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Review articles

European and Oriental mistletoe: From mythology to contemporary integrative cancer care

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Abstract

Medical uses of European mistletoe (*Viscum album* L.) and Oriental mistletoe (*Viscum cruciatum* Sieb.) have been common since early times, included cancer therapy. The two mistletoes are mentioned in Classical sources (e.g. Dioscorides and Pliny) and by medieval European practitioners (e.g. Paracelsus) and Arab physicians (e.g. al-Kindi, al-Ghafiqi, and Ibn al-Baytar). These plants are also known as symbols of love and feature in legends throughout ancient and modern Europe. Contemporary traditional medicine uses of mistletoes are found in Lebanon, Israel, Egypt, Turkey, and Pakistan.

In 1916, Rudolf Steiner mentioned for the first time mistletoe extracts as possible for cancer therapy. *V. album* has gained notable attention due to its central role as leading remedy in cancer care in Anthroposophic medicine.

Contrary to the abundance of studies on *V. album*, there is lack of clinical trials concerning anti-cancer activities of *V. cruciatum*. We conclude a discrepancy between the paucity of research data concerning *V. cruciatum* and its attributed efficacy as suggested in historical and ethno-botanical literature. Thus, based on the significant findings achieved in *V. album* research, we recommend targeting research on the therapeutic potential of *V. cruciatum* in cancer care.

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Keywords: *Viscum album*; *Viscum cruciatum*; Oncology; Cancer; Islamic medicine; Anthroposophic medicine

Prologue

Viscum album (known as mistletoe) is an important medicinal herb rooted in traditional Middle Eastern and European pharmacopeia. Its use at a modern oncology center, as illustrated by Dr. N's integrated chemotherapy and *Viscum* treatment, is not self-evident and illumines the major change that has occurred in the last three decades regarding herbal medicine: progression from anecdotal myth and documented historical accounts to contemporary evidence-based modern care. Our article focuses on historical and ethno-botanical knowledge of two mistletoes that grow in southern and central Europe (European mistletoe, *V. album* L.) and in the Middle East (Oriental mistletoe, *Viscum cruciatum* Sieb.). Our purpose is to encourage open-mindedness

to the potential of traditional herbs in modern cancer care and research.

Botanical perspective

Mistletoe is a semi-parasitic evergreen shrub, with 70 known kinds (Family Viscaceae [Loranthaceae]) in the world, most of them tropical [1]. Mistletoes are widespread around the Mediterranean basin.

V. album L. (European [common, white-berry] mistletoe) is the most common *Viscum* species used in medicine. It is an evergreen parasitic plant, growing on branches of trees where it forms pendant bushes. It is found on various deciduous trees, mainly ash, hawthorn, lime, larch, cedar of Lebanon, and rarely oak or pear. It grows throughout southern and central Europe and eastward to the Caucasus [2]. The genus name is the Latin name of the plant, as it was widely known in Europe; it also

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means birdlime [1]. *V. cruciatum* Sieb. Ex Boiss. (Oriental [red-berry] mistletoe) is a perennial, dioecious hemi-parasitic plant with pistillate flowers that produces red berries. It grows sporadically around the Mediterranean (Israel, Jordan, N. Africa, southern Portugal, south-west Spain, Australia, and Asia). Its hosts are in the first place olive, but also almond, lemon, buckthorn, azerolier, and blackberry [3].

Historical perspective

The medical uses of the mistletoes are common since early times. In Classical times Dioscorides (1st century CE) described the *Ixos*, which was identified with white mistletoe (*V. album*), and listed its medical uses: to treat swellings, to soothe, to eliminate pus, to cure stomach ulcers, to treat problems of the spleen, and to remove stones from the urinary tract [4]. Pliny (1st century CE) describes mistletoe and the methods of making birdlime out of it, as well as the superstitions about it of the Gauls, including its worship on the fifth day of the moon (the day their month and year begin) [5]. Paracelsus (15th century) and Matthioli (16th century) mention mistletoe for the treatment of epilepsy [6].

