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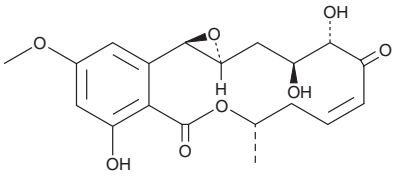
PRODUCT INFORMATION

Hypothemycin

Item No. 27913

CAS Registry No.: 76958-67-3
Formal Name: (1aR,3S,4S,6Z,9S,15bR)-1a,8,9,15b-tetrahydro-3,4,12-trihydroxy-14-methoxy-9-methyl-3H-oxireno[k][2]benzoxacyclotetradecin-5,11(2H,4H)-dione
Synonym: NSC 354462
MF: $C_{19}H_{22}O_8$
FW: 378.4
Purity: ≥95%
UV/Vis.: λ_{max}: 221, 267, 310 nm
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years
Item Origin: Fungus/*Phoma* sp.



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Hypothemycin is supplied as a solid. A stock solution may be made by dissolving the hypothemycin in the solvent of choice, which should be purged with an inert gas. Hypothemycin is soluble in the organic solvent DMSO at a concentration of approximately 10 mg/ml.

Description

Hypothemycin is a resorcylic acid lactone polyketide originally isolated from *H. tricothecoides* that has diverse biological activities.[1-6] Hypothemycin inhibits MEK (IC_{50} = 15 nM) and other protein kinases containing a conserved cysteine residue in the ATP-binding domain, including ERK, PDGFR, VEGFR, PKD1, and MAPKAP5/MK5.[3,4] It also inhibits transforming growth factor β-activated kinase 1 (TAK1) *in vitro* (IC_{50} = 33 nM).[5] Hypothemycin inhibits proliferation of cancer cell lines dependent on activating mutations, including A549, MV-4-11, and EOL1 cells (IC_{50}s = 6, 0.006, and 0.0004 µM, respectively) and reduces tumor growth in Ma44 and HCT116 mouse xenograft models when administered at a dose of 25 mg/kg per day.[4,6]

References

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3. Zhao, A., Lee, S.H., Mojena, M., *et al.* Resorcylic acid lactones: Naturally occurring potent and selective inhibitors of MEK. *J. Antibiot. (Tokyo)* **52(12),** 1086-1094 (1999).
4. Schirmer, A., Kennedy, J., Murli, S., *et al.* Targeted covalent inactivation of protein kinases by resorcylic acid lactone polyketides. *Proc. Nat. Acad. Sci. USA* **103(11),** 4234-4239 (2006).
5. Fakhouri, L., El-Elimat, T., Hurst, D.P., *et al.* Isolation, semisynthesis, covalent docking and transforming growth factor beta-activated kinase 1 (TAK1)-inhibitory activities of (5Z)-7-oxozeaenol analogues. *Bioorg. Med. Chem.* **23(21),** 6993-6999 (2015).
6. Tanaka, H., Nishida, K., Sugita, K., *et al.* Antitumor efficacy of hypothemycin, a new Ras-signaling inhibitor. *Jpn. J. Cancer Res.* **90(10),** 1139-1145 (1999).

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