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Eucalyptus globulus and *Plectranthus amboinicus*: a comparative nonclinical acute toxicology study of their emulsions in *Wistar* rats

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Eucalyptus globulus L., Myrtaceae, and *Plectranthus amboinicus* L., Lamiaceae, are widely used in folk medicine due to their main biological activities, mainly in the respiratory tract such as bronchodilator, expectorants, antimicrobials and anti-inflammatory properties. This study aimed to evaluate and compare the nonclinical acute toxicity of two emulsions containing the essential oil obtained from *E. globulus* leaves (EOEEG) (1,8-cineol: 84,35%, α-pinene: 1,72%) and from *P. amboinicus* leaves (EOEPA) (carvacrol: 33,5%, γ-terpinene: 14,77%). The chemical composition was obtained by GC-MS. The emulsions were obtained by the phase inversion emulsification method (PIT method). Toxicity study was based on 'Guide for conducting nonclinical toxicology study and pharmacology safety necessary for the development of drugs' and it was approved by the Ethics Committee on Animal Research (CEPA) nº 1005/14 and 1205/14. *Wistar* rats, both sexes, were divided into groups: control (orally water, n=12) and treated (single dose 1000 mg/kg EOEEG, o.w., n=12, or single dose 1000 mg/kg EOEPA, o.w., n=12). We performed a pharmacological screening to detect signs of activity in the central nervous system described by Almeida et al. (1999); food and water consumption; weight evolution; hematological and biochemical parameters of blood. The statistical analysis was performed by one-way ANOVA test through the software GraphPad Prism 6.0, and the results were considered significant when they presented values of $p < 0.05$. After 14 days, there were not deaths in the groups and EOEPA-treated animals showed behavioral changes, reflecting discomfort under the essential oil. A significant decrease was observed in water and feed intake only for EOEPA-treated group, which may be associated with general stress due to the drug exposure. The weight evolution showed significant differences only in the first week for EOEEG-treated males. Hematological parameters of EOEEG-treated animals revealed increased hemoglobin and hematocrit (males), and increased leukocytes and monocytes (females), while EOEPA-treated group showed increased erythrocytes, hemoglobin and hematocrit (males), and leukocytes and lymphocytes (females). Biochemical analyzes of EOEPA-treated animals showed increase of total proteins and GGT (males), reduction of uric acid (males), decrease of LDH (females), increase of cholesterol (females), increase of calcium (females) and decrease of creatinine (females), while EOEEG-treated group presented reduction of LDH and creatinine (females). The majority of these blood changes are within the normal reference values established for rats, suggesting that hepatic and renal functions remained unchanged, indicating that the emulsions have a relatively low acute toxicity profile.

Keywords: Herbal emulsion; acute toxicity; biochemical and hematological.

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