Historical Aspects of Antitumor Compounds from Plants, Including Homoharringtonine (Omacetaxine mepesuccinate, Synribo™)

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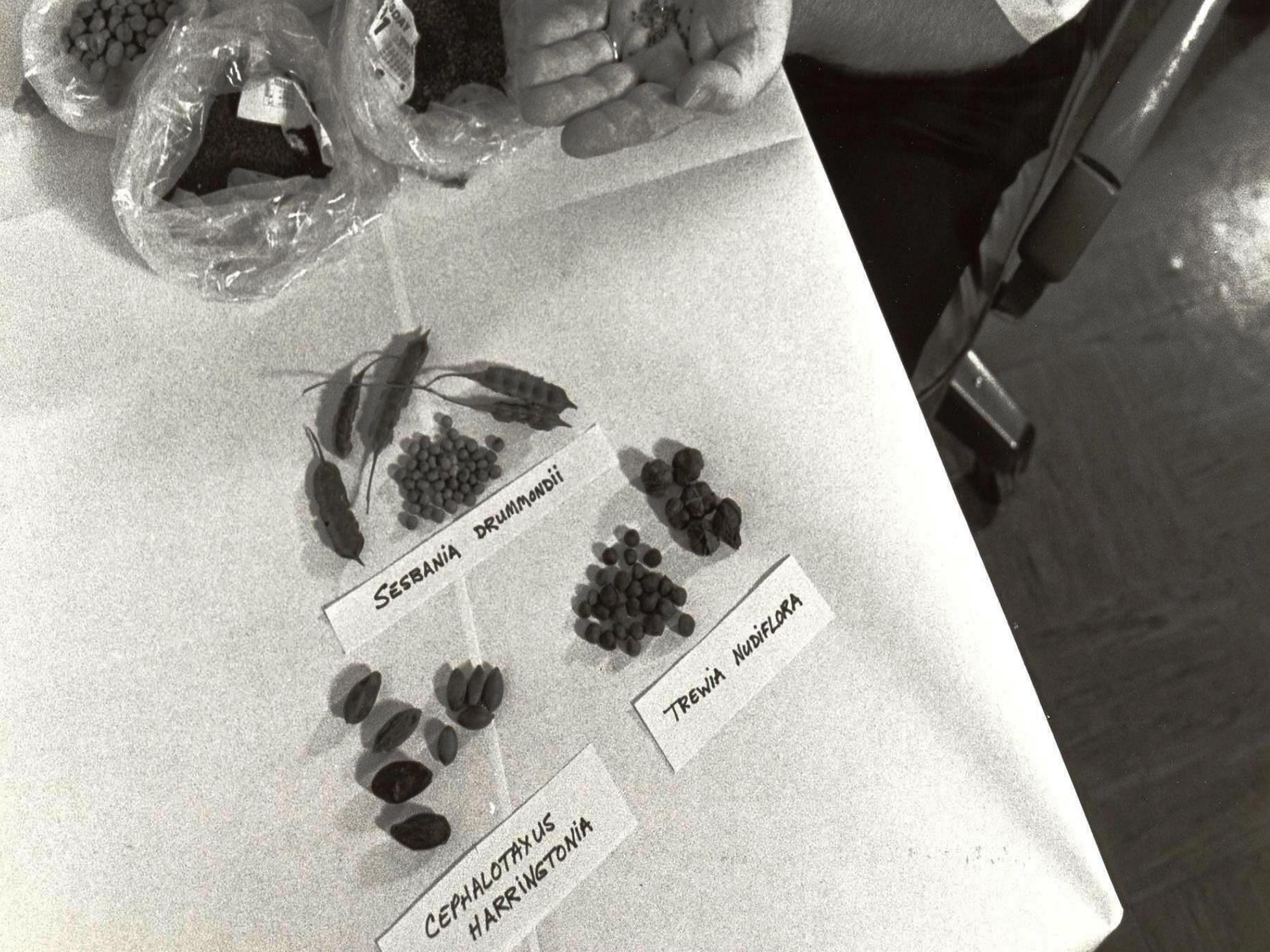
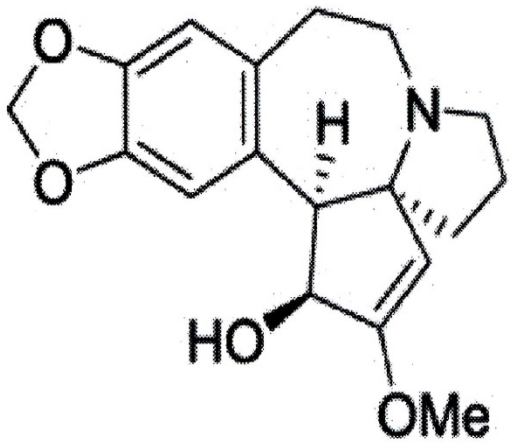
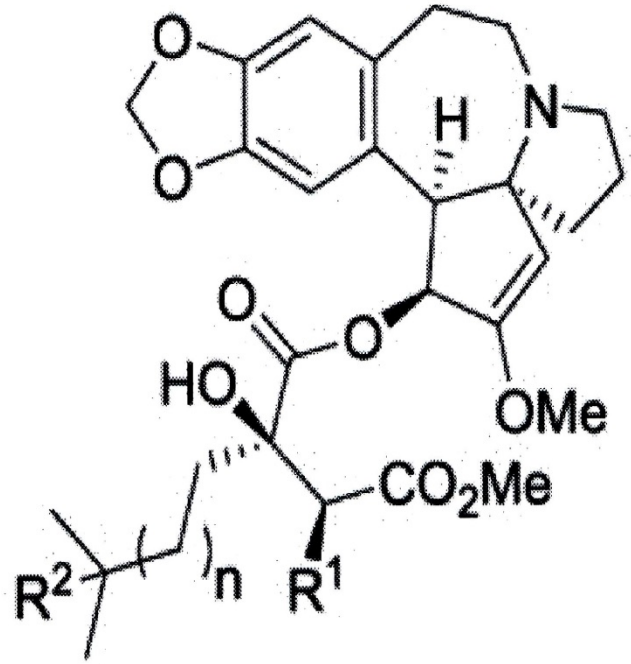

