Product Data Sheet

Product Name: S-MTC
Cat. No.: GC31243

Chemical Properties

Cas. No.	156719-41-4		
SMILES	N[C@@H](CCCNC(SC)=N)C(O)=O		
Formula	$C_7H_{15}N_3O_2S$	M.Wt	205.28
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	S-MTC		

Protocol

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Cell experiment:

Mixed cortical glial and neuronal cultured cells are prepared from E15 to E18 embryos obtained from Spargue-Dawley rats. On day 7 after plating, the culture medium is removed and replaced with freshly prepared culture medium in the presence of either Aβ1-42 (1, 5, 10, or 20 μM), Aβ42-1, or peroxynitrite (100 or 200 μM) with or without either NG-nitro-L-arginine (L-NOARG,10 or 100 μM), S-MTC (10 or 100 μM), N-iminoethyl-L-lysine (10 or 100 μM), N-(3-(aminomethyl)benzyl)acetamidine (1400W,1 or 5 μM), 2-(4-carboxyphenyl)-4, 4, 5, 5-tetramethylimidazoline-1-oxyl-3-oxide (carboxy-PTIO,10 or 100 μM), or 6-hydorxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (10 or 100 μM) alone or in combination. The cultured cells are then incubated for 20 h. For the time-course studies, the cultured cells are pre-treated with the described culture medium containing Aβ1-42 (10 μM). Either L-NIL (100 μM), L-NOARG (100 μM), 1400W (5 μM), S-MTC (100 μM), carboxy-PTIO (100 μM) or Trolox (100 μM) are administered at 1, 4, and 8 h later. Assessments are carried out 20 h after Aβ1-42 administration. The viability of cultured cells is evaluated by using MTT and neutral red colorimetric assays. MTT reduction and NR uptake are quantified at 570 and 540 nm, respectively, by using a micro-plate reader[1].

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Animal experiment:

mice[2]Male NIH Swiss mice, weighing 18-22 g, are used. S-MTC (1.0 μg/mouse) is administered i.c.v. (15-min pretreatment time). In one set of experiments (#1, #2, and #3), opioid antagonists and NOS-inhibitors are administered 15–30 min prior to the 60-min HBO2 treatment (180 min prior to antinociceptive testing). In another experiment (#4), opioid antagonist and NOS-inhibitor pretreatment is administered 60 min following cessation of the 60-min HBO2 treatment (15–30 min prior to antinociceptive testing). For i.p. or s.c. pretreatments, the volume of injection is 0.1 mL/10 g body weight with control animals receiving an i.p. or s.c. injection of vehicle (sterile saline) only. For i.c.v. pretreatments, the volume of microinjection is 5.0 μL per mouse with control animals receiving an i.c.v. microinjection of vehicle (sterile saline) only.Rats[3]Male, Sprague-Dawley rats (350-450 g) are used. On the day after catheterisation (day 1), animals (n=7) receive bolus i.v. injections (0.1 mL) of either saline (vehicle), and 0.3 and 3 mg/kg S-MTC (n=4), or 0.1, 1 and 10 mg/kg S-MTC (n=3). On day 3, the dose regimen is switched to ensure that each animal has received all the doses of S-MTC. On each day, drugs are given in ascending dose-order, and at least 60 min is allowed between doses. The intervening day (day 2) is allowed for wash-out of any drug effects.

References:

[1]. Law A, et al. Neuroprotective and neurorescuing effects of isoform-specific nitric oxide synthase inhibitors, nitric oxide scavenger,

and antioxidant against beta-amyloid toxicity. Br J Pharmacol. 2001 Aug;133(7):1114-24.
[2]. Zelinski LM, et al. A prolonged nitric oxide-dependent, opioid-mediated antinociceptive effect of hyperbaric oxygenin mice. J Pain. 2009 Feb;10(2):167-72.
[3]. Wakefield ID, et al. Comparative regional haemodynamic effects of the nitric oxide synthase inhibitors, S-methyl-L-thiocitrulline and L-NAME, in conscious rats. Br J Pharmacol. 2003 Jul;139(6):1235-

Product Data Sheet

43.

Background

S-MTC is a selective type I nitric oxide synthase (NOS) inhibitor.

S-MTC (10 or 100 μM) reduces cellular NO release in the absence of Aβ1-42. At 100 μM, S-MTC decreases cell viability. S-MTC (100 μM) significantly lowers nitrite production (11.2±1.1 μM) when compared to control (no NOS inhibitor exposure; 19.6±1.2 μM). Nitrite productions after Aβ1-42 and L-NOARG (100 μM) or Aβ1-42 and S-MTC (100 μM) treatments are significantly lower than Aβ1-42 alone (33.5±2.0 and 34.5±1.6 μM, respectively). S-MTC (100 μM) is able to significantly reduce nitrite production (25.2±1.1 μM) as compared to Aβ1-42 treatment alone (38.3±2.7 μM), when administered after Aβ1-42 at the 1 h time point. S-MTC (100 μM) concentration decreases both MTT (87±1% of control) and NR (80±1% of control, respectively) levels. The co-administration of S-MTC (100 μM) and Aβ1-42 significantly reverses the effects of Aβ1-42 alone (72±2% vs 61±2% of control)[1].

S-MTC (S-methyl-L-thiocitrulline) is a selective neuronal NOS-inhibitor. Following pretreatment with S-MTC (i.c.v.), the HBO2-induced antinociception is significantly antagonized. In Experiment #2, different groups of mice are pretreated with naltrexone hydrochloride (NTX) (3.0 mg/kg, i.p.), L-NAME (1.0 μg/mouse, i.c.v.), S-MTC (1.0 μg/mouse, i.c.v.) or N5-(1-iminoethyl)-L-ornithine (L-NIO) (3.0 mg/kg, s.c.) 15-30 min prior to HBO2 treatment. The antinociceptive effect assessed 90 min after HBO2 treatment is completely abolished by NTX and L-NAME, antagonized by two-thirds by S-MTC and largely unaffected by L-NIO (F=25.57, p

[1]. Law A, et al. Neuroprotective and neurorescuing effects of isoform-specific nitric oxide synthase inhibitors, nitric oxide scavenger, and antioxidant against beta-amyloid toxicity. Br J Pharmacol. 2001 Aug;133(7):1114-24. [2]. Zelinski LM, et al. A prolonged nitric oxide-dependent, opioid-mediated antinociceptive effect of hyperbaric oxygenin mice. J Pain. 2009 Feb;10(2):167-72. [3]. Wakefield ID, et al. Comparative regional haemodynamic effects of the nitric oxide synthase inhibitors, S-methyl-L-thiocitrulline and L-NAME, in conscious rats. Br J Pharmacol. 2003 Jul;139(6):1235-43.

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