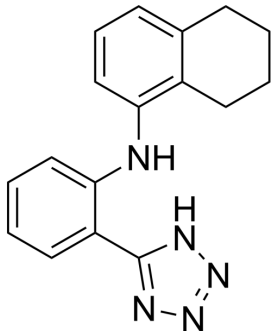
BL-1249

Cat. No.:	HY-108596
CAS No.:	18200-13-0
Molecular Formula:	$C_{17}H_{17}N_5$
Molecular Weight:	291.35
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (171.61 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4323 mL	17.1615 mL	34.3230 mL
	5 mM	0.6865 mL	3.4323 mL	6.8646 mL
	10 mM	0.3432 mL	1.7161 mL	3.4323 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 (8.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BL-1249 is a nonsteroidal anti-inflammatory agent (NSAID) and a potassium channel activator. BL-1249 potently activates $K_{2P}2.1$ (TREK-1) and $K_{2P}10.1$ (TREK-2) with EC_{50} values of 5.5 μM and 8.0 μM, respectively. BL-1249 extracellular application activates all TREK subfamily members but has no effect on other K_{2P} subfamilies. BL-1249 exhibits more selective for the bladder (EC_{50} of 1.26 μM) than vascular tissue (EC_{50} of 21.0 μM)[1][2].

IC_{50} & Target

EC50: 5.5 μM (TREK-1) and 8.0 μM (TREK-2)[1]

In Vitro

BL-1249 produces a concentration-dependent membrane hyperpolarization of cultured human bladder myocytes, assessed as either a reduction in fluorescence of the voltage-sensitive dye bis-(1,2-dibutylbarbituric acid)trimethine oxonol (EC_{50} of 1.26 μM) or by direct electrophysiological measurement EC_{50} of 1.49 μM). BL-1249 produced a concentration-dependent hyperpolarization with an EC_{50} of 21.0 μM in human aortic smooth muscle cells[1].

	In in vitro organ bath experiments, BL-1249 produces a concentration-dependent relaxation of 30 mM KCl-induced contractions in rat bladder strips (EC_{50} of 1.12 μM), yet has no effect on aortic strips up to the highest concentration tested (10 μM). The bladder relaxation produced by BL-1249 is partially blocked by Ba^{2+} (1 and 10 mM)[1]. BL-1249 is a selective agonist of the TREK subfamily when applied extracellularly, having preferential action on K_{2P}2.1(TREK-1) and K_{2P}10.1(TREK-2) over K_{2P}4.1(TRAAK) and establish that its mechanism of action relies on gating at the selectivity filter C-type gate[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BL-1249 (1 mg/kg) inhibits isovolumic bladder contractions in vivo. The short duration of the effect of BL-1249 on bladder contraction (30 min) is likely due to a fast elimination half-life of the compound after i.v. administration (0.69 h)[1]. BL-1249 (1 mg/kg) has little effect on mean arterial blood pressure, an observation again consistent with the in vitro bladder to vascular relaxant selectivity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Tertyshnikova S, et al. BL-1249 [(5,6,7,8-tetrahydro-naphthalen-1-yl)-[2-(1H-tetrazol-5-yl)-phenyl]-amine]: a putative potassium channel opener with bladder-relaxant properties. J Pharmacol Exp Ther. 2005 Apr;313(1):250-9.

[2]. Pope L, et al. Protein and Chemical Determinants of BL-1249 Action and Selectivity for K2P Channels. ACS Chem Neurosci. 2018 Dec 19;9(12):3153-3165.

[3]. Iwaki Y, et al. Towards a TREK-1/2 (TWIK-Related K+ Channel 1 and 2) dual activator tool compound: Multi-dimensional optimization of BL-1249. Bioorg Med Chem Lett. 2019 Jul 1;29(13):1601-1604.

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