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Characterization of Coating Systems

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ABSTRACT

Polymeric film coatings have been applied to solid substrates for decorative, protective, and functional purposes. Irrespective of the reasons for coating, certain properties of the polymer films may be determined as a method to evaluate coating formulations, substrate variables, and processing conditions. This article describes experimental techniques to assess various properties of both free and applied films, including water vapor and oxygen permeability, as well as thermal, mechanical, and adhesive characteristics. Methods to investigate interfacial interactions are also presented.

KEYWORDS: Polymeric film, permeability, mechanical testing, adhesion, interface.

INTRODUCTION

Many technologies can be employed to modify the release of oral solid dosage forms. One such method is the use of polymer films to surround the dosage form and alter drug release. These coatings can also be used to improve the appearance and enhance the mechanical strength of the dosage form as well as to protect the active against exposure to environmental factors. Irrespective of the reasons for coating, certain properties of the polymer films may be determined as a method to evaluate coating formulations, substrate variables, and processing conditions.

Specific to coating processes, properties of both free and applied films are generally studied. Free films can be obtained by the casting method, where a polymeric solution or dispersion is cast onto a nonstick substrate and the solvent is evaporated. To avoid different film surfaces that may result from casting polymeric dispersions, a spray atomization technique may be employed.[1] A spray box apparatus, shown in Figure 1, consists of a rotating drum inset in a box with heat introduced to facilitate solvent evaporation. The polymeric material is then sprayed onto the nonstick surface of the rotating drum. This technique better simulates coating processes and produces more uniform surfaces.[2] In contrast to the study of free films, evaluation of applied films allows one to evaluate substrate variables, processing parameters, and storage conditions as well as coating formulation variables. This article describes experimental techniques to assess various properties of both free and applied films.

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WATER VAPOR PERMEABILITY

Water vapor permeability experiments are used to evaluate the effectiveness of a film coating as a barrier to water. Several variables have been shown to influence water vapor permeability, including film composition, film thickness, and film preparation technique.[3-6] For free films, water vapor transmission cells are assembled (Figure 2). These cells consist of a glass or aluminum container with a saturated salt solution inside. The film is attached over the opening of the container, such that water vapor movement can occur only through the film. The transmission cells are placed in a desiccator of known humidity, creating a water vapor pressure gradient. The change in weight of the transmission cell is followed over time and the weight change is plotted versus time. The slope of the line from this graph, calculated using linear regression, is the water vapor transmission rate (WVTR). The permeability constant (P_{erm}) of the film can then be calculated using Equation 1, where L is the film thickness, A is the area the exposed film, and ΔP is the vapor pressure gradient.

$$P_{erm} = \frac{WVTR \times L}{A \times \Delta P} \quad (1)$$

Water vapor permeability of *applied* films can also be determined by modifying the free film transmission cell apparatus.[7] In this method, a coated tablet is suspended on a wire loop above a saturated salt solution in a closed environment, as seen in Figure 3. The tablet is weighed over time and WVTR and P_{erm} are calculated. This method is especially useful to investigate the influence of excipients in the tablet core on water vapor permeability.

OXYGEN PERMEABILITY

The rate of oxygen permeability is a measure of the effectiveness of the coating material as a barrier to oxygen and

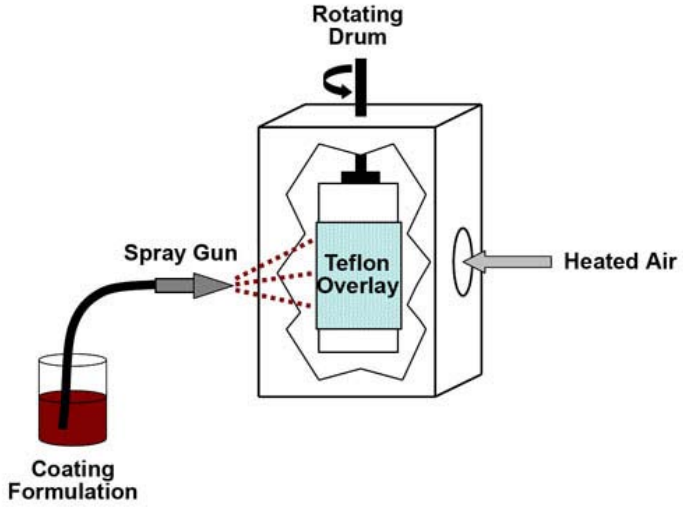

Figure 1. Schematic of a spray box apparatus for producing free films.

