Therapeutic Coatings for Medical Device Implants

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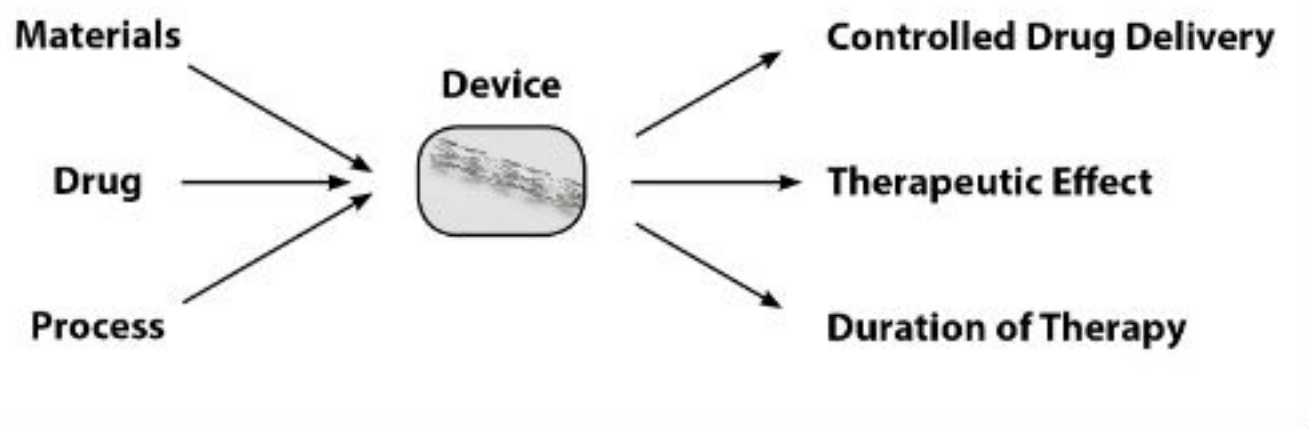
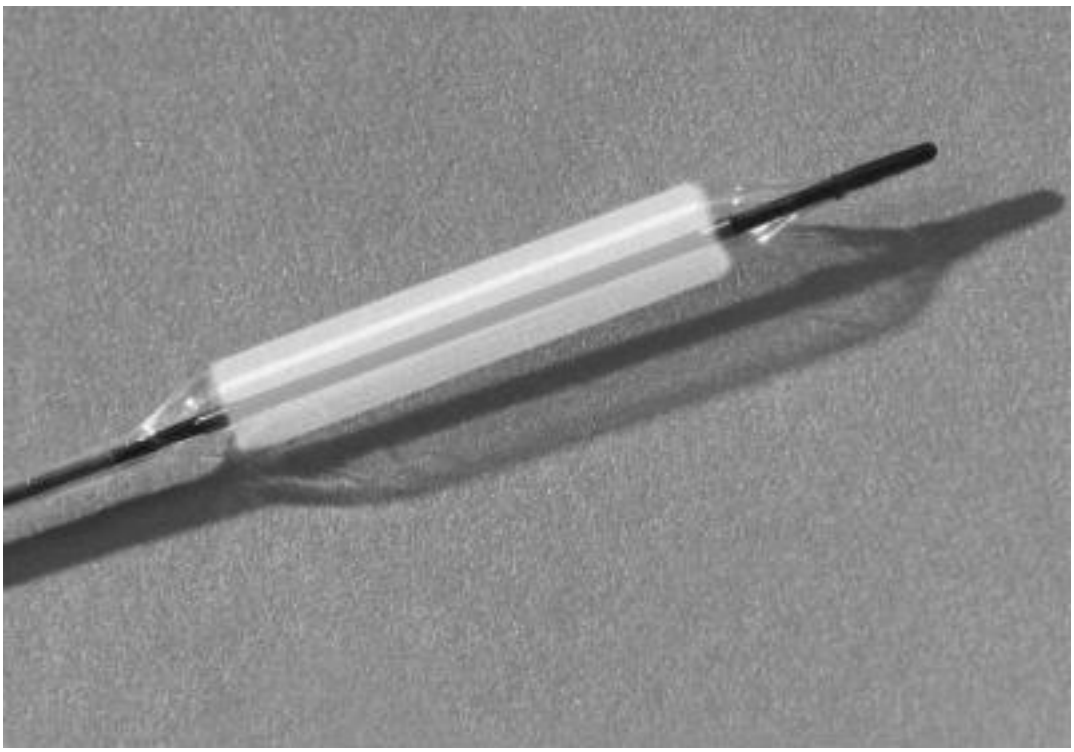
Drug delivery coatings are not a new technology to the medical device industry. However, as more implantable devices are tasked with achieving a greater level of healthcare, they do offer great benefit to design engineers. This article reviews drug coating technology and looks at application areas where it has made a significant impact.



