Correlation of Free Salicylic Acid Content to the Water Vapor Transmission Properties of Aqueous Film Coating Systems

INTRODUCTION

Aqueous film coating of solid oral dosage forms is carried out for various purposes such as improvement of product aesthetics, packaging efficiency, patient compliance, swallowability, and stability. In drug product stability, film coatings have typically been used to protect the dosage form from the effects of ultraviolet radiation, moisture, and oxidation.

The performance characteristics that a fully formulated film coating system imparts to the dosage form are dependent on the raw material ingredients and their respective levels in the film coating system. These ingredients also determine the ease at which the system is applied in production. Success of the film coating system is achieved when an optimal balance is struck between the functionality it is intended to provide and the ease at which the system can be applied in production.

Protection of a dosage form from atmospheric moisture can be important in situations where the drug substance or drug product is negatively impacted by its presence. Issues can range from hydrolysis of the drug substance to changes in appearance or disintegration characteristics of the dosage form.

This study was conducted to investigate the water vapor transmission rate (WVTR) properties of common aqueous film coating polymers and fully formulated coating systems. It involved observing the characteristics of film coated Acetylsalicylic Acid (ASA) tablets in relation to the water-permeation properties of the coating system applied.

METHODOLOGY

1. Cast Film Preparation

All samples were dispersed via low shear mixing into distilled water for a period of 45 minutes. Applicable samples were stored for a period of time to allow for deaeration. Dispersions were cast with a BYK-Gardner knife onto Teflon-lined glass plates and allowed to dry overnight.

Prior to analysis, all samples were permitted to equilibrate at 25°C/50%RH for 48 hours. All film samples were cast to yield a dry film thickness of 0.1034 millimeters (0.004 inch/101.6 microns).

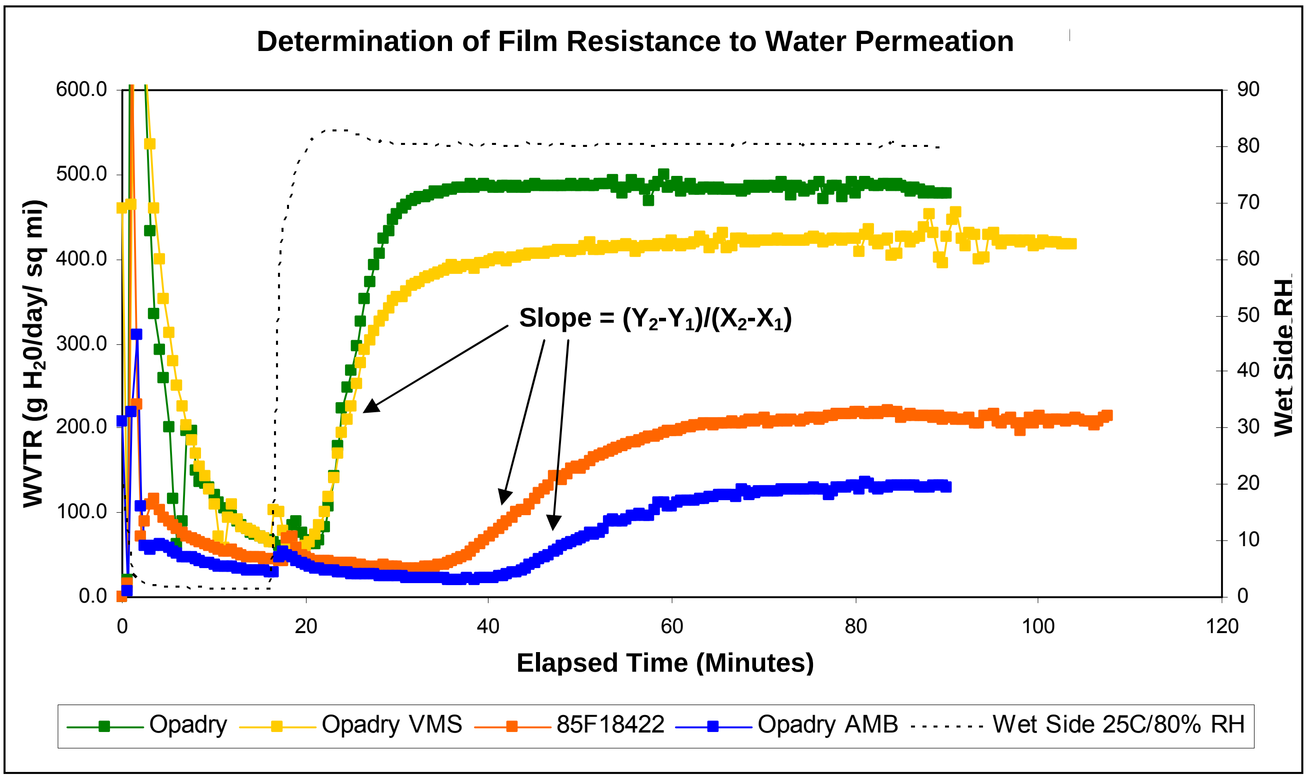
Hypromellose (HPMC), hydroxypropylcellulose (HPC), sodium carboxymethylcellulose (NaCMC), and polyvinyl alcohol (PVA) were the neat polymeric materials evaluated.

