Solvantless coating for Tablets: An alternative to conventional coating technique

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ABSTRACT

There are many ways to coat tablets. Coatings are a very important part in the formulation of pharmaceutical dosage form to achieve excellent formulation quality (e.g., color, texture, mouth feel, and taste masking), physical and chemical protection for the drugs in the dosage forms, and modification of drug release characteristics. Most film coatings are applied as aqueous or organic-based polymer solutions. Such film coating brings their own disadvantages. Solventless coatings are alternative technique of coating. Solventless coating technologies can overcome many of the disadvantages associated with the use of solvents (e.g., solvent exposure, solvent disposal, and residual solvent in product) in pharmaceutical coating. Solventless processing reduces the overall cost by eliminating the tedious and expensive processes of solvent disposal/treatment. In addition, it can significantly reduce the processing time due to reduction of step of drying/evaporation. These environment-friendly processes are performed without any heat in most cases (except hot-melt coating) and thus can provide an alternative technology to coat temperature-sensitive drugs. This review includes various solventless coating methods like magnetic assisted impaction coating, hot-melt coating, supercritical fluid spray coating, electrostatic coating, dry powder coating, and photocurable coating that can be used to coat the pharmaceutical dosage forms.

Introduction

Pharmaceutical solid dosage forms such as tablet, pellets, pills, beads, spherules are coated for different reasons such as aesthetic property, to enhance drug stability (from light, moisture, oxygen), to separate reactive components in formula, modified drug release, identification, prevention from gastric acid and enzyme, improved mechanical strength [1]. Film coating can be carried out using either an organic solvent or water [2]. The liquid coating technology can obtain extremely uniform smooth, gleaming coating surface. Organic solvents are toxic, flammable, vapor of organic solvent causes environmental pollution and hazard to coating equipment operator, long processing time due to evaporation of solvent, vaporization of organic solvents is energy consumptive, high cost of solvent, strict environmental regulation placed on use of organic solvent [3]. USFDA, Environmental Protection Agency and Occupational Safety and Health administration (OSHA) have strict requirement regarding use of solvent in pharmaceutical industry [4]. Thus, aqueous based coating is increasingly used compared to organic based coating. However aqueous based coating also having following drawbacks:

- Degradation of certain drugs due to use of heat and water.
- Validation of coating dispersion for controlling microbial presence.
- High energy consumption and long processing time

In order to overcome the drawbacks of liquid coating technology, solventless coating has emerged. Solventless coating eliminates many problems associated with the use of solvent i.e., residual solvent, solvent exposure, solvent disposal in coating. As there is no use of solvent, it eliminates the solvent evaporation step and
thus reduces the processing time also solventless coating reduces overall cost because it eliminates the tedious and costly process of solvent disposal and treatment. Solventless coating can be applied to thermosensitive drugs except hot melt coating[5]. It can obtain much thicker coat than conventional liquid coating and Process can be recycled. The main aim of this review is to discuss mechanism, current status and future development of the solventless coating techniques such as powder coating, hot melt coating, photocurable coating, magnetically assisted impaction coating, supercritical fluid coating, Plasma enhanced chemical vapor deposition. Solventless coating can be classified as:

Compression Coating

It involves the compaction of granular materials around a preformed tablet core using specially designed tableting equipment. Compression coating is a dry process. Finished product is a tablet within a tablet. Advantages of the method include the capability to physically separate two incompatible drugs within the same dosage form, which is commonly achieved using multilayer tablets or compression coated dosage forms. In addition incompatible ingredients can be conventionally separated by this process.[6] However this process has disadvantages of mechanical complexity and therefore has not proven the preferred method for the tablet coating. The only requirement for producing the compression-coated tablet dosage form is that the core material should possess the ability to flow into a die during production. Microcrystalline cellulose, colloidal silica, mannitol, lactose are some directly compressible excipients. Modified compression coating machine is also available which has specially modified punches to carry out the coating process. At first stage the punches forms the cup of coating material in lower die, then in second stage drug is filled in that cup with compression using another modified punch and finally coating material compressed on the top to cap the drug filled cup [7,8].