SESBANIA DRUMMONDII
TREWIA NUDIFLORA
CEPHALOTAXUS HARRINGTONIA



Cephalotaxine



Harringtonine : R^1 = H, R^2 = OH, n = 1

Isoharringtonine : R^1 = OH, R^2 = H, n = 1

Homoharringtonine : R^1 = H, R^2 = OH, n = 2

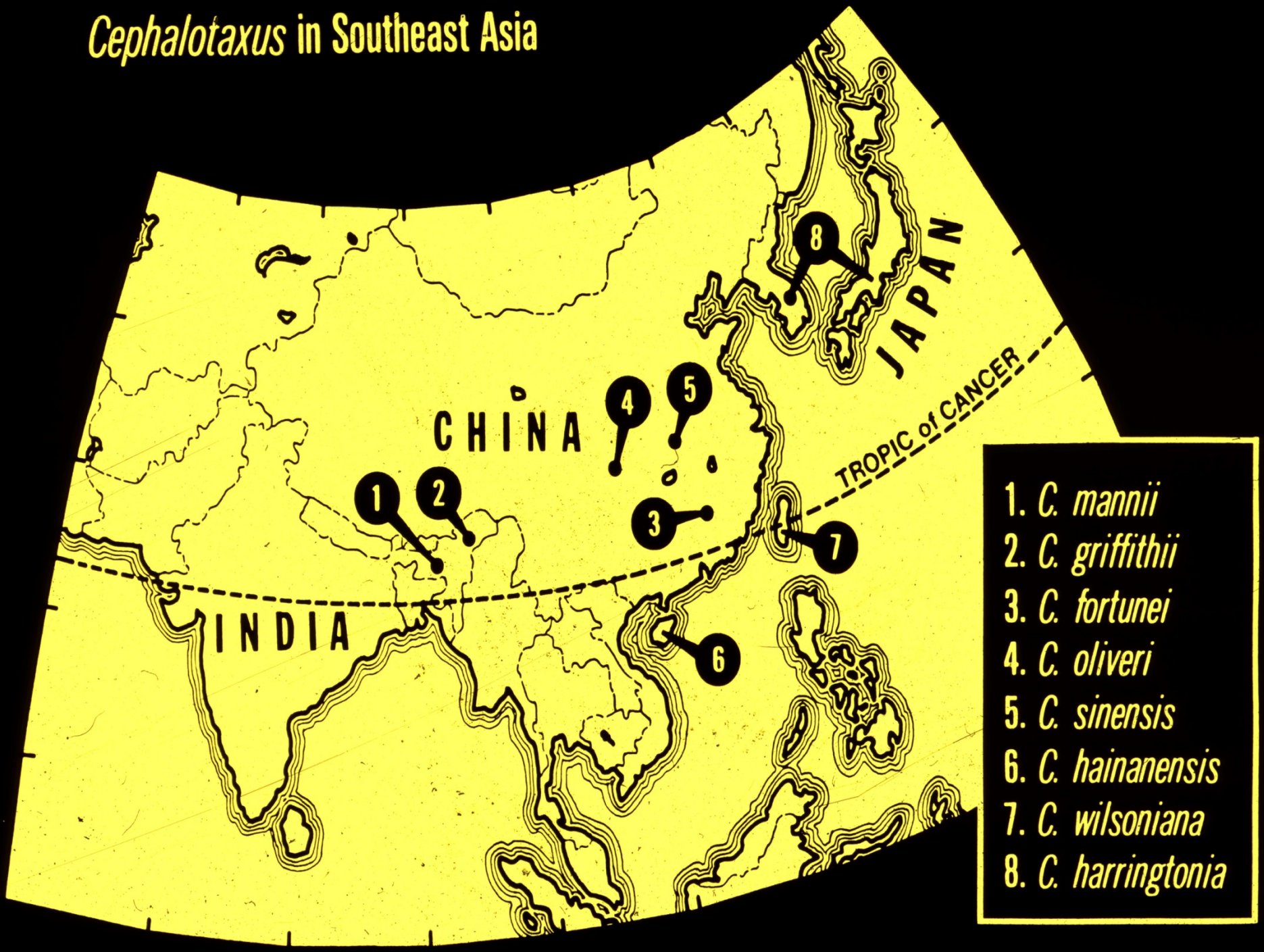
Deoxyharringtonine : R^1 = H, R^2 = H, n = 1

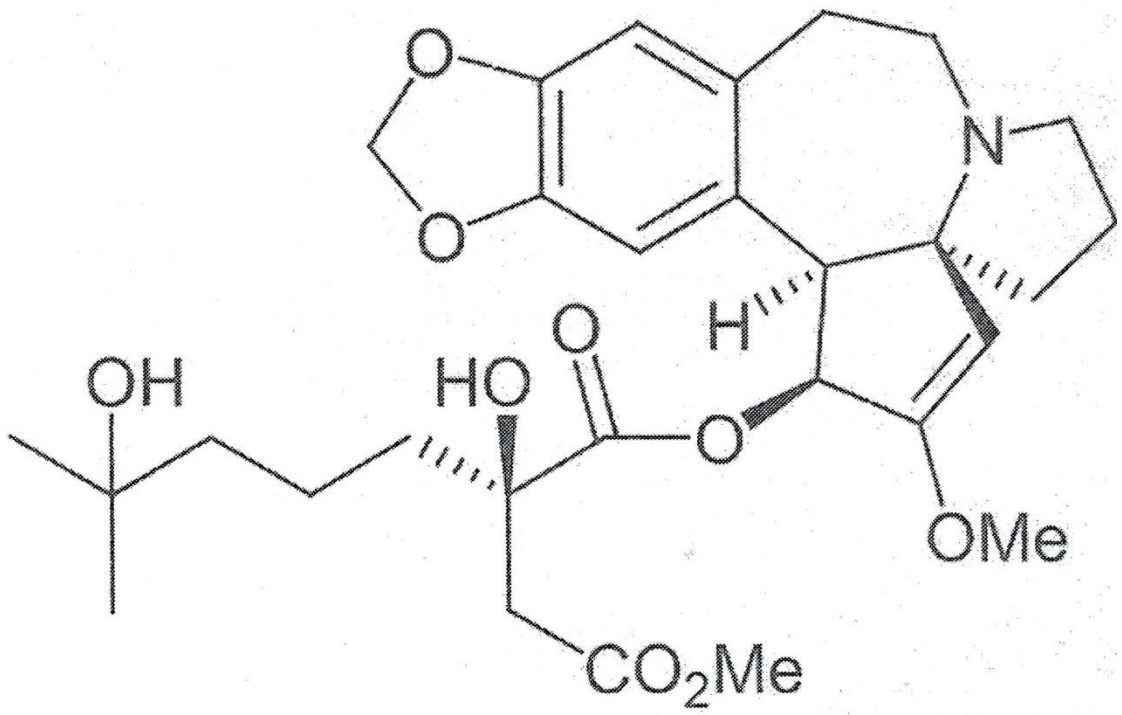
Activity of *Cephalotaxus* Alkaloids Against P388 Leukemia*

