L-765314

Cat. No.: HY-101385

CAS No.: 189349-50-6

Molecular Formula: $C_{27}H_{34}N_6O_5$

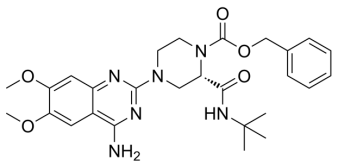
Molecular Weight: 522.6

Target: Adrenergic Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

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 : 50 mg/mL (95.68 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9135 mL	9.5675 mL	19.1351 mL
	5 mM	0.3827 mL	1.9135 mL	3.8270 mL
	10 mM	0.1914 mL	0.9568 mL	1.9135 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 (4.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.78 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

L-765314 is a potent and selective α1b adrenergic receptor antagonist with K_is of 5.4 nM and 2.0 nM for rat and human α1b adrenergic receptor, respectively.

IC_{50} & Target

Ki: 5.4±0.6 nM (rat α1b receptor), 2.0±0.66 nM (human α1b receptor), 50±8 nM (rat α1d receptor), 34±6 nM (human α1d receptor), 500±20 nM (rat α1b receptor), 420±62 nM (human α1b receptor)[1].

In Vitro

L-765314 exhibits two displacement sites. The high-affinity site accounts for approximately 25% of binding (IC_{50}) 1.90 nM

	and represents binding to the R1b sites. The low-affinity site accounts for the residual 75% of binding (IC_{50}) 790 nM and represents binding to the R1a sites[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The results of plasma assayed by liquid chromatograph/mass spectrometer (LCMS) show that the mean C_{max} of L-765314 (A322312) is 1.05 μM and the $t_{1/2}$ is 0.5 h. L-765314 shows weak potency for inhibiting the pressor response to either phenylephrine or A-61603 (AD_{25}>3 mg/kg for each). On the basis of the inhibition of pressor responses to the R1a subtype selective agonist A-61603, L-765314 appears to be selective versus the R1a receptor up to a dose of 0.3 mg/kg. The results of hypotensive potency in rats show that both L-765314 and terazosin tend to decrease heart rate (about 25 bpm at 1 mg/kg iv) [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] The potency of terazosin and L-765314 for inhibiting the pressor responses to phenylephrine and A-61603 is evaluated in anesthetized male Sprague-Dawley rats (n=4). The rats are dosed i.v with either vehicle or ascending doses of test compounds, and the peak changes in mean arterial pressure are measured. The dose of antagonist eliciting a 25 mmHg decrease in mean arterial pressure (AD_{25}) is calculated as an index of hypotensive potency. The rats are dosed i.v with L-765314 at 3 mg/kg , and the plasma is assayed by LCMS for parent compound[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Neuropharmacology. 2023 Oct 13:109757.

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REFERENCES

[1]. Patane MA, et al. 4-Amino-2-[4-[1-(benzyloxycarbonyl)-2(S)- [[(1,1-dimethylethyl)amino]carbonyl]-piperazinyl]-6, 7-dimethoxyquinazoline (L-765,314): a potent and selective alpha1b adrenergic receptor antagonist. J Med Chem. 1998 Apr 9;41(8):1205-8.

[2]. Tobias Böhmer, et al. The α1B-adrenoceptor subtype mediates adrenergic vasoconstriction in mouse retinal arterioles with damaged endothelium. Br J Pharmacol. 2014 Aug; 171(16): 3858–3867.

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