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Advancements in Pharmaceutical Film Coating: A Comprehensive Review of Methods, Applications, and Optimization Strategies

Dr. Indira Parab[1], Priya Patwa[2], Deepak Yadav[3], Sujeet Yadav[4]

Ideal Cures Pvt. Ltd., R&D department, Vasai Taluka, Thane, Maharashtra-401208, India
Email: Indira.Parab[at]idealcures.com

Abstract: ***The pharmaceutical industry is continuously innovating, regarding to film coating and other aspects of the industry. Pharmaceutical film coating is regarded as an important component in the manufacture of solid pharmaceutical dosage forms due to its exceptional organoleptic qualities. Additionally, it can change the drug's release characteristics as well as the physical and chemical stability of dosage forms. The process of film coating is technology-driven, and improvements in coating technology, apparatus, analytical methods, and coating materials are essential to the development of coated dosage forms. The proper formation of a film is achieved through the optimization of various process parameters which has been described in the current review. The review offers a concise exploration of film coating, encompassing its application types, methods, and the process parameters that impact them.***

Keywords: Film coating, functional, non-functional, process parameter, advancement

1. Introduction

Oral dosage forms remain one of the most widely used and convenient dosage form. They are multi-component complex systems that can come in a variety of different forms, including powders, granules, compressed tablets, chewable tablets, and capsules [1]. Tablets provide several benefits, including ease of administration, high patient compliance, and cost effectiveness, making them one of the most preferred oral dosage forms. Coating is an important technique in the pharmaceutical manufacturing of tablets that is widely used for practical and aesthetic purposes [2]. Among the three different coating techniques (sugar coating, film coating, and press coating), film coating is the most frequently employed method to address different challenges that arise during the production, transportation, storage, and clinical use of drug products. For example, Film coating can act as a barrier to moisture, oxidation, and light, thereby protecting the core tablets. Additionally, film coating can be used to mask the bitter taste of the API and furthermore, it can control the drug release patterns of tablets in terms of site, rate, and time [3]. As a result, tablet film coating is frequently employed to accomplish a range of pharmacological and therapeutic objectives.

Film Coating is a modern and widely used technology for coating oral solid dosage forms in the pharmaceutical and food sectors. In the process of film coating, solid dosage forms like tablets, capsules, pellets, or granules are coated with a thin, uniform layer of polymer-based solution generally consisting of a polymer, plasticizer, glidant, colourant and solvent as mentioned in table 1. Polymer is the backbone of the coating layer. Polymers used can be cellulose ethers e.g., Hydroxy Propyl Methyl Cellulose (HPMC), Hydroxy Propyl Cellulose (HPC), Ethyl cellulose or Vinyl polymers e.g., polyvinyl pyrrolidone or acrylic acid polymers e.g., Eudragit®, Ecopol® range of polymer. A plasticizer is used to improve the physical property of the polymer and influence film formation e.g., polyols or organic esters. Anti-tacking agent used to avoid tackiness and smooth film formation e.g., talc. Colorants are added to enhance the appearance of the dosage form. Colorants used can be natural based, FD&C or D&C colors. Opacifier is also involved to improve the product appearance and to protect the drug against the light e.g., Titanium dioxide (TiO_2), However, in 2021, the European Food Safety Authority (EFSA) announced that it is carcinogenic and would no longer consider it safe as a food additive. Hence, Calcium carbonate can be used as a replacement of TiO_2.

Table 1: Common components of film coating

Components	Example
Polymer	• Cellulose ethers e.g., Hydroxy Propyl Methyl Cellulose (HPMC), Hydroxy Propyl Cellulose (HPC), Ethyl cellulose • Vinyl Polymers e.g., Polyvinyl pyrrolidone • Acrylic acid polymer e.g., Eudragit, Ecopol grades • Natural based polymer e.g., Sodium alginate, Shellac, Zein
Plasticizer	• Polyols or organic esters e.g., Propylene glycol, Polyethylene glycol (PEG)
Anti-tacking agent	• Talc
Colourants	• FD& C colours e.g., brilliant blue, Allura red, erythrosine • Natural colourants e.g., Carmine, beta-carotene, riboflavin • D&C colours e.g., Yellow No.10, Red No. 27, etc.
Opacifier	• Titanium Dioxide (TiO_2) • Calcium carbonate ($CaCO_3$)
Solvents	• Aqueous e.g., Water • Organic e.g., Isopropyl Alcohol (IPA), Methylene Dichloride (MDC)

