

Evaluation of neuroprotective effect of 1-benzyl-4-((6-alkoxy-3-oxobenzofuran-2(3H)-ylidene) methyl) pyridinium derivatives on beta amyloid (A β) induced toxicity in PC12 cells

Z. Golej^{1,*}, M. Soodi¹, H. Nadri²

¹Department of Toxicology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

²Department of Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

Background and Aims: Alzheimer's disease (AD) is an age-related neurodegenerative disease that was characterized with cholinergic neurons destruction and affects learning and memory, then acetylcholinesterase (AChE) inhibitors such as donepezil can improve AD symptoms. It is reported that novel series of benzofuranone-ylidene-methyl benzylpyridinium derivatives which are donepezil derivatives can potentially inhibit AChE. This study is performed to evaluate the protective effects of these new analogues of Donepezil on beta amyloid induced toxicity.

Methods: PC12 cells were treated with different concentration of new analogues (10⁻¹¹-10⁻⁶ mol/l) for 1 hours, then pre-aggregated A β was added. After 24 hours, cell viability was measured by MTT assay. Donepezil was used as positive control.

Results: incubation of cells with A β peptide for 24h significantly decreased cell viability relative to control. Pre-treatment of PC12 cells with test substances and donepezil could protect cells from A β induced toxicity. The protective effects of new analogues were comparable with donepezil and some of them were more potent than it.

Conclusions: present study showed that all synthesized compounds have moderate to high protective effect against A β induce toxicity and some of them were effective than donepezil. Also protective effects of these compounds did not related to AChE inhibitory activity of them. It is suggested that other mechanism are involved.

Keywords: Beta amyloid; Neurotoxicity; Benzylpyridinium; Cholinesterase inhibitor