Streszczenie rozprawy doktorskiej

Synteza i właściwości nowych glikopeptydów o działaniu przeciwzamarzającym

Synthesis and characterization of novel antifreeze glycopeptides (AFGP)

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Antifreeze glycopeptides (AFGP) are a class of biological antifreeze agents found in Arctic and Antarctic species of fish. These biopolymers enable living at temperatures below the freezing point of the body fluids. AFGP are composed of 4 to 55 tripeptide units alanine-alanine-threonine, glycosylated at the threonine side chains with the disaccharide *β*-D-galactosyl-(1→3)-α-*N*-acetyl-D-galactosamine, with a molecular mass of 2.6 - 33.7 kDa. The antifreeze phenomenon relies on regulation of ice nucleation and ice crystal growth. AFGP molecules are supposed to directly interact with the ice surface with implications on ice crystal growth. However, the exact mechanism of action of AFGP remains unclear. Due to their interesting properties AFGP have many potential applications. Therefore it is crucial to develop an efficient synthetic strategy of obtaining these fine chemicals in order to meet the industrial needs.

The main goal of the presented doctoral dissertation was to optimize the synthesis of monoglycosylated AFGP analogues. In order to provide glycopeptides with defined composition and stereochemistry the microwave-assisted solid phase peptide synthesis was performed. An important step in the research was the development of methodology for the introduction of a methylamine at the peptide C-terminus carried out on solid support.

Two groups of compounds were obtained. Tri- and pentapeptides were designed to determine conformational preferences using circular dichroism spectroscopy (CD) and

nuclear magnetic resonance spectroscopy (NMR) in order to elucidate the stereochemical influence of the amino acid configuration on the three-dimensional structure. Based on the experimental NMR data, the molecular dynamics calculations were performed to obtain a better representation of the molecule structure. The all-D-configured peptides turned out to adopt a much more rigid structure in comparison to the corresponding peptides containing only L-amino acids. Furthermore, the D-configured peptides showed the ability to "lock" the orientation of the carbohydrate unit, while the peptides containing L-amino acids were fully flexible.

In case of longer AFGP sequences, the research was focused on their antifreeze activity. The conformational preferences were determined via CD spectroscopy, indicating that the AFGP analogues adopt polyproline II (PP II) helix. Subsequently, the adsorption process of AFGP analogues onto different surfaces was investigated using atomic force microscopy (AFM).

As a result, desired AFGP analogues were obtained via optimized solid phase peptide synthesis. A successful, novel approach was developed during the research.
Finally, presented study, though did not fully explain the mechanism of action of AFGP, provided interesting structural and conformational information about the influence of amino acid stereochemistry on the peptide backbone stability. Conducted AFM research revealed an unusual pattern of hydration of AFGP molecules adsorbed on mica surface.