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Novel tricycloundecane derivatives as potential N-methyl-D-aspartate receptor and calcium channel inhibitors for neuroprotection

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Neurodegenerative disorders are debilitating conditions characterized by progressive dysfunction and death of neuronal cells by means of apoptosis, necrosis or autophagic degeneration. Amidst the proposed mechanisms of neurodegeneration, the effects of excitotoxicity via glutamate receptor stimulation on neuronal cells are prominent. Numerous molecules have been synthesized to regulate glutamate receptors but some, such as dizolcipine and phencyclidine, have been marked by undesirable side effects. Uncompetitive blockers such as memantine and amantadine proved to be neuroprotective with fewer side effects and are approved for clinical use. This has led to the development of structurally related polycyclic molecules such as NPG1-01, which exhibit neuroprotective properties through NMDA receptor and VGCC inhibitions with lower side effect profile. In this study, a series of compounds were synthesized for evaluation of inhibition of calcium influx through NMDA receptor channels and voltage-gated calcium channels (VGCC). The structures were confirmed using NMR, IR and MS. Compounds (2, 3, 6, 7 and 10) demonstrated potential ability to attenuate calcium influx through NMDA receptor and/or VGCC. Based on the significant activity of compound 2 & 3, a new series of tricycloundecane derivatives have been proposed. However, the true potential benefit of the already synthesized novel compounds as neuroprotective agents and safety in patients is yet to be established. Additional derivatives have been designed and are in the process of being synthesized. The compounds could serve as lead structures for the development of novel neuroprotective drugs.

Biography

Ayodeji O Egunlusi is a Pharmacist who is currently busy with his PhD. He had participated in the young scientist program organized by the Novartis Pharma (Basel). His PhD entails the design and synthesis of novel molecules as potential neuroprotective agents. Few compounds have been synthesized and screened for neuroprotective activities.

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