

Immune Stimulation and Surveillance

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This article is the forth of a series by Dr William Barnes which explore the structure and function of the immune system, and how it fits into the changing medical paradigm.

Introduction

In the treatment of cancer there are a number of tasks. Often, the first task of treatment is tumour removal or destruction whether we are dealing with primary or secondary disease.

The most successful treatment in Primary disease is surgery. In secondary disease conventional methods include chemotherapy, Radiotherapy, Hormone therapy and immune therapy. Hyperthermia has also been mentioned as a therapy in this role. Immune therapy has to this time, been relatively unsuccessful.

Having been successful in tumour removal or destruction, the next task in treatments is to prevent local recurrence and distant metastatic spread. Here the support and training of the immune system is paramount. As previously discussed, a common side effect of tumour is destructive therapy is immune suppression or depletion. Support and repair of immune function can be achieved with some known therapies; this article will describe the role of mistletoe in this context.

Mistletoe

There are few plants that have received as much scientific examination and research in the treatment of cancer as mistletoe (*viscum album*).

Originally discussed in European folklore, Rudolph Steiner, philosopher and founder of the Anthroposophical Society, first suggested its use in cancer therapy.

Primarily, it was used by practising doctors using anthroposophical techniques, yet mistletoe gained limited success and recognition, Since then more rigorous research in scientific institutions has widened its acceptance as a valid immune therapy.

Mistletoe is a good example of a therapy used in treatments based on esoteric philosophies which has now been adopted by practitioners who are more scientifically and pragmatically orientated.

Mistletoe epitomises the struggle in the medical world: some practitioners suggest the value is in using the whole plant as a botanical extract; while others want extraction of the active components as a standardised pharmaceutical.

The argument to retain the whole plant was championed by Dr Rita Leroi an early researcher and anthroposophical doctor, who says, “a number of immunological and cytostatic elements are frequently combined. The combination already exists in mistletoe, confirming that Steiner was right in suggesting that this plant be used in cancer therapy. It is important that the full extract be used, for nature herself has created a model here- avoiding one-sided action on the part of the individual tumour’s active constituents, (and hence their toxicity) by combining them in a biological whole.”

The scientific community’s argument requires scientific analysis and purification of active ingredients. This is summed up by a Norwegian Research team Holtskog *et al*: “Because of the widespread therapeutic use of Iscador (mistletoe extract derived by fermentation), it is important to establish to what extent it contains toxins, as well as study whether cystostatic components are present in the extract.”

In their paper published in 1988 the team concludes that not all the properties of mistletoe are due to cytotoxic actions, but that mistletoe somehow activates the defence system of the host.

To date, the only preparations used are the full extract, and no great problems with toxicity have been reported.

The Plant

Mistletoe is a semiparasitic plant growing on the trunks of a variety of host trees. It has no root system. It is very active in photosynthesis and draws its nutrients directly from the host. Some researchers have described it as somewhere between a plant and an animal.

Constituents

Over the years, numerous constituents of the mistletoe plant have been examined in great detail. Primarily, the active ingredients can be divided into carbohydrates (polysaccharides and oligosaccharides) and proteins (viscotoxins and lectins). The actions of these substances involve both control of cell division and support of the immune system.

Preparation

One of the problems hampering the full therapeutic evaluation of mistletoe is the multitude of different extracts available.

Initially, the main extraction process was by fermentation with bacteria called lactobacillus plantorum. This preparation was used by injection. The main preparation prepared by this method in use today is Iscador.

The other main method of preparation now in use, is whole plant water extraction with no fermentation and sterilised by filtration. The dose is expressed in mg with 100mg of plant yielding a 100mg-ampoule dose. Preparations using this process include Helixor and Eurixor.

Therapeutic Effects

Therapeutic effects of mistletoe can be divided into three main areas;

1. cytotoxic
2. Immune stimulation
3. Cellular protection

Table 1 lists these actions.

Table 1			
Structure Type	Substance Category	Effects on Tumour Cells	Effects on Immune Cells
Glycoproteins	Mistletoe lectins 1, 11 and 111	Inhibition of protein synthesis	Release of TNF & Interleukins 1, 2, 6
Polypeptides	Viscotoxins	Cytotoxicity thru Leaks in membranes	Macrophage activation
Peptides	Peptides	Cytotoxicity	Macrophage activity
Polysaccharides	Arabinogalactones		Stimulation of Tcells
Oligosaccharides		Tumour Inhibition	Interferon increase in NK activity

Cellular Protection

There is a lot of agreement in German literature reporting the beneficial role mistletoe plays during and after conventional therapy. The explanation for this lies not only in immune support, but also a new action, that of DNA repair in white blood cells.

Certain chemotherapies have been shown to damage DNA structure in phagocytes (white blood cells) and certain factors in mistletoe reconstitute the DNA, restoring the phagocytic action.

One of the major problems with chemotherapy and radiotherapy is therefore overcome. This effect has been born out in clinical trials.

Clinical Results

Mistletoe has been tested extensively in laboratory tests and clinical trials. Mistletoe has been shown to be an effective treatment in metastatic liver disease, gastric cancer, bowel cancer, lung cancer, leukaemia and breast cancer.

In a prospective trial on breast cancer published in 1988, 643 patients were divided into 3 trial groups following initial surgery to remove the breast tumour. 192 patients received Helixor; 177 patients received CMF (cyclophosphamide methotrexate) and 5FU, a first line chemotherapy for breast cancer; 177 had no follow up treatment.

The results are presented in Table 2; the lymph node involvement indicates the increasing degree of severity.

This result shows similar in 0 and 1-4 node groups between Helixor and CMF, but better long term survival in the Helixor group than the CMF group with more advanced disease at diagnosis, showing the value of this low toxicity therapy. The second group of 19 was given the standard chemotherapy plus a concurrent regime of Helixor. The results are listed in Table 3.

Stages of Axillary lymph Nodes (under arm)	Therapy	Survival Rate	
		3 years	5 years
Nodes 0 (no nodes infected)	HELIXOR	88.1	78.8
	CMF	88.7	80.4
	control	88.5	75.9
Nodes infected 1-4	HELIXOR	77.2	64.6
	CMF	82.2	65.5
	Control	71.9	51.0
Nodes Infected > 4	HELIXOR	62.8	45.5
	CMF	48.7	39.2
	control	44.8	37.0

This small-randomised trial clearly shows the benefit of combination therapy in colorectal cancer.

As of 1996 there were more than 1000 scientific publications on mistletoe, its ingredients, its pharmacology and therapeutic effects.

Toxicity

To date no serious toxicity has been detected in both animal and human studies. More specifically high dose therapy in humans has revealed no signs of liver, kidney or bone marrow injury.

Administration & availability

Mistletoe in all its preparations is an injectable medicine and as such needs to be given under medical supervision.

At this time it is not registered for general use in Australia, however it is available in New Zealand and Germany. A consenting medical practitioner can administer it under the special access scheme of the therapeutic goods act. Under this scheme the patient must qualify by having a terminal disease (Category A patient).

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SURVIVAL RATES		
	1 year	2 years
Control	70%	32.2%
Helixor	90%	60.0%

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