



The development of cracks on delayed release film of hygroscopic cores: A review of the tablet and coating formulations, coating processes and storage conditions.

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ABSTRACT

Methacrylic Acid Copolymer Dispersion NF (aqueous dispersion of Methacrylic Acid Copolymer Type C in water) has been used extensively for delayed release coating in the pharmaceutical industry. However, a concern is that the Methacrylic Acid Copolymer Dispersion NF may cause cracks to develop in the coating film in hygroscopic tablets. These develop because the polymer is inherently brittle and therefore cracks during storage, especially when exposed to elevated heat and/or humidity. A crack in the coating film develops as the polymer is unable to accommodate the stresses that are generated during the coating process or because of changes in, e.g., tablet dimensions during storage. The important factors to maintain the integrity of the coating film are (i) formulation of the tablet core and its hardness, (ii) formulation of the coating dispersion, and (iii) coating process parameters. Tablet core hardness, its relaxation properties, water content, content of the insoluble component in the coating formulation, and temperature and relative humidity (RH) of the inlet air influences the film quality and integrity. In this paper, the probable causes for the development of cracks in the film coating on a hygroscopic core are discussed with reference to the properties of the tablet core, coating formulations (e.g., polymers, plasticizers, insoluble excipients) and the coating process parameters.

KEY WORDS: Methacrylic acid, delayed release, cracks, insoluble excipients, environment, hygroscopic tablet

INTRODUCTION

Methacrylic Acid Copolymer NF is available in three types i.e., A, B and C. Today, many pharmaceutical manufacturers use an aqueous dispersion of Methacrylic Acid Copolymer NF Type C for delayed release coating of tablets. However, one of the problems is the

development of cracks in the film when applied to hygroscopic tablets. The cracks in the film develop during storage (Figure 1) and are not observed during the coating or immediately after the coating process. Elevated temperatures and humidity affect crack formations in the film. In general, temperature and humidity fluctuates during the summer season. More cracks are observed in the films

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Figure 1 Cracks on the delayed release film of hygroscopic tablet cores.

applied to hygroscopic tablet cores during the summer season, especially in the tropics due to variations in temperature and humidity.

The potential causes for developing cracks on the delayed release film are believed to be associated with three main factors. These factors are (i) tablet core attributes, (ii) mechanical properties of the film, and (iii) coating process parameters. Generally, tablet core attributes and coating process parameters are studied extensively during formulation, scale-up and process development. However, the mechanical properties of the film and the stretching effect of the hygroscopic tablet cores are generally not considered during the development of the delayed release coating formulation and processing. Therefore, the typical consequences are market complaints, enormous resource and time involvement for trouble shooting, and even product recall. The mechanical properties of the film depend on the following factors:

- 1 Tensile strength which is the maximum stress applied up to the point at which the film specimen breaks.
- 2 Young's Modulus or elastic modulus which is a measure of the film stiffness which is the most basic and structurally important of all the mechanical properties. The elastic modulus is

the ability of the film to withstand high stress while undergoing little elastic deformation.

- 3 Strain or Elongation at Break (EaB) is the stretching of the film under applied stress. The strain is typically reported as percent elongation at the break. Elongation of a film generally increases as plasticizer to dry polymer is increased.
- 4 Glass transition temperature (T_g) is the temperature at which the mechanical behavior of a film changes from rubbery to glass or glass to rubbery state. Below this temperature, the polymer exists in a glassy state and is brittle. It is characterized by a substructure in which there is minimum potential for polymer chain movement. Above the T_g , the polymer is in a rubbery state, which is characterized by increased polymer chain movement and polymer elasticity.

Delayed release film coatings applied to hygroscopic tablet cores crack because of micro-level expansion and contraction in the tablet core or plasticization caused by moisture in the surrounding area. The expansion and contraction of the tablet core and further plasticization due to moisture contribute to an increase in the internal stresses and strains in the film. If the mechanical strength of the film is weak, it will exceed the EaB due to the stretching effects causing the film to crack. This article discusses the causes for film cracking e.g., the tablet core and coating formulation attributes together with the coating process parameters. However, the main focus of this paper is coating formulation attributes and ways to improve the mechanical strength of the film.