Alkaloid	Dose mg/kg	Survivors	Survival Time Days (T/C)	T/C × 100
Harringtonine	1.0	6/6	36.5/9.0	405
Isoharringtonine	7.5	6/6	24.5/9.0	272
Homoharringtonine	1.0	6/6	30.5/9.0	338
Deoxyharringtonine	2.0	6/6	18.0/10.0	180

* CCNSC data for maximum T/C dose.

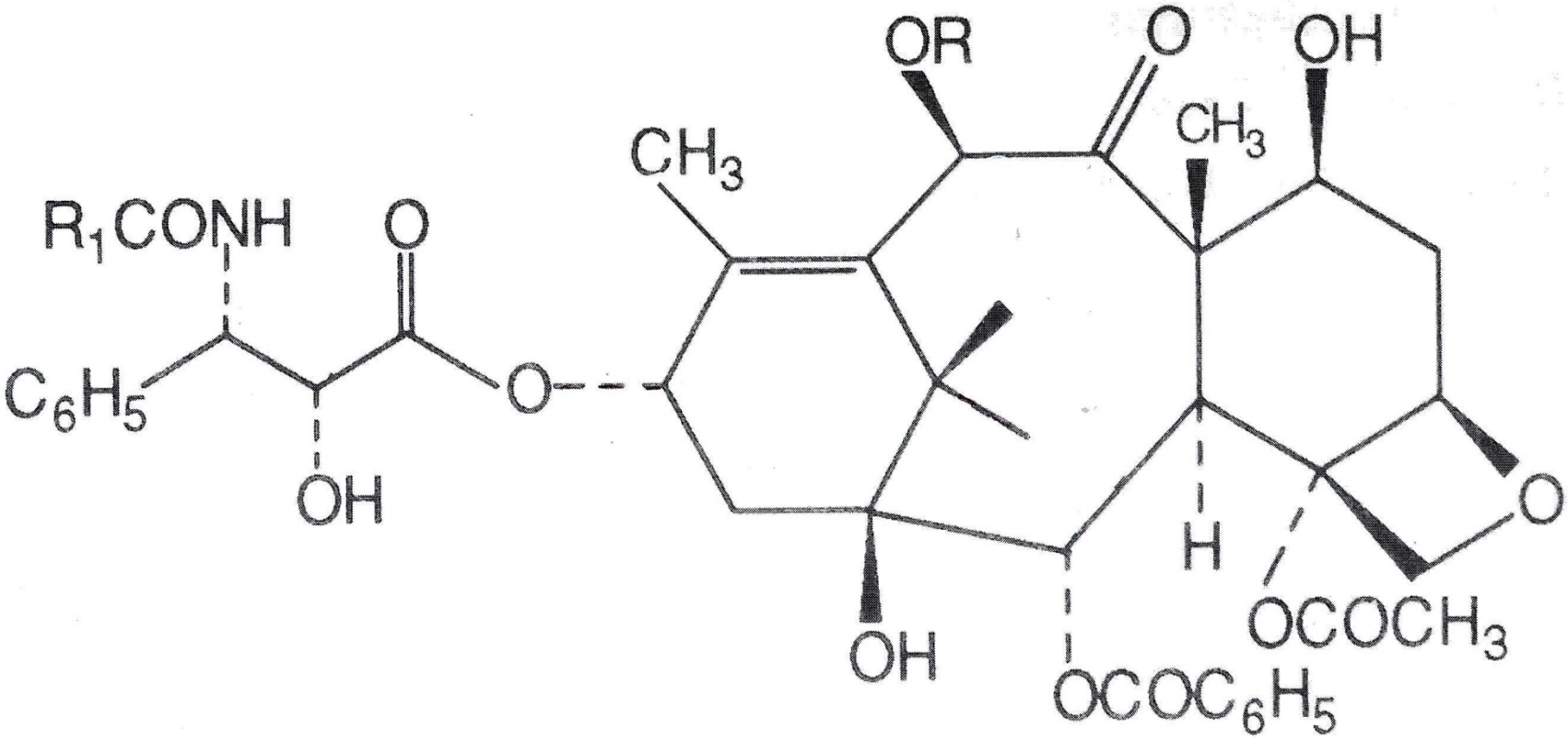
Cephalotaxus in Southeast Asia



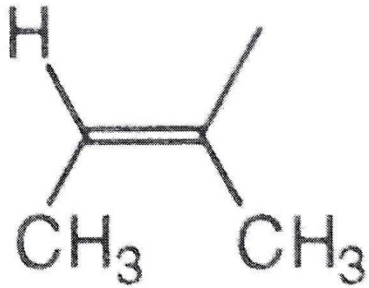


Homoharringtonine

NSC 141633, CAS number 26833-87-4, HHT, sHHT, Omacetaxine mepsuccinate, Synribo



