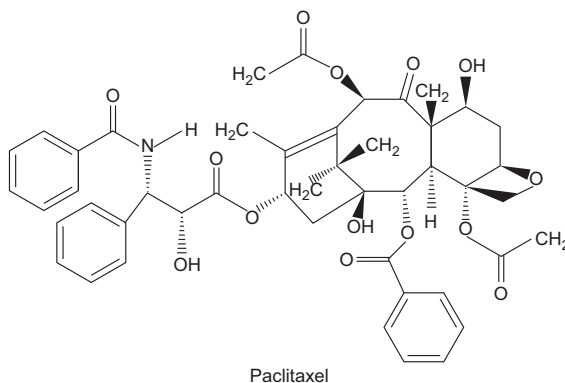


#### d. Origin of Paclitaxel

Paclitaxel (Taxol<sup>®</sup>), an anticancer drug, was discovered in extracts of the Pacific yew tree, *Taxus brevifolia*. In 1963, a crude extract from Pacific yew bark was found to have activity against tumors in experimental animals (31). In 1991, the active component, paclitaxel, was approved by the FDA as an anticancer drug. Paclitaxel, which is a class of drugs 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 (32). Docetaxel (Taxotere<sup>®</sup>) is a semisynthetic analog of paclitaxel (33) having a mechanism and anticancer properties similar to those of paclitaxel. Docetaxel can be synthesized using a precursor extracted from needles of the European yew, *Taxus baccata* (34). Paclitaxel finds use in treating various cancers, in a formulation where paclitaxel is bound to albumin (35,36,37). The albumin confers water-solubility to paclitaxel, which is not soluble in water.



#### e. Origin of Cladribine

Cladribine (2-chloro-2'-deoxyadenosine) is a small molecule that is a nucleotide analog. Cladribine is an analog of deoxyadenosine. After administration, cladribine enters various cells and once inside the cell, the enzyme deoxycytidine kinase 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

<sup>31</sup>Socinski MA. Single-agent paclitaxel in the treatment of advanced non-small cell lung cancer. *Oncologist* 1999;4:408–16.

<sup>32</sup>Pusztai L. Markers predicting clinical benefit in breast cancer from microtubule-targeting agents. *Ann. Oncol.* 2007;18(Suppl. 12):xii15–20.

<sup>33</sup>Bissery MC, Guénard D, Guéritte-Voegelein F, Lavelle F. Experimental antitumor activity of taxotere (RP 56976, NSC 628503), a taxol analogue. *Cancer Res.* 1991;51:4845–52.

<sup>34</sup>Verweij J. Docetaxel (Taxotere): a new anti-cancer drug with promising potential? *Br. J. Cancer* 1994;70:183–4.

<sup>35</sup>Socinski MA. Update on taxanes in the first-line treatment of advanced non-small-cell lung cancer. *Curr. Oncol.* 2014;21:e691–703.

<sup>36</sup>Socinski MA, et al. Weekly nab-paclitaxel in combination with carboplatin versus solvent-based paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small-cell lung cancer: final results of a phase III trial. *J. Clin. Oncol.* 2012;30:2055–62.

<sup>37</sup>Viudez A, et al. Nab-paclitaxel: a flattering facelift. *Crit. Rev. Oncol. Hematol.* 2014;92:166-80.