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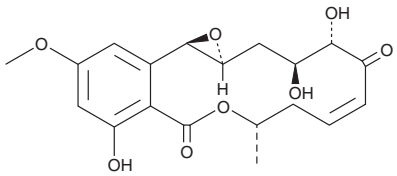
PRODUCT INFORMATION

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: ≥98%
Supplied as: A solid
Storage: -20°C
Stability: ≥2 years
Item Origin: Fungi/*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 DMSO.

Description

Hypothemycin is a resorcylic acid lactone polyketide originally isolated from *H. tricothecoides* that has diverse biological activities, including fungicidal, kinase inhibitory, and anticancer properties.[1-6] It is active against the pathogenic fungi *P. litchii*, completely inhibiting spore germination when used at a concentration of 0.78 µg/ml.[2] 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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