Review of mistletoe literature from the 1st half of 2025

Botany

Dołkin-Lewko A, Pulat E, Wojcik R, et al.: Distinctive traits of European mistletoe (*Viscum album spp. austriacum*) and its impact on host tree wood (*Pinus sylvestris*). Plants 2025;14:1489. https://doi.org/10.3390/plants14101489: In view of the increasing spread of European mistletoe (*Viscum album* L.) in Central European forests as a result of climate change, which can cause premature death of host trees, this study aimed to characterise the specific anatomical features of mistletoe and analyse the morpho-anatomical response of pine trees (*Pinus sylverstris*) to infestation. The results showed that mistletoe infection induce callose formation in the cell walls of pine tracheids, a defense mechanism that restricts water flow to the mistletoe. In addition, unique structural features of mistletoe were identified, including structural dimorphism with the inner system forming only vessels and parenchyma cells, in contrast to the outer system, composed of protective, ground, and conductive tissues, and which displays an uneven distribution of chlorophyll and starch grains along the plant axis. Futhermore, starch and chlorophyll were present in the parenchyma cells of the haustorium. Starch presence there may potentially enable internal photosynthesis, and the compounds formed after starch hydrolysis may facilitate water uptake from the hostʼs xylem sap.

Huang XY, Zhang YB, Scalon MC, et al.: Survival secrets of mistletoes: high drought tolerance in canopy habitats. Tree Physiol 2025;18. doi: 10.1093/treephys/tpaf071: The interaction between mistletoes and their host trees influences — as previously noted — both the physiological performance of the hosts and their climate change-induced mortality. The aim of this study was therefore to measure various functional traits of eight mistletoe-host species pairs that are directly related to hydraulics and drought resistance. Compared to their host trees, mistletoes were more drought tolerant, characterised by a more negative midday leaf water potential during the dry season, a lower turgor loss point, and a lower water potential at 12% loss of conductivity. Additional characteristic traits included higher Huber values, sapwood and vessel density, and lower leaf size, specific leaf area, vein density, and stomatal density. At the same time, mistletoes were less hydraulically efficient than their hosts, demonstrated by lower leaf- and sapwood-specific hydraulic conductivity and hydraulically weighted vessel diameter. Paradoxically, water-use efficiency was still lower in mistletoes. These findings highlight the response capacity of mistletoes, enabling them to adjust their hydraulic strategies based on host-specific conditions, providing insights into their drought tolerance mechanisms.

Ramm H: Was Misteln erfolgreicher macht. Obst & Garten 2025;1:18-20: In order to understand the dispersal dynamics of mistletoe and develop effective control strategies, a detailed knowledge of its biology is essential, particularly the conditions that allow it to establish and spread most successfully. Warming trends as a result of climate change indirectly promote the spread of mistletoe by expanding the habitat of mistletoe-dispersing bird species such as the blackcap (*Sylvia atricapilla*). This species has adapted its migration behavior to the milder winters over the past decades and prefers to spend the winter in regions with a sufficient supply of mistletoe berries. Due to their important role in seed dispersal, blackcaps are considered as a key factor for the mass distribution of mistletoe.

Teixeira-Costa L, Wiese L, Speck T, et al: Starting strong: development and biomechanics of the seedling-host interaction in European mistletoe (*Viscum album*). Journal of Experimental Botany 2025. https://doi.org/10.1093/jxb/eraf129: In the present study, the process of attachment of European mistletoe (*Viscum album* L.) to its host tree at the seedling stage was investigated. Using a combination of germination experiments, microtomography, histological analysis, and biomechanical tests, this work investigates the role of the three key attachment structures involved in this process: the seed coat, hypocotyl, and holdfast. The viscin layer, a sticky coating on the seed, provides initial adhesion before the growing hypocotyl expands towards the host surface, where it flattens and forms a holdfast that strengthens adhesion and aids tissue penetration. Tensile tests revealed that these three attachment structures withstand similar forces in the early stages, considerably higher than the weight of the seedling. Within a few months, the endophytic system ‚interlockes' with the

host‘s bark, forming a stable connection that not only transports water but also increased the mechanical strength of the structure.

