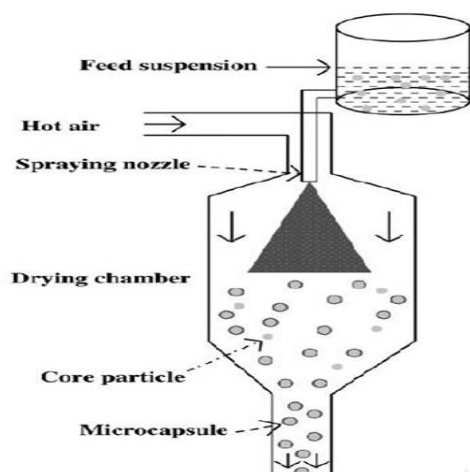


Figure 3: Spray Congealing (Vinensia.com)

e) Fluidized bed coating techniques^[17,20]

A fluidized bed is a bed of solid particles with a stream of air or gas passing upward through the particles at a rate great enough to set them in motion. As the air travels through the particle bed, it imparts unique properties to the bed. For example, the bed behaves as a liquid. The fluid bed can be used to dry the wet product, agglomerate particles, improve flow properties, or produce coated particles for controlled release or taste masking. However, the conventional fluidized bed cannot be used for handling fine particles (less than 40 microns) due to their poor fluidization. Coating and granulation of fine particles (15 micron cornstarch and 12 micron aluminum) are performed using the Mini Glatt Fluidized Bed. The fluidized bed process can be used with both thermoset and thermoplastic powder coatings.

I. Top spray coating^[20,21]

With top spray coating in the fluid bed (batch and continuous), particles are fluidized in the flow of heated air, which is introduced into the product container via a base plate. The coating liquid is sprayed into the fluid bed from above against the air flow (countercurrent) by means of a nozzle. Drying takes place as the particles continue to move upwards in the air flow. Small droplets and a low viscosity of the spray medium ensure that the distribution is uniform. Dripping of the coated particles depends on the formulation of the coating material. Top spray fluid-bed coaters produce highest yields of encapsulated particles. Depending on the application, the system is sub-divided into pre-heating zones, spray zones & drying zones.

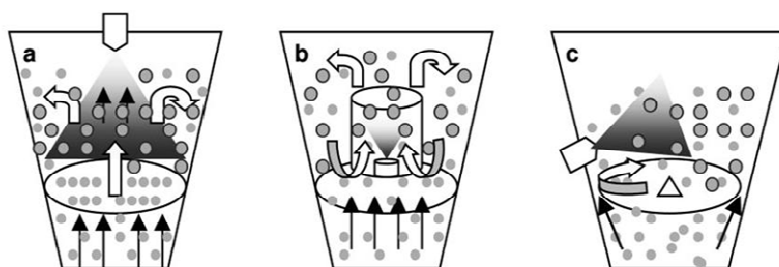


Figure 4: Schematics of a fluid-bed coater; (a) Top spray; (b) bottom spray; (c) tangential spray (ispub.com)

II. Bottom spray coating (Air suspension process, wurster coating)^[6- 22]

Wurster coaters are bottom spray fluid bed coaters that have been extensively used in the pharmaceutical industry for coating of small particulates. They offer excellent heat and mass transfer within the product bed and are able to form uniform coats. Within the coating chamber, particles are suspended on an upward moving air stream. Particles are recirculated through coating zone portion of the chamber, where coating material, usually a polymer solution is spray applied to the moving particles. During each pass through the coating zone, the core material receives an increment of coating material. The air distribution plate in the precision coater consists of a perforated plate connected to the swirl accelerator. The swirl accelerator functions to swirl and accelerate the inlet air to impart spin and high velocity to the particles as they transit through the partition column where coating takes place. This process can change the fluid dynamics of the particles. In bottom spray fluid bed processes, the area of the air distribution plate directly under the partition column has more perforated area than the periphery region of the air distribution plate, resulting in a higher central air velocity through the partition column. This creates a region of lower pressure that draws in particles by the venturi's effect and lifts particles up the partition column (up-bed zone) according to Bernoulli's law. As such, particles from the product bed enter the partition column (horizontal transport zone) and decelerate in the expansion chamber (deceleration zone)—falling outwards freely in an inverted u-shape trajectory back onto the product bed staging area (down-bed zone). The particles then reenter the partition column through the partition gap and repeat the fountain-like cyclic flow. Particles receive coating droplets during the passage through the spray zone within the partition column, and this cycle is repeated until the desired coating level is achieved. The cyclic process is repeated several hundred times during processing, depending on the purpose of microencapsulation and the coating thickness desired. Particle size ranges from 35- 5000 μ . Although it is a time consuming process, the multilayer coating procedure helps in reducing particle defects. Fluid dynamics was found to be important in controlling product quality and productivity in bottom spray fluid bed coaters.

