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Evaluation of Moisture Sorption Methods for Aqueous Moisture Barrier Coatings

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Introduction

Moisture is the most deleterious environmental factor with regard to chemical stability of actives (Monkhouse, 1984). Protection from environmental moisture is therefore an important concern in formulation development. Additionally, solid dosage forms containing elevated levels of residual water frequently exhibit physical changes such as altered dissolution, which can be associated with moisture-induced changes in crystal structure. The mechanism by which moisture exerts such physical and chemical changes generally entails adsorption of water vapor onto solid surfaces, with preferential location in amorphous domains, e.g. crystal lattice defects and amorphous polymers. The high concentration of water in these regions, acts as a potent plasticizer, enhancing molecular mobility.

On the macroscopic level, gross changes in mechanical properties, e.g. hardening of tablets, partial swelling or disintegration, adhesion of dosage forms to each other and microbial spoilage are also possible. Well-known examples of moisture sensitive actives include aspirin, ranitidine, temazepam, most vitamins and numerous herbals.

Formulators frequently guard against these unwanted effects by applying a moisture barrier coating to the affected dosage form. Traditionally such barrier coatings were based on combinations of hydrophobic or lipophilic additives and hydrophobic film forming polymers such as shellac, cellulose acetate phthalate (CAP) and ethyl cellulose. While effective, such systems require use of organic solvents with the attendant need for extensive environmental and safety precautions and costs. Additionally, the potential delay of drug dissolution caused by the hydrophobic barrier is frequently a concern. To overcome these shortcomings, water-dispersible moisture barrier coating systems have increasingly gained favor.

For rational development of moisture barrier systems, a fundamental understanding of compositional factors that affect rate and extent of moisture sorption is important. This understanding allows for appropriate choices and levels of pigments, fillers, polymers, plasticizers and other additives. The objectives of this study were therefore to a) establish suitable methods to assess water vapor resistance of coatings, b) screen potential coating components for their barrier properties and c) develop an experimental, water-dispersible moisture barrier coating and compare to commercially available systems.

Experimental methods

Two methods were compared for their suitability to measure water repellency of barrier film coatings. These were direct gravimetric measurement of moisture sorption rates on coated and uncoated tablets exposed to various relative humidities, and measurement of water vapor transmission rate of free films.

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Moisture sorption rates on coated tablets: Hygroscopic tablets (400 mg) comprising 5% croscarmellose as a hygroscopic wicking agent, 10% copper sulfate as a hygroscopic, hydrate-forming, model active and colorimetric moisture indicator and q.s. microcrystalline cellulose were compressed on Manesty™ Beta press. An additional model formulation comprising 325 mg aspirin was also evaluated. The tablets were coated in a O'Hara Labcoat™ IIX coater equipped with a 15" perforated pan. Tablets were coated to 4 and 5% weight gain. Moisture uptake by uncoated and coated tablets was measured gravimetrically following the exposure to 75% relative humidity (RH) at 25°C. Compositional film coating variables included hygroscopicity of film forming cellulose polymer, inclusion of water-soluble plasticizers and inclusion of inorganic and lipophilic additives.

Water vapor transmission rate (WVTR) of free films: Free films were cast onto glass plates. After equilibrating at 50% RH and room temperature, the water vapor transmission rate was measured using ASTM procedure E96 as follows: a film sample is sealed to the open mouth of a test dish containing desiccant. The assembly is then stored at 50% RH for 48 hours. The test unit is weighed periodically and the weight is plotted as a function of time. WVTR is calculated from the following equation:

$$WVTR = G/t\,\frac{x}{A.} = \frac{g.mm}{(m^2)(24\ Hour)}$$

Where, G is the weight gain in time, t, A is the area of exposed film and x is the film thickness.

Comparisons with commercially available coating systems: Based on an understanding of fundamental compositional factors a novel water-dispersible moisture barrier system, Aquarius™ experimental moisture barrier coating system, was developed. Copper sulfate and aspirin tablets were coated with white pigmented versions of Aquarius experimental moisture barrier coating system, Opadry™ AMB complete film coating system, and Sepifilm™ LP 770 film coating system. Moisture barrier properties were assessed using the gravimetric moisture sorption method at 75% RH and 25°C. In addition general coating performance parameters such as coating times, % solids and appearance characteristics were evaluated.