Tokarieva O, Bilonozhko Y, Heinze B, et al.: Mistletoe distribution in some cities and forests of Austria. Austrian Journal of Forest Science 2025;142:39-60: This article also focuses on the fact that mistletoe species are part of the biodiversity of cities, forests and other tree-covered areas, but as a hemiparasite they are also a possible threat to trees, in particular in view of increasing drought stress as a consequence of climate change. The distribution of mistletoe largely depends on the woody host species and their growing density. Therefore the tree cadasters of the Austrian cities Vienna and Graz were analysed, as well as the data of the Austrian National Forest lnventory around Vienna. Field–work and visual assessments of the trees were conducted to determine the prevalence of mistletoe infection. The most common host trees for mistletoe in Vienna and Graz (*Acer*, *Tilia*, *Populus*) and Austrian forests (*Pinus*, *Quercus*) were identified. The results allow to predict the spread of particular mistletoe species to adjacent areas and to identify mistletoe-resistant trees, that remain healthy and live longer and may help to mitigate the effects of climate change.

Zaemdzhikova G, Glogov P, Bozhilova M, Kechev M: First record of *Drosophila suzukii* (Diptera: Drosophilidae) on the fruits of Viscum album spp. album in Bulgaria. Historia Naturalis Bulgarica 2025;47(6):137-144: The invasive fly species *Drosophiia suzukii* (Matsumura) was recorded for the first time as a pathogen on the fruit of European mistletoe (*Viscum album ssp. album*) in Bulgaria. Fruits were collected there in April 2023 at seven locations. At three of these locations, the mistletoe was found on black locust tree (*Robinia pseudoacacia* L.) and at four locations on Canadian poplar (*Populus x canadensis*). Analysis showed that the infestation rate of mistletoe fruits by *Drosophila suzukii* was influenced by the host tree of mistletoe and is approximately ten times higher on black locust tree than in Canadian poplar.

Biochemistry/Chemisty

Megalinska A, Bilyk Zh, Panchuk O, et al.: Comparative analysis of *Viscum album* L. antibacterial, hemagglutinating, cytostatic activity depending on the host plants. Fitoterapiia. Chasopys – Phyto–therapy Journal 2025;1,142–150, https://doi.org/10.32782/2522-9680-2025-1-142: The aim of this study was to investigate the antibacterial, cytostatic, and hematopoietic activities of aqueous total extracts and lectin-enriched extracts of the white-berried mistletoe in relation to the host plant, as well as the litholytic activity of a lectin-enriched extract from rowan mistletoe. The results showed an antibacterial activity depending on the host tree with the highest activity in the extract obtained from rowan mistletoe. Lectin-enriched extracts of all tested variants showed a hemagglutinating activity, with hemagglutination titers also varying according to the host tree species; hemagglutina–ting activity was highest for blood groups A and B. Cytostatic activity was found in all samples, with extracts obtaines from poplar and maple being the most cytotoxic. The lectin-enriched extract from rowan mistletoe showed *in vitro* litholytic activity against oxalates and urates.

Processing

Coteli E: Utilization of mistletoe for the synthesis of copper nanoparticles and its clinical applica–tions. European Journal of Chemistry 2025;16:53-63. bttps: //dx.doLorg/10.5155/eurjchem. 16 1 53-63.2629: In this study, the synthesis, analytical and *in vitro* clinical application (anti-oxidant capa–city and antibacterial activity) of copper nanoparticles (CuNPs) prepared according to the principle of “green synthesis“ using aqueous extracts from the leaves, fruits and twigs of pine mistletoe (*Viscum album ssp. austriacum*) and the metal salt copper sulfate ($CuS0_4$) were investigated. It was found that CuNPs obtained from aqueous fruit extracts were smaller in size and present at higher concentra–tions than those derived from leaves and twigs, while the shape was sherical in all extracts. It was also observed that the CuPNs in the three extracts, which contain different secondary plant metabo–lites ,were formed by various functional groups. Additionally, the CuPNs obtained from the fruit extract showed therapeutic potential in the treatment of free radical-induced diseases. Furthermore, the CuPNs synthesised from all three extracts showed strong antibacterial activity against pathogens,

indicating their potential as antimicrobial agents for applications in the food, textile and pharma–ceutical industries.

Coteli E: Antioxidant, antidiabetic, and antimicrobial potentials of silver nanoparticles synthesized from *Viscum album*. Journal of Agricultural Sciences (Torim Bilimleri Oergisi) 2025;31(2):373-391. doi: 10.15832/ankutbd.1553350: In this *in vitro* study, silver nanoparticles (AgNPs) were produced for the first time from the aqueous extracts of leaves, fruits and twigs of pine mistletoe (*Viscum album ssp. austriacum*) using the "green synthesis" principle with the addition of silver nitrate ($AgNO_3$) and the antioxidant, antidiabetic and antimicrobial potential of these nanoparticles was determined The AgNPs obtained from all three extracts had a spherical shape and the AgNPs obtained from the extract of the fruit part were smaller than the AgNPs obtained from the other plant parts. In addition, it was found that the AgNPs from the leaf, fruit and branch extracts are present in a high concentration and a pure crystalline form (74 to 83 percent) and their structure size is always in the nanometer range. It was also shown that the AgNPs from all three plant part extracts, but especially from the fruit extract, have very good antioxidant, antidiabetic and antimicrobial properties.

