Radosław Kitel1,2, Łukasz Filipczyk2, Marcin Herok2, Aleksandra Rusin2, Wiesław Szeja1. **Perspectives on development of novel apoptosis inducers derived from genistein as lead compounds for anticancer drug development**. 1Department of Organic Chemistry, Bioorganic Chemistry and Biotechnology, Silesian University of Technology, 2Center for Translational Research and Molecular Biology of Cancer, Maria Skłodowska-Curie Memorial Center and Institute of Oncology,

Streszczenie

Among many examples of natural compounds, isoflavones still represents a group of molecules that are most investigated in anticancer drug development. A number of compounds which belong to this group have anticancer properties which have been confirmed both in in vitro and in vivo models. Molecule of particular interest is genistein, which is able to inhibit the growth of many cancer cell lines. Anticancer activity of genistein is a result of interaction of this molecule with many molecular targets, including protein tyrosine kinases (PTKs), which play crucial role in tumor development and metastases. Unfortunately, genistein has a number of weaknesses, of which the most serious is weak solubility in aqueous solutions. Therefore much efforts have been made to develop novel derivatives of genistein with increased anticancer properties and better pharmacokinetic properties. Based on our previous results we have identified several compounds from our library of glycoconjugates derived from genistein with strong proapoptotic activity. Taking this into account we have started project entitled Design, synthesis and anticancer properties of genistein glycoconjugates. The Project's research program covers the filed of anticancer drug discovery and its main objective is to obtain apoptotic inducers which could serve as innovative structures for further development. This project consists of three main interrelated parts which include almost all aspects of modern drug discovery process: computer-based drug discovery, synthesis and extensive biological evaluation of synthesized compounds in order to identify the exact mechanism of action of them. To address the gap between monolayer cell culture and in vivo models in our research we have employed testing of activity in three-dimensional cancer cell culture, shortly called spheroids. Our results clearly show that proper derivatization of genistein could lead to novel class of compounds which could serve as leads for development of novel anticancer drugs.

The project is realized within the VENTURES programme (VENTURES/2012-9/6) of Foundation for Polish Science, cofinanced from European Union, Regional Development Fund