Advanced Antithrombotic and Batericidal Nitric Oxide Releasing Materials/Devices: Development, Characterization and Biomedical Applications

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Nitric oxide (NO), generated within our bodies via oxidation of L-arginine by nitric oxide synthase (NOS), controls many important physiological processes. Although NO's role as a potent vasodilator is well known, NO is also very effective at preventing platelet activation, adhesion, and aggregation, key steps in the formation of blood clots induced by the contact of flowing blood with foreign materials. In addition, NO is known to be a potent antimicrobial agent, inhibit smooth muscle cell proliferation, promote wound healing and the growth of new blood vessels. Therefore, it should be possible to prevent infections and clotting widely associated with a variety of medical devices (e.g., intravascular catheters, urinary tract catheters, extracorporeal blood loops, implanted vascular grafts, etc.). by developing polymeric materials that release low levels of NO gas over extended time periods. In this presentation, it will be shown that a variety of hydrophobic polymers (PVC, polyurethane, silicone rubber, etc.) often utilized as blood contacting materials in biomedical devices/systems can be formulated to release NO gas for days and weeks with NO fluxes at or above those generated by cells in our bodies. The NO release can be accomplished by incorporating diazeniumdiolate species (nitric oxide adducts of secondary amines), or S-nitrosothiols as NO donors, either as dispersions within polymers or tethered covalently to the polymer backbones. In some cases, the use of certain additives to promote longer-term NO release by controlling the pH within the organic polymer phase is required. An additional approach, especially well suited for use with multilumen catheters, is to create NO releasing device using electrochemical reduction of nitrite ions via a Cu wire working electrode within a catheter lumen. In this presentation, the chemistry of these different NO release methods will be reviewed, and results regarding the *In vitro* and *in vivo* antimicrobial and antithrombotic activity of the various NO release approaches will be summarized. It will be shown that these various NO release strategies clearly reduce platelet adhesion/activation *in vivo* and can dramatically decrease bacteria adhesion and biofilm formation on the surface of polymeric materials.