III. Tangential spray coating (Rotor pellet coating)^[21- 23]

The tangential spray consists of a rotating disc at the bottom of the coating chamber, with the same diameter as the chamber. During the process the disc is raised to create a gap between the edge of the chamber and the disc. The tangential nozzle is placed above the rotating disc through which the coating material is released. The particles move through the gap into the spraying zone and are encapsulated. As they travel a minimum distance there is a higher yield of encapsulated particles. It is ideal for coating with high solid content. Very thick film layers can be applied by means of the rotor method.

f) Interfacial polymerization^[24, 25]

Interfacial polymerization method for forming polyamide membranes involves the reaction occurring at the liquid-liquid interface existing between an aqueous solution of an aliphatic diamine and a water immiscible organic solution of a dicarboxylic acid halide. The polymerization reaction depends on the fact that acid halides (sebacoyl chloride), are nearly water insoluble, and diamines (hexanediamine), have an appreciable partition coefficient toward the water immiscible organic phase. Hence, the hexadiazine diffuses to the organic phase, and the polycondensation reaction occurs forming the polyamide membrane. So in this technique the capsule shell will be formed at or on the surface of the droplet or particle by polymerization of the reactive monomers. Various polymer-coating materials used includes; polyamides (nylon), polyurethanes, polysulfonamides, polyesters, polycarbonates, and polysulfonates.

g) In-situ polymerization^[26-28]

Like IFP the capsule shell formation occurs because of polymerization monomers added to the encapsulation reactor. In this process no reactive agents are added to the core material, polymerization occurs exclusively in the continuous phase and on the continuous phase side of the interface formed by the dispersed core material and continuous phase. Initially a low molecular weight prepolymer will be formed, as time goes on the prepolymer grows in size, it deposits on the surface of the dispersed core material there by generating solid capsule shell. e.g.

encapsulation of various water immiscible liquids with shells formed by the reaction at acidic pH of urea with

formaldehyde in aqueous media. In one process, e.g. Cellulose fibers are encapsulated in polyethylene while 0.5mcm/min. Coating thickness ranges 0.2-75 μm . The coating is uniform, even over sharp projections.

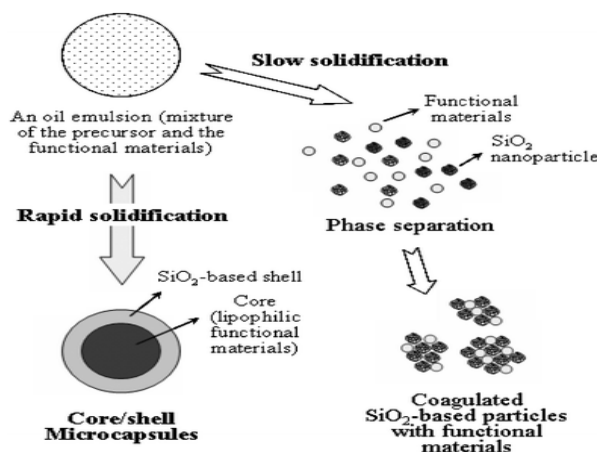


Figure 5: Silica based In situ polymerization

h) Matrix polymerization^[29]

In a number of processes, a core material is imbedded in a polymeric matrix during formation of the particles. A simple method of this type is spray-drying, in which the particle is formed by evaporation of the solvent from the matrix material. However, the solidification of the matrix also can be caused by a chemical change.

i) Pan coating^[14]

The microencapsulation of relatively large particles by pan coating method has become wide spread in the pharmaceutical industry. Solid particles greater than 600 μm in size are generally considered essential for effective coating. The coating is applied as a solution or as an atomized spray to the desired solid core passed over the coated materials during coatings is being applied in the coating pans.

j) Multi orifice centrifugation^[14]

The liquid material to be coated is extruded through the nozzle of the inner tube into the coating fluid contained in the outer tube. Initially, the fluid extrudes as a rod surrounded by the coating fluid, but the rod ultimately breaks up into droplets, which are then immersed, in the coating fluid. As the extruded droplets pass through the

nozzle orifice of the outer tube, the coating fluid forms a surface coat, which encases the extruded particle. This is then passed through hardening bath where coated particles are strengthened. The centrifugation method is capable of producing microcapsules in the 100-200 μm range. Centrifugal extrusion processes generally produce capsules of a larger size, from 250 microns up to a few millimeters in diameter. Liquids are encapsulated using a rotating extrusion head containing concentric nozzles. In this process, a jet of core liquid is surrounded by a sheath of wall solution or melt. As the jet moves through the air it breaks, owing to Rayleigh instability, into droplets of core, each coated with the wall solution. While the droplets are in flight, a molten wall may be hardened or a solvent may be evaporated from the wall solution. Since most of the droplets are within $\pm 10\%$ of the mean diameter, they land in a narrow ring around the spray nozzle. Hence, if needed, the capsules can be hardened after formation by catching them in a ring-shaped hardening bath. This process is excellent for forming particles 400-2,000 μm (16-79 mils) in diameter. Since the drops are formed by the breakup of a liquid jet, the process is only suitable for liquid or slurry. A high production rate can be achieved, i.e., up to 22.5 kg (50 lb) of microcapsules can be produced per nozzle per hour per head.

k) Vibrational nozzle^[8, 14, 17]

Core-Shell encapsulation or Micro granulation (matrix-encapsulation) can be done using a laminar flow through a nozzle and an additional vibration of the nozzle or the liquid. The vibration has to be done in resonance of the Rayleigh instability and leads to very uniform droplets. The liquid can consist of any liquids to work), e.g. solutions, emulsions, suspensions, melts etc. The solidification can be done according to the used gelation system with an internal gelation (e.g. sol-gel processing, melt) or an external (additional binder system, e.g. in a slurry). The process works very well for generating droplets between 100-5,000 μm (3.9-200 mils), applications for smaller and larger droplets are known. With capacities of 1-10,000 kg per hour (2-22,000 lb/h) at working temperatures of 20-1,500°C (68-2,700°F) (room temperature up to molten silicon). Nozzle heads are available from one up to several hundred thousand.

l) Solvent evaporation [8, 14, 17, 30]