Taxol $R = Ac, R_1 = C_6H_5$

Cephalomannine $R = Ac, R_1 =$ 

Antitumor Alkaloids from *Cephalotaxus harringtonia*: Structure and Activity. Powell, R. G.; Weisleder, D.; Smith, C. R., Jr. *J. Pharm. Sci.* 1972, *61*, 1227-1230.

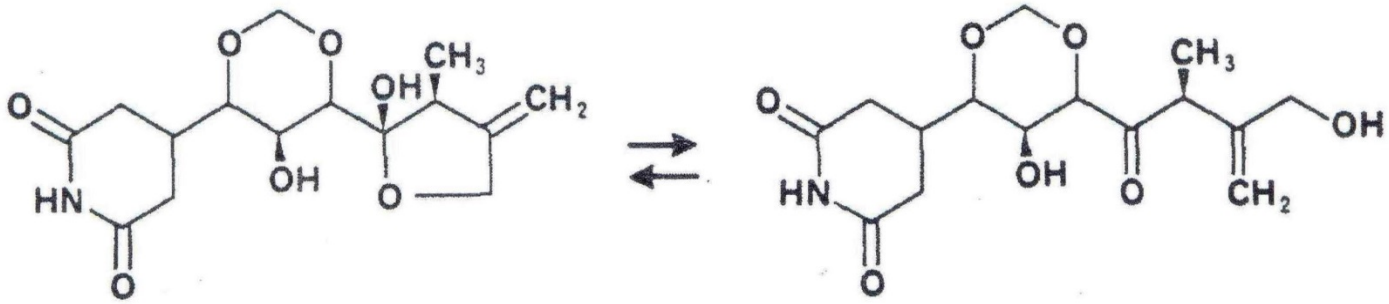
Isolation of Antitumor Alkaloids from *Cephalotaxus harringtonia*. Powell, R. G.; Rogovin, S. P.; Smith, C.R., Jr. *Ind. Eng. Chem. Prod. Res. Dev.* 1974, *13*, 129-132.

