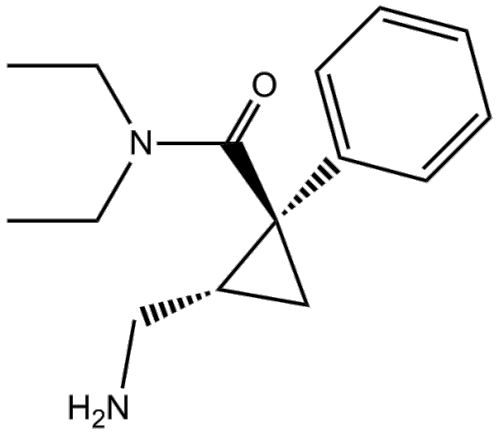
Product Data Sheet

Product Name: Milnacipran
Cat. No.: GC14330

Chemical Properties

Cas. No.	92623-85-3		
Chemical Name	(1R,2S)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropane-1-carboxamide		
SMILES	CCN(CC)C(=O)C1(CC1CN)C2=CC=CC=C2		
Formula	C15H22N2O	M.Wt	246.35
Solubility	Soluble 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]:	
Cell lines	TetHeLaG2m cells (modified HeLa cell line stably expressing half-edited GluR2 pre-mRNA)

Product Data Sheet

Preparation Method	TetHeLaG2m cells were cultured in MEM-α medium supplemented with 10% Tet System-approved fetal bovine serum, 0.75μg/mL puromycin, 100 IU/mL penicillin, and 100μg/mL streptomycin at 37°C, 5% CO_2. TetHeLaG2m cells were plated at 2×10^5 cells/well in 6-well plates and treated with 0.1-10μM Milnacipran for 24 hours. After treatment, RNA was extracted and reverse transcribed, and nested PCR with BbvI restriction digestion was performed to determine GluR2 Q/R site-editing efficiency. Real-time quantitative PCR was used to measure mRNA expression levels of ADAR2, GluR2, pre-GluR2, and β-actin.
Reaction Conditions	0.1-10μM; 24h
Applications	Milnacipran increased GluR2 Q/R site-RNA editing efficiency at 10μM. Milnacipran decreased ADAR2 mRNA, GluR2 pre-mRNA expression, increased GluR2 mRNA expression.
Animal experiment [2]:	
Animal models	C57BL/6J mice, wild-type mice, Ay mice
Preparation Method	Mice were intraperitoneally injected with Milnacipran (20-60mg/kg) 30 minutes before food presentation after a 23-hour fast. In separate experiments, mice were intraperitoneally injected with Milnacipran (30mg/kg) twice daily for 3 days. For hypothalamic gene expression and hormone analysis, mice were intraperitoneally injected with Milnacipran (30mg/kg) in the light cycle and sacrificed at 30, 60, or 120 minutes for blood and hypothalamus collection.
Dosage form	20, 30, 60mg/kg; i.p.; single injection or twice daily for 3 days

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

Applications	Milnacipran suppressed food intake in fasted C57BL/6J mice with effects lasting 5 hours, reduced food intake in wild-type and Ay mice after fasting and after dark cycle onset, twice-daily 30mg/kg for 3 days decreased food intake and body weight, increased hypothalamic POMC and CART mRNA levels, and reduced plasma corticosterone levels at 60 and 120 minutes in the dark cycle.

References:[1] Sawada J, Yamashita T, Aizawa H, et al. Effects of antidepressants on GluR2 Q/R site-RNA editing in modified HeLa cell line. Neuroscience Research. 2009 Jul;64(3):251-258.[2] Nonogaki K, Nozue K, Kuboki T, et al. Milnacipran, a serotonin and norepinephrine reuptake inhibitor, induces appetite-suppressing effects without inducing hypothalamic stress responses in mice. Am J Physiol Regul Integr Comp Physiol. 2007 May;292(5):R1775-81.

