Product Data Sheet

Product Name: Cutamesine (SA4503)
Cat. No.: GC33697

Chemical Properties

Cas. No.	165377-43-5		
SMILES	COC1=CC=C(CCN2CCN(CCCC3=CC=CC=C3)CC2)C=C1OC		
Formula	$C_{23}H_{32}N_2O_2$	M.Wt	368.51
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	Cutamesine (SA4503)		

Protocol

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Kinase experiment [1]:

Preparation Method	Cutamesine (SA4503) Binding affinities to sigma-1□2 receptor subtypes were assessed with 5 nM (+)-[^{3}H]pentazocine or 5 nM [^{3}H]DTG with 200 nM (+)-[3H]pentazocine. Incubations in the (+)-[^{3}H]pentazocine and [3H]DTG binding studies were carried out at 37°C for 150 min or at 25°C for 90 min.
Reaction Conditions	10^{-12}M-10^{-3}M Cutamesine (SA4503) at 37°C for 150 min or at 25°C for 90 min.

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Applications	Competition binding experiments showed that Cutamesine (SA4503) had a high affinity for (+)-[Hlpentazocine binding sites in guinea pig brain membranes . The IC50 value of this compound for the sigma-1 receptor subtype was 17.4 + 1.9 nM. Cutamesine (SA4503) had a low affinity for the sigma-2 receptor subtype, with an IC50 value of1784.1 + 314.4 nM. The inhibitory potency of Cutamesine (SA4503) for the sigma-1 receptor subtype was about 100 times higher than that for the sigma-2 receptor subtype.

Cell experiment [2]:

Cell lines	Cultured cortical neurons(DIV4)
Preparation Method	Dissociated cortical neurons were cultured for 4 or 5 days before Cutamesine (SA4503) was applied. Twenty-four hours after Cutamesine (SA4503) addition, H202 was applied for 12 h. Then, the cell viability was analyzed.
Applications	Cutamesine (SA4503) prevents cultured cortical neurons from cell death caused by H2O2 application. The survival effect by Cutamesine (SA4503) reached a plateau at 0.1 μM.

Animal experiment [3]:

Animal models	Transgenic G93A [B6SJL-Tg (SOD1-G93A) 1Gur/J] mice

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Preparation Method	Cutamesine (SA4503) was dissolved in saline and subcutaneously administered at a dose of 1 mg/kg once daily to 5-week-old mice to the time of death
Dosage form	1 mg/kg Cutamesine (SA4503) once a day
Applications	Cutamesine (SA4503) prolonged the survival of SOD1 G93A mice

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References:

[1]. Matsuno K, Nakazawa M, et,al. Binding properties of SA4503, a novel and selective sigma 1 receptor agonist. Eur J Pharmacol. 1996 Jun 13;306(1-3):271-9. doi: 10.1016/0014-2999(96)00201-4. PMID: 8813641.

[2]. Tuerxun T, Numakawa T, et,al. SA4503, a sigma-1 receptor agonist, prevents cultured cortical neurons from oxidative stress-induced cell death via suppression of MAPK pathway activation and glutamate receptor expression. Neurosci Lett. 2010 Jan 29;469(3):303-8. doi: 10.1016/j.neulet.2009.12.013. Epub 2009 Dec 16. PMID: 20025928.

[3]. Ono Y, Tanaka H, et,al. SA4503, a sigma-1 receptor agonist, suppresses motor neuron damage in in vitro and in vivo amyotrophic lateral sclerosis models. Neurosci Lett. 2014 Jan 24;559:174-8. doi: 10.1016/j.neulet.2013.12.005. Epub 2013 Dec 12. PMID: 24334165.

Background

Product Data Sheet

Cutamesine (SA4503) is a potent and selective agonist for the sigma 1 receptor subtype in the brain. Cutamesine (SA4503) inhibited specific (+)-[3H]pentazocine binding in a competitive manner(IC_{50} = 17.4 +/- 1.9 nM) in guinea pig meninges[1□4].

Cutamesine (SA4503) prevents cultured cortical neurons from cell death caused by H2O2 application. The survival effect by Cutamesine (SA4503) reached a plateau at 0.1 μM[3]. Cutamesine(SA4503) reduces the activation of the MAPK/ERK pathway and down-regulated the ionotropic glutamate receptor, GluR1[2]. Cutamesine(SA4503) protects motor neuron NSC34 cells against superoxide dismutase 1 and serum free neurotoxicity. It upregulates the phosphorylation levels of Akt and extracellular signal-regulated kinase (ERK) 1/2 [2].

Cutamesine (SA4503) extended the survival time, but it did not delay the disease onset in the SOD1G93A mice. The extended survival time in the Cutamesine (SA4503) group may be associated with the suppression of the progression of motor neuron damage by the upregulation of phosphorylated Akt and ERK1/2. From these results, Cutamesine (SA4503) may have the protective effect against FALS, because SOD1G93A mice are model of FALS [2]. When examined the effects of Cutamesine (SA4503) on the cholinergic dysfunction-induced memory impairments in a passive avoidance task. Single administration of Cutamesine (SA4503) significantly reduced the scopolamine-induced memory impairment [5]. Cutamesine (SA4503) produced a significant decrease and rise in the number of spontaneously active SNC and VTA DA neurons in rats. Cutamesine (SA4503) produced a significant increase in the number of spontaneously active VTA DA neurons relative to SNC DA neurons Repeated administration of Cutamesine (SA4503) produced a greater change in the firing pattern of spontaneously active VTA[6]. Repeated treatment with Cutamesine (SA4503) (0.3 mg/kg) improved the behavior disorder similar to depressive symptoms in rats in olfactory bulb resection group. Cutamesine (SA4503) also reversed the reduction of NMDA receptor subunit (NR)1 protein expression in the prefrontal cortex, hippocampus, and amygdala of olfactory bulbectomy rats, but did not affect NR2A or NR2B[7].

References:
[1]: Lever JR, Gustafson JL, et,al. Sigma1 and sigma2 receptor binding affinity and selectivity of SA4503 and fluoroethyl SA4503. Synapse. 2006 May;59(6):350-8. doi:

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10.1002/syn.20253. PMID: 16463398.
[2]: Ono Y, Tana19996ka H, et,al. SA4503, a sigma-1 receptor agonist, suppresses motor neuron damage in in vitro and in vivo amyotrophic lateral sclerosis models. Neurosci Lett. 2014 Jan 24;559:174-8. doi: 10.1016/j.neulet.2013.12.005. Epub 2013 Dec 12. PMID: 24334165.
[3]: Tuerxun T, Numakawa T, et,al. SA4503, a sigma-1 receptor agonist, prevents cultured cortical neurons from oxidative stress-induced cell death via suppression of MAPK pathway activation and glutamate receptor expression. Neurosci Lett. 2010 Jan 29;469(3):303-8. doi: 10.1016/j.neulet.2009.12.013. Epub 2009 Dec 16. PMID: 20025928.
[4]: Matsuno K, Nakazawa M, et,al.Binding properties of SA4503, a novel and selective sigma 1 receptor agonist. Eur J Pharmacol. 1996 Jun 13;306(1-3):271-9. doi: 10.1016/0014-2999(96)00201-4. PMID: 8813641.
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