On October 26, 2012, the United States Food and Drug Administration (FDA) approved Synribo® (omacetaxine mepesuccinate) to treat adults with chronic myelogenous leukemia (CML)

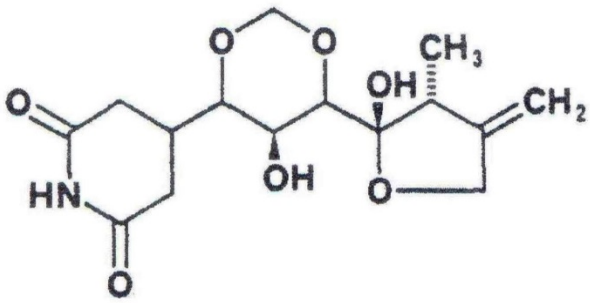
Homoharringtonine and Omacetaxine for Myeloid Hematological Malignancies. Lu, S.; Wang, J. *J. Hematol. Oncol.* 2014, *7*:2 (http://www.jhoonline.org/content/7/1/2)

Cephalomannine: A New Antitumor Alkaloid from *Cephalotaxus mannii*. Powell, R. G.; Miller, R. W.; Smith, C. R., Jr. *J. Chem. Soc. Chem. Commun.* 1979, *3*, 102-104.

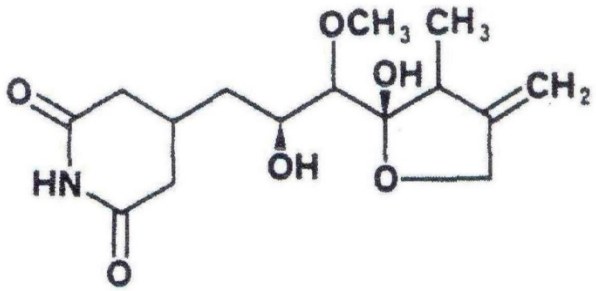
Antileukemic Alkaloids from *Taxus wallichiana* Zucc. Miller, R. W.; Powell, R. G.; Smith, C.R., Jr.; Arnold, E.; Clardy, J. *J. Org. Chem.* 1981, *46*, 1469-1474.



