Reducing Coated Tablet Defects from Laboratory through Production Scale: Performance of Hypromellose or Polyvinyl Alcohol-Based Aqueous Film Coating Systems

INTRODUCTION

The purpose of this study was to investigate the effect of film coating formulations in reducing or preventing coating defects on a soft and friable multivitamin tablet. Pigmented, fully-formulated film coating systems, containing either hypromellose (HPMC) or polyvinyl alcohol (PVA) as the base polymers, were used in the study. The effects of pan speed and scale-up were also investigated as both may have detrimental impact when coating tablets of poor mechanical strength.

METHODS

Multivitamin tablets 1000 mg, (7.2kp breaking force, 1.2% friability) were chosen as the substrate. The coating systems evaluated were hypromellose-based Opadry®, complete film coating system (03B50680), and polyvinyl alcohol-based Opadry® II,high performance film coating system (85F90618), both supplied by Colorcon.

The tensile strength (MPa) of the coating formulations was determined using an Instron Mini 44 materials analyzer on cast films of 10 cm (L) x 1 cm (W) with a film thickness of 0.2 – 0.025 cm (n=10). The films were allowed to equilibrate for 24 hr. at 23°C/50% RH prior to testing. Both coating formulations were also coated onto flat-faced placebo tablets (3.0% applied weight gain) and the film removed from the surface of the tablets (n=10) using the Instron Mini 44 to determine the adhesion (kPa) characteristics of the coatings. Viscosity measurements were made using a Brookfield LV-DVII digital viscometer at solids concentrations in water of 10.0,12.5, 15.0, 17.5, and 20.0% w/w.

Color development and uniformity testing were performed using a Diano Color Products Milton Roy Colormate employing the Commission Internationale de l'Eclairage (CIE) L* a* b* system. Total color difference from target reference was determined by calculating the distance between two points in the color space using the following equation:

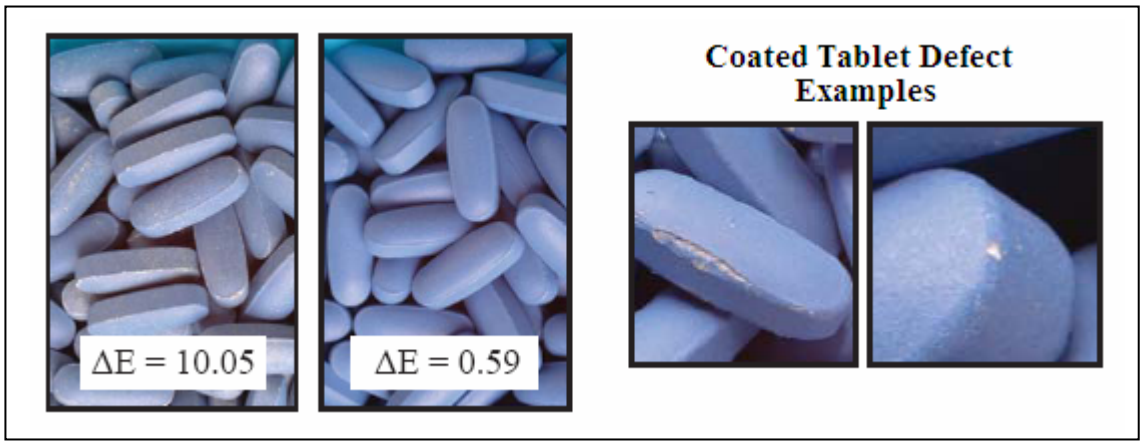
$$\Delta E^* = [(L^*1 - L^*2)^2 + (a^*1 - a^*2)^2 + (b^*1 - b^*2)^2]^{1/2}$$

The standard deviation of color difference between calculated ΔE values of the individual tablets from each set of samples were compared as a measure of coating uniformity.

To calculate defect rates, tablet samples (n=100) were taken every 5 minutes after 1.5% applied WG and individually inspected for any imperfection in the coating where the core was exposed.

Figure 1. Color Development Examples

ΔE ≤ 1.0 = no visual difference



The laboratory-scale coating trials were conducted in 24" full-perforated pan (O'Hara Technologies Labcoat II). Production-scale trials were conducted in a 48" fully-perforated pan (O'Hara Technologies Fastcoat). Both pans were fitted with 1.0 mm spraying systems VAU anti-bearding spray guns. The target coating weight gain for all trials was 3.0%.

