

233a Transnitrosation and Release Kinetics of Nitric Oxide (NO) with Cysteine-Modified Biomaterials

Jun Gu and Randy S. Lewis

In order to increase the haemocompatibility of biomaterials, biomaterial surfaces were modified such that the biomaterials utilized naturally-occurring nitric oxide (NO) compounds readily available in the blood to inhibit platelet adhesion. For our studies, S-nitroso-bovine serum albumin (BSANO) was used as the model NO compound and polyethylene terephthalate (PET) was used as the model polymer. The mechanism for inhibiting platelet adhesion involves the transnitrosation (transfer) of NO from BSANO to immobilized cysteine on the biomaterial to form S-nitroso-cysteine (CysNO), followed by the release of NO from CysNO. NO is a known inhibitor of platelet adhesion.

A kinetic model showed that the immobilized cysteine redox state (whether cysteine forms disulfide bonds or remains reduced) following the release of NO is critical for long term functioning of the biomaterial. The kinetic model is sensitive to the forward transnitrosation kinetic rate constant and the NO release rate constant. Spectrophotometer measurements of the NO release from free CysNO showed that the release is highly susceptible to pH. The maximum release occurs at physiological pH (near 7.4), demonstrating that blood provides an optimized environment for the release of NO from CysNO.

A chemiluminescence-based method was used to monitor BSANO in the solution and the cysteine surface concentration during the transnitrosation between immobilized cysteine and BSANO. Based on the transnitrosation and CysNO data, key parameters of the kinetic process were calculated. The experimental results showed that the cysteine on the polymer is not fully oxidized following the release of NO, thus the cysteine-modified polymer effectively extracts and releases NO for long periods of time. In addition, the cysteine surface concentration remains stable after 5 hours. These key findings suggest the long term ability of the cysteine-modified polymer to continually release NO to inhibit platelet adhesion.