Tablet core attributes

A number of researchers, as well as, the authors' own experiences have confirmed that both the physicochemical properties such as hygroscopicity, viscoelastic recovery and hardness of the tablet core and the difference in thermal expansion coefficients of the tablet core and the coated film are associated with the

tablet cores, and contribute to development of cracks in delayed release films (1, 2).

Physicochemical properties

The physicochemical properties of the ingredients (i.e., the active pharmaceutical ingredient (API) and fillers) and tablet core hardness affect film cracking during storage. Hygroscopicity is an important physicochemical property of drug substances or major fillers which is thought to cause film cracking because the dimensions of the hygroscopic cores can change during storage. The probable reason for the change in the tablet dimension is attributed to a subsequent gain and loss of moisture from the tablet, which is triggered by the change in relative humidity (RH) (3). The tablet core changes dimension because of thermal expansion and moisture absorption at 30°C and 45% RH, and thermal expansion and water loss at 45°C and 20% RH (4). It is because moisture promotes hydration of any hygroscopic fillers resulting in a widening of the tablet core pore structure causing the core to swell and expand (5). Similarly, it is believed that, the removal of water contracts the core. The internal stress of the film increases due to the swelling and contraction of the core which weakens the film (6-8). Initially, the cracks in the film develop (i) at the filler-polymer interface and (ii) at the edge of the tablet. The explanation is, that the film thickness is thinner and the volumetric expansion is greater, at the edge of the tablet (9). Another reason is that the T_g of the a polymeric film is affected more by the hygroscopic nature of the core, than the pigment concentration (10). In addition, hygroscopic excipients such as microcrystalline cellulose, crospovidone, and copovidone undergo plastic deformation during compression. The viscoelastic recovery during relaxation changes the dimensions of such tablet cores. Therefore, the change of a tablet dimension is greater during storage than during the coating process. A high tablet hardness value can also affect film cracking due to weak film-substrate adhesion (11).

Dimensional changes of hygroscopic tablet cores are inevitable during the summer season in temperate climates and generally in the tropics. Therefore, testing tablet core hygroscopicity is important to prevent film cracking. Drop test and dynamic vapor sorption (DVS) are generally used to test the hygroscopicity of a tablet core. The simplest way to test the hygroscopicity of a tablet core is the drop test. One drop of coating dispersion is placed on top of the tablet. The spreading of the dispersion on the tablet surface is observed against time. The drop test also provides an approximation of spray rate and drying requirements, in addition to, the hygroscopicity of the tablet core. Spray rate and drying temperature are believed to influence film cracking. The DVS study indicates the percent water uptake at specific humidity.

The film coating cracks due to an increase in internal stresses in the polymer, especially if the mechanical strength of the film is not strong enough to withstand effects of stretching. Internal stresses within a film develop when polymeric dispersions are applied to solid substrates and due to the dimensional changes in the tablet core. There are three probable reasons for stress development during the coating process. The reasons are (i) shrinkage of the film upon solvent evaporation, (ii) generation of thermal stress due to the difference in thermal expansion of the substrate and film and (iii) volumetric stress as the substrate swells upon storage (12). Therefore, it is necessary to increase the mechanical strength of the film to withstand the stresses that develop during the coating process or changes in the dimensions of the tablet core. In addition, as a precautionary measure, a moisture barrier seal coating could be applied before the application of the delayed release coating to increase the mechanical strength of the film.

Differences in thermal expansion

Usually catastrophic film cracking occurs when the total internal stress of the film is close to

twice the tensile strength of the film (1). This is because the total internal stress of the film increases due to a wide variation in the expansion coefficients of the excipients in the tablet core and coating formulations (1, 13).

Film cracking due to differences in the excipient thermal expansion in the core and the coating film are generally seen during the coating process (Figure 2) rather than during storage.

