Product Data Sheet

Product Name: U-101017 (PNU 101017)
Cat. No.: GC31013

Chemical Properties

Cas. No.	170568-47-5		
SMILES	O=C(C1=C2N(C=N1)C3=C(C=C(Cl)C=C3)C(C(N4C[C@@H](C)N[C@@H](C)C4)=O)=C2)OC(C)(C)C		
Formula	$C_{23}H_{27}ClN_4O_3$	M.Wt	442.94
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	U-101017 (PNU 101017)		

Protocol

Animal experiment:

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.

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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.

Background

U-101017 is a partial agonist of benzodiazepine receptor and GABAA receptor, with anxiolytic effects.

PNU-101017 potentiates GABA-stimulated Cl- currents at low concentrations (<1 μM)[1]. U-101017 concentration-dependently inhibits the binding of [3H]FNZ to the membrane preparation of rat cerebral cortex in vitro with Ki of 3.37±0.22 nM[2].

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 [3H]FNZ binding to the mouse cerebral cortex. U-101017 dose-dependently decreases the levels of cGMP with ED50s 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].

[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.