Materials

1. Aquarius experimental moisture barrier coating system, White, marketed by Aqualon a Business Unit of Ashland Inc., Wilmington, DE.
2. Opadry AMB complete film coating system, White, marketed by Colorcon, Inc. of Westpoint, PA.
3. Sepifilm™ LP 770 film coating system, White, marketed by Seppic, a subsidiary of Air Liquide, of Paris, France.
4. Klucel™ pharm hydroxypropylcellulose, marketed by Aqualon a Business Unit of Ashland Inc., Wilmington, DE.
5. Benecel™ pharm hypromellose, marketed by Aqualon a Business Unit of Ashland Inc., Wilmington, DE.
6. Aqualon sodium carboxymethylcellulose pharm, marketed by Aqualon a Business Unit of Ashland Inc., Wilmington, DE.
7. Cupric sulfate anhydrous, marketed by Spectrum Chemicals, Gardena, CA.
8. Ac-Di-Sol™ croscarmellose sodium, NF, marketed by FMC Corporation, Philadelphia, PA.
9. Microcrystalline cellulose: Avicel™ PH-102 Microcrystalline cellulose, NF, marketed by FMC Corporation, Philadelphia, PA.
10. Acetyl salicylic acid, USP, marketed by Ria International, East Hanover, NJ.
11. HyQual™ magnesium stearate, NF, marketed by Mallinckrodt Inc., a Division of Tyco International, St. Louis, MO.
12. Cab-O-Sil™ amorphous fumed silica (colloidal silicon dioxide), NF, marketed by Cabot Corporation, Tuscola, IL.
13. Hystrene™ 5016 NF Stearic acid, marketed by CK Witco, Memphis, TN.
14. Pregelatinized corn starch, Spress™ B820, marketed by Grain Processing Corporation, Muscatine, IA.
15. Lactose monohydrate, NF: Lactose Fast Flo, marketed by CHR Hansen, New Berlin, WI.

Results and Discussion

1. Influence of Film Composition

Effect of Hydrophilicity of the Film Forming Polymer: Film WVTR testing on neat polymer films indicates that moisture transmission is directly proportional to the hydrophilicity of the film forming polymer employed and follows the following rank order: Sodium carboxymethylcellulose (CMC)>> hypromellose (HPMC)>> Hydroxypropylcellulose (HPC) (Figure 1a). For reference, equilibrium moisture content at 75% RH, 25°C is approximately 25%, 15% and 11% for CMC, HPMC and HPC respectively. Similar behavior was reported by Okhamafe and York (2). A possible explanation is that the hydrophilic polymers interact strongly with water molecules, resulting in increased moisture sorption and plasticization, which in turn increases the diffusion constant for water vapor. Since WVTR is a product of the diffusion rate constant and the solubility coefficient, WVTR increases significantly. It is therefore apparent that the more hydrophilic the film is, the greater is the permeability to moisture. Copper sulfate tablets coated with pure polymer show the same trend with less moisture uptake into HPC coated tablets relative to HPMC coated tablets (Figure 1b).

Effect of Inorganic Additives: Figure 2a shows that inclusion of an inorganic additive with plate-like morphology in HPC free films resulted in further reductions in film WVTR. It appears that the platy particles align perpendicular to the direction of the draw down. However, when applying analogous coating compositions onto copper sulfate model tablets, the moisture uptake increased for tablets that were coated with the combination of HPC and platy inorganic additive (Figure 2b). This divergence between results from free film WVTR studies and coated tablet moisture uptake could be due to different film formation processes. During casting of free films the inorganic platy additives align in the direction perpendicular to the drawdown, thereby increasing the tortuosity of the diffusion path. The film formation during pan coating occurs through sequential droplet deposition followed by rapid drying with increased likelihood of random alignment of any insoluble particulates. These randomly aligned inorganic additive particles would therefore tend to act as locators for film defects rather than as a diffusion barrier.