The coating material is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core material to be encapsulated is dissolved or dispersed in the coating polymer solution. This mixture is added to the liquid manufacturing vehicle phase with agitation, the mixture is heated to evaporate the solvent for polymer. Here the coat material shrinks around the core material and encapsulate the core. Microspheres of 5-fluorouracil have been prepared, using three grades of ethyl cellulose as wall forming materials, and utilizing a solvent evaporation technique under ambient conditions.

m) Spray drying [31, 32]

Spray drying is a mechanical microencapsulation method developed in the 1930s. An emulsion is prepared by dispersing the core material, usually an oil or active ingredient immiscible with water; into a concentrated solution of wall material until the desired size of oil droplets are attained. The resultant emulsion is atomized into a spray of droplets by pumping the slurry through a rotating disc into the heated compartment of a spray drier. There the water portion of the emulsion is evaporated, yielding dried capsules of variable shape containing microencapsulated materials from aqueous slurry that are produced by chemical methods.

n) Rotational suspension separation [33]

Rotational suspension separation or the spinning disk method is a wet particle coating technique. The internal phase is dispersed into the liquid wall material and the mixture is advanced onto a turning disk. Droplets of pure shell material are thrown off of the rim of the disk along with discrete particles of core material enclosed in a skin of shell material. After having been solidified by cooling, the microcapsules are collected separately from the particles of shell material.

2) Dry particle coating technology [1, 34]

Dry particle coating is used to create new-generation materials by combining different powders having different physical and chemical properties to form composites, which show new functionality or improve the characteristics of known materials. Materials with relatively large particle size (1-200 μm) form a core and these core (host) particles are mechanically coated with fine submicron (guest) particles; no liquid of any kind (solvents, binders or water) is required. Dry particle coating involves mechanically fixing fine particles (guests) onto the surface of relatively larger particles (hosts).

Advantages

- To coat particles without using of organic solvent or water dispersion.
- Compared to solvent and water based coating, the dry coating method is favorable regarding environmental friendliness, safety and cost.
- It might be a very suitable coating method in order to coat foods and drugs which are sensitive to organic solvents or water.
- During the traditional coating process based on organic solvent, the solvent needs to be recovered due to environmental pollution.
- Coating processes with aqueous dispersions are time and energy consuming caused by the low concentration of coating polymer and large amounts of water which need to be evaporated.

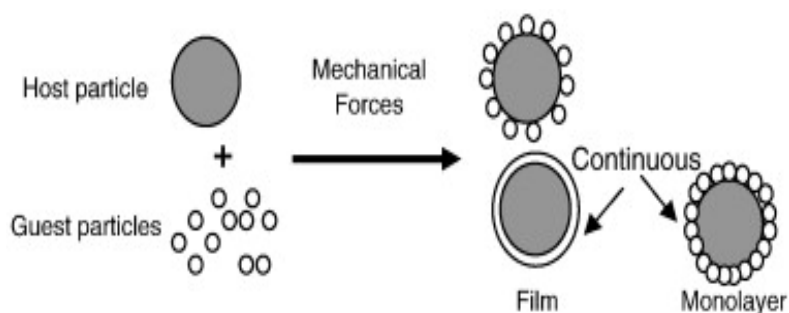


Figure 6: Mechanism of dry coating ^[1]

Dry Particle coating techniques

a) Hot melt coating ^[35-37]

A hot-melt coating material, as its name implies, is applied in its molten state over the substrate and then solidified upon cooling. Generally, materials with molten viscosities less than 300 centipoise and melting points less than 80°C, because the liquefied coating substances are maintained at 40–60°C above their melting point prior to spraying, can

be used when the molten droplet size, inlet and outlet air temperature, and volume of fluidization air are well controlled. Lipid excipients are highly compatible with ingredients including flavoring agents, artificial sweeteners and surfactants. Coated drug particles can be used in tablets, including chewable and flash melt forms where an interesting aspect of lipid coatings is their plasticity and resistance to fracture under pressure. They can also be used in capsules, suspensions and sachets.

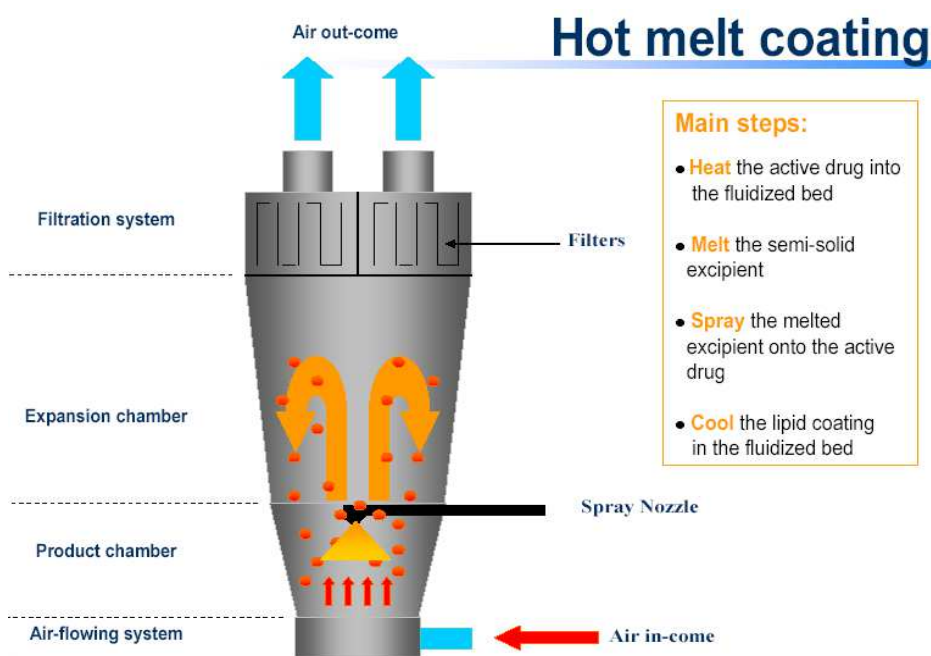


Figure 7: Hot melt coater

Most commonly used coating materials and their melting points:

