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Synthesis of 5,6-diaryl-1,2,4-triazine derivatives with ethyl acetate moiety as novel neuroprotective agents against H₂O₂ and A β -induced neurotoxicityHamid Irannejad¹ and Tuba Tuylu Kucukkilinc²¹Mazandaran University of Medical Sciences, Iran²Hacettepe University, Turkey

Alzheimer's disease is a neuropathologic disorder characterized by intracellular neurofibrillary tangles and amyloid aggregates in the CNS. In recent years numerous approaches have been used to combat AD like small molecule inhibitors of A β aggregation, anti-inflammatory agents, cholinesterase, β - and γ -secretase. Herein, we report synthesis of some 5,6-diaryl-1,2,4-triazines 3a-f and 8a-e as potential agents for treatment of AD. We evaluated them against both H₂O₂ and β -amyloid induced toxicity in PC-12 and SH-SY5Y cells and the extent of cell viability and apoptosis were assessed. The synthesis of compounds (3a-f) was started by 1,2-diketones, in which triazine ring closure was performed by thiosemicarbazide and alkylation by ethyl chloroacetate to afford compounds 3a-f. Synthetic route for compounds 8a-e was started by an acylation reaction of anisole with phenylacetic acid derivatives. The oximation in the alpha position of carbonyl group was performed by use of sodium methoxide and butyl nitrite. The next two steps, were performed similarly to afford final compounds 8a-e. All compounds showed significant neuroprotective activity with EC₅₀ values ranging from 14-30 μ M. Most compounds could increase cell viability compared to amyloid treated group. Surprisingly, 3-thioxo-1,2,4-triazin-2(3H)-yl) acetate derivative 8e was the most potent compound in both tests with EC₅₀ of 14 μ M and could increase 40% of cell viability revealed by cytometric analysis with Annexin V/PI staining. It was also shown that 8e has more neuroprotective activity than Quercetin. Morphologic evaluation of cells by DAPI staining and TUNEL assay showed the effectiveness of this compound to improve neurite outgrowth in neuronal cells.

Biography

Hamid Irannejad has completed his Doctor of Pharmacy at Kerman University of Medical Sciences and PhD at Tehran University of Medical Sciences, Iran. His Postdoctoral studies were accomplished at University of Siena, Italy, under the supervision of Prof. Maurizio Botta. Currently, he is serving as an Assistant Professor at Mazandaran University of Medical Sciences. He has published nearly 20 papers in reputed journals in the field of Medicinal Chemistry.

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