Effect of Lipophilic Plasticizers: A divergence in results between free film and coated tablet moisture uptake data was also seen for lipophilic, water-insoluble plasticizers. Free film WVTR testing showed that the inclusion of lipophilic plasticizers to the polymer slightly reduces the water vapor transmission (Figure 3a). On the other hand, tablets coated with solution of polymer with lipophilic plasticizers had an opposite effect and showed no improvement in the barrier properties (Figure 3b). It is possible that phase separation occurred during the high shear atomizing spray application in the coating pan. Low MW lipophilic plasticizers have no effect on the barrier properties.

Effect of Water Soluble Plasticizers: As shown in Figure 4a, presence of water-soluble plasticizer is detrimental in free films, whereas water soluble plasticizer had only marginal effect on the moisture uptake of coated copper sulfate tablets (4b).

2. Performance comparisons

Comparison of moisture uptake rates: Aquarius experimental moisture barrier provided similar moisture barrier functionality on coated copper sulfate tablets when compared to Opadry™ AMB (Figure 5a). Sepifilm™ LP770 allowed significantly more moisture uptake. Figure 5b shows that on the aspirin formulation, the Aquarius experimental moisture barrier performed significantly better than Opadry AMB.

General coating performance: Processing conditions for each coating system were optimized for the particular tablet formulation and coating pan configuration at hand.

As shown in Table 1, Aquarius experimental moisture barrier can be sprayed at 20% solids versus the 12-15% of Sepifilm™ LP770, and can be coated much faster as a result.

Although Opadry AMB can also be sprayed at high solids; the tackiness of the coating limits the application speed. Aquarius experimental moisture barrier can be applied at nearly twice the spray rate of Opadry AMB system.

Conclusions

Based on a study of compositional variables, a novel, water-dispersible moisture barrier coating system has been developed. This system has improved barrier function and processing efficiencies as compared to other commercially available coating systems.

Additionally, this study highlights the importance of selecting appropriate test methods. WVTR measurement on free films provided largely contradictory data when compared to actual moisture uptake of coated tablets. Free film testing is widely used to assess gas permeability of coatings in a variety of applications; however results should be used cautiously in the context of spray-coated tablets.

References:

1. Monkhouse, D. C, Drug Dev. Ind. Pharm., 10 (1984) 1373-1412.
2. Okhamafe, O.A et al, Pharm Acta Helv, 60 (3), 1985

Table 1: Coating Parameters for Aquarius™ experimental moisture barrier coating system and other commercially available barrier systems (All were white pigmented systems, coated in a O'Hara Labcoat IIX Coater 15" Coating Pan)

Parameters	Aquarius Experimental Moisture Barrier Coating System	Opadry AMB	Sepifilm™ LP770
% Solids	19	20	14
Viscosity (cps)	341	230	448
Spray Rate (g/min)	20	10	20
Coating Time for 5 % weight gain (min)	39	75	54
Coating Time for 4% weight gain (min)	32	60	43
Bed Temperatures (°C)	40-45	55-59	40-45
Atomization Air Pressure (PSI)	20	45	20

Figure 1a
Effect of polymer hydrophilicity on WVTR of neat polymer films.
The rank order for hydrophilicity is CMC> HPMC >HPC.

