WHITE PAPER

Radiochemicals

^{3}H Vinca Alkaloids for Oncology Research

Microtubules are cylindrical cellular cytoskeleton components comprised of polymerized dimers of alpha- and beta-tubulin. They play an especially crucial role in eukaryotic cell division by construction of the mitotic spindle which helps choreograph chromosome alignment and separation during mitosis. Microtubule disrupting drugs stall mitosis in the metaphase stage and prevent it from proceeding to completion thus inhibiting cell division and are therefore highly effective. Because of this critical function in rapidly growing tumor cells; microtubule disruption is an inviting target for oncology drugs especially when used in combination with more than one drug. However, one significant problem in the use of these combined chemotherapeutic agents is the development of multi-drug resistance to them by tumor cells. The mechanism of such drug resistance is attributed to over expression of the MDR1 gene product P-glycoprotein by tumor cells.[1,2,3]

P-glycoprotein is part of the superfamily ATP-binding (ABC) cassette transporters and is normally expressed in most cells but is present in elevated levels in healthy cells of the adrenal gland, gastrointestinal tract, kidney and liver. In these cells, P-glycoprotein appears to function as a successful biological defense mechanism against toxic xenobiotics by actively transporting them out of the cells. However, the over expression of P-glycoprotein in tumor cells facilitates their multi-drug resistance protection by transporting the administered chemotherapeutic agents out of the cell before they are effective. This clearly compromises the effectiveness of the powerful multi-drug treatment strategy and is a significant clinical challenge to patient improvement. An intense research effort has therefore been focused on elucidating the details of P-glycoprotein mediated drug efflux as well as the discovery of inhibitors for its activity.

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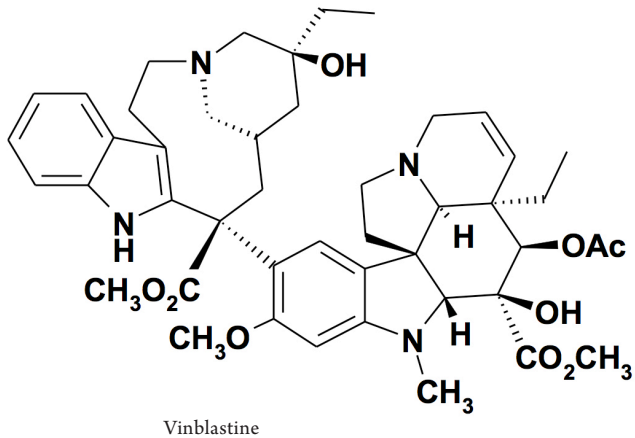
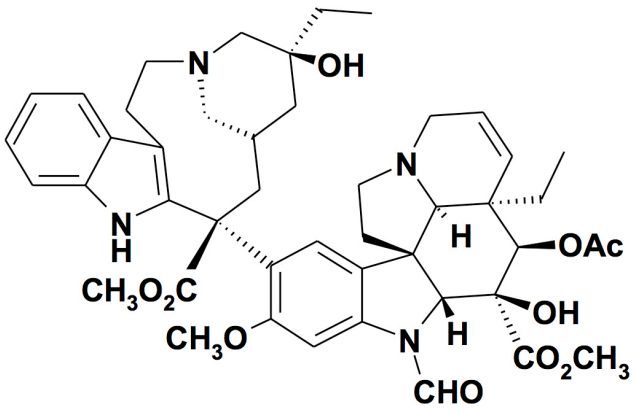
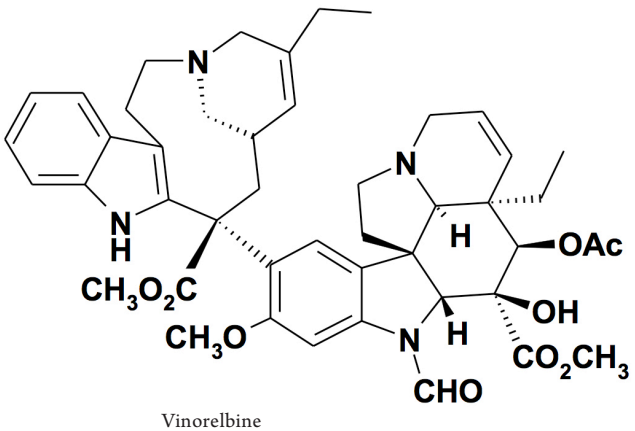
Vinca Alkaloids



Vinblastine



Vincristine



Vinorelbine

Among the most potent microtubule disrupting agents are the vinca alkaloids shown below. Vinblastine and vincristine, natural products isolated from the Madagaskar periwinkle, are widely used in cancer chemotherapy as is their structurally related semi-synthetic vinca analogue, vinorelbine. These alkaloids are frequently used in combination with other non-structurally related oncology drugs in a multi-drug administration patient regimen.

To support this critical oncology research, PerkinElmer now makes available tritiated versions of these three alkaloids as their sulfate salts at high specific activity and radio purity. They are **[^{3}H(G)] vinblastine sulfate (NET1176), [^{3}H(G)] vincristine sulfate (NET1210) and [^{3}H(G)] vinorelbine sulfate (NET1211).** Use of these valuable radioligands will no doubt play a role in finding a cure for various cancers.[4,5]

By using radioactive isotopes to directly replace non-radioactive atoms, the biology of the substance you are studying is not altered. The use of radiochemicals is of critical importance in the drug development process for use as radioligands in lead discovery, as metabolic tracers in development, and ADME-Tox studies.

References

1. M. Kavallaris, J.-P. Annereau, J.-M. Barret, *Seminars in Oncology,* **2008,** 35, S22-S27.

2. J.A. Silverman, *Pharmaceutical Biotechnology,* **1999,** 12, 353-386.

3. A.B. Shapiro, V. Ling, *Acta Physiologica Scandinavica, Supplementum,* **1998,** 163, 227-234.

4. P. Pitchakarn, S. Ohnuma, K. Pintha, W. Pompimon, S.V. Ambudkar, P. Limtrakul, *J. Nutrional Biochem.,* **2012,** 23, 76-84.

5. N. Aouali, H.E. Btaouri, C. Dumontet, L. Eddabra, S. Malagarie-Cazenave, C. Madoulet, H. Morjani, *Oncology Reports,* **2011,** 25, 1161-1167.

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