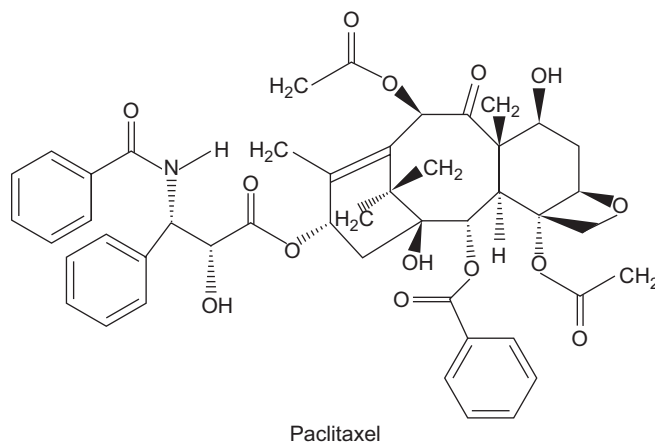


called taxanes, acts on the cytoskeleton of the cell. Specifically, the drug acts on tubulin, disrupts the normal behavior of the cytoskeleton in mediating cell division, and causes cell death (22). Docetaxel (Taxotere[®]) is a semi-synthetic analogue of paclitaxel (23) having a mechanism and anti-cancer properties similar to those of paclitaxel. Docetaxel can be synthesized using a precursor extracted from needles of the European yew, *Taxus baccata* (24).



e. Origins of cladribine

Cladribine (2-chloro-2'-deoxyadenosine) is a small molecule that is a nucleotide analogue. Cladribine is an analogue of deoxyadenosine. After administration, cladribine enters various cells and once inside the cell, an enzyme catalyzes the attachment of three phosphate groups. The result is the conversion of cladribine to cladribine triphosphate. Cladribine triphosphate, in turn, inhibits DNA synthesis, inhibits DNA repair, and results in apoptosis (death of the cell). The drug is most active in cells with high levels of the deoxycytidine kinase, such as lymphocytes (25). Cladribine is used for treating multiple sclerosis and a type of leukemia (hairy cell leukemia).

The connection between deoxynucleotides and killing lymphocytes, as it applies to cladribine, is as follows. Inherited deficiencies of the enzyme adenosine deaminase interfere with lymphocyte development while sparing most other organ systems (26). The

²² Puzstai L. Markers predicting clinical benefit in breast cancer from microtubule-targeting agents. *Ann Oncol.* 2007;18 (Suppl 12):xii,15–20.

²³ Bissery MC, Guénard D, Guéritte-Voegelein F, Lavelle F. Experimental antitumor activity of taxotere (RP 56976, NSC 628503), a taxol analogue. *Cancer Res.* 1991;51:4845–4852.

²⁴ Verweij J. Docetaxel (Taxotere): a new anti-cancer drug with promising potential? *Br J Cancer.* 1994;70:183–184.

²⁵ Piro LD, Carrera CJ, Beutler E, Carson DA. 2-Chlorodeoxyadenosine: an effective new agent for the treatment of chronic lymphocytic leukemia. *Blood.* 1988;72:1069–1073.

²⁶ Carson DA, Kaye J, Seegmiller JE. Lymphospecific toxicity in adenosine deaminase deficiency and purine nucleoside phosphorylase deficiency: possible role of nucleoside kinase(s). *Proc Natl Acad Sci USA.* 1977;74:5677–5681.