

Product Data Sheet

Product Name: Trofinetide (NNZ-2566)

Cat. No.: GC30804

Chemical Properties

Cas. No. 853400-76-7

SMILES O=C(O)CC[C@@H](C(O)=O)NC([C@@]1(C)N(C(CN)=O)CCC1)=O

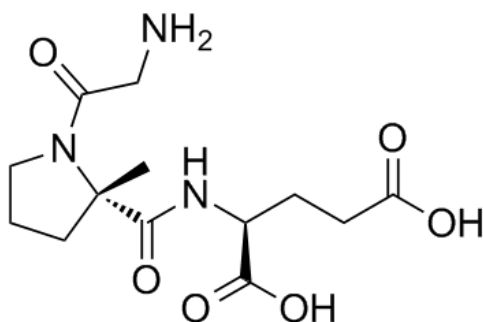
Formula $C_{13}H_{21}N_3O_6$ M.Wt 315.32

Solubility Water : ≥ 50 mg/mL (158.57 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

Cell lines BV2 cells

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

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Preparation Method BV2 cells were cultured in DMEM supplemented with 10% fetal bovine serum (FBS) at 37°C in 5% CO₂. Cells were plated onto a 96-well plate at a density of 3×10^3 cells/ml for 24h, and the cells were incubated with different concentrations of Trofinetide 1μM for 2h, followed by co-incubation with Aβ42 oligomers (10μM) for an additional 24h. After 72 hours, cell viability was analyzed.

Reaction Conditions 1μM; 2h

Applications Trofinetide pretreatment significantly rescued Aβ42-induced cytotoxicity in BV2 cells.

Animal experiment [2]:

Animal models Male Sprague-Dawley rats

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Male Sprague-Dawley rats were weighed and anaesthetized with 5% halothane/O₂ and maintained with 3% halothane/O₂ throughout surgery. A blunt 22G×8.5mm guide cannula was stereotaxically implanted and rested on the dura, positioned to enable an injection cannula to be lowered adjacent to the middle cerebral artery (0.2mm anterior, 5.2mm lateral to Bregma) and was anchored in place with dental cement. To enable intravenous (i.v.) infusion of Trofinetide, rats were surgically fitted with an indwelling catheter into the jugular vein and housed individually in metabolic cages before induction of the stroke-like injury. Three to four days following surgery, a stroke-like injury was induced. A 15.8mm 30G needle connected to a 1ml syringe with polythene tubing was inserted into the guide cannula, and ET-1 (100pmol in 3μl) was infused over a period of approximately 3min to induce vasoconstriction of the middle cerebral artery. Following stroke injury, Trofinetide or vehicle was administered intravenously via the indwelling catheter (10mg/kg/h for 4h, starting 3h after stroke). Five days following drug treatment, rats were sacrificed, and the brains were taken for histological analysis.

Dosage form 30mg/kg/h for 4h; i.v.

Applications Trofinetide treatment reduced brain injury size in rats subjected to focal stroke.

References:

- [1] Chen M, Ning Y, Yang H, et al. Trofinetide Improves Cognitive Function in APP/PS1 Mice by Suppressing Inflammation and Apoptosis[J]. Molecular Neurobiology, 2026, 63(1): 129.
- [2] Bickerdike M J, Thomas G B, Batchelor D C, et al. NNZ-2566: A Gly–Pro–Glu analogue with neuroprotective efficacy in a rat model of acute focal stroke[J]. Journal of the neurological sciences, 2009, 278(1-2): 85-90.

Background

Trofinetide (NNZ-2566) is a synthetic analogue of the endogenous N-terminal tripeptide Glycine Proline-Glutamate (GPE) with neuroprotective effects ^[1]. Trofinetide can cross the blood-brain barrier

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and improve synaptic function, repair synaptic structure, reduce neuroinflammatory substances in the brain, and enhance antioxidant response^[2]. Trofinetide has been widely used in Fmr1 knockout mice to correct learning and memory deficits, abnormal hyperactivity, and social interaction impairments^[3].

In vitro, Trofinetide pretreatment at 1 μ M for 2 hours effectively reversed the cytotoxicity of A β 42 (10 μ M; 24h) on BV2 cells and increased cell viability^[4]. Treatment with 10 μ M Trofinetide for 24h reversed okadaic acid-induced cell death in isolated embryonic striatal neurons^[5].

In vivo, Trofinetide treatment via continuous intravenous infusion at a rate of 3mg/kg/h for 12 hours inhibited neuroinflammation and proinflammatory cytokine expression induced by experimental penetrating ballistic-like brain injury in rats^[6]. Intravenous infusion of Trofinetide (10mg/kg/h) for 4 hours significantly reduced infarct size in rats caused by middle cerebral artery occlusion (MCAO) and attenuated weight loss^[7].

References:

- [1] Neul J L, Percy A K, Benke T A, et al. Trofinetide for the treatment of Rett syndrome: a randomized phase 3 study[J]. Nature Medicine, 2023, 29(6): 1468-1475.
- [2] Hudu S A, Elmigdad F, Qtaitat A A, et al. Trofinetide for Rett syndrome: highlights on the development and related inventions of the first USFDA-approved treatment for rare pediatric unmet medical need[J]. Journal of Clinical Medicine, 2023, 12(15): 5114.
- [3] Deacon R M J, Glass L, Snape M, et al. NNZ-2566, a novel analog of (1–3) IGF-1, as a potential therapeutic agent for fragile X syndrome[J]. Neuromolecular medicine, 2015, 17(1): 71-82.
- [4] Chen M, Ning Y, Yang H, et al. Trofinetide Improves Cognitive Function in APP/PS1 Mice by Suppressing Inflammation and Apoptosis[J]. Molecular Neurobiology, 2026, 63(1): 129.
- [5] Bickerdike M J, Thomas G B, Batchelor D C, et al. NNZ-2566: A Gly–Pro–Glu analogue with neuroprotective efficacy in a rat model of acute focal stroke[J]. Journal of the neurological sciences, 2009, 278(1-2): 85-90.
- [6] Wei H H, Lu X C M, Shear D A, et al. NNZ-2566 treatment inhibits neuroinflammation and pro-inflammatory cytokine expression induced by experimental penetrating ballistic-like brain injury in rats[J]. Journal of neuroinflammation, 2009, 6(1): 19.
- [7] Bickerdike M J, Thomas G B, Batchelor D C, et al. NNZ-2566: A Gly–Pro–Glu analogue with neuroprotective efficacy in a rat model of acute focal stroke[J]. Journal of the neurological sciences, 2009, 278(1-2): 85-90.

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