Opadry®, Opadry® amb, Opadry® VMS, and Opadry® II (85F series) were the fully formulated coating systems evaluated. It is important to note that Opadry amb and Opadry VMS are moisture barrier systems, with amb developed for the pharmaceutical market and VMS for the nutraceutical market.

2. Water Vapor Transmission Analysis

Samples were measured for WVTR on a WPA-100 Water Permeability Analyzer from VTI Corporation. Cast films were placed in a 6.39 square centimeter cell at a nitrogen flow rate of 200 cubic centimeters/minute. Each material was measured at 25°C/60%RH, 25°C/80%RH, and 40°C/75%RH conditions. The resistance of the film to water vapor permeation was calculated from the slope of the WVTR versus time plot, as seen in Figure 1.

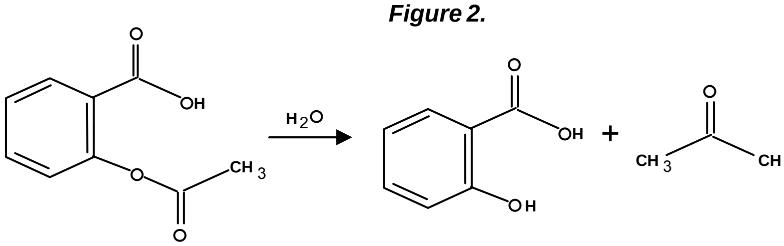
Figure 1. Determination of Film Resistance to Water Permeation



3. Tablet Film Coating

Acetylsalicylic Acid (ASA), which is susceptible to hydrolysis, was used to correlate the results obtained from the water permeation studies to the performance of the sprayed film on the surface of a tablet. Figure 2 shows the primary hydrolytic degradant that was monitored during the course of the stability study, Salicylic Acid.

Figure 2.



Acetylsalicylic Acid Salicylic Acid Acetic Acid

ASA tablets (325 mg) were aqueously film coated in a side-vented pan with one of two fully formulated coating systems to an actual four percent weight gain (determined gravimetrically). The choice of the systems was based on the fact that each system contained the same polymer as the primary film former, yet differed in the primary function for which each was optimized. Opadry amb was developed as an aqueous moisture barrier to provide moisture protection to hygroscopic and moisture-sensitive drug products. Opadry II (85F) is a problem-solver system created to enhance productivity and adhere to hydrophobic substrates, while still imparting fair moisture barrier properties.

