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Multifunctional N-cinnamoyl-memantine analogues as potential anti-alzheimer's disease agents

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Neurodegenerative diseases affect millions of people worldwide and are becoming more prevalent, particularly in the elderly. Amongst the neurodegenerative disorders, Alzheimer's disease (AD) is the most common form of dementia. Since the most AD cases are known to be nongenetic, it is believed that the complex of various risk factors leading to oxidative stress, combined with the aging process may cause this illness. Therefore, antioxidants (e.g. hydoxycinnamic acids-caffeic, ferulic and etc.) possessing the therapeutic potential to overcome the oxidative stress might reduce the risk of development of this severe pathology.

Objective: In this study we aim to link together memantine (Mem) with 3,4-dihydroxy, alfa-methyl, 3-methyl, 3-NO_2, 4-NO_2, 4-Cl-3-NO_2 substituted cinnamic acids (CA) by applying TBTU reagent. The newly compounds have been screened in vitro for their neuroprotective effects.

Methods: Measurment of neuroprotective effects of amides against copper-induced toxicity in APPswe cells

APPswe cells were seeded into 96-well plates at a density of 5×104 cells/well. APPswe cells were divided into three groups: control group (DMEM/F12 medium), copper-injured group (300 μM copper; model group), and copper-injured groups treated with compounds, in which cells were treated with 0.032 μM, 0.16 μM, 0.8 μM, 4 μM, 20 μM, and 100 μM tested compounds. The cell viability of APPswe cells was measured at 36 h incubation by MTS assay.

Measurment of neuroprotective effects against glutamate-induced toxicity in SH-SY5Y cells

The SH-SY5Y cells were seeded into 96-well plates at a density of 5×104 cells/well. Cells were divided into three groups: control group (DMEM medium), glutamate-injured group (7 mM glutamate; model group), and glutamate-injured groups treated with compounds, in which model groups were treated with 0.032 μM, 0.16 μM, 0.8 μM, 4 μM, 20 μM, and 100 μM tested compounds. The cell viability of SH-SY5Y cells was measured at 48 h incubation by MTS assay.

Results: The results of copper-induced toxicity reveal that amongst the tested amides, compounds CA(3-NO_2)-Mem, CA(4-Cl-3-NO_2)-Mem, CA(4-NO_2)-Mem, CA(alfa-CH_3)-Mem displayed neuroprotective effects, ranging from 0.032 μM to 20 μM, whereas CafA-Mem and CA(3-CH_3)-Mem did not show neuroprotective effects on APPswe cells.

Moreover, amides CA(3-NO_2)-Mem, CA(4-Cl-3-NO_2)-Mem, and CA(alfa-CH_3)-Mem treated at 0.032 μM increased cell viability against glutamate-induced neurotoxicity in SH-SY5Y cells.

Conclusion: Combined, these active compounds may have neuroprotective effects with a correlation with the glutamate receptors.

References

1. Vassar, R., Kovacs,D.M., Yan, R., Wong, P.C. The β-secretase enzyme BACE in health and Alzheimer's disease: regulation, cell biology, function, and therapeutic potential. Journal of neuroscience 2009, 29, 12787-12794.
2. Shi, X.-P., Tugusheva, K., Bruce, J.E., Lucka, A., Chen-Dodson, E., Hu, B., G.-X., Wu, Price, E., Register, R.B., Lineberger, J. Novel mutations introduced at the β-site of amyloid β protein precursor enhance the production of amyloid β peptide by BACE1 in vitro and in cells. Journal of Alzheimer's Disease 2005, 7, 139-148.
3. Parfenova, H., Basuroy, S., Bhattacharya, S., Tcheranova, D., Qu, Y,. Regan, R.F., Leffler, C.W. Glutamate induces oxidative stress and apoptosis in cerebral vascular endothelial cells: contributions of HO-1 and HO-2 to cytoprotection, American Journal of Physiology-Cell Physiology 2006, 290 C1399-C1410

Biography

Maya G. Chochkova is affiliated to South-West University. she is a recipient of many awards and grants for her valuable contributions and discoveries in major area of subject research. Her international experience includes various programs, contributions and participation in different countries for diverse fields of study. Her research interests include Antioxidant Activity, Antioxidant Assays, Alkaloids, Antioxidants and DPPH.