Product Data Sheet

Product Name: MONNA
Cat. No.: GC18358

Chemical Properties

Cas. No.	1572936-83-4		
Chemical Name	2-[(4-methoxy-2-naphthalenyl)amino]-5-nitro-benzoic acid		
SMILES	COC1=CC(NC2=C(C(O)=O)C=C([N+]([O-])=O)C=C2)=CC3=CC=CC=C31		
Formula	$C_{18}H_{14}N_2O_5$	M.Wt	338.3
Solubility	DMF: 30 mg/ml,DMSO: 30 mg/ml,DMSO:PBS(pH 7.2) (1:3): 0.25 mg/ml,Ethanol: slightly soluble	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	MONNA		

Protocol

Cell experiment [1]:

Cell lines	Single airway smooth muscle cells

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Preparation Method	Single airway smooth muscle cells were isolated using a collagenase/proteinase mixture consisting of (per 5mL of Hanks Ca^{2+}-free solution): 15mg/ml of collagenase (type II), 10mg/ml bovine serum albumin, 10mg/ml trypsin inhibitor and 1mg/ml proteinase. In order to examine the effects of MONNA on cytosolic [Ca^{2+}] in isolated cells, MONNA (1μM) was applied three times for 30s. Cells were plated and incubated in 0.4μM fluo-4AM (Molecular Probes) for 6–8min at room temperature in Hank's Ca^{2+}-free solution to which 100μM Ca^{2+} was added. During experiments, dishes containing cells were continuously perfused with Hanks solution (Solution C) at 35±2℃. Additionally, the cell under study was continuously superfused with Hanks solution by means of a custom built close delivery system with a pipette tip diameter of 200μm placed approximately 300μm from the cell. The Hanks solution in the close delivery system could be switched to a drug-containing solution with a dead-space time of less than 5s. Cells were imaged using an iXon 887 EMCCD camera coupled to a Nipkow spinning disk confocal head.
Reaction Conditions	1μM; 30s
Applications	MONNA caused reproducible elevations in intracellular Ca^{2+} concentration in isolated mouse bronchial smooth muscle cells.

Animal experiment [2]:

Animal models	Female Wistar rats

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Preparation Method	Female Wistar rats of 130-150g of weight (6-7 weeks) were housed in cages on a standard 12/12h light/dark cycle and had free access to food and water before experiments. Rats were sacrificed in a CO_2 chamber at the end of experiments. Neuropathic pain was induced by L5/L6 spinal nerve ligation [SNL]. In order to determine the effect of MONNA in nerve injuryinduced neuropathic pain, rats were treated with MONNA (1-10μg; i.t.) or vehicle (1% or 15% DMSO; i.t.) daily for 3 days, starting on day 4 after nerve injury (SNL). Then, tactile allodynia was assessed from 7 to 21 days after injury.
Dosage form	1-10μg/day; 3 days; starting on day 4 after SNL; intrathecal injection
Applications	MONNA reverted SNL-induced tactile allodynia in a dose-dependent manner in injured L5 dorsal root ganglia of rats.

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References:
[1] Dwivedi R, Drumm BT, Alkawadri T, et al. The TMEM16A blockers benzbromarone and MONNA cause intracellular Ca^{2+}-release in mouse bronchial smooth muscle cells. *Eur J Pharmacol*. 2023;947:175677.
[2] García G, Martínez-Rojas VA, Oviedo N, Murbartián J. Blockade of anoctamin-1 in injured and uninjured nerves reduces neuropathic pain. *Brain Res*. 2018;1696:38-48.

Background

MONNA is a specific blocker of ANO1 (anoctamin-1/TMEM16A) calcium-activated chloride channels, with an IC_{50} of 0.08μM for xANO1 in Xenopus laevis oocytes[1]. MONNA modulates epithelial chloride transport and smooth muscle contraction by selectively blocking ANO1-mediated chloride currents[2]. MONNA is commonly used in research on

diseases such as hypertension, cystic fibrosis, bronchitis, asthma, and hyperalgesia[3] [4].

In vitro, MONNA (1μM; 30s) caused reproducible elevations in intracellular Ca^{2+} concentration in isolated mouse bronchial smooth muscle cells[5].

In vivo, MONNA (1μM; 30min perfusion) reversed the U46619-induced decrease in coronary flow in Langendorff-perfused rat hearts[6]. MONNA (10μg/day; 3 days; starting on day 4 after SNL; intrathecal injection) reduced SNL-induced up-regulation of anoctamin-1, ATF-3, and caspase-3 protein expression in injured L5 dorsal root ganglia of rats[7].

References:
[1] Oh SJ, Hwang SJ, Jung J, et al. MONNA, a potent and selective blocker for transmembrane protein with unknown function 16/anoctamin-1. *Mol Pharmacol*. 2013;84(5):726-735.
[2] Liu Y, Liu Z, Wang K. The Ca^{2+}-activated chloride channel ANO1/TMEM16A: An emerging therapeutic target for epithelium-originated diseases?. *Acta Pharm Sin B*. 2021;11(6):1412-1433.
[3] Galietta LJV. TMEM16A (ANO1) as a therapeutic target in cystic fibrosis. *Curr Opin Pharmacol*. 2022;64:102206.
[4] Boedtkjer DM, Kim S, Jensen AB, Matchkov VM, Andersson KE. New selective inhibitors of calcium-activated chloride channels - T16A(inh) -A01, CaCC(inh) -A01 and MONNA - what do they inhibit?. *Br J Pharmacol*. 2015;172(16):4158-4172.
[5] Dwivedi R, Drumm BT, Alkawadri T, et al. The TMEM16A blockers benzbromarone and MONNA cause intracellular Ca^{2+}-release in mouse bronchial smooth muscle cells. *Eur J Pharmacol*. 2023;947:175677.
[6] Askew Page HR, Dalsgaard T, Baldwin SN, et al. TMEM16A is implicated in the regulation of coronary flow and is altered in hypertension. *Br J Pharmacol*. 2019;176(11):1635-1648.
[7] García G, Martínez-Rojas VA, Oviedo N, Murbartián J. Blockade of anoctamin-1 in injured and uninjured nerves reduces neuropathic pain. *Brain Res*. 2018;1696:38-48.