- Partially hydrogenated palm oil (58–63°C) and cottonseed oil (61–65°C)
- Beeswax (62–65°C), paraffin wax (55°C), carnauba wax (84°C)
- Polyethylene glycol 3350 (54–58°C)
- Glycerol behenate (69–74°C) and
- Gelucires (different melting points for different grades).

The coating liquid is maintained at a constant temperature during application, which can be as high as 140–150°C. Small pellets, granules, and with mean particle size ranging from 100 to 2000 m can be coated with hot-melt coating process by using a fluidized bed process. Turbo Jet Coating process is adapted to coat solid particles by suspending them in a spiral of ascending air that provides the homogeneous distribution of individual particles. The molten lipid is dispersed from the bottom of the tank and tangential to the particle flow. Here, lipid crystallization within the nozzle expansion is prevented by a micro-environment surrounding the nozzle out-let. An advantage of this technique is its ability to suspend particles within the ascending air stream, allowing the coating of very fine particles^[38].

Hot-melt coating by direct blending^[39]

Although the technique does not require complicated equipment, the obtained results are quite surprising and it can be applied for a wide range of different size substrates as well as multiple coated layers. The method consists of the following five steps: (i) melting coating agent, (ii) drug dissolution or dispersion in the molten coating material, (iii) good mixing of the substrate and molten coating agent, (iv) Cooling with continued stirring of the mixture, and (v) congealing the coated particles. Hot melt direct blending coating, involves application of a molten coating material onto beads or capsules in a heated tablet coating pan. In the hot-melt pan coating cetyl alcohol and Gelucire® (Gelucire) 50/13 were used as coating agents.

Modified version: Solid Dispersion Hot-Melt Fluid Bed Coating^[40]

In this modified version they eliminated the spraying step and thereby, the need for nozzles, steam jackets, and/or heating tape from the process. Non-pareils and PEG as a divided solid (particle size 1.41–3.36 mm) were fluidized together, and the inlet air temperature was increased to transfer PEG onto the non-pareils. The typical steps of hot-melt coatings were followed. Multiple coatings were applied by using this modified hot-melt process. Coating materials in diminishing rank order of melting points were used to produce additive coating layers resulting in multiple coatings.

b) Supercritical fluid coating^[41]

Carbon dioxide is an ideal supercritical medium for pharmaceutical purposes due to its relatively low critical temperature (31.1°C) and critical pressure (72 bar). For a successful coating, the supercritical fluid ideally dissolves only the coating material, leaving the core completely undissolved. Rapid expansion of supercritical solutions (RESS) is the most common supercritical fluid process in pharmaceutical applications. The coating agent is solubilized in supercritical carbon dioxide in a high-pressure vessel. The active ingredients are dispersed in the supercritical solution. When the suspension is rapidly expanded, the *solvent power* of carbon dioxide is reduced. The coating material precipitates onto the particles of drug dispersed in the medium. Most of the coating compounds including polymers, have very low solubility in supercritical fluids (<1 wt %) except for low molecular weight fractions. In many cases, cosolvents (methanol and acetone) are used to increase the solubility of the compounds in supercritical fluids. Coating materials were mainly lipids, (e.g., mono-di-and tri-glycerides of various fatty acids), fatty alcohols, fatty acids, and combinations of these materials with other lipids.

Supercritical CO₂ is widely used because of its advantages:

- Low critical temperature value
- Nontoxic, non-flammable
- Readily available
- Highly pure
- Cost-effective

The most widely used methods are as follows:

a) Polymer Encapsulation by Rapid Expansion of Supercritical Fluids

Supercritical fluids are highly compressed gasses that possess several advantageous properties of both liquids and gases. The most widely used being supercritical carbon dioxide (CO₂), alkanes (C₂ to C₄), and nitrous oxide (N₂O). A small change in temperature or pressure causes a large change in the density of supercritical fluids near the critical point. Supercritical fluid containing the active ingredient and the shell material are maintained at high pressure and then released at atmospheric pressure through a small nozzle. The sudden drop in pressure causes desolvation of the shell material, which is then deposited around the active ingredient (core) and forms a coating layer. Active ingredient and shell material must be very soluble in supercritical fluids. In general, very few polymers with low cohesive energy densities are soluble in supercritical fluids such as CO₂. The solubility of polymers can be enhanced by using co-solvents. In some cases nonsolvents are used; this increases the solubility in supercritical fluids, but the shell materials do not dissolve at atmospheric pressure.

b) Gas anti-solvent (GAS) process

Gas anti-solvent (GAS) process also called supercritical fluid anti-solvent (SAS). Supercritical fluid is added to a solution of shell material and the active ingredients and maintained at high pressure. This leads to a volume expansion of the solution that causes super saturation such that precipitation of the solute occurs. Thus, the solute must be soluble in the liquid solvent, but should not dissolve in the mixture of solvent and supercritical fluid. On the other hand, the liquid solvent must be miscible with the supercritical fluid. This process is unsuitable for the encapsulation of water-soluble ingredients as water has low solubility in supercritical fluids. It is also possible to produce submicron particles using this method.

c) Particles from a gas-saturated solution (PGSS)

This process is carried out by mixing core and shell materials in supercritical fluid at high pressure. During this process supercritical fluid penetrates the shell material,

causing swelling. When the mixture is heated above the glass transition temperature (T_g), the polymer liquefies. Upon releasing the pressure, the shell material is allowed to deposit onto the active ingredient. In this process, the core and shell materials may not be soluble in the supercritical fluid.

