- 2018/31/B/ST8/03277 [2019-2022] Nowe biomateriały zawierające polisacharydy jako efektywna platforma do adsorpcji i uwalniania czynników wzrostu fibroblastów: zastosowania w diagnostyce i w leczeniu chorób cywilizacyjnych - dr hab. A. Michna

Research project objectives/ Research hypothesis

The experimental and theoretical studies of this project are focused on acquiring a new knowledge on the formation of the effective biomaterials (the polysaccharide-based films). This allows to elaborate an effective procedure that can be applied for delivering the biologically active fibroblast growth factors (FGFs) to tissues, that is of significance for diagnostics and treatment of diabetes, obesity, and osteoporosis, and for designing novel intelligent dressings. One of the main objective of the research projects is developing a quantitative description of adsorption of biocompatible polyelectrolytes, of various charges, shapes, forming the anchoring layers on the solid/liquid interface. This allows forming effective biomaterials with defined structures. The adsorption and stability of the biomaterials, created by sequential adsorption of oppositely charged polyelectrolytes, under well-defined conditions of shear flows will be determined. The mechanisms of the proteins binding with biocompatible scaffolds (various types of the biomaterials) will be clarified. Finally, the process of release of fibroblast growth factor 21 (FGF 21) and fibroblast growth factor 23 (FGF 23) from biomaterials in various shear flow conditions will be evaluated. Theoretical calculations based on the hybrid random sequential adsorption (RSA) model will be carried out for a quantitative interpretation of experimental results, i.e., the calculation of protein-carrier binding energy.

The following research tasks will be realized:

- the kinetics of the adsorption of biocompatible polyelectrolytes forming the anchoring layers, of controlled properties, at solid/liquid interfaces under well-defined transport conditions is determined
- the effect of coverage of the anchoring layer, its charge and the conformation of adsorbed polyelectrolytes on the structure and the coverage of the subsequent layers forming a biocompatible film is evaluated
- a methodology for determining the electrokinetic, optical, and structural parameters of multilayers created by synthetic polyelectrolytes and polysaccharides adsorbed on macroscopic surfaces of various roughness.
- the stability new polysaccharide-based biomaterials formed by sequential adsorption of oppositely charged polyelectrolytes (up to 6 layers) is determined. The obtained results will be quantitatively evaluated, i.e. the adsorption constant and binding energy biomaterial- substrate will be determined using a new theoretical approach
- the kinetics of the FGF 21 and FGF 23 binding to the most stable biomaterials is evaluated
- the release kinetics of FGF 21 and FGF 23 from biomaterials under various conditions, including physiological conditions, is determined
- a theoretical description of FGF 21 and FGF 23 desorption from solid surfaces using the hybrid RSA model is determined

Research hypothesis: Adsorption and desorption of the polyelectrolytes are mainly controlled by the electrostatic interactions.

Research project methodology

The proposed research methods enable complete physicochemical characteristics of the polyelectrolytes in bulk, and the polyelectrolyte films at solid/ electrolyte interfaces. Diffusion coefficients and electrophoretic mobilities of the polyelectrolytes will be measured by dynamic light scattering (DLS) and laser Doppler electrophoresis (LDE) as a function of solution ionic strength, pH, and electrolyte type. The diffusion coefficients and electrophoretic mobilities allow determining the polyelectrolyte size distributions, zeta potentials, and the electrokinetic charge that are of vital importance for their bulk characterization. Electrokinetic (streaming potential measurements), optical waveguide lightmode spectroscopy (OWLS), quartz crystal microbalance with dissipation (QCM-D), atomic force microscopy (AFM) will be applied for the determination of the process of formation and stability of polyelectrolyte multilayers and the protein binding and release from the biomaterials. The experimentally determined kinetics of the polyelectrolyte adsorption and the stability will be interpreted theoretically in terms of the hybrid RSA model using original computer software. The main advantage of the RSA

modeling is high efficiency of calculations, generating large populations of polyelectrolytes and obtaining the precise results.

Expected impact of the research project on the development of science

These investigations will promote the development of the research methodology useful for determining the process of formation of new polysaccharide-based biomaterials under *in situ* conditions.

The planned research will allow a deeper insight into the mechanisms of the protein binding to biomaterials.

This knowledge is exploited to define the relevant physicochemical parameters ensuring effective immobilization and release of the biologically active FGFs.