Radiation Crosslinked Poly(vinyl alcohol)/Poly(vinyl pyrrolidone)/Poly(ethylene glycol) Hydrogels for Biomedical Applications

Valerie R. Binetti, William Wolf, Huaitzung A. Cheng, Michele Marcolongo, Anthony Lowman
Drexel University, Philadelphia

Statement of Purpose: Poly(vinyl alcohol) (PVA) and poly(vinyl pyrrolidone) (PVP) hydrogels have been investigated for various biomedical applications including cartilage repair [1], nucleus replacement [2], and meniscal replacement [3], two significant disadvantages to freeze/thaw PVA/PVP hydrogels are their low compressive moduli and high swelling ratio (V/V_o). The moduli of PVA/PVP gels can be increased in various methods from creating composite materials from the PVA/PVP gels [3], to various forms of crosslinking. Chemical crosslinking, with agents such as glutaraldehyde, are use to increase the moduli and decrease V/V_o of PVA hydrogels but have been shown to be cytotoxic [4]. Radiation crosslinking, such as electron beam (e-beam) crosslinking, of the PVA/PVP hydrogel eliminates the need for multiple freeze/thaw cycles of the hydrogel and crosslink the gel without the use of cytotoxic crosslinkers such as dialdehydes. Poly (ethylene glycol) (PEG) is added to the PVA/PVP hydrogel to change the solubility point of the solution, allowing more polymer to be added to the hydrogel network in a given volume, which in turn increases the modulus of the hydrogel but depending on the molecular weight of the PEG can either increase or decrease the V/V_o. The purpose of this study is to determine the effect of adding PEG to the PVA/PVP hydrogel and e-beam crosslinking the PVA/PVP/PEG hydrogel by measuring the compressive modulus and swelling ratio of the hydrogels.

Methods: PVA (99.0-99.8% hydrolyzed, MW=145,000) was chemically stabilized with PVP (MW=58,000) in a ratio of 99:1 to form a solution in deionized water at different weight percents. Barium sulfate (1-10 μm) and PEG (MW=10,000) were added to the solution and the hydrogel was formed by a series of autoclaving cycles. Gels were also made without the addition of PEG as a baseline. Upon gel formation, samples were subjected to one cycle of freezing at -20 °C for 21 h and thawing at room temperature for 3 h. E-beam irradiation was done at E-BEAM Services in Cranbury, NJ using a 4.5 MeV electron beam accelerator. The irradiation doses were approximately 20 and 30 kGy. Gels were heated to 95°C before being transferred into molds for testing.
Mechanical Testing: Cylindrical hydrogel samples (n=3) were molded, about 9.5 mm in diameter and 5-7 mm in thickness. Unconfined, uni-axial compression was applied using an Instron 50N load cell, model 4442. The samples were preloaded to 0.2 N, and compressed further to a total strain of 35%. Chord modulus was measured between 10 and 20% strain. *Swelling Studies:* Hydrogels were immersed in a solution of PEG in PBS to examine the changes of the properties over time in an osmotic environment. The PEG solutions were made to an approximate osmotic pressure of 0.20 MPa by dissolving 128.2 g of PEG in 1 L of solution [5]. The ratio of gel volume to swelling media volume was 1:70. V/V_o was calculated from the masses of the samples before and after swelling in air and heptane (n=3).

Results: Hydrogels did not form from solutions below 13.4 wt% PVA without irradiation, therefore neither mechanical nor swelling studies could be performed on 8.9 wt% PVA at 0 kGy. At 13.4 wt% unirradiated PVA solutions without PEG did not form gels, whereas unirradiated solutions with PEG did gel and had a modulus of 0.04 MPa at 24 h. Solutions at both PVA concentrations (13.4 and 8.9 wt%) tested formed gels when irradiated at doses of 20 and 30 kGy, only solutions with PEG were irradiated. At 20 kGy compressive modulus decreased from 0.06 to 0.02 MPa with decreasing PVA concentration, modulus at 30 kGy decreased from 0.10 to 0.02 MPa (Figure 1). Swelling ratio decreases with decreasing PVA content, independent of e-beam irradiation. At 20 kGy V/V_o decreased from 1.50 to 0.94 from with decreasing PVA concentration; V/V_o at 30 kGy decreased from 1.33 to 1.05.

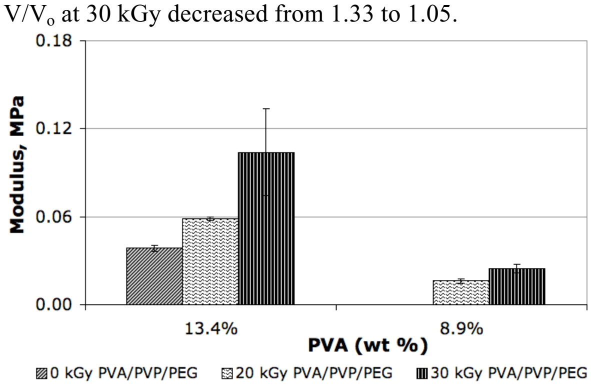

Figure 1. Compressive Modulus at 24 Hours (n=3)

Conclusions: E-beam irradiation is needed to form a gel above 8.9 wt% PVA. At 13.4 wt% PVA the addition of PEG formed a hydrogel with a modulus of 0.04 MPa. Electron beam irradiation at doses of 20 and 30 kGy increased modulus and decreased swelling for these selected concentrations of PVA in the family of PVA/PVP/PEG hydrogels, due to an increase in crosslinking of the network.

References:

1. Spiller, K. L. *et al.* Acta Biomater. 2008; 4: 17-25.
2. Thomas, J. *et al.* J Biomed Mater Res A. 2003;67A: 1329-1337.
3. Holloway, J. L. *et al.* Acta Biomater. 2010; 6:4716-4724.
4. Gough, J. E. *et al.* J Biomed Mater Res. 2002; 61:121-130.
5. Urban, J.P. *et al.* Spine. 1988;13:179-87.