

Product Data Sheet

Product Name: URB597

Cat. No.: GC15951

Chemical Properties

Cas. No. 546141-08-6

Chemical Name [3-(3-carbamoylphenyl)phenyl] N-cyclohexylcarbamate

SMILES C1CCC(CC1)NC(=O)OC2=CC=CC(=C2)C3=CC(=CC=C3)C(=O)N

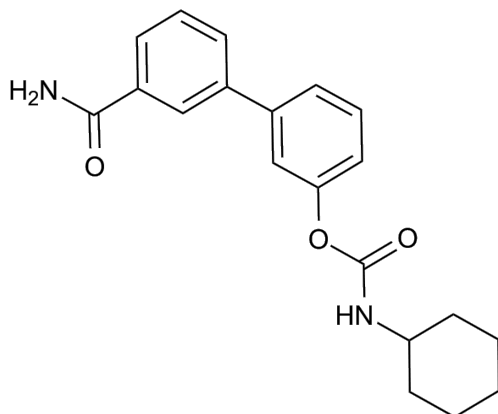
Formula $C_{20}H_{22}N_2O_3$ M.Wt 338.4

Solubility ≥ 16.9 mg/mL in DMSO, ≥ 4.55 mg/mL in EtOH with ultrasonic and warming
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

BV-2 cells (mouse microglia cell line)

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Preparation Method	BV-2 cells were maintained in DMEM/F-12 medium containing 5% fetal bovine serum, 4mM L-glutamine, and 1% penicillin-streptomycin at 37°C, 5% CO₂. BV-2 cells were pre-treated with 5μM URB597 for 4 hours and incubated with 30μM Aβ25-35 for 24 hours. After treatment, cell viability was evaluated by MTT and Trypan blue assays, FAAH activity was measured, morphology was analyzed by phalloidin staining, migration was assessed by scratch assay, phagocytosis was evaluated by FITC-dextran uptake, Rho GTPases activity was detected by pull-down assay, and mRNA expression of cytokines and markers was analyzed by qPCR.
Reaction Conditions	5μM; 28h
Applications	URB597 reversed Aβ25-35-induced cell death, inhibited FAAH activity, rescued the control phenotype of BV-2 cells, reduced migration. URB597 reduced the increase of RhoA protein activation and increased Cdc42 protein activation, decreased mRNA expression of IL-1β and TNF-α and increased TGF-β and IL-10 expression, decreased iNOS expression and increased Arg-1 expression in BV-2 cells co-treated with Aβ25-35.
Animal experiment [2]:	
Animal models	Male Swiss mice
Preparation Method	Mice were subjected to chronic constriction injury (CCI) of the left sciatic nerve under xylazine (10mg/kg i.p.) and ketamine (100mg/kg i.p.) anesthesia. Starting 3 days after surgery, mice were orally administered URB597 (1-50mg/kg) once daily for 4 days. On day 7 after surgery, 2h after the last drug administration, pain withdrawal thresholds to mechanical or thermal stimuli were measured, plasma extravasation was assessed by Evans' blue dye extravasation in paw tissue, and spinal cord fatty acid ethanolamide levels were quantified.

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Dosage form	1-50mg/kg; p.o.; once daily for 4 days
Applications	URB597 reduced mechanical hyperalgesia, thermal hyperalgesia and mechanical allodynia, reduced plasma extravasation, increased spinal cord levels of anandamide, PEA and OEA in CCI mice.
References:[1] Grieco M, De Caris MG, Maggi E, et al. Fatty Acid Amide Hydrolase(FAAH) Inhibition Modulates Amyloid-Beta-Induced Microglia Polarization. Int J Mol Sci. 2021 Jul 19;22(14):7711.[2] Russo R, LoVerme J, La Rana G, et al. The Fatty Acid Amide Hydrolase Inhibitor URB597(Cyclohexylcarbamic Acid 3'-Carbamoylbiphenyl-3-yl Ester) Reduces Neuropathic Pain after Oral Administration in Mice. J Pharmacol Exp Ther. 2007 Jul;322(1):236-242.	

Background

URB597 is an orally active fatty acid amide hydrolase (FAAH) inhibitor ($IC_{50}=0.5-5nM$). URB597 inhibits FAAH-mediated degradation of endocannabinoids anandamide, OEA and PEA to enhance endocannabinoid tone. URB597 alleviates hyperalgesia via CB1/CB2 receptor signaling. URB597 suppresses microglial LPS-induced COX-2 and iNOS expression to reduce PGE2 and NO release. URB597 modulates the Nrf2/HO-1 pathway to attenuate neuroinflammation. URB597 can be used for research on chronic pain, anxiety, depression and neuroinflammation^[1-4].