The tradition of “kissing under the mistletoe” originated in Scandinavian legend. Bakder, the god of peace, was killed by an arrow made of mistletoe and was resurrected by the other deities. Common mistletoe was then entrusted to the goddess of love, who established it as a symbol of love; it was customary that anyone passing beneath it should receive a kiss [1]. A festival in honour of the mistletoe, called Guilanlen, was celebrated in France as late as the 16th century; in England the plant is still hung in the room at Christmas [6].

Common mistletoe was deemed sacred in pre-Christian Europe (Gaul, Britain and Ireland). It was considered as Druidic herb, associated with welcoming the New Year (the original Golden Bough). It was cut only from oak trees by Druids in white robes at a particular phase of the moon, using golden sickle (along with the sacrifice of victims and the fasting of devotees) [1,6]. Thus obtained, the plant was considered a cure-all, a charm against disaster and the emblem of fertility. As such it was a special object of worship among ancient Britons, who named it with various superlatives, some of which exist to the present day in Welsh [6].

In German folklore mistletoe bestows the power to see ghosts and make them speak. In traditional European medicine it was believed that the medicinal uses of the common mistletoe varied according to the host tree; the Druids held mistletoe on oak supreme (probably compounds that effect protein synthesis, and benefit the immune and circulation systems and the heart) [1].

Common mistletoe (*V. album*) has a pungent, bitter-sweet taste, and is a warming herb that lowers blood pressure, stimulates the immune system, slows heart beat, relaxes spasms, and has sedative, diuretic, and anti-cancer effects. The plant is used internally, for mild hypertension, hardening of the arteries, nervous tachycardia, nervous tension, and cancer (mainly of lung and ovaries). Externally the common mistletoe is used for arthritis, rheumatism, chilblains, leg ulcers, and varicose veins. It is also used for the treatment of mild hypertension (with *Cartaegus*

laevigata and *Mellisa officinalis*) and hardening of the arteries (with *Ginkgo biloba* and *Vinca major*) [1].

The medicinal uses of mistletoe in the middle ages

Many authors of Arabic medical books mention mistletoe (*bantumah*, *dibq*, *shagar ed dibq*, *zarq et tayr* in Arabic) identified in various dictionaries as *V. album* [7–10]. But this plant does not grow in the Middle East. We suggest that the plant used by the medieval Middle Eastern physicians, herbalists and pharmacologists was the local *V. cruciatum*; in those times they often could not differentiate species of the same genus, so many names were collective [11].

These sources also describe mistletoe’s nature and various uses, including medicinal. It was used as laxative and a solvent of corrupt humours, to cleanse the system of adust bile and phlegm (with walnuts and castor oil) and remove obstructions, and as a remedy for lumbago and piles. Applied externally, it was used to promote suppuration, or cause dispersion of tumours or enlargements [6].

According to al-Kindi (9th-century Iraqi physician), the mistletoe resin was a medication for mouth cancer, tooth decay, and stomach ulcers [10].

al-Ghafiqi (12th-century Andalusian physician) described the use of the plant to knit broken bones (drunk with Armenian clay); its decoction prevented cough. This author noted that it was a bitter and constricting drug [12].

Ibn al-Baytar (13th-century Spanish physician, specialist in medicinal plants of the Levant) notes in his book on medicinal substances that the plant grew in Andalusia and in the Levant (al-Sham region), especially in the area of Shechem (“Nablus”), where they customarily fried the fruit in olive oil to improve its colour. Ibn al-Baytar also claimed that the plant grew mainly on olive, almond, and pear trees. He cited various physicians who listed the medical properties and uses of the plant; they included knitting broken bones and treating cracks in the skin, torn muscles, cough (boiled with figs), and skin diseases. In his view the plant was cold, constricting, and dry [13,14].

The Jewish physician R. Nathan Ben Yoel Falaqera (13th century, Spain), wrote in his book *Sori Ha-Guf* that the fruit is black and as small as peas. It is a hot and dry drug, used to treat the joints and bad nails [15].

According to Daud al-Antaki (16th-century Turkish physician) and known physicians that he mentioned, mistletoe is a cold, dry and astringent drug, and rather bitter. It healed damaged muscles, treated blood spitting, opened obstructions, cleansed the mind and the stomach, knitted fractures, cured cough and skin diseases, and dried haemorrhoids [16].

