STATINS AS NEUROPROTECTANTS: A COMPARATIVE IN VITRO STUDY OF LIPOPHILICITY, BLOOD-BRAIN-BARRIER PENETRATION, LOWERING OF BRAIN CHOLESTEROL AND NEUROPROTECTION

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Introduction: There is growing evidence in the literature to support the hypothesis that statins may act as neuroprotectants in several neuropathological conditions, including Alzheimer's disease. However, the mechanisms for neuroprotection are only partially understood, and pleiotropic phenomena could be involved.

Aims: The scope of this work was to evaluate how several parameters regarding to statins could be related with the potential neuroprotection associated to these drugs.

Methods: A comparative study of the 9 known statins (lovastatin, mevastatin, pravastatin, simvastatin, cerivastatin, atorvastatin, fluvastatin, pitavastatin and rosuvastatin) was developed, analyzing chemical structure and lipophilicity, blood-brain-barrier penetration (BBB) through PAMPA methodology and 3-hydroxy-3-methylglutaryl co-enzyme A reductase inhibition through in vitro assays. The cholesterol modulation was also evaluated in neurons, glia and human hepatocyte cell lines. Furthermore, neuroprotection of the 9 statins against a neuron cell death based on tau hyperphosphorylation induced by okadaic acid was studied.

Results: The results indicate that monacolin J derivatives (natural and semi-synthetic statins) are the best candidates for the prevention of neurodegenerative conditions due to their higher BBB penetration capacity, cholesterol lowering effect on neurons with a high safety profile, and protection against cell death caused by okadaic acid.

Conclusions: Among the nine statins studied, simvastatin presented the best characteristics for preventing neurodegenerative conditions.