

Introduction: European mistletoe extracts have been widely used in cancer treatment for at least 100 years. In the present work, the antitumoral potential of *Viscum album* ethanolic soluble substances was evaluated in a topic and transdermal hydrogel formulation.

Methods: *V. album* whole plant, collected in winter from the host tree *Abies alba*, was submitted to ethanolic maceration. This lyophilized ethanolic extract was chemical characterized by thin layer chromatography, HPLC-UV and HPLC-MS. Aqueous fermented extract (1:5 from *V. album* spp *abietus*, Iscador®) was also evaluated. Using a thermal sensitive polymer and skin permeation enhancers, two hydrogel formulations were developed: *V. album* dry extract (VA_DEH) and *V. album* aqueous fermented extract (VA_AEH). These formulations were submitted to the stability and rheological assays, as well as cytotoxic tests using tumoral (Yoshida) and non-tumoral (HaCat) cell lines. The VA_DEH transdermal potential was evaluated by ex vivo assay, in a Franz-cell type apparatus.

Results: Phytochemical analyses of VA_DEH indicated the presence of flavonoids and chlorogenic acid. Hydrogels were classified as non-Newtonian fluids and presented different sol-gel transition temperatures: 12 °C (VA_DEH) and 17 °C (VA_AEH). The pH values were compatible with topic formulations and both hydrogels showed microbiological stability under time and conditions tested. Both hydrogels presented a promising antitumoral activity, when compared to the normal cells, with special focus on VA_DEH ($p < 0.05$). VA_DEH permeation was detected after 8 h of experiment, reaching 4.60 µg of chlorogenic acid permeated, at 24 h.

Conclusion: The present results highlight a new *V. album* transdermal application for cancer treatment, opening innovative possibilities to the currently injectable formulation already used in medical practice.

Keywords: mistletoe; *Viscum album*; hydrogel; transdermal; in vitro; ex vivo; cancer

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Oral Mistletoe and Cancer Part 1

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Introduction: Mistletoe therapy (MT) is used as an adjunct to conventional therapy in cancer patients due to its known immunological properties. However minimal evidence has been presented on oral mistletoe and MT in the UK. The aim of this study was to understand UK clinicians' preferred route of administration by conducting in-depth, semi-structured interviews. Questions used were standardised to gain a comparable insight into route of administration; patient demographics and clinicians' individual experience and perceptions of MT, focusing on oral mistletoe and cancer.

Methods: Doctors prescribing mistletoe were contacted via centres listed on <https://www.mistletoetherapy.org.uk/> between June and July 2020. 17 questions were devised for the virtual Zoom interviews - conducted by one researcher whilst another transcribed. Recordings ensured transcription accuracy. The interview questionnaire was piloted to check feasibility. The qualitative data was coded into key themes and analysed.

Results: Six clinicians were recruited and interviewed. MT provision varied amongst clinicians with all mentioning no national standardised protocol. Oral and subcutaneously administered mistletoe were the most common, followed by intravenous. Four doctors preferred prescribing subcutaneous mistletoe due to visible skin reactions to help determine optimal dose, whilst two doctors solely prescribed oral mistletoe. Overall, there was no suggestion that one route of administration had greater

outcomes than another. However, it was indicated that the therapeutic effects of oral mistletoe are unknown, and it could be a placebo effect.

Conclusion: This study highlights diversity of MT provision amongst UK clinicians, including route of administration. Preferences were established on practicality, experiences, case reports and manufacturer's guidance, with no national or international standardised guidelines. This suggests the need for further research into mistletoe provision in the UK.

Keywords: Mistletoe Therapy, cancer, oral mistletoe, semi-qualitative study, cancer

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Development of an Interactive Database to Quantitatively Assess the Impact of Medication on micronutrient status

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Introduction: A significant, but disparate and poorly collated literature exists describing the impact of medication/s on micronutrient status. Currently no tools allow this data to be easily accessed and used to quantitatively determine the single or cumulative impact of medication/s on nutritional status. The aim of this research was to provide on-line access to the relevant data to deliver validated corrective dietary recommendations.

Methods: A search was performed of electronic databases of peer reviewed literature using keywords and the Medical Subject Headings of classes of drugs as defined in the British National formulary and 26 recognised micronutrients and descriptors of microbiome. Studies were screened and reviewed in detail.

Results: 1050 references were identified with 4073 incidences of medication/s interacting with the physiological status of the above micronutrients. These were assessed as-major/moderate/minor based upon the conclusion/s of the publication. An algorithm was developed that enabled the likely impact of individual medications to be quantified and interrogated, with aggregation of cumulative scores from multiple inputs. Weighted inputs relating to life-stage, lifestyle and dietary preferences can also be aggregated with medication/s effects enabling rapid assessment of the impacts these issues might induce in micronutrient status to be delivered in an easy-to-understand summary report. This has been evaluated in bariatric surgery patients and athletes. (1,2).

Conclusion: The tool enables a rapid assessment of the cumulative impact of medication/s on micronutrient status to be made, with a hyperlink to the relevant abstract, enabling validation of conclusions. Potential minor and moderate negative impacts resulting from inputs are advised to be corrected firstly by recommended changes to diet, with any major deficiencies addressed by additional relevant supplementation wherever necessary. This development can be linked to international formularies and complements healthcare provider's clinical skills thereby contributing to optimise patient's micronutrient status by delivering personalised evidence-based recommendations.

Keywords: literature review; micronutrient status; interactions

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The Society for Integrative Oncology Practice Recommendations for online consultation and treatment

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