

Unconventional therapies for cancer: 3. Iscador

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This article, on Iscador, is third in the series that reviews the evidence for the safety and effectiveness of 6 unconventional therapies commonly used by Canadian cancer patients. The purpose and methodology of the review of these therapies appear in part 1 (CMAJ 1998[7]:897-902). Annotated bibliographies providing more detailed references are available in print from the Canadian Breast Cancer Research Initiative (CBCRI; address appears at end of article). The reference lists and the lay summaries of the findings (published in 1997) can be found on the CBCRI's Web site (www.breast.cancer.ca). The following article adapts the lay summary of information on Iscador for clinicians and provides references for the key findings. [Copies of this and other articles in the series can be found on CMAJ's Web site (www.cma.ca/cmaj/series/therapy.htm).]

Iscador is the trade name of the most commonly available brand of an extract of *Viscum album*, a European species of mistletoe, which differs from the North American species. Mistletoe is a semiparasitic plant that lives symbiotically with several tree species, including oak, pine, elm and apple. Considered sacred in ancient times, it has been used for centuries in Europe to treat a variety of acute and chronic health conditions.

The use of mistletoe as a cancer therapy was popularized in the early 20th century by Rudolf Steiner, PhD (1861–1925). Steiner founded anthroposophy, a conceptual framework that blends spiritual and scientific principles and applies them to healing practices with a focus on cancer treatment. He theorized that the human body is subject to various forces, some of which result in cell growth and multiplication (“lower organizing forces”) and some of which control and organize cell growth to form tissues and organs (“higher organizing forces”). Steiner believed that the balance between these forces determined an individual’s susceptibility to cancer, with a serious imbalance promoting the development of cancer. He considered mistletoe to have a number of characteristics that suggested it could resist natural forces, and he therefore proposed that mistletoe preparations would stimulate the “higher organizing forces” that he believed were deficient in cancer patients.

Today, mistletoe preparations are principally advocated by physicians practising in special anthroposophic medical clinics in Switzerland and Germany. These clinics have been operating since the 1920s and have treated more than 80 000 patients. They offer a variety of other components in conjunction with Iscador, such as dietary, artistic and movement therapies, that are also designed to promote the “higher organizing forces.” In several European countries and in South Africa, Iscador is registered for commercial purposes and can be legally prescribed. It is not commonly used in North America but can be obtained from the manufacturer (Weleda AG) in Germany or Switzerland.

Although there have been few claims that Iscador reduces tumour size, proponents believe that it stimulates the immune system, promotes the reversion of cancerous cells to more differentiated forms, improves general well-being and may improve survival, especially in patients with cancer of the cervix, ovary, breast, stomach, colon and lung.¹ Proponents also recommend its use in patients who have certain conditions that place them at increased risk of cancer, such as



Education

Éducation

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The Canadian Breast Cancer Research Initiative does not endorse the use of any particular unconventional therapy. It urges patients to evaluate all evidence carefully and to consult their caregiver in order to make thoughtful and fully informed personal decisions.

This article has been peer reviewed.

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THERAPIES EVALUATED IN THIS SERIES

1. Essiac (158[7]:897-902)
2. Green tea (158[8]:1033-5)
3. Iscador
4. Hydrazine sulfate
5. Vitamins A, C and E
6. 714-X



ulcerative colitis, cervical dysplasia, leukopenia, Crohn's disease, papillomatosis of the bladder or colon, and senile keratosis.

Iscador is prepared by fermenting an aqueous extract of the whole mistletoe plant with the bacterium *Lactobacillus plantarum*. The product is then mixed and filtered to remove the bacteria before being standardized and packaged in ampules for injection. Some proponents recommend the use of mistletoe preparations derived from specific trees or modified by the addition of very dilute concentrations of metals such as mercury, silver or copper, depending on the type of cancer diagnosed.

Iscador is injected subcutaneously into the abdominal wall, near the tumour site if possible. Anthroposophic practitioners may, in some cases, inject Iscador directly into the tumour. The treatment regimen is adjusted according to the patient's general condition. A typical course of treatment lasts several weeks and requires that injections be given early in the morning 3–7 times per week, with gradual increases in the concentration of Iscador in accordance with a protocol set by Steiner. A long-term maintenance dose may be recommended depending on the person's health and tumour status.

Proponents advise that Iscador is compatible with chemotherapy and radiotherapy. It is usually administered before surgery.

