

Abstract

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Title of diploma thesis: Study of selected iron chelators for oxidative stress prevention in PC12 cell line

Parkinson's disease is a progressive neurodegenerative disease with motoric symptoms (tremor, rigidity, akinesia, postural disorders), which are connected with the loss of dopaminergic neurons in *Substantia nigra pars compacta*. Oxidative stress has been associated with pathological processes of PD as an initiator or a member of pathological cascades. Moreover, oxidative stress plays a role in development of several diseases, e.g. cardiovascular disorders. Damages caused by oxidative stress are based on reactive oxidative species (ROS). The most common and the most toxic compound is hydroxyl radical, which is created by chemical reaction with iron as a catalyst (Fenton reaction). Iron chelators act as protectors against oxidative harm in tissues. They chelate iron ions, therefore prevent their catalytic activity and formation of ROS. This study deals with the determination of cytotoxicity and protective effects of clinically used iron chelators (deferoxamine – DFO, deferiprone – L1, deferasirox – ICL670A) in PC12 cell line as *in vitro* model of dopaminergic neurons with PD, using 6-hydroxydopamine (6DA) as of oxidative stress inducer.

In this study we used PC12 cell line that was treated for 7 days with nerve growth factor (50 ng/l). 72-hour incubations were performed for tests of iron chelators cytotoxicity. 24-hour incubations were performed for tests of iron chelators protective effects, using 100 μ M 6DA. Lactate dehydrogenase assay was used for assessment of cellular viability.

100 μ M ICL670A showed the highest cytotoxicity (74% of dead cells). 1 and 10 μ M L1 showed the lowest cytotoxicity (15 and 17 % of dead cells, respectively). In tests of protective effects 100 μ M L1 displayed the best efficiency (66,8 % living cells) and DFO was the worst. Therefore chelators L1 and ICL670A tend to have the greatest potential for future studies of iron chelation therapy.