is especially important when working with active pharmaceutical ingredients that degrade by oxidative processes. Film composition and film thickness have been shown to significantly influence oxygen vapor transmission.[8,9] The majority of published work has been focused on assessing oxygen permeation of free films, where a test specimen is placed between two chambers, as shown in Figure 4. After purging with nitrogen gas, one side of the chamber is exposed to pure oxygen and the diffused molecular oxygen is quantified by a coulometric sensor. With more sophisticated equipment, the relative humidity of both gases can be monitored and adjusted.

The oxygen permeability of *applied* films can be determined using a nondestructive electron paramagnetic resonance (EPR) spectroscopic technique described by Felton and Timmins.[10] This method involves the insertion of a lithium phthalocyanine crystal inside the dosage form and is based on that reported by Liu and coworkers,[11] who implanted these oxygen-sensitive crystals in vivo to determine partial oxygen pressure (pO_2)

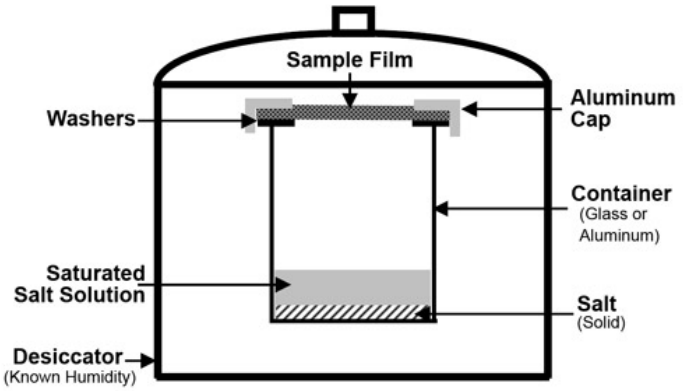

Figure 2. Schematic of a water vapor transmission cell to assess water vapor permeability of free films.

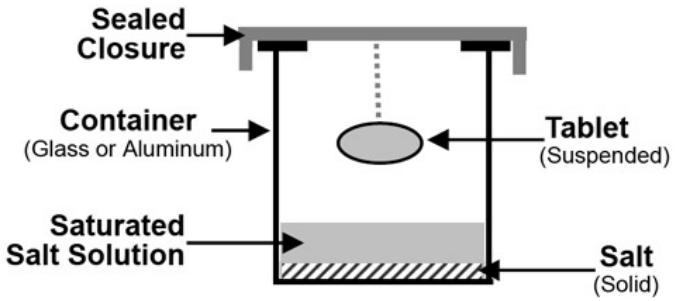

Figure 3. Schematic of a water vapor transmission cell to assess water vapor permeability of applied films.

in rats following stroke and traumatic brain injuries. The peak-to-peak linewidth of the first derivative of the EPR spectra of the lithium phthalocyanine crystals is proportional to pO_2. The pO_2 can be plotted versus time (Figure 5) and the slope calculated using linear regression to obtain the oxygen permeation rate. As shown in Figure 6, the rate of oxygen permeation through an applied film is significantly slower than through uncoated tablets.

Thermal Properties

Glass Transition Temperature

One of the most common polymer properties determined for amorphous polymers is the glass transition temperature (Tg). The Tg is the temperature at which the mechanical properties of a polymer change from a brittle to a rubber state. At temperatures above the Tg, there is an increase in free volume and the polymer chains are able to move. An increase in Tg is generally related to a restriction in mobility of the polymer chains or an increase in the crystallinity of the polymer. The Tg is typically measured using a differential scanning calorimeter (DSC), where a sample and reference pan are heated at a programmed rate, and thermal transitions, where more