By the 18th century the medical use of *V. album* had become widespread in Europe and was associated with superstitious and magical practices [17–20]. In the 19th century several physicians in Europe and the USA started to study the plant and its medicinal uses with modern tools, and thereafter used it in various forms to treat, among other things, menorrhagia and post-partum haemorrhage, and as a substitute for digitalis. The active materials of

the plant's berries and leaves were studied from the 19th century as well [6].

Ethno-botanical research

The berries of *V. cruciatum* are edible in the Levant, and are sometimes soaked in olive oil to heighten their red colour [21]. In traditional medicine in Israel *V. cruciatum* was commonly used to treat constipation in young children and adults (fleshy fruits). All part of the plants are used against general pain, backache, and arthritis. The main technique is a bath to which the water of boiled leaves and fruits is added. Decoction made from the leaves is successfully used for the treatment of intestinal cancer [22].

In traditional medicine in Egypt the plant is used for the treatment of epilepsy, arteriosclerosis, and diseases of cardiac arteries, and as a hypotensive [23].

In traditional medicine in Lebanon the berries are soaked or boiled in water and used as an antispasmodic, to stop internal haemorrhage, to lower blood pressure, and to check dysmenorrhoea. According to priests and specialists, powdered leaves are used with caution for epilepsy, nervous spasms, bloody dysentery and palsy. Macerated fresh leaves (with honey) are used for nervousness and convalescence [24]. *V. cruciatum* was also recorded as used against hysterical psychosis [24].

According to the well known British herbalist Culpeper, both leaves and berries of the "mistletoe" (bird-lime) were hot and dry. It "mollifies hard knots, tumours"; mixed with wax and resin it "mollifies the hardness of the spleen, and helps old ulcers and sores". Mixed with sanderic and orpiment, it "helps to draw off foul nails". Made into powder and drunk, it is good for "falling-sickness". Juice brewed out of its wood was used to treat ear inflammation. It was also use to treat nervous diseases such as "convulsive fist, palsy, and vertigo." The author concludes his entry: "The bird-lime which is made of the berries of Mistletoe is a powerful attractive, and is good to ripen hard tumours and swellings" [25].

V. album is used extensively in Turkish traditional medicine, and is sold in shops specializing in traditional *materia medica*. Its main medicinal uses are for pains, allergy, bedwetting children, hypotension, tuberculosis, stomach and duodenal ulcers; as a prophylactic in arteriosclerosis, and for stomachache and wounds [26].

V. album is known as medicinal plant in Pakistan [27]. In India, dried berries are sold in the markets and bazaars. A few physicians practising in India in the 19th century investigated the content of local mistletoe growing on *Nux vomica* trees, and reported that it contained poisonous properties similar to those of the tree on which the plant grows (strychnine in the case of *Nux vomica*). Some physicians even used leaves of such mistletoe (growing on that tree) as a substitute for *Nux vomica* [6].

Mistletoe and cancer treatment in Anthroposophic medicine

In 1908 Rudolf Steiner (1861–1925, founder of Anthroposophic sciences), mentioned mistletoe extracts as a possibility

for cancer therapy [28]. Ita Wegman (1876–1943), one of the first Anthroposophic physicians, took up his proposal and with a pharmacist in Zürich developed the first mistletoe medication, *Iscar*, which was renamed to *Iscador* in 1926 [29]. From 1920 until his death, Rudolf Steiner described more precisely the connection of cancer and mistletoe, and shared his ideas with doctors at various conferences and in clinical consultations, mostly in the Klinisch-Therapeutisches Institut, founded by Ita Wegman in Arlesheim near Basel. In 1935 a society for cancer research (Verein für Krebsforschung) was founded and researchers, including Werner Kaelin and Alexander Leroi, worked on the improvement of the various *Iscador* medications. Based on this society's activity, the Hiscia Institute was founded in 1949 for practical research. It was followed by the formation the Lukas Klinik, which to this day is a specialist oncological-Anthroposophic clinic [30].

