Cytogenotoxic effects of a characterized aqueous extract of *Baccharis articulata* (Lam.) Pers. (Asteraceae) on normal cells.

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Introduction: Cold aqueous extract of *Baccharis articulata* (Ba-CAE) induces the death of human peripheral blood mononuclear cells (PBMCs) and exerts mutagenic effects on mice at 6h post-injection (p.i). The aim was to investigate whether the PBMCs death is due to apoptosis, and whether this extract exerts mutagenic effects on mice at 24 and 48 h p.i. In addition, Ba-CAE was chemically characterized.

Materials and methods: PBMCs were exposed to extract (10, 20, 40, 80, 160, 320, 640 and 1280 μg/mL) for 18-24 h. Cell viability was determined by trypan blue dye exclusion method. Apoptosis was determined by Hoechst 33258 staining, TUNEL, and DNA fragmentation analysis by agarose gel electrophoresis. BALB/c mice were injected with extract (1800, 900 and 450 mg/kg) and sacrificed at 24 and 48 h p.i. Bone marrow samples were used to assess chromosome mutations by the micronucleus test. The main metabolites in the Ba-CAE were identified and quantified by HPLC.

Results: A dose-dependent toxicity of Ba-CAE was demonstrated on PBMCs (CC50=165μg/mL). Hoechst staining showed several apoptotic figures. The percentage of TUNEL-positive per 400 cells was: control: 7±1%, cells treated: 10μg/mL(8±1%), 20μg/mL(9±3%), 40μg/mL(43±11%)*, 80μg/mL(58±18%)*, 160μg/mL(62±13%)*, 320μg/mL(68±20%)**, 640μg/mL(73±10%)**, 1280μg/mL(88±13%)**; *p<0.01; **p<0.001. The agarose gel electrophoresis showed the typical DNA laddering in cells treated with Ba-CAE. Both at 24 and 48 h, the extract increased the frequency of micronuclei in polychromatic erythrocytes (Tukey test, p<0.05). HPLC analysis demonstrated the presence of luteolin (1.96 ± 0.27%), acacetin (1.12 ± 0.14%) and chlorogenic acid (0.29 ± 0.05%).

Conclusion: Ba-CAE induced apoptosis and mutagenic effects on normal cells. The phytotherapy use of this medicinal herb should be limited as it may cause serious damage to cells when used improperly.

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