

Crystallization mechanism of the PVA-Theta hydrogel as load bearing synthetic articular cartilage

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Statement of Purpose: PVA hydrogel is a candidate material for synthetic articular cartilage due to its viscoelastic nature, high water content, and biocompatibility. Potential devices are resurfacing patches, osteochondral plugs or interpositional implants. PVA hydrogels in different forms exhibit acceptable strength and stiffness for osteochondral plugs. However when used as interpositional implants, which require stronger and stiffer materials, PVA hydrogel lacks the strength and toughness. One method to strengthen PVA hydrogels is to increase its crystallinity and to reduce its water content. However the reduction water content also reduces the lubricity of the gels and could compromise the counterface cartilage during in vivo use. Therefore, increasing crystallinity with minimal loss on water content is desirable. The crystallinity of PVA hydrogels can be increased by dehydration followed by annealing – yet this method reduces the water content of the gel unless a non-volatile substance, such as polyethylene glycol (PEG), is kept in the pores of the hydrogel during annealing. The crystallization kinetics of PVA thetadgels during high temperature annealing is not well understood, especially the changes that take place during the steps of dehydration, annealing, and rehydration. In this study we used wide angle x-ray diffraction (WAXD) to investigate these changes.

Materials and Methods: 15% (w/w) PVA (MW=115,000) and 28% PEG solution was prepared in deionized water at 90°C. The solution was molded and cooled down to room temperature for gelation for 24h. Two gel groups were prepared: One group was used in their ‘as-gelled’ form (AG). The other group was immersed in DI water after gelation for PEG removal and was used in this ‘dePEGed’ form (DP). The crystallinity of the gels were measured during (i) gelation (6h, 12h, 24 (AG)), (ii) DePEGing (1h, 6h, 12h, 24h equilibrium (DP eq)), (iii) dehydration under vacuum at room temperature (6, 12, 24h and equilibrium), (iv) high temperature annealing under 500 mmHg at 160°C for 1h subsequent to equilibrium dehydration (v) rehydration subsequent to equilibrium dehydration and annealing (6,12, 24h, 3 days and equilibrium). Both dehydrated and annealed gels groups were rehydrated in DI water. A PANalytical X'Celerator powder diffractometer was used to determine the crystallinity of the PVA hydrogels. The diffraction pattern was obtained from 5 to 90° 2θ at a rate of 8.5°/min. The peaks were fit using a commercial peak-fitting package, JADE with an overall residual error of less than 3%. Crystallinity (X) was the ratio of the area under the crystalline peaks at 17°, 19°, 23° and 40°. The PVA crystallinity values for the equilibrium gels were reported as tested (GX) and also as true PVA crystallinity (CX) by normalizing gel crystallinity values by the PVA content. The equilibrium water content (EWC) of the rehydrated gels at equilibrium was determined by measuring the weight loss during complete dehydration at 90°C. The total creep strain (TCS) of the samples was determined on a custom made mechanical tester in DI at 40°C by applying a 100N load for 10h followed by a 10h relaxation period under 10N load.

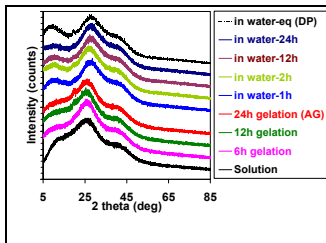


Fig 1. Crystallinity behavior of PVA-PEG solution during gelation and DePEGing

increased and another peak appeared at 40° after 12h. Annealing slightly increased the crystallinity of the dried DP gel and the peak at 22° appeared. The main difference in the WAXD pattern of annealed and dried-only gels was observed after rehydration (Fig 2b). Crystalline peaks at 19° and 40° of the dried DP disappeared and the CX value of the rehydrated PVA DP-dry gel decreased from 42 to 7% upon rehydration whereas the DP annealed gel did not show any difference in the WAXD pattern and the crystallinity slightly increased (Fig 2a, Table 1). Dehydration and annealing showed