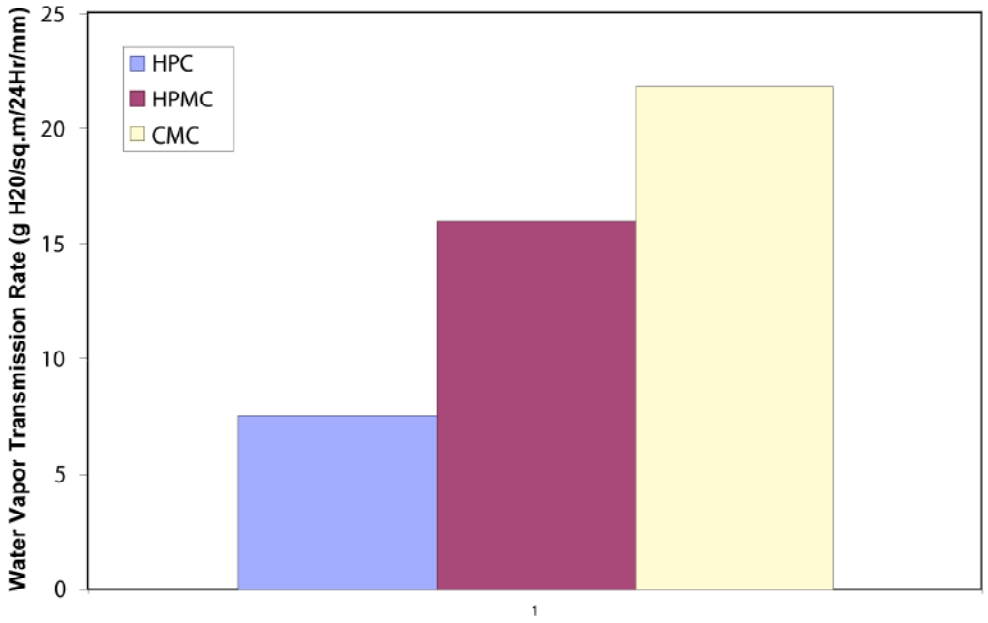

Figure 1b
Effect of polymer hydrophilicity on moisture uptake of copper sulfate tablets coated with polymer only.
HPMC is more hydrophilic than HPC.

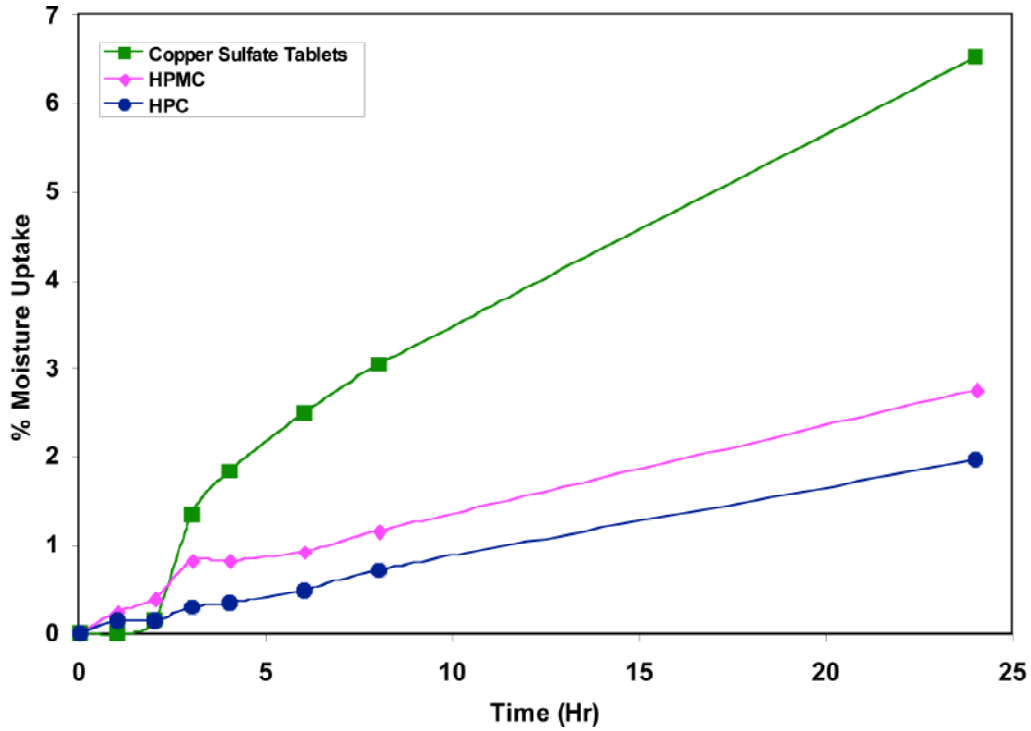

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Figure 2a
Effect of including an inorganic, platy additive on the WVTR of HPC films