In Steiner's days the active ingredients of the viscum (e.g., lectines and viscotoxines) and its immunological effects were not yet known. Steiner's unconventional way of discovering the oncological indication of mistletoe is intriguing: what was his vision of this mysterious half-parasite, seen down the centuries in so many exotic ways as a healing plant? Steiner saw parallels between the behaviour of cancer in the human body and the behaviour of the mistletoe living on trees. According to Anthroposophy, mistletoe withdraws from the normal laws of plant growth: it does not grow in the earth but on trees; it flowers and fruits not in summer but in winter. Likewise, cancer cells do not obey the normal rules of growth. But most mistletoes can live in balance with the trees, whereas cancer cells exhaust and destroy the human body. Steiner described the mistletoe, if prepared in a special way, as a plant which can help the human body to rediscover the balance, and even stimulate its own healing forces to overcome the disease of cancer. He found the correspondence of mistletoe and cancer, so to speak, in the image, on a spiritual level. Steiner's perspective on cancer treatment with mistletoe inspired the first Anthroposophic doctors to develop and improve mistletoe therapy. It is remarkable that the amount of recent research on mistletoe therapy confirms many of the original considerations. For example, the statement, in anthroposophic terms, that mistletoe helps the 'I-organisation' (the unconscious, body-orientated part of our spirit) not to be fixed in the physical body, but to be actively engaged in the living and healing forces of the body, is reflected in modern knowledge of psycho-immuno-oncology.

Mistletoe therapy has become the best-known Anthroposophic therapy, and in German-speaking central Europe it is now one of the most commonly prescribed complementary therapies for cancer [31]. In 2007, 9.2 million daily doses were sold in Germany, amounting to 22.5% of all chemotherapy agents that year [32]. Other Anthroposophic viscum preparations besides *Iscador* are *Abnoba viscum*, *Iscusin*, and *Helixor*.

Discussion and conclusions

The two mistletoes discussed in this paper share significant references in medical history and ethno-botanic literature. In modern times *V. album* has won notable attention due to its

central role as leading remedy in cancer care in Anthroposophic medicine. Subsequent *in vitro* and clinical studies followed *V. album*'s use in Anthroposophic clinics in central and western Europe. Laboratory studies indicate that *V. album* induces cancer cell apoptosis [33], cytotoxic activity [34], DNA repair in peripheral blood mononuclear cells [35], angiogenesis inhibition [36], antiproliferative effects in cancer cell lines [37], maturation and activation of human dendritic cells [38], and stimulation of GM-CSF, IL-5 and IFN γ production [39]. Clinical trials indicate that *V. album* may improve quality of life of patients with breast cancer [40,41] and reduce side effects of chemotherapy [42] and radiotherapy. Preliminary studies suggest that *V. album* may also improve survival of patients with malignancies of breast [43], cervix [44], ovary [45], uterus [46], and colon [47], and of those with melanoma [48], and also lower recurrence of superficial bladder cancer [49]. A systematic review of 37 clinical studies on mistletoe therapy showed a structural improvement of quality of life; significantly fewer adverse effects from chemotherapy, radiation or surgery, tumor remission, and survival benefit, were shown in eight of 17 studies [50]. Ostermann et al. reported of pooled analysis of clinical studies and suggested that adjuvant treatment viscum treatment is associated with a better survival of cancer patients [51]. Nevertheless, a Cochrane Database systematic review published in 2008 by Horneber et al. concluded that the evidence from randomized controlled trials to support the impact of *V. album* on survival is weak and that more high quality, independent clinical research is needed to assess viscum's safety and effectiveness [52].

Compared with the abundant studies on *V. album*, clinical trials on anti-cancer activities of *V. cruciatum* are lacking. Two *in vitro* studies demonstrate the herb's cytotoxic activity against larynx cancer [53] and melanoma, renal and breast cancer cell lines [54]. We determine a discrepancy between the paucity of research data on *V. cruciatum* and its efficacy as suggested in historical and ethno-botanical literature. Considering the significant findings achieved in *V. album* research, we recommend directing research at the therapeutic potential of *V. cruciatum* in cancer care.

Conflict of interest

We hereby state that there is no conflict of interest.

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