

# Poly (vinyl alcohol)-Acrylamide Hydrogels as Load-Bearing Cartilage Substitute

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**Statement of Purpose:** Poly(vinyl alcohol) (PVA) has been advanced as a biomaterial for the fabrication of medical devices to be used as synthetic articular cartilage because of its viscoelastic nature, high water content, and biocompatibility. Key material requirements for such devices are high creep resistance to prevent mechanical instability in the joint and high water content to maintain a lubricious surface to minimize wear and damage of the cartilage counterface during articulation. The creep resistance of PVA hydrogels can be increased by high temperature annealing; however this process also collapses the pores, reducing the water content and consequently reducing the lubricity of the hydrogel surface [1]. We hypothesize that a hydrophilic compound such as poly(acrylamide) (PAAm) can prevent the pore collapse by filling the pores during annealing and the hydrophilic nature of the PAAm would increase the ability to retain water subsequently resulting in a hydrogel with high lubricity while still maintaining a high creep resistance.

**Materials and methods:** PVA-AAm interpenetrating networks (IPN) hydrogels were prepared by dissolving PVA in deionized (DI) water at 90°C. The solution was mixed with an aqueous solution of AAam monomer at 40°C in the presence of 1:3 ratio of ammonium persulfate to azobisisobutyronitrile, for a total initiator concentration of 0.1 wt% of AAam monomer. The resulting solution was pre-polymerized at 45°C then poured into a glass mold. The solution was placed in a -17°C freezer then thawed followed by a polymerization process (1h to 45°C, 2h at 45°C, 1h to 55°C, 4 h at 55°C). The polymerized IPN was then placed in a -17°C freezer for 16 hours with a subsequent 8h thawing. The gel was then soaked in PEG with constant agitation until equilibrium was reached, followed by soaking in DI water in order to remove any unreacted AAam monomer. The gels were then dried in a convection oven at 25°C for 14 hours, ramped to 80°C in 8 hours, then kept at 80°C for 20 hours prior to annealing. Annealing was carried out under a 500mmHg argon partial pressure at 160°C for 1 hour in a vacuum oven. The annealed gels were rehydrated in DI water until equilibrated. As a comparison, PVA-PEG gels were prepared by mixing 15% (w/w) PVA solution at 90°C to 28% (w/PEG)/w(PEG+water) PEG. The solution was cooled down to room temperature. Two groups were prepared: "as-gelled" (AG) and "de-PEGed" (DP). The latter was immersed in saline solution in order to remove the PEG from the hydrogel and the AG gel was dried similar to the AAam gels, with a subsequent annealing period of 20h at 160°C under argon in a self-persurized vessel. The equilibrium water content (EWC) was measured using a Thermogravimetric Analyzer (TGA). Creep behavior was determined by applying a 100N load for 10 hours followed by a relaxation period under a 10N load for 10 hours on cylindrical samples. The gels were imaged using a confocal laser scanning microscope. Relative coefficient of friction (COF) was determined in DI water at 40°C against an annular fixture mounted on a controlled stress rheometer (AR-2000, TA Instruments) with an inner radius of 0.72cm and a contact area of 0.36cm<sup>2</sup> at a constant angular velocity of 0.1 rad/s. The COF between the IPN and the counterface was calculated using the method of Kavehpour and McKinley [2]. The COF was measured by averaging the reading over 90s of load application. The Instron Insight 2 (MTS) pulling at a rate of 20in/min was used to determine the tear strength of the gels per ASTM D624.

**Results:** The equilibrium water content of the IPNs showed an expected increase with increasing AAam concentration, due to the hydrophilic nature of PAAm (Table 1). The EWC for 15-5, 15-10, and 15-15 PVA-AAm was 50, 72 and 83%, respectively. The EWC of the 15-15 PVA-AAm gel was comparable to that of the 15-28 PVA-PEG AG SRA. The pore size of the annealed PVA-AAm gels was significantly smaller than the annealed PVA-PEG (Fig1).The confocal images show an increase in pore size with increasing AAam content. On the other hand, creep resistance of the PVA-AAm gels decreased with increasing AAam content both before and after annealing (Fig 2, Table 1).Annealing markedly improved the creep resistance of all formulations

studied (Fig 2, Table 1). The initial elastic response of the gels to the 100N load increased with increasing AAam content for both annealed and non-annealed gels (Table 1). While the viscoelastic strain for the non-annealed form of the gels showed small variations with AAam content, after annealing viscoelastic strain increased from 1% at the 15/0 PVA/AAm ratio to 13% at the 15/15 PVA/AAm ratio. Nevertheless, creep resistance of PVA-AAm gels is still higher than that observed on PVA-PEG gels.

