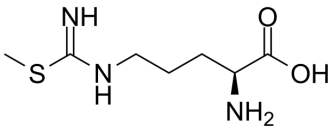
S-MTC

Cat. No.:	HY-U00432
CAS No.:	156719-41-4
Molecular Formula:	$C_7H_{15}N_3O_2S$
Molecular Weight:	205.28
Target:	NO Synthase
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	S-MTC is a selective type I nitric oxide synthase (NOS) inhibitor.
IC_{50} & Target	NOS[1]
In Vitro	S-MTC (10 or 100 μM) reduces cellular NO release in the absence of $A\beta_{1-42}$. 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 $A\beta_{1-42}$ and L-NOARG (100 μM) or $A\beta_{1-42}$ and S-MTC (100 μM) treatments are significantly lower than $A\beta_{1-42}$ 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 $A\beta_{1-42}$ treatment alone (38.3±2.7 μM), when administered after $A\beta_{1-42}$ 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 $A\beta_{1-42}$ significantly reverses the effects of $A\beta_{1-42}$ alone (72±2% vs 61±2% of control)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	S-MTC (S-methyl-L-thiocitrulline) is a selective neuronal NOS-inhibitor. Following pretreatment with S-MTC (i.c.v.), the HBO_2-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 N^5-(1-iminoethyl)-L-ornithine (L-NIO) (3.0 mg/kg, s.c.) 15-30 min prior to HBO_2 treatment. The antinociceptive effect assessed 90 min after HBO_2 treatment is completely abolished by NTX and L-NAME, antagonized by two-thirds by S-MTC and largely unaffected by L-NIO ($F=25.57$, $p<0.0001$)[2]. At a dose of 0.3 mg/kg, S-MTC (SMTC) causes a rise in mean blood pressure (BP). At doses of 1.0, 3.0 and 10 mg/kg, S-MTC causes falls in heart rate, rises in BP and vasoconstriction in all three vascular beds [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	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 $A\beta_{1-42}$ (1, 5, 10, or 20 μM), $A\beta_{42-1}$, or peroxynitrite (100 or 200 μM) with or without either N^G-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 $A\beta_{1-42}$ (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 $A\beta_{1-42}$ 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2][3]	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 HBO_2 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 HBO_2 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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):1235-43.

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