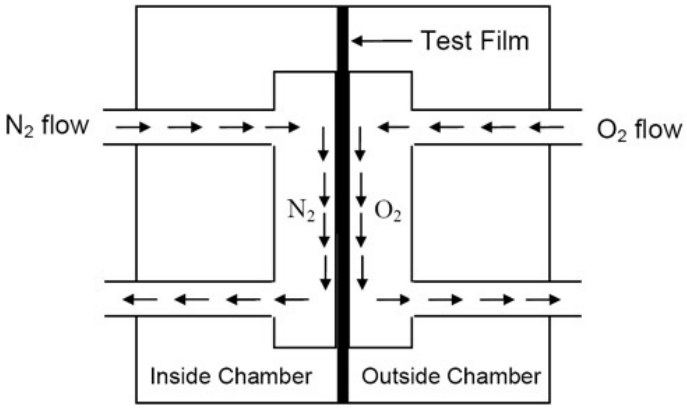

Figure 4. Schematic of an instrument to quantify oxygen permeation through free films.

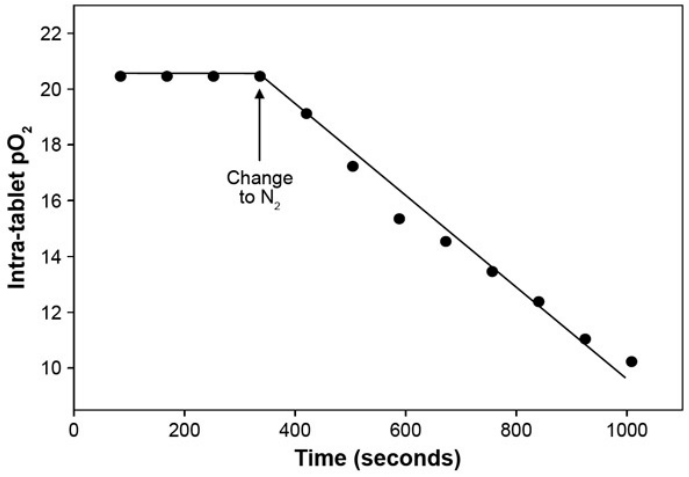

Figure 5. Partial oxygen pressure inside an uncoated tablet as a function of time following gas switching to nitrogen.

energy is absorbed or emitted, are determined. There are numerous examples in the literature of Tg studies having been conducted to evaluate polymer properties and interactions with excipients.[12-17] The DSC instrument can also be used to determine melting temperature, detect polymorphism, study polymer miscibility, and investigate oxygen degradation.[18-21] Several variations in DSC testing have been developed, including a triple cell system for more precise measurements of enthalpy, temperature-modulated units to separate reversing and nonreversing transitions, and high-sensitivity models.

Thermogravimetric Analysis

Another temperature-related test that is often conducted on polymeric materials is thermogravimetric analysis (TGA). A typical TGA apparatus consists of a microbalance, a furnace, a computer interface, and a temperature controller. A sample is placed on the microbalance and the furnace is heated. The test determines mass change as a function of temperature or time and is used to determine residual solvents in a sample and to evaluate thermal stability. TGA can be combined with additional instrumentation, such as mass spectroscopy (MS), gas chromatography (GC), or Fourier transform infrared (FTIR) spectroscopy, to analyze the evolved gaseous material.[22]

Minimum Film Forming Temperature

The minimum film forming temperature (MFT) is the minimum temperature at which a polymeric material will coalesce to form a film. At temperatures below the MFT, a white opaque or powdery material is formed, whereas a clear, transparent film is formed at temperatures equal to or greater than the MFT. Obviously, the MFT has implications in coating processes and the bed temperature of the coating equipment must be above the MFT to ensure film formation. To determine the MFT experimentally, a temperature gradient plate with drying air blown across the surface is used. The polymeric material is then poured onto the plate and visually inspected to determine the lowest temperature at which a clear and transparent film is formed. Many excipients in the coating formulation can affect this parameter[23] and, in some cases, the MFT may be below room temperature.[24]

Mechanical Testing

Polymer films must be mechanically strong such that they do not break or fracture during processing, packaging, shipping, and storage. A series of experimental techniques have been used to assess the mechanical strength of polymer coatings and these data have been used to predict such properties as dissolution or the incidence of film defects.[25-27] Researchers have also used mechanical testing to evaluate the effectiveness of plasticizers and predict long-term storage stability.[17,28-30] There are several mechanical tests available to the pharmaceutical scientist and some of the more common techniques are discussed below.