similar effects on the crystallinity of AG gels, which exhibited strong diffraction peaks after dehydration and annealing (Fig 2a). AG annealed gel showed higher crystallinity than its DP counterpart. In contrast to DP annealed gels, rehydrated AG annealed PVA exhibited substantially different WAXD pattern than its annealed dry state; crystallinity values of AG annealed gel decreased after rehydration (Fig 3). The increase in crystallinity also resulted in higher creep resistance and low EWC for both AG and DP annealed gels (Table 1). We found a strong negative correlation between CX and TCS ($\gamma_s = -0.7$) and CX and EWC (negative ($\gamma_s = -0.9$)).

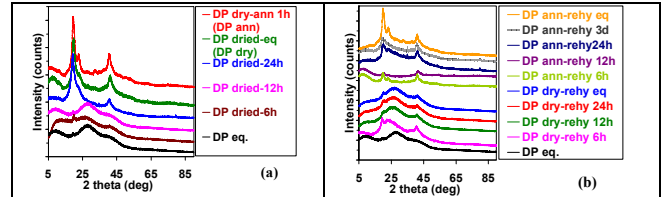


Fig 2 Crystallinity behavior of PVA-PEG DP gel during a) vacuum drying -annealing and b) subsequent rehydration

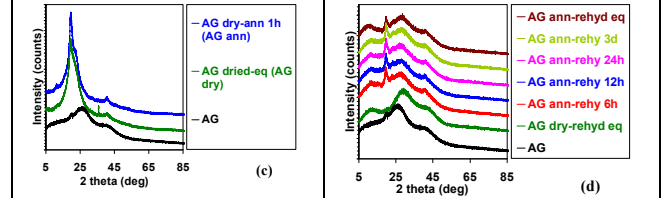


Fig 3 Crystallinity behavior of PVA-PEG DP gel during a) vacuum drying -annealing and b) subsequent rehydration

The increase in the crystallinity of PVA in both DP and AG form upon dehydration and annealing is likely due to the chain proximity caused by removal of the free and bound water from gel network. Removal of water and the increased chain proximity presumably increased hydrogen bond formation between OH groups in PVA chains thus the crystallinity. The fact that the subsequent annealing step is more effective than dehydration alone is probably due to the increased mobility of the chains caused by the additional energy at high annealing temperature. The higher PVA crystallinity in annealed AG is probably due to the presence of PEG during annealing. We postulate that PEG separates the bound water molecules, which cannot be removed by vacuum dehydration, from PVA, removing their steric hindrance of crystallization. Also the decrease in the PVA crystallinity after rehydration in annealed AG gels is probably due to removal of PEG which was likely stabilizing these dissolving crystals in PVA.

Table 1 EWC Crystallinity and TCS value of PVA theta hydrogels

	EWC (%)	Gel X (%)	CX (Corrected PVA X) (%)	TCS (%)	Appearance
DP	91±1.7	0.9±0.4	10±5	88±1.0	Opaque
DP dry	4.1±1	37±4	39±4	-	Transparent
DPdry-rehyd	74±4.9	1.7±0.3	7±1	30±1.5	Transparent
DP annealed	3±0.4	42±12	43±13	-	Transparent
DP ann- rehyd	55±1.4	21±7	48±10	19±4	Transparent
AG	62±2.1	1±0.3	3±1	-	Opaque
AG dry	10±1	7±3	8±2	-	Opaque
AG dry-rehyd	89±1.0	0.3±0.2	2±2	82±1.0	Opaque
AG annealed	7±0.8	24±6	86±20	-	Opaque
AG ann-rehyd	83±1.0	5±2	42±10	65±4	Opaque

Conclusion: Annealing and dehydration increased crystallinity of the PVA-PEG theta gels. Annealing resulted in more stable crystalline network and mechanically stronger gels. Highly crystalline PVA hydrogels are promising candidates as artificial cartilage substitutes.

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References: 1) Bodugoz-Senturk, H et al. Biomaterials, 2008, 29(2)141-9.