Woiniak M, Baranowska M, Waskiewicz A, Cofta G: Activity of *Viscum album* L. extract against wood-rot fungi and its potential. Wood Material Science & Enegeneering 2025. https://doi.org/10.1080/17480272.2025.2479230: To investigate the antifungal efficacy of *Viscum album* extracts in the wood industry, extracts from the bushes (without fruit) of the three subspecies *Viscum album ssp. album* (poplar), *Viscum album ssp. austriacum* (pine) and *Viscum album ssp. abietis* (silver fir) were prepared. All extracts tested at a concentration of 100 mg/mL completely inhibited the growth of all fungal species. Fungi causing brown rot, such as *Coniophora puteana*, were inhibited more strongly than those causing white rot (*Trametes versicolor*). The treated wood also showed lower mass losses caused by rot fungi compared to the untreated wood. The content of phenolic com–pounds, which contribute significantly to the antifungal effect, was depended on the mistletoe sub–species, but phenolic acids always dominated. The results indicate that the use of mistletoe extracts can be a sustainable source of antifungal agents, particularly to improve resistance to *C. puteana* and *T. versicolor*.

Preclinic

Cell cultures

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;49:289-314: In this research, the tumour-suppressing capabilities of water-extracted Korean mistletoe (*Viscum album* var. *coloratum*) and its purified lectin component (*V. album* var. *coloratum* agglutinin, VCA) using two distinct mouse melanoma models B16BL6 and B16F10 cell lines were investigated. The aqueous extract showed a dose-dependent cytotoxicity, which was stronger for VCA. Both agents induced substantial apoptosis with a significant progression from early to late apoptotic stages.

Weissenstein U, Tschumi S, Leonhard B, Baumgartner S: A fermented Mistletoe (*Viscum album* L.) extract elicits markers characteristic for immunogenic cell death driven by endoplasmic reticulum stress *in vitro*. BMC Complementary Medicine and Therapies 2025;25:175. https://doi.org/10.1186/s12906-025-04909-8. To investigate the induction of immunogenic cell death (ICD) in cancer cell lines by mistletoe extracts, three human breast cancer cell lines (SKBR3, MDA-MB-231, MCF-7) and one murine melanoma cell line (B16F10) were incubated for 24 or 48 hours with different doses of the aqueous, fermented *Viscum album* extract Iscador Qu (VAE). The ICD-activating paclitaxel and tunicamycin served as positive controls. To determine whether VAE triggers ribotoxic stress, the expression of endoplasmic reticulum stress regulators (p-eIF2a, ATF4 and CHOP), the expression of damage-associated molecular patterns (DAMPs) such as calreticulin (CRT), Hsp70, Hsp90, HMGB1 and ATP, apoptosis and the induction of mitochondrial reactive oxygen species (ROS) were investi–gated. In all cell lines, the effects of VAE were concentration-dependent and resulted in a significant increase in the exposure of three DAMPs (CRT, Hsp70, and Hsp90) on the surface of early apoptotic

cells. Furthermore, VAE induced phosphorylation of the ER stress protein eIF2α in all tested cancer cell lines and increased calreticulin exposure on the surface of pre-apoptotic SKBR3 breast cancer cells and B16F10 mouse melanoma cells. The ER stress protein CHOP was significantly induced by VAE at a concentration of 400 µg/mL only in the triple-negative breast cancer cell line MDA-MB-231. In the breast cancer cell line SKBR3, VAE in the concentration of 20 and 30 µg/mL significantly reduced the expression of the ER stress protein ATF4. In addition, VAE increased mitochondrial ROS production and ATP release. HMGB1 release was not induced by VAE. This *in vitro* study demonstrated for the first time the potential of a mistletoe extract to induce surrogate markers of immunogenic cancer cell death.

