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Mistletoe: Beyond Magic And Mysticism

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Mistletoe comes to us entwined in a long history of magic and mysticism. Ancient peoples believed it would ward off witchcraft. To this end, the Gypsies wore a sprig around their necks. The Druids thought the plant cured sterility and used it as an antidote for poison.[1] Many Americans, even those who would otherwise scoff at superstition, have kissed under the mistletoe.

The main mistletoe species are European varieties (*Viscum album L.*, abbreviated as VAL), American varieties (the most common of which is *Phoradendron serotinum*) and Korean mistletoe (*Viscum album coloratum*). Herbalists have traditionally used a tea of American mistletoe leaves to induce vomiting, purge the bowels, soothe the nerves and mitigate some heart problems. Native Americans used it to induce abortion.[2] European mistletoe is said to increase urination and relax blood vessels-- with an initial rise, then fall in blood pressure. Some authorities, however, believe using European mistletoe to treat high blood pressure requires further substantiation.[3]

Since the 1960s, mistletoe has gained the attention of the medical community as a possible treatment for cancer and, recently, as a potential treatment for AIDS. Although most research uses the European variety, the active components are thought to be similar among the varying species. Because mistletoe is semiparasitic, its chemical constituents may also vary according to the kind of tree it grows on.

Eating mistletoe, especially its berries, has been considered highly toxic, particularly for children. However, recent examination of the medical literature and poison center charts failed to produce convincing evidence of severe toxicity, except possibly for infants who eat the berries.[4]

Because mistletoe preparations contain tyramine (a metabolite of the amino acid tyrosine), patients on any types of monoamine oxidase (MAO) inhibitor antidepressants such as Nardil® should not take them.[5] MAO inhibitors prevent the enzymatic breakdown of neurotransmitters such as

noradrenaline and tyramine (structurally similar to noradrenaline), thereby liberating noradrenaline stores. The resultant extra tyramine can overstimulate the sympathetic nervous system, leading to problems such as dangerously high blood pressure.

Useful Lectins

Although mistletoe contains biologically important alkaloids and polysaccharides, research centers on its protein constituents--viscotoxin and three lectins called ML-I, ML-2 and ML-3.[6] Lectins are proteins or glycoproteins (proteins with a carbohydrate group attached) that bind to sugars, with each different lectin binding to a specific sugar. This is particularly important because when normal cells become tumor cells, some sugars on the cell surface change, thereby giving it a unique composition of sugars. Mistletoe lectins appear to bind only to these specific sugars. This is probably how they eliminate cancer cells.

Because stomach acids tend to destroy proteins, mistletoe preparations are typically administered by subcutaneous injection. The three standardized mistletoe preparations primarily used are the European IscadorTM, HelixorTM and EurixorTM. IscadorTM, a fermented product, contains the lectins ML-2 and ML-3, but not ML-1.[7] HelixorTM is a non-fermented extract containing all three lectins.[8] A newer extract, EurixorTM has been standardized to the ML-1 content.[9] One mistletoe extract, T4GEN®, is the first multiple molecule medicine to receive a U.S. patent. In this case, the term "multiple molecule" means the drug is standardized to all three of the active mistletoe lectins.

Mistletoe lectins are useful because they can kill cancer cells. Normally when cells become damaged or mutated, they die by a process known as apoptosis, a sort of mini-suicide. Cancer cells, however, somehow shut off this apoptosis program and continue dividing and growing, thereby forming a tumor. Research shows that when mistletoe lectins bind to tumor cells, they can induce apoptosis. Of the different mistletoe protein constituents, ML-3 is the most effective, and viscotoxins have no therapeutic effect.[10]

Mistletoe also prevents angiogenesis, the formation of new blood vessels critical for continued tumor growth. In one experiment using mice, Korean mistletoe extract prevented blood vessel growth, with resultant "starving" of the tumor cells.[11]

Mistletoe extracts also have profound effects on the immune system, increasing the proliferation and activity of various immune cells.[12] Compounds with such immunomodulating effects may help treat viral infections such as HIV and cancer.

Human Research

Many human studies support using mistletoe as companion therapy for standard cancer treatments and for decreasing some of the side effects of radiation therapy and chemotherapy. Laboratory research on mistletoe extracts indicates that they may actually stabilize DNA, preventing it from

mutating.[13] This property may not only help prevent cancer, it may prove useful in conjunction with chemotherapy to prevent tissue damage.

One investigation showed that Iscador MTM (the M means it is from mistletoe found on apple trees) treatment improved DNA repair in breast cancer patients.[14] This is important since DNA repair is decreased by chemotherapy and radiation therapy. Faulty DNA repairs in lymphocytes (white blood cells critical to cancer surveillance) are common in cancer patients and cancer-prone patients, and decreases lymphocyte ability to recognize and remove cancer. In this experiment, patients in advanced stages of breast cancer were given one dose of Iscador MTM intravenously, followed by daily subcutaneous injections for seven days. Blood samples were evaluated for DNA repair mechanisms in blood lymphocytes. At days seven and nine, there was a 2.7-fold average increase in DNA repair, with 12 out of 14 of these patients showing improvement.

Another study showed that although mistletoe did not decrease progression of advanced pancreatic cancer (a malignancy with a dismal prognosis), it did improve patients' quality of life.[15] Patients were given subcutaneous injections of the EurixorTM preparation twice weekly with no simultaneous administration of other therapies. Evaluation by questionnaire indicated that quality of life was stable, which is unusual in patients receiving cancer therapies.

A trial on patients with advanced gliomas (a type of brain tumor) showed that EurixorTM enhanced immune function and improved quality of life during radiation therapy.[16] These patients were randomly divided to receive either subcutaneous injections of mistletoe extract twice weekly for three months plus standard cancer treatments or standard cancer treatments alone. The patients receiving mistletoe showed a significant increase in the number of lymphocytes and overall immune function.

The new mistletoe extract T4GEN® is currently undergoing clinical trials for AIDS treatment.[17] Unlike most AIDS drugs that target the virus, this mistletoe extract is expected to act by augmenting the immune system.

Because constituents in mistletoe extracts vary, comparing study results is difficult. The best types of extracts and dosages have yet to be determined. Nevertheless, mistletoe extracts have caught the attention of pharmaceutical companies. As research continues and positive results accumulate, mistletoe extracts may become an important part of both cancer and AIDS therapy.

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References

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