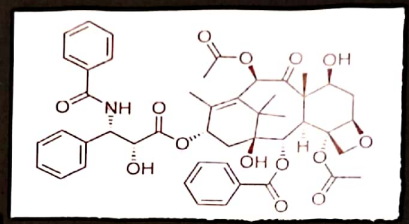
TAXOL

Taxol or paclitaxel

- Common anti-cancer drug,
- Chemotherapeutic drug i.e. a chemical used to treat and control a disease such as cancer (chemotherapy)
- First extracted from the bark of yew trees.
- Isolation of taxol from natural sources was very wasteful as it used a lot of bark of trees that were a threatened and old species.
- A semi-synthetic method was developed that uses a natural precursor (hence semi-synthetic) from the leaves of different but more common and faster-growing yew trees.
- Natural precursor is 10-deacetylbaccatin – DAB.
- Process involves many steps, different solvents and low yield – not very sustainable!

MONROE E. WALL & MANSUKH C. WANI
AT THE RESEARCH TRIANGLE INSTITUTE, RESEARCH TRIANGLE PARK, NORTH CAROLINA, IN 1971

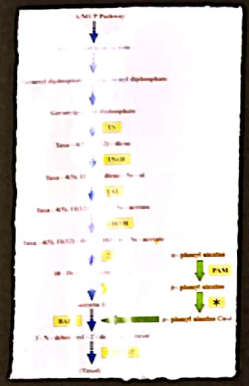


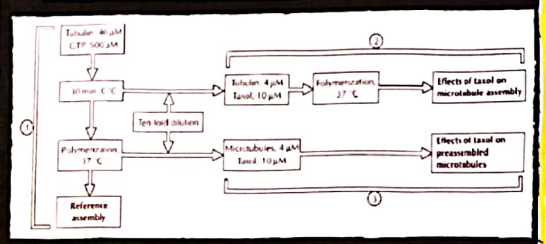
FORMULA = $C_{47}H_{51}NO_{14}$

MOLAR MASS = 853.910 g mol

Taxol

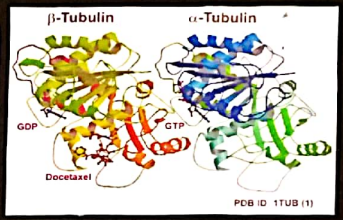
- Taxol is an alkaloid derived from the Pacific yew (*Taxus brevifolia*), a gymnosperm that grows in western North America.
- In the 1960's the National Cancer Institute ran a large scale anticancer screening program. Most samples submitted were synthetic compounds, but there was also a program for screening natural products isolated from plants and fungi. Bark from the Pacific yew had some activity in a simple assay procedure.
- Testing in animals and then humans showed that it helped with lung cancer, breast cancer, and ovarian cancer, as well as Kaposi's sarcoma (common in AIDS).
- Huge amounts of bark were harvested to purify the drug, increasing as it continued to show promise as a cancer treatment. It would be easy to drive the tree to extinction, since harvesting the bark kills the trees.
- It is now produced from a line of tissue culture cells derived from the Pacific yew. The cells make and secrete taxol, which is then purified.
- Taxol binds to the mitotic spindle and stabilizes the structure so it can't be re-used. This prevents further cell division.

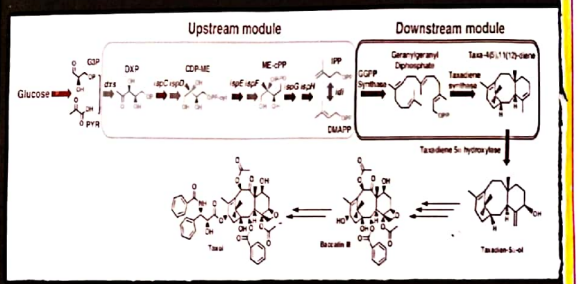




The Pacific Yew

- The Pacific yew (*Taxus brevifolia* Nutt.) is a medicinal drug that is used to produce paclitaxel (taxol).
- In 1962, several samples were collected at random and screened.
- A potent cytotoxic effect was documented in one *in vitro* system.
- After a lengthy development process, clinical studies started 13 years later in 1984.
- Another 10 years is taken before paclitaxel was approved in the treatment of anthracycline-resistant metastasizing mammary carcinomas.



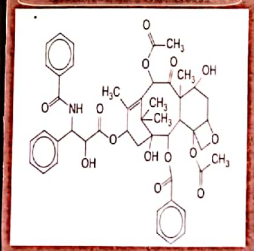


Pacific yew. The bark of Pacific yew (*Taxa brevifolia*) is a source of taxol, a compound used to treat women with ovarian cancer. The leaves of a European yew species produce a similar compound, which can be harvested without destroying the plants. Pharmaceutical companies are now refining techniques for synthesizing drugs with taxol-like properties.

MSJ Chem
Tutorials for IB Chemistry

Taxol

The structure of Taxol can be found in section 37 of the IB data booklet.



Taxol has low solubility in water.
Water solubility is important because a drug must be fully dissolved to be safe for injection.
To increase its water solubility, Taxol is dissolved in alcohol with the addition of polyoxyethylated (35) castor oil.

Taxol – Side Effects

- Administered by IV because it irritates skin and mucous membranes on contact
- Allergic reactions as mentioned
- Other side effects
  - abnormally low neutrophil, which can leave the patient vulnerable to infection
  - abnormally low platelet counts, which can cause hard-to-control bleeding
  - anemia and bone and muscle pain