COATING FORMULATION

Polymers

Methacrylic Acid Copolymer Dispersion NF Type C is a combination of Methacrylic Acid and Ethyl Acrylate at a ratio of about 1:1. It is an aqueous dispersion with 30% w/w solids. It contains 0.7% sodium lauryl sulfate (SLS) and 2.3% polysorbate 80 (vegetable origin) with respect to dry polymer as emulsifying agents (14, 15). Polysorbate 80 is incorporated to decrease the minimum film forming temperature (MFT).

Inherently, Methacrylic Acid Copolymer Dispersion NF forms a very brittle film due to its low elasticity. The viscosity, molecular mass, T_g , EaB and the hydrophilic nature of the copolymer affect its elasticity. The viscosity of the Methacrylic Acid Copolymer Dispersion NF is low (3-10 mPa.s), measured using a Brookfield viscometer) and the molecular mass is about 320,000 g/mole (15, 16). It has been reported that resistance to cracking increases due to the increasing effective tensile strength with increasing polymer viscosity and molecular mass (1, 17). T_g of the Methacrylic Acid Copolymer Dispersion NF is about 110°C, which drops to about 60°C with the addition of a plasticizer. The T_g of the formed film further drops to 41.9°C when stored at 52% RH for 1 month (18). The polymer generally behaves as a hard, brittle glass at temperatures below the T_g , whereas the mechanical properties of the polymer change to soft and flexible at



Figure 2 Cracks in the film created during the coating process.

temperatures above the T_g . T_g influences the molecular movement in the side chain followed by the polymer backbone, caused by heat applied during the coating process and during storage (16). The EaB of the Methacrylic Acid Copolymer film containing 10% w/w triethyl citrate (TEC) to dry polymer is about 1% increasing to about 7% with 15% containing w/w TEC (11, 16). The EaB decreases with increasing water uptake. Methacrylic Acid Copolymer Dispersion NF films are hydrophilic by nature i.e., water uptake of the Methacrylic Acid Copolymer film containing 20% w/w TEC at 60% RH is about 2% within 1 to 3 hours (18). The water vapor transmission rate (WVTR) containing 10% w/w TEC is about 100 g/(m².day) (16). Moisture adversely impacts the film structure as any absorbed water plasticizes the polymer resulting in an increased polymer chain mobility, deformation, elasticity and flexibility (19 - 21).

In delayed release film coatings, a certain film thickness is required for the desired release to occur. In addition, the WVTR of the film increases with decreasing film thickness, which is greater for hygroscopic tablet cores (22-24). Therefore, the amount of dry polymer to be applied per square centimeter surface area of the tablet and the film thickness are important parameters for hygroscopic tablet cores. The recommended weight of dry polymer for delayed release coating is 4-6 mg/cm² for round tablets (16, 25) and 5-10 mg/cm² for oblong-shaped tablets (16). The reasons for applying a specific amount of dry polymer per square

centimeter tablet surface area are to ensure that the release properties, and to achieve the required tensile strength and elastic modulus of the film. Based on the authors' experience it is possible to obtain enteric properties with about 3 mg/cm² of the dry polymer. The application of a low amount of polymer compromises the tensile strength and elastic modulus of the film. Hence, the mechanical strength of the film formed, using a lower amount of polymer, will be weaker compared to the recommended amount of the polymer. Another important factor is the weight gain of the coating. The film thickness is related to the weight gain of the coating. It may be possible to achieve delayed release with a 5% w/w weight gain of the coating with an average film thickness of 30µm - 45µm. However, such a film could be chipped off (breached coating) from the weakest surface due to mechanical stress during handling. The breached coating may not be seen during, or immediately after, the coating. In general, recommended weight gain of the coating for delayed release characteristics is between 8%- 12% w/w. The weight gain of the coating depends on the nature of the material, as well as, on the processing conditions. The spray droplets must spread on impact and coalesce to form an intact film. Temperature and relative humidity of the inlet air influence the coalescence of the spray droplets. A porous film is generally formed if the droplets are over dried before impacting the tablet surface.

