Ethoxzolamide

Cat. No.: HY-B1480

CAS No.: 452-35-7

Molecular Formula: $C_9H_{10}N_2O_3S_2$

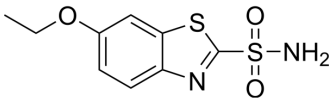
Molecular Weight: 258.32

Target: Carbonic Anhydrase; Bacterial

Pathway: Metabolic Enzyme/Protease; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (387.12 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.8712 mL	19.3558 mL	38.7117 mL
5 mM	0.7742 mL	3.8712 mL	7.7423 mL
10 mM	0.3871 mL	1.9356 mL	3.8712 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: ≥ 2.08 mg/mL (8.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (8.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (8.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ethoxzolamide is a carbonic anhydrase inhibitor with K_i of 1 nM.

IC_{50} & Target

Ki: 1 nM (carbonic anhydrase)[1]

In Vitro

Ethoxzolamide (ETZ) treatment causes >90% inhibition of reporter GFP fluorescence in infected macrophages. Moreover, in

	a 9-day macrophage survival assay, Ethoxzolamide (ETZ) treatment significantly inhibits the ability of M. tuberculosis to grow intracellularly[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	It is discovered that the lipid-soluble ethoxzolamide is converted in vivo to a water-soluble metabolite, while retaining high activity againstt the enzyme. At the minimal dose for maximal effect (4 mg/kg i.v. at 45 min) the IOP lowering is 4.2 mmHg, the concentration in anterior uvea is 2.5 pmol/kg, and the fractional inhibition of the enzyme (i) is 0.9995. The effect declines rapidly, attributable to the very short half-life of drug in plasma, leading to depletion of free drug in the anterior uvea and other tissues[1]. Ethoxzolamide (ETZ) strongly downregulates GFP reporter fluorescence in mouse lungs, with 3-fold inhibition of GFP signal compare to that in the mock-treating control. There is a significant reduction of bacterial survival in the lungs of ETZ-treating mice compare to the mock-treating control[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	BMDMs are treated with 80 μM Ethoxzolamide (ETZ) or an equivalent volume of DMSO every 2 days for 9 days total. At days 3, 6, and 9, intracellular bacteria are quantified by lysing macrophage monolayers and performing serial dilution plating of lysates on 7H10 agar. For fluorescence microscopy experiments, macrophages are seeded on glass coverslips before infection with M. tuberculosis CDC1551. Samples are treated every 2 days with 100 μM Ethoxzolamide (ETZ) or an equal volume of DMSO for 9 days[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Rats (male, 300–325 g) are randomly selected into 2 groups (n=6 each group) and Ethoxzolamide (EZ) is administered at a dose of 0.18 mg/kg (in PEG 300: ethanol, 1:1) via i.v. injection through the tail vein. Blood samples (about 50-100 μL) are collected in heparinizing tubes at 0, 15, 30, 60, 120, 180, 240, 360, 540, and 1440 min post-injection, via tail snip with isoflurane as anesthetic. Plasma samples are prepared and stored at -80 °C until analysis. To study the distribution in brain, rats in group 1 are scarified at 6 hours and rats in group 2 are scarified at 24 hours to collect the brain tissues. Those blood samples from group 2 are analyzed to generated PK profile[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Maren TH, et al. Relations among IOP reduction, ocular disposition and pharmacology of the carbonic anhydrase inhibitor ethoxzolamide. Exp Eye Res. 1992 Jul;55(1):73-9.

[2]. Benjamin K. Johnson, et al. The Carbonic Anhydrase Inhibitor Ethoxzolamide Inhibits theMycobacterium tuberculosis PhoPR Regulon and Esx-1 Secretion and Attenuates Virulence. Antimicrob Agents Chemother. 2015 Aug; 59(8): 4436–4445.

[3]. Song Gao, et al. Development and validation of an UPLC-MS/MS method for the quantification of ethoxzolamide in plasma and bioequivalent buffers: Applications to absorption, brain distribution, and pharmacokinetic studies. J Chromatogr B Analyt Technol Biomed Life Sci. 2015 Apr 1; 0: 54–59.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA