Lubricious coatings for medical devices

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Lubricious coatings have a wide variety of applications with regard to medical plastics and devices. Lubricity, biocompatibility, anti-thrombogenicity and anti-microbial activity are desirable properties for medical devices. This paper describes a unique water-based lubricious coating, LubriLAST which can easily lend these properties to a medical plastic and which can be used with a wide variety of substrates.

The ability for a coating to be not only lubricious, but anti-microbial is becoming increasingly important. RepelaCOAT™ offers both lubricity and antimicrobial activity. The coating can also be modified so as to render it able to elute drugs in a controlled manner. This attribute is attractive for a number of medical applications.

Introduction

Devices used in the medical industry are constructed of plastics, metals or ceramics and are often hydrophobic, non-slippery, and/or non-biocompatible. High friction properties are unfortunate since such devices should exhibit low friction surfaces in order to facilitate insertion into blood vessels, the urethra or other body conduits during certain procedures. Pressure from managed care to reduce patient trauma and shorten hospital stays, encourages device manufacturers to ensure that their catheters, guidewires and other invasive devices have low friction surfaces. Device manufacturers often enjoy a market advantage if their devices exhibit low friction profiles. In today's competitive market, a device with a coating that gives it additional advantages such as improved biocompatibility, infection control and/or controlled release of bioactive compounds is especially appealing.

Current lubricious coating technologies

Device surfaces are often coated with low friction materials such as polytetrafluroethylene (PTFE), glycerin or silicone fluid to render the surface slippery. Unfortunately, hydrophobic polymer coatings such as these often render the devices difficult for the physician to manipulate. Silicone fluids and glycerin are greasy and sticky. PTFE coatings are slippery even when dry. Furthermore, the use of PTFE coatings is restricted due to coating stiffness, poor bonding and a limited supply of medical grade raw materials. Lastly, all of these coatings suffer from the limitation of not being able to incorporate drugs or other bioactive agents. A "slippery when wet" hydrogel-like surface that is high friction, that offers the user flexibility in terms of bioactive compound incorporation and exhibits low bacterial adhesion is therefore desirable.

The technology involved in coating hydrophobic surfaces with hydrophilic polymers or hydrogels that hydrate and become "slippery when wet" is available. However, hydrated, traditional hydrophilic polymer coatings have little physical integrity due to the high water content and a considerable amount of research has been done to improve the durability and substrate adhesion of traditional hydrophilic coatings.

A common approach is to physically anchor a long-chain hydrophilic polymer in a supporting polymer network that is normally non-swellable in water. One end of the long hydrophilic polymer becomes entwined within the supporting polymer and the free end is able to become hydrated. This is known as an "interpenetrating network" (IPN) and is characteristic of many commercially available lubricious coatings. A schematic diagram is shown in **Figure 1**. With many coatings, the hydrophilic polymer is dissolved in an organic solvent along with the polymer that will form the supporting matrix. The device is coated with the solution and the solvent is allowed to dry. Another approach is to graft one end of a functionalised hydrophilic polymer to the substrate. This is often accomplished via a reactive bridge between the insert substrate surface and a functional group on the hydrophilic polymer, also shown schematically in **Figure 1**. This results in a very thin hydrophilic layer that is chemically linked to the surface.

These approaches begin to overcome many of the inherent limitations of hydrophilic coatings such as limited wet strength, poor adhesion and fragility. Unfortunately, these processes fall short in that they tend either to rely on cumbersome processing techniques (such as UV curing) or organic solvent handling. Given the current regulatory climate, it is desirable for companies to avoid using organic solvents in order to eliminate the possibility of residual solvents within the device and to minimize processing, waste handling and hazardous material reporting costs.

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Figure 1. Interpenetrating network (top) and grafting of hydrophilic polymer (bottom).

Table

Common substrates which have been coated with LubriLAST include:

HDPE	FEP
LDPE	Latex
Polyurethane	Silicone
Polycarbonate	Stainless steel (various alloys)
Polyimide	Nitinol
Polypropylene	Aluminium
PVC	Platinum
Nylon	Gold
PEBAX	
PVDF	

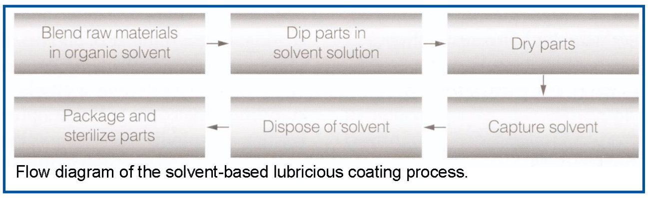

Figure 4. Solvent-based lubricious coating process flow diagram.