Yang YJ, Kim MJ, Heo JW, et al.: Korean mistletoe (*Viscum album var. coloratum*) ethanol extracts enhance intestinal barrier function and alleviate inflammation. Antioxidants 2025;14:370. https://doi.org/10.3390/antiox14030370: This study aims to evaluate the effects and potential molecular mechanisms of an ethanolic extract from Korean mistletoe (*Viscum album var. coloratum*), focusing on intestinal barrier function and tight junctions in an interleukin-6-induced Caco-2 cell monolayer model and a dextran sodium sulfate induced ulcerative colitis mouse model. The extract was non-cytotoxic in Caco-2 cells, demonstrated strong antioxidant activity, alleviated significant barrier dysfunction and protected tight junction proteins *in vitro*. Furthermore, the extract alleviated clinical symptoms and histopathological damage, upregulated tight junction proteines, and suppressed the inflammatory cytokines *in vivo*.

Murine test systems

Eimam GD, El-Dardiry MA, Badawi M, et al: Effect of *Viscum album* extract on the angiogenic process during the muscular phase of experimental trichinellosis. Egyptian Academic Journal of Biological Sciences, E. Medical Entomology & Parasitology 2025;17:13-22: Albendazole is the current treatment for trichinosis. However, there are uncertainties about its efficacy in removing the encapsulated phases. Therefore, this study investigated the efficacy of a *Viscum album* extract (VA, not a comercial product) as a potential substitute for the treatment of encapsulated larvae in striated muscle, both in combination with albendazole and as monotherapy. For this, infected male CD1 Swiss Albino mice were divided into four groups: Group G1 was non-treated to serve as a control, G2 was treated with albendazole, G3 with VA, and G4 with a combination of AV and albendazole. Among others, assessment was conducted by counting the number of larvae. The group treated with combination therapy had the lowest number of larvae and achieved the highest reduction rate at 93%. VA also showed a pronounced antiangiogenic effect. In addition, the inflammatory response was significantly reduced in the groups treated with VA. The results indicate that VA – especially in combination with albendazole – is a potential therapeutic agent for the treatment of encapsulated larval stages, as VA deprives the larvae of their food source and positively modulated the inflammatory response in favour of the host.

Clinic

Combination with oncological therapies

Thronicke A, Grabowski P, Roos J, et al.: Combined immune checkpoint blockade and Helixor® therapy in oncology: real-world tolerability and subgroup survival (ESMO GROW). Int. J. Mol. Sci. 2025;26:3669. https://doi.org/10.3390/ijms26083669: In this real-world data study, 405 patients, predominantly with non-small cell lung cancer, who were enrolled from the Oncology Network registry in accordance with the ESMO-GROW guidelines, received either PD-1/PD-L1 inhibitors as monotherapy (344 patients) or in combination with the mistletoe extract Helixor (61 patients). The primary and secondary objectives were tolerability and overall survival. The treatment discontinuation rate associated with adverse side effects was lower in the combination group, and the survival rate was significantly higher compared to the group receiving PD-1/PD-L1 therapy alone, particularly in female patients.

Case reports

Kaesbach S, Hintze A, Engelbrecht S, et al.: ER+ HER2- invasive breast cancer: tumor remission following Viscum album extract/influenza vaccine treatment – a report of 2 cases. Complement Med Res 2025;32:176–181. DOI: 10.1159/000544082: The first case describes a 60-year-old female patient with a local recurrence of hormone receptor-positive (HR+) Her2/neu-negative (HER2-) breast cancer who declined all conventional therapies. She was treated subcutaneously and intra–tumorally with *Viscum album* extracts (VAE) and influenza vaccines (IV) and concurrent with VAE-induced hyperthermia. After five months, almost complete remission was observed, which persisted for three years. The second case concerns a 57-year-old female patient who suffered from right sided metastatic HR+ HER2- breast cancer and also declined conventional treatment. The patient was trea–ted with 17 monthly VAE-induced hyperthermia cycles, eight of which included intratumoral VAE and four of these eight involved intratumoral IV administration. Almost 2 years after treatment start, a follow-up showed marked morphological and metabolic reduction of the breast tumour on the right side, stable local lymph node metastases in the right axilla, complete remission of pulmonary metas–tases, the single bone metastasis, and the majority of hilomediastinal lymph node metastases but a new metabolic highly active left adrenal lesion. Since then, the patient has declined further radio–logical follow-up examinations, but remains in a good condition and shows no clinical signs of disease progression.

