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# Neuroprotective effects of a novel organoselenium probucol analogue

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Recent studies based on oxidative models of neuropathologies have shown that probucol, a hypocholesterolemic drug, displays neuroprotective properties. Here we investigated the potential neuroprotective effects of probucol and two new organoselenium analogues [2,6-di-tert-Butyl-4-selenocyanatophenol (Compound 1, C1) and 4,4′-Diselanediylbis (2,6-di-tert-butylphenol) (Compound 2, C2)] under in vitro and in vivo conditions. The in vitro protective effects against glutamate-induced oxidative cell death were investigated using cultured HT22 hippocampal neurons. Regarding the in vivo model, adult Wistar rats were subjected to experimental focal ischemic stroke. C2, which was selected based on its beneficial in vitro effects and low in vivo toxicity, was administered (20 and 50 mg/kg, i.p.) at 1, 24, 48 and 72 h after ET-1 administration. Behavioral tests related (adhesive removal test, cylinder test and beam balance) were performed on day 5. After the behavioral tests, all animals were perfused and the brains were collected to evaluate reactive gliosis. Glutamate caused a concentration- and time-dependent death of cultured HT22 neuronal cells, which was preceded by increased levels of oxidants (reactive species) and depletion of reduced glutathione (GSH). Although probucol displayed no beneficial effects, both analogues significantly protected against glutamate-induced oxidative cytotoxicity. Such protection was paralleled by a decrease in the levels of reactive species, although glutamate-induced GSH depletion was not changed by the probucol analogues. Of note, C2 displayed significant protective effects against ET-1-induced ischemic injury in vivo, leading to a substantial improvement in behavioral tests, as well as a significant decrease in ET-induced striatal gliosis. The study presents two new probucol analogues that, in sharp contrast to the parent compound (probucol), mitigated glutamate-induced damage in vitro and protected neurons from oxidative death. One of these analogues (C2), which exhibited no evident toxicity in vivo, attenuated ischemic brain injury in rats, leading to significant functional improvements.