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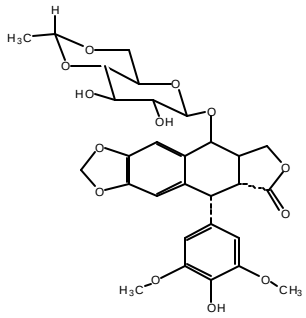
ProductInformation

ETOPOSIDE
Sigma Prod. No. E1383



E1383 Etoposide

CAS NUMBER: 33419-42-0
SYNONYMS: EPEG[1]; VP-16; VP-16213; NK 171; NSC-141540; 4'-Demethylepipodophyllotoxin 9-(4,6-O-Ethylidene-β-D-Glucopyranoside)[2]

PHYSICAL DESCRIPTION:
Appearance: Powder, white to white with a yellow cast.
Molecular formula: $C_{29}H_{32}O_{13}$
Molecular weight: 588.6
Melting point: 236-251°C
pK_a: 9.8.[1]
E^M(283nm) = 4245 (Absolute Methanol)
Purity: Not less than 98% (Thin-Layer Chromatography)[3]

METHOD OF PREPARATION:
Etoposide is semisynthetically prepared from podophyllotoxin.[4] Various synthetic methods have been reported.[5]

SOLUBILITY / SOLUTION STABILITY:
Etoposide is poorly soluble in water but soluble in organic solvents such as ethanol, methanol and DMSO to different extents.[4,6,7] Aqueous solutions are most stable at pH 4-5.[5] A 50 mM solution can be prepared in dimethyl sulfoxide as a stock solution. Dilutions of about 1000-fold can be made in media such as RPMI or Hank's Balanced Salt Solution (HBSS). Etoposide was reportedly dissolved in a small volume of DMSO and diluted to the appropriate concentration with 0.9% sodium chloride (final volume of DMSO did not exceed 1%).[7] Etoposide can also be dissolved in Tween 80 or in a mixture containing polyethylene glycol 300, ethanol, and Tween 80 then diluted with water or balanced salt solutions for use in cell culture or in animals.[8]

Solutions of 0.25 g/L in either 0.9% sodium chloride, 5% dextrose or a solution of dextrose:NaCl (4%:0.18%) were stable for about 96 hours while a 1 g/L solution was stable for 5 hours at room temperature. Stability of solutions was not affected by storing at 4°C or at -20°C nor by storing in the light or dark.[9]

USAGE/APPLICATIONS:
Etoposide inhibits DNA synthesis and is very active against cells in the late S and G_2 phases of the cell cycle.[10] Metabolic activation of etoposide by oxidation into the O-quinone derivative may play a significant role in its activity against DNA.[11] Etoposide induces double- and single-strand breaks in DNA in intact cells and in the nuclei but not in purified DNA preparations.[5] The DNA lesions may be due to the interference of etoposide with the scission-reunion reaction of mammalian topoisomerase.[12] Etoposide has been shown to cause significant inhibition of the uptake of uridine and thymidine in intact HeLa cells at 100 µM.[13]. The teratogenic and cytogenic effects in mice were reported as well as effects on experimental tumors.[7,8] Discussion of the physicochemical properties, possible mechanisms of action, metabolism and bioanalysis of etoposide, have also been published.[7,9,12,13,14,15]

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GENERAL NOTES:
Etoposide is a derivative of podophyllotoxin (Sigma Product No. P4405) with antimitotic and antineoplastic properties. As an antineoplastic agent the pharmaceutical grade is reportedly used in the treatment of different malignant neoplasms such as leukemia, and tumors of the brain lung, testis and stomach.[10] The product is toxic and a possible carcinogen. See information on the label and the Sigma Material Safety Data Sheet for handling information.

CITED REFERENCES:

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6. Martindale, *The Extra Pharmacopoeia*, 28th ed., 208 (1982).
7. Sieber, S.M. et al., *Teratology* 18, 31, (1978).
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11. van Maanen, J.M.S., *Human Toxicology*, 5, 136, (1986).
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14. Lee, K.-H. and Wang, H.-K., J. *Food and Drug Analysis*, 3, 209, (1995) (review).
15. Gupta, R.S, *Drug Resistance in Mammalian Cells, Volume II ,Anticancer and Other Drugs*, Chapter 5, 89, CRC Press, Boca Raton, FL, (1989) (review).

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Fujii, M.F. et al. "Effects of Mitomycin-C and Etoposide in Cell Culture and in Nude Mice: The Role of G-CSF Mutein" *Cancer Investigation*, 11(3), 283-290, (1993).