Limitations

- Poor solubility of most coating materials in supercritical fluid
- The requirement of the core to be insoluble.
- There is some necessary investment in high-pressure processing equipment.

c) Vapor coating of powders^[42]

A liquid or powder material can be dispersed by the application of electrostatic fields. The phenomena, referred to as "electrodispersion" is the dispersion by an intense electric field of part of a static bed of liquid or powder into a stable cloud of rapidly moving particles, and the maintenance of a dynamic equilibrium between the static and dispersed phases. The density of the dispersed cloud of particles varies with a number of factors, including the field strength and the nature of the powder. The electrodeposition effect is employed to produce a uniform and durable coating of controlled thickness on the individual particles, by the generation of a vapor of the desired coating--typically a metal or semiconductor material--and allowing the vapor to permeate the dispersed particles. The electric field ensures that only the particles are coated, and the dispersed particles, having the same charge, repel each other, avoiding agglomeration. Possibilities include the manufacture of slow dissolving coatings on pharmaceutical powders.

Modification: Fluidized bed chemical vapour coating

- Fluidized bed chemical vapor deposition is one of the most efficient techniques to functionalize, to deposit on, or to coat each individual particle of a powder.
- From gaseous species. It combines two processes. One is the deposition itself, the other aims in suspending the particles in the deposition zone, most often by flowing gas upwards through the powder.
- It is generally transport limited. Eg. Coatings of titania.

d) Electrostatic fluidized bed coating^[43, 44]

In such systems, the powder material which is essentially 100% solids is kept fluidized in a bed by dry air passing through a porous base plate. The powder particles are charged either by means of an electrode in the fluid bed beneath the surface of the fluidizing powder or by charge transfer from the pre-ionized air. The fluidizing effect plus the charge repulsion effect of the powder particles result in an upward motion of the particles to form a cloud above the

bed. An elongated substrate or any other object passing axially across or vertically through the bed and through the powder cloud becomes deposited with a layer of the powder material. Electrostatically assisted fluidized bed coating does not dip the part into the powder; it generates a cloud of charged particles (much like a conventional electrostatic gun) through which a heated or an unheated part passes. It generally applies a thin coat vs. the thicker coat from fluidized bed coating.

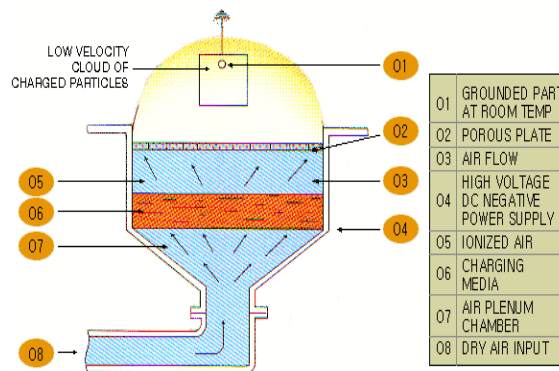


Figure 7: Electrostatic Fluidized bed coater

e) Rotating (Centrifugal) fluidized bed granulator/coater^[2]

It consists of a chamber and a porous cylindrical air distributor made of stainless sintered mesh. The horizontal cylinder (air distributor) rotates around its axis of symmetry inside the chamber. There is a stationary concentric cylindrical metal filter inside the air distributor to retain any elutriated fine powder. A binary spray nozzle mounted on the metal filter sprays mist of coating material into the powder bed. A pulse air-jet nozzle is also placed inside the

metal filter, which cleans the surface of the metal filter in order to prevent it from clogging. An air knocker is installed outside the chamber to prevent powder adhesion onto the air distributor mesh and the front cover. In a rotating fluidized bed, powder samples are introduced inside the air distributor and are forced to the wall by centrifugal force due to the rotation of the distributor. Air flows radially inward through the air distributor, and the forces on the powder are balanced by the airflow (drag force and buoyancy) and the centrifugal force.

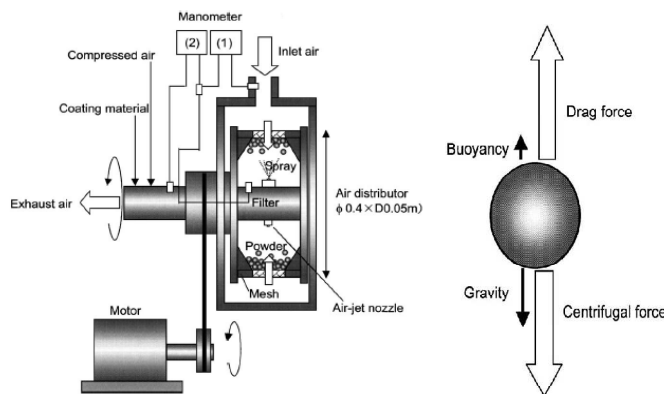


Figure 8: Rotating fluidized bed coater cum granulator^[2]

f) Magnetically assisted impaction coating (MAIC, pronounced “mace”)^[1, 45, 46]

