# *Taxus*: Renewed Interest in this Genus and Implications for New Zealand

**J.M. Follett and J.A. Douglas**
New Zealand Institute for Crop & Food Research Ltd, Ruakura Agricultural Centre, Hamilton

## BACKGROUND

A tree crop, which may be of interest to the New Zealand nursery industry, is the yew (*Taxus baccata*). A member of the family Taxaceae it is a slow-growing and long-living, dioecious evergreen tree which can grow to a height of around 20 m. It is extremely tolerant of variations in temperature, light, soil moisture, and pH. The yew, which is a native of Europe and West Asia, is widely cultivated and is often found near churches and other meeting places, as it was considered a sacred tree before Christianity, and is still associated with places of worship. In the Middle Ages it was valued as a wood for long bows and is now often used in gardens as an ornamental species and for topiary.

The yew is poisonous and was blamed for untimely deaths as early as 51 B.C. In North America; native Americans are known to have used the bark from Pacific yew (*T. brevifolia*) as a disinfectant and as a treatment for skin cancer (Nicolaou et al., 1996).

## MODERN DEVELOPMENTS

Interest in the medicinal properties of the yew tree was reawakened in the early 1960s when the U.S. National Cancer Institute (NCI) started screening natural sources for possible medicinal properties (Abell, 1997). Extracts collected from the bark of the Pacific yew (*T. brevifolia*) were found to kill artificially preserved leukemia cells. In 1967 the active ingredient was identified, isolated, and named taxol or paclitaxel. In 1978 researchers were able to demonstrate taxol's mode of action against cancerous cells. It was found that taxol binds to microtubules, which act as part of the cells' internal skeleton, causing them to become rigid. This disrupts cell division especially in rapidly dividing cells such as those found in tumours (Schiff et al., 1979; Horwitz et al., 1992). Today taxol is used to treat breast and ovarian cancer (Nicolaou et al., 1996).

Unfortunately the bark from a mature Pacific yew provides only 500 mg taxol, enough for only one ovarian cancer treatment programme (Abell, 1997) when ovarian cancer afflicts 20,000 women annually in the U.S.A. alone. Producing taxol from yew bark from natural populations has led to the decimation of wild yew populations in North America, and subsequently to shortages of taxol (Webb, 1997) resulting in a search for other sources. Research has identified taxol in other *Taxus* species and in other plant components including the foliage. This means that, in the long term, sustainable yields of taxol and taxol precursors could be produced from large yew orchards that were regularly trimmed to harvest the foliage.

## RESEARCH IN NEW ZEALAND

Any industry based on harvesting *Taxus* foliage in New Zealand would require suitable planting stock. In 1993 Crop & Food Research began an initial survey of the concentrations of taxol and taxol-related chemicals (taxanes) in existing populations

of Irish yew (*T. baccata*), Japanese yew (*T. cuspidata*), and the Japanese plum yew (*Cephalotaxus harringtonia*). No taxanes were found in the Japanese plum yew, only low concentrations in the single tree of the Japanese yew, but significant amounts were found in the Irish yew. This initial survey was followed by a comprehensive survey of Irish yew tree foliage from Northland to Southland. Trees were sampled and the foliage analysed using an HPLC to identify the concentrations of the taxanes (10-deacetylbaccatin III, baccatin III, cephalomannine, and taxol) (Lauren et al., 1995). This survey of 72 trees found individual trees varied in taxol concentration from 7 to 510 mg $kg^{-1}$ (Lauren et al., 1995). On the basis of these analyses five trees, including one golden-leafed cultivar (*T. baccata* Aurea Group), with high concentrations of taxanes were propagated. The trees are being grown at two sites to determine whether the high taxane concentrations within the plant are stable.

**Propagation.** The propagation of *Taxus* species is well documented with most Northern Hemisphere nurseries using cuttings collected from September to December (March to June in New Zealand) (Thomsen, 1978; Bauer, 1978; van Hof, 1978). Rooting hormones are often used (van Hof, 1978; Scheer, 1976; Verkade, 1976; von Kornya, 1976) along with a variety of rooting mixes based on either sand (van Hof, 1978) or peat (Thomsen, 1978) or combinations which often include perlite (Scheer, 1976; von Kornya, 1976). Most nurseries report good survival and plant growth using these methods with Verkade (1976) quoting rooting percentages of 90% to 95%.

