Nicotine protects dopaminergic neurons from the neurotoxicity of aminochrome

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Although detrimental consequences of smoking are well established, nicotine by itself might possess positive and even therapeutic potential. Experimental evidence indicates that nicotine is protective for Parkinson disease vulnerable dopamine neurons. At physiological pH dopamine oxidizes in dopaminergic neurons to aminochrome, which is the precursor of neuromelanin, an event that occurs in vivo since the neuromelanin have been found in dopaminergic neurons in substantia nigra. Aminochrome can polymerize to neuromelanin or can be reduced by DT-diaphorase. However, aminochrome can be neurotoxic when form adducts with alpha-synuclein or it can be reduced by flavoenzymes that catalyze one electron reduction of quinones. In order to determine whether nicotine plays a protective role in aminochrome neurotoxicity, the aim of this study was examined the potential role of nicotine in the RCSN-3 cells. RCSN-3 cells were incubated with 50 µM Aminochrome cell death was 23% (p < 0.001) and 50 µM Aminochrome + 100 µM Dicoumarol (specific inhibitor for DT-diaphorase) cell death was 54% (p < 0.001) compared to the control cells. To determine the protective role of nicotine, the cells were pre-incubated with 20 µM Nicotine for 1 h and then with 50 µM Aminochrome + 100 µM Dicoumarol cell death significantly decreased (8%; p<0.001). To verify that this protection is mediated by nicotine, cells were pre-treated with 10 µM mecalamine (inhibitor of nicotinic receptors) and then treated with 20 µM Nicotine + 50 µM Aminochrome + 100 µM Dicoumarol where increased cell death a 49% (p<0.001) Which proves that nicotine is protecting dopaminergic neurons from the toxicity to aminochrome.

Keywords: Nicotine, DT-diaphorase and Aminochrome.