XXII POLISH CONFERENCE ON BIOCYBERNETICS AND BIOMEDICAL ENGINEERING



Abstract Book

Warsaw, May 19-21, 2021

Thermosensitive hydrogel/short electrospun fibers as a smart scaffold for tissue engineering

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The aim of these studies was to obtain a thermosensitive injectable hydrogel system consisting of methylcellulose (MC)/agarose hydrogel and short electrospun poly(l-lactide) acid (PLLA) nanofibers as a scaffold for tissue engineering application. Hydrogel components provide many benefits such as biocompatibility, high processability, and 3-D highly hydrated structure. The thermosensitivity of this biomaterial allows it to remain as a sol at room temperature and become a highly crosslinked gel in the physiological temperature after injection. It is an effect of reversible crosslinking of MC starting from dehydration known as "water cages destruction," followed by fibril formation. Agarose plays a supportive role in MC crosslinking as a dehydration accelerator [1]. Filling hydrogel with short electrospun nanofibers strengthens hydrogel mechanically and enriches its structure with bioactive fibers. Such an approach improves the mimicry of native ECM, providing an appropriate environment and support for cell growth and regeneration.

In these preliminary studies, scanning electron microscopy (SEM) was used to determine the hydrogel/short fibers system's morphology. The viscosity measurements allowed to assess hydrogels' injection ability after fibers addition by comparing viscosities with the literature reports.

The morphology of 5 wt. % MC/ 5 wt. % Agarose filled with 7.5 mg/ml of PLLA fibers (Fig. 1.) showed a structure, which according to Padhi et al. [2], are similar to native ECM of rats spinal cord. Table 1 shows a few examples of the viscosity results for hydrogels vs. hydrogels loaded with PLLA fibers at room temperature. The viscosities are below 1000 mPa • s, which according to Bradshaw et al. [3], is the limit of liquid injectability through 23 and 25 gauge needles.



| Material | Viscosity [mPa • s] |
|--|------------------------|
| 3 MC/3 Agarose | 121.44 ± 11.7 |
| 3MC/3 Agarose/7.5 mg/ml PLLA fibers | 179.7 ± 15.2 |
| 5 MC/ 5 Agarose | 725.2 ± 55.6 |
| 5 MC/ 5 Agarose/7.5 mg/ml PLLA fibers | 890 ± 90.9 |

Fig. 1. SEM image of a hydrogel loaded with fibers.

Table. 1. Viscosities of hydrogels before and after the addition of short fibers.

The SEM imaging showed a resemblance between the structure of the obtained hydrogel system and native ECM. Simultaneously, viscosity studies confirmed hydrogel/short fibers systems' injectability, thereby demonstrating its high potential in tissue engineering applications. References:

[1] B. C. Martin, E. J. Minner, S. L. Wiseman, R. L. Klank, R. J. Gilbert 2008 J. Neural Eng 5, pp. 221

[2] A. Padhi, A.S. Nain, 2020 Ann Biomed Eng 48, pp. 1071–1089

[3] J. Bradshaw, S. White, 2018 ONdrugDelivery Magazine 91, pp.16-21