The development and adoption of therapeutic coatings for medical devices has created new product categories, enhanced the functionality of devices, and improved patient outcomes. The therapeutic effect, duration of therapy, and deliverability of these combination devices are influenced by the choice of therapeutic agent, coating materials, and the means by which coatings are applied to the medical device (Figure 1).

Devices

Therapeutic coatings have been incorporated onto implantable medical devices for a variety of acute and chronic applications. Perhaps the best known is the drug-eluting stent. The polymeric coating on a drug-eluting stent provides controlled, site-specific delivery of anti-restenotic drugs that dramatically lower the restenosis rates found with bare metal stents. More recently, percutaneous angioplasty balloons coated with anti-restenotic drugs and excipients (drug coated balloons or DCBs) (Figure 2) have been developed to quickly transfer a therapeutic drug from the device to the arterial site, then provide longer-term control of restenosis. Other devices take advantage of surface modification to impart their therapeutic effect. For example, embolic protection devices are enhanced by the incorporation of a hemocompatible coating that, while not eluting a therapeutic agent from the device, reduces clot formation on the surface of the device.

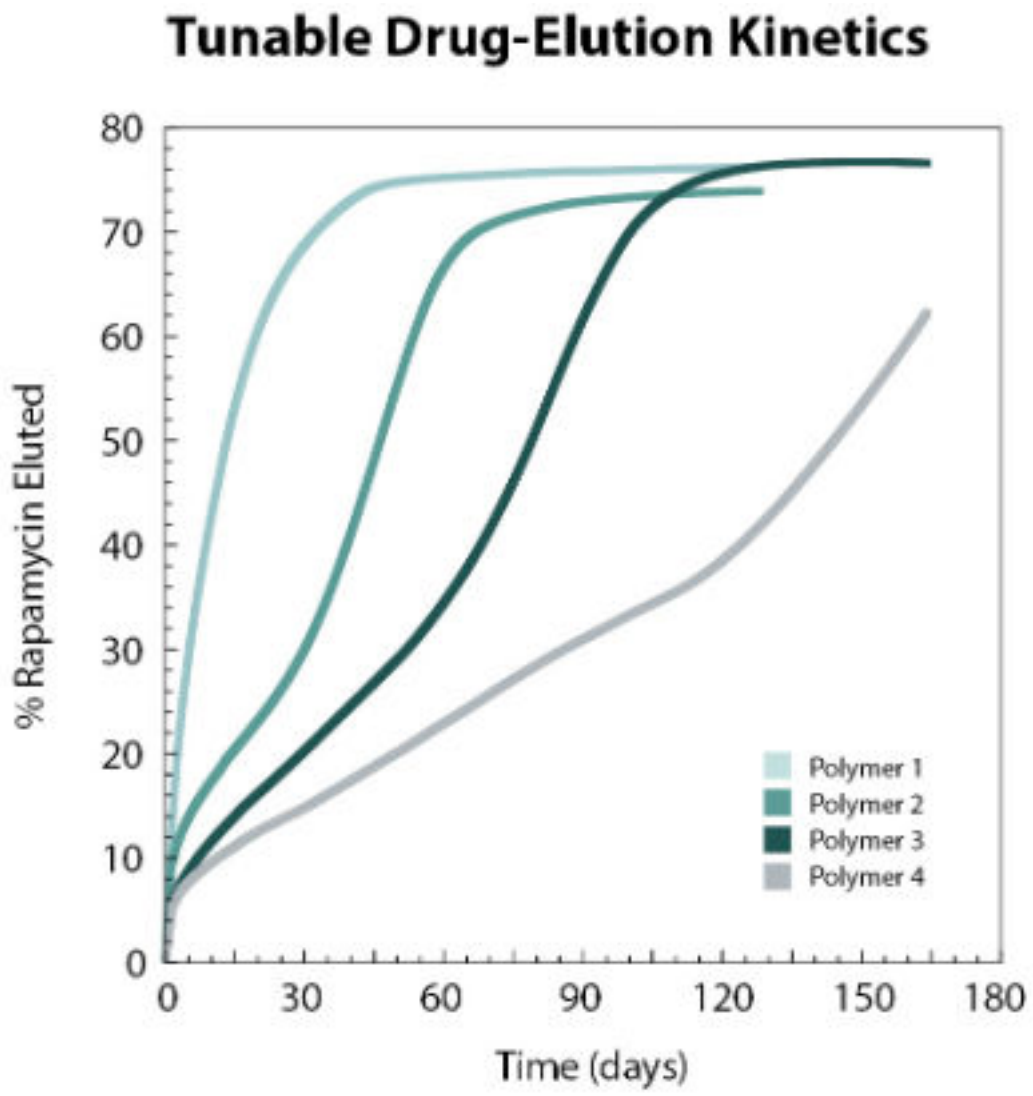


Therapeutic Effects

The coating materials and formulations available make possible the delivery of a wide range of therapeutic drugs and the ability to elicit a range of tissue responses. For instance, a device that is highly prone to infection may benefit from a coating that delivers antimicrobial drugs to stop foreign cell growth, while a device that requires rapid incorporation into the surrounding tissue may call for a coating that provides a surface onto which cells may easily attach and grow. The desired therapeutic outcome impacts the time over which the therapeutic coating acts. For example, an anti-inflammatory compound may need to be delivered for weeks or months in order to prevent restenosis, while an antimicrobial may only need to stay resident at the site for several days in order to effectively prevent infection.