Figure 1: Compression coated tablet

Magnetically Assisted Impaction Coating (MAIC)

Several dry coating methods have been developed such as compression coating, plasticizer dry coating, heat dry coating and electrostatic dry coating [9]. These methods generally allow for the application of high shearing stresses or high impaction forces or exposure to higher temperature to achieve coating. The strong mechanical forces and the accompanying heat generated can cause layering and even embedding of the guest particles onto the surface of the host particles. Many food and pharmaceutical ingredients, being organic and relatively soft, are very sensitive to heat and can quite easily be deformed by several mechanical forces. Hence, soft coating methods that can attach the guest (coating material) particles on to the host (material to be coated) particles with a minimum degradation of particle size, shape and composition caused by the build up of heat are the better candidates for such applications. The magnetically assisted impaction coating (MAIC) devices can coat soft organic host and guest particles without causing major changes in the material shape and size. Although there is some heat generated on a micro scale due to the collisions of particles during MAIC, it is negligible. This is an added advantage when dealing with temperature sensitive powders such as pharmaceuticals.

Figure 2: Compression coating Process

Mechanism of coating in the MAIC process is
(a) Excitation of magnetic particle,
(b) De-agglomeration of guest particles,
(c) Shearing and spreading of guest particles on the surface of the host particles,
(d) Magnetic-host-host particle interaction,
(e) Magnetic–host–wall interaction and
(f) Formation of coated products.

Apparatus for MAIC

Apparatus for MAIC consist of processing vessel surrounded by the series of electromagnets connected to the alternating current .The host and guest materials are placed in the vessel along with the measured mass of the magnetic particles. The magnetic particles are made of barium ferrite and coated with polyurethane to prevent contamination of the coated particles. When a magnetic field is present the magnetic particles are agitated and move furiously inside the vessel, resembling a fluidized bed system. These agitated magnetic particles then impart energy to the host and guest particles, causing collisions and allowing coating to be achieved by means of impaction or peening of the guest particles onto the host particles .The magnetic particle motion studies
suggests that the primary motion due to the magnetic field is the spinning of the magnetic particles, promoting deagglomeration of the guest particles as well as the spreading and shearing of the guest particles onto the surface of the host particles. However, the effect of the translational speed is also significant as it allows for the impaction of one particle onto another, promoting coating[10].

Figure 3: Experimental setup of MAIC

**Hot melt coating**

In hot melt coating method, the coating material is applied in its molten state on the substrate then solidified by cooling. Hence, the necessity of the application of any solvent is fully eliminated. The choice of the coating excipients depends primarily on its function (e.g., retarding the drug-release rate, preventing environmental degradation and masking unpalatable taste) in the dosage form. Lipid, waxes, fatty bases and hydrogenated vegetable oils are the most suitable coating material in hot melt coating. It offers several benefits and potential for a wide variety of application in pharmaceutical formulation like tablets and pellets. During the hot melt coating method, the required weight gain with lipid materials are less than those commonly employed with polymers to achieve the same effect. As the lipid based coatings are less expensive and processing time is short, hot melt coating is also cost effective [25]. A difficulty in hot melt coating is maintaining adequate operational safety, as high temperatures, close to 200°C, are employed. The choice of coating excipients depends primarily on its “functional” (such as retardation drug release rate, prevention of environmental degradation, and masking of unpleasant taste) in the dosage form. For sustain release applications, coating excipients of special interest can be divided broadly as natural and synthetic waxes, hydrogenated vegetable waxes, polyglycolysed glycerides. Examples of some marketed hot melt coating excipients are Gelucires, Precirol, Stearines, Myvaplex, Compriot 888ATO [11-14]. The various technologies of hot melt coatings are:

1. Fluidized bed coating (top spray and bottom spray),
2. Spray congealing/coating,
3. Pan coating (pan spray and pan pour).

