

P017 Neuroprotective actions of a novel 2-amido-3-hydroxy-pyridin-4(1H)-one iron chelators against Alzheimer's disease relevant insults

Francisco Molina-Holgado, Alessandra Gaeta, Paul Francis, Robert J Williams, Robert C Hider
King's College London, London, UK

Alzheimer's disease is associated with amyloid beta (A β) aggregation and there is evidence of iron-mediated oxidative stress in the pathogenic process. In this context iron chelation by compounds such as 2-amido-3-hydroxypyridin-4(1h)-ones (AG compounds), may have therapeutic potential. In the present study primary cultured cortical neurones were exposed to ferric nitrilotriacetate (FeNTA 10 μ M) or A β 1-40 (3 or 20 μ M) and cultures treated with AG compounds (10, 30 or 100 μ M) or vehicle either immediately or up to 6h after the insult. Cytotoxicity was assessed at 24h by LDH release, MTT turnover, expression of the synaptic marker synaptophysin and morphometric analysis by Hoechst 33324/propidium iodide staining. FeNTA and A β 1-40 induced significant cell death which was reversed by a range of AG compounds in a concentration-dependent manner with the greatest protection observed with AG6. FeNTA-induced reductions in the levels of synaptophysin were reversed by AG6. Morphological analysis revealed preservation of cell bodies and processes. The present study suggests that pyridin-4(1h)-one-based iron chelators may have therapeutic potential in neurodegenerative conditions such as Alzheimer's disease.
Supported by BTG plc.