Nitric Oxide Releasing Coatings for Medical Devices

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Introduction:

Nitric oxide (NO) is a vital biological molecule. It plays a significant role in diverse biological processes such as host defense, cardiovascular regulation, signal transduction, neurotransmission and wound healing. In addition to helping body cells to communicate with each other by transmitting signals throughout the entire body, NO assists the immune system at fighting off bacteria and defending against tumors. Furthermore, it helps reduce inflammation and regulate blood pressure by dilating arteries. NO is also a well known inhibitor of platelet adhesion and smooth muscle cell proliferation. Agents that release or generate NO locally have been proposed as systematic drugs to prevent and treat restenosis and thrombus formation when delivered to treatment sites inside an individual that have come in contact with medical devices such as cardiovascular drug-eluting stents, catheters and adhesion prevention barriers including meshes.

Researchers have sought various ways to deliver NO to damaged tissues and organs at risk of injury. However, the prior work suffers from the following drawbacks (a) the rate of release of nitric oxide and drug molecule cannot be controlled and (b) Some of the NO donors reported so far release toxic and carcinogenic nitrosamines upon decomposition under oxygenated conditions. In light of the above drawbacks, therefore, there is a need for new molecules and compositions capable of delivering NO and drug to treatment sites in a controlled manner and which can overcome the aforementioned shortcomings

In this paper, we present NO and drug releasing polymers wherein the rate of release of NO and drug molecule can be controlled[1]. These novel NO and drug releasing polymers are derived from monomers comprising of a drug molecule and a NO releasing moiety linked to each other via a hydrolytically degradable linker. This hydrolytically degradable linker comprises of repeat units derived from safe and biocompatible molecules such as glycolic acid, lactic acid, p-dioxanone and caprolactone, key components of all commercially available absorbable medical devices. The hydrolytic degradation rate of these NO and drug-releasing polymers are controlled by the number of repeat units in the linker as well as by the choice of the safe and biocompatible molecules from which the repeat units are derived. For example, NO and drug releasing macromers and oligomers comprising of degradable linker containing repeat units derived from glycolic acid will hydrolyze faster than the one comprising repeat units derived from p-dioxanone. Similarly, these NO and drug releasing polymers comprising of degradable linkers containing repeat units derived from lactic acid and caprolactone should take much longer to hydrolyze than the ones wherein the degradable linker comprises of repeat units derived from glycolic acid and p-dioxanone.

Key aspects along with potential applications of these NO and drug releasing polymers will be presented. *In Vitro* hydrolysis profiles will be discussed during presentation. We believe that innovative technology behind these polymers will enable us to fulfill the unmet needs of the healthcare community.

Results and Discussion:

We have developed a number of diol containing monomers with pendant drug and NO releasing groups. Figure 1 displays selected examples of these diols. These diols are used to prepare polyesters and polyurethanes with pendant drug and NO releasing groups for applications in NO releasing medical device coatings.

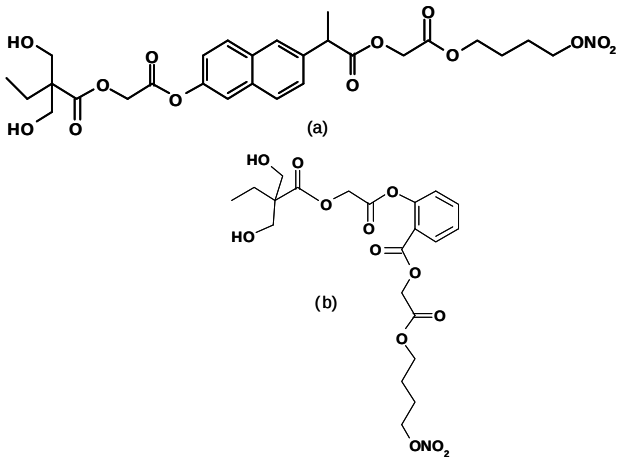

Figure 1. (a) Hydrolytically degradable diol with pendant NO and Naproxen releasing moiety (b) Hydrolytically degradable diol with pendant NO and Aspirin releasing moiety.

Conclusions: We have developed a variety of hydrolytically degradable NO and drug releasing polymers wherein the rate of release of NO and drug molecule can be controlled. These polymers are expected to find use in a variety of biomedical applications including NO and drug eluting cardiovascular stents, controlled NO and drug delivery, wound care applications, implantable medical devices, pharmaceutical, anti-cancer and anti-microbial compositions and medical device coatings.

References:

(1) Bezwada, Rao S., US Patent Application pending No.61/153349