Tensile Testing

A tensile test consists of a free film strip that is placed between 2 grips and then stretched at a constant rate until the film fractures. The force and displacement values are recorded during the test and these data are converted to stress and stain using Equations 2 and 3, where σ is stress, F is the applied force, A is the initial cross-sectional area of the

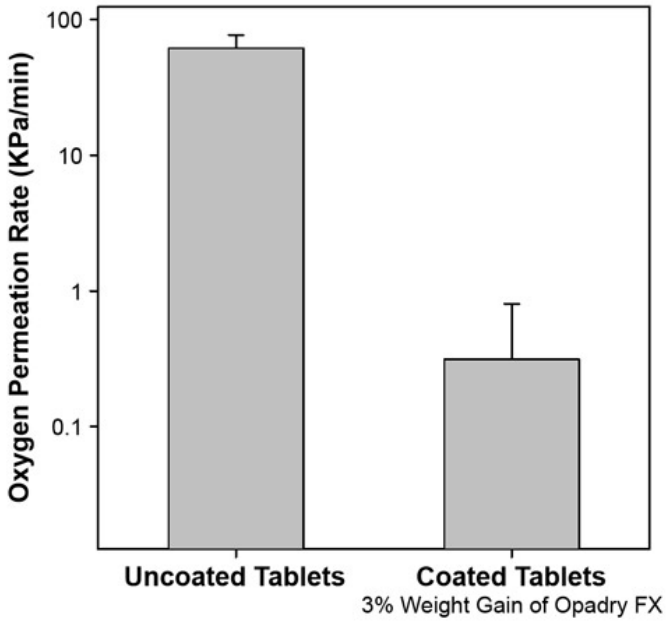

Figure 6. Rate of oxygen permeation into uncoated and coated tablets.

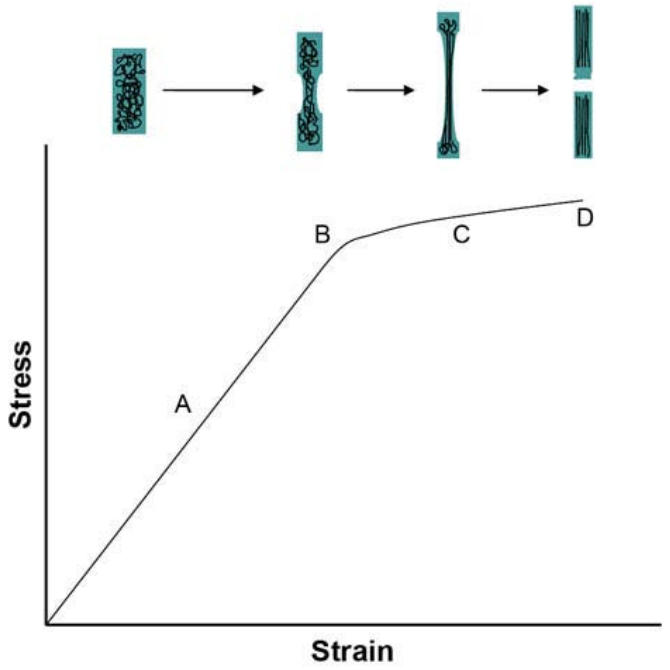

Figure 7. Example of a stress-strain curve. A, Elastic deformation, where stress is proportional to strain; B, Yield point; C, Plastic deformation, where polymer chains orient themselves with the applied stress; D, Break.

film, ε is strain, L is the initial length between the grips and ΔL is the increase in the length of the film at fracture.

$$\sigma = \frac{F}{A_{initial}} \tag{2}$$

$$\varepsilon = \frac{\Delta L}{L} \tag{3}$$

Data generated during tensile testing of free films are often plotted as stress versus strain, as shown in Figure 7. During the test, elastic deformation occurs initially, where stress is proportional to strain. After a yield point, plastic deformation occurs, where polymer chains orient themselves with the applied stress. Finally, the film fractures. At least 5 replicates should be done per sample and the data should be discarded if the film slips or fractures at the grips. Since temperature and humidity can have profound effects on the mechanical properties of films, tensile testing should be conducted under controlled environmental conditions.

