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The influence of mechanical stretching and freeze-thaw processing on the properties of polyvinyl alcohol hydrogels for drug delivery applications

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Introduction

The study describes the development of physically cross-linked polyvinyl alcohol (PVA) hydrogels using uniaxial orientation via freeze-thawing (F/T). Although cryogels have shown significant improvements in long-term stability, high tensile strength, high elastic mechanical character and high degree of swelling [1,2], stretching hydrogels in between freeze-thawing cycles could change its properties and might be modulated for drug delivery systems. It has been proved that the stretched hydrogels are mechanically stronger and easier to handle than typical hydrogels of the same composition and dimensions [3]. In addition, the stretching process can induce a uniaxial polymer chain alignment while maintaining sufficient porosity and water content (>95%) [3]. Therefore, the hypothesis of this study is the stretched PVA/CAF hydrogel can highly improve the drug releasing rate and its tensile strength.

Methods

- The pure PVA hydrogels and caffeine-contained PVA hydrogels were created by freeze-thaw processing with 20 minutes fast freezing using liquid nitrogen and 4 hours thawing at 4°C.
- The orientated hydrogels were produced by applying a uniaxial orientation cycle (100% stretching strain per cycle) after each F/T cycle.

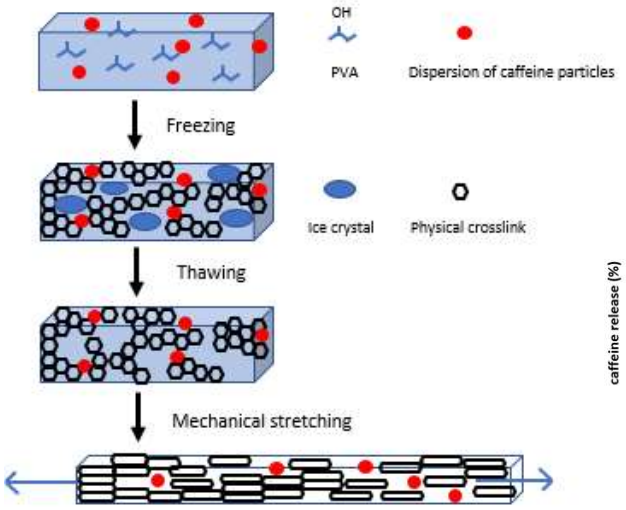

Figure 1: *Schematic diagram of the orientated PVA/CAF hydrogel preparation using freeze-thaw method*

Results

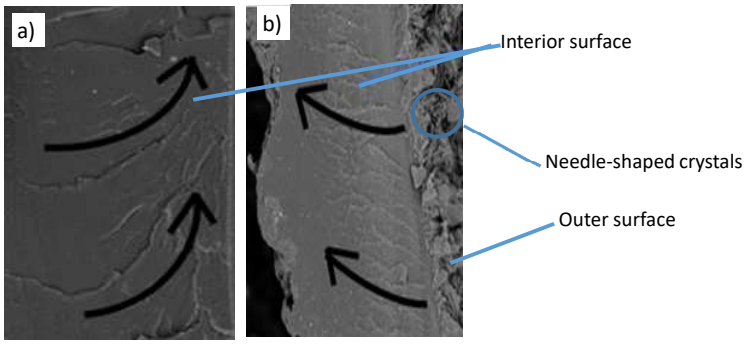

Figure 2: *SEM micrographs of the interior part of (a) PVA 2FT2S and, (b) PVA/CAF 2FT2S hydrogel samples. (*FT=freeze/thaw, S= stretching)*

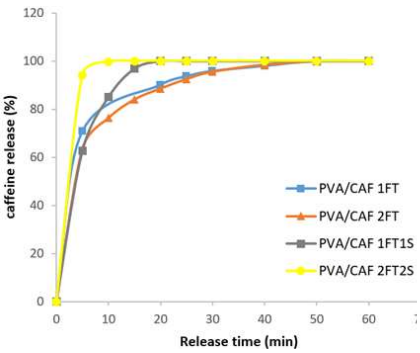

Figure 3: *Drug releasing rate of PVA/CAF hydrogels*

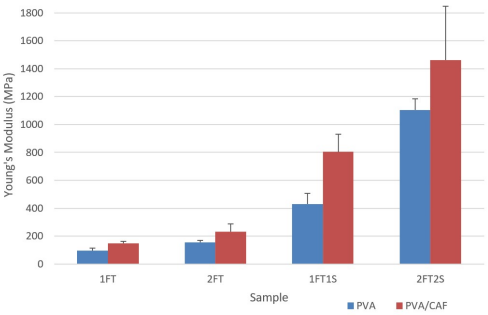

Figure 4: *Tensile strength of PVA and PVA/CAF hydrogels*

Discussion

- The chemical, mechanical and thermal properties for all dried xerogel samples were evaluated and the results shows that the PVA/CAF hydrogel with two F/T cycles followed by two stretching cycles (e.g. PVA/CAF 2FT2S) gave the best response.
- PVA/CAF 2FT2S was found to show best fit (R^2=0.9904) in the Hixson-Crowell drug release model with the fastest drug releasing rate in 15 minutes due to the increase of surface area-to-volume ratio on the hydrogel.
- **Hixson-Crowell euqation**: $\sqrt[3]{W_o} - \sqrt[3]{W_t} = \kappa t$
- When there were more mechanical stretching cycles applied on the hydrogel, the polymer chains alignment increase and consequently caused the increase of swelling degree.
- PVA/CAF 2FT2S has the highest Young's modulus of 1462 MPa which makes the hydrogel very stiff in comparison to all the hydrogel samples.

Table 1: *Release behaviour of the drug-loaded PVA/caffeine hydrogels.*

PVA/CAF	Zero-order	First-order	Higuchi	Korsmeyer-Peppas		Hixson-Crowell
	R^2	R^2	R^2	R^2	n	R^2
1FT	0.9960	0.9809	0.9808	0.9642	0.1427	0.9871
2FT	0.9800	0.9993	0.9956	0.9992	0.2564	0.9957
1FT1S	0.9696	0.9770	0.9902	0.9941	0.4020	0.9984
2FT2S	0.8033	0.9513	0.8591	0.9062	0.0579	0.9904

References

1. Fumio *et al.*, Int J of Pharm, 58:pp. 135–142, 1990.
2. Hassan & Peppas, Macromolecules, 33:pp.2472–2479, 2000.
3. Zhang *et al.*, Biomaterials, 35:pp. 3243–3251, 2014.

Acknowledgements

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