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Peniocerol, a sterol isolated from *Myrtillocactus geometrizans*, inhibits cell proliferation and tumor growth in colon cancer xenografts *in vivo*

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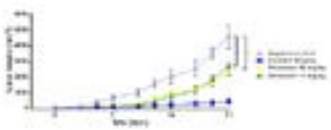
Introduction: Cancer worldwide is one of the leading causes of mortality, in 2012 there were 14 million new cases reported, as well as 8.2 million deaths related to cancer. It is expected that the number of new cases will increase by 70% in the next 20 years. In addition to the above, patients sometimes do not respond to treatment, have recurrence of cancer cells have chemoresistance and the drugs currently used in chemotherapy are limited. Therefore, there is a need to discover and develop new drugs for the treatment of cancer. Which requires the exploration of all possible strategies, one of the most important is the use of natural products, which has allowed making significant contributions, such as taxol isolated from *Taxus baccata* and vincristine isolated from Catharanthus roseus, both currently used in the clinic. In the research carried out by our working group, the natural product peniocerol, an isolated sterol from *Myrtillocactus geometrizans* (Mart.Ex Pfeiff) Console, has been studied.

Objective: To evaluate both the cytotoxic activity of peniocerol *in vitro* against the human HCT-116 colon cancer cell line and its antitumor effect in a mouse colon cancer xenograft model.

Methods: HCT-116 cells were treated with various concentrations of peniocerol. Crystal Violet Assay was used to evaluate the inhibition effect. Cell apoptosis was detected through Annexin–V FLUOS/PI double-labeled cytometry assays. The antitumor activity of peniocerol was assessed in a mouse colon cancer xenograft model. The tumors were analyzed to evaluate the expression of the Caspasa-3 and PCNA, by Western blot and Immunohistochemistry assays, respectively.

Results: Peniocerol induced growth inhibition and apoptosis *in vitro* in a time- and dose-dependent manner. The administration of peniocerol (30 mg/kg or 15 mg/kg) once a week for 21 days inhibited tumor growth. However, a greater antitumor effect was achieved when peniocerol was administered (15 mg/kg) three times a week for 21 days. The expression of Caspase-3 was increased and the expression of PCNA was decreased, in tumors treated with peniocerol.



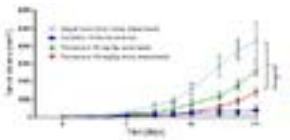


Figure 1: Antitumoral activity of peniocerol administrated once a week during 3 weeks in an experiment *in vivo*. Groups of six nu/nu mice inoculated with 1.5 x 10^6 HCT-116 cells. The mice were treated with 30 mg/kg and 15 mg/kg peniocerol, cisplatin or negative control, on days 0, 7 and 14. The size of the tumors was measured three times per week. The bars indicate the standard deviation of the mean * p> 0.05 compared to the vehicle (ANOVA and t test).

Figure 2: Antitumoral activity of peniocerol administered every third day for 21 days. Groups of six nu/nu mice inoculated with 1.5 x 106 HCT-116 cells. Mice were treated with 15 mg/kg peniocerol, cisplatin or negative control, on days 0, 2, 4, 7, 9, 11 and 14. The size of the tumors was measured three times per week. The bars indicate the standard deviation of the mean * p> 0.05 compared to the vehicle and ** p> 0.001 compared to peniocerol administered once a week (ANOVA and t test).

Biography

Beatriz Del Carmen Couder García is pursuing her Doctor of Science in Biomedical Sciences at the Nacional Autonomous University of Mexico (UNAM). She has obtained her Master of Science degree in Biochemical Engineering at the Technological Institute of Tuxtla Gutiérrez. She is an Agro-industrial Engineer from the Polytechnic University of Chiapas. Her research interests include *in vitro* and *in vivo* research in the antitumor evaluation of natural products and the mechanism of action.

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