It is also called as soft coating technique developed by Aveka a US based company. Soft coating methods that can attach the guest particles onto the host particles with a minimum degradation of particle size, shape and composition caused by the buildup of heat, are the better candidates for such applications. MAIC coats particles onto particles by a peening process. By adding a small coating particle and a large core particle into an assembly of small oscillating magnets, the small particles are readily coated onto the core particles. Using this process, the core particle

as small as 0.25 microns can also be coated. Materials that have been used in this process include glasses, pigments, metals, metal oxides, polymers, organic and inorganic powders. One of its major advantages is Shorter processing time and lower energy demand. The limitation of batch type processing can be overcome by the use of a continuous type MAIC device reported by Kooyer and Hendrickson (WO9707900). This device is capable of separating coated substrate from the magnetic elements during continuous operation. The Aveka MAIC continuous process is a patented process to coat small dry particles on large dry particles.

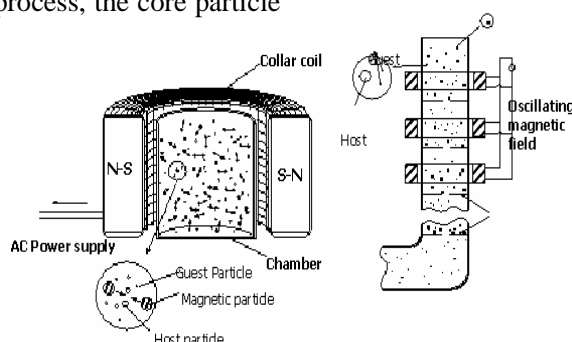


Figure 9: Schematic of the MAIC process^[1]

a) Hybridizer^[1]

The hybridizer consists of a very high-speed rotating rotor with six blades, a stator and a powder re-circulation circuit made with ceramic or stainless steel. The powder (host and guest particles) placed in the processing part of the vessel is subjected to high impaction and dispersion due to the high rotating speed of the rotor. The particles undergo many collisions, and this allows for break-up of fine agglomerates and powder coating due to the embedding or filming of the guest particles onto the surface of the host particles.

Advantages

- Very short processing times are required to achieve coating.
- The device consists of a re-circulating unit that continuously moves the particles in and out of the processing vessel and against the blades of the rotor.
- There is a temperature build-up due to the high impaction forces caused by the high rotation speeds, which aids in coating the guest particles onto the surface of the host particles.

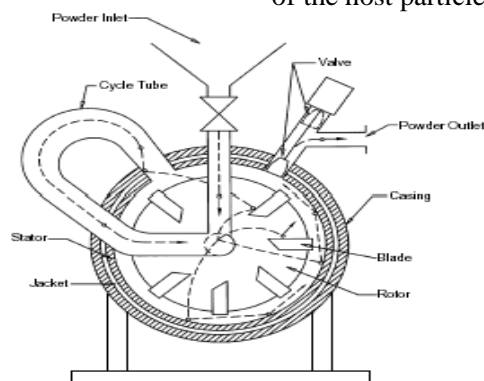


Figure 10: Schematic of hybridizer^[1]

h) Theta Composer^[1]

The theta composer consists of a slow rotating elliptical vessel (around 30 rpm) and a faster (500–3000 rpm) elliptical rotor. As the rotor rotates anticlockwise (900–1200 rpm) inside the vessel (it rotates between 30–40 rpm, clockwise), the powder mixture consisting of host and guest particles is subjected to shear and compressive stresses as it is forced into the small clearance between the vessel and the rotor. As the rotor continues to move and the clearance between the vessel wall and the rotor becomes large, there is bulk mixing of the host and guest particles. The total blending of the particles will be done in the low-

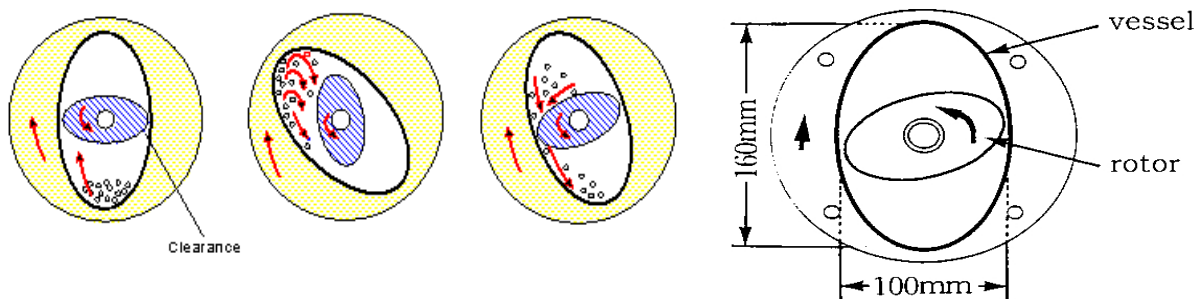


Figure 11: Schematic of theta composer

speed rotation oval shaped container and the high-speed oval shaped rotor rotating at the centre, each rotates in the opposite directions. At the same time, as the strong compression and shearing forces are repeatedly added to the materials, precise blending and composite fabrication are accelerated.