In vitro, BV-2 cells were treated with 5 μ M URB597 for 28 hours after amyloid β -peptide 25-35 induction. URB597 decreased RhoA activity and increased Cdc42 activity, reduced migration, enhanced phagocytic capacity of BV-2 cells. URB597 downregulated iNOS and proinflammatory cytokines IL-1 β and TNF- α expression, upregulated Arg-1 and anti-inflammatory cytokines TGF- β and IL-10 expression in BV-2 cells. URB597 shifted BV-2 cells toward an anti-inflammatory phenotype^[5]. HepG2 and Hep3B cells were treated with URB597 for 24 hours. URB597 increased TIMP3 expression, elevated cell surface MICA/B levels, reduced soluble MICA/B levels in culture media of HepG2 and Hep3B cells^[6]. 4T1 and HeyA8 cells were treated with 0-50 μ M URB597 for 72 hours. URB597 decreased viability of cells^[7].

In vivo, C57BL/6J mice received a single intraperitoneal injection of 0.5mg/kg URB597. URB597

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improved task accuracy and correct response number, reduced premature responses in distractor-cue trials^[8]. Chronic constriction injury of the sciatic nerve Swiss mouse models received oral URB597 at 1-50mg/kg once daily for 4 days. URB597 reduced mechanical hyperalgesia, thermal hyperalgesia and mechanical allodynia, decreased ipsilateral plasma extravasation, elevated spinal anandamide, PEA and OEA levels^[9]. C57BL/6J mice received a single intraperitoneal injection of 4mg/kg URB597. URB597 reduced saliva volume in male mice at 1 hour. URB597 reduced saliva volume in female mice at 3 hours^[10].

References:

- [1] Leung K. 6-Hydroxy-[1,1'-biphenyl]-3-yl-cyclohexyl-[¹¹C-carbonyl]carbamate. 2012 Oct 24 [updated 2013 Mar 21]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004–2013.
- [2] Bouskila J, Bleau M, Micaelo-Fernandes C, et al. The Vertical and Horizontal Pathways in the Monkey Retina Are Modulated by Typical and Atypical Cannabinoid Receptors. *Cells*. 2021 Nov 13;10(11):3160.
- [3] Clapper JR, Mangieri RA, Piomelli D. The endocannabinoid system as a target for the treatment of cannabis dependence. *Neuropharmacology*. 2009;56 Suppl 1(Suppl 1):235-43.
- [4] de Ceballos ML. The endocannabinoid system offers a target for Alzheimer's disease treatment through inhibition of fatty acid amide hydrolase (FAAH). *FEBS J*. 2025 Aug;292(16):4156-4159.
- [5] Grieco M, De Caris MG, Maggi E, et al. Fatty Acid Amide Hydrolase (FAAH) Inhibition Modulates Amyloid-Beta-Induced Microglia Polarization. *Int J Mol Sci*. 2021 Jul 19;22(14):7711.
- [6] Sekiba K, Otsuka M, Seimiya T, et al. The fatty-acid amide hydrolase inhibitor URB597 inhibits MICA/B shedding. *Sci Rep*. 2020 Sep 23;10:15556.
- [7] Slivicki RA, Xu Z, Mali SS, et al. Brain permeant and impermeant inhibitors of fatty-acid amide hydrolase suppress the development and maintenance of paclitaxel-induced neuropathic pain without producing tolerance or physical dependence in vivo and synergize with paclitaxel to reduce tumor cell line viability in vitro. *Pharmacol Res*. 2019 Apr;142:267-282.
- [8] Contarini G, Ferretti V, Papaleo F. Acute Administration of URB597 Fatty Acid Amide Hydrolase Inhibitor Prevents Attentional Impairments by Distractors in Adolescent Mice. *Front Pharmacol*. 2019 Jul 19;10:787.
- [9] Russo R, LoVerme J, La Rana G, et al. The Fatty Acid Amide Hydrolase Inhibitor URB597 (Cyclohexylcarbamic Acid 3'-Carbamoylbiphenyl-3-yl Ester) Reduces Neuropathic Pain after Oral Administration in Mice. *J Pharmacol Exp Ther*. 2007 Jul;322(1):236-242.

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[10] Andreis K, Billingsley J, Shirazi KN, et al. Cannabinoid CB1 receptors regulate salivation. Sci Rep. 2022 Aug 19;12:14182.

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