Non-Silicone Based Nano Thickness Coating to Improve Protein Compatibility

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ABSTRACT

Medical devices have relied to a large extent on silicone oil surface treatment. A drawback of silicone oil is that it may induce aggregation of proteins in vivo or in vitro. The conformational change of proteins may lead the immune system to consider the aggregated protein as a foreign object, thus stimulating an immune response (Jones, Kaufmann, & Middaugh, 2005). Because of this concern, market demand for silicone-free medical devices has increased. The purpose of this study is to demonstrate technical concepts of silicone-free surface coating that could be used to design a protein compatible and lubricious surface for drug delivery devices.

A proprietary acrylate derivative coating material was developed and its effectiveness as a silicone oil coating material replacement for a syringe system was demonstrated. The materials, which can be synthesized by plasma polymerization for nano thickness coating, have excellent protein drug compatibility. Medical devices coated with the newly developed materials dramatically reduce the loss of expensive protein drugs because of its low protein absorption. In addition, the coating materials show better protein compatibility than silicone oil. The coating minimizes the risk of immunogenicity related to protein-silicone oil interactions.

This acrylate derivative coating is stable and provides good lubricity and water vapor barrier.

Keywords: nanocoating, silicone replacement, protein drug compatible coating, medical devices, syringe

1 INTRODUCTION

Silicone oil may induce aggregation of proteins. The conformational change of proteins may lead the immune system to consider the aggregated protein as a foreign object, thus stimulating an immune response (Jones, Kaufmann, & Middaugh, 2005). Because of this concern, market demand for silicone-free medical devices has increased. The purpose of this study is to demonstrate technical concepts of silicone-free surface coating that could be used to design a protein compatible surface.

2 METHOD

Using plasma polymerization technology (Figure 1), a few proprietary monomers containing acrylate derivatives were polymerized and covalently bonded onto a plastic substrate to form a nano-scale thin film.

The coating was applied to a Cyclic Olefin Copolymer (COC) (Figure 2) syringe material. After coating, the coated surfaces were characterized by contact angle measurement, protein adsorption, coating stability, syringe and piston sliding force, coated surface morphology, water vapor transmission rate (WVTR), and protein stability tests.

Radioactive iodine (I^{125}) labeled human serum albumin (HSA) and erythropoietins (EPO) were used for the protein adsorption study. 1.2 ml of I^{125} labeled protein solution was injected into a 3ml syringe (Figure 3). After incubation and rinsed, the amount of protein bound to the container surface was read by a gamma counter.

3 RESULTS

An acrylate derivative coating was successfully applied to the interior surface of a Cyclic Olefin Copolymer (COC) syringe. Water contact angle was measured on the coated and non-coated COC surfaces. The result showed that surface properties of the substrates changed dramatically from hydrophobic to hydrophilic after coating as shown in Figure 4. HSA and EPO protein adsorption were reduced by 50 times and 20 times respectively, when compared to a neat or silicone oil coated surface. The stability of the coating was evaluated by subjecting the test article to 20-40 kGy of gamma irradiation, followed by 3 weeks of aging at 60^{o}C. Two types of COC syringes were evaluated in this study. There is no indication of increase in HSA adsorption after 3 week of aging at 60^{o}C as shown in Figure 5.

The main concern of high piston sliding force in the absence of silicone oil coating was addressed via testing (Figure 6). It was demonstrated that the sliding force of a piston on a silicone oil coated syringe versus an acrylate derivative coated syringe barrel were comparable.

Another concern was a possible increase in water loss through the coating interface between the piston and barrel. A water loss study for a 3 ml ISO standard COC syringe

suggested that the water vapor barrier for the coated syringe is better than or equivalent to the silicone oil coated syringe, Table 1.

4 CONCLUSIONS

A proprietary acrylate derivative coating material was developed and its effectiveness as a silicone oil coating material replacement for a syringe system was demonstrated. The materials, which can be synthesized by plasma polymerization, have excellent protein drug compatibility. Medical devices coated with the newly developed materials dramatically reduce the loss of expensive protein drugs because of its low protein absorption. In addition, the coating materials show better protein compatibility than the non-coated materials and silicone coated material. The coating may minimize the potential risk of immunogenicity related to protein-silicone oil interactions.

This proprietary acrylate derivative coating is stable and provides good lubricity and water vapor barrier.