Stress is a measure of the film's strength, whereas strain is a measure of film ductility. Other useful data that can be determined from stress-strain testing include Young's modulus and the area under the stress-strain curve. Young's modulus is the slope of the linear region of the stress-strain curve and is a measure of the stiffness of the film or its elasticity. The greater the slope, the higher the modulus and the stiffer the material. The area under the curve is the work required to fracture the film and is a measure of film toughness. The ratio of tensile strength to Young's modulus has been used to predict crack resistance, with high values exhibiting greater resistance to cracking.[25]

Compression Testing

Compression testing of applied films is similar to tensile testing of free films in that uniform displacement rates are applied to a sample and force and displacement values are recorded; the primary difference is in the direction of the applied stress. Compression testing can be used to investigate the effects of substrate, storage conditions, and physical aging of the applied film[31,32] and can provide qualitative information on adhesion.[33] Compressional forces are critical when tableting coated pellets and thus compression testing of coated pellets is especially important when these units will be tableted. If the compressional force exceeds the coating strength, the film will fracture and faster dissolution will result.[34] Slower drug release has also been reported due to the formation of matrix tablets as the polymer coatings fuse during compression.[35] To reduce friction during compression and to prevent direct contact, readily compressible excipients are often blended with the coated pellets before tableting.[36]

Puncture Strength

Bodmeier and Paeratakul[37] have suggested that films in the dry state may not predict the behavior of films when in contact with biological fluids. Water may plasticize the film and conventional plasticizers may leach out. Thus, the puncture test has been developed to evaluate films in their hydrated state. The apparatus consists of a platform assembly containing a free film that is submerged in a dissolution bath. A puncture probe attached to a load cell is then driven into the film. Data determined from this experiment include the puncture strength (force at puncture divided by the cross-sectional area of the dry film) and the percent elongation at puncture.

Dynamic Mechanical Analysis

Dynamic mechanical analysis (DMA) is another type of test used to study the mechanical properties of films. In DMA testing, a free film is placed between 2 grips, 1 that is stationary and the other oscillatory. The free film is then deformed by torsion oscillation as a function of temperature. The storage modulus, loss modulus, and damping coefficient (ratio of loss modulus to storage modulus) are

determined. Several different modes are available, including fixed frequency, creep relaxation, and stress relaxation. DMA can be used to determine the Tg as well as other smaller, sub-Tg transitions, which can provide some indication of polymer structure.[38]

POLYMER ADHESION

In film-coating processes, adhesion between the polymeric film and substrate is a major consideration. Poor adhesion could result in the coating flaking or peeling from the substrate core and moisture could accumulate at the film-substrate interface.[39] In addition, poor adhesion can compromise the mechanical protection the coating provides.[40] Polymer adhesion is related to both film-substrate interfacial interactions and internal stresses within the film. Internal stresses arise due to shrinkage of the film upon solvent evaporation, thermal stress due to the difference in thermal expansion of the substrate and film, and volumetric stress as the substrate swells during storage. Equation 4 can be used to estimate total internal stress (P) within a film coating,[41-44] where E is the elastic modulus of the film, ν is Poisson's ratio, Φ_s is the volume fraction of solvent at the solidification point of the film, Φ_r is the volume fraction of solvent in an air dried film, $\Delta\alpha_{cubic}$ is the difference in coefficient of thermal expansion between the film and substrate, ΔT is the difference between the Tg of the film and the temperature during manufacturing and storage, ΔV is the volumetric change of the substrate, and V is the original volume of the substrate core.

$$P = \frac{E}{3(1-\nu)}\left[\frac{\Phi_s - \Phi_r}{1-\Phi_r} + (\Delta\alpha_{cubic}\Delta T) + \left(\frac{\Delta V}{V}\right)\right] \quad (4)$$

Several methods have been used to either predict or determine film-tablet adhesion. Contact angles between polymeric solutions or dispersions and tablet surfaces provide information regarding substrate wettability, with the more wettable surface theorized to produce better interfacial interactions and thus stronger adhesion. One must be mindful, however, that it is the film that adheres to the substrate, not the polymer solution or dispersion.

