

Product Data Sheet

Product Name: AMG 9810

Cat. No.: GC11926

Chemical Properties

Cas. No. 545395-94-6

Chemical Name (Z)-3-(4-(tert-butyl)phenyl)-N-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)acrylamide

SMILES O=C(/C=C/C1=CC=C(C=C1)C(C)(C)C)NC2=CC=C3OCCOC3=C2

Formula $C_{21}H_{23}NO_3$

M.Wt 337.42

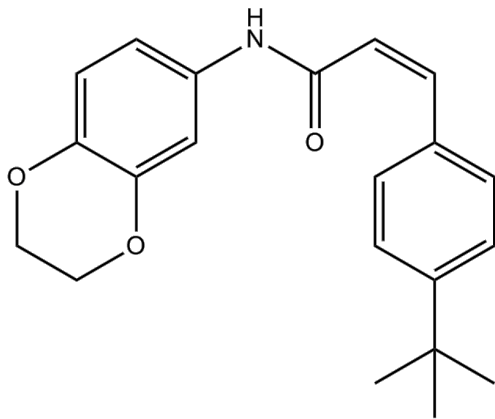
Solubility $\geq 33.7\text{mg/mL}$ in DMSO

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]:

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell lines	HEK _n cells
Preparation Method	HEK _n cells were plated in 24-well plates (2×10^4 cells per well in 1 mL of culture medium) or in 6-well plates (9.6×10^4 cells per well in 2 mL of culture medium) and incubated overnight at 37°C. The culture medium was replaced with or without various concentrations of SB-705498 and AMG 9810, at a final concentration of 0.1% v/v DMSO, and the MTT assay was performed after 24, 48, and 72 hours of incubation.
Reaction Conditions	0–5 μM; 24–72h
Applications	AMG 9810 was cytotoxic to these cells at the higher concentrations tested and when exposed for longer in culture.

Animal experiment [2]:

Animal models	Male Wister rats
Preparation Method	Animals (n = 12) were randomly allocated before surgery to vehicle, OLDA (30mg/kg), or AMG 9810 (30mg/kg) treatment groups. Dummy cannulas were removed and the thermocouple wire sensors were inserted in the guide cannula. Animals were then left undisturbed in the telemetry cages for 60 minutes to measure baseline temperatures and gross activities. The injection solutions (1mL DMSO, 15mg OLDA in 1mL DMSO, and 15mg AMG 9810 in 1mL DMSO) were prepared for administration in a blinded manner.
Dosage form	30mg/kg; ip; single injection
Applications	AMG 9810 injection can induce mild hyperthermia in rats immediately.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

- [1]. Park M, Naidoo A A, Burns A, et al. Do TRPV1 antagonists increase the risk for skin tumorigenesis? A collaborative in vitro and in vivo assessment[J]. Cell Biology and Toxicology, 2018, 34(2): 143-162.
- [2]. Tejada de Rink M M, Naumann U, Kollmar R, et al. A Single Injection of N-Oleoyldopamine, an Endogenous Agonist for Transient Receptor Potential Vanilloid-1, Induced Brain Hypothermia, but No Neuroprotective Effects in Experimentally Induced Cerebral Ischemia in Rats[J]. Therapeutic Hypothermia and Temperature Management, 2020, 10(2): 91-101.

Background

AMG 9810 is a highly selective and competitive TRPV1 antagonist (human: $IC_{50} = 24.5nM$; mouse: $IC_{50} = 85.6nM$) [1]. AMG 9810 blocks TRPV1 channels activated by capsaicin, acidic conditions, heat, and endogenous ligands such as anandamide, inhibiting ion influx into cells and thereby attenuating the transmission of pain and heat-sensitive signals [2-3]. AMG 9810 exhibits anti-hyperalgesia, anti-inflammatory, and analgesic effects [4].

In HEK293 cells, AMG 9810 (0–5 μM ; 24–72h) was cytotoxic to these cells at the higher concentrations tested and when exposed for longer in culture [5]. In T84 cells, AMG 9810 (100nM; 30min) can block the increase in $[Ca^{2+}]_i$ induced by capsaicin and resiniferatoxin [6]. In chinese hamster ovary (CHO) cell, AMG 9810 (3–1000nM; 10min) penetrates faster than capsaicin and is more potent than capsaicin [7].

In Male Wistar rats, AMG 9810 (30mg/kg; ip; single injection) injection can induce mild hyperthermia in rats immediately [8]. In C57BL/6 mice, AMG 9810 (1nmol; intrathecal injections; single injection) completely blocked NADA-induced allergy 15 and 60 minutes after injection [9].

References:

- [1]. Gavva N R, Tamir R, Qu Y, et al. AMG 9810 [(E)-3-(4-t-butylphenyl)-N-(2, 3-dihydrobenzo [b][1, 4] dioxin-6-yl) acrylamide], a novel vanilloid receptor 1 (TRPV1) antagonist with antihyperalgesic properties[J]. The journal of pharmacology and experimental therapeutics, 2005, 313(1): 474-484.
- [2]. Gomtsyan A. Aryl-Urea Class and Related TRPV1 Antagonists[J]. Vanilloid Receptor TRPV1 in

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

- Drug Discovery: Targeting Pain and Other Pathological Disorders, 2010: 293-310.
- [3]. Hakimzadeh E, Oryan S, Shamsizadeh A, et al. Endocannabinoid system and TRPV1 receptors in the dorsal hippocampus of the rats modulate anxiety-like behaviors[J]. Iranian Journal of Basic Medical Sciences, 2012, 15(3): 795.
- [4]. Gomtsyan A. Aryl-Urea Class and Related TRPV1 Antagonists[J]. Vanilloid Receptor TRPV1 in Drug Discovery: Targeting Pain and Other Pathological Disorders, 2010: 293-310.
- [5]. Park M, Naidoo A A, Burns A, et al. Do TRPV1 antagonists increase the risk for skin tumourigenesis? A collaborative in vitro and in vivo assessment[J]. Cell Biology and Toxicology, 2018, 34(2): 143-162.
- [6]. Bouyer P G, Tang X, Weber C R, et al. Capsaicin induces NKCC1 internalization and inhibits chloride secretion in colonic epithelial cells independently of TRPV1[J]. American Journal of Physiology-Gastrointestinal and Liver Physiology, 2013, 304(2): G142-G156.
- [7]. Pearce L V, Ann J, Blumberg P M, et al. Combination of a Rapidly Penetrating Agonist and a Slowly Penetrating Antagonist Affords Agonist Action of Limited Duration at the Cellular Level[J]. Biomolecules & Therapeutics, 2019, 27(5): 435.
- [8]. Tejada de Rink M M, Naumann U, Kollmar R, et al. A Single Injection of N-Oleoyldopamine, an Endogenous Agonist for Transient Receptor Potential Vanilloid-1, Induced Brain Hypothermia, but No Neuroprotective Effects in Experimentally Induced Cerebral Ischemia in Rats[J]. Therapeutic Hypothermia and Temperature Management, 2020, 10(2): 91-101.
- [9]. Pitcher M H, Price T J, Entrena J M, et al. Spinal NKCC1 blockade inhibits TRPV1-dependent referred allodynia[J]. Molecular pain, 2007, 3: 1744-8069-3-17.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA