Double-compartment hydrogel particles for targeted delivery and sustained release of hesperidin

M. Tsirigotis-Maniecka[1*], R. Gancarz[1], K. A. Wilk[1]

[1]*Department of Organic and Pharmaceutical Technology, Faculty of Chemistry, Wroclaw University of Science and Technology, Wroclaw, Poland*

**e-mail address: marta.tsirigotis@pwr.edu.pl*

There has been considerable interest in application of hydrocolloids as stable targeted delivery systems for therapeutic agents [1]. Double-compartment (complex) nano- and microsized structures, composed of biocompatible and biodegradable materials (eg. sodium alginate (SA) and carboxymetylocelullose (CMC)), are being increasingly exploited for successful encapsulation of pharmaceuticals [1]. The polymeric particles have been in focus of our actual research due to their functionality and ease of controlled cargo release in response to a particular trigger - ionic strength, pH or temperature.

The objective of our study was to develop a targeted delivery system for hesperidin - a low-molecular phenolic glycoside of natural origin, in order to enhance its pharmacological activities: antioxidant [2], anti-inflammatory [3], and recently revealed therapeutic potential in the treatment of nephrolithiasis [4]. We designed, developed and extensively studied pH-responsive biodegradable double-compartment hydrogel carrier system devoted to encapsulate the bioactive compound to facilitate its protection in adverse environment and distribution to specific locations within the organism. We fabricated a double-compartment delivery system composed of CMC microparticles filled with SA nanoparticles loaded with hesperidin. Nanoparticles were formed with methods based on internal and/or external gelation, and subsequently were incorporated into CMC microparticles with dripping technique. Additionally, hesperidin was also encapsulated directly in single-compartment SA and CMC microparticles fabricated with the external gelation method. All obtained particles were characterized in terms of their morphology and size using polarization microscopy and scanning electron microscopy (SEM). Furthermore, the hydrodynamic diameter, size distribution and zeta potential of the nanoparticles were measured by dynamic light scattering (DLS). The cargo encapsulation was confirmed by spectroscopic analysis (FTIR), while the processes efficacies were derived from the spectrophotometric measurements (UV-Vis). The effect of different pH values (2, 7, 10) on the stability and diffusion kinetics of the microparticles was evaluated. The release profiles of the fabricated microsystems were studied *in vitro* in the simulated gastric (pH 2, 37^{o}C) and intestinal (pH 7.5, 37^{o}C) environment in order to provide the most effective carrier system in terms of functionality of the fabricated hydrocolloid particles, their ability to encapsulate the studied cargo, protect it under adverse conditions and release it under required ones.

The optimization of the fabrication processes provided nano- and microproducts with sizes in range of 100 – 300 nm and 800 – 1000 μm respectively, and of acceptable loading efficiency, but different stability within various pH conditions. Comparing results obtained for single-compartment and double-compartment microparticles it can be concluded, that filling micro-hydrogel structures with nanoparticles loaded with hesperidin provided more stable carrier protecting the bioactive compound from uncontrolled leaching more effectively, and significantly prolonged its release under simulated intestinal conditions.

Acknowledgement

This research was supported by the statutory activity subsidy granted by the Polish Ministry of Sciences and Higher Education to the Faculty of Chemistry of Wrocław University of Technology.

[1] S. Labbaf, S. Deb, G. Gamma, E. Stride and M. Edirisinghe**,** *J. Colloid. Interface. Sci.*, 2013, **409**, 245

[2] K.M. Kamel, O.M. Abd El-Raouf, S.A. Metwally et al., *J. Biochem. Mol. Toxicol.*, 2014, 28, **7**, 312.

[3] A.S.A. Abuelsaad, G. Allam and A.A.A. Al-Solumani, *Mediat. Inflamm.* 2014, **1**, 13

[4] R. Gancarz and E. Klepacz, Patent application P.410626, 2015