Nitisinone

Cat. No.: HY-B0607

CAS No.: 104206-65-7

Molecular Formula: $C_{14}H_{10}F_3NO_5$

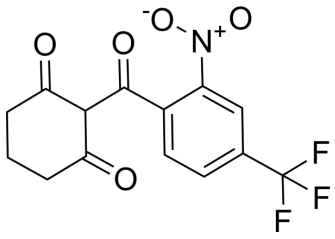
Molecular Weight: 329.23

Target: HPPD

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (126.57 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0374 mL	15.1870 mL	30.3739 mL
	5 mM	0.6075 mL	3.0374 mL	6.0748 mL
	10 mM	0.3037 mL	1.5187 mL	3.0374 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 (7.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nitisinone is an orally active, competitive and reversible 4-hydroxyphenylpyruvate dioxygenase (4-HPPD) inhibitor with an IC_{50} of 173 nM. Nitisinone promotes tyrosine accumulation in a dose-dependent manner. nitisinone can be used in studies of hereditary tyrosinemia type 1 (HT-1) (a rare genetic disorder) and albinism[1][2][3][4].

In Vitro

Nitisinone (0.01-10 μM; 72 h) promotes tyrosine accumulation in a dose-dependent manner[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Human primary fibroblasts (HFb)

Concentration:	0.01-10 μM
Incubation Time:	72 h
Result:	Exhibited massive intracellular accumulation of tyrosine in human cell cultures.

In Vivo

Nitisinone (5, 10 mg/kg; p.o.; 5 days aweek for 6 weeks) inhibits HPPD in a dose- and time- dependent manner in rat liver[2].
Nitisinone (4 mg/kg; p.o.; single daily; one day interval for 1 month) elevates tyrosine in both OCA-1A and OCA-1B model[3].
Nitisinone (4 mg/kg; p.o.; single daily; one day interval for 1 month) increases coat and iris pigmentation and melanin content in the melanosomes of ocular tissues in a mouse model of OCA-1B[3].
Note: Oculocutaneous albinism, type 1 (OCA1). There are 2 forms of OCA1, OCA-1A and OCA-1B. Individuals with the former lack functional tyrosinase and therefore lack melanin, while individuals with the latter produce some melanin[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Wistar rats (120-150 g)[2].
Dosage:	5, 10 mg/kg
Administration:	Oral gavage; 5 days aweek for 6 weeks.
Result:	Inhibited HPPD in a dose- and time- dependent manner in rat liver. (rat liver form animal model, incubate with 0-200 nM Nitisinone for 3 min).

Animal Model:	C57BL/6J mice (WT mice), $Tyrc^{-2J/c-2J}$ mice (model of OCA-1A) and $Tyrc^{-h/c-h}$ mice (model of OCA-1B) (all are 3 to 4-month-age)[3].
Dosage:	4 mg/kg
Administration:	Oral gavage; single daily; every other day for 1 month.
Result:	Elevated plasma tyrosine levels 4- to 6- fold compared with placebo-treated controls, after 1 month in both OCA-1A and OCA-1B model. Increased pigmentation in the irides and pigmentation in areas of new hair growth upon physical, in OCA-1B model. Significant increased in the number of pigmented melanosomes in OCA-1B model. Showed substantial pigmentation in the irides of $Tyrc^{-h/c-h}$ pups born of Nitisinone-treated mothers.

CUSTOMER VALIDATION

- Int Immunopharmacol. 2022 Aug 6;111:109098.

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REFERENCES

[1]. Laschi M, et al. Inhibition of para-Hydroxyphenylpyruvate Dioxygenase by Analogues of the Herbicide Nitisinone As a Strategy to Decrease Homogentisic Acid Levels, the Causative Agent of Alkaptonuria. ChemMedChem. 2016 Apr 5;11(7):674-8.

[2]. Ellis MK, et al. Inhibition of 4-hydroxyphenylpyruvate dioxygenase by 2-(2-nitro-4-trifluoromethylbenzoyl)-cyclohexane-1,3-dione and 2-(2-chloro-4-

methanesulfonylbenzoyl)-cyclohexane-1,3-dione. Toxicol Appl Pharmacol. 1995 Jul;133(1):12-9.

[3]. Onojafe IF, et al. Nitisinone improves eye and skin pigmentation defects in a mouse model of oculocutaneous albinism. J Clin Invest. 2011 Oct;121(10):3914-23.

[4]. Aktuglu-Zeybek A, et al. Nitisinone: a review. Orphan Drugs: Research and Reviews, 2017, 7.

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