Safety

There is usually some local inflammation at the injection site and an increase in body temperature that is sometimes accompanied by headache and chills.^{2,3} The review of the literature revealed no other evidence of toxic effects from mistletoe preparations when used as directed. However, ingestion of the plant or intravenous administration of some of the constituents may cause seizures, bradycardia and even death.⁴

Laboratory and clinical evidence

Since researchers have used several different preparations of mistletoe extracts in their studies, including non-fermented preparations of mistletoe and specially prepared extracts, the literature review was expanded to include information on mistletoe products other than Iscador.

Several studies using cell systems have confirmed the biological activity of mistletoe extracts. Specifically, the extracts appear to increase DNA stability⁵ and inhibit cell growth.^{6,7} Increases in a number of indices of immune function have been reported in animals studies,^{8–11} but the extent to which these effects are of clinical significance in humans is unknown. Some animal studies have suggested that mistletoe has antitumour activity.^{9,12}

Since mistletoe products have been widely used in Germany and Switzerland for many years, many of the clinical studies (case reports and clinical trials) have been reported in German-language journals. However, a number of clinical studies and review articles have now appeared in the English-language literature.^{13,14} Several studies indicated an improvement in immune function,^{3,15,16} quality of life^{17,18} and even survival.¹⁴ However, most of the studies had significant design limitations, making it difficult to interpret their results and seriously limiting the value of their findings.

Constituents of Iscador

Although the proponents of Iscador advise that optimal effects require the use of whole-plant products, researchers have endeavoured to identify the most active constituents. Mistletoe preparations contain a number of biologically active constituents, but these vary widely depending on whether the extract is crude or fermented, on the host species from which the mistletoe has been obtained and on the season during which it was harvested. These variations make it difficult to predict the likely effects of nonstandardized mistletoe preparations. Nonetheless, laboratory research using cell cultures and a variety of animal systems has identified the 2 key components of mistletoe preparations: viscum (also known as mistletoe lectin I, ML-I or VAL) and viscotoxin.¹⁹

Viscum is a lectin (a complex protein–sugar compound that can bind to cell surfaces) that appears to interfere with intracellular protein synthesis,^{20,21} stimulate the production of cytokines (which increase the production of leukocytes)^{3,22} and activate leukocytes.²³ Viscum may also affect the processes of metastasis and apoptosis.²⁴ Viscotoxin, also a lectin, has a molecular structure similar to that of viscum, but it appears to be more cytotoxic and to induce cellular necrosis.¹²

In addition to viscum and viscotoxin, extracts of mistletoe contain polysaccharides and alkaloids, some of which have been shown to have biological activity.^{25,26} Researchers are continuing to study the activity of these constituents and their possible role as therapeutic agents.

Conclusion

Mistletoe products have been in widespread use, particularly in Europe, for at least 70 years. Although there is laboratory evidence of biological activity that may be beneficial to cancer patients, the evidence of clinical benefit from human studies remains weak and inconclusive. Because of the absence of serious side effects and the limited evidence that mistletoe products may offer some therapeutic advantage, further research is warranted. New



multicentred clinical trials are under way in Europe and are in the planning phase in the US and Canada.

Innovative and collaborative research needed to meet the needs of growing numbers of patients and their physicians for information on unconventional therapies is now being sponsored by the Canadian Breast Cancer Research Initiative. Open communication between patients and physicians is also necessary to maintain an appropriate therapeutic partnership. A guide for patients to help them choose unconventional therapies has been prepared (page 1161) in the hope that it will help physicians to initiate communication with patients interested in exploring unconventional therapies. It lists important questions for patients to ask and identifies some sources of information.

This article reports some of the work carried out by the Task Force on Alternative Therapies of the Canadian Breast Cancer Research Initiative (CBCRI). The CBCRI is the main funder of breast cancer research in Canada and was established in 1993 as a consortium of the Canadian Cancer Society (CCS), the National Cancer Institute of Canada (NCIC) — which also serves as the administrative home of the CBCRI — and the federal government (through the participation of the Medical Research Council of Canada and the National Health Research and Development Programme). In addition to the author, a number of other CBCRI staff worked on the project, including Dr. Carmen Tamayo (research associate), Ms. Rebecca McDonald and Ms. Jess Merber. Others contributed to the reviews of specific agents. The task force was chaired by Ms. Donna Cappon. Dr. Kaegi was the Director of Medical Affairs and Cancer Control for the CCS and the NCIC and staff partner with the task force.

Hydrazine sulfate will be the topic of the next article in the series, to appear in the May 19 issue.

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Peer-reviewed journals dealing with unconventional therapies:
Alternative Therapies in Health and Medicine
The Journal of Alternative and Complementary Medicine

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