**Fluidized bed coating**

Fluidized bed coating method proved capable of coating nonpareils from 10 to 35 mesh [0.500 to 2.00 mm) and tablets up to 1 g. Spray coating/congealing, whereby slurry of molten matrix material and substrate is sprayed through into a cooling chamber, where the droplets solidify rapidly. Atomization methods for spray coating are Ultrasonic atomization, Hydraulic (airless) atomization, and Pneumatic atomization [30]. Third approach is pan coating; conventional pan coater can be used for the hot melt coating. Only the difference is that the coating agent is in molten state instead of solution state. There are two types of pan coating processes, one is pan pour another is pan spray. It was observed that the pan spray coating technique is the best technique to control the release due to uniform film formation, while pan pour technique shows variation in the release of drug from the same batch this was due to non-uniform coating and very low coating efficiency [15].
Table 1: Hot Melting Coating Lipid Exipients

<table>
<thead>
<tr>
<th>S.No</th>
<th>Characteristic</th>
<th>Method/Equipment</th>
<th>Information</th>
<th>Impact on hot melting coating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Melting</td>
<td>Differential scanning colorimetry (DSC)</td>
<td>Stability at high temperature, Narrow melting Range</td>
<td>Melting Temperature Setting Process temperature for coating Agent</td>
</tr>
<tr>
<td>2</td>
<td>Crystalization</td>
<td>Differential scanning colorimetry (DSC)</td>
<td>Crystalization temperature</td>
<td>Setting product temperature in the fluid Bed</td>
</tr>
<tr>
<td>3</td>
<td>Viscosity</td>
<td>Rehometer</td>
<td>Viscosity as a function of temperature</td>
<td>Setting Process temperature for coating Agent/Viscosity &lt; 300 mPas</td>
</tr>
<tr>
<td>4</td>
<td>Wettability</td>
<td>Goniometer/onlipid exipients films</td>
<td>Hydrophobicity of the lipid coating</td>
<td>Selection of material depending on the drug release required</td>
</tr>
<tr>
<td>5</td>
<td>Concentration of crystallization</td>
<td>Dilatometer</td>
<td>Reduction of volume upon cooling formation of the cracks</td>
<td>Selection of the material uniformity of the lipid coating Steeting of the crystallization parameter for lipid coating</td>
</tr>
<tr>
<td>6</td>
<td>Water sorption</td>
<td>Dynamic vapour Sorption (DVS)/on lipid exipients</td>
<td>Protection of coating material versus Water</td>
<td>Selection of material for protective coat</td>
</tr>
<tr>
<td>7</td>
<td>Digestibility</td>
<td>In vitro digestion (pH-state apparatus)</td>
<td>Degradation of the coating by digestive lipase in the gastrointestinal tract</td>
<td>Selection of the material depending on the drug release required</td>
</tr>
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</table>

Hot-melt coating offers many advantages in comparison to conventional coating techniques. Principally the technique does not require the use of solvents (aqueous or organic) and consequently: (i) cost intensive solvent treatment can be avoided; (ii) processing times reduced (as hot-melt coating allows higher and uniform application rates of coating agent and there is no solvent to evaporate); and (iii) the risk of microbial contamination is reduced due to a water-free process. Furthermore, this technique works with conventional coating systems such as fluid bed coaters that can be modified for this approach.

**Supercritical fluid spray coating**

The supercritical fluid spray coating process consists of dissolving the coating material or drug in supercritical carbon dioxide, and gradually reducing the solvent power of carbon dioxide to enable the coating material to precipitate onto drug particles dispersed in the medium. Although this process is technically a solvent-based coating process, the use of carbon dioxide as the supercritical fluid avoids some of the challenges associated with traditional solvent-based processes. In the absence of co-solvents, the coating materials used in supercritical fluid coating are limited mainly to lipids (fats and waxes) [16].

Microencapsulation using supercritical fluid technology combines a liquid-like density and solvating power with gas-like transport properties (like viscosity, diffusivity). Carbon dioxide is the most widely used supercritical fluid because of its relatively low critical temperature (31°C) and pressure (74 bar). The use of supercritical fluid technology, especially CO₂ for encapsulation purposes is mainly due to the mild processing

Condition, allowing microencapsulation of sensitive ingredients for cosmetics, pharmaceuticals [17].

Supercritical fluids are especially suitable for particle formation, as they display a large change in density near the critical point which enables their solvating power to be carefully controlled by small changes in temperature or pressure. The coating material must have sufficient solubility in liquid or that a coating of sufficient thickness to provide the desired level of protection is formed when conditions inside the autoclave are adjusted to insolubilize the coating material. Ideally, deposition should occur as a defect-free film or coating [18].