The coating solution or suspension is sprayed onto a revolving tablet bed inside a pan and simultaneous drying is carried out by passing hot air through the tablet bed, which allows the solvent to be removed, leaving a thin film on the surface of each tablet core [4]. The film coating process usually occurs in three steps i.e., wetting, spreading and coalescence as shown in the figure 1. The process starts by wetting the tablets with fine droplets of the film coating material followed by the spreading of the coating material on the surface of the of the core and coalescence of each droplet to form a smooth film. Film coating is classified into two types functional and non-functional film coating. Functional film coating is used to modify the release pattern of the tablet that is either immediate release or delayed release or can also be used to protect from moisture in case of moisture sensitive core API or as can be used for taste-masking of the bitter tasting API, whereas, non-functional film coating is important in enhancing patient compliance because it affects the final appearance and organoleptic qualities of the manufactured tablets, which are important parts of the brand image [5,6]. Film coating can be done by three methods i.e., Organic solvent-based film coating, Aqueous film coating and Solvent based film coating which has been covered further in the review. [7]

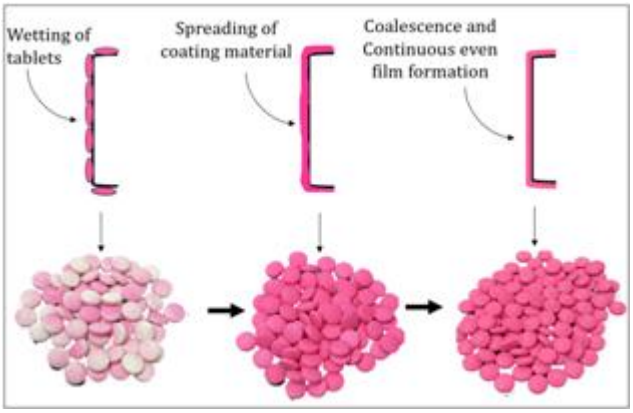

Figure 1: A Coating trial with INSTACOAT 4G demonstrating the mechanism of action of film formation

Film coating is the process of consistently depositing and drying a uniform coating formulation onto the surface of a substrate to generate a uniform film. Thus, process parameter control is critical for a proper tablet coating. A poorly designed film coating method can result in a variety of tablet flaws such as chipping, edge erosion, twinning, colour variation from tablet to tablet, poor solubility, elegance, and product stability [8-10]. In order to establish a robust process, a process optimization study to identify the crucial film coating parameters is essential. The one factor at a time (OFAT) approach was previously used to optimize process parameters, but it was time intensive and less sensitive to parameter interactions. A quality by design (QbD) technique including multivariate analysis can be advantageous because the study can be done by varying numerous elements at the same time. A QbD strategy begins by establishing the target product profile (TPP) based on prior knowledge of formulation and process, followed by identifying critical quality attributes (CQAs) that have a substantial impact on reaching the target profile. The CQAs are often a mixture of formulation-related characteristics such as critical material attributes (CMAs) or critical process parameters (CPPs). Once the CQAs are determined, the manufacturer will be able to establish a design space based on their impact on the target profile. Design space development can assist in understanding the effects of a combination of process factors to get the intended response and implementing a control strategy to monitor the product throughout its life cycle [11,12]. The critical process parameter involved in the film coating are inlet air temperature and bed temperature, spray rate, speed of coating pan, distance of spray gun to bed and atomization of air pressure [13-15].

In this review, we have provided an overview of film coating and the characteristics that govern it, as well as the most technological breakthroughs in the process.

2. Classification of Film coating

Film coating is categorized into functional and non-functional film coatings based on its intended purpose as shown in Figure 2.

2.1 Functional Film coating

As previously stated in this assessment, functional FC is mostly utilized to offer additional value to products. These values may comprise one or more functions such as increasing the product's stability and altering its release pattern to produce drug targeted products.