One technique used to quantify film-tablet adhesion is the peel test, which uses a modified tensile tester to peel the film from the tablet surface at a 90° angle. The peel strength, however, is dependent on the elasticity of the film and the uniformity of adhesion, both of which can produce deviations in the data.[39] The most widely accepted methodology to determine polymer adhesion is the butt adhesion test, where the entire film is removed normal to the surface of the tablet. A schematic of the apparatus is shown in Figure 8. This technique eliminates variations due to the elasticity of the film and is less influenced by the uniformity of adhesion. Ideally, flat-faced tablets are used, but concave tablets can also be tested by adding a rubber or foam backing to ensure uniform contact between the film surface and the force gauge.

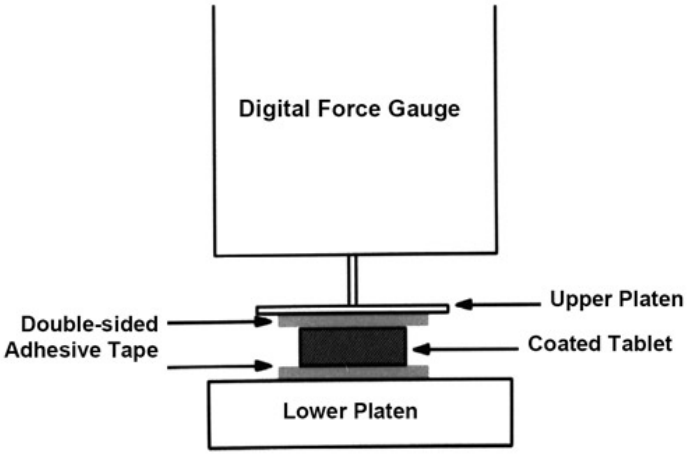

Figure 8. Schematic of a butt adhesion test.

An example of a force-deflection profile obtained from butt adhesion testing is shown in Figure 9. The figure is similar to a stress-strain profile obtained from tensile testing of free films. Graphing the force-deflection data permits the visualization of the development of the force within the sample during the adhesion test. The force of adhesion is the force at which the film is removed from the substrate surface. Elongation at adhesive failure is the distance the platen moved at film removal and reflects the ductility of the film. The modulus of adhesion is analogous to Young's modulus in the tensile testing of free films and is the slope from the linear region of the force-deflection diagram. And, finally, adhesive toughness is the area under the curve and represents the work required to remove the film from the tablet surface.

Several variables have been shown to influence the adhesive properties of an applied film. Fisher and Rowe[45] showed that the compressional force used during tableting significantly influenced adhesion of organic-based cellulosic films. Above a critical force, increased compressional force during tableting resulted in decreased adhesion, which was attributed to a decrease in the effective area of contact between the film and tablet surface. Below the critical compression pressure, the tablet laminated, rather than the film being separated from the tablet surface, a process known as cohesive failure. When intermolecular bonding forces between the film and the tablet surface are stronger than those bonds formed between the powdered particles within the tablet, lamination of the tablet compact will occur during an adhesion test. With cohesive failure, particles from the tablet are found on the surface of the film coating. Data from cohesive failure should not be compared with that from adhesive failure, as different forces are involved in each process. Experimental procedures can be modified to obtain adhesive failure.

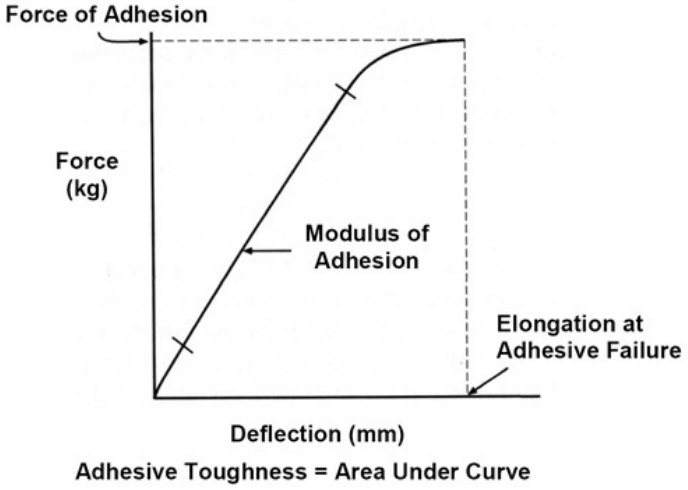

Figure 9. Schematic of a force-deflection profile obtained from a butt adhesion test.