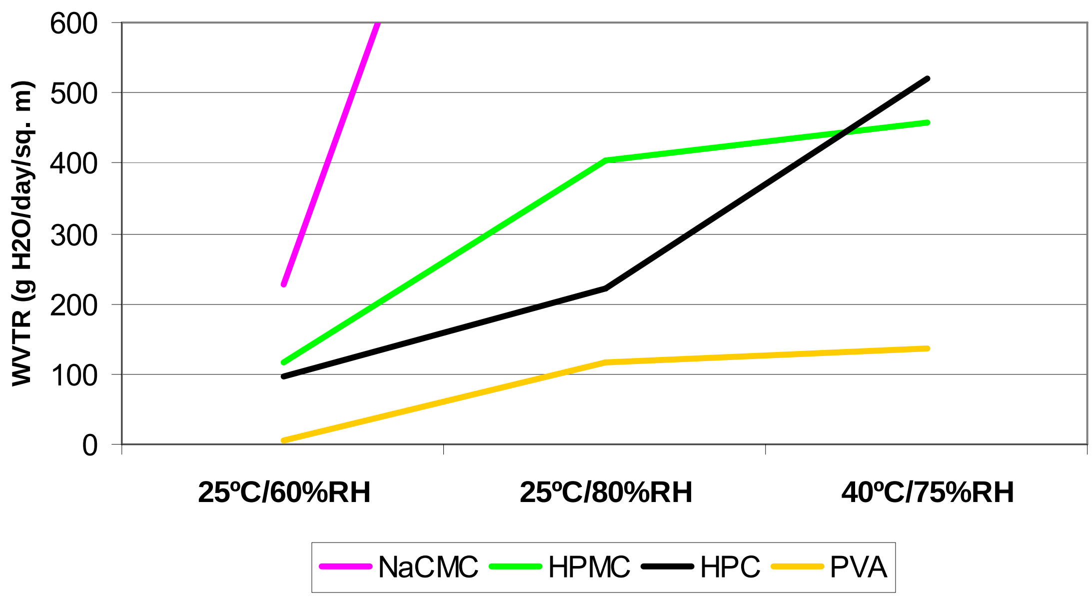
RESULTS

1. Neat Polymer — WVTR Properties

Experimental results indicated that at 25°C/60%RH or 25°C/80%RH, the order of moisture barrier protection is: PVA > HPC > HPMC >> NaCMC. When tested at 40°C/75%RH conditions the order is: PVA > HPMC > HPC>> NaCMC.

The WVTR properties of PVA are similar, at 25°C/80%RH and 40°C/75%RH, indicating excellent resistance to the transport of moisture at accelerated conditions.

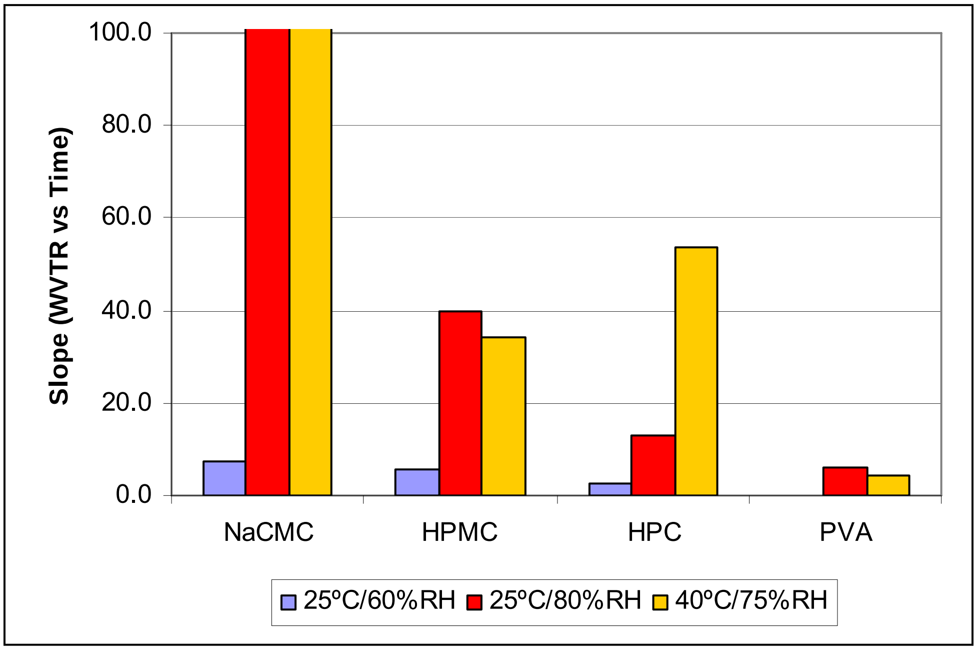
Figure 3. Neat Polymer — WVTR Properties



2. Neat Polymer Moisture Permeation Resistance

The order of film resistance to permeation at 25°C/60%RH or 25°C/80%RH is: PVA > HPC > HPMC >> NaCMC. When tested at 40°C/75%RH conditions, the order is: PVA > HPMC > HPC >> NaCMC.

