

Magnetic alginate hydrogels: the role of particles' surface functionalization

Mariusz Barczak¹

Piotr Borowski¹, Cristina Gila-Vilchez^{2,4}, Miguel Alaminos^{3,4}, Fernando González-Caballero^{2,4}, Modesto T. López-López^{2,4}

¹Department of Theoretical Chemistry, Institute of Chemical Sciences, Faculty of Chemistry, Maria Curie-Skłodowska University, 20031, Lublin, Poland

²Department of Applied Physics, Faculty of Sciences, University of Granada, 18071, Granada, Spain

³Tissue Engineering Group, Department of Histology, University of Granada, Granada, Spain

⁴Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain

mariusz.barczak@mail.umcs.pl

Introduction

Hydrogels can be considered as three-dimensional, hydrophilic networks of flexible polymer chains swollen by water or other fluid. They are able to store a large amount of water (even up to thousands times their dry weight) while maintaining the structure that can be cast into practically any shape or form [1]. They are soft and capable of retaining large amounts of water thus closely resemble living tissues. Mainly for that reason hydrogels are considered as particularly promising materials in the rapidly developing field of tissue engineering as matrices for replacing and regenerating different tissues and organs [2-4].

There is a plethora of different hydrogelators which can be used to fabricate hydrogels; among them alginate-based hydrogels are considered as one of the preferred formulations, mainly due to low cost and excellent biocompatibility of alginate hydrogelators [5,6]. To fabricate "smart" materials, alginate hydrogels can be doped with magnetic particles. Incorporation of magnetically-susceptible species into hydrogel structure may provide additional features like, for example, stimuli-responsive action, improved thermal properties or tailorable rheological properties without affecting biocompatibility [7,8]. The rheological properties of the magnetic hydrogels (also called ferrogels) in the presence of magnetic field are then predominantly controlled by the factors related to the type, size, shape and concentration of the incorporated magnetic particles [9-11].

Functionalized magnetic particles can be used to modulate the interactions between them and the polymer filaments that form the hydrogels having a direct impact on the properties of the hydrogels, as has been

recently shown [9]. However, apart from bulk iron providing magnetic field actuation, the surface of magnetic particles can be used to tune specific or nonspecific interactions with the hydrogelator moieties [12], which in turn can affect the final properties of resulting hydrogels and even provide more favorable features like better adhesion of biological species (e.g., cells).

Goal

The main objective of this work was to determine the role of surface functionalization of iron particles on the properties of the resulting alginate magnetic hydrogels [13]. We hypothesize that different surface chemistries of iron particles can affect chemical interactions between the both phases in a distinct way, and these changes will contribute to the different microstructure, mechanical properties, and biocompatibility of ferrogels. Alginate was chosen as a model matrix due to its high biocompatibility allowing its use in biomedical applications. A set of different surface functionalizations of iron/silica core-shell microparticles has been chosen. Interactions between specific surface groups and alginate chains have been elucidated with the aid of DFT quantum chemistry calculations to get a more detailed insight into those interactions.

Results

Iron microparticles were modified by introducing a number of functionalities on their surface, ranging from amine to phenyl groups. Although surface functionalizations have not significantly affected the properties of the microparticles themselves, they changed remarkably the final properties of magnetic hydrogels obtained by embedding the iron microparticles into the pre-polymerized alginate matrix (cf. Figure 1). Thus, the successful dispersion of functionalized microparticles was twofold beneficial [13]:

(i) magnetic activity was introduced in-situ,
(ii) enhancement of the macroscopic and mechanical properties was achieved thanks to the altered interactions of alginate with functionalized surface.

Among all the systems studied, amine functionalized IMP-based hydrogels (1-ALG, 2-ALG and 5-ALG) exhibited superior properties when compared with the hydrogel prepared with the use of their non-functionalized counterpart (R-ALG). Properties such as hydrogel integrity, water-holding capability, storage modulus of the amine-based hydrogels (1-ALG and 2-ALG) were significantly altered in comparison with pure hydrogel (R-ALG) or phenyl-

functionalized one (4-ALG). For example, storage moduli for the 1-ALG and 4-ALG are 410 and 483 Pa, respectively, while for the R-ALG and 4-ALG - 137 Pa and 141 Pa, respectively (cf. Figure 2). SEM images revealed that the lack of adequate surface chemistry limits the contact between both phases, which are connected only by limited number of anchoring points. In contrast, amination of the iron surface results in more tight covering of most of the microparticles' surface by multiple connections (cf. figure 1). Theoretical DFT calculations revealed that alginate chains are chemically active not only because of the presence of carboxyl groups but also other non-carboxylic oxygen arrangements which can interact with functionalities. Even blocking of all carboxyl groups by calcium cations during alginate crosslinking does not limit the possibility of tuning of alginate interactions with appropriately modified surfaces [13]. Biocompatibility *in vitro* of the obtained hydrogels depends on the surface chemistry of functionalized microparticles and thus, apart from the macroscopic and mechanical properties, also the cell viability depends on the functionalization (cf. Figure 3).