- **Slow revolution of outside vessel:** Promotion of favourable bulk mixing.
- **High speed rotation of inside rotor:** high shear stress required for coating and
- **Elliptical Shape:** Stress & relaxation

Features^[49]

- Rotation of the vessel assists to create the totally homogenous powder composites without any thermal deterioration.
- Instant compression and shearing to the particles minimize the temperature rise of the materials.
- Simple structure and easy for operation and maintenance with short processing time.
- Suitable rotating conditions for the materials can be selected as required.
- Suppress hygroscopicity
- Improve handling and Increase flowability

i) Mechanofusion^[1]

It is specifically designed for particle to particle fusion at high shear and compressive force which also results in control particle shape. It can't be used for continuous production since it is batch operated device. The device contains a rotating outer vessel, a stationary inner piece and a stationary scraper as its cardinal parts. By generating a

mechanical-chemical reaction between two or more materials, a new material with different properties is created. A measured amount of host and guest particles is placed into the rotating vessel. As the vessel rotates at speeds between 200 and 1600 rpm, the powder is forced outward towards the walls of the vessel. The gap between the inner piece and the rotating drum is controlled, and as a result, the particles passing through the gap are subjected to intense shearing and compressive forces. These forces generate sufficient heat energy to fuse the guest particles onto the surface of the host particles. The gap size between the inner piece and the walls of the vessel is very important in order to control the thickness of coating. The gap between the scraper and the wall of the vessel is also controlled.

Features / Benefits

- Produce composite particles, control particle shapes.
- Eliminates the need for pre-mixing particles during particle performance improvement processes.

- Water cooled jacket to control product temperature.
- Compact design
- Local temperature build-up due to these strong forces acting on the particles, which can result in the fusion of the surface of the host and guest particles
- Ultimately it enhances and eases the coating process.

j) Spheroidization

Meltable materials are utilized for coating in such processes with a Core Up to 0.5 mm in diameter. It is more suitable for smooth continuous coating with improved flow properties. The particles are rapidly passed through an intensely heated area; the outside material melts, flows, and, as it cools, forms a smooth surface. If there are small meltable particles on the outside of the core material, these will melt and flow to provide a better coating. If the core is thermoplastic, it softens and allows the coating particles to become more strongly adhered.

k) Particle coating via atomic layer deposition ^[50, 51]

Atomic layer deposition (ALD) is similar to chemical vapor deposition (CVD) both of which utilized gaseous reagents in order to nurture a film. In ALD, we split the CVD reaction into two surface half reactions means it exposes the surface to one reagent at a time. By splitting the reaction up into two steps, the surface will react with each reagent in sequence only until the surface is completely coated with a new atomic layer. The process, depicted in Figure 14, starts with an A reactant reacting with functional surface groups on the particle. New functional groups are now in place and the surface is exposed to the B reactant that reacts with the new groups. Again, the reaction is self-limiting and reaction stops when all of the sites have been converted back to the original surface species. At this point, the process can be repeated sequentially until the desired film thickness is achieved. Each monolayer (one complete AB cycle) will result in a film thickness on the order of 1 angstrom (0.1 nanometers).

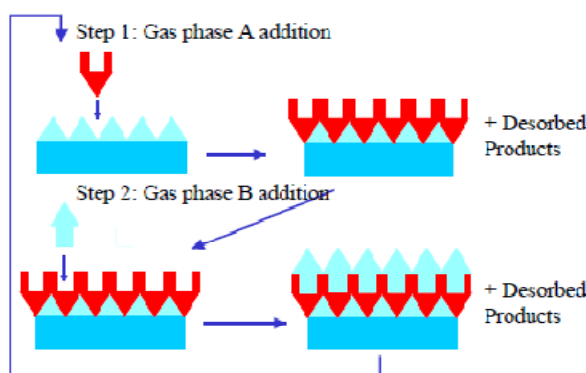


Figure 12: Schematic of the ALD process

3. Conclusion

Here in this review both wet and dry particle coating techniques are highlighted with modification in respective fields. Particle engineering is now become essential so as to improve flow properties as well as compaction. Particle coating is also very useful to separate incompatibilities as well as for taste masking.

4. References

[1] Pfeffer R, Dave R. Synthesis of engineered particulates with tailored properties using dry particle coating. Powder

Technology 2001;117:40–67.

[2] Watano S, Nakamura H, Hamada N, et al. Fine particle coating by a novel rotating fluidized bed coater. Powder Technology 2004;141:172– 6.

[3] Banker GS. Film coating theory and practice. J Pharm Sci 1966;55:81–9.

[4] Pickard JF, Rees JE. Modern trends in pharmaceutical coating. Pharm Ind 1972; 34:833–9.

[5] Lachman L, Liberman H, Kanig J. The Theory and Practice of Industrial Pharmacy. Third Edition ed: varghees publisher; 2010.