5. Electrostatic dry coating: The electrostatic coating process is very useful in paint technology, food technology, metal coatings, finishing industry and coating of living cells. It is also useful in the coating of tablets as well as capsules. The principle of electrostatic powder coating involves spraying of a mixture of finely grounded particles and polymers onto a substrate surface without using any solvent and then heating the substrate for curing on oven until the powder mixture is fused into film. There are two types of spraying units, according to the charging mechanism a) corona charging and b) tribocharging.[19-21]

Mechanism of Corona charging

This is done Characterized by the electrical breakdown and then ionization of air by imposing high voltage on a sharp pointed needle like electrode (i.e. charging pin) at the outlet of the gun. The powder particles pick up the negative ions on their way from the gun to the substrate. The movement of particles between the charging gun and the substrate is mainly governed by the combination of electrical and mechanical forces. The mechanical forces produced by the air blows the powder towards the substrate from the spray gun. For the corona charging, the electrical forces are derived from the electrical field between the charging tip of the spray gun and the earthen substance, and from the repulsive forces between the charged particles. The electrical field can be adjusted to direct the powder's flow, control pattern size, shape, and powder density as it is released from the gun[22].

Mechanism of tribo charging

Unlike corona charging guns, the tribo charging makes the use of the principle of friction charging associated with the dielectric properties of solid materials and therefore no free ions and electrical field will be present between the spray gun the grounded substance. For tribo charging guns, the electrical forces are only regarded to the repulsive forces between the charge particles. After spraying when charged particles move into the space adjacent to the substrate, the attraction forces between the charged particles and the grounded substrate makes the particle to deposit on the substrate. Charged particles are uniformly sprayed onto the earthen substrate in virtue of mechanical forces and electrostatic attraction. Particles accumulate on the substrate before the repulsion force of the deposited particles against the coming particles increase and exceeds the electrostatic attraction. Finally once the said repulsion becomes equivalent to the said attraction, particles cannot adhere to the substrate any more, and the coating thickness does not increase anymore[23].

Dry Powder coating

From a mechanistic perspective, dry powder coating processes consist of the same sequence of steps that are employed with conventional solvent based coatings. In all cases the process begins with the pretreatment of coating material. This is followed by the application of coating material to the substrate, relying on the adhesive nature of the formulation to maintain uniformity of coating during the film formation process. Film formation occurs by a process of evaporation, coalescence and sintering which are influenced by process and formulation considerations. As the amount of volatile solvent used approaches zero the evaporation process may be neglected, as is the case for many dry powder applications. Pre-treatment of the coating material varies greatly based on the type of coating process utilized. For dry powder coating applications, careful consideration of material particle size will be essential to
ensure appropriate uniformity for the coating. It is generally recommended that coating material diameter be less than 1% the size of the coating substrate. This allows for acceptable uniformity of the material on the substrate surface, improving adhesion, appearance and processing times. During the dry powder coating process, the substrates are often heated above the glass transition temperature of the layering materials so that the coating materials soften and adhere to the substrate. For conventional film coating, spreading and adherence is well defined based on surface free energies and capillary forces where mobility is not a limiting interaction. Dry powder coating applications also rely on mechanical compaction that occurs naturally during the process to facilitate adhesion and coalescence. During this process stresses on the coating layer result in consolidation of the bed and deformation driven spreading across the interface. When coatings exhibit plastic behavior, the deformation is irreversible and the mechanical compaction leads to greater adhesion of the surface layer due to a larger surface area for contact between substrate and coating, as well as possible mechanical interlocking of the materials. Adhesion and spreading behavior can also be modified through the application of a sub-coat to the substrate. This allows for a change of interfacial energy by the application of a new material that can facilitate adhesion of powder coat. The subcoating layer corresponding to 2–3% weight gain of the uncoated core has been reported. Low melting point, hydrophilic polymers (polyethylene glycol 3350) have been extensively used in the literature, however, other materials, with amphiphilic amphiphilic and hydrophilic properties have also been reported. To further promote adhesion with the coating layer, the subcoat can actually be intentionally selected to be partially molten at the processing temperatures. The molten priming layer promotes the adhesion of the powder coating particles by forming liquid bridges with the tablet surface. The interfacial interactions between the tablet surface and the polymeric particle are rather complex and depend on interfacial tension, wetting and adhesion. Since the spreading of the priming layer on the surface of the coating cores is crucial, the best subcoating material is selected by measuring the contact angle with water of the tablet surface and those of the primer and of the polymeric material to be layered. The closer the contact angle values, the more efficient will be the adhesion of the powder to the surface. The mechanism of film formation of the powders layered onto the solid cores can be summarized by (i) coalescence and sintering of the particles of the polymeric materials in a process that involves the partial fusion of the polymer; (ii) leveling of the coating material includes densification of the layer with reduction of the empty spaces and smoothing of the surface; (iii) cooling of the layer and hardening of the coating. A schematic of this process is shown in Fig. 5.

