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Strategies for Developing Medical Coatings Based on Dyna-Tek's Technologies

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Introduction

This white paper is focused on promising adaptations of Dyna-Tek's coating technologies ((A) Polysilazane-based coatings and (B) Triazolone technology) to fulfill the needs of the Medical Coatings and Drug Delivery Industry. Hydrophobic and hydrophilic coatings are discussed we well as drug delivery and medical imaging opportunities.

In general, hydrophobic coatings are considered a commodity market, whereas hydrophilic coatings are more difficult to produce and still considered specialty chemicals.[i] Hydrophobic surfaces are self-lubricating, even when not wet. Super-hydrophobic surfaces are known to prevent the adhesion of bacteria and, therefore, biofilm formation upon implanting. Hydrophilic surfaces have to be wetted to be lubricating. They are surfaces of choice on catheters, guide wires and sheaths, because they permit easy insertion into the body. Hydrophilic surfaces are well suited to host biofilms unless chemical defense measures are taken.[1]

The Global Market for hydrophobic surfaces in medicine in 2014 was 3.12 Billion dollars, and for hydrophilic surfaces 6.53 Billion dollars. In general, the ageing population and the population growth in Asia are considered the drivers (average CAGR 2014-2019: 6.5%).[1]

Rationale

In this paper, the principal differences between the (bio)physical and (bio)chemical properties of the already existing, conventional coating technologies for medical devices, and Dyna-Tek's TRISILON Technology will be compared. TRISILON possesses several advantages over competing technologies, because it is non-toxic and highly versatile with regard to materials properties and adaptability to multiple applications.

Biofilm Formation at Surfaces within the Human Body Generally speaking, pathogenic microbes forms biofilms on surfaces during hospital infections.[ii] Biofilm-associated infections are one of the most prevalent risk factors of medical procedures that involve implantation of foreign objects (e.g. artificial bone replacements, breast implants, stents) or the installation of tracheal tubes, peripherally inserted central

[1] Zhao, G.; Usui, M. L.; Lippman, S. I.; James, G. A.; Stewart, P. S.; Fleckman, P.; Olerud, J. E., Biofilms and Inflammation in Chronic Wounds, *Adv Wound Care (New Rochelle)* **2013**, *2*, 389.

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catheters or urinary catheters.[iii] Basically all nosocomial infections in humans are caused by commensal species including *Staphylococcus aureus, S. epidermidis, E. coli, Acinetobacter baumannii*, *Pseudomonas aeruginosa* and many other Gram-positive cocci or Gram-negative rods.[iv] These infections cannot be prevented by killing the bacteria within the human body because that would require concentrations of antibiotics that would kill the host. Therefore, the (bio)physical and (bio)chemical properties of the surfaces that are inserted/ implanted are most important, because they will determine whether pathogenic biofilms can form easily, or whether the formation of such biofilms can be prevented, at least for some the time the surface will be within the human body.[v]

Medical Coatings

Bacteria will eventually form biofilms on virtually all surfaces that are in long-term contact with the human body. However, also medical devices that come only in short contact with body tissues and fluids have to be sterile to prevent the transfer of often multi-drug resistant pathogens from the hospital environment to the host. These materials should possess coatings, which survive the harsh sterilization procedures[vi] and prevent the adhesion of bacteria. The five established sterilization methods are ethylene oxide (single and multiple cycles), gas plasma, steam, vapor phase liquid chemical and γ-irradiation (single and multiple cycles).[vii] However, most coatings do not withstand ethylene oxide and gas plasma treatment, as well as higher doses of γ-irradiation, which are often required.

All surfaces that come in contact with the human body can cause tissue rejection. A suitable coating has to reduce rejection and other immune responses to not to endanger the health of the patient.[viii]

Surfaces of medical devices are either hydrophilic (in contact with aqueous body fluids and tissue) or hydrophobic (not in contact with any part of the body containing water or proteins). To these surfaces, antimicrobial additives are often added, resulting in antimicrobial coatings.[ix]

Lubricant coatings are required to minimize the effort (and the access site trauma associated) to insert a medical device into a particular site of the human body.[x]

The typical advanced coating in modern medicine is multifunctional:

1) It has to adhere strongly to the materials of which medical devices are made. The most important (in that sequence) are stainless steel, aluminum, titanium, silver, and ceramics, such as bioglass (composed of SiO_2, Na_2O, CaO and P_2O_5 in specific proportions)[xi] and alumina (Al_2O_3).[xii] Since many modern devices are made of more than one of these materials, a suitable coating has to strongly adhere to all of them. On the other hand, medical tubing (e.g. catheters) is made of silicone rubber of fluoropolymers.[9]
2) It has to provide either a hydrophilic or hydrophobic environment. For numerous applications, well-adapted surface properties are desirable, which are neither strictly hydrophilic nor hydrophobic. However, conventional coatings cannot be adapted easily.

3) Antibiotic components have to be integrated into the coating and be released very slowly. For this purpose, the antibiotic components have to be either attached to or integrated into the coating. Attached (organic) antibiotics are often cleaved off their tethers by bacteria, whereas inorganic antibiotics (e.g. copper or silver nanoparticles) slowly leach out of the coating. The latter are usually active for a much longer time, which is desirable.[xiii]
4) Implants, which are in contact with the bloodstream require coatings that prevent the formation of blood clots (hemocompatible coatings). For that purpose, either chemotherapeutic drugs (e.g. camptothecin) or blood clotting inhibitors (e.g. heparin) are physically adsorbed or chemically attached. Chemotherapeutic drugs kill basically all human cells getting in contact with the surface, heparin and similar drugs. The problem is again that the drugs desorb from the surfaces relatively quickly.

Potential Applications of Polysilazane Designer Polymers

Hydrophilic Coatings based on polysilazane designer polymers are very suitable for needles, catheters and short-term implants (less than a week). They can easily be sterilized and are chemically stable. However, biofilms can grow on hydrophilic surfaces if no chemical measures are taken that prevent bacterial growth, leading to nocosomial infections. One easy strategy to prevent bacterial growth will be the incorporation of bactericidal silver nanoparticles into the structure. The real advantage of hydrophilic coatings based on polysilazane chemistry is that they can be mass-produced, whereas most hydrophilic surfaces are still regarded as specialty chemicals.

(Super)hydrophobic coatings are ideal for surgical instruments, because they prevent the adhesion of bacteria. Polysilazane designer polymers will permit strongly adhesive coatings, which are required for surgical precision. They easily withstand thermal sterilization procedures, which are required for hospital use.

The aforementioned content draws specific excerpts from several reports and white paper written by Prof. Stefan Bossman. For more detailed information, please contact us at info@dyna-tek.com. Some information will require the exchange of NDA's.

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