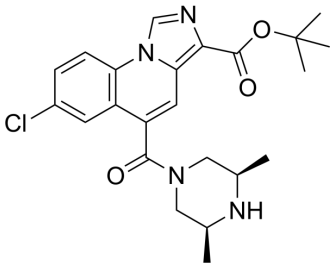
U-101017

Cat. No.:	HY-19250
CAS No.:	170568-47-5
Molecular Formula:	$C_{23}H_{27}ClN_4O_3$
Molecular Weight:	442.94
Target:	GABA Receptor
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	U-101017 is a partial agonist of benzodiazepine receptor and GABAA receptor, with anxiolytic effects.
In Vitro	PNU-101017 potentiates GABA-stimulated Cl^- currents at low concentrations (<1 μM)[1]. U-101017 concentration-dependently inhibits the binding of [^{3}H]FNZ to the membrane preparation of rat cerebral cortex in vitro with K_i of 3.37±0.22 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pre-ischemic treatment with either PNU-101017 significantly protects the CA1 neuronal population, and PNU-101017 reduces the loss to 50%. Delaying PNU-101017 administration until immediately after reperfusion does not reduce the neuroprotective activity[1]. U-101017 (30 μmol/kg, p.o.) time-dependently blocks [^{3}H]FNZ binding to the mouse cerebral cortex. U-101017 dose-dependently decreases the levels of cGMP with ED_{50}s of 260.0 (163-425) and 0.37 (0.12-1.04) in nonstressed and foot shock-stressed mice, respectively. Flumazenil, an antagonist of GABAA receptors, has no significant effect on cGMP in nonstressed mice, but pretreatment with flumazenil significantly blocks U-101017 (10 μmol/kg, p.o.)-induced reductions in cGMP. In stressed mice, flumazenil is ineffective in altering cerebellar cGMP, but pretreatment with these doses of flumazenil significantly ($p < 0.01$) blocks U-101017-induced attenuation of stress-induced elevations in cGMP [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Three groups of gerbils (N=9-11/group) are treated i.p. with either vehicle (0.05 N HCl), PNU-101017 (30 mg/kg) or diazepam (10 mg/kg) 30 min prior to ischemia and again 2 h after reperfusion. Two other groups receive PNU-101017 or diazepam immediately after reperfusion and again 2 h later. The tested doses of PNU-101017 and diazepam are selected from past studies demonstrating their neuroprotective efficacy in the gerbil forebrain ischemia model. The administration of the second dose at 2 h after reperfusion is consistent with previous dosing with other effective compounds tested in the gerbil. The 0.05 N HCl vehicle has been employed for i.p. dosing with other test compounds and is devoid of toxicity or acute distress production. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Hall ED, et al. Comparative neuroprotective properties of the benzodiazepine receptor full agonist diazepam and the partial agonist PNU-101017 in the gerbil forebrain ischemia model. Brain Res. 1998 Jul 6;798(1-2):325-9.

[2]. Sethy VH, et al. The novel anxiolytic U-101017: in vitro and ex vivo binding profile and effect on cerebellar cGMP. Pharmacol Biochem Behav. 1997 Oct;58(2):609-13.

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