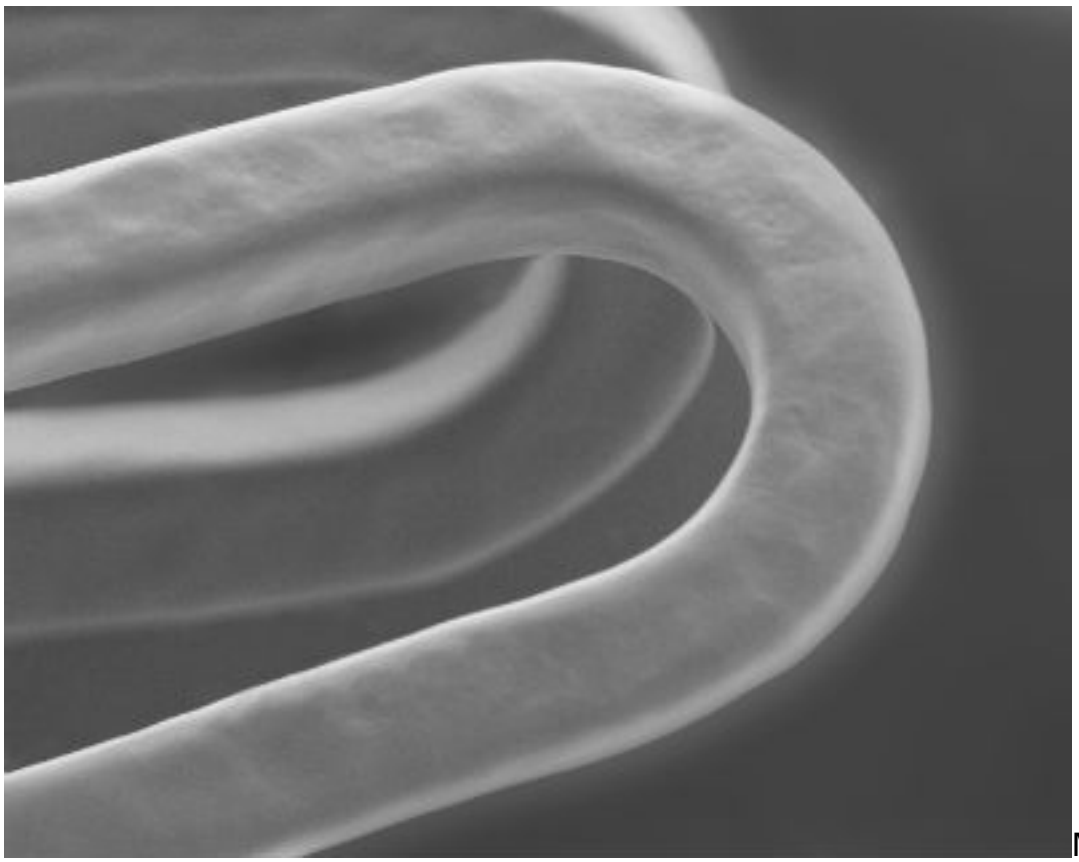
Coating Materials

Selection of the appropriate coating material enables a device to deliver the proper therapeutic effect. For passive therapeutic coatings, such as polymeric hydrogels, the ability to covalently bond a molecule to the surface of a device provides for a more durable hemocompatible effect.



The active peptides and proteins of some therapeutic coatings elicit a stronger response from the body only when they are presented in a certain orientation, such as end-point attachment. An example of this approach is the bio-engineered OrbusNeich Genous coronary stent, which is coated with immobilized anti-CD34 monoclonal antibody that captures beneficial cells circulating in the blood stream to enhance endothelialization, protect against blood clots, and minimize restenosis.