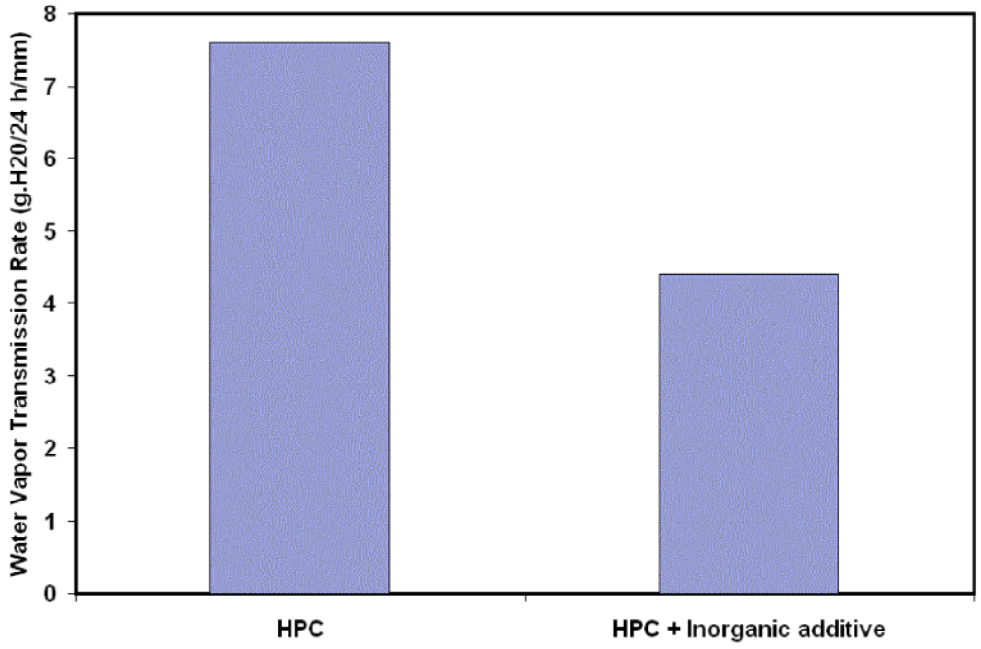

Figure 2b
Effect of including and inorganic platy additive
on moisture uptake of coated copper sulfate tablets

