Product Data Sheet

Product Name: AR-M 1896
Cat. No.: GC11955

Chemical Properties

Cas. No.	367518-31-8		
SMILES	CC(C[C@@](/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/C/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/[C@](N)([H])CC1=CNC2=CC=CC=C12)([H])[C@@](O)([H])C)([H])CC(C)C)([H])CC(O)=N)([H])CO)([H])C)([H])CC3=CC=C(O)C=C3)([H])CC(C)C)([H])C(O)=N)C		
Formula	$C_{54}H_{81}N_{13}O_{14}$	M.Wt	1136.31
Solubility	Soluble to 1 mg/ml in 20% formic acid	Storage	Desiccate 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	AR-M 1896		

Protocol

Cell experiment [1]:

Cell lines	Rat pheochromocytoma (PC12) cells stably transfected with GFP-tagged galanin receptor subtype 2 (GalR2) and non-transfected (native) PC12 cells
Preparation Method	PC12 and GFP-GalR2-transfected PC12 cells were cultured. Cells were exposed to AR-M 1896 (100nM; 24h).

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Reaction Conditions	100μM; 24h.
Applications	In GFP-GalR2-transfected cells, AR-M 1896 induced caspase-dependent apoptotic cell death, as shown by a significant increase in apoptotic nuclei and caspase-3-like activity. AR-M 1896 also led to a down-regulation of phosphorylated Akt (pAkt) and phosphorylated Bad (pBad), indicating inhibition of the PI3K/Akt survival pathway. In contrast, in non-transfected native PC12 cells, AR-M 1896 did not significantly induce apoptosis. Flow cytometry analysis indicated that treatment in transfected cells resulted in a significant population of cells in the sub-G1 phase, indicative of cell death.

Animal experiment [2]:

Animal models	Sprague-Dawley rats with median nerve chronic constriction injury (CCI)
Preparation Method	Rats received intraplantar injection of AR-M 1896 (0.1μM/paw) on day 5 and day 7 after CCI. The forepaw withdrawal threshold was assessed using von Frey filaments, and neuronal activation (c-Fos expression) in the cuneate nucleus (CN) was examined after electrical stimulation of the injured nerve on day 7.
Dosage form	0.1μM/paw; intraplantar injection; Two doses (on day 5 and day 7 post-CCI).

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications	AR-M 1896 administration slightly aggravated CCI-induced mechanical allodynia (tactile hypersensitivity). Furthermore, AR-M 1896 significantly increased the number of c-Fos-positive neurons in the cuneate nucleus following electrical stimulation of the injured median nerve.

References:
[1] Tofighi R, Joseph B, Xia S, et al. Galanin decreases proliferation of PC12 cells and induces apoptosis via its subtype 2 receptor (GalR2). Proc Natl Acad Sci U S A. 2008 Feb 19;105(7):2717-22.
[2] Chen SH, Lue JH, Hsiao YJ, et al. Elevated galanin receptor type 2 primarily contributes to mechanical hypersensitivity after median nerve injury. PLoS One. 2018 Jun 21;13(6):e0199512.

Background

AR-M 1896 is a novel, highly selective galanin type 2 receptor (GalR2) agonist (IC_{50}=1.76nM)[1-2]. AR-M 1896 modulates neuropeptide signaling pathways by

specifically activating the GalR2 receptor, thereby exerting neuroprotective, anti-inflammatory, and pain-modulating effects. AR-M 1896 can be used in research related to acute myocardial infarction, neuropathic pain, and epilepsy[3-4].

In vitro, treatment of primary cultured cortical neurons ischemia model with AR-M 1896 (1nM to 10μM) for 15min did not increase neuronal viability or reduce lactate dehydrogenase (LDH) release in a dose-dependent manner, unlike galanin[5]. Treatment of rat pheochromocytoma (PC12) cells stably transfected with GFP-labeled galanin type 2 receptor (GalR2) with AR-M 1896 (100nM) for 24h induced caspase-dependent apoptosis, inhibited the PI3K/Akt signaling pathway, and caused cell cycle arrest in the sub-G1 phase[6].

In vivo, AR-M 1896 (0.1μM/paw) was administered to rats via plantar injection on days 5 and 7 after median nerve chronic constriction injury (CCI). AR-M 1896 slightly aggravated CCI-induced mechanical allodynia and significantly increased the number of c-Fos-positive neurons in the cuneate nucleus (CN) after electrical stimulation of the injured nerve[7]. AR-M 1896 (3pmol) and calcitonin gene-related peptide (CGRP; 10pmol) were co-administered to CD-1 mice via intradermal injection; AR-M 1896 significantly suppressed CGRP-induced inflammatory skin edema (plasma extravasation)[8].

References:
[1] Liu HX, Brumovsky P, Schmidt R, et al. Receptor subtype-specific pronociceptive and analgesic actions of galanin in the spinal cord: selective actions via GalR1 and GalR2 receptors. Proc Natl Acad Sci U S A. 2001 Aug 14;98(17):9960-4.
[2] Serebryakova L, Pal'keeva M, Studneva I, et al. Galanin and its N-terminal fragments reduce acute myocardial infarction in rats. Peptides. 2019 Jan;111:127-131.
[3] Pirondi S, Fernandez M, Schmidt R, et al. The galanin-R2 agonist AR-M1896 reduces glutamate toxicity in primary neural hippocampal cells. J Neurochem. 2005 Nov;95(3):821-33.
[4] Kerekes N, Mennicken F, O'Donnell D, et al. Galanin increases membrane excitability and enhances Ca(2+) currents in adult, acutely dissociated dorsal root ganglion neurons. Eur J Neurosci. 2003 Dec;18(11):2957-66.
[5] Li Y, Mei Z, Liu S, et al. Galanin Protects from Caspase-8/12-initiated Neuronal Apoptosis in the Ischemic Mouse Brain via GalR1. Aging Dis. 2017 Feb 1;8(1):85-100.
[6] Tofighi R, Joseph B, Xia S, et al. Galanin decreases proliferation of PC12 cells and

induces apoptosis via its subtype 2 receptor (GalR2). Proc Natl Acad Sci U S A. 2008 Feb 19;105(7):2717-22.
[7] Chen SH, Lue JH, Hsiao YJ, et al. Elevated galanin receptor type 2 primarily contributes to mechanical hypersensitivity after median nerve injury. PLoS One. 2018 Jun 21;13(6):e0199512.
[8] Schmidhuber SM, Rauch I, Kofler B, et al. Evidence that the modulatory effect of galanin on inflammatory edema formation is mediated by the galanin receptor 3 in the murine microvasculature. J Mol Neurosci. 2009 Feb;37(2):177-81.