The HPMC-based Opadry was applied to the tablets at the maximum recommended solids concentration of 15%. The PVA-based Opadry II was applied at the recommended 20% solids concentration.

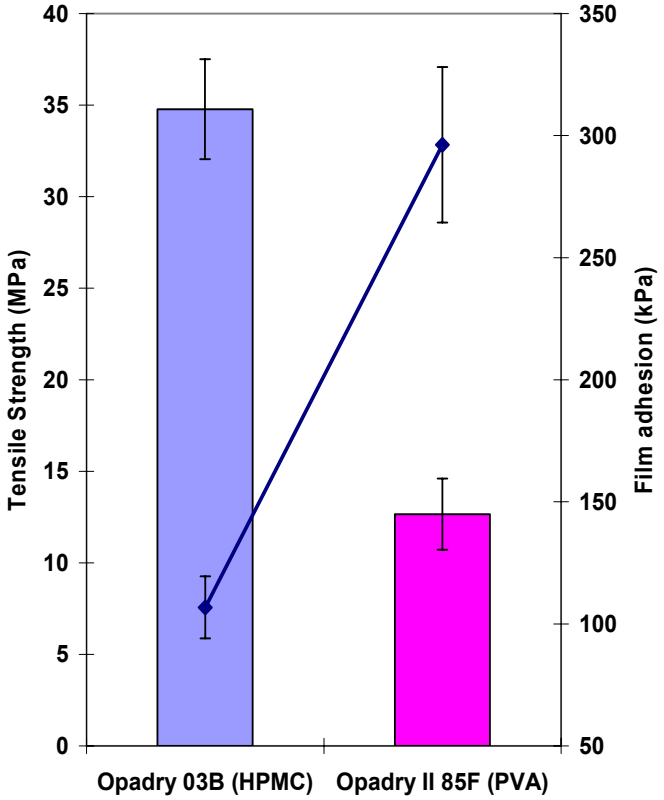
On laboratory scale, the influence pan speed was evaluated at high and low settings for each coating formulation. On production scale, the pan speed target was scaled (via linear pan wall velocity) based on the laboratory scale pan speeds that produced the best overall results with regard to defects.

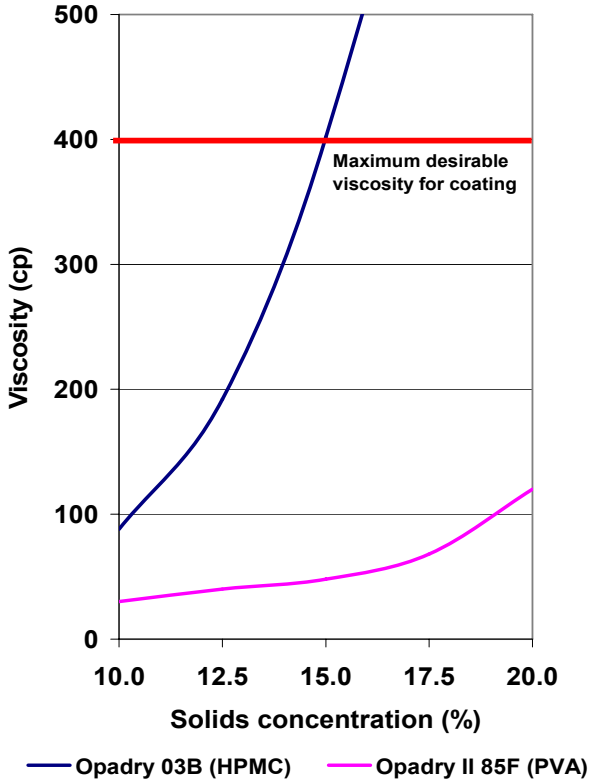
Table 1.

Coating Trial	1	2	3	4		5	6
Polymer system	HPMC	HPMC	PVA	PVA		HPMC	PVA
Pan diameter (in/*cm*)	24/*61*	24/*61*	24/*61*	24/*61*		48/*122*	48/*122*
Pan load (kg)	20	20	20	20		180	180
Solids conc. (%)	15	15	20	20		15	20
Pan speed (rpm)	8	14	8	14		4	7
Spray guns (number)	2	2	2	2		4	4
Spray rate (g/min)	60	60	60	60		430	430
Bed temperature (ºC)	45	45	45	45		45	45
Air flow (f³min / *m³hr*)	250/*425*	250/*425*	250/*425*	250/*425*		1800/*3060*	1800/*3060*
Atomizing air (psi / *bar*)	30/*2.1*	30/*2.1*	30/*2.1*	30/*2.1*		45/*3.1*	45/*3.1*
Patterns air (psi / *bar*)	20/*1.4*	20/*1.4*	20/*1.4*	20/*1.4*		30/*2.1*	30/*2.1*