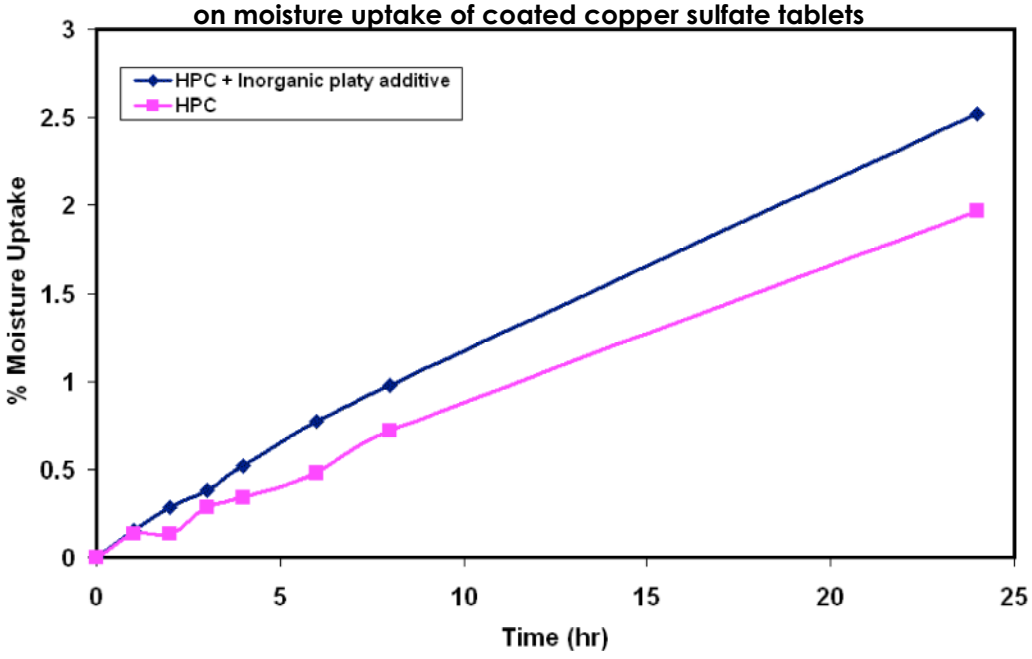

Figure 3a
Effect of lipophilic plasticizer on WVTR of HPC and HPMC films

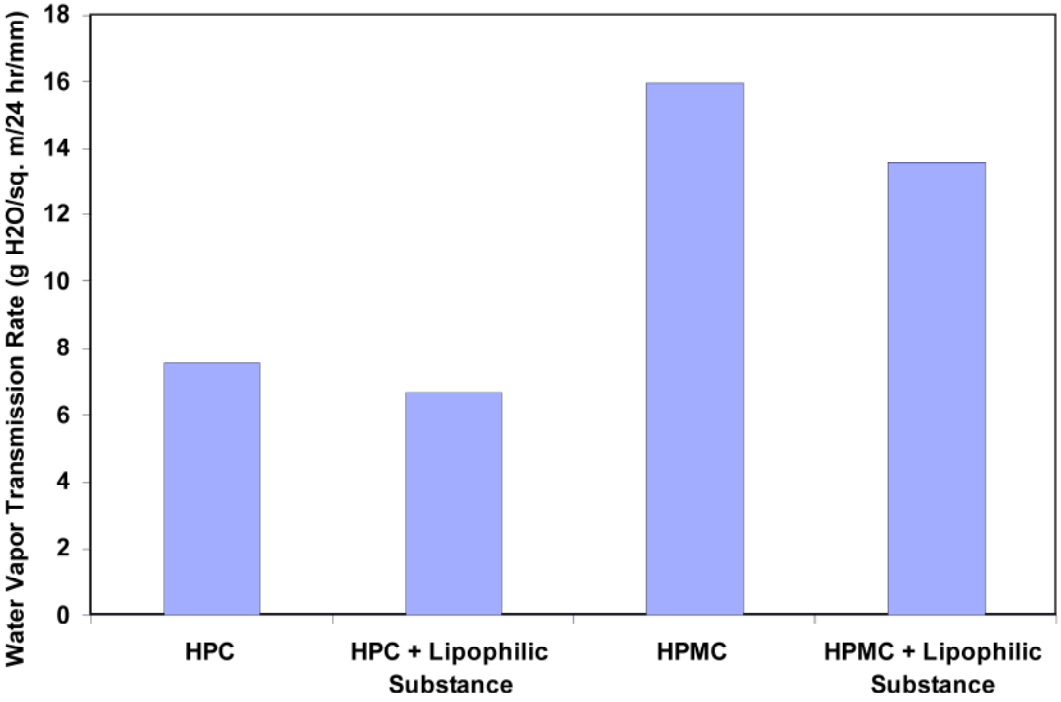

Figure 3b
Effect of lipophilic plasticizer on moisture uptake of coated copper sulfate tablets