Aqueous based lubricious coatings

LubriLAST, a simple, aqueous-based coating, has been shown to overcome many of the physical and processing limitations of current hydrophilic coatings. It produces a superior IPN type lubricious coating that is slippery only when wet. The coating consists of a chemically cross-linked supporting polymer network with long-chain hydrophilic molecules intertwined within it. The lubricity of the coating is seen in **Figure 2** in which the coefficient of friction of LubriLAST is compared with polyethylene, and PET. An often-used hydrophilic molecule is poly(vinylpyrrolidone) (PVP). Since the supporting polymer network is cross-linked, it possesses superior cohesive properties; it will not "slough off" as readily as polymers deposited by simple evaporation (**Figure 3**).

Eliminating organic solvents gives a manufacturer the ability to incorporate bioactive ingredients that are incompatible with organic solvents or that could be degraded upon exposure to them. Also, LubriLAST can be used successfully with substrates that are not solvent-compatible. Another advantage of using an aqueous base is the elimination of residual organic solvents that can compromise the safety of the device. Regulatory requirements in both the US and Europe discourage the use of solvents and thus aqueous processing is preferred. Elimination of organic solvents improves industrial hygiene and worker conditions. Increasingly, products that are environmentally friendly are seen as having a market advantage.

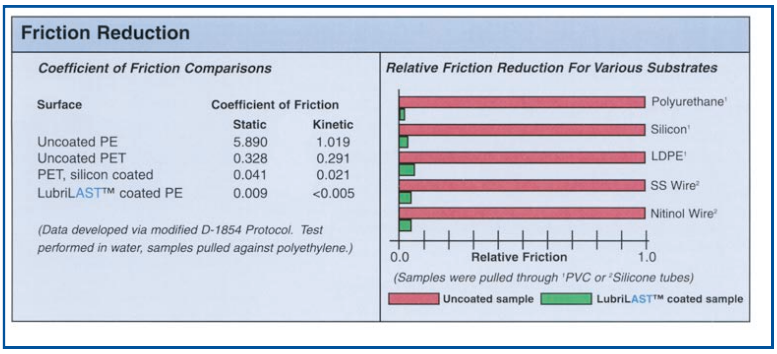

Figure 2. Coefficient of friction of LubriLAST, polyethlylene, and PET.

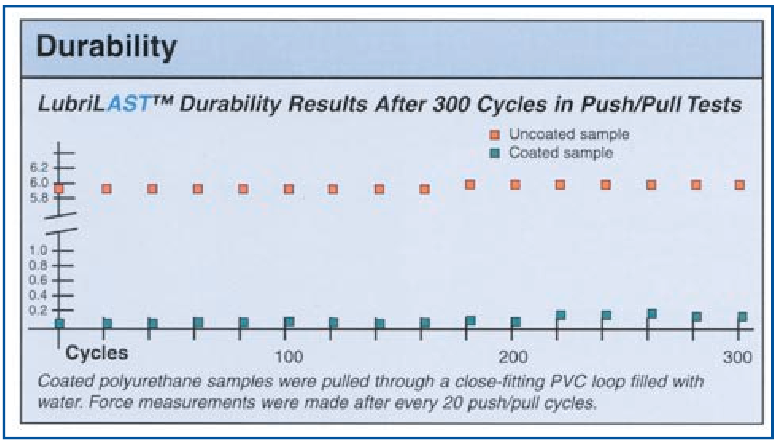

Figure 3. Durability of LubriLAST in push/pull tests.

Process and chemistry

The hydrophilic molecule is blended with an aqueous polymer dispersion. A cross-linking agent that cross-links the supporting polymer matrix is added to enhance coating integrity. This cross-linker can cure at room temperature. However, it is best to cure at about 60°C to facilitate the reaction as well as to achieve the strongest supporting network. The process is straightforward. Unlike coatings that use organic solvents such as shown in **Figure 4**, there is no need to incorporate special processing equipment or ventilation. Additionally, costs associated with disposal of hazardous waste are all but eliminated.

Figure 5. Zone of inhibition tests for aqueous based lubricious coating.