Cuttings (15 cm long) from trees with high taxane concentrations were collected in late August 1994. These cuttings were then dipped in plant rooting hormone powder containing 0.8% ß-indolebutyric acid before being lined out in three different rooting media — straight sand, standard potting mix, and a vermiculite and perlite mix (1:1, v/v). The cuttings were kept in a glasshouse under mist. There was no significant difference in the number of rooted cuttings produced by different treatments or trees. Approximately 50% of all cuttings produced roots after 6 months. The relatively low rooting percentage, compared with figures for overseas nurseries, is probably the result of collecting cuttings in late winter rather than in the more traditional autumn-early winter period.

**Production.** A large number of production trials are currently in progress overseas to determine the growing conditions required for optimum taxol production in the field (Wheeler and Piesch, 1993). To date no trials have been established in New Zealand to determine the growing conditions required to optimise taxol production.

## DISCUSSION

The survey has demonstrated that there are a number of high-taxane-yielding trees amongst the existing *T. baccata* population in New Zealand. Provided the taxane concentrations remain stable, these selected trees could provide the basis for establishing orchards to provide the raw material for extracting and manufacturing taxol for the treatment of ovarian cancer. At least one North American company has taken this approach with large scale biomass production for the long term economical supply of taxanes for the pharmaceutical industry (Wheeler and Piesch, 1993). Taxol is a complex molecule and while research is being undertaken to develop biotechnology fermentation methods of producing it, the lower cost method of extracting it from managed plantations is likely to remain in place.

If New Zealand is to develop a successful industry growing *Taxus* species for the production of taxol, the nursery industry will need to be able to rapidly supply large numbers of selected trees capable of producing high taxol or taxol-related compounds in the foliage.

## LITERATURE CITED

**Abell, A.** 1997. Improving access to yew tree extracts. UCResearch, University of Canterbury, Christchurch. pp. 46.

**Bauer, C.** 1978. Propagation of *Picea glauca* 'Conica'. Comb. Proc. Intl. Plant Prop. Soc. 28:353-354.

**Horwitz, S.B.** 1992. Mechanism of action of taxol. Trends Pharmacol. Sci. 13:134.

**Lauren, D.R., D.J Jensen,** and **J.A. Douglas**. 1995. Analysis of Taxol, 10-deacetylbaccatin III and related compounds in *Taxus baccata*. J. Chromatography A 712:303-309.

**Nicolaou, K.C., R.K. Guy,** and **P. Potier**. 1996. Taxoids: New weapons against cancer. Scientific Amer. pp 84-88.

**Scheer, C.** 1976. *Taxus* propagation by cuttings. Comb. Proc. Intl. Plant Prop. Soc. 26:173-174.

**Schiff, P. B., J. Fant**, and **S. B. Horwitz**. 1979. Promotion of microtubule assembly in vitro by taxol. Nature 22:665.

**Thomsen, A**. 1978. Propagation of conifers by cuttings and grafting. Comb. Proc. Intl. Plant Prop. Soc. 28:215-220.

**van Hof, E**. 1978. Rooting *Taxus* cuttings with no heat. Comb. Proc. Intl. Plant Prop. Soc. 28:515-516.

**Verkade, G**. 1976. Propagation of *Taxus* by cuttings. Comb. Proc. Intl. Plant Prop. Soc. 26: 177.

**von Kornya, J.P**. 1976. Propagation of *Taxus* cuttings. Comb. Proc. Intl. Plant Prop. Soc. 26:178-179.

**Webb, G.** 1997. Camptothecin and taxol natural anti-cancer agents. HerbalGram No. 40:21.

**Wheeler, N.C**., and **R.F. Piesch**. 1993. Intensive cultivation of *Taxus* species for the production of Taxol. Comb. Proc. Intl. Plant Prop. Soc. 43:222-227.