Case series

Gardin N, Gardin-Machado B: Mistletoe (*Viscum album* L.) for human papillomavirus: a seven-case series. Phytomedicine Plus 2025;5(2): 00805. https://doi.org/10.1016/j.phyplu.2025.100805: This case series describes the clinical course of seven female patients with HPV treated with mistletoe extracts. In four patients, the persistence of HPV infection was six months or longer, in three patients, the diagnosis was recent. All patients received Viscum mali ointment for topical (vaginal) application, and the six patients with high-risk HPV or cervical intraepithelial neoplasia also received subcutaneous injections of Helixor or Iscador in individual doses two to three times a week. In addi–tion, Calendula officinalis was used as vaginal ovules for inflammation in the genital area and Thuja occidentalis ointment for verrucous lesions. Depending on the severity, treatment lasted between 4 and 16 weeks. All medications were well tolerated, with only mild skin reactions occurring at the injection site of the mistletoe preparations. After treatment, six of the seven patients had negative hybrid capture tests for HPV. One of these six patients required a repeat course of treatment, after which the HPV hybrid capture test turned negative. In one patient, treatment failed to eradicate HPV. The findings suggest that mistletoe extracts have therapeutic potential in genital HPV infections.

Non-oncological indications

Grah C, Gatov I, Oei SL, et al.: New therapy for chronic sarcoidosis with *Viscum album* L. and Ferrum chloratum preparations: results of a retrospective survey. Journal of Evidence-Based Integrative Medicine 2025;30:1-9. doi: 10.1177/2515690X251345931: To assess the efficacy of a multi-component therapy developed in the Department of Pneumology at Gemeinschaftskranken–haus Havelhöhe based on *Viscum album* extracts (Iscucin Salicis) and Ferrum chloratum – applied according to the Havelhöhe sarcoidosis protocol (HSP) – the course of the disease was examined in a total of 956 sarcoidosis patients treated with this therapy regimen. Complete data sets were avai–lable for 124 patients, which enabled an evaluation of clinical efficacy during a mean follow-up period of 23 months. In this sub-cohort, the response rate with regard to pulmonary manifestations was 69%. At the start of the study, 81 of the 124 patients (65%) reported clinically relevant fatigue, which improved significantly in 48 patients (59%) during HSP therapy. At the last follow-up visit, 103 patients (83%) did not need glucocorticosteroids or other medications and were receiving only HSP. Pharmacovigilant monitoring demonstrated a safe HSP therapeutic profile, with only 10 (8%) subjects experiencing grade 1 adverse events.

Veterinary medicine

Cakiroglu H, Deveci Ozkan A, Erman G, et al.: Comparative analysis of IscM and IscQu in feline oral squamous cell carcinoma treatment: cytotoxic and apoptotic insights. Front. Vet. Sci. 2025;12. doi: 10.3389/fvets.2025.1549550: Feline oral squamous cell carcinomas are the most common malignant oral tumours in cats, which are characterised by invasive and aggressive behaviour regardless of their location. For the study, primary cultures of three of these squamous cell lines were used from surgi–cal tissue samples removed from cats. The cytotoxic and apoptotic effects of Iscador M and Qu were evaluated using cell viability assays. Both Iscador M and Iscador Qu induced apoptotic cell death and promoted cell cycle arrest in all three cell lines tested. Iscador Qu showed a relatively stronger pro-apoptotic effect compared to Iscador M, although no significant differences were observed among the cell lines.

Viana Valle AC, Viana Valle MLP: Fibrosarcoma in a young dog treated with injectable *Viscum album* therapy: a case report. Pubvet 2025. https://doi.org/10.31533/pubvet.v19no3e1747: This case report presents a case of fibrosarcoma located in the esophagus, diagnosed in a young dog, potentially linked to a chronic inflammatory response triggered by a parasitic infestation. The dog was treated with a homeopathic *Viscum album* preparation in D3 three times a week for 60 days subcutaneously as monotherapy, with the priority of preserving the dog's quality of life. After six months of treatment, the dog exhibited a clinical course unlike the typically expected for this con–dition, with no evidence of tumour growth. Similarly, there were no significant side effects. The the–rapy was therefore assessed as safe and easily practicable, especially in young animals.

Viana Valle AC: Integrative treatment of mammary neoplasm in a cat induced by injectable hormonal contraceptive. Integrative Journal of Veterinary Biosciences 2025;9(1):1-4: Mammary neoplasms are among the most common malignancies in cats, which in some cases may be asso–ciated with the prolonged use of injectable hormonal contraceptives. This case study reports on a cat diagnosed with mammary carcinoma, potentially induced by the administration of hormonal contra–ceptives. Due to financial constraints, the recommended ovariohysterectomy, mastectomy, and chemotherapy were not performed. Instead, the cat received the homeopathic injection preparation *Viscum album* D3 as the primary therapeutic agent, which was administered subcutaneously every other day for 60 days. The treatment protocol resulted in a marked reduction in tumour volume, improved overall patient condition, and no observed adverse effects.