**Microstructural and Diffusive Characterization of Calcium Alginate Hydrogels**

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Hydrogels are three-dimensional polymeric networks that contain a significant amount of water, which co-determines their structure. Natural hydrogels such as calcium-alginate have been extensively used in food and drug applications and claimed to provide control over bioactive compound release to the surrounding digestive fluids1. Few studies focus on hydrogel mesh properties and for those studies that consider this, it is measured when the hydrogel is freshly prepared. Yet, alginate hydrogels respond to environmental changes, as occur in the gastrointestinal tract, affecting their mesh size and diffusion into and from the hydrogel network.

In this study, we systematically characterized microstructural changes of alginate hydrogel microcapsules and corresponding diffusion properties under different pH and ionic strength conditions. Hydrogel mesh size was estimated based on swelling ratio and storage modulus. The kinetics of diffusion within the hydrogel was studied using fluorescence microscopy, by conducting one-dimensional diffusion experiments of tetramethylrhodamine (TRITC) dextran within a hydrogel-filled capillary tube. The experimental data were modelled in COMSOL2, using a finite element analyzer that enables simulation of solute diffusion, to find diffusion coefficients throughout the hydrogel.

The calculated mesh size of alginate hydrogel (5% w/v) increased with decreasing pH, from 5.7 ± 0.2 nm to 10.5 ± 0.4 nm. In response, the diffusion coefficient of TRITC-dextran (40 kDa) increased from 1.3 ± 0.05∙10-10 m2/s to 1.9 ± 0.08∙10-10 m2/s, respectively. An increase in mesh size and solute diffusivity was also observed at elevated ionic strength. These findings provide valuable information for the correlation between hydrogel mesh size and solute diffusivity under digestive conditions, which are essential for, amongst others, intestinal targeted delivery systems.

*Reference:*

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2. Dosmar, E. *et al.* Compartmental and COMSOL Multiphysics 3D Modeling of Drug Diffusion to the Vitreous Following the Administration of a Sustained-Release Drug Delivery System. *Pharmaceutics 2021, Vol. 13, Page 1862* **13**, 1862 (2021).