Hypothemycin

Cat. No.: HY-107417

CAS No.: 76958-67-3

Molecular Formula: $C_{19}H_{22}O_8$

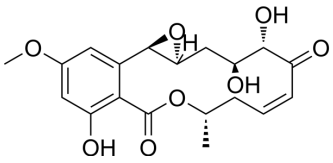
Molecular Weight: 378.37

Target: VEGFR; MEK; ERK; PDGFR; FLT3

Pathway: Protein Tyrosine Kinase/RTK; MAPK/ERK Pathway; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (264.29 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6429 mL	13.2146 mL	26.4292 mL
	5 mM	0.5286 mL	2.6429 mL	5.2858 mL
	10 mM	0.2643 mL	1.3215 mL	2.6429 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.61 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Hypothemycin, a fungal polyketide, is a multikinase inhibitor with K_is of 10/70 nM, 17/38 nM, 90 nM, 900 nM/1.5 μM, and 8.4/2.4 μM for VEGFR2/VEGFR1, MEK1/MEK2, FLT-3, PDGFRβ/PDGFRα, and ERK1/ERK2, respectively[1][2].

IC_{50} & Target

VEGFR2 10 nM (Ki)	VEGFR1 70 nM (Ki)	MEK1 17 nM (Ki)	MEK2 38 nM (Ki)
FLT-3 90 nM (Ki)	PDGFRα 1.5 μM (Ki)	PDGFRβ 900 nM (Ki)	ERK1 8.4 μM (Ki)

	ERK2 2.4 μM (Ki)
In Vitro	Hypothemycin inhibits eosinophilic EOL1 cell carrying mutations in FIP1L1-PDGFRα, acute myeloid leukemia MV-4-11 cell carrying mutations in FLT3-ITD, melanoma COLO829 cell carrying mutations in BRAF V600E, HUVEC cell carrying mutations in VEGFR, mastocytoma P815 cell carrying mutations in c-KIT D814Y, NSCLC A459 cell carrying mutations in KRAS, and ovarian SKOV-3 cell carrying mutations in HER2 with IC_{50}s of 0.4 nM, 6 nM, 50 nM, 70 nM, 370 nM, 6.0 μM, and 7.0 μM, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Hypothemycin (10 mg/kg) kills T. brucei in infected mice, completely curing the infection in one third of animals, although high doses of Hypothemycin (>10 mg/kg) leads to side effects[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Adult female Balb/c mice (weighing 18–22 g) infected with T. brucei[1]
Dosage:	10 mg/kg
Administration:	Administered once daily via intraperitoneal injection for 7 days.
Result:	Showed a dose-dependent reduction in parasitemia in infected mice. Prolonged survival of infected mice over 30 days, with a cure rate of 33%.

REFERENCES

[1]. Schirmer A, et al. Targeted covalent inactivation of protein kinases by resorcylic acid lactone polyketides. Proc Natl Acad Sci U S A. 2006 Mar 14;103(11):4234-9.

[2]. Nishino M, et al. Hypothemycin, a fungal natural product, identifies therapeutic targets in Trypanosoma brucei. Elife. 2013 Jul 9;2:e00712.

Caution: Product has not been fully validated for medical applications. For research use only.

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