Therefore, it is of utmost importance to optimize the polymer content in the coating formulation and weight gain of the coating for hygroscopic tablet cores. The purpose is to optimize the mechanical strength and to minimize the WVTR of the film using optimum film thickness. Failure to do so can result in film cracking of hygroscopic tablets during storage, especially at higher temperatures (30°C-45°C) and relative humidity (50 to 70% RH).

Plasticizers

Plasticizers serve several purposes when they are added to the coating formulations of Methacrylic Acid Copolymer Dispersion NF.

They can minimize film cracking by increasing the flexibility of the polymer, reduce brittleness, increase toughness and tear resistance, and allows the polymer molecules to move more easily which enhances the crack resistance of the film (16).

The mechanical properties of the film depend on the hydrophilic-lipophilic character and on the amount of the plasticizer added to the coating formulation. Plasticizers simultaneously reduce the T_g and increase the elasticity. The more hydrophilic the plasticizer is, the lower the resulting T_g (26). The EaB of the film increases with increasing plasticizer concentration. Formulations containing high plasticizer concentrations generally require lower processing temperatures and less time for film coalescence and curing. Therefore, high plasticizer content is beneficial in terms of production cost, as well as, the mechanical strength of the film. There are concerns with using higher amounts of plasticizer because they may cause coagulation of the dispersion making it difficult to spray. In addition, a high plasticizer content can contribute to sticking or agglomeration of the coated product during storage, compromising the release properties of the drug (16). The elastic modulus of the polymeric films decreases as the level of plasticizer increases for the water-soluble plasticizers. On the other hand, insufficient amounts of plasticizer do not prevent the formation of cracks in the film coating (1).

The plasticizers used in the Methacrylic Acid Copolymer Dispersion NF formulation are TEC, 1, 2 - propylene glycol (which may to some extent evaporate during coating and storage), polyethylene glycol (PEG 6000) and lipophilic dibutyl sebacate (11, 16). It is important to remember that moisture is also reported to be a superior plasticizer for Methacrylic Acid Copolymer Dispersion NF (18). The recommended, and most widely used plasticizer for Methacrylic Acid Copolymer Dispersion NF, is TEC which is hydrophilic by nature. TEC is a non-polymeric plasticizer

which evaporates along with the water during the coating and curing process, as well as, during storage. It has been reported that approximately 20% of TEC is lost during the coating process at an inlet temperature of 35°C increasing to approximately 35% at an inlet temperature of 65°C even though the boiling point of TEC is 288°C (27). This phenomenon could be explained by Dalton's laws of partial pressure. In a mixture of low boiling water, TEC or other oily liquids could be somewhat volatile. Therefore, inlet temperature during the coating process influences the evaporation of TEC. TEC is also lost through evaporation through any permeable packaging material at elevated temperatures (27). Hence, if the TEC concentration in the coating formulation is reduced, the film strength will be compromised as TEC will evaporate during the coating and curing processes. Such a film can easily crack due to the changes induced by temperature and RH during storage. Therefore, it is critical to optimize the plasticizer level in the coating formulation for hygroscopic tablets to reduce the brittle character of the film. Methacrylic Acid Copolymer Dispersion NF has a low elasticity and usually requires 5-20% w/w of plasticizer with respect to the dry polymer (16).

Insoluble excipients

Insoluble excipients are added to polymeric film coating formulations to prevent, or to reduce, agglomeration of the solids during the coating process, and product stickiness during storage. It has been reported that the inclusion of insoluble excipients in coating formulations restrict the mobility of the polymer chains (28). The decrease in the polymer mobility generally causes an increase in T_g and a decrease in tensile strength of the film (28). Therefore, the internal and thermal stresses of the film increases due to a change in T_g . These stresses act as a nucleus for crack propagation during storage. In addition, the amount of insoluble excipients in the coating formulation influences the amount of polymer in the coating

formulation. Higher concentrations of insoluble excipients in the coating formulation require greater amounts of polymer to completely surround the insoluble particles. The mechanical properties of the film, the appearance, and the permeability of the polymeric film change significantly once the critical pigment volume concentration (CPVC) is exceeded (29). The mechanical properties of the polymeric film decrease if the insoluble particles are not completely covered by the polymer. The crack resistance of the polymeric film decreases with an increase in insoluble excipients, irrespective of the type of excipients used (13). The reason for the decrease in crack resistance is attributed to the polymer-excipient interfacial bonding. It is believed that the polymer-excipient interfacial bonding is most likely dipole-dipole bonding, which is weaker, compared to hydrogen bonding, which holds the polymer molecular segments together (29).

