

Review of the mistletoe literature from the second half of 2025

Botany

Çakir F, Çiçek N, Yücedağ C: Impacts of pine mistletoe on the physiological traits and plant nutrients of Anatolian black pine. European Journal of Plant Pathology 2025, pp 11. <https://doi.org/10.1007/s10658-025-03059-4>: This study investigates the effects of pine mistletoe (*Viscum album* subsp. *austriacum*) on the physiological traits and plant nutrients of Anatolian black pine (*Pinus nigra* subsp. *pallasian*). For this 15 uninfected (control) and 15 moderately infected Anatolian black pine trees were sampled from both thin and medium diameter classes. The infected trees exhibited significant reductions in chlorophyll content and mineral nutrients, alongside increase in proline, malondialdehyde (MDA), and hydrogen peroxide (H₂O₂) increased, particularly in trees with medium stem diameters. These findings suggested that mistletoe infection caused a notable decline in photosynthetic efficiency and nutrient absorption and therefore has a detrimental effect on the Anatolian black pine.

Biology

Campos-Dominguez L, Christenhusz M, Bell D, et al: The genome sequence of the European mistletoe, *Viscum album* L. (Santalales: Viscaceae). Wellcome Open Research 2025, pp 14. <https://doi.org/10.12688/wellcomeopenres.24920.1>: In this study a genome assembly from a female specimen of *Viscum album* (European mistletoe, Streptophyta, Magnoliopsida, Santalales, Viscaceae) was presented. The genome sequence had a total length of 94,261.04 megabases. Most of the assembly (98.67%) was scaffolded into 49 chromosomal pseudomolecules, including the B₁ chromosome. The genome assembly was generated as part of the 'Darwin Tree of Life Project', which produces reference genomes for eukaryotic species found in Britain and Ireland.

Alma MH, Karadag M, Atalar MN, et al: Determination of the chemical content of the ethyl acetate and ethanol extracts of *Viscum album* L. subsp. *austriacum*. 9th International Tourism and Development Congress October 2025, Kahramanmaraş, Türkiye: *Viscum album* L. has been proven as an effective medicinal plant for the treatment of hypertension, diabetes, arthritis, inflammation, and cancer. This study therefore investigated the phenolic compound content of the ethanol and ethyl acetate extracts of *Viscum album* L. ssp. *austriacum*. In the ethyl acetate extract, chlorogenic acid, quercetin-3-glucoside, quercetin-3-galactoside and quercimeritrin were determined in high amounts, while in the ethanol extract, chlorogenic acid – but in lower concentrations than in the ethyl acetate extract – quercetin-3-glucoside, naringenin and naringin were detected as the predominant compounds. All these compounds exhibit antioxidant, anti-bacterial, anti-inflammatory and antitumour properties.

De Souza HMR, de Carvalho AGA, Nonato de Oliveira Melo M, et al: Gas and liquid chromatography-mass spectrometry investigation of *Viscum album* lipophilic extracts. Analytical Letters 2025, pp 19. <https://doi.org/10.1080/00032719.2025.2565255>: As there is little information on the chemical composition of the lipophilic constituents of *Viscum album* available, this study aimed to perform a comprehensive analysis of the lipophilic extracts via gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-high performance mass spectrometry (LC-HRMS) to reveal their complex chemical composition and to understand the impact storage time and the host tree. Lipophilic extracts of pine mistletoe (*Pinus sylvestris*) were used, as well as extracts from the host trees apple, oak, fir and elm (*Malus domestica*, *Quercus* sp., *Abies alba* and *Ulmus* sp.). A total of 103 metabolites were identified, including pentacyclic triterpenes, fatty acids, phytosterols, flavonoids, organic acids, amino acids and lipids, with the composition varying depending on the year of extraction and the host tree.