References

- [1] D. Seliktar, *Science*, 336 (2012) 1124.
- [2] J.L. Drury, D.J. Mooney, *Biomaterials*, 24 (2003) 4337.
- [3] N.A. Peppas, et al., *Advanced Materials*, 18 (2006) 1345.
- [4] H. Geckil, et al., *Nanomedicine*, 5 (2010) 469.
- [5] A. Espona-Noguera et al., *International Journal of Biological Macromolecules*, 107 (2018) 1261.
- [6] H. Wang et al., *ACS Biomaterials Science & Engineering*, 5 (2019) 3654.
- [7] J. Supramaniam et al., *International Journal of Biological Macromolecules*, 118 (2018) 640.
- [8] C. Gila-Vilchez et al., *Smart Materials & Structures*, 28 (2019) 035018.
- [9] A.B. Bonhome-Espinosa et al., *Soft Matter*, 13 (2017) 2928.
- [10] C. Gila-Vilchez et al., *Journal of Rheology*, 62 (2018) 1083.
- [11] C. Gila-Vilchez et al., *Philosophical Transactions Mathematical Physical and Engineering Sciences*, 377 (2019) 20180217.
- [12] E. Tanasa et al., *Nanomaterials*, 9 (2019) 1384.
- [13] M. Barczak et al., *Carbohydrate Polymers* 247 (2020) 116747.

Acknowledgement

Mariusz Barczak thanks to Polish National Agency for Academic Exchange (NAWA) for supporting the research and his stay at the University of Granada in the frame of the Bekker programme fellowship no. PPN/BEK/2018/1/00235/U/00001.



This study was also supported by project FIS2017-85954-R (Ministerio de Economía, Industria y Competitividad, MINECO, and Agencia Estatal de Investigación, AEI, Spain, cofunded by Fondo Europeo de Desarrollo Regional, FEDER, European Union).

Figures

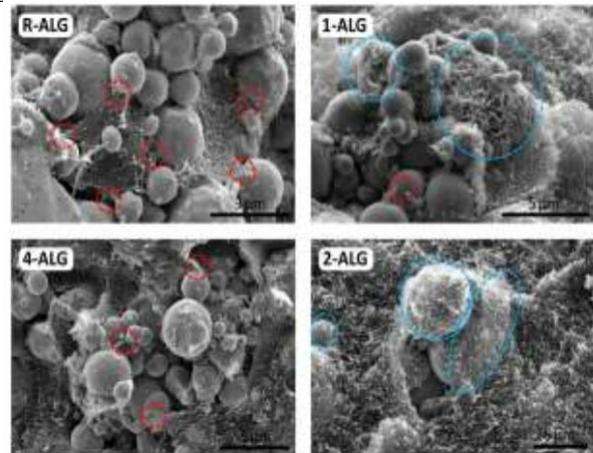


Figure 1: SEM microphotographs of the selected hydrogels (red circles show cobweb-like single point type joints, blue circles – multi point joints of the microparticles with alginate network) [13].

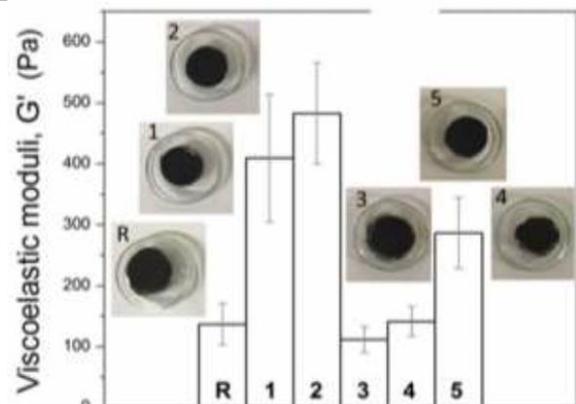


Figure 2: Comparison of the values of storage modulus (G') of the hydrogels studied without the presence of magnetic field [13].

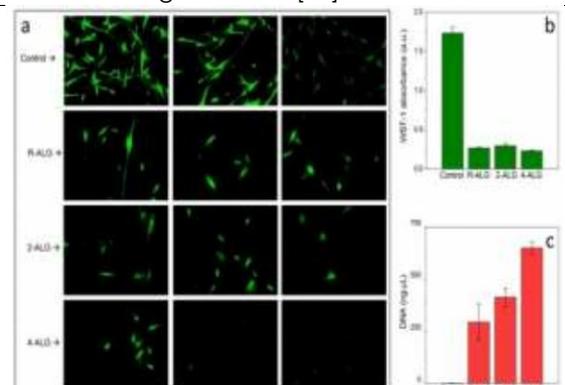


Figure 3: (a) Cytotoxicity of the selected hydrogels revealed by the fluorescence microscopy, (b) WST-1 absorbance test, (c) and DNA quantification in the cell medium [13].