Background

Milnacipran is an inhibitor of the serotonin transporter (K_i = 31 nM) and the monoamine transporter (K_i = 8.5 nM). Milnacipran boosts synaptic monoamine levels and helps regulate pathways related to descending pain inhibition, easing chronic pain. Milnacipran is useful for research on major depressive disorder, fibromyalgia, anxiety disorders, and neuropathic pain[1-4].

In vitro, treatment with 0.1-10μM Milnacipran for 24 hours increased GluR2 Q/R site RNA editing efficiency, decreased ADAR2 mRNA expression, and elevated GluR2 mRNA and GluR2 pre-mRNA expression in modified HeLa cells stably expressing GluR2 pre-mRNA[5]. Treatment with 2.5-40μg/mL Milnacipran for 24-48 hours increased chromosomal aberrations, sister chromatid exchanges, and micronucleus frequency, decreased mitotic index, and increased comet tail length, tail intensity, and tail moment in peripheral blood lymphocytes[6]. Treatment with 10-100μM Milnacipran for 24 hours did not affect cell viability in esophageal squamous cell carcinoma cell lines (KYSE30, KYSE150, KYSE180, KYSE450)[7].

In vivo, intraperitoneal injection of 3-30mg/kg Milnacipran or intrathecal injection of 2.1-21μg/site Milnacipran inhibited pain in C57BL/6 mouse models of mechanical allodynia[8]. Intrathecal injection of 0.1-10μg/site Milnacipran or intraperitoneal injection of 1, 10mg/kg Milnacipran dose-dependently inhibited itch-related behaviors in serotonin-induced ICR mice[9]. Single intraperitoneal injection of 30mg/kg Milnacipran suppressed food intake after fasting in C57BL/6J mice and Ay mice. Twice-daily

intraperitoneal injection of 30mg/kg Milnacipran for 3 days decreased food intake and body weight and increased hypothalamic POMC and CART mRNA levels in mice[10].

References:

[1] Gupta H, Girma B, Jenkins JS, et al. Milnacipran for the Treatment of Fibromyalgia. Health Psychol Res. 2021 Jul 10;9(1):25532.
[2] Keks NA, Hope J, Keogh S, et al. Milnacipran: serotonin-noradrenaline reuptake inhibitor approved for fibromyalgia may be a useful antidepressant. Australas Psychiatry. 2018 Oct;26(5):537-540.
[3] Spencer CM, Wilde MI. Milnacipran. A review of its use in depression. Drugs. 1998 Sep;56(3):405-27.
[4] Kyle JA, Dugan BD, Testerman KK. Milnacipran for treatment of fibromyalgia. Ann Pharmacother. 2010 Sep;44(9):1422-9.
[5] Sawada J, Yamashita T, Aizawa H, et al. Effects of antidepressants on GluR2 Q/R site-RNA editing in modified HeLa cell line. Neuroscience Research. 2009 Jul;64(3):251-258.
[6] Avuloglu Yilmaz E, Unal F, Yuzbasioglu D, et al. Evaluation of cytogenetic and DNA damage induced by the antidepressant drug-active ingredients, trazodone and milnacipran, in vitro. Drug Chem Toxicol. 2016;Early Online:1-10.
[7] Bao S, Zhang Y, Zeng J, et al. Innovative role of the antidepressant imipramine in esophageal squamous cell carcinoma treatment: Promoting apoptosis and protective autophagy. International Immunopharmacology. 2025;147:113969.
[8] Andoh T, Kitamura R, Kuraishi Y. Milnacipran inhibits oxaliplatin-induced mechanical allodynia through spinal action in mice. Biol Pharm Bull. 2015;38(1):151-154.
[9] Andoh T, Gotoh Y, Kuraishi Y, et al. Milnacipran inhibits itch-related responses in mice through the enhancement of noradrenergic transmission in the spinal cord. J Pharmacol Sci. 2013;123:199-202.
[10] Nonogaki K, Nozue K, Kuboki T, et al. Milnacipran, a serotonin and norepinephrine reuptake inhibitor, induces appetite-suppressing effects without inducing hypothalamic stress responses in mice. Am J Physiol Regul Integr Comp Physiol. 2007 May;292(5):R1775-81.