



Short communication

Influence of imperatorin on the anticonvulsant activity and acute adverse-effect profile of lamotrigine in maximal electroshock-induced seizures and chimney test in mice

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Abstract:

The influence of imperatorin (IMP) on the anticonvulsant activity and acute adverse-effect potential of lamotrigine (LTG, a second-generation antiepileptic drug) was studied in the maximal electroshock-induced seizure (MES) model and chimney test in mice. In order to assess the nature of interaction between IMP and LTG in the MES test, total brain LTG concentrations were evaluated with high-pressure liquid chromatography (HPLC).

Results indicate that IMP administered *ip*, 30 min before the test, at a dose of 50 mg/kg significantly enhanced the anticonvulsant action of LTG in the MES test by reducing the median effective dose (ED₅₀) of LTG from 6.11 to 2.47 mg/kg ($p < 0.05$). In contrast, IMP administered *ip* at doses of 30 and 40 mg/kg did not significantly potentiate the anticonvulsant activity of LTG against MES-induced seizures, although a reduction of the ED₅₀ values for LTG from 6.11 to 5.77, and 4.28 mg/kg, respectively, was observed. On the other hand, IMP administered *ip*, at doses of 30, 40 and 50 mg/kg had no impact on the acute adverse effects of LTG, and the median toxic doses for LTG (TD₅₀) were almost unchanged, ranging from 22.13 to 30.04 mg/kg in the chimney test. The protective index (TD₅₀ to ED₅₀ ratio) for LTG administered alone was 4.90 and increased to 5.21, 6.77, and 8.96 for LTG in combination with IMP at doses of 30, 40 and 50 mg/kg, respectively. Pharmacokinetic evaluation of total brain LTG concentration with HPLC revealed that IMP at the dose of 50 mg/kg did not affect total brain LTG concentration in experimental animals and thus, the observed interaction between IMP and LTG in the MES test was pharmacodynamic in nature.

The present study demonstrates that IMP ameliorates the pharmacological profile of LTG, when considering both, the antiseizure and acute adverse effects of the drug in preclinical study on animals. The combination of LTG with IMP can be of pivotal importance for epileptic patients as a potentially advantageous combination if it is proven that the results of this study can be extrapolated to clinical settings.

Key words:

imperatorin, lamotrigine, maximal electroshock seizure test, chimney test, protective index