The elastic modulus and adhesion of the polymeric film on the substrate influence film cracking. The particle morphology e.g., size and shape of the insoluble excipients and fillers added to the coating formulation influence the elastic modulus of the polymeric film (30). A lamellar shape causes the greatest increase in elastic modulus, followed by acicular-shaped particles, cubic particles and spherical particles. The greatest increase in the modulus occurred with the addition of talc and yellow or black iron oxide. The addition of aluminum lakes to film coating formulations resulted in small changes in the elasticity of the film.

The particle size of the insoluble excipients in film coating formulations affects polymer adhesion onto the substrate. Pigment particles embed themselves within the polymeric film and at the film-tablet interface, and thus disrupt interfacial contact between the film and the tablet surface (6). The adhesion of the polymeric film on the substrate is strong when smaller yellow iron oxide pigment was

incorporated into the film coating formulation compared to larger particles (31).

Antiadherents

Talc is commonly used as an antiadherent for Methacrylic Acid Copolymer Dispersion NF. It is obtained from natural sources and therefore, the quality and physical characteristics of talc, such as particle size, may vary depending on the supplier. Talc is hydrophobic by nature and therefore it is added to the formulation to take up any water. Talc may contain free iron ions and the magnesium in the talc can influence the pH of the coating solution. Talc is commonly used to reduce the stickiness or tackiness of the polymeric film. Relatively high amounts of talc (depending on the amount of dry polymer) are required to reduce the tackiness of a polymeric film. High amounts of talc may cause clogging of the spray nozzle and sedimentation. Additionally particle size affects nozzle clogging and sedimentation.

Glyceryl monostearate (GMS) could be used as an alternative to talc (32). It has been reported that, 5% GMS is as effective, as 50% talc in reducing the tackiness of several acrylic polymeric films (33). Coating process parameters (e.g., coating and curing temperature), and plasticizer content also influence the extent of stickiness and tackiness. In some cases, it can also affect dissolution. Particle size and shape of talc influences the tensile strength, elastic modulus, and CPVC value of the film (29). Talc increases the CPVC value of the film in comparison to the iron oxide pigmented film (34). Crack resistance of the film decreases with increasing CPVC value. The CPVC of the polymeric film produced using the coarser particle (surface area 2.99 m²/g) and finer particle (surface area 14.33 m²/g) of talc is 12.0–15.0% v/v and 25.0–35.0% v/v respectively (34). The CPVC value of talc was determined using the Brunauer–Emmett–Teller (BET) nitrogen adsorption. It has been reported that the platelet-like particles of talc tend to align

themselves parallel to the planar structure within the polymeric film (34). This alignment of the particles is thought to contribute to the relatively high CPVC values of the polymeric films. Internal and thermal stresses of the film increase due to an increase in the CPVC values and thus lead to the formation of cracks in the film. The particle size of talc also influences the WVTR of the polymeric film. The permeability to moisture of the polymeric film manufactured using larger particles (median particle size of 20.5 mm) is low compared to the finer particles (median particle size of 12.5 mm) of talc (35). The recommended typical amount of talc as an antiadherent is 25 – 100% w/w with respect to the amount of polymer (15).

