

Seasonal variation in cytotoxicity of the volatile oil from *Anethum graveolens* L. (Apiaceae) against human prostate and breast tumoral cells

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According to the World Health Organization, about 8.8 million people worldwide died of cancer in 2015. That is nearly one in six of all global deaths, or the second leading cause of global death. Prostate cancer is the most common type of cancer in men while breast cancer is in women(1). The current severe global profile and the limitations of available treatments urge the searching for new and more effective drugs. In this context, herbal drugs and their bioactive compounds are a potential source of new cytotoxic agents. In our systematic search for new bioactive compounds, Anethum graveolens L. (dill) volatile oil was selected for an in vitro cytotoxicity screening. Dill oil is widely applied in pharmaceutical, cosmetics and food industries. Previously, researches ascribed to this oil a variety of biological activities such as: antioxidant, antiprotozoal, antifungal, insecticidal, antihelmintic, fumigant toxicity among others, motivating this present work to evaluate its potential cytotoxic activity against cells of those most incident cancers. Furthermore, the seasonal variation effect on this action was also investigated. Aerial parts from A. graveolens were collected during the four annual seasons, in the surroundings of Piedade city, located about 170 Km from the city of São Paulo, in the São Paulo State, Brazil. The oil from pools of fresh plant organs was extracted by hydrodistillation, in a Clevenger-type apparatus for three hours and its cytotoxicity was then evaluated against prostate (PC-3) and breast (MCF-7) cancer cell lines by the sulforhodamine B colorimetric assay (2). Doxorubicin was the positive control, while α- phellandrene was tested as an analytical marker of this plant oil. The oil yield values varied: 0.15; 0.06; 0.03 and 0.02 % m/ m (wet base), respectively in the winter (wint), summer (sum), autumn (aut) and spring (spr). Results showed that all the oils presented different levels of cytotoxicity on both tumoral cells, along all the seasons. In general, the oils were more active against the prostate cell line. The volatile oil from plants collected in the winter was the most cytotoxic against both cell lines (IC₅₀(PC-3): 1.81 μ g/mL, CI₅₀ (MCF-7): 15.26 μ g/mL). The IC₅₀ values of the plants collected in the other seasons on PC-3 and MCF-7 cells were, respectively: 11.11/25.96 (aut); 14.16/23.51 (spr) and 13.21/32.36 (sum) µg/mL, while for the marker (α-phellandrene) it presented 11.11/25.96μg/mL. To our knowledge, there is no previous study on this oil against PC-3 cells in literature, or a season-based approaching for MCF-7 cells. Results confirmed the cytotoxic potential of this oil and the seasonal variation on its yield and activity. The oil from the winter season is the most promising one. An analysis of the previous study on chemical composition, in relation to this data, is in progress to indicate the potential bioactive constituents.

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