![Figure 5: Schematic of film formation in dry powder coating systems.](image)

The melt viscosity-temperature relationship can be described by the Arrhenius equation, presented in equation below:

\[ t = \frac{kR}{\nu} \]  

where \( k \) is a constant, \( E \) is the activation energy for viscous flow, \( R \) is the universal gas constant and \( T \) is the absolute temperature. Since viscosity decreases when temperature increases, higher processing and curing
temperatures can be used to produce a higher quality film, even if degradation phenomena may also be accelerated:

$$\mu = Ae^{E/RT}$$  
Arrhenius equation describing polymer viscosity as a function of temperature

### Photo Curable Coating

Unlike other solventless coating techniques that rely on changes in the physical state of the coating material to obtain a coating, photocuring is a chemical approach proposed to rapidly coat tablets at or below room temperature with an extremely rapid rate [23-24]. Photocuring systems generally consist of 4 major components:

- Specially functionalized liquid pre-polymers or monomers
- An initiator.
- UV/visible light source,
- Pore forming agents.

It is common to define photocuring as a process of rapid conversion of specially formulated (usually liquid) solventless compositions into solid films by irradiation with ultraviolet or visible light. A large proportion of the curing reactions described above are carried out with light in the ultraviolet region. This is due to the fact that ultraviolet light is more energetic and, therefore, more efficient in rupturing chemical bonds. On the other hand, the use of visible light has many attractions, such as safety and ease of handling. So, lately, curing with visible light is receiving attention as well.[26-27]

Photocuring can be divided into two groups, those that cure by free-radical mechanism and those that cure by an ionic mechanism viz. cationic (mostly), anionic mechanism. There are also some compositions that cure simultaneously by both mechanisms.

#### 7.1 Pre-polymer or monomer: They should be stable to UV exposure during the entire coating process. They should be able to polymerize by UV-curing process while maintaining acceptable film firmness, integrity and stability. They should be in the liquid state so that they can be easily spread on the tablets, granules.

Two major classes of photocurable siloxanes are acrylic acid derivatives and enethiols. Most important resins and reactive diluents used in photocurable coatings are epoxy acrylate, polyester acrylate, polyurethane acrylate, hexanediol diacrylate, unsaturated polyester, trimethylolpropane triacrylate, tripropylene glycol diacrylate. Co-polymerizable liquids with relatively low viscosity are used as reactive diluents. Photo curable polydimethylsiloxane is widely used as a photocuring material due to its good thermal stability and extraordinary flexibility in addition; photo curable siloxanes are used in transdermal drug delivery systems, composite dental fillings and other medical products [28-31].

Acrylic siloxanes are prone to inhibition by oxygen and moisture present in the atmosphere hence system needs to purge with nitrogen. However, ene-thiol systems are not affected by either oxygen or moisture. This characteristic allows the use of such photocurables in open systems such as pan coaters. In addition, it was previously shown that the ene-thiol system cures faster and more completely than acrylate siloxanes.[32]

#### 7.2 Photo initiators or catalysts: Photo initiators start a reaction which results in the formation of a solid coating. Their reaction products add to the unsaturated components and become a part of the polymer layer. They are generally stable against temperature increase. Such formulations are applied as a layer, under normal room light conditions and they cure only when exposed to intensive UV light. Most of the photo initiators contain a benzoyl group, which is mainly responsible for the absorption of the energy from the light. By the absorption of radiation energy formation of a radical pair takes place. During UV curing these radicals add to the double bounds of the unsaturated reaction partner [33-34].