Pigments

Two types of pigments i.e., opacifying agents (Titanium Dioxide (TiO₂)) and coloring agents are used in the coating formulation of Methacrylic Acid Copolymer Dispersion NF. Pigments significantly impact the mechanical, adhesive, and drug-release properties of the resulting film. Water vapor permeability of the polymeric film increases with increasing pigment concentration. This is because the polymer cannot hold the pigments together, resulting in the creation of a void, increasing permeability and decreasing the mechanical strength of the film (36, 37). Therefore, a greater coating thickness is required to ensure delayed release. There is a significant increase in the T_g of the Methacrylic Acid Copolymer film with increased concentration of TiO₂ when applied to hydrophilic tablets (10). The T_g of the Methacrylic Acid Copolymer Dispersion NF film coated on hydrophilic and hydrophobic tablets with 0% v/v TiO₂ with respect to the dry polymer is 36.5°C and 49.3°C whereas with 20% v/v with respect to the dry polymer is 49.3°C and 51.9°C respectively (10). Therefore, the tensile strength of the film decreases with increasing TiO₂ concentration as evidenced from the EaB. The EaB of the polymeric film produced using TiO₂ at 2% w/w concentration with respect to the polymer is

about 40%, decreasing to about 10% at 6% w/w concentration of TiO_2 (38). The reason for a decrease in the EaB is attributed to the CPVC value of the polymeric film produced using TiO_2 , which is 13.5 - 15.0% v/v (34). Film adhesion on the tablet surface increases, with an increase in the TiO_2 concentration until optimal concentration has been reached, after which film adhesion decreases. This is because exceeding the optimal concentration of TiO_2 increases the internal stress of the polymeric film causing weaker film adhesion. An increase in the internal stress and weaker film adhesion causes film cracking. The crack resistance of the polymeric film containing TiO_2 is greater compared with talc. This is attributed to the difference in particle shape of the talc (plate-like) and TiO_2 (round irregular) (13).

The commonly used lakes in the Methacrylic Acid Copolymer Dispersion NF formulations are yellow ferric oxide, red ferric oxide, and aluminum lakes i.e., Blue No. 1 and Yellow No. 6. A significant portion of the polymer is associated with the lakes, leaving less polymer available for film formation (29). The CPVC of the polymeric film containing the aluminum lakes is high compared to the iron oxide pigmented films. The rationale is that aluminum lakes are highly aggregated pigments with a large surface area which requires a lot of energy for dispersion. The aggregation of the aluminum lakes limits the external surface available to the polymer, leading to the relatively high CPVC value. The particles of both the insoluble colors i.e., yellow ferric oxide and red ferric oxide aggregate. A more open structure is formed by the yellow ferric oxide and is associated with fewer polymers compared to red ferric oxide (29). The CPVC values of the polymeric films produced using aluminum lake Yellow No. 6, yellow ferric oxide and red ferric oxide are 12.0–13.5 % v/v, 10.0 - 12.0 % v/v and 8.5–10.0% v/v respectively (34). The higher the CPVC values, the lower the mechanical properties of the polymeric film.

A large pigment concentration may cause coagulation of the anionic polymers e.g., Methacrylic Acid Copolymer Dispersion NF. This is because pH values below 5 influences the zeta potential of the spray suspension resulting in coagulation. To prevent coagulation of the polymer due to the impact of insoluble excipients and high plasticizer concentration the addition of 1 N NaOH or low viscous hydrocolloids such as Na-CMC is recommended to stabilize the dispersion before mixing it with the pigment suspension (16).

Optimizing the total insoluble excipients in the Methacrylic Acid Copolymer Dispersion NF tablet core formulation is one of the most critical considerations, especially when it is applied to hygroscopic tablet cores, to ensure the mechanical integrity of the film. Ideally, the insoluble excipients should range from 35 to 50% w/w of dry polymer, when applied to hygroscopic tablet cores. At this concentration the polymer completely covers the insoluble excipients as fewer polymers are associated with the insoluble excipients.

