

***Viscum album* L. homeopathic mother tinctures: Metabolome and antitumor activity**

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Background: *Viscum album* L. is a semiparasitic plant with antitumor activity attributed to the aqueous extracts. However, European *V. album* ethanolic extracts (VAE) have also demonstrated *in vitro* activity in tumor models.

Aims: Evaluate the metabolic profiles of fifty VAE harvested during summer and winter seasons and their antitumor activity through 2D and 3D models.

Methodology: VAE were prepared by maceration from: *V. album* ssp. *album* growing on *Malus domestica*, *Quercus* sp. and *Ulmus* sp.; *V. album* ssp. *austriacum* from *Pinus sylvestris*; *V. album* ssp. *abietis* from *Abies alba*. Chemical analyses were performed through liquid chromatography coupled with high resolution mass spectrometry and Partial Least Squares Discriminant Analysis (PLS-DA) was performed in the Metaboanalyst 4.0. The antitumor potential of the selected VAE was evaluated in 2D and 3D models (MDA-MB-231 cancer cells) by MTT, crystal violet and glycolytic pathway analysis.

Results and discussion: The first 3 principal components in PLS-DA explained 60% and 40% of data variation in positive and negative modes respectively. Three groups were formed and showed chemical similarity among *V. album* subspecies. The compounds responsible for group separation were tentatively identified as: pinobankasin or naringeninhexoside; isorhamnetin-3-hexoside, meglutol and different amino acids. The summer VAE at 0.5% v/v induced higher cytotoxic damage than the winter preparations, and *Abies alba* and *Quercus* sp. VAE promoted 49% and 42% reduction of tumor viability in 3D model (72h incubation), respectively. MDA-MB-231 glycolytic pathway in 2D model showed a decrease in the glucose consumption and extracellular lactate production. Also, PFK (6-phosphofructo-1-kinase) and PK (Pyruvate kinase) activities were inhibited by *Abies alba* and *Quercus* sp. VAE at 48h of incubation.

Conclusion: VAE extracts showed different metabolomes and the glycolytic pathway should be an important target involved in the inhibition of tumor growth by these extracts.

Key words: *Viscum album*, antitumor, metabolome, glycolysis