

Highly diluted compounds effects on B16-F10 melanogenesis, reactive species production and tumorigenesis

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ABSTRACT

Background: Cutaneous melanoma is a highly malignant tumor derived from skin epidermis pigment-producing melanocytes. During melanin biosynthesis and other tumorigenic process, oxygen and nitrogen reactive species are produced and might be critically involved in melanogenesis. Reactive species play key roles on regulation of many types cell proliferation, including melanoma cells.

Aims: We evaluated M8 (*Aconitum napellus* 20dH, *Arsenicum album* 18dH, *Asa foetida* 20dH, *Calcarea carbonica* 16dH, *Conium maculatum* 17dH, *Ipecacuanha* 13dH, *Phosphorus* 20dH, *Rhus toxicodendron* 17dH, *Silicea* 20dH, *Sulphur* 24dH, *Thuja occidentalis* 19dH) and M1 (*Chelidonium majus* 20dH, *Cinnamon* 20dH, *Echinaceae purpurea* 20dH, *Gelsemium sempervirens* 20dH plus all M8 compounds) effects on cell proliferation, melanogenesis and reactive species.

Methodology: Melanin content was measured in B16-F10 cells after 96 hours of treatment with highly diluted compounds, as well as superoxide anion, hydrogen peroxide and nitric oxide. Furthermore, cell proliferation was investigated by crystal violet and cell viability by trypan blue exclusion method after 48 hours of treatment.

Results: M1 and M8 treatment led to statistically significant increase in B16-F10 melanin content and a decrease in nitrite concentration, a nitric oxide derivative. Superoxide anion and hydrogen peroxide production was not changed, but a decrease in cell proliferation after treatment was observed. NO is known to be involved in tumor progression. NO treated B16-F10 cells exhibited higher metastatic capacity and endogenous NO has antiapoptotic effects. Thereby, low NO levels could account cell proliferation reduction and *in vivo* tumorigenesis reduction [1]. It is speculated that melanocytes are programmed to survive in order to preserve their photoprotective role, thus in a compensatory manner the cell may synthesize melanin in response to cell proliferation reduction.

Conclusion: These results suggest that tumorigenesis reduction observed on *in vivo* models by M8 [1] may be due to changes in cell metabolism as well as in cell proliferation. However further studies are needed to better understand M1 and M8 mechanisms of action.

Keywords: melanoma, melanogenesis, oxygen reactive species

References:

[1] Guimarães FSF, Andrade LF, Martins ST, Abud APR, Sene RN, Wanderer C, et al. *In vivo* and *in vitro* anticancer properties of *Calcareo carbonica* derivative complex (M8) treatment in a murine melanoma model. BMC Cancer, 2010, 10:113.



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