Nano- and microstructures formed by self-assembly of block copolymers – preparation and applications as carriers for bioactive substances

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Compartmentalization is an essential feature found in living cells to ensure that biological processes occur without being affected by undesired external influences.[1] Over the years various self-assembled soft-matter structures have been developed to. mimic cellular compartmentalization. In particular *liposomes*, *polymersomes* and *coacervates* have been applied for this purpose. *Polymersomes* are vesicular structures formed by self-assembly of appropriate block copolymers. These polymeric vesicles are usually composed of *amphiphilic block copolymers* (containing the hydrophobic and hydrophilic blocks).[2] The amphiphilic polymersomes are considered to be analogues of well-known liposomes, but they are more stable. Recently, the formation of polyion complex vesicles (*PICsomes*), a new type of polymersomes, by the simple mixing of two water-soluble oppositely charged block copolymers in an aqueous medium have been reported.[3,4] These PICsomes have many advantages compared with amphiphilic polymersomes, such as elimination of organic solvents form preparation procedures and easy encapsulation of substances.

The project aims on preparing polymeric nano- and microstructures and on assessing the possibility of their application as carriers of selected compounds (dyes and bioactive substances). For this purpose, we plan to synthesize novel adequately designed copolymers and explore methods of preparation of polymersomes, coacervate microdroplets, and polymeric micelles. These structures will be obtained by self-assembly of pairs of oppositely charged diblock copolymers, in which the ionic block will consist of a strong or weak polyelectrolyte, and amphiphilic diblock copolymers. The effect of pH, ionic strength, temperature, and the presence of serum proteins on the stability of nano/microstructures will be determined. Biocompatibility is a crucial parameter for structures that are considered as potential drug carriers. For this reason, both the copolymers and the nano/microstructures will be tested for their effect on normal cells. Our further efforts will be focused on efficiency of encapsulation of model substances (both amphiphilic and hydrophobic), including various dyes and commercially-available drugs, in these structures. This will allow determining the nature of compounds that can be incorporated and transported by the investigated structures.

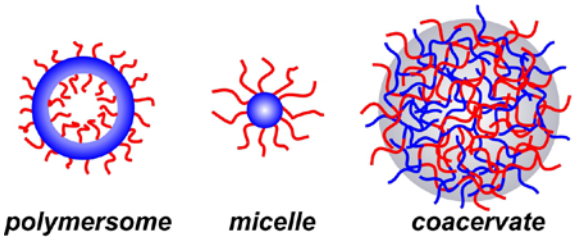

***Figure 1**. Schematic illustration of polymer vesicles, micelles and coacervates.*

The results of our project will contribute to better knowledge on the preparation of various polymeric nano/microstructures from a variety of block copolymers. Especially, the results are of great importance for the development of PICsomes, which membrane is made of pair copolymers consisting of neutral/zwitterionic and strong/weak polyelectrolyte blocks. The studies will also help in deeper understanding the mechanisms of cytotoxicity of block copolymers and the effect of their structure (the type of blocks and their lengths) on interactions with lipid membranes. The successful implementation of the project will contribute to increase the knowledge on efficiency of accumulation of model bioactive substances in the nano/microstructures. This knowledge will be useful in the preparation of new functional colloidal systems for biomedical, biotechnological and pharmacological applications (for example controlled drug delivery systems). The tangible result of the project will be novel polymeric nano/microstructures stable under physiological conditions that can be used to incorporate and transport the bioactive substances, including drugs. Nano/microstructures, especially polymersomes with high stability and resistance to many external stimuli, and the ability to encapsulate hydrophilic and hydrophobic active substances are excellent candidates for use in biotechnology, pharmaceutical, environmental, and catalysis.

[1]Schoonen L, van Hest JCM, Adv. Mater. 2016, 28, 1109.
[2]Discher BM, Won Y-Y, Ege DS, Lee JC-M, Bates FS, Discher DE, Hammer DA, Science 1999, 284, 1143.
[3]Koide A, Kishimura A, Osada K, Jang W-D, Yamasaki Y, Kataoka K, J. Am. Chem. Soc. 2006, 128, 5988.
[4]Kania G, Kwolek U, Nakai K, Yusa S, Bednar J, Wójcik T, Chłopicki S, Skórka T, Szuwarzyński M, Szczubiałka K, Kepczynski M, Nowakowska M, J. Mater. Chem. B 2015, 3, 5523.