

Product Data Sheet

Product Name: 3-hydroxy-DL-Kynurenine

Cat. No.: GC45336

Chemical Properties

Cas. No. 2147-61-7

Chemical Name $\alpha,2$ -diamino-3-hydroxy- γ -oxo-benzenebutanoic acid

SMILES OC1=CC=CC(C(CC(N)C(O)=O)=O)=C1N

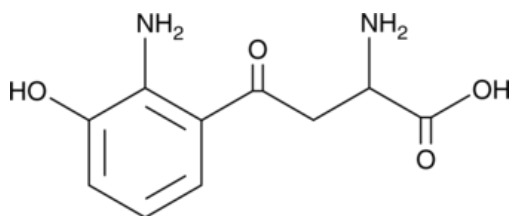
Formula $C_{10}H_{12}N_2O_4$ M.Wt 224.2

Solubility DMF: 0.5 mg/ml, DMSO: 1 mg/ml, Ethanol: 2 mg/ml, PBS (pH 7.2): 0.5 mg/ml
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Murine CD4⁺ T cells

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

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CD3/CD28 bead-stimulated CD4⁺ T cells were incubated for 72 hours in the presence of 3-hydroxy-DL-Kynurenine at concentrations varying from 0 to 100µM.

Reaction Conditions 0-100µM; 72h

Applications 3-hydroxy-DL-Kynurenine significantly inhibited CD4⁺ T-cell proliferation in a dose-dependent manner with IC₅₀ of approximately 70µM.

Animal experiment [2]:

Animal models Male Wistar rats

Preparation Method 3-hydroxy-DL-Kynurenine was administered as a single 50nmol intrastriatal injection dissolved in 1µL DMSO into the rat striatum.

Dosage form 1µL of 50nmol; intrastriatal injection; a single administration

Applications 3-hydroxy-DL-Kynurenine induced lesion around the injected area characterized by a dose-dependent, well-defined cavity surrounded by necrosis and reactive gliosis.

References:

[1]Sarah S Zaher, Germain C, Fu H, et al. 3-hydroxykynurenine suppresses CD4⁺ T-cell proliferation, induces T-regulatory-cell development, and prolongs corneal allograft survival. Invest Ophthalmol Vis Sci. 2011 Apr 22;52(5):2640-8.

[2]Nakagami Y, Saito H, Katsuki H. 3-Hydroxykynurenine toxicity on the rat striatum in vivo. Jpn J Pharmacol. 1996 Jun;71(2):183-6.

Background

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3-hydroxy-DL-Kynurenine is a potential endogenous neurotoxin which significantly inhibited CD4⁺ T-cell proliferation in a dose-dependent manner with IC₅₀ value of approximately 70μM. 3-hydroxy-DL-Kynurenine is a metabolic intermediate of the kynurenine pathway, the major metabolic pathway of tryptophan (Trp). Increased levels of 3-hydroxy-DL-Kynurenine have been described in several neurodegenerative disorders^{[1][2]}.

In vitro, human colon cancer HCT116 cells treated with 3-hydroxy-DL-Kynurenine (0.008-2mM) for 6-48h disrupted TCA cycle metabolism, depleted glutathione levels and reduced cell viability in a dose-dependent manner^[3]. Neuronally derived hybrid cell line (N18-RE-105) was treated with increasing concentration of 3-hydroxy-DL-Kynurenine for 24h. 3-hydroxy-DL-Kynurenine was toxic to greater than 85% of cultured cells at concentrations in excess of 100μM. N18-RE-105 exposed to 500μM 3-hydroxy-DL-Kynurenine for 2h did not induced significant cell lysis, yet marked cell death emerged 22h after harvest^[4]. Human neurons and astrocytes treated with 3-hydroxy-DL-Kynurenine (0.1–1000μM) for 24h significantly increased intracellular NAD⁺ levels at a low concentration of 100nM but substantially decreased NAD⁺ levels at higher concentrations. Treatment with 3-hydroxy-DL-Kynurenine increased extracellular LDH activity at concentrations above 100nM in both cell types^[5].

In vivo, kynurenine 3-monooxygenase (KMO) is a pivotal enzyme in the kynurenine pathway (KP) and normally oxidizes kynurenine (KYN) to 3-hydroxy-DL-Kynurenine in the presence of reduced NADPH and molecular oxygen. Endotoxic shock was induced in KMO^{-/-} C57BL/6N mice with 15mg/kg LPS. KMO^{-/-} mice given 10mg/kg 3-hydroxy-DL-Kynurenine i.p. every 12h after LPS survived significantly longer than PBS-treated KMO^{-/-} mice by inhibiting inflammation via halving serum IL-6 and blocking ATF4 nuclear translocation^[6]. Intrastriatal injection of 1μl of 3-hydroxy-DL-Kynurenine (50nmol) dissolved in DMSO into Wistar rats brain induced lesion at the injected area characterized by a dose-dependent, well-defined cavity surrounded by necrosis and reactive gliosis^[7].

References:

- [1] Okuda S, Nishiyama N, Saito N, and Katsuki H. 3-Hydroxykynurenine, an endogenous oxidative stress generator, causes neuronal cell death with apoptotic features and region selectivity. J Neurochem. 1998 Jan;70(1):299-307.
- [2] Sarah S Zaher, Germain C, Fu H, et al. 3-hydroxykynurenine suppresses CD4⁺ T-cell proliferation,

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induces T-regulatory-cell development, and prolongs corneal allograft survival. Invest Ophthalmol Vis Sci. 2011 Apr 22;52(5):2640-8.

[3] Buchanan J L, Rauckhorst A J, Taylor E B. 3-hydroxykynurenine is a ROS-inducing cytotoxic tryptophan metabolite that disrupts the TCA cycle. bioRxiv. 2023 Jul 10:2023.07.10.548411.

[4] Eastman C L, Guilarte T R. Cytotoxicity of 3-hydroxykynurenine in a neuronal hybrid cell line. Brain Res. 1989 Aug 28;495(2):225-31.

[5] Braidy N, Grant R, Brew B J, et al. Effects of Kynurenine Pathway Metabolites on Intracellular NAD Synthesis and Cell Death in Human Primary Astrocytes and Neurons. Int J Tryptophan Res. 2009;2:61-9.

[6] Hoshi M, Kubo H, Ando T, et al. 3-Hydroxykynurenine Regulates Lipopolysaccharide-Stimulated IL-6 Production and Protects against Endotoxic Shock in Mice. Immunohorizons. 2021 Jun 28;5(6):523-534.

[7] Nakagami Y, Saito H, Katsuki H. 3-Hydroxykynurenine toxicity on the rat striatum in vivo. Jpn J Pharmacol. 1996 Jun;71(2):183-6.

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