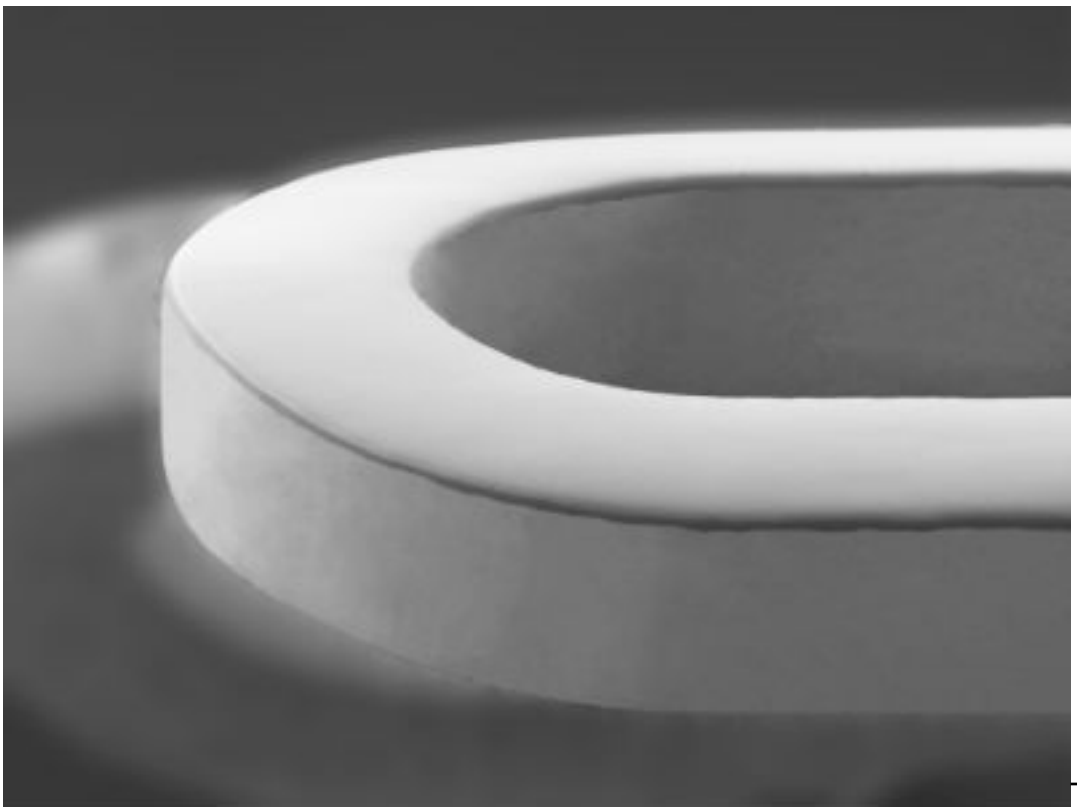
Materials for the active delivery of a therapeutic agent include a wide range of polymers and small-molecule matrices. For many drug-polymer systems, the release of the drug is dominated by the diffusion of the drug through the polymer matrix. In these cases, the glass transition temperature (T_g) of the polymer has a large effect on the drug release, with lower T_g polymers releasing the drug faster than high T_g materials. The compatibility of the drug-polymer system should be evaluated as this will give information on how quickly the drug will come out of the system. As a general rule, the more similar the hydrophilicity or hydrophobicity between the drug and polymer, the longer the drug will stay in the polymer matrix (Figure 3).



