Cytotoxicity of natural chemicals against normal and tumor cell lines

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Introduction: More recently there has been observed an increased number of scientific studies with medicinal plants in search of bioactive molecules to be used in the development of new drugs. Plant species are sources of a great diversity of natural chemicals with various pharmacological activities. In this context the discovery of new antineoplastics, has been the aim of innumerable research groups using medicinal plants as source of drugs. The effective results obtained from studies using the species Catharanthus roseus and Podophyllum peltatum that produce the antineoplastic secondary metabolites vinblastine, vincristine and etoposide, respectively, motivated us to investigate the efficacy of the triterpenes betulinic acid, oleanolic acid and ursolic acid synthesized in Jacaranda decurrens, a species endemic to the Brazilian Cerrado region. Objective: The aim of this work was to validate the cytotoxic effectiveness of the triterpenes betulinic acid, oleanolic acid and ursolic acid against 3T3, MRC5 and MCF7 cell lines. Methods: The synthetic substances cyclophosphamide (Cytoxan®), cisplatin (Tecnoplatin®), doxorubicin (doxorubicin®), the semi-synthetic etoposide (Posidon®) and the phytomedicine vincristine sulfate (Zodiac®) were used as reference. The cytotoxic activity was evaluated for each chemical individually, betulinic acid, oleanolic acid and ursolic acid. Experiments were carried out in triplicate and the concentration used was 25, 5 and 1μg against 3T3 and MRC5 normal strains, and MCF7 tumor cell line, grown in specific media. The cell lines were cultured in 5% CO₂ incubated at 37°C for 48 hours. The results were analyzed using the MTT colorimetric test for cell viability by spectrophotometry at 570nm. Results: Obtained results showed that the triterpenes tested showed IC₅₀ > 25μg for both normal strains 3T3 and MRC5, however for MCF7 tumor cell line showed IC₅₀ = 1μg for vincristine, ursolic acid, etoposide and cisplatin, IC₅₀ = 5 for doxorubicin, and IC₅₀ > 25μg for oleanolic acid, betulinic and cyclophosphamide. Conclusion: The data obtained indicate that among the triterpenes tested ursolic acid is the most promising for the development of an anticancer agent since it showed to be selective regarding the tumor cell line, while oleanolic acid and betulinic did not show this selectivity in the concentrations tested.

Keywords: medicinal plants, secondary metabolite, phytomedicine, antineoplastic drug.