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Synthesis and properties of peptide dendrons and their dimers with a "bola" structure

Abstract

Diseases of the nervous system (cancer, neurodegenerative diseases) are currently the second cause of death in developing countries. Modern medicine is expanding the range of possible therapies by increasing the use of nanoparticles such as polymers and dendrimers. The latter are of great interest due to their high monodispersity, well-defined synthesis methods and practically unlimited possibilities of building complex multifunctional structures.

Research on peptide dendrimers has been carried out for years at the Institute of Organic Chemistry of the Polish Academy of Sciences under the leadership of Prof. Z. Lipkowska. These branched macromolecules both in terms of structure and biological properties mimic natural peptides present in plant and animal organisms, and thus are potential antimicrobial, anticancer compounds and can be carriers of, for example, drugs or nucleic acids. Such constructs combining multiple beneficial properties allow the final structure to be biocompatible and biodegradable.

The aim of my research was to design and develop a strategy for the synthesis of nanoparticle peptide dendrons and their dimers with a "bola" structure using a classical method in solution or on a solid support, and studying the structure and properties of the obtained compounds. The biological target set for the obtained nanocompounds were diseases of the nervous system, in particular glioma cell lines.

In the first part of my research, I developed optimal synthesis conditions for peptide dendrons functionalized with cinnamic acid derivatives or imidazole derivatives. The second part of my research concerned the development of a proper methodology for the synthesis of peptide dendrimers of the "bola" type having stable and degradable organic linkers in their structure.

For selected compounds, studies and analyses of the relationship between structure and biological activity of dendrimers have been carried out, including studies of molecular conformation by circular dichroism, studies of antioxidant properties, studies of complexing properties, interactions of dendrons with secondary structures (PLGA and PLL), and cytotoxicity studies against several glioma lines