VERMINOSIDE AND VERBASCOSIDE FROM *KIGELIA AFRICANA*: CYTOTOXIC AND GENOTOXIC EFFECTS IN HUMAN LYMPHOCYTES

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Verminoside and verbascoside are the major constituents of *Kigelia Africana*, plant used in African folk medicine for its emollient, anti-eczema and anti-psoriasis properties. Remedies from root bark are also used for the treatment of venereal diseases and naphtoquinones extracted from *Kigelia africana* showed cytotoxic activity against melanoma and renal carcinoma cells (1). We have demonstrated that verminoside is able to inhibit in vivo iNOS expression in LPS-induced 774.A1 macrophages, suggesting an anti-inflammatory activity of the compound in a concentration related manner. The potential applications of these natural compounds as ingredients in cosmetic and pharmaceutical formulations prompted us to investigate on the cytotoxic and genotoxic activities of verminoside and verbascoside, using genetic toxicity tests recommended in preclinical studies by US Food and Drug Administration (FDA). In particular we tested in vitro cytotoxic and genotoxic activities of verminoside and verbascoside in human lymphocytes from three heathy unrelated subjects. We determined mitotic index and exclusion of trypan blue dye as markers of cell proliferation and cell viability and used chromosome aberration test and Sister Chromatid Exchange (SCE) analysis as indicators of genetic damage induced by the compounds on normal cells. Our results showed that verminoside and verbascoside (from 0.01 to 0.1 mM) induced a significant ($P<0.05$) concentration-dependent reduction of the mitotic index associated to a time-dependent reduction of cell viability. Moreover, we found a concentration-dependent increase in chromosome aberrations after a 72 hour-incubation and an enhancement of about 2 fold induction of sister chromatid exchanges. Interestingly, preliminary data indicated that the induction of the clastogenic effects and sister chromatid exchanges implicates an up-regulation of the total Poly(ADP-ribose) polymerase (PARP-1) protein levels, a gene regulating genomic stability and activated by agents inducing DNA strand breaks. In conclusion our results suggest that both verminoside and verbascoside could have genetic toxicological properties that have to be taken into account in pharmacological and clinical applications.

1. Houghton P. J. et al. (1994) Planta Med. 60:430-433.