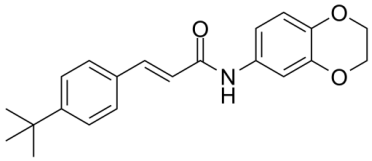
Data Sheet

Product Name:	AMG9810
Cat. No.:	CS-6481
CAS No.:	545395-94-6
Molecular Formula:	C21H23NO3
Molecular Weight:	337.41
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Solubility:	DMSO : ≥ 33 mg/mL (97.80 mM)



BIOLOGICAL ACTIVITY:

AMG9810 is a selective and competitive vanilloid receptor 1 (**TRPV1**) antagonist with **IC_{50}** values of 24.5 and 85.6 nM for human and rat TRPV1, repectively. IC50 & Target: IC50: 24.5 nM (human TRPV1), 85.6 nM (rat TRPV1)[1] **In Vitro:** AMG9810 is a competitive antagonist of capsaicin activation (IC_{50} value for human TRPV1, 24.5±15.7 nM; rat TRPV1, 85.6±39.4 nM) and blocks all known modes of TRPV1 activation, including protons (IC_{50} value for rat TRPV1, 294±192 nM; human TRPV1, 92.7±72.8 nM), heat (IC_{50} value for rat TRPV1, 21±17 nM; human TRPV1, 15.8±10.8 nM), and endogenous ligands, such as anandamide, N-arachidonyl dopamine, and oleoyldopamine. AMG9810 blocks capsaicin-evoked depolarization and calcitonin gene-related peptide release in cultures of rat dorsal root ganglion primary neurons. AMG9810 inhibits capsaicin-, proton-, heat-, and endogenous ligand-induced uptake of $^{45}Ca^{2+}$ into TRPV1-expressing cells[1]. **In Vivo:** AMG9810 is effective at preventing capsaicin-induced eye wiping in a dose-dependent manner, and it reverses thermal and mechanical hyperalgesia in a model of inflammatory pain induced by intraplantar injection of complete Freund's adjuvant. At effective doses, AMG9810 does not show any significant effects on motor function. AMG9810 is the first cinnamide TRPV1 antagonist reported to block capsaicin-induced eye wiping behavior and reverse hyperalgesia in an animal model of inflammatory pain[1]. AMG9810, promotes mouse skin tumor development. The topical application of AMG9810 results in a significant increase in the expression level of the epidermal growth factor receptor (EGFR) and its downstream Akt/mammalian target of rapamycin (mTOR)-signaling pathway[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Cultured adult rat dorsal root ganglia neurons in 96-well plates are washed twice with release buffer to initiate the assay. CGRP release is induced by incubation of neurons with capsaicin for 10 min at room temperature. The cultures are preincubated with increasing concentrations of capsazepine or AMG9810 for 15 min, followed by 300 nM capsaicin activation for 10 min at room temperature. The extracellular medium is collected and the CGRP content is determined using a commercially kit[1]. **Cell Assay:** [2]To assess cyotoxicity of AMG9810, N/TERT1 cells are treated with different concentrations of AMG9810 (0.25, 0.5, 1, 5 μM) and cultured for various periods of time (24, 48, 72 h). The CellTiter 96 AQueous One Solution is added to each well and then cells are kept in a 37°C, 5% CO_2 incubator for 1 h. Absorbance is then measured at 492 and 690 nm with a plate reader[2]. **Animal Administration:** [1]Rat: AMG9810 is dissolved in DMSO. Rats are acclimated for 30 to 45 min in a 30×30×30-cm Plexiglas chambers before the intraperitoneal injection of either vehicle (DMSO) or AMG 9810. Injections are made over a 5-s period in the lower right ventral quadrant of the abdomen either 15, 30, or 60 min before intraocular application of capsaicin. Intraocular application of capsaicin (3 μg/20 μL in 10% ethanol/PBS) or vehicle (20 μL in 10% ethanol/PBS) is done with a pipette, and the number of front paw eye wipes is counted over a 5-min period in 1-min intervals [1].

References:

[1]. Gavva NR, et al. AMG9810 [(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 Pharmacol Exp Ther. 2005 Apr;313(1):474-84.

[2]. Li S, et al. TRPV1-antagonist AMG9810 promotes mouse skin tumorigenesis through EGFR/Akt signaling. Carcinogenesis. 2011 May;32(5):779-85.

CAIndexNames:

2-Propenamide, N-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[4-(1,1-dimethylethyl)phenyl]-, (2E)-

SMILES:

O=C(NC1=CC=C(OCCO2)C2=C1)/C=C/C3=CC=C(C(C)(C)C)C=C3

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