Tetrahydrobiopterin

Cat. No.: HY-107383

CAS No.: 17528-72-2

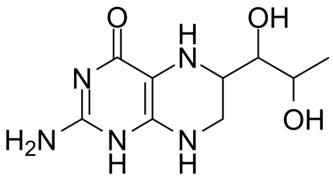
Molecular Formula: $C_9H_{15}N_5O_3$

Molecular Weight: 241.25

Target: NO Synthase; Endogenous Metabolite

Pathway: Immunology/Inflammation; Metabolic Enzyme/Protease

Storage: -20°C, protect from light, stored under nitrogen
* In solvent : -80°C, 2 years; -20°C, 1 year (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (207.25 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.1451 mL	20.7254 mL	41.4508 mL
	5 mM	0.8290 mL	4.1451 mL	8.2902 mL
	10 mM	0.4145 mL	2.0725 mL	4.1451 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 (10.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (10.36 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tetrahydrobiopterin ((Rac)-Sapropterin) is a cofactor of the aromatic amino acid hydroxylases enzymes and also acts as an essential cofactor for all nitric oxide synthase (NOS) isoforms.

IC_{50} & Target

Human Endogenous Metabolite

In Vitro

MicMicroglial cell cultures under hyperoxia are supplemented or not with an effective dose of Tetrahydrobiopterin (BH4) (100 μM). Exposure of microglial cells to hyperoxia-induced oxidative stress for 24 h reveals a robust increase in TSP-1 mRNA expression and protein compare to normoxia (21% O_2). Tetrahydrobiopterin supplementation significantly prevents hyperoxia-induced microglial activation by diminishing Iba-1 and TSP-1 expression? and prevents microvascular injury in

	choroidal explants[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To assess the levels of Tetrahydrobiopterin in the retina, three to five pools of retinas are collected from WT and hph-1mice at postnatal age 7, 14, and 22 and evaluated by LC-MS/MS. LC-MS/MS analysis confirm a significant decrease by approximately 90% in the concentration levels of Tetrahydrobiopterin in retinal tissue from hph-1 mice (0.0009±0.0006; p<0.0001, 0.01±0.001; p<0.0001 and 2.45±0.40; p<0.005) compare to the WT group (0.014±0.001, 0.092±0.01, and 23.13±6.44) at P7, P14, and P22, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Microglia cell line (SIM-A9) is used and cultured. Briefly, microglial cells (800, 000 cells per well) are cultured in 6-well plates with DMEM/F12 (1:1) supplementing with 10% fetal bovine serum (FBS), 5% of horse serum (HS), and 1% penicillin/streptomycin. After 24 h, the cells are starved with DMEM/F12 (1:1) free of FBS and HS for 6 h. Then, microglial cells cultures in presence or absence of 100 μM of Tetrahydrobiopterin are exposed to hyperoxia (75% oxygen and 25% nitrogen) in a modular incubator chamber and maintained in a humidified CO_2 incubator at 37 °C for 24 h. Microglial cells in matching controls are incubated at 37 °C in an incubator with 95% air and 5% CO_2 and collected at the same time point. Cell lysates are quickly processed for RNA. The conditioning media is stored at -80 and later used in choroidal explant assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice pups are exposed with their mothers in a 75% oxygen environment from postnatal day 7 to P9 using oxycycler to induce retinal vaso-obliteration (VO). Animals are anesthetized and injected intravitreally at P7 with 100 μM of Tetrahydrobiopterin or vehicle (sterile PBS 1×) using a syringe equipped with 50-gauge glass capillary. At P9, mice pups are sacrificed and retinas are dissected and stained overnight at 4 °C with fluorescein-labeled Griffonia Simplicifolia Lectin 1 (GSL 1), isolectin B4 (1:100) with 1 mM $CaCl_2$ in PBS. Quantification of VO is assessed using the computer software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Rivera JC, et al. Tetrahydrobiopterin (BH4) deficiency is associated with augmented inflammation and microvascular degeneration in the retina. J Neuroinflammation. 2017 Sep 6;14(1):181.

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