RESULTS

Coating Formulation Film Analysis and Viscosity Profiles



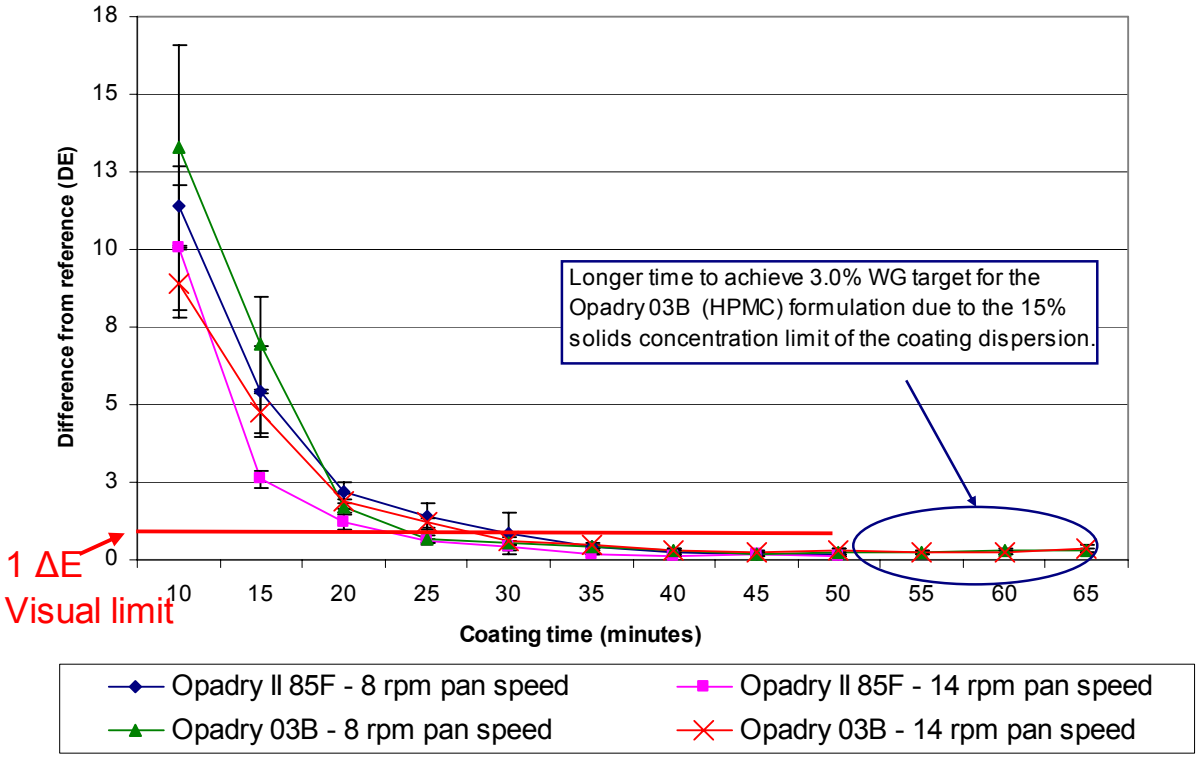


Historically, film strength has been shown to be a critical attribute in reducing the incidence of coated tablet edge defects.[1] It is also recognized that film adhesion plays an equally important role and a robust coating formulation must balance each of these factors.[2]

Film testing showed that the HPMC-based Opadry coating system exhibited substantially higher film strength than the PVA-based Opadry II. Conversely, the PVA-based Opadry II exhibited three-fold higher film adhesion compared to the HPMC based system.

