



Abstract

Microcoleus autumnalis Cyclopeptides Present Protective Properties against Oxidative Stress [†]

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Abstract: Oxidative stress is a common pathological mechanism in neurodegenerative diseases. Aging leads to mitochondrial dysfunction and produces a reduction in endogenous antioxidant systems efficiency, with a consequent increase in reactive oxygen species (ROS) release. This unbalance among protecting and damaging molecules impairs neuronal function, even causing cell death. Therefore, the search for new drugs with antioxidant and neuroprotective effects is a great challenge. In this work, the bioactivity of three new cyclopeptides (1–3), isolated from the freshwater cyanobacterium *Microcoleus autumnalis*, was tested in SH-SY5Y human neuroblastoma cells. This species is a prolific source of bioactive metabolites, anatoxin being the best-characterized molecule due to its neurotoxicity. In this context, cytotoxicity of compounds was firstly analyzed. None of the *M. autumnalis* metabolites induced toxic effects up to 50 μM after 24 h of incubation. In view of the lack of neurotoxicity produced by compounds 1–3, their antioxidant and neuroprotective ability was analyzed. With this objective, SH-SY5Y cells were co-treated with compounds (0.001, 0.01, 0.1, and 1 μM) and 150 μM H_2O_2 for 6 h. The effect of compounds 1–3 on cell viability under oxidative stress conditions was determined, finding that the three compounds were able to protect neuronal cells from oxidative damage. Next, mitochondrial function was evaluated by monitoring mitochondrial membrane potential. In this assay, only compound 3 recovered the organelles from the depolarization generated by H_2O_2 . Finally, intracellular ROS content was assessed, observing that 1–3 decreased the levels of these harmful molecules. In conclusion, *M. autumnalis* cyclopeptides presented neuroprotective effects mainly mediated by their ability to reduce ROS levels. These results suggest that compounds 1–3 act as direct antioxidants and could be interesting compounds for further studies in neurodegenerative diseases.

Keywords: *Microcoleus autumnalis*; cyanobacteria; antioxidant; neuroprotection



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