Stability of Therapeutic Self-Assembled Monolayers During Drug Loading and *In-vitro* Drug Delivery

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Introduction: Self-assembled monolayers (SAMs) are defined as monomolecular films of a surfactant formed spontaneously on a substrate upon exposure to a surfactant solution [1]. The many possible interfacial reactions at the reactive functional groups of the SAMs surface opposite the substrate are very promising in terms of potential biomedical applications. A variety of biomolecules like proteins, peptides, antibodies, and DNA have been immobilized at the SAM's terminal group [2]. We have successfully attached therapeutic drugs to SAMs for the purpose of drug delivery. In this study, we investigate the stability of such SAMs (T-SAMs) during drug loading and *in vitro* drug delivery experiments.

Methods: Hydroxyl-terminated (-OH) SAMs were formed by immersing sputter coated gold substrates in a 2mM absolute ethanol solution of 11-mercapto-1-undecanol. T-SAMs were prepared as follows: aspirin, the model drug, was treated with thionyl chloride and dissolved in dry-tetrahydrofuran (THF). Hydroxyl-terminated SAMs formed on gold substrates were immersed in the prepared solution for 1 hour under nitrogen forming T-SAMs$_{(Aspirin)}$. *In vitro* drug-delivery experiments were carried out by immersing the T-SAMs$_{(Aspirin)}$ on gold in PBS at 37 °C for different time periods. The SAMs, T-SAMs, and drug-eluted samples were investigated by XPS. High resolution S 2p spectra were examined for the peaks at the binding energies (BE) of 162 eV and 169 eV, which have been assigned to thiol and oxidized (oxi.) thiol species respectively [3,4].

Results / Discussion: Fig 1-3 shows the high resolution XPS S 2p spectra of the gold substrates with –OH terminated SAMs, T-SAMs$_{(Aspirin)}$, and after 30 days of *in vitro* drug delivery. The molar concentration (%) of the thiol (BE = 162.2 ± 0.4 eV) and oxi. thiol (BE = 169.3 ± 0.6 eV) components in the XPS S 2p spectra were calculated by keeping the relative peak widths of both the components constant in all the measured spectra. It is vital to note that approximately 40 % of the thiol species in T-SAMs$_{(Aspirin)}$ were oxidized during the procedures for attaching the drug (Fig. 2), possibly from dissolved oxygen in the organic solvents. The peaks that belong to thiol species were completely absent after 30 days immersion in PBS (Fig. 3). This significant alteration could be because of the oxidation during the PBS treatment [3]. It has been shown that the oxi.thiols (sulfonates, sulfonates, etc.) do not have strong affinity towards gold that sulfur does [3,4]; hence the SAMs which are bonded through oxi.thiols are likely to be desorbed from the substrates. Detailed knowledge of this process is crucial for the drug delivery applications, since the drug carriers (SAMs) have to be attached to the substrates until the drug elution period is complete to ensure reproducible dosage.

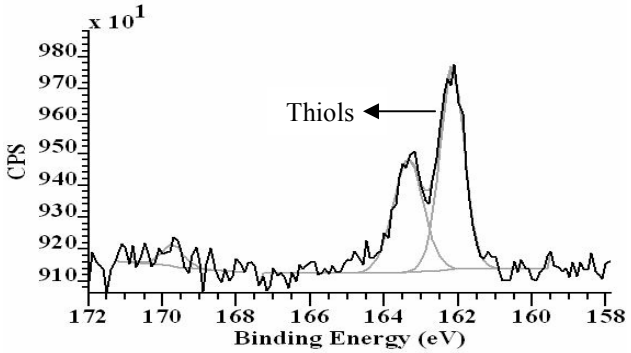

Figure 1. High resolution XPS spectra of S 2p region for the SAMs on gold substrates

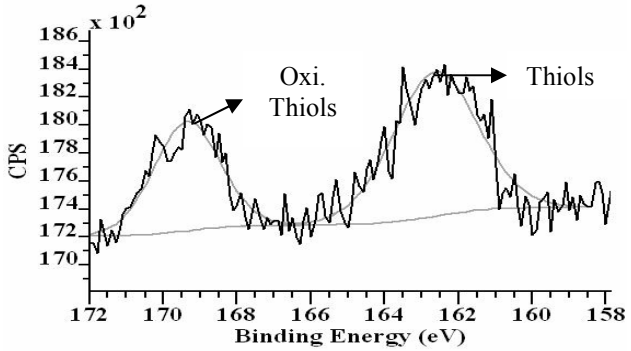

Figure 2. High resolution XPS spectra of S 2p region for the T-SAMs on gold substrates

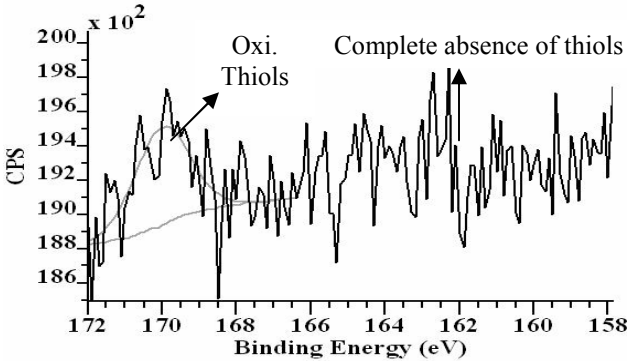

Figure 3. High resolution XPS spectra of S 2p region for the Aspirin eluted gold substrates after 30 day IN-vitro drug delivery

Conclusions: XPS studies showed that 40 % and 100 % of thiols were oxidized during the experiments on drug loading and *in vitro* drug delivery experiments respectively. It is ideally desired to keep the degree of oxidation of thiols to a minimum during the drug loading procedure to ensure greater stability of T-SAMs which would result in lesser variation in the amount of drug released in long term drug elution.

References:

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