**Novel Hydrogel for the Replacement of the Nucleus Pulposus**

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**INTRODUCTION**

Back pain induced by the degeneration of the hydrogel core of the intervertebral disc, the nucleus pulposus (NP), is currently a major public health issue. Different treating approaches exist such as vertebral fusion and total disc replacement with for example a SB Charité Prosthesis. However, recent trends in surgery are shifting towards preservation techniques and a new strategy will be to replace the NP by an adequate material that restores all its functions. Synthetic hydrogels have been developed over the last years for their hydrophilic character and potential biocompatibility but none gained universal acceptance as NP prostheses up to now. The goal of this study is to create a novel hydrogel based on Tween 20 trimethacrylate (T3) as a crosslinker and N-vinyl-2-pyrrolidone (NVP) in order to restore disc height but also the AF loading. Mechanical properties of the novel hydrogel as well as the swelling behaviour were investigated.

**METHODS**

A well mixed solution of T3 (synthesized in the lab from Tween 20 purchased at Sigma-Aldrich, Switzerland), NVP (Sigma-Aldrich, Switzerland), photoinitiator Irgacure 12959 (Ciba, Switzerland) and deionised water was used to cast samples of 2 cm in diameter and 5 mm high in silicon moulds resistant to UV light. Samples were exposed for 30 min to UV light with an intensity of 140 mW/cm² measured between 270 and 370 nm (SolaCheck, Solatell, UK). The samples were then redimensioned with a punch to cylinders of 8 mm of diameter and 5 mm high. The swelling behaviour of the hydrogel samples was assessed as a function of T3 concentration. The swelling ratio at each concentration of T3, the degree of crosslinking of the network is higher with a higher T3 concentration. The swelling behaviour of the hydrogel samples with concentration of T3 of 4.5 vol%, 8 vol% and 15 vol% was followed gravimetrically by measuring the weight gain with the time of immersion in PBS at room temperature. Every 15 minutes, the samples were weighed after drying the surface. The measurements were taken until equilibrium was reached. During the swelling process a considerable increase of the dimensions of the original samples was observed. All measurements were triplicated to ensure reproducibility.

The swelling ratio was calculated as follows:

$$SR = \frac{W_f}{W_d} = \frac{(W_w - W_d)}{W_d}$$

where $W_w$ is the weight of PBS in the swollen hydrogel after the equilibrium has been reached at room temperature, $W_d$ is the weight of the dry sample and $W_f$ is the weight of the dry hydrogel at time 0. The solute diffusion in the hydrogel, in this case saline (PBS), was characterized by the phenomenological equation, that represents the fraction of released drug molecules from a polymer as a function of time,

$$M_t / M_\infty = K t^{n'}$$

where $M_t$ is the swelling ratio at time $t$, $M_\infty$ the swelling ratio at equilibrium, $K$ is a constant related to the characteristics of the gel and $n'$ is the exponent describing the Fickian or anomalous swelling mechanism. For cylindrical samples, when $n'>0.45$ non-Fickian diffusion is observed, while $n'\leq 0.45$ represents a Fickian diffusion. The values of $n'$ and $K$ were calculated from the slopes and intercepts of $\ln(M_t / M_\infty)$ vs $\ln t$.

Hydrogel samples with 8vol% of T3 at swelling equilibrium were tested under confinement with large deformations in a custom device, as shown in Figure 1.

**RESULTS**

Figure 2 shows the variation of the mass of samples as a function of the swelling time for hydrogels with composition indicated. All samples showed similar behaviour, with an initial rapid swelling phase, a slower uptake and finally an asymptotic equilibrium.

As showed in Table 1, all hydrogel compositions exhibited a Fickian diffusion of the solute. $n'$ is related to the pore size and as $n'$ increases, the pore size increases too.

Swollen hydrogels showed similar behaviour in confined compression as the bovine NP. In Figure 3, it can be noticed however that the hydrogel has a significantly higher preloading force value.

**DISCUSSION**

The swelling behaviour of the novel hydrogels can be easily tuned by changing the composition of the system. As the amount of crosslinker is doubled, the water absorbed by the hydrogel is divided by two. The SR values vary from 1.5 to 5.6 and are in the range of the SR values of the native NP (1.8 to 9). The material will therefore be able to transfer the loads to the AF as a native NP. The diffusion of the saline through the hydrogel follows Fick’s law and is proportional to the square root of time at early stages of swelling. Here again, $n'$ is dependent on the T3 concentration and decreases as the latter increases. For a higher concentration of T3, the degree of crosslinking of the network is higher and therefore, the pore size is smaller.

Comparing the bovine NP to the novel hydrogel developed here showed that the hydrogel has similar viscoelastic behaviour within the range of the tested frequencies. The significantly higher preloading force value predicts that the material will probably have the capacity of restoring disc height.

The developed hydrogel in this study could be a good candidate for the replacement of the human NP as it transfers loads to the AF and restores disc height.

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**Figure 1:** a) Compression chamber composed of a silicon membrane and two porous filters, b) compression plates.

Five hydrogel samples were submitted to a 12.5% strain at a 1N preload. 20 cycles at 1 and 0.01 Hz were performed, repeated three times for each sample. Bovine NP samples, punched from bovine spinal units, were compared to the hydrogel samples. The testing devices were paired and Bovine NP samples were tested at the same conditions.