- [6] Wurster DE. Winstonsin. In: Foundation) AR, editor. Winstonsin (Alumini Research Foundation)1953.
- [7] Berienger P, Gupta P. Remington Pharmaceutical Sciences. 21st ed: Lipincott williumms & wilkins; 1990.
- [8] Cole G. Pharmaceutical Coating Technology. 3rd ed. london: Tayler and Francies; 2001.
- [9] Mawatari Y, Koide T, Tatemoto Y. Liquid coating. Adv Powder Technol 2001; 12:157.
- [10] Farid DJ. Dissolution of compacted aspirin microcapsules. Indian Journal of Pharmaceutical Sciences 1991;5:222-3.
- [11] Kramer PA. Albumin microspheres as vehicles for achieving specificity in drug delivery. Journal of Pharmaceutical Sciences 1974;63:1646-7.
- [12] Sachan NK, Singh B, Rao R. Controlled drug delivery through microencapsulation. Malesian journal of Pharmaceutical sciences 2006;4:65-81.
- [13] Arshady R. Microspheres and microcapsules, a survey of manufacturing techniques: part III: Solvent evaporation. Polymer Engineering Science 1990;30:915-24.
- [14] Lachman L, Liberman HA. Microencapsulation. In: Lachman L, editor. The theory and practice of industrial pharmacy. bombay: varghese publication; 2008. p. 412-33.
- [15] Green BK. Coacervation. 1955. p. 1-7.
- [16] Green BK, Schleicher L. Coacervation phase sepration. 1956.
- [17] Feld K M, LI SP, Kowarski CR. Recent advances in microencapsulation technology and equipment. Drug Development and Industrial Pharmacy 1988;14:353-76.
- [18] Donbrow M. Recent advances in microcapsule delivery systems. Topics in Pharmaceutical Sciences,BREIMER. Amsterdam: Elsevier Science Publishers B.V.; 1987. p. 33-45.
- [19] Scott MW, Robinson MJ, Paul VF. spray drying and cingealing. J Pharm Sci 1964;53:670.
- [20] Cole GC. Introduction and overview of pharmaceutical coating. Pharmaceutical coating technology 1995;110:1-5.
- [21] Battista JV, Wuster DE. Fluidized bed powder handling & coating. 1967.
- [22] Wurster DE, Lindlof JA. wuster process. 1966.
- [23] Vinesia.com. Pharmaceutical coating. In: vinesia.com, editor. Formulation2010.
- [24] Saihi D, Vroman I, Giraud S. Microencapsulation of ammonium phosphate with a polyurethane shell. Part II. Interfacial polymerization technique. Reactive and Functional Polymers 2006; 66:1118-25.
- [25] Sun Q, Deng Y. In Situ Synthesis of Temperature-Sensitive Hollow Microspheres via Interfacial Polymerization. J Am Chem Soc 2005;127:8274-5.
- [26] Seok SI. Core/shell silica-based in-situ microencapsulation: A self-templating method Chem Commun 2006:189-90.
- [27] Jang IB, Sung JH. Synthesis of microcapsule containing oil phase via in-situ polymerization. Journal of Materials Science 2005;40:1031-3.
- [28] Brown EN. In situ poly(urea-formaldehyde) microencapsulation of dicyclopentadiene. Journal of Microencapsulation 2003;20:719-30.
- [29] Xie XL. Effect of talc/MMA in situ polymerization on mechanical properties of PVC-matrix composites. Journal of Applied Polymer Science 2001; 80:2105-12.
- [30] Ming L, Poncelet D. Microencapsulation by solvent evaporation: State of the art for process engineering approaches. International Journal of Pharmaceutics 2008;363:26-39.
- [31] Re MI. Microencapsulation by spray drying. Drying Technology: An International Journal 1998;16:1195-236.
- [32] Sheu TY. Microencapsulation by Spray Drying Ethyl Caprylate in Whey Protein and Carbohydrate Wall Systems. Journal of Food Science 1995; 60:98-103.

- [33] Desai KH. Recent Developments in Microencapsulation of Food Ingredients. *Drying Technology* 2005;23:1361–94.
- [34] Dave R, Banerjee A. Dry particle coating for improving the flowability of cohesive powders. *Powder Technology* 2005;158: 21–33.
- [35] Epstein N, Grace JR. *Handbook of powder science and technology*. New York: Van Nostrand Reinhold Company; 1997. p. 509-536.
- [36] Kennedy JP, Niebergall PJ. Development and optimization of a solid dispersion hot-melt fluid bed coating method. *Pharm. Dev. Technol.* 1996 apr;1(1):51-62.
- [37] Faham A, Prinderre P, Farah N, Eichler KD, Kalantzis G, Joachim J. Hot-melt coating technology I: Influence of Compritol 888 ATO and granule size on theophylline release. *Drug Dev. Ind. Pharm.* 2000a;26:167-176.
- [38] Benameur H, Barthelemy P. Method for coating solid particles with a thermofusible agent and resulting coated solid particles. European patent, EP1301176 B1; 2004:1–20.
- [39] Le H, Le H. Preparing a sustain release dosage form of nifedipine by hot-melt coating method. *AAPS Pharm. Sci. Tech.* 2007;9(S2):Article -002651.
- [40] Kennedy JP, Niebergall PJ. Development and optimization of a solid dispersion hot-melt fluid bed coating method. *Pharm Dev Technol* 1996 1:51-62.
- [41] Perutt M, Jung J. Particle design using supercritical fluids: Literature and patent survey. *The Journal of Supercritical Fluids* 2001;20:179–219.
- [42] Mortan D, David H, Bay K, Potter E. Vapour coating of powders. USP 4440800 1984.
- [43] Richard DS. method of powder coating with electrostatic fluidized bed. 1987. p. 1-7.
- [44] Beriatta M. Influence of process parameters in electrostatic fluidized bed coating. *Surface and Coatings Technology* 2006; 200:4619–29.
- [45] Singh R, Ata A, Fitz-Gerald J. *Surf. Modif. Technol. 10th International Proceedings on Surface Modification Technologies*, 1997.
- [46] Ferguson, J.D., A.W. Weimer, and S.M. George, Atomic layer deposition of ultrathin and conformal Al₂O₃ films on BN particles. *Thin Solid Films*, 2000. 371(1-2): p. 95-104.
- [47] Ritali, M. and M. Leskela, *Atomic Layer Deposition. Handbook of Thin Film Materials*, ed. H. Nalwa. Vol. 1. 2001, San Diego: Academic Press.

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