The photochemical formation of a radical pair can be monomolecular reaction or bimolecular reaction. Photoinitiators of the monomolecular type are more effective than bimolecular combinations (for instance benzophenone/amine). Photoinitiators derived from phosphine oxides (mono- and bisacryl phosphine oxides) are of special interest these days. The mechanism of the photochemical curing process can be described in following three steps: Initiation, Propagation, Termination. Examples of monomolecular-type photoinitiators are Benzoin ether, Diethoxy acetophenone, Hydroxyketones, Aminoketones, Bisacryl phosphine oxides, etc.

**UV/Vis light source**

An often-used lamp type is the 80 W/cm medium-pressure mercury lamp, which emits a broad spectrum in the short wavelength range from 200 to 320 nm but also at discrete wavelength numbers of 360, 410, and 430 nm.

**Pore forming agents**

The initial study performed by Wang and Bonger, where UV light was used to cure derivatized silicon polymer films on non-pareil beads in small-scale coating equipments, but film formed by this method is complete and almost perfect barrier to drug diffusion, such drug release depend on defects or weak points in the coating. Therefore they found need to incorporate pore forming agents in the polymeric film to prepare functional coatings (e.g. Immediate, sustained, or delayed release). Example
of pore forming agents are Lactose, sodium chloride, Explotab, Ac-Di-Sol, PEG 800, etc.

Mechanism

Light generates a polymerization reaction that involves free radical, cationic, or anionic mechanisms, depending on the functional groups of the prepolymer or monomers and the initiators or catalyst used.[35] Chemical reaction of the functionalized liquid prepolymer or monomers results in transition from liquid to solid film. Oxygen can slow down and/or reduce the extent of curing in some acrylate-functionalized silicone systems by quenching excited states and scavenging free radicals from the initiator and the growing polymer network. Thus, photocurable systems are usually purged with nitrogen to reduce this complication. Photocuring is a common solvent-free technique used in the paint, adhesive, and photo-imaging industries. Although photo curing is used widely in the medical, dental, and chemical industries, it has few, if any, commercial applications in pharmaceutical manufacturing.

Composite dental fillings, preventive treatment for caries, Assembly of medical devices, Wound dressing. This is used to form films of varnishes, paints, and coatings for paper, plastic, wood, metal surfaces. Utilized in dental restorative fillers and in preparations of some contact lenses. Functional pharmaceutical coatings (eg, immediate, sustained, or enteric coatings) composed of powdered pore-forming agents (superdisintegrants or simple pore formers) added to an acrylate silicone matrix. That study evaluated different formulation and processing factors to delineate the design space for manufacturability of this solventless coating system. Using a variety of pore-forming materials, it was found that the ratio of the amount of solid pore-forming agent (S) to the volume of liquid prepolymer (L), or the S/L ratio; The particle size of the pore-forming agent; The concentration of the initiator; The light intensity; the exposure time of light; Ratio of solid pore-forming agent (S) to liquid pre-polymer (L) is the most significant parameter which determines the coating efficiency and coating uniformity [35-40].

Conclusion

All the coating methods reported above are solventless coating methods which eliminates or minimizes the various drawbacks associated with the conventional solvent-based coating methods. The conventional pan coater, fluidized bed coater and spray dryer can be used with slight modification for most of the solventless coating methods. But electrostatics coating magnetically assisted coating and supercritical fluid coating needs specialized designed apparatus. Plasticizer dry coating and heat dry coating have to overcome difficulties in obtaining uniform and smooth coating before their commercial application, rest of other methods are able to produce coat with sufficient thickness and smoothness. Electrostatic coating is capable of applying different coating colors on the same formulation. Though these methods have greater advantage over conventional coating methods, before commercialization of these methods further work should be focused on scale-up tests, functional detection of coated solid dosage forms such as drug release profile and clinical tests to make them more useful, economical and safe.

Conflict of interest statement

We declare that we have no conflict of interest.

References


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