When dynamic covalent chemistry meets bioactive glasses – novel multi-level crosslinked, injectable, self-healing chitosan-based hydrogels

Szymon Salagierski [1], Michal Dziadek [1], Barbara Zagrajczuk [1], Patrycja Domalik-Pyzik [2], Andrada Serafim [3], Izabela-Cristina Stancu [3], Katarzyna Cholewa-Kowalska [1]

[1] Department of Glass Technology and Amorphous Coatings, AGH University of Science and Technology, Krakow, Poland
[2] Department of Biomaterials and Composites, AGH University of Science and Technology, Krakow, Poland
[3] Advanced Polymer Materials Group, University Politehnica of Bucharest, Bucharest, Romania

Hydrogel materials are a three-dimensional crosslinked network of polymer chains. High porous structure and presence of many functional groups confers their attractive properties such as large water content and great swelling. Due to their beneficial rheological properties, hydrogels can be used as injectable materials with high surgical handiness, ideal for minimally invasive surgery.

In this study, silicate and borate bioactive glasses (BGs) were used as modifiers in the dynamic covalent chitosan-based hydrogels crosslinked with dextran dialdehyde. We have shown for the first time that both silicate and borate BGs can play a dual role in the obtained hydrogels – they serve a functional component, modifying hydrogel properties, and provide additional multi-level crosslinking mechanisms.

The aim of this study was to obtain injectable hydrogel materials based on chitosan and evaluate the effect of different BGs on the crosslinking process and physicochemical, biological and rheological properties of hydrogels. After the materials were freeze-dried their microstructure, porosity and mineralization was assessed by SEM/EDX and ATR-FTIR. Mineralization process in wet state was evaluated using µCT. Additionally, rheological, self-healing properties and injectability were investigated. The *in-vitro* studies were carried out with the Human Umbilical Vein Endothelial Cells (HUVECs).

Two main mechanisms of the crosslinking effect of BGs, resulting from the release of their degradation products can be identified. Boron and silicon provide dynamic covalent ester bonds. Calcium and sodium-mediated deprotonation of the NH_3^+ groups of chitosan enables the formation of additional imine bonds. BGs significantly improve stiffness, compressive strength, and viscoelastic characteristics of hydrogels, as well as greatly reduce crosslinking time. Hydrogels modified with BGs showed good injectability and self-healing properties. Furthermore, no cytotoxic effect of hydrogels was observed in direct contact with HUVECs.

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