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Phenolic alkaloid oleracein E attenuates oxidative stress and neurotoxicity in $AlCl_3$-treated mice

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Abstract

Aims: Chelation therapy and antioxidant supplements have been demonstrated to be useful in ameliorating aluminum (Al) induced neurotoxicity. Oleracein E (OE) is a phenolic antioxidant alkaloid which possesses a rare tetrahydroisoquinoline/pyrrolidone tricyclic skeleton and a catechol moiety. The aim of this study was to investigate whether OE can chelate with Al and alleviate $AlCl_3$-induced oxidative stress and neurotoxicity.

Main methods: Kunming mice were administered $AlCl_3$ (40 mg/kg/d, i.p., 28 days), with co-administration of OE (3 mg/kg/d, 15 mg/kg/d, i.g.) and the positive control piracetam (PA, 400 mg/kg/d, i.g.). The Al contents in the brain and plasma were determined using ICP-MS. Al chelating ability of OE was assayed using UV spectroscopy. MDA, GSH, SOD or CAT, in the brain or plasma were determined. HE staining was used to examine hippocampal morphology alterations. IHC staining was employed to measure the expression of apoptotic-related proteins Bax, Bcl-2 and Caspase-3.

Key findings: $AlCl_3$ remarkably increased the brain and plasma Al contents, increased lipid peroxidation and induced hippocampal neuronal damage. OE chelated with Al to form a stable complex. An increase in brain Al content by OE (15 mg/kg) likely occurred through chelating with Al, which reduced the toxicity of free Al ion in the brain. OE significantly decreased MDA by regulating some antioxidant biomarkers. Furthermore, OE significantly ameliorated the protein expression changes in some apoptotic indices induced by $AlCl_3$.

Significance: The phenolic alkaloid OE, as an antioxidant, Al chelator and apoptosis inhibitor,