ABSTRACT

Cyanobacteria are photosynthetic Gram-negative bacteria. They are considered as one of the oldest life forms on the Earth. These organisms constitute a rich source of biologically active metabolites, including toxins and compounds with potential biotechnological and pharmaceutical applications. Due to their biological activity, peptides and their derivatives have attracted the attention of scientific community. The greatest interest in this field of research has been focused on cyanobacteria originating from tropical regions. However, the results obtained within this PhD thesis indicate a similar potential of microorganisms from the Baltic Sea.

In this study, *Nostoc edaphicum* strain CCNP1411 isolated from the Gulf of Gdańsk (Baltic Sea) was used and cultured for biomass. The analyses of mass fragmentation spectra obtained with application of tandem mass spectrometry allowed for identification of ten peptides classified to nostocyclopeptide (Ncp) group of compounds. This includes six new analogues containing (with one exception) seven amino acid residues, occurring in cyclic as well as in linear form. It was shown that four cyclic Ncps have their linear counterparts with a *C*-terminal aldehyde group. Moreover, the linear analogues were present in higher concentrations than their cyclic forms. This fact indicated that despite the conformational determinants resulting from the presence of Gly and Gln, the macrocyclization process is also dependent on other amino acid residues.

Six Ncps were tested for their activity against the human 20S proteasome (h20S). The chymotrypsin-like (CH-L) activity of h20S was inhibited in the presence of linear forms of Ncps, but only those that contained a *C*-terminal aldehyde group in their structure. For the cyclic variants, no such effect was observed. In contrast, one of the cyclic forms inhibited the trypsin-like (T-L) activity of the h20S proteasome. This is the first report on Ncps activity against proteasome. The 20S proteasome is a proteolytic complex that takes part in the regulation of basic cellular processes in eukaryotic organisms. Dysfunction of this proteolytic complex leads to many pathological disorders, including cancer. Since the selective activity of Ncps against h20S was confirmed within this PhD thesis, these compounds, as novel inhibitors, may be considered as tools in studies on the regulation of cellular processes.

The other group of peptides produced by the Baltic strain of *N. edaphicum* CCNP1411 were cyanopeptolins (Cps). The identified compounds (thirteen analogues) were found to differ in amino acid composition and side chain modifications. Biochemical assays using key metabolic enzymes indicated the effect of the amino acid located between Thr and Aph on biological activity of these peptides. In the case of Cps containing Arg at this position, a strong activity against trypsin and moderate against chymotrypsin was observed. In contrast, peptides containing Tyr were selectively active only against chymotrypsin. Proteases are known to be involved in a number of metabolic processes, therefore regulators (activators and inhibitors) of these proteins are sought for their application in medical therapies. Cps, as trypsin and chymotrypsin inhibitors, can be therefore the starting material for development of new drugs.

The results of the present study undoubtedly reveal the potential of the Baltic strain *Nostoc edaphicum* CCNP1411, as a source of compounds with significant biological activity and provide a strong basis for further research into the possible pharmaceutical or biotechnological application.