2.1.1Taste masking

Unpleasant taste is a significant barrier to patient compliance, especially in juvenile and geriatric populations. Thus, masking bitter taste in oral dosage forms is a critical aspect for improving patient compliance and therapeutic efficiency. A variety of approaches have been tried for taste masking, including chemical modification (prodrug approach), salt creation, interaction with ionogenic polymers (methacrylates), complexation, insertion of flavor enhancers (e.g., sweeteners) in the formulation, and surface coating [16]. The most efficient and often used technique for taste masking among them is film coating, which is especially well suited for microencapsulating tiny particles to create taste-masked multi-unit dosage forms [17]. Nishiyama et al. used a combination of water insoluble and soluble polymers (ethylcellulose and hypromellose) to film coat orally disintegrating tablets, to mask the unpleasant taste of lafutidine [18].

2.1.2 Improved drug stability

External environmental elements such as temperature, humidity, and light, as well as excipient and API compatibility, can affect the stability of APIs or medicinal formulations. Moisture can induce drug degradation through hydrolysis and instability. concerns during storage. Moisture-absorbed drug products can expand, split, and dissolve inside the container, causing major changes in product appearance and reducing the drug product's shelf life [19]. Light can also accelerate the oxidation and hydrolysis of APIs. To prevent these external variables from producing API or pharmacological product instability, film coating can be added to the surface of core tablets [20]. Some of the commercially available ready-mix powder for improved

drug stability are INSTACOAT® EMB, INSTAMOISTSHIELD® and INSTAMOISTSHIELD® AQUA II. Tablets containing light-sensitive medicines (such as sorivudine, nifedipine, sulfisomidine, and molsidomine) are photo stabilized using film coating [21].

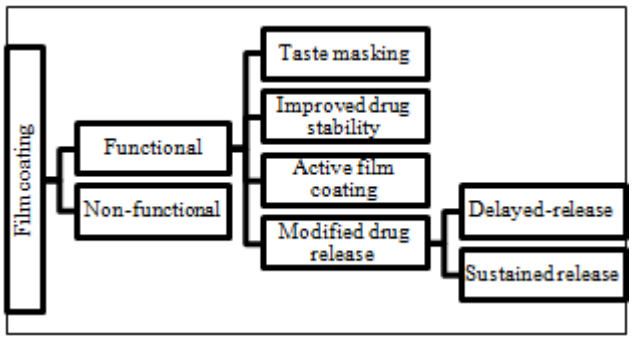

Figure 2: Classification of film coating

2.1.3Active film coating

Active film coating is a method of coating a solid dosage unit (tablet or pellet) with an API-containing solution or suspension. This coating technology addresses formulation which needs quick drug release and better product stability, and it is especially beneficial for generating fixed-dose combination (FDC) products to manage drug release rate or physically restrict interaction between APIs [22,23]. In active film coating, the API is directly mixed with the film-forming agent, additionally, there are no restrictions on the choice of the film-forming agent [24]. The compatibility of film-forming agents and APIs should be validated because APIs are directly present in the coated film. A functional separation layer (e.g., enteric, or hydrophobic layer) can be put between the core tablet and the active coating layer if necessary. Desai et al. investigated an active film coating method for stabilizing peliglitazar, a PPAR/agonist. Because Peliglitazar is acid-/base-catalyzed, the active film coating technique was used to improve the stability of the peliglitazar tablet formulation by spraying pharmaceuticals with coating ingredients over a placebo core tablet. This active film coating method produced tablets with acceptable chemical stability, which could be due to a higher drug to excipient ratio in the film coat of non-reactive coating materials when compared to standard dry or wet granule formulations [25].

2.1.4. Modified drug release

Modified drug release is frequently advantageous for enhancing drug effectiveness and patient compliance or prolonging the duration of action [26]. As a result, tablet film coating with different polymers is being actively pursued in order to produce modified drug release by altering the pace and/or sites of drug release. The following are some examples of film coating methods for customized drug release.

(a) Delayed drug release

Delayed or enteric-coated dosage forms are frequently achieved by using pH sensitive-polymeric coats capable of delaying the release of certain API's either to protect the drug from the acidic environment in the stomach (i.e., proton pump inhibitors) or to protect the stomach from the irritant effect of the drug due to chronic use as nonsteroidal anti-inflammatory drugs like diclofenac sodium [27, 28]. Commercially available ready to use ready-mix for delayed release film coating are available under INSTACOAT® EN series from Ideal cures Pvt. Ltd. Acid-resistant polymers are often employed to prevent medication release at pH 1.2. They, on the other hand, exhibit a large increase in solubility at pH levels greater than 5.5, bypassing the stomach and releasing the drug in the small intestine [29, 30]. Film coating for delayed medication release has also been attempted for colon-targeted drug administration or chronotherapeutic drug delivery synchronized with circadian rhythms.

