Mussel-Inspired Catechol Biomaterials for Surgical Repair and Drug Delivery

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Abstract:

The adhesive proteins employed by mussels have very specialized amino acid compositions undoubtedly related to the particular challenges of achieving permanent adhesion in the wet marine environment. Mussel adhesive proteins (MAPs) are known to contain high levels of the catecholic amino acid 3,4-dihydroxy-L-alanine (DOPA). Catechols are versatile in a chemical sense, participating in redox reactions, high affinity coordination of metal ions, and strong interfacial activity, leading to important roles for catechols in a variety of biological processes such as pigment formation, neurotransmission, iron sequestration, and in the case of mussel byssal proteins-mechanical adhesion. The rich chemical and biochemical landscape of catechols has led to numerous opportunities for the development biologically inspired materials for a variety of applications. In this talk I will summarize our work on understanding the mechanochemistry of mussel adhesive proteins and to design mussel-inspired synthetic catechol materials for use in surgical adhesion/wound closure, antifouling coatings and in drug delivery.

Our basic research is devoted to undertsanding the role of DOPA in mussel adhesive proteins. For example, single molecule force spectroscopy provides a powerful tool for probing the mechanochemical behavior of DOPA at solid-liquid interfaces. These experiments have revealed new details of the chemical interactions between DOPA and inorganic or organic surfaces. More recently, we have explored the unique role of Fe(III) in the mussel byssus, providing the strongest evidence yet for Fe(III) induced covalent cross-linking of catechols, and demonstrating the mechanical toughening of catechol polymer networks through the formation of coordination bonds between Fe(III) and catechols.

On the translational side, synthetic catechol polymer medical sealants and adhesives are being developed, exploiting the same cohesive and adhesive interactions of catechols that are believed to be important in mussel adhesion. Examples of surgical applications where these materials are candidates for use in humans, include vascular wound closure and sealing of spontaneous or fetal surgery-associated cases of fetal membrane rupture.

We have also developed a variety of surface modification strategies inspired by mussel adhesive proteins, involving catechol containing molecules Highly versatile in their ability to modify a variety of different materials by dip-coating, these coatings are able to confer a variety of functional properties to substrates. Several examples of these will be given, with an emphasis on grafting of antifouling polymers onto surfaces via catechol-based chemistry, for the purposes of controlling protein, cell and bacterial adhesion on surfaces, including the surfaces of nanoparticles.

In the area of drug delivery, we are developing novel catechol polymer conjugates of the proteasome inhibitor bortezomib (BTZ) for pH-sensitive delivery to cancer cells. One design takes advantage of the facile conjugation of BTZ to catechols to form pH-sensitive drug delivery vehicles that are stable and inactive in the bloodstream but dissociate in the acidic tumor interstitium or intracellular environment to liberate the drug, activating its proteasome inhibiting function and thereby potentially increasing the efficacy and reducing the peripheral toxicity of BTZ.