Medical device designers have a choice of durable or degradable polymer materials for drug delivery coatings. Durable polymers were used in the early generation drug-eluting stents (e.g., Cordis Cypher, Boston Scientific Taxus, Boston Scientific Promus, Abbott Xience, and Medtronic Resolute stents), which have been successfully implanted in millions of patients (Figure 4). Durable polymers can allow for longer delivery times and the underlying matrix does not change over time. In contrast, recent commercial drug-eluting stents (e.g., OrbusNeich Combo stent) use degradable polymer coatings (Figure 5). These materials enable control over the release of the drug by both diffusion (similar to durable systems) and degradation of the polymer, which can change the polymer T_g, coating thickness, and encapsulation of the drug over time. Some devices utilize both durable and biodegradable coatings, such as a stent coated on the inner and outer lumen for two different drug delivery modes of action.

Equally important to the ability of the polymer to control the drug release is the ability of the coating system to ensure delivery of the therapy to the treatment site. Coating materials should be evaluated for adhesion to the underlying substrate and resistance to flaking or cracking as the device is deployed to the desired location. In some instances, such as with drug-coated balloons, coating materials need to balance the retention of the coating during transit with the need to deliver the drug very quickly once the device reaches the treatment site.

Processing



The means by which a therapeutic coating is applied to an implant can significantly impact the performance of the coating. A variety of coating techniques enable conformal coatings as well as coatings that cover only a portion of the device, such as a luminal or abluminal coating, which enables targeted delivery to specific tissues in contact with the device. Coating techniques offer control over the thickness of the coating, which can be adjusted to provide a sufficient reservoir for the therapeutic agent while not causing a large dimensional change to the device that may hinder delivery, placement, or other attributes. For solvent-based coating processes, the rate at which the solvent is dried from the coating can affect the structure of the coating and the drug release rate. Slower dry times, for example, can allow for greater segregation of the drug from the polymer, resulting in an enrichment at the surface of either the drug or polymer compared to the bulk coating composition. Solvent evaporation and other aspects of the coating process can also impact the form of the drug (crystalline, amorphous, etc.), which can, in turn, influence how quickly the drug elutes from the coating and how rapidly the drug is absorbed into the surrounding tissue.

Conclusion

The use of therapeutic coatings on medical devices has led to enhanced device performance and improved patient outcomes. The selection of coating materials, therapeutic agent, and processing methods all play a critical role in the deliverability, therapeutic effect, and duration of therapy. A skilled development team can help navigate the interconnectedness of the coating choices to ensure the desired therapeutic properties are achieved.

For more information, visit www.surmodics.com [1].

Links:
[1] http://www.surmodics.com