Di H, Shen C, Zhang S, et al.: *Viscum coloratum* (Komar.) Nakai: a review of botany, phytochemistry, pharmacology, pharmacokinetics and toxicology. Biomolecules 2025;15:974. <https://doi.org/10.3390/biom15070974>: This review article summarises the botany, traditional uses, phytochemistry, pharmacology and pharmacokinetics of *Viscum coloratum* (Komar.) Nakai, which is used in traditional Chinese medicine for the treatment – amongst other conditions – of rheumatism, paralysis, back pain, muscle weakness, excessive menstruation, bleeding during pregnancy, foetal restlessness and dizziness. To date, 111 compounds have been isolated and identified from this plant, including flavonoids, phenylpropanoids,

terpenoids, diarylheptanoids, alkaloids, polysaccharides and lectins, which have anti-inflammatory, anti-cancer, antioxidant and anti-cardiovascular disease effects. However, some constituents – particularly alkaloids and lectins – may induce toxicity due to excessive intake or accidental ingestion. Despite these warnings, only a few toxicological studies have been conducted to date, meaning that the safety of this plant is not yet sufficiently investigated.

Kalinić L, Šrajter Gajdošik M, Pavić V, et al: Analyses of spatiotemporal variation of antioxidative activity in common mistletoe (*Viscum album* L.) accompanied by antibacterial activity of green synthesized silver nanoparticles. *ChemistrySelect* 2025;10,e05741(1 of 13). doi.org/10.1002/slct.202405741: In this study the impact of location and sampling time on the content of bioactive compounds and antioxidative activity in freshly harvested mistletoe leaves, twigs, and commercial tea mixtures was investigated. Additionally a suitable green synthesis procedure for antimicrobial silver nanoparticles (AgNPs) from mistletoe extract was presented. The samples harvested in October contained significantly higher levels of bioactive substances compared with those collected in February. However, fresh samples and commercial tea mixtures showed no significant differences. AgNPs were successfully synthesised using a methanolic mistletoe extract, which had a potent antimicrobial activity against the human pathogens *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus*.

Preclinic

Cell cultures

Hong CE, Lyu SY: Mistletoe lectin induces apoptosis and modulates the cell cycle in YD38 oral squamous cell carcinoma cells. *BIOCELL* 2025;49(2):269-288. https://doi.org/10.32604/biocell.2025.060411: As treatment outcomes for patients with oral squamous cell carcinoma (OSCC) are still poor, this study investigated the antiproliferative and molecular effects of the protein agglutinin (VCA), derived from Korean mistletoe (*Viscum album* var. *coloratum*), on human YD38 OSCC cells. VCA exhibited dose-dependent cytotoxicity against YD38 cells, with a significant increase in both early and late apoptotic populations at 100 and 1,000 ng/ml VCA. In addition, significant changes in cell cycle distribution, increased levels of cleaved poly(ADP-ribose) polymerase (PARP) and cleaved caspase-3 were detected, indicating an activation of the caspase-dependent apoptotic pathway and associated with a potent anti-tumour effect against YD38 OSCC cells.

Hong CE, Lyu SY: Comparative anticancer mechanisms of *Viscum album* var. *coloratum* water extract and its lectin on primary and metastatic melanoma cells. *BIOCELL* 2025;49(2):289-314. doi:10.32604/biocell.2025.061334: The anti-tumour properties of an aqueous extract of Korean mistletoe (*Viscum album* var. *coloratum*) and its purified lectin component (*V. album* var. *coloratum* agglutinin, VCA) were analysed using the two melanoma cell lines B16BL6 and B16F10. The aqueous extract exhibited dose-dependent cytotoxicity in both cell lines, which was even more significant in VCA. Both compounds induced substantial apoptosis with a significant progression from the early to the late stage of apoptosis, demonstrating particularly high efficacy in the induction of caspase-dependent apoptosis.

Lyu SY, Meshesha SM, Hong CE: Synergistic effects of mistletoe lectin and cisplatin on triple-negative breast cancer cells: insights from 2D and 3D *in vitro* models. *Int. J. Mol. Sci.* 2025, 26, 366. https://doi.org/10.3390/ijms26010366: This study investigated the potential synergistic effects of mistletoe lectin (*Viscum album* L. var. *coloratum* agglutinin, VCA) isolated from Korean mistletoe and cisplatin on the highly invasive, triple-negative (TNBC) breast cancer cell line MDA-MB-231. The combination therapy of VCA and cisplatin synergistically inhibited cell proliferation, induced apoptosis and arrested the cell cycle in the G2/M phase. Furthermore, it reduced cell migration and invasion, as well as the expression of the angiogenesis-specific factors VEGF-A and HIF-1 α .