Colon-targeted drug delivery systems are necessary for the local treatment of colon-specific disorders such as Crohn's disease, IBS, and colon cancer [31,32]. Goyanes et al. manufactured a controlled-release tablet for budesonide administration in the colon. A capsule-shaped tablet (caplet) containing 9 mg budesonide was 3D printed and then coated with Eudragit® L100 in a spray fluidized bed coater. The drug release patterns of the coated caplets were further investigated in a dynamic dissolving buffer system that mimicked gastrointestinal circumstances. After 1 hour, in the small intestine, the drug started to release and then continued in a sustained manner throughout the conditions of distal intestine and colon [33].

Chronotherapeutic drug release involves the delayed release of API for a programmable amount of time to fulfill chronotherapeutic needs, particularly for circadian symptoms. Cardiovascular illness, bronchial asthma, rheumatoid arthritis, and sleep disturbances are examples of chronic diseases with circadian symptoms that most commonly reoccur at night or early in the morning [34,35]. Although medications are supplied at bedtime, pulsatile drug release synchronized with the disease's circadian cycles can selectively cover the important phase of the disease without forcing the patient to wake up for drug consumption. Enteric film coating can be used to achieve chronotherapeutic medication release. Luo et al. manufactured an enteric coated bilayer tablet containing a fixed dose combination of telmisartan and pravastatin sodium that corresponded to circadian rhythmic fluctuations in hypertension and cholesterol production for once-daily bedtime administration [36].

(b) Sustained drug release

Sustained release dosage form was developed when the drug requires a consistent blood level and reduced dosing frequency. This can be accomplished using a variety of approaches, including increasing the particle size of the drug, encapsulating the drug in an appropriate matrix, complex interactions between the API and ion-exchange resins, and coating the API or Dosage form containing the API [37]. The rate of drug release can be influenced by physicochemical qualities and the amount of polymers employed for surface coating [38]. It is also adjusted by varying the coating layer's thickness, tortuosity, and permeability [39]. Venlafaxine HCl, an antidepressant, has a short half-life (approximately 5 hours), necessitating a sustained-release formulation to reduce dose frequency. Using a standard ethyl cellulose dispersion solution

(Aquacoat® ECD 30) and polyacrylate-based coating agents (Eudragit®), Jain et al. created a reservoir type aqueous and organic coated tablet of venlafaxine for prolonged drug release [40].

2.2 Non-functional film coating

Non-functional film coating, along with tablet form and size, plays an important role in enhancing patient compliance since it influences the final appearance and organoleptic qualities of the manufactured tablets, both of which are important parts of the brand image [41]. Furthermore, it plays a key function in assisting senior people suffering from dysphagia since the presence of a film coat on the dosage form can make swallowing easier [42]. According to the US FDA, the presence of a film coating can either enhance or facilitate tablet mobility when compared to a non-coated tablet of the same shape and size [43].

3. Methods of film coating

3.1 Solvent-free coating

In the coating process, the use of solvents and heat exposure can raise product instability, processing costs, and the possibility of environmental and safety issues [44]. As a result, solvent-free coating approaches have been intensively pursued to overcome the disadvantages of solvent-based coating. Solvent-free coating can minimize production time and expense by avoiding expensive and time-consuming solvent disposal processes Furthermore, because it does not usually require drying, solvent-free coating is suitable for heat-sensitive pharmaceuticals [45]. Although solvent-free coating may eliminate some of the problems associated with solvent-based coating, the need for coating conditions, equipment, and coating materials limits its widespread use in the pharmaceutical sector [46]. Solvent-free coating offers advantage of reduced environmental consideration, reduced residue, cost efficient, increased regulatory compliance, and improved product stability [47].