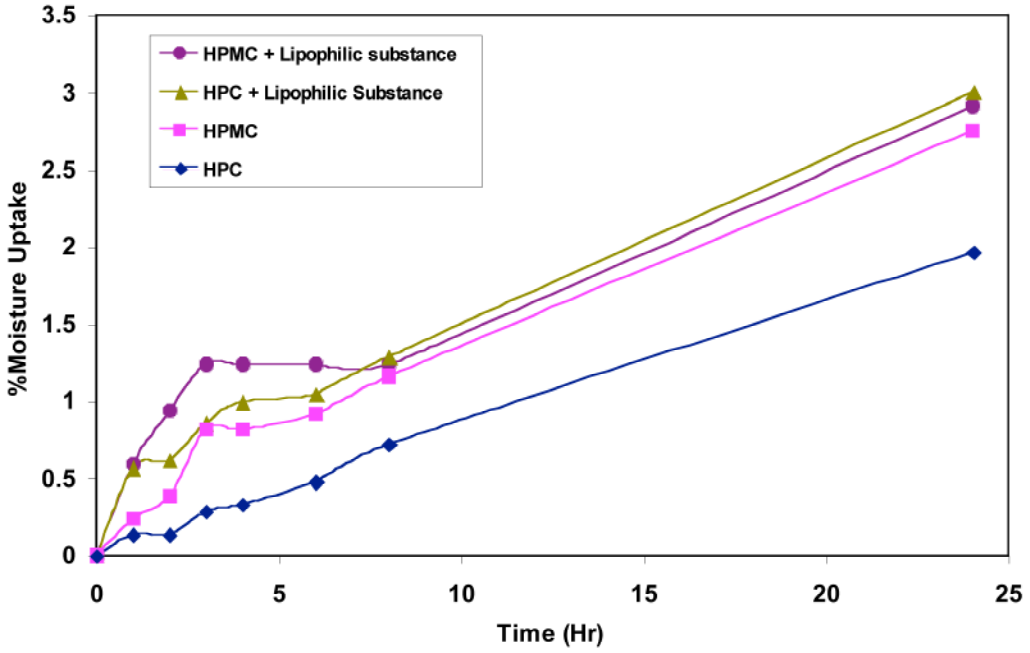

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Figure 4a
Effect of water soluble plasticizer on WVTR of free films

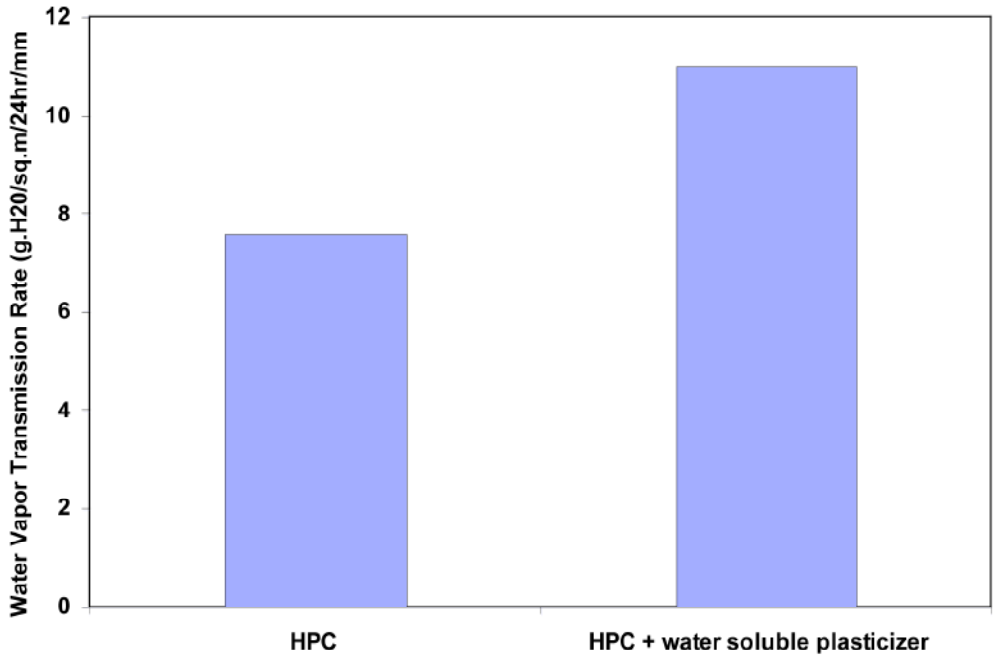

Figure 4b
Effect of water soluble plasticizer on moisture uptake of coated copper sulfate tablets

