Shape Memory Polymers with Phenolic Acid-Based Antioxidant Properties

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Statement of Purpose: Reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2) and hydroxyl radical (OH^-), are produced during cellular oxidative metabolism. In healthy tissue, the elimination and production of ROS is well-balanced. However, in damaged tissues, excess ROS causes oxidative stress, which damages cells and disrupts wound healing processes. Therefore, effective ROS scavenging by antioxidant biomaterials may aid in wound repair following traumatic injury. SMP foams are a class of smart materials that have the ability to return from a deformed, secondary shape to their primary shape after exposure to a stimulus, such as heating. Under dry conditions up to ~50°C, SMP foams maintain a compressed shape for easy storage and storage. Then, when the foams are exposed to water in body temperature blood, they expand to their primary shape within ~2 minutes. These materials have been pursued for hemostatic applications due to their rapid blood clotting.

Here, we have synthesized antioxidant SMPs foams to be used as hemostatic agents. Plant-based phenolic acids (PAs) antimicrobial and free radical-scavenging activities.[1] Therefore, the incorporation of PAs into SMP foams could provide a multifunctional biomaterial system.[2] In our previous research, we incorporated p-coumaric (PCA), vanillic (VA), and ferulic (FA) acids into SMP foams, which demonstrated excellent antimicrobial and antioxidant properties, cell compatibility, and hemocompatibility. In this work, we have further studied antioxidant SMP foams in terms of oxidative degradation and cellular ROS scavenging.

Methods: *Foam Synthesis*: PAs were reacted with polyols and excess hexamethylene diisocyanate (HDI) at 50°C for 48 hours to form an isocyanate (NCO) pre-polymer. A hydroxyl (OH) solution was prepared with the remaining PA and polyols, catalysts, surfactant, and deionized water. The OH solution was reacted with the NCO pre-polymer at 50°C to form SMP foams. *Oxidative degradation*: Cylindrical samples (10 mm length. 8 mm diameter) were submerged in 20% H_2O_2 at 37°C to evaluate oxidative degradation under accelerated conditions. Mass loss; surface chemistry via attenuated total reflectance-Fourier transform infrared (FTIR) spectroscopy; glass transition temperature via differential scanning calorimetry; and pore morphology via scanning electron microscope (SEM) were characterized over up to 20 d. *Cellular ROS scavenging*: Human hepatocellular carcinoma (HepG2) cells were seeded into a 96 well plate. The next day, 2′,7′-dichlorofluorescein diacetate (DCFH-DA) was added to each well as a ROS indicator.[3] Then, foam samples were placed into the wells with fresh media. After 1 hour, samples were removed, cells were washed, and 2,2′-azobis (2-amidinopropane) dihydrochloride (ABAP) was added as a peroxyl radical generator. The plate was analyzed in a plate reader every 5 min for 1 hr with 485 nm excitation and 538 nm emission.

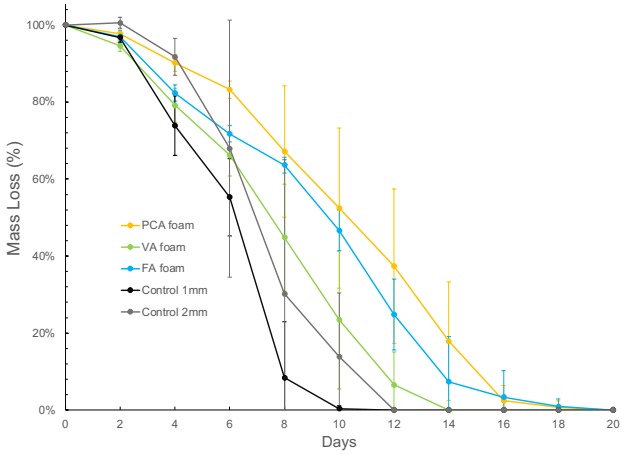
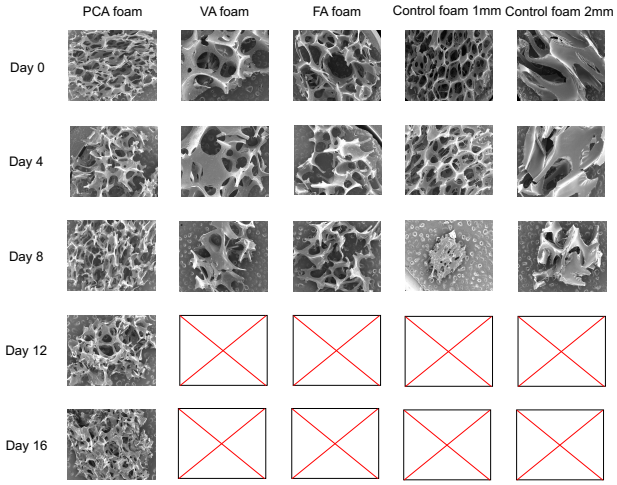


Figure 1. Mass loss of PA foams in 20% H_2O_2.**Figure 2**.



The pore morphology of PA foams during degradation.

Results: Control foams underwent 100% mass loss in 10-12 d, **Figure 1**. All PA foams exhibited slower oxidative degradation in high concentrations of H_2O_2, and PCA foams had the highest stability, which correlates with high antioxidant activity of PCA. The pore morphology, **Figure 2**, shows that PA foams maintain pore structure with less shrinking and collapse than the control foams, with the highest stability evident in the PCA foam. The FTIR spectra indicated that the PAs were released from the foams during degradation, which may have increased H_2O_2 scavenging. Tg's of PA foams remained constant during degradation.

Conclusions: PA foams show evidence of antioxidant activity via enhanced oxidative stability. Cellular ROS scavenging experiments are currently underway. This system could provide an antioxidant biomaterial that improves healing in wounds with ROS imbalance.

References: 1. Liu J. et al. Pharmaceutics. 2020; 12:419. 2. Monroe M.B.B. et al. ChemPhysChem. 2018; 19:1999-2008. 3. Kellett M.E. et al. FoodChem. 2018; 244359-363.