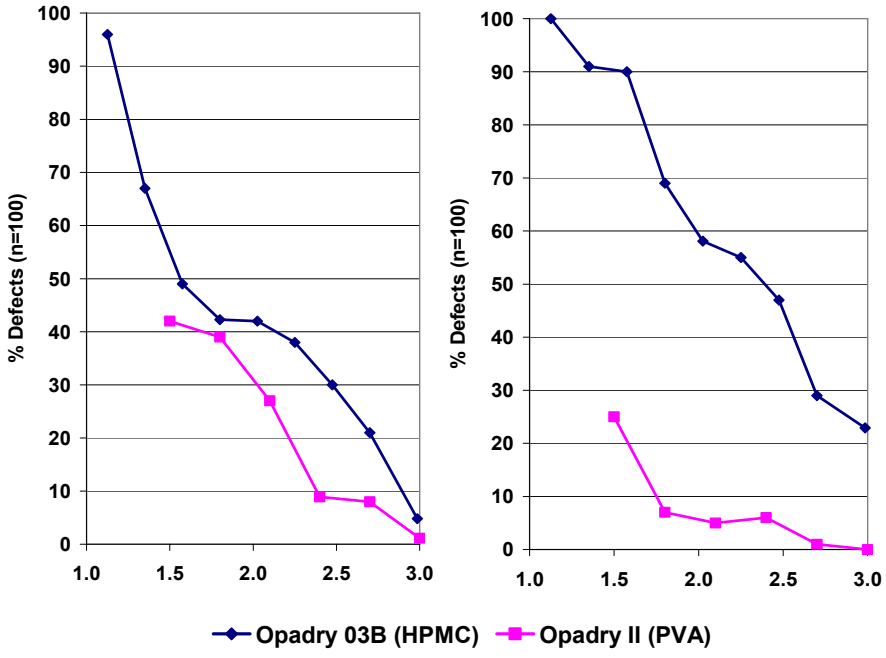
The PVA-based coating system also exhibited very low viscosity compared to the HPMC-based system. The low viscosity of this system enables a higher solids concentration of coating to be delivered to the tablets resulting in faster protection of the tablets and shorter process times.[2] Lower viscosity coating formulations can also be beneficial in terms of more efficient atomization, less build-up of material on the spray guns and ease in pumping.

Figure 2. 24" Scale- Color Development and Uniformity



Color development data exhibited similar trends across the four laboratory scale trials. At early stages in the trials (10-15 min), higher pan speeds were seen to improve color uniformity. Both the HPMC-based and PVA-based coating systems achieved target color and uniformity in ~40 minutes. The HPMC-based took 15 minutes longer to reach the target 3.0% weight gain due to the reduced solids concentration of the coating suspension.

