A high dose of 3-phenyl-4-(phenylseleno) isoquinoline causes acute toxicity in C57bl/6 mice

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Introduction: Selenium stands out by presenting both structural and enzymatic roles in selenoproteins. Several organoselenium compounds studied demonstrated pharmacological proprieties, among them 3-phenyl-4-(phenylseleno) isoquinoline, tested in this study, a selective, reversible and mixed inhibitor of the isoform B of cerebral monoamine oxidase in vitro. Nevertheless, isoquinolines can cause toxicity, typically related to the oxidation of endogenous thiols. Furthermore, isoquinoline derivatives were found in the brain exhibiting both neuroprotective and neurotoxic action.

Material and Methods: Male C57bl/6 mice (25-35 g) received 3-phenyl-4-(phenylseleno) isoquinoline dissolved in canola oil at a dose of 500 mg/kg per oral. The animals were observed for 72 hours, during this period food and water consumption and the body weight gain were monitored. After that, brain, kidney, liver and blood of mice were removed for biochemical assays.

Results and discussion: The food consumption was not altered; but water consumption and the body weight gain were reduced. These alterations are in accordance with other studies, which demonstrated that treatment with organoselenium compounds, even at doses that do not cause toxic effects, reduces food and water intakes and the body weight gain, probably by an anorexigenic effect of this class of compounds. Treatment did not influence the cell viability (by MTT assay) and δ-aminolevulinic acid dehydratase activity in brain, liver and kidney. The cerebral Na⁺, K⁺-ATPase activity was inhibited by compound. This is a sulfhydryl enzyme and its reduced cysteinylic residues are target of organoselenium compounds, which can interact oxidizing them to disulfides, these oxidizing agents can cause the loss of catalytic activity. The serum parameters, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) activities and urea was unmodified. Conclusion: A high dose of 3-phenyl-4-(phenylseleno) isoquinoline caused systemic toxicity, demonstrated by a decrease in the water consumption, in the body weight gain and the inhibition of cerebral Na⁺, K⁺-ATPase activity.

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