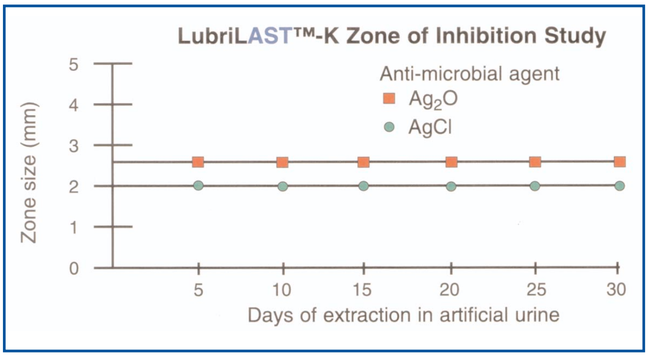

Figure 5a.

Properties

Perhaps the most important attribute of the aqueous-based system is the compatibility with nearly all medical materials. The substrates listed in the **Table** have been successfully coated with aqueous formulations with no change in the underlying properties or shape. Sensitive crystallized polyurethanes do not "relax" since there is no solvent present to attack the microstructure. Aqueous-based lubricious coatings can be applied both to the outer surface and to the lumen of tubing as small as 7 French. They can be applied to complex geometries, to thin wires and to springs with minimal bridging.

Aqueous-based systems offer flexibility in formulation. By varying the chemistries and "recipes", different coating properties can be enhanced. For example, balloons and guidewires require a very flexible and resilient coating. On the other hand, introducer sheaths and stents require lubricious coating that is extremely durable. By modifying the supporting polymer network, these different specifications can be met.

Another important property of aqueous-based lubricious coatings is the ability to incorporate bioactive agents which are released *in vivo*. The coating then has the potential for use in drug delivery devices or therapeutic intervention. This property has been demonstrated in the incorporation of silver oxide within the coating. Zone of inhibition studies demonstrate that there is antimicrobial activity on the surface even after 30 days of soaking in artificial urine. Conventional antimicrobial coatings show a huge spike of activity at a constant level (**Figure 5** and **6**).

Biocompatibility

Hydrogels, by their chemistry, imply biocompatibility and haemocompatibility. In order to evaluate this biocompatibility, hydrogels have gone through a number of tests with successful results (**Figure 7**).

To summarize the characteristics of LubriLAST coating:

- Non-solvent, aqueous-based
- Smooth device insertion and removal
- Easy device handling "slippery when wet"
- Stable and durable with long shelf life
- Biocompatible
- Works on a broad range of substrates
- Flexible formulation facilitating drug agent incorporation
- Choice of any agent/combination

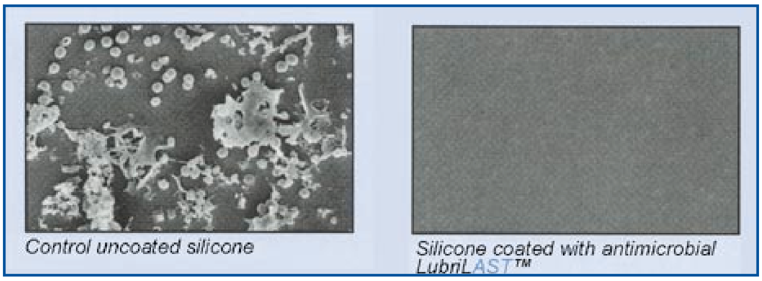

Figure 6. Bacterial adherence photographs of aqueous based hydrophilic coating with incorporated antimicrobial agents (coated and uncoated).

Other benefits/applications

Devices

Lubricious coatings have been used on a wide variety of medical devices including those in the areas of cardiology, urology and neurology and in many diagnostic applications. Angioplasty balloons, Foley catheters, urethral stents, microcatheters and guidewires all benefit from the incorporation of a lubricious coating. Haemodialysis equipment is also coated for reduced patient trauma.

Tissue Biocompatibility

- Systemic (Acute) Toxicity
- Cytotoxicity
- Sensitization Test in guinea pigs
- Acute Intracutaneous Reactivity
- Pyrogen Material Mediated test

Hemocompatibility

- Direct Hemolysis
- In-vivo thromogenic resistance study
- Complement Activation
- Coagulation Study

Figure 7. Biocompatibility tests.

Bioactivity

LubriLAST can be modified to exhibit other properties such as haemocompatibility, antimicrobial characteristics, and reduced protein and cell adhesion. A modified formulation of the lubricious coating, RepelaCOAT™, has been introduced which combines antimicrobial effectiveness with the original lubricious "slippery when wet" properties. This has resulted in a coating with a two-fold effect – it to prevent device-induced infections and helps to reduce patient trauma by rendering the device surface slippery and easy to insert.

Conclusion

Lubricious coatings have been a topic of interest for some time. They offer excellent wet friction reduction, high durability and simple processing techniques that make an attractive option for many manufacturers.