Gelatin-Ovalbumin Hybrid Hydrogels: Characterization and their potential as a Dual Growth Factor Delivery Device

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Statement of Purpose: Growth factors are an important component of tissue engineering along with cells and scaffolds (Tabata Y. PSTT. 2000;3:80-89). One strategy to deliver growth factors *in vivo* is ionic complexation of the growth factor to protein matrices. In this study, the feasibility of a protein hybrid hydrogel for dual delivery of growth factors was undertaken. The hypothesis is that spatiotemporal control of growth factor release is possible from protein hybrids given proper selection of the components. It was reasoned that a globular-fibrous hybrid would be immiscible and therefore allow for the desired spatiotemporal control.

Methods: Gelatin from porcine skin (type A, pI 9) and albumin from chicken egg white (Grade II, pI 4.8) were obtained from Sigma Chemical Co. (St. Louis, MO) and used as received. Aqueous solutions of 5 wt% gelatin A and ovalbumin were mixed in varying blends (20%, 40%, 60%, 80% gelatin A). The ovalbumin sol-gel transition was obtained through various methods of acid, alkaline, and heat treatments. Hydrogel films were dried and crosslinked with 50 mM glutaraldehyde. These hybrid hydrogels were characterized in terms of their swelling, thermal, degradable, and microstructural properties. *In vitro* release studies were carried out with two model proteins, lysozyme and bovine serum albumin.

Results: After lyophilization, these hybrid gels have two distinct "domains" on a macroscopic level, Figure 1.

Figure 1. Gelatin A-Ovalbumin hybrid hydrogels after lyophilization.

Gelatin A-Ovalbumin hybrid hydrogel swelling results demonstrated reduced water adsorption under an alkaline processing method, Figure 2.

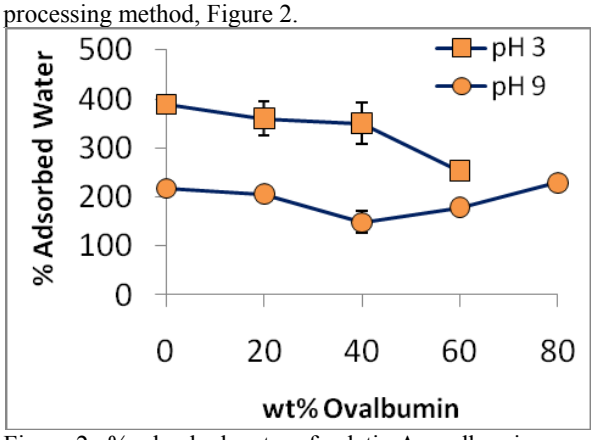

Figure 2. % adsorbed water of gelatin A-ovalbumin films. The amount of adsorbed water was measured in 20 mM phosphate-buffered saline at 37°C (n=3).

In vitro enzymatic degradation under a tissue healing response showed films with a higher concentration of ovalbumin had greater longevity, Figure 3.

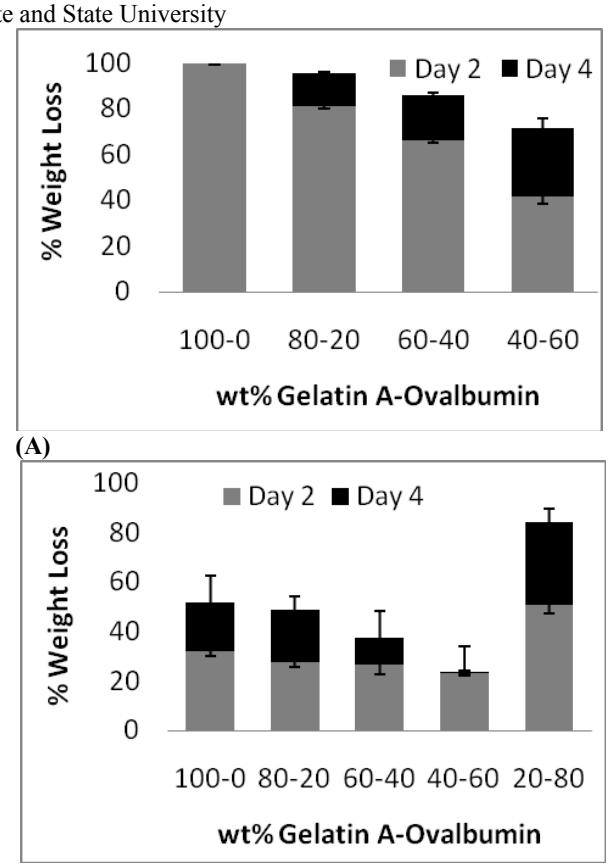

Figure 3. Collagenase degradation of gelatin A-ovalbumin films. The weight loss of films in 300 U/ml enzyme solutions at 37°C (n=3). Panel A: films prepared at pH 3. Panel B: films prepared at pH 9.

Conclusions: At this point, two macroscopic "domains" in the lyophilized hybrid gels is understood to be phase separation of the gelatin and ovalbumin. Crosslinked gelatin A-ovalbumin hybrid gels at pH 9 adsorbed less water under equilibrium conditions and degraded slower in the presence of collagenase, undoubtedly due to more lysine available for crosslinking in alkaline prepared gels. At the same time, this supports the idea of temporal control over growth factor release by varying the crosslinking within the matrices.