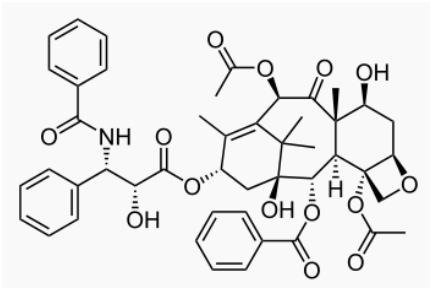
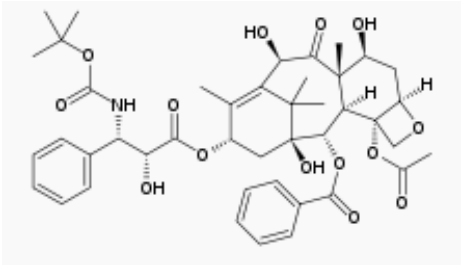
Taxus: from poison to cancer chemotherapy

Taxus baccata: berry and needle leaves



Taxol® molecule
Anti-cancer drug
Extracted from the taxus bark



Taxotere® molecule
Anti-cancer drug
Synthesized from the taxus baccata needles

Document 1 **Taxus: toxic!** (from ①)

The toxicity of its leaves has been known since Antiquity. The Gauls were used to coating the extremity of their arrows with taxus sap. In the ancient Celtic world, the yew tree had extraordinary importance; a passage by Caesar narrates that Catuvolcus, chief of the Eburones poisoned himself with yew rather than submit to Rome.
But, in spite of its high toxicity, this tree became vary famous in pharmacology.

Document 2 **From taxus toTaxol** (from ② ③ ④)

After some years of informal arrangements, in July 1960, the National Cancer Institute (NCI) commissioned botanists to collect samples from about 1,000 plant species per year. On 21 August 1962, one of those botanists, Arthur Barclay, collected bark from a Pacific yew tree, Taxus brevifolia, in a forest north of the town of Packwood, Washington. The material was then processed by a number of specialists, and one of the Taxus samples was found to be cytotoxic in a cellular assay on 22 May 1964. They named the active ingredient 'taxol' in June 1967.The chemical structure was published in 1971.
The use of taxol has been approved by the Food and Drug administration for use in treatment of two cancers, ovarian and breast cancers. Due to the success in clinical trials, the NCI offered drug companies the right to develop the drug competitively. In 1991, the company Bristol-Meyers Squibb (BMS) won this right.

Document 3 **From extraction to synthesis** (from ②)

The concentration of taxol in the bark of the tree is extremely low. A 100 years old tree might yield 3kg of bark which provides enough taxol for one 300mg dose. By 1991, harvest of bark was up to around 425,000kg, at 3kg a tree that is over 100,000 trees that year.
The problem is that bark cannot be harvested without killing the tree. A sustainable harvest had to be found for the long term viability of the yew tree and to provide enough taxol for BMS.
Thus, between 1983 and 1993, more than 30 teams worldwide worked endlessly on the synthesis of taxol. It was the ICSN team (Institut de Chimie des Substances Naturelles) that won that race synthesizing Taxotere, from the needles of a European yew tree, which is a source renewed every year contrary to bark. Taxotere, a parent to taxol, is twice as effective in the treatment of cancers. Today, taxotere and taxol, synthesized the same way, are the active ingredients of many drugs that are used to fight several types of cancer. For instance, Paclitaxel Teva® is a generic which contains taxol.

Bibliography
① *http://en.wikipedia.org/wiki/Taxus_baccata*
② *http://www.colostate.edu/Depts/Entomology/courses/en570/papers_1996/hill.html*
③ *http://en.wikipedia.org/wiki/Taxol*
④ *http://www.news-medical.net/health/Paclitaxel-History.aspx*

Questions

1. What was botanist Arthur Barclay looking for in the sixties? What is the name of the substance he studied more specifically? How did he get it then? Will this substance be considered natural or synthetic?
2. What got researchers to work on the synthesis of this substance?
3. Will Taxotere® be considered natural or synthetic?
4. Paracetamol is the active ingredient of Doliprane®. Judging from the text and this example, define what the active ingredient of a drug is.
5. What is the active ingredient of Paclitaxel Teva®? What does generic mean?
6. Classify synthesized taxotere and taxol extracted from the bark of a Western yew tree: according to their effectiveness, then to their impact on the environment.
7. Taxol is a chemical species contained in the bark of taxus. Find two other natural species with acknowledged medicinal properties.