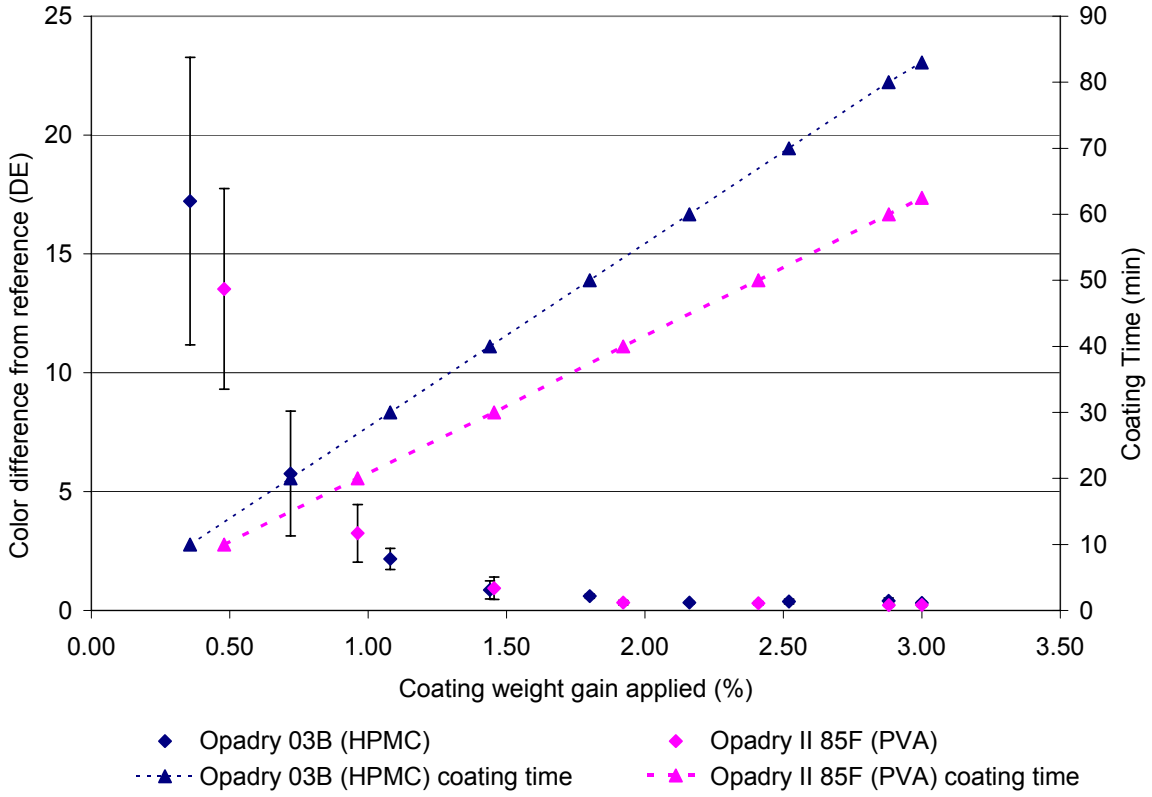
Figure 3. 24" Scale- Defect Results



Increased pan speed resulted in a significant increase in defects for the tablets coated with the HPMC-based system. The defect rate was lower overall for the PVA-based film coated tablets and, interestingly, the higher pan speed resulted in even fewer defects with the PVA-based coating system.

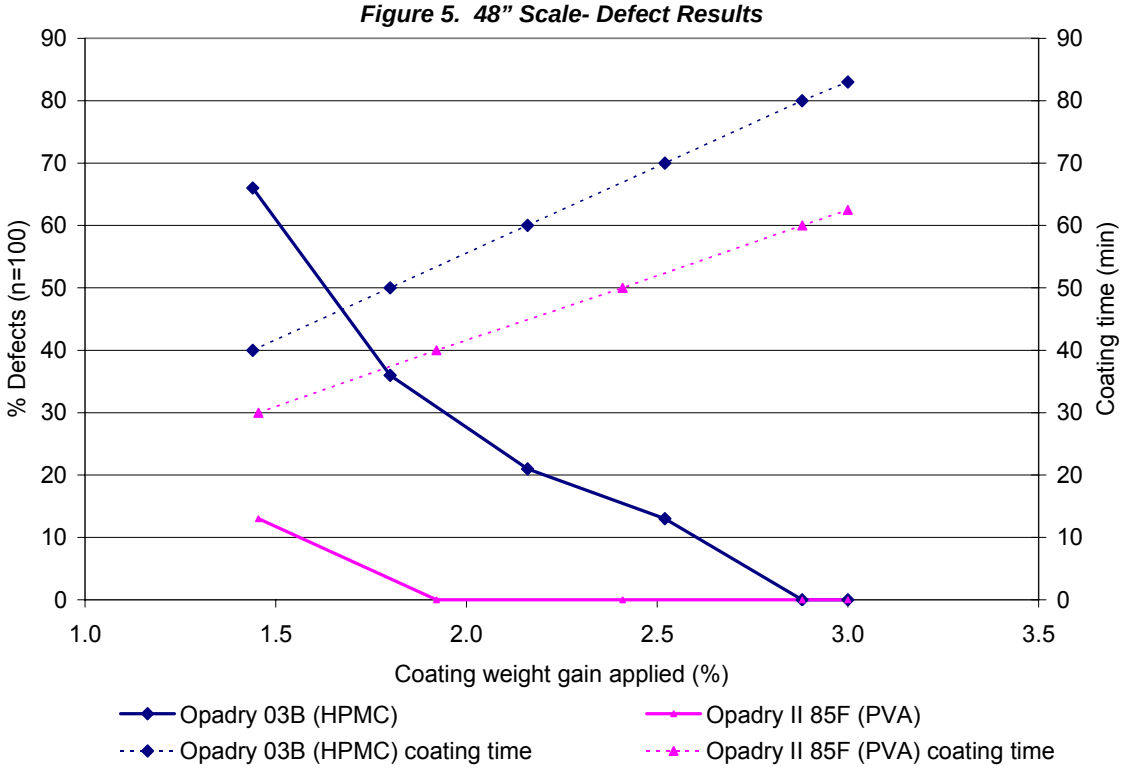
These results may be due to the differences in the surface characteristics of the applied films. The frictional attributes of varying coating systems were examined by Hughes et al. In their studies, it was found that PVA-based coating systems exhibited a higher degree of "slip" than HPMC systems.[3] This higher slip may have provided for less frictional force on the tablets as they tumbled in the pan resulting in more efficient mixing by the baffles, less attrition and lower defects.