3.2 Aqueous-film coating

Aqueous coating is a widely used film coating method in current pharmaceutical practice. Initially, Aqueous film coating techniques were viewed with misunderstanding due to the realities of extended processing time and unattractive appearance of coated product. In terms of operator safety, environmental pollution, and explosion danger, it outperforms organic solvent-based coatings. Despite these advantages over organic solvent-based coating methods, aqueous coating has some disadvantages, such as an energy- and time-consuming water evaporation process, a longer processing time, validation of coating dispersion to control microbial presence, and potential activity loss of certain drugs due to water or high coating temperature [45,46]. Furthermore, for a homogenous coating solution, an aqueous coating solution containing water-insoluble polymers requires the inclusion of a suitable suspending agent or plasticizer [47]. Although aqueous film coating has several drawbacks, it avoids the safety concerns associated with organic solvent-based coating and is thus still commonly utilized in the pharmaceutical business. Process automation, process validation, and the development of more efficient equipment, such as side-vented perforated coating pans and fluidized bed equipment, are ongoing attempts to minimize processing time and enhance productivity [48]. Aqueous film coating can be done by solutions directly or by dispersion and redispersible. Benefits of redispersible powder formulations include decreased flocculation when subjected to severe shear pressures or temperature variations, lower storage and shipping costs, and improved microbiological stability [49].

3.3 Organic film coating

In the early 1950s, film coating was done using polymers soaked in organic solvents, which had various advantages over sugar coating, such as less processing time, the ability to make thin smooth continuous coatings, and a lower risk of hydrolysis [49]. Although the use of organic solvents is not desirable, due to the limited water solubility of coating ingredients, film coating with hydrophobic or lipophilic polymers needs the use of organic solvents. Highly hydrophobic polymers are advantageous as moisture-protective coating polymers because they can minimize the final film's water vapor permeability by stopping water molecules from moving. As a result, organic solvent-based coating is advantageous for moisture-sensitive pharmaceuticals. The rate of evaporation of the solvent is critical for the end product's quality, and several variables such as temperature, atmospheric pressure, and air movement should be controlled to maximize the evaporation rate [50]. Despite medicinal needs, organic solvent-based coating has many key limitations due to residual solvent toxicity, flammability, and environmental safety concerns [47]. Even with sufficient ventilation, totally removing organic solvent vapors from the coating chamber is challenging, raising the danger of toxicity and explosion. Environmental and regulatory concerns might raise production costs. Hence, film coating with organic solvent is very limited in use.

4. Process parameter affecting film coating.

The mass of tablets from the compression unit operation determines the batch size in the conventional solvent-based pan coating process. The spinning pan permits tablets to circulate along the coater walls during the manufacturing operation. Droplets of coating solution are deposited on the surface of tablets as they pass through the spray zone, forming a coating film [51]. Tablets are oriented differently as they move through the spray zone during each cycle, which causes the surfaces they face toward the spray gun to shift often, coating the tablets' whole surface. The produced film must be smooth and uniform after drying by a combination of hot airflow supplied from the upper section of the coater and conduction from the heated tablet bed. However, the coating process's intricacy frequently results in coating flaws such as bridging, cracking, and orange-peel roughness [52]. These flaws are primarily due to insufficient procedure parameters. As a result, optimizing coating formulas (compositions), process variables, and equipment settings is crucial for achieving a consistent and smooth coating layer [53]. Some of the process parameters that

affects coating on solid dosage forms have been listed below and the summary of the same is provided in table 2.

4.1 Inlet air temperature and bed temperature

The drying kinetics of the spray droplets as they travel from the spray nozzle to the tablet surface are dictated by the inlet air (flow rate), which is another essential processing parameter in film coating. An earlier study found that inlet air temperature has a considerable impact on both tablet bed and exhaust air. Inlet air temperature also influences the temperature of heat-sensitive products, which affects the formulation's stability. The effects of intake air are primarily related to drying difficulties. Inadequate drying can result in too wet tablet surfaces, which can cause twinning, tablet agglomeration, and surface breakdown. If drying occurs too quickly, the polymer-containing droplets may dry before striking the tablet surface (spray drying) or may not spread properly throughout the tablet surface, resulting in a rougher film surface, and resulting in the blockage of the spray gun. [54]. The temperature of the bed is significant because it affects the evaporation of the coating dispersion solvent. An increase in the amount of heat of the incoming process air causes an increase in the tablet bed temperature. The temperature of the tablet bed rises as the amount of heat in the incoming process air rises. But the bed temperature is usually 5-10°C lower than the inlet air temperature.