Markowitsch SD, Albrecht L, Meiborg M, et al.: Mistletoe extracts inhibit progressive growth of prostate cancer cells. *Cells* 2025;14:1535. https://doi.org/10.3390/cells14191535: This *in vitro* study investigated the effect of mistletoe extracts from the host trees *Tilia* (lime), *Populus* (poplar), *Salix* (willow) and *Crataegus* (hawthorn) on the growth and proliferation of prostate cancer cells (PCa cells) and analysed clonogenicity, apoptosis, cell cycle, and cell cycle-regulating proteins such as cyclin-dependent kinases and cyclins, as well as the expression of CD44 marker, splice variants, and integrin α and β receptors. All mistletoe

extracts showed significant dose-dependent inhibition of cell growth and suppression of cell proliferation and clonogenicity. The extracts from *Populus* and *Salix* induced cell cycle arrest in the G2/M phase and increased apoptosis. Both extracts downregulated CDK1 and cyclin A and altered CD44 expression. Integrin $\alpha 5$ and $\alpha 6$ were downregulated by all extracts, leading to inhibition of cell growth and proliferation of PCA cells *in vitro*.

Viana Valle AC, Cunha de Carvalho A, Araujo A, et al.: Anti-inflammatory activity of *Viscum album* D6 preparations in eye drops formulation. Research and Development 2025;6:1-6. <https://doi.org/10.11648/j.rd.20250601.11>: This *in vitro* study investigated the effect of a homeopathic formulation of *Viscum album* eye drops (*Viscum* 6DH) on ocular inflammation using human keratinocytes (HaCaT) and mesenchymal stem cells (MSCs). The *Viscum album* 6DH eye drops showed no cytotoxicity towards the cells, and a significant acceleration in wound healing was observed. Furthermore, in a cytokine assay using the mesenchymal stem cells exposed to inflammatory induction and treated with the eye drops, a marked reduction in IL-8 and IL-12p70 levels was observed following treatment.

Murine test systems

Hao Z, Liu Y, Wang Y, et al: *Viscum coloratum* (Kom.) Nakai inhibits osteoclastogenesis in RANKL-induced osteoclast differentiation through the PI3K/AKT/mTOR pathway. Research Square 2025, pp 23. <https://doi.org/10.21203/rs.3.rs-6704733/v1>: *Viscum coloratum* (Kom.) Nakai has been widely used in traditional Chinese medicine and clinical treatment for rheumatoid arthritis (RA), as it alleviates clinical symptoms and reduces osteoclastogenesis-related gene expression in a mouse model. However, whether *Viscum coloratum* could inhibit osteoclastogenesis and what mechanisms underlie this was first investigated in this study using the mouse monocyte-macrophage leukaemia cell line RAW 264.7. It was demonstrated that the extract from *Viscum coloratum* has a significant effect against RANKL-induced (receptor activator of NF- κ B ligand) osteoclast differentiation, identified by inhibiting the formation of TRAP-positive (tartrate-resistant acid phosphatase) multinucleated osteoclasts and TRAP activity, as well as a reduction in the expression of the osteoclast-specific gene NFATc1 (nuclear factor of activated T cells 1). Osteoclastogenesis was inhibited by regulating the PI3K/AKT signalling pathways, and Viscumneoside III was identified as the main active compound.

Clinic

Clinical laboratory diagnostics

Lee Y, Kim MJ, KangYJ, et al.: Helixor A enhances natural killer cell activity by induction of PAI-1 expression through the p38/MAPK signaling pathway. International Immunopharmacology 2025;165:115531. <https://doi.org/10.1016/j.intimp.2025.115531>: Studies have shown that mistletoe extracts such as Helixor A can be used for the treatment of endometriosis, as they increase the cytotoxicity of NK cells by inducing CD107a expression. However, the molecular mechanisms underlying its effect on NK cells in these patients are not fully understood. This study demonstrated that Helixor A enhances the cytotoxic activity of mNK cells by upregulating p38/MAPK activation and PAI-1 expression. Furthermore, increased expression of NK cell-activating receptors such as NKp44 and NKp30, as well as enhanced production of IFN- γ and TNF- α , was observed in mNK cells treated with Helixor. Overexpression of PAI-1 enhanced the cytotoxicity of NK cells and increased the phosphorylation of p38 in mNK cells, suggesting that PAI-1 may regulate the p38/MAPK signalling pathway.

