

Product Data Sheet

Product Name: CL 316,243 (disodium salt)

Cat. No.: GC43276

Chemical Properties

Cas. No. 151126-84-0,138908-40-4

Chemical Name 5-[(2R)-2-[[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-1,3-benzodioxole-2,2-dicarboxylic acid, disodium salt

SMILES C1C=CC=CC([C@@H](O)CN[C@H](C)CC2=CC=C(OC(C([O-])=O)(C([O-])=O)O3)C3=C2)=C1.[Na+].[Na+]

Formula $C_{20}H_{18}ClNO_7 \cdot 2Na$

M.Wt 465.8

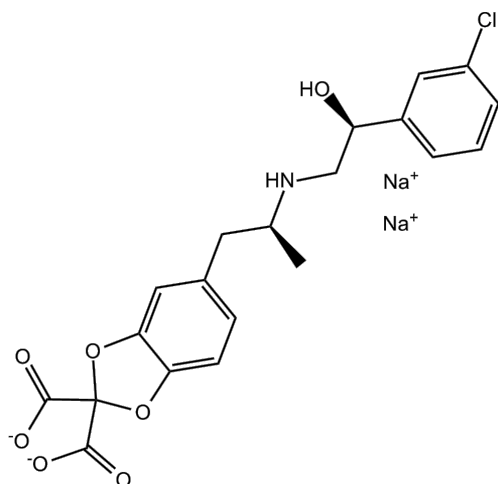
Solubility DMSO: 15mg/mL, H₂O: 4 mg/mL
(ultrasonic and warming and adjust pH to 12 with 1 M NaOH and heat to 60°C)

Storage Desiccate 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

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

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Cell experiment [1]:

Cell lines White and brown preadipocytes

Preparation Method At the third day of culture CL 316,243 (disodium salt) (10 nM) or isoproterenol (1mM) was added to the culture medium . Cells were harvested at day 10 and analysed.

Reaction
Conditions CL 316,243 (disodium salt) (10 nM); 7 days

Applications In both types of adipocyte culture lipid accumulation was first detectable at day 6 (around confluence) . Until day 10 an almost linear increase in lipid content occurred. overall lipid accumulation was about 30% higher in white adipocyte cultures than in brown ones.

Animal experiment [2]:

Animal models Insulin resistance model

Preparation Method Nine to ten week old male WT and MKR mice were injected intraperitoneally with CL-316,243 (1 mg/kg /day) or with an equivalent volume of vehicle (sterile water and phosphate buffered saline) for three weeks.

Applications CL 316,243 (disodium salt) (1 mg/kg ; ip), 3 weeks

After treatment with CL-316,243, the circulating glucose and insulin concentrations in the MKR mice improved, an increase in the expression of peroxisomal fatty acid oxidation genes was observed in addition to a decrease in the expression of retinaldehyde dehydrogenases.

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References:

- [1]. Klaus S, Seivert A, Boeuf S. Effect of the beta(3)-adrenergic agonist CL316,243 on functional differentiation of white and brown adipocytes in primary cell culture. *Biochim Biophys Acta*. 2001 May 28;1539(1-2):85-92.
- [2]. Kumar A, Shiloach J, Betenbaugh MJ, Gallagher EJ. The beta-3 adrenergic agonist (CL-316,243) restores the expression of down-regulated fatty acid oxidation genes in type 2 diabetic mice. *Nutr Metab (Lond)*. 2015 Mar 8;12:8.

Background

CL 316,243 (disodium salt) is a highly potent β 3-adrenoceptor selective agonist with an EC₅₀ of 3 nM. It is a potent adipocyte lipolysis stimulator that increases thermogenesis and metabolic rate of brown adipose tissue and has the potential to treat obesity, diabetes, and urge urinary incontinence^[1].

CL 316,243 (disodium salt) (10 nM, 10 days) treated with white and brown adipocytes, lipid accumulation was first detected on day 6 (confluence) and lipid content increased almost linearly until day 10. Overall lipid accumulation in white adipocyte cultures was approximately 30% higher than in brown adipocyte cultures^[2]. CL 316,243 (disodium salt) inhibits spontaneously contracting, isolated rat detrusor strips in a concentration dependent manner with a mean concentration inhibiting 50% of maximal response of 2.65 nM^[3].

Following treatment with CL 316,243 (disodium salt) (1 mg/kg; i.p.; 3 weeks), expression of peroxisomal FA oxidases ACAA1 and HSD17b4 was increased in adipose tissue of MKR mice^[4]. CL 316,243 (disodium salt) (1 mg/kg; SC; 2 weeks) reduced serum levels of glucose, insulin, triglycerides, free fatty acids, and tumor necrosis factor- α (TNF- α), and increased adiponectin^[5]. CL 316,243 (disodium salt) (0.3 and 1 mg/kg; 2 weeks; subcutaneous injection) dose-dependently reduced the weight/volume of the inguinal fat pad^[6].

[1]. Bloom JD, Dutia MD, Johnson BD, Wissner A, Burns MG, Largis EE, Dolan JA, Claus TH. Disodium (R,R)-5-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]-amino] propyl]-1,3-benzodioxole-2,2-dicarboxylate (CL 316,243). A potent beta-adrenergic agonist virtually specific for beta 3 receptors. A promising antidiabetic and antiobesity agent. *J Med Chem*. 1992 Aug 7;35(16):3081-4.

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- [2]. Klaus S, Seivert A, Boeuf S. Effect of the beta(3)-adrenergic agonist CL316,243 on functional differentiation of white and brown adipocytes in primary cell culture. *Biochim Biophys Acta*. 2001 May 28;1539(1-2):85-92.
- [3]Woods M, Carson N, Norton NW, Sheldon JH, Argentieri TM. Efficacy of the beta3-adrenergic receptor agonist CL-316243 on experimental bladder hyperreflexia and detrusor instability in the rat. *J Urol*. 2001 Sep;166(3):1142-7.
- [4]. Kumar A, Shiloach J, Betenbaugh MJ, Gallagher EJ. The beta-3 adrenergic agonist (CL-316,243) restores the expression of down-regulated fatty acid oxidation genes in type 2 diabetic mice. *Nutr Metab (Lond)*. 2015 Mar 8;12:8.
- [5]. Shin W, Okamatsu-Ogura Y, Matsuoka S, Tsubota A, Kimura K. Impaired adrenergic agonist-dependent beige adipocyte induction in obese mice. *J Vet Med Sci*. 2019 Jun 6;81(6):799-807.
- [6]Danyasz W, Han Y, Li F, Nicoll J, Buch P, Hengl T, Ruitenbergh M, Parsons C. Browning of white adipose tissue induced by the β_3 agonist CL-316,243 after local and systemic treatment - PK-PD relationship. *Biochim Biophys Acta Mol Basis Dis*. 2018 Sep;1864(9 Pt B):2972-2982.

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