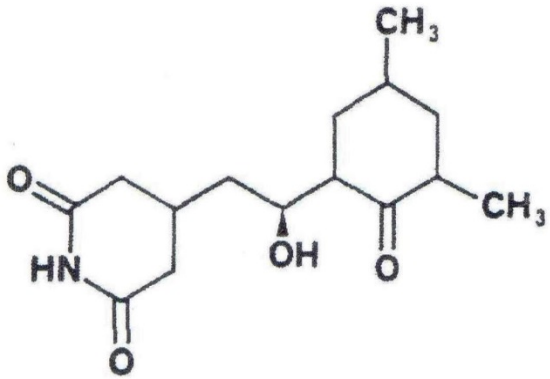
Sesbanimide A



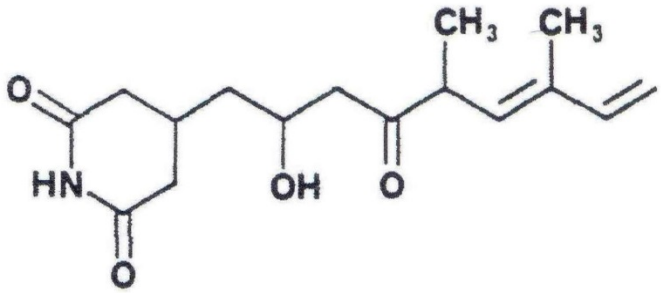
Sesbanimide B



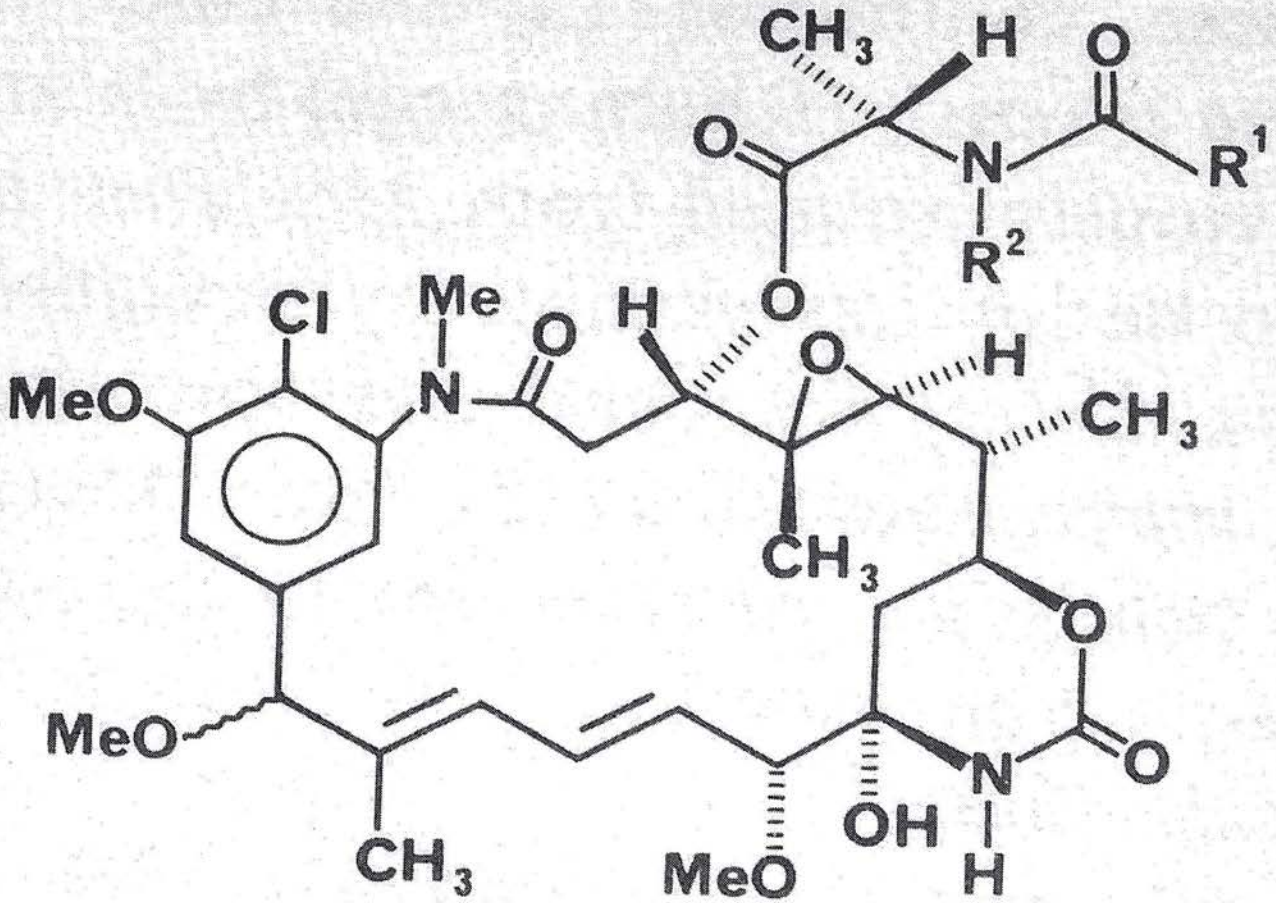
Sesbanimide C



Cycloheximide



Streptimidone



Trewiasine, $R^1 = CH(CH_3)_2$; $R^2 = CH_3$

Dehydrotrewiasine, $R^1 = C(CH_3){=}CH_2$; $R^2 = CH_3$

Demethyltrewiasine, $R^1 = CH(CH_3)_2$; $R^2 = H$

SUMMARY

Plant seeds can be rich sources of potential antitumor active compounds.

Thorough literature searches and accurate botanical identifications are essential before beginning studies of plant collections. (*Cephalotaxus Mannii* collection re-identified as *Taxus wallichiana* as an example)

Voucher specimens are critical to confirm identity of original samples and to assist in recollections. GPS coordinates as to location of the collection should also be reported.

Possibility of endophytes should be considered.