Feasibility

Duncan LJ, Bryant S, Feder G, et al.: The mistletoe and breast cancer (MAB) study: a UK mixed-phase, pilot, placebo-controlled, double-blind, randomised controlled trial. Cancers 2025;17:3169. <https://doi.org/10.3390/cancers17193169>: The aim of this study was to test the feasibility of a mixed-phase, pilot, placebo-controlled, double-blind trial on mistletoe therapy (MT) with an embedded qualitative study in the UK National Health Service (NHS) setting. For this, 45 female patients diagnosed with early or locally advanced breast cancer should be recruited via an NHS oncology centre. Participants were randomly allocated to receive either Iscador Malus, Iscador Pinus or physiological saline solution (placebo). To collect data, participants kept a diary and completed questionnaires on quality of life. Qualitative interviews were

also conducted with the patients, oncologists and nurses. Of the 67 patients approached to take part in the study, 15 gave their consent, 14 were randomised and 2 withdrew during the trial. The additional treatments, the extra time required, the additional injections and the possibility of placebo allocation were cited as barriers to the low recruitment rate. However, treatment adherence was very good during participation in the study.

Efficacy/Safety

Hong SS, Choi M, Rho SY, et al.: Immediate postoperative abnobaVISCUM® F as an adjuvant treatment in patients receiving standard care after pancreatic cancer resection. *Yonsei Med J* 2025;66(11):762-770.

<https://doi.org/10.3349/ymj.2024.0493>: This retrospective study investigated the antitumour effect of abnobaVISCUM Fraxini in patients with resected pancreatic cancer. The 985 patients were divided into a Viscum group comprising 310 patients who received at least 12 Viscum treatments and a control group comprising 590 patients. The disease-free survival (DFS) and overall survival (OS) were compared using a matched-pair analysis. Both groups showed similar DFS ($p = 0.518$), whilst the Viscum group demonstrated better OS ($p < 0.001$). Subgroup analyses revealed better OS for the Viscum group in tumour stages T1 ($p = 0.014$), T2 ($p = 0.012$), N0 ($p = 0.010$), N1 ($p = 0.001$), in patients with R0 resection ($p < 0.001$) and in patients who did not receive adjuvant chemotherapy or chemotherapies other than Folfirinox ($p < 0.001$).

Combination with other oncological therapies

Heidari SS, Ahmadi R, Siavashpour M, et al.: Mistletoe extract (Iscador®) in cancer patients undergoing chemotherapy for prostate and bladder tumors: a prospective observational study. *Avicenna J Phytomed* 2025.

The aim of this prospective observational study was to investigate the effects of the mistletoe extract Iscador, used as an add-on therapy, on health-related quality of life (HRQoL) and haematological toxicities in patients with metastatic prostate and bladder cancer. Patients were treated either with chemotherapy alone or in combination with Iscador. HRQoL was assessed at baseline and after each chemotherapy cycle. A total of 116 patients, including 59 with prostate cancer and 57 with bladder cancer, were enrolled. Analysis of the HRQoL symptom scales revealed a significant improvement in fatigue ($p = 0.014$), pain ($p = 0.023$), insomnia ($p = 0.017$) and diarrhoea ($p = 0.031$) in the mistletoe therapy group compared with the control group. In patients with bladder cancer, however, no significant differences in the HRQoL scales were observed between the two treatment groups. Similarly, there were no significant differences between the two groups with regard to haematological toxicities.