Samples	EWC (%)	TCS (%)	Tear (N/mm)	X (%)	RCOF
<b>PVA-PEG</b>					
15-28 DP	91±1.7	87±1.4	0.3±0.1	3 ±0.4	0.30±0.001
15-28 AG SRA	79±0.6	59±2.7	9±0.2	44 ±7	0.40±0.001
<b>PVA-AAm Non-annealed</b>					
15-0	74±1.2	59±0.8	13±3	7±0.3	0.35 ± 0.038
15-5	78±0.1	57±1.4	13±1	6 ±0.2	0.24 ± 0.05
15-10	85±1	72±0.9	4±0.1	5±0.1	0.045 ± 0.003
15-15	87±1.5	70±2	3±0.2	5 ±0.1	0.037 ± 0.001
<b>PVA-AAm Annealed</b>					
15-0	37±1.2	14±2.1	87±4	52 ±1	0.33±0.03
15-5	50±0.1	19±4.5	33±11	15 ±1	0.34±0.13
15-10	72±1.0	28±1.8	10±1	11 ±0.2	0.18±0.02
15-15	83±1.5	53±2.3	8±1	20 ±1.0	0.12±0.003

The total creep strain after 10-hours of loading decreased with decreasing equilibrium water content and showed a very strong correlation ( $\gamma_s=0.9$ ). The tear strength decreased with increasing AAam content (Table 1).

The tear strength observed for the 15-10 PVA-AAm gels was comparable to that of the 15-28 PVA-PEG AG SRA gels. Addition of the hydrophilic AAam group in to the PVA network substantially decreased the friction coefficient corroborating our hypothesis (Fig 3). The relative coefficient of friction of the PVA-AAm gels decreased with increasing acrylamide content increased the RCOF in both the

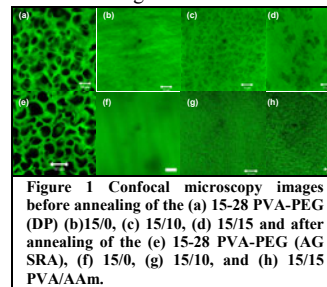
before and after annealing. Annealing

PVA/AAm and PVA/PEG gels (Fig 3, Table 1). The relative COF of the PVA-AAm gels was lower than that of the treated PVA-PEG gels (Fig 3). There was a somewhat strong negative correlation between relative coefficient of friction and equilibrium water content ( $\gamma_s=-0.49$ ). The x-ray diffraction data showed a decrease in the crystallinity of PVA segments with increasing AAam content (Table 1), suggesting that the polyacrylamide impeded PVA's ability to organize into crystals. Presumably, this decrease in PVA crystallinity also contributed to the decrease in the creep resistance of the PVA/AAm gels.

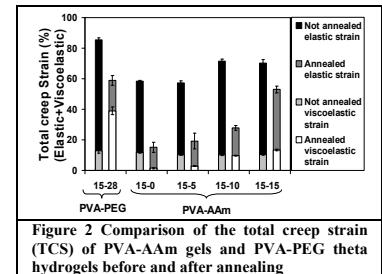
**Conclusions:** Incorporation of AAam component in to PVA networks substantially improved the lubricity of the resulting gels while maintaining a high creep resistance. PVA-AAm hydrogels are promising candidate hydrogels for use as synthetic articular cartilage.

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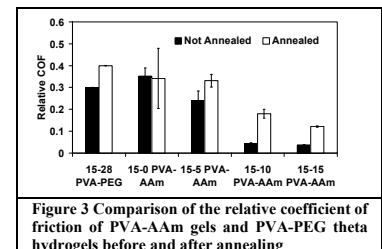
**References:** 1) Bodugoz-Senturk, H et al. *Biomaterials*, 2008, 29(2): 141-9; 2) Kavehpour HP et al. *Tribology Letters*, 17(2), pp. 327-335, 2004.



**Figure 1** Confocal microscopy images before annealing of the (a) 15-28 PVA-PEG (DP) (b)15/0, (c) 15/10, (d) 15/15 and after annealing of the (e) 15-28 PVA-PEG (AG SRA), (f) 15/0, (g) 15/10, and (h) 15/15 PVA/AAm.



**Figure 2** Comparison of the total creep strain (TCS) of PVA-AAm gels and PVA-PEG theta hydrogels before and after annealing



**Figure 3** Comparison of the relative coefficient of friction of PVA-AAm gels and PVA-PEG theta hydrogels before and after annealing