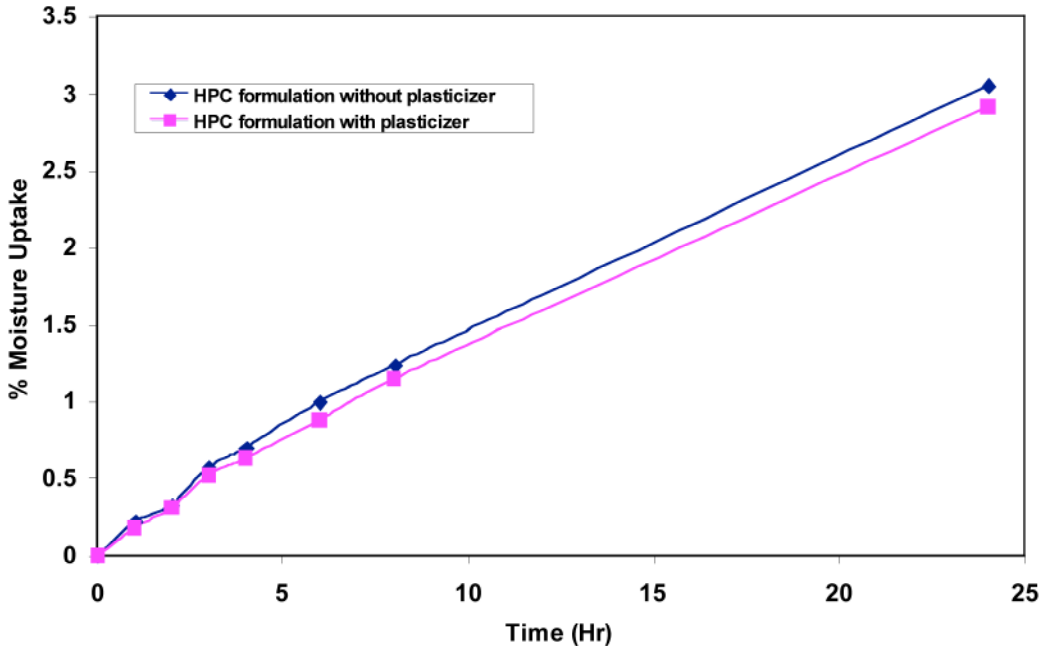

Figure 5a
Comparison of Aquarius™ experimental moisture barrier coating system to commercial moisture barrier systems. Copper sulfate tablets were coated to 5% weight gain on a O'Hara Labcoat IIX, 15" pan.

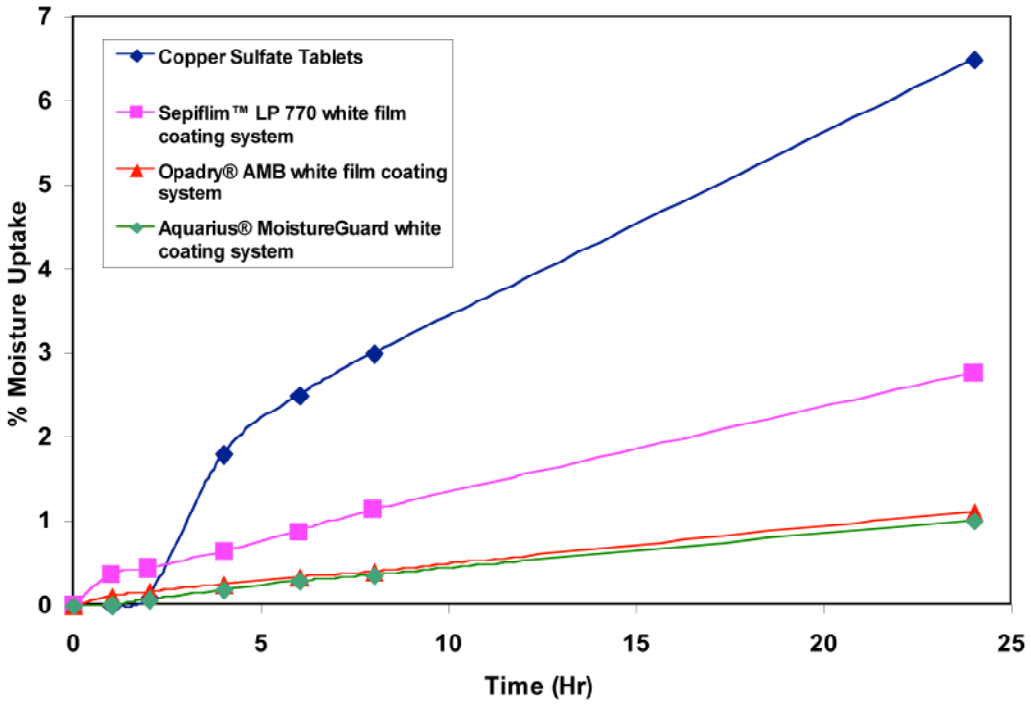

Figure 5b
Comparison of Aquarius experimental moisture barrier coating system and other marketed moisture barrier systems. Aspirin tablets were coated to 4% weight gain on a O'Hara Labcoat IIX, 15" pan.