Excipients used in tablet formulations can influence film-tablet adhesion. Since adhesion between a polymer and tablet surface is due primarily to hydrogen bond formation, hydrophobic agents may decrease adhesion by presenting a surface consisting of mainly nonpolar hydrocarbon groups, the extent of which is dependent on the nature and concentration of the excipient.[46,47] Other studies have shown that solvent,[48,49] film thickness,[49] surface roughness,[46] plasticizers,[50] surfactants,[51] insoluble pigments,[50,52] and curing[53] can influence film-tablet adhesion.

Surface Roughness

Several techniques can be used to determine the roughness of both uncoated and coated surfaces. Surface roughness of uncoated tablets has been shown to influence polymer adhesion,[46,48,49] with rougher surfaces providing greater interfacial contact. The surface roughness of coated substrates at minimum influences the aesthetic appearance and potentially can influence drug release. Electron microscopy is commonly employed to provide qualitative information about surface morphology. In contrast, profilometry is a quantitative method that involves a sensing head moving across a relatively *large* area of the substrate. Another technique to quantify surface roughness is atomic force microscopy (AFM), which uses a sensor to examine relatively *small* areas of a substrate.

Scanning thermal microscopy uses principles similar to AFM, except the tip is replaced with a thermal probe to simultaneously gather topographical and thermal information. The power required to maintain the tip temperature is monitored. The heat flow between the tip and sample will vary with the thermal properties of the sample. This technique is used to study local thermal events, such as melting temperature, Tg, and water loss, to distinguish between active and inactive ingredients, and investigate multiphase polymer systems.[54,55]

Interfacial Interactions

Polymeric coatings are generally applied to solid substrates using a spray atomization technique, where polymer-containing solutions or dispersions are atomized with air and delivered to the substrate surface as fine droplets. These droplets spread across the surface and solvent evaporation causes the droplets to closely pack and the polymer chains coalesce to form the film. Since most solid dosage forms are designed to dissolve in water-based biological fluids and the majority of coating systems used today are aqueous-based, dissolution of the outermost surfaces of the substrate occurs during the coating process, permitting physical mixing at the film-tablet interface and the potential for migration of drug or excipient into the film.[56] This physical mixing and migration of components into the coating can affect the mechanical, adhesive, and drug-release properties of the polymer film.

Several techniques can be employed to assess drug migration into film coatings. One such method is confocal laser scanning microscopy (CLSM). This technique has been used in the biological sciences for many years but has only recently been used in systems of pharmaceutical interest.[57] One of the advantages of CLSM is the ability to depth profile in a nondestructive manner; however, a major limitation to the use of CLSM is that a fluorescent compound must be used. The CLSM images of the surface of an uncoated and coated pellet are shown in Figure 10, where the fluorescent area is the drug of interest, and it is apparent from these images that the drug migrated into the coating. In this example, the drug was water-soluble and partitioned into the coating material, an ethylcellulose in isopropyl/water solvent, and these CLSM findings accounted for the significantly faster dissolution profiles that were observed.

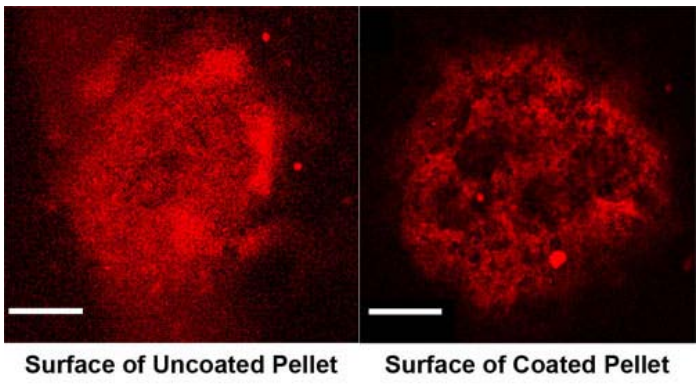

Figure 10. Confocal laser scanning microscopy of the surface of uncoated and coated pellet. The red fluorescent signal is the drug. White line represents 100 microns.