Figure 4. 48" Scale- Color Development and Uniformity



On production scale, based on applied coating weight gain, color development was consistent between the two coating systems. Either coating system reached the target color and acceptable color uniformity at <2.0% applied weight gain. Again, the coating trial utilizing the HPMC-based coating system took longer to reach the target color due to the lower solids concentration of the applied suspension.

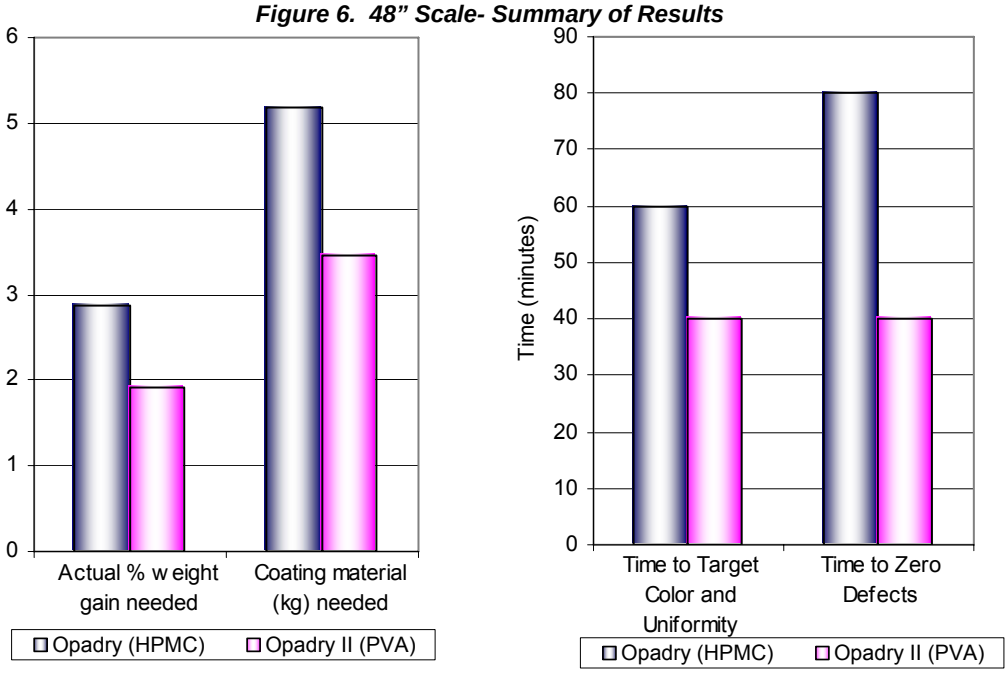
Figure 5. 48" Scale- Defect Results



The defect rates for both the HPMC- and PVA-based coating systems were significantly lower on production scale than seen on laboratory scale. This is consistent with the findings of Mueller et al. who investigated the influence of scale-up on the abrasion of tablets and postulated that larger pan loads resulted in less tablet impacts with the pan walls and baffles.[4]

On production scale, the tablets coated with the PVA-based coating system were free of defects at the same point in the process where the tablets reached their target color and uniformity. In the case of the HPMC coated tablets, it was necessary to apply coating well past the point of good color uniformity to cover edge defects that were created earlier in the process.

Figure 6. 48" Scale- Summary of Results



CONCLUSIONS

It is important to consider the composition of the film coating formulation as well as coating process parameters when developing strategies for coating soft or friable tablets. While both the HPMC- and PVA-based coating systems provided acceptable results, the PVA-based system provided faster protection of the core at lower application levels. It was also found that film parameters, other than tensile strength, should be considered when selecting a film coating formulation. Appropriate selection of the film coating system early in the development process can result in significant material and process time savings over the lifetime of a product.

Reprint of poster presented at AAPS – Nov 2007. Author: Charles R. Cunningham.

References

1. Rowe, R.C.; "Coating Defects – Causes and Cures", Manufacturing Chemist, 49-50; April 1993.
2. Barkley, A., Levine, S., Signorino, C.; "The Evolution and Evaluation of Tablet Coatings"; Tablets and Capsules; April 2006.
3. Hughes, K.W., Wan, P., "Investigation into the Flow Properties of Coated and Uncoated Tablets and its Relevance to Blister Packaging Efficiency", AAPS Annual Meeting, November, 2005.
4. Mueller, R., Kleinebudde, P.; "Influence of Scale-Up on the Abrasion of Tablets in a Pan Coater"; European Journal of Pharmaceutics and Biopharmaceutics; 64 (2006) 388-392.

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