Effects of aqueous and hydroalcoholic extracts and ultra-highly diluted solutions of *Palicourea marcgravii* (Rubiaceae) in rats

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ABSTRACT

Palicourea marcgravii (Pm) is the most important toxic plant in Brazil. It is responsible for about half of all bovine deaths by natural poisoning in the country. The poisoning has a hyperacute evolution resulting in sudden death, which is attributed to the monofluoroacetic acid. This substance has high toxicity to several mammals, including humans. The homeopathic therapeutics uses ultra-highly diluted and dynamized solutions and there is enough evidence to investigate them as possible protection against poisonings. The aims of the present work were to compare the toxic effects of aqueous (AE) and hydroalcoholic (mother tincture - MT) extracts of Pm in rats, evaluate the effects of ultra-highly diluted and dynamized solutions (Pm 6CH and Pm 30CH) over the development of tolerance to the toxic effects of Pm and evaluate clinical, necroscopic and histopathological alterations in non-intoxicated rats treated with these solutions. AE and MT groups were formed of 10 animals each which received the extract in doses of 0.4g/kg, 0.8g/kg, 2g/kg and 4g/kg, intragastrically. The UD₆EA and UD₃₀EA groups were formed of five rats each, which received respectively 1 mL of Pm 6CH e Pm 30CH solutions, by oral route, three times a day, for eight days. Then, they were intoxicated with 2g/kg of Pm aqueous extract, intragastrically and received the correspondent ultra-highly diluted and dynamized preparations hourly until death. The UD₆ and UD₃₀ groups were formed of five rats each and received respectively 1 mL of Pm 6CH and Pm 30CH, orally, three times a day for 63 days. The animals were evaluated using clinical parameters, including the direct observation of their behavior at the open field and at the elevated plus-maze, and the study of the macro and microscopic lesions. Hyperacute death occurred after administration of the doses of 0.4g/kg, 0.8g/kg, 2g/kg e 4g/kg. In the AE group, prostration and nervous hyperexcitability followed or not by convulsive crisis were observed. In the MT group, the animals presented marked nervous depression without convulsion. Hepatic congestion and evidence of cardiac dilation were observed in the necropsy. Hydropic vacuolar degeneration of the renal distal convoluted tubules and congestion of several organs were observed in the histopathological examination. The latencies for the emergence of the first clinical signs, the convulsions and death occurrence were different in the animals of groups AE₁ (Pm 2g/kg), UD₆EA and UD₃₀EA, but was considered inadequate the animals amount. Groups UD₆ and UD₃₀ did not show any clinical, behavioral, necroscopical or histopathological differences when compared to the control group. The conclusions were that the aqueous extract causes nervous excitability and convulsions while the mother tincture causes nervous depression. There is cumulative effect of the toxic substances present in the plant, and there is not evidence that the ultra-highly diluted and dynamized preparation increases the tolerance to Pm intoxication.

Keywords: *Palicourea marcgravii*, ultra-highly diluted, monofluoroacetic acid.

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