Table 2: Process parameter affecting film coating

Sr. no.	Process parameter	Effects of respective conditions	
		High	Low
1.	Inlet air temperature and bed temperature	- Blockage of spray gun -Film peeling and flacking of the tablet	-Swelling of core containing disintegrates -No film formation
2.	Spray rate	-Sticking and picking, cracking, and splitting of the film, bridging swelling of core -Hydrolysis of the active ingredient	-Orange peel effect -Sedimentation of the suspension in the tube
3.	Speed of coating pan	-Edge erosion of the tablet	-Non-uniform colour distribution -Sticking and picking
4.	Distance of spray gun to bed	-Orange peel effect -Loss of coating suspension due to spray coating -Coating film will be too thin	-Swelling of cores -Hydrolysis of the active ingredient -No film formation -Sticking and picking -Non-uniform colour distribution
5.	Atomization of air pressure	-Loss of coating suspension due to spray coating -Orange peel effect	-Cracking and splitting of the film. -Sticking and picking

4.2. Spray rate

One of the most critical coating process characteristics is spray rate. Droplet size and velocity both increase as spray rate increases. Spray rate influences coating quality not only as an individual parameter, but also as a composite parameter in conjunction with atomization air and pattern air [55]. Because the mean droplet size does not change much when the atomization air/spray rate ratio is fixed, the atomization air/spray rate ratio is one of the most critical parameters influencing droplet size and coating quality [56]. A high spray rate, may result in coating flaws such as twinning, picking and adhering, and logo bridging. However, a low spray rate, on the other hand, may result in spray drying and a decrease of coating efficiency [57].

4.3. Speed of coating pan

Pan speed was found to be the most significant factor related to coating uniformity [58]. Pan speed affects the product's movement and mixing effect, as well as the color distribution on the tablet and the contact time between the tablets. High speed of pan can lead to edge erosion of the tablet and if in case the speed of the pan is low it results into non-uniform colour distribution as well as sticking and picking.

4.4 Distance of spray gun to bed

It is the distance between the tip of the nozzle and an imaginary flat surface on the tablet cascading bed. As a result, this variable may be subjective and operator dependent. As the droplets move in this region, the solvent can evaporate, causing the droplets to shrink, or the droplets can coalesce, causing the droplets to grow [59]. Droplet velocity diminishes and agglomeration occurs as the droplets of coating solution migrate away from the nozzle tip, resulting in increasing droplet size (diameter). Coating process efficiency diminishes as the gun-to-bed distance grows. Droplets may dry before reaching the tablet surface, resulting in a rough tablet surface [60]. In contrast, if the gun-to-bed distance is short, sprayed droplets stick to the tablet surface before drying, causing the tablet surface to become wet. Twinning or coating surface dissolution can occur on wet tablet surfaces [54].

4.5 Atomization of air pressure

The droplet size and velocity of the solution or suspension exiting the spray nozzle are determined by the atomization air pressure utilized in coating procedures. [61]. The coating solution is disintegrated into droplets that are forced into the spray nozzle by high-pressure atomization air. When spraying just with atomization air, coating solution droplets may flow directly into a restricted area of the tablet surface, causing coating uniformity issues [62]. Excessive atomization air pressure can cause smaller droplets to dry entirely before reaching the tablet surface, resulting in spray drying, efficiency loss, and, in rare situations, logo infilling or "orange peeling" coating flaws. A low atomization air pressure, on the other hand, can result in poor atomization of the coating suspension, resulting in larger droplets that may not be dispersed and cured properly after they contact the tablet substrate [55].

5. Conclusion

Pharmaceutical film coating has evolved significantly in terms of technology, materials, and applications. It plays a crucial role in improving drug efficacy, patient compliance, and overall product quality. The variety of types and classifications allow for tailored solutions to meet the

specific needs of different pharmaceutical formulations, making it a vital component of modern drug manufacturing processes. The continued advancement of film coating technology is likely to further enhance drug delivery and patient outcomes in the pharmaceutical industry. We should expect more breakthroughs in film coating techniques to improve drug delivery and patient outcomes as technology and research evolve.

6. Future scope

Film coating holds significant promise and is likely to evolve in response to various factors, including advancements in technology, regulatory changes, market demands, and environmental considerations. As new technologies and materials become available, film coating methods are likely to adapt and continue to play a vital role in drug delivery and product development.

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