Solid contents and solvent system

The solids concentration governs solidification, which impacts the mechanical properties of the film. Diluting the Methacrylic Acid Copolymer Dispersion NF at a high concentration makes the solvent poorer. In a poor solvent there is much more intermolecular association of the polymer, but in a good solvent the polymer chains are free to move and are independent of each other (1). The poorer the solvent system (indicated by lower intrinsic viscosity), the lower the tensile strength and elastic modulus of the film (1). BASF, one of the manufacturers of Methacrylic Acid Copolymer Dispersion NF, recommend diluting the dispersion to a solid content of 20% w/w with a range of 15-30%, whereas Evonik recommends 15-25% w/w. Low solids content means more water in the final dispersion for spraying.

There are two concerns with excess water in the coating formulation. First, that the polymer will be excessively plasticized as the solids content in the coating formulation is low and water acts as plasticizer. Second is an increase in the total coating time. On the other hand, too high a solids content in the coating formulation is associated with film cracking (11). In addition to film cracking, a well-controlled coating process is needed to guarantee good film formation, and the high solids content can cause nozzle blocking (16).

Therefore, the total solids content in the coating formulation must be optimized for hygroscopic tablet cores to optimize the mechanical strength of the film and the total coating time. Ideally, the solids content in the Methacrylic Acid Copolymer Dispersion NF formulation of the hygroscopic tablet core should range between 20 and 22% w/w.

COATING PROCESS PARAMETERS

Four process parameters i.e., spray rate, atomizing air pressure, inlet air temperature, and RH of the inlet air have been reported to cause film cracking (11, 39). Temperature and absolute RH of the inlet air greatly affect the mechanical strength of the film. The inlet air temperature during the coating and curing processes influences the loss of TEC resulting in films with poor mechanical strength. The RH of the inlet air can affect the water evaporation rate, water penetration, surface roughness, total coating time, and polymer plasticization resulting in an increase in internal and thermal stress of the film making it weaker at the initial stage. A film formed with a lower mechanical strength cannot withstand the additional stress when exposed to heat and humidity during storage. The recommended absolute RH of the inlet air for a moisture labile drug is 5 g/m³ (40). The same absolute RH of the inlet air could be considered optimum for hygroscopic tablet cores to ensure optimal mechanical strength of the film. Therefore, it is important to optimize the total coating time. Temperature

and absolute RH of the inlet air, plasticizer concentrations and coating spray rate influence the total coating time.

CONCLUSIONS

The developments of cracks in delayed release film coatings during storage are mainly associated with the material attributes of the tablet core and coating dispersion formulations. Other factors, such as tablet core attributes (tablet hygroscopicity and hardness), temperature and absolute relative humidity of the inlet air during the coating and curing process also act as drivers for film cracking (Figure 3).

Inherently, Methacrylic Acid Copolymer Dispersion NF film is brittle due to its low elasticity. The mechanical strength of the film is generally compromised when the delayed release coating formulation of Methacrylic Acid Copolymer Dispersion NF is not optimized for the weight of polymer to be applied per square centimeter of surface, plasticizer amount, total insoluble excipients with respect to the dry polymer, and solids content. The EaB of the Methacrylic Acid Copolymer Dispersion NF film is about 1% with 10% w/w TEC with respect to the dry polymer. The polymer may not completely cover the insoluble excipients, if the formulation contains more than 50% w/w insoluble excipients to dry polymer. Less solids content in the formulations means more water. The excess water in the coating formulation can excessively plasticize the polymer resulting in further decrease in the EaB due to an increase in both internal and thermal stress. In other word, the poorer the solvent system, the lower the tensile strength and elastic modulus of the film will be. Therefore, the film formed with a non-optimized coating formulation is rigid and

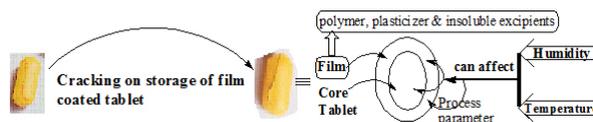


Figure 3 Factors affecting coated tablets that can cause the film to crack.

tough instead of soft and tough. The rigid and tough film cannot withstand the stress and strain when exposed to heat and humidity as the moisture further plasticizes the film resulting in an increase in both internal and thermal stress. Finally, total coating time using a non-optimized coating formulation will be longer which will impact the mechanical properties of the film, along with production costs.

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