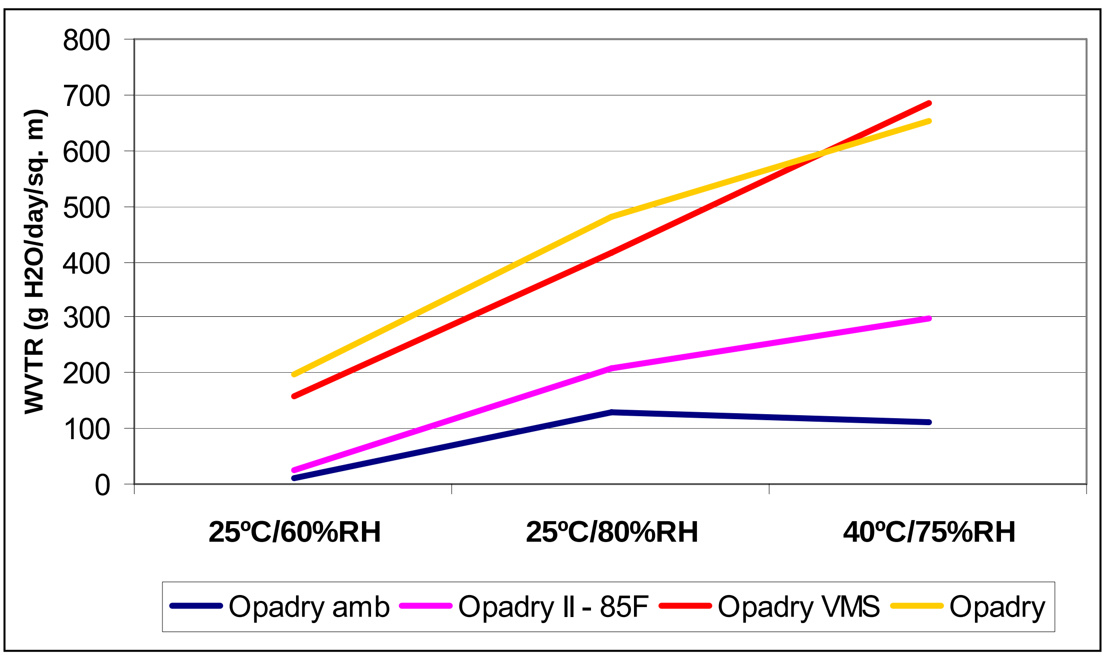
Figure 4. Neat Polymer Moisture Permeation Resistance



3. Coating Formulation — WVTR Properties

WVTR results at multiple conditions highlight the order of moisture barrier protection as follows: Opadry amb > Opadry II – 85F > Opadry VMS ≡ Opadry

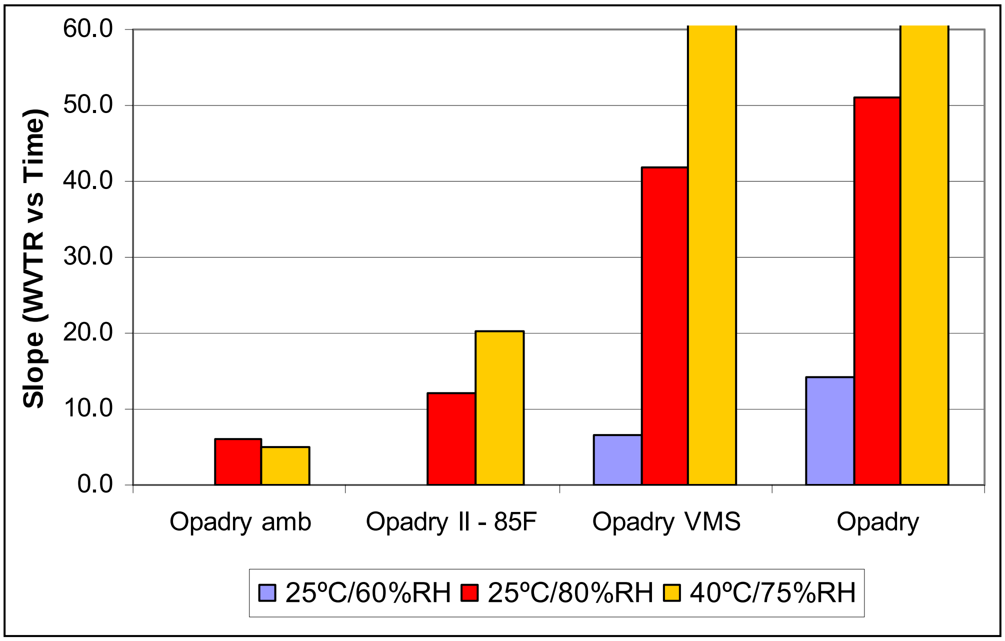
Figure 5. Coating Formulation — WVTR Properties



