HYALURONATE-BASED NANOCAPSULES: FROM CONCEPT TO BIOMEDICAL APPLICATION

<u>Joanna Szafraniec</u>^{a,b}, Małgorzata Janik^a, Agnieszka Błażejczyk^c, Edyta Kuś^c, Joanna Wietrzyk^c, Stefan Chłopicki^d, Szczepan Zapotoczny^a

^a Department of Physical Chemistry and Electrochemistry, Faculty of Chemistry, Jagiellonian University, Ingardena 3, 30-060 Krakow, Poland
^b Department of Pharmaceutical Technology and Biopharmaceutics, Jagiellonian University Medical College, Faculty of Pharmacy, Medyczna 9, 30-688 Krakow, Poland
^c Laboratory of Experimental Oncology, Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Weigla 12, 53-114 Wroclaw,

Poland

^d Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Bobrzynskiego 14, 30-348 Krakow, Poland

In the present work we describe core-shell nanocapsules able to serve as potential nanodelivery system of lipophilic compounds. A series of hydrophobically modified hyaluronic acid was synthesized in EDC-NHS coupling reaction and used to obtain capsules templated on hydrophobic core in surfactant-free process. The relationship between the properties of the formed nanocapsules and the composition of the polysaccharide derivatives was studied using dynamic light scattering, electron microscopy as well as nanoparticle tracking analysis. Physicochemical parameters as well as stability of capsules over time were examined in order to found the most suitable formulation ensuring transport through the blood vessels. *In vitro* uptake of nanocapsules by endothelium was tested, while for *in vivo* studies the capsules were administered to mice either intravenously or orally and their biodistribution was characterized in healthy as well as endotoxemic mice to test the increased targeting to organs in the setting of severe systemic inflammation. Acute oral toxicity was examined as well.

Biocompatible hyaluronate-based nanocapsules with liquid cores described herein represent a tunable nanodelivery system for lipophilic active compounds to liver and lungs after oral administration that may be useful in liver or lung-targeted therapies.