Factorial Analysis of Factors Governing Silver Release from a Hydrophilic Coating

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Introduction: Hydrophilic coatings are common components used in catheters, guidewires, and other blood contacting surfaces. Chiefly, they act as low-friction, non-thrombogenic surfaces which enhance device performance. "First generation" hydrophilic coatings simply fulfilled their functions without additional features. As the field advances, there is a desire for coatings that combine other functionalities with lubricity and non-thrombogenicity, such as the ability to release therapeutic drugs, or deliver anti-biofilm agents. For example, several forms of silver releasing catheters are known to be effective in reducing catheter infection rates[1]. However, these catheters are not known to have lubricious or non-thrombogenic surfaces, and could possibly benefit from the same.

Hydak® hydrophilic coatings (Biocoat, Inc. Horsham, PA) are bilaminar, comprised of an acrylic-based base coat and a lubricious top coat containing hyaluronic acid, with coefficients of friction ranging from 0.003 to 0.03. Though these coatings are currently used in medical devices to ensure smooth passage through tissue, they might serve as suitable delivery matrices for antimicrobial agents and other therapeutic drugs. In this study, possible factors that might influence silver release from the coatings were systematically studied in a factorial design.

Methods: Two factorial studies were conducted. The first experiment followed a 4 x 2 factorial design to determine the main effects due to the base coat. No top coat was used in this set. See Table 1 for factors and levels.

Table 1.

Factor	Low Value	Hi Value
Water Uptake of acrylic	Hydak B-23KX	Hydak G-23
Amount of Silver Zeolite Loading	95:5 (Coating: Ag Zeolite)	90:10 (Coating: Ag Zeolite)
Grade	Non-medical Grade	Medical Grade
Solids Level of Base Coat Solution	5%	10%

Polyester rods were coated in triplicate with base coat containing varying amounts and grades of silver zeolite powder (Agion Technologies, Wakefield, MA) and placed into 50-mL centrifuge tubes containing approximately 40 mL of 0.9% sodium acetate solution. These tubes were then placed in a shaken incubator (New Brunswick Scientific Orbital Shaking Incubator, Edison, NJ) at 37º C for 24 hours. Afterward, solutions were extracted from the tubes and read on an atomic absorbance machine (Buck Scientific, East Norwalk, CT) at 328 nm.

The second study was a 2 x 2 factorial analysis (Table 2.), and the same method was repeated with the groups specified below. Some of these samples used a top coat, Hydak L-110.

Table 2.

Factor	Low Value	Hi Value
Presence of Top Coat	None	Hydak L-110
Crosslinking Density of Base Coat	Normal (Hydak B-23KX)	2x Normal (Hydak B-23KX[2])

Results: Among both studies, the amount of silver per area of coated rod released by 24 hrs into approximately 40 mL of 0.9% sodium acetate solution ranged from 0.08 to 2.4 $\mu g/cm^2$.

The 4 x 2 analysis yielded main effects for four primary parameters, and eleven higher order interactions. Effects and interactions with relative dimensionless magnitudes less than 1.0 were neglected. The effects and interactions with the highest relative values were: Water uptake of Acrylic (1.77), Silver zeolite loading (2.37), solids level of base coat (2.83), and an interaction between water uptake and solids level in the base coat (2.35.)

In the second experiment, the main effect of the crosslinking density was three-fold higher than the effect of the top coat, and there was no interaction between top coat and cross linking density. Rods with high crosslinking density released more silver at 24 hrs, counterintuitively, possibly because they are slightly hydrophilic increased the water uptake of the basecoat.

Conclusions: The solids level parameter relates to coating thickness, while grade parameter relates to zeolite particle size and shape. Large zeolite particles may penetrate the topmost portion of the base coat, enabling them to release more silver, but this did not seem to be the case. Instead, coating thickness and silver loading were related in the first experiment, and the second experiment showed that cross linking density of the base coat plays a role in release kinetics. Overall, Hydak coatings loaded can yield desirable silver release characteristics for antimicrobial applications.

References: Casey AL, et al. Lancet Infect Dis. 8(12): 763-76, 2008.