4. Coating Formulation Moisture Permeation Resistance

The order of film resistance to permeation at the conditions tested for the fully formulated coating systems is: Opadry amb > Opadry II – 85F > Opadry VMS > Opadry

Figure 6. Coating Formulation Moisture Permeation Resistance

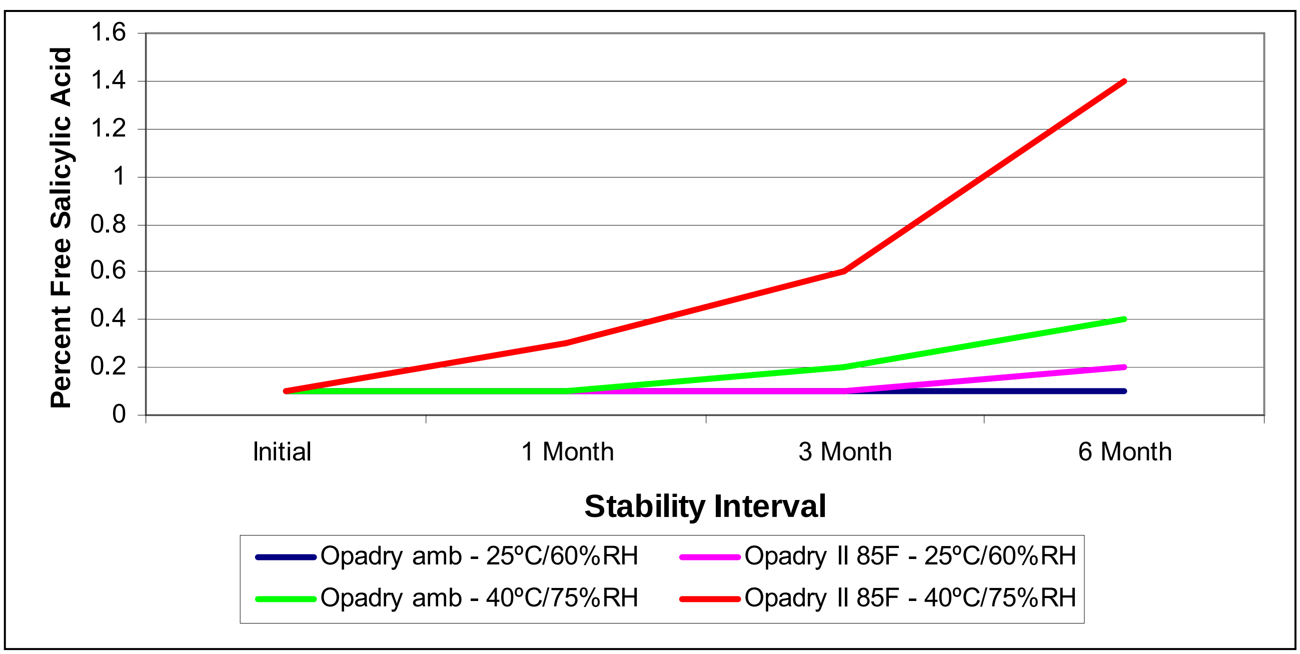


5. ASA Tablet — Free Salicylic Acid Content

WVTR results at 25°C/60%RH conditions indicate that two coating formulations have very high resistance to water vapor permeation. This correlates well with free Salicylic Acid (FSA) levels through six months at this condition. Virtually no change is observed from zero to six months for both coating formulations.

At 40°C/75%RH testing conditions, the WVTR of Opadry II (85F) is higher than Opadry amb by a factor of three. When comparing the FSA levels of Opadry II (85F) to those of Opadry amb at all stability intervals, the results differ by a factor of three.

Figure 7. ASA Tablet — Free Salicylic Acid Content



Both coating systems provided adequate protection through six months at 40°C/75%RH to comply with the USP specifications for FSA content and dissolution.

CONCLUSIONS

WVTR analysis was successfully employed to characterize the barrier properties of neat polymers and fully formulated aqueous film coating systems.

Opadry amb, Opadry II (85F), and Opadry VMS yielded higher resistance to water permeation than traditional Opadry systems.

Free Salicylic Acid levels of ASA tablets coated with Opadry amb and Opadry II (85F) correlated very well to WVTR values at 25°C/60%RH and 40°C/75%RH.

Thus, aqueous film coating systems can be successfully employed to protect a dosage from the effects of moisture.

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