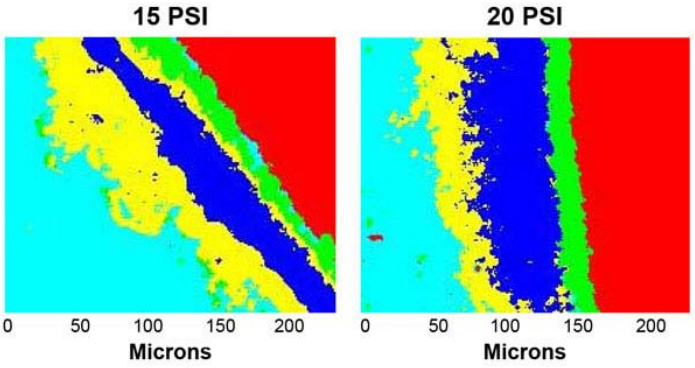

Figure 11. Influence of atomization air pressure used during the coating process on the interfacial thickness of an applied polymer. Images obtained using x-ray photoelectron spectroscopy and a classification system. Yellow inidicates the tablet/coating interface; Light blue, tablet; Dark blue, coating; Green, air/coating interface; Red, air.

Another technique that can be used to investigate the film-tablet interfacial region is x-ray photoelectron spectroscopy (XPS). XPS is a surface-sensitive technique that has been used to determine both elemental analysis and chemical structure of materials.[58-60] In a preliminary study, Felton and Perry[56] combined XPS with intermittent ion bombardment to depth profile and quantified film-tablet interfacial thickness. This technique required the use of unique identifiable components in both the film coating and the substrate. Moreover, sample preparation was quite tedious. A recent modification used the same XPS instrument but combined it with a classification method, which permitted the investigators to study any system containing carbon and eliminated complicated sample preparation. An example of the data obtained from XPS with classification is shown in Figure 11, where the interfacial region was found to be dependent on the atomization air pressure used during the coating process. At higher atomization pressures, finer droplets impinge on the tablet surfaces, allowing for quicker solvent evaporation and less surface dissolution, resulting in a narrower interfacial region.

Film Thickness and Uniformity

In coating processes, an assumption is made that all substrates are coated uniformly. However, variations between batches, between substrates in a given batch, and even within individual substrates have been reported. To study film thickness and uniformity, several approaches have been tried. Microscopic examination can be used, but is a tedious process. Weighing marked tablets before and after coating can also be used. Although not as tedious as microscopic examination, this technique provides no information about how the film is distributed on the substrate. Another method that has some promise in the study of film thickness and uniformity is laser-induced breakdown spectroscopy (LIBS), an elemental analysis technique based on the detection of atomic emission from a plasma formed by a high-energy laser.[61] LIBS requires that the coating and substrate cores be constructed with specific targets, but no additional sample preparation is required. Multiple areas of a single tablet can be tested to provide information on uniformity of film distribution. The technique, however, is destructive, as the laser drills into the sample.

Terahertz-pulsed imaging is a relatively new, nondestructive technique that can be used to determine the thickness of an applied polymeric coating.[62] A terahertz pulse, of wavelengths between the microwave and IR regions, hits the substrate surface and a portion of the pulse is reflected from internal layers of the substrate, with the return pulse being delayed as it passes into the coating. In addition, terahertz-pulsed spectroscopy can be used to gain information on chemical constituents in the film and the data obtained can be converted into visual images. This system does not require that material components have specific properties and is nondestructive.

Computer-aided tomography (CAT) medical imaging has been extended into pharmaceutical systems to visualize structural features in solid dosage forms. With this method, x-rays are transmitted onto a sample and a detector on the opposite side measures the intensity of the transmitted x-rays. The entire sample can be rotated and scanned to create 2-dimensional and 3-dimensional images. Film thickness and uniformity are only a few parameters that can be investigated with CAT scanning.[63]

Conclusions

This paper reviewed various techniques that can be used to quantify properties of free and applied films. These methods can be used by the pharmaceutical scientist to facilitate a better understanding of the principles involved in coating and to avoid or resolve problems encountered during coating processes.

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