1. **Viscum album topic and transdermal formulations: development, stability and in vitro cytotoxicity evaluation**

**Pharmacology of Traditional Medicine**

**Background:** In complementary medicine, European mistletoe extracts have been widely used in cancer treatment for at least 100 years. However, the complex phytochemical composition of mistletoe extract, as well as the low water solubility of important pharmacological metabolites, has motivated the development of new delivery systems.

**Objective:** development of topic and transdermal *V. album* formulations and their *in vitro* antitumoral potential.

**Methodology:** *V. album* ethanolic extract was prepared by maceration from berries, stems and leaves collected from *Abies alba* host tree. Then, the dry extract was prepared by lyophilization and submitted to a chemical characterization by thin layer chromatography, HPLC-DAD and HPLC-MS. Aqueous fermented extract from the same host tree was also used. *V. album* extracts (ethanolic and aqueous) and thermal sensitive polymer were mixed to prepare a hydrogel. The stability and rheology of both formulations were conducted in order to characterize the physicochemical properties. The *in vitro* antitumoral activity was carried out using tumoral (Yoshida) and non-tumoral (HaCat) cell lines. The transdermal properties of new formulations were evaluated by *in vitro* assays, using pig ear as membrane, in Franz-cell type apparatus.

**Results:** The hydrogels were classified as non-Newtonian fluids and presented different transition temperatures: 15 ºC (hydrogel with dry extract) and 18 ºC (hydrogel containing aqueous extract). The hydrogel containing 5% of dry or aqueous extract presented pH and microbiological stabilities for 180 days. The total flavonoid content in the hydrogel varied around 20%, which is in accordance with Brazilian quality guidelines. Both formulations presented selectivity towards tumoral when compared to normal cells, with higher antitumoral activity from the dry extract, compared to the aqueous one (p<0.05), in a dose dependent manner. A permeation potential related to hydrogel containing dry extract was detected after 8 hours application on pig ears, according to the methodology used.

**Conclusion:** The present results highlight the new *V. album* transdermal application for cancer treatment, opening innovative possibilities to the current injectable formulations.

**Key words**: *Viscum album*, dry extract, hydrogel, transdermal, cytotoxicity

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