Case reports

Peter L: Möglichkeiten und Grenzen einer perioperativen Misteltherapie: Ein Fallbericht. *Der Merkurstab. Zeitschrift für Anthroposophische Medizin* 2025;78(4):243-246. DOI: <https://doi.org/10.14271/DMS-21942-DE>

This case report describes the clinical course of a patient with a deep-seated rectal carcinoma metastasised to the liver. Following transcutaneous CT-guided microwave ablation of the liver metastases and subsequent chemoradiotherapy, the patient underwent from July 2023 a subcutaneous mistletoe therapy with Iscador Qu c. Cu up to Series II, administered three times a week, and from October 2023 an intra- and peritumoral mistletoe therapy with abnobaVISCUM Fraxini in concentrations between 40 and 100 mg, as the patient refused rectal resection with creation of a permanent colostomy. In January 2024, despite mistletoe therapy, significant tumour progression was observed, and the patient again was advised to undergo curative surgery in terms of rectal resection with colostomy creation. After extensive reflection, the patient agreed to this. At the subsequent follow-up, conducted in May 2024, the patient was still tumour-free, but mistletoe therapy was no longer being used.

Reviews

Hong CE, Lyu SY: Mistletoe in cancer cell biology: recent advances. *Curr. Issues Mol. Biol.* 2025;47:672.

<https://doi.org/10.3390/cimb47080672>: This review article summarises the latest findings on the molecular mechanisms, immunomodulatory properties and clinical applications of mistletoe therapy in cancer treatment between 2020 and 2025. The finding that mistletoe extracts can induce immunogenic cell death (Weissenstein et al. 2025, see review of the mistletoe literature, first half of 2025) represents a paradigm shift in the understanding its anticancer effects. Thus, mistletoe extracts trigger endoplasmic reticulum (ER)

stress, leading to calreticulin exposure in 18–51% of cancer cells and a 7-fold increase in adenosine triphosphate (ATP) release. Also, it is accompanied by a 15.8% rise in the pro-inflammatory interleukin (IL)-6 and a 26.4% reduction in the immunosuppressive IL-10. In the clinical setting, real-world data studies involving more than 400 patients with non-small cell lung cancer showed that the combination of mistletoe therapy with PD-1/PD-L1 inhibitors doubled median overall survival. Furthermore, a phase I study at Johns Hopkins University confirmed the safety of intravenous mistletoe therapy at a dose of 600 mg, administered three times a week. Advanced analytical approaches including metabolomics, chronobiology, and machine learning are enabling precision medicine applications. These findings position mistletoe therapy as a scientifically validated part of integrative oncology.

Veterinary medicine

Beermann A, Hamza E, Reinhard S, et al: Selected microRNAs as biomarkers in sarcoid-affected horses under immunotherapy with a mistletoe extract. *Journal of Veterinary Diagnostic Investigation* 2025;1-8.

doi: 10.1177/10406387251362820: This case-control study investigated whether certain microRNAs (miRNAs) are potential prognostic markers for equine sarcoid (ES) disease. For this purpose, 45 affected and 15 healthy horses, which were comparable in breed, age and sex, were examined, and three miRNAs (eca-miR-127, eca-miR-379 and eca-miR-432) were analysed in horses treated either with mistletoe extract (*Viscum album* L.), administered subcutaneously or orally, or with placebo. The results showed that eca-miR-432 was expressed at significantly lower levels in affected horses than in healthy animals. However, none of the investigated miRNAs had prognostic significance or showed changes in their expression following treatment with mistletoe extract.

Kalil RFT, Viana Valle AC: *Viscum album* as a treatment for liver neoplasm in dogs. *Aracê* 2025;7:955-960.

<https://doi.org/10.56238/arev7n1-058>: In July 2024, an ultrasound scan revealed nodular changes in the liver of a 10-year-old French Bulldog, and cytology confirmed hepatocellular cancer. As the dog was not stable enough for surgery, the owner decided on treatment with homeopathic *Viscum album* in potencies D3, D6, D9, D12, D30, D2 and 200 CH, which were administered subcutaneously and applied to the VG14 acupuncture point to stimulate the immune system. The acupuncture treatments were continued at home by the owner – following prior instruction from the veterinarian – from Monday to Saturday over a period of 3 months. In October 2024, a follow-up ultrasound scan of the abdomen was carried out, during which no nodular structures were any longer visible in the liver, so the dog was classified as being in remission. No tumour cells were found during the follow-up appointments every three months either, meaning the patient remained in complete remission.