5 FIGURES AND TABLE

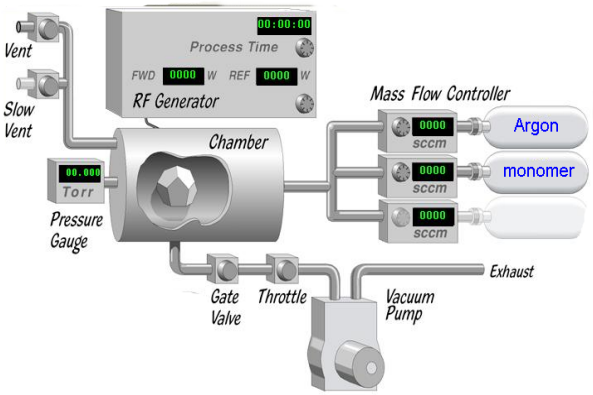

Figure 1: Plasma polymerization system.

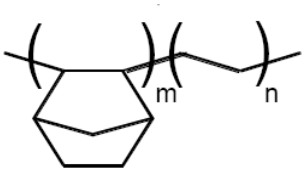

Figure 2: Chemical structure of COC.

Figure 3: Protein adsorption study.

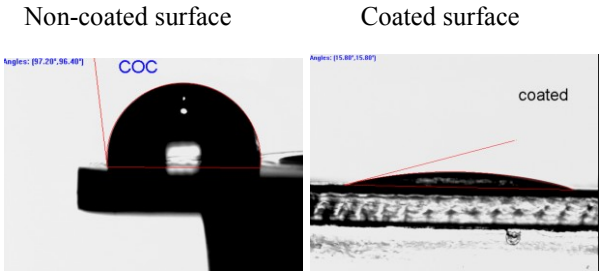

Figure 4: Contact angle of non-coated and coated surface.

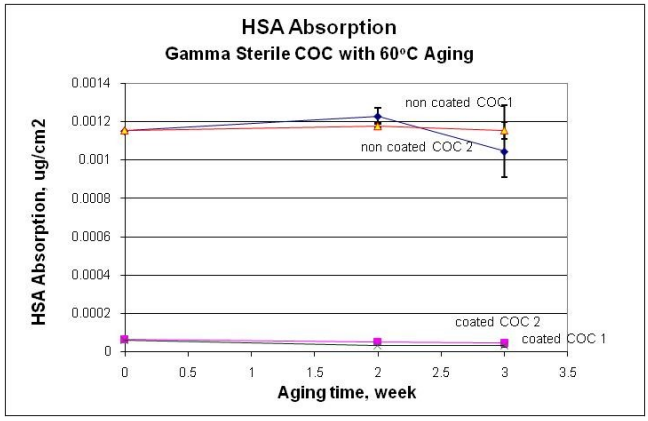

Figure 5: Polyolefin syringe HSA adsorption as a function of aging time.

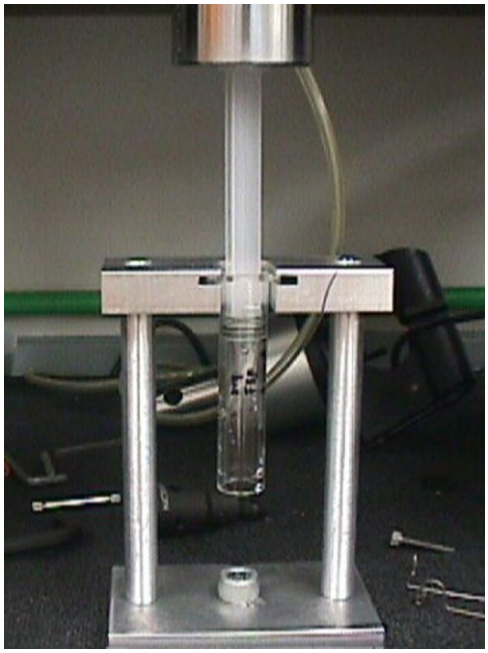

Figure 6: Syringe sliding force test.

Syringe	WVTR, g/day
Acrylic derivative coated syringe	5.68E-05
Silicone oil coated - syringe	8.64E-05

Table 1: Water vapor transmission rate (WVTR) for the acrylic derivative coated versus silicone oil coated syringe.

REFERENCE

[1] Jones, L. S., Kaufmann, A., & Middaugh, C. R. (2005). Silicone oil induced aggregation of proteins. *Journal of Pharmaceutical Sciences*, *94 (4)*, 918-927.