

Product Data Sheet

Product Name: L-755,507

Cat. No.: GC15743

Chemical Properties

Cas. No. 159182-43-1

Chemical Name (S,Z)-N'-hexyl-N-(4-(N-(4-(2-((2-hydroxy-3-(4-hydroxyphenoxy)propyl)amino)ethyl)phenyl)sulfamoyl)phenyl)carbamimidic acid

SMILES CCCCCC/N=C(O)/NC1=CC=C(S(NC2=CC=C(CCNC[C@@](O)([H])COC3=CC=C(O)C=C3)C=C2)(=O)=O)C=C1

Formula C₃₀H₄₀N₄O₆S M.Wt 584.73

Solubility DMF: 30 mg/mL, DMSO: 25 mg/mL, Ethanol: 30 mg/mL, Ethanol: PBS (pH 7.2) (1:3): 0.25 mg/mL
 Storage Desiccate at RT

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.

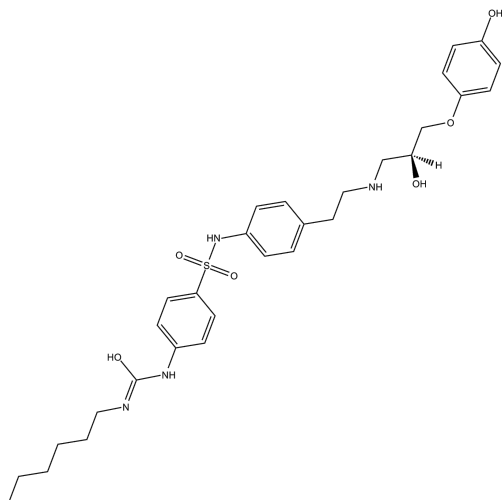
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment: The cytosensor microphysiometer is used to measure $\beta 3$ -AR-mediated increases in ECAR. In brief, CHO $\beta 3$ cells are seeded into 12-mm Transwell inserts at 5×10^5 cells/cup and left to adhere overnight. On the day of experiment, cells are equilibrated for 2 h, and cumulative concentration-response curves to L755507, zinterol, or L748337 are constructed in paired sister cells with each concentration of drug exposed to cells for 14 min. Results are expressed as a percentage of the maximal response to L755507. In experiments examining the effect of inhibitors, cells are treated for 30 min before stimulation with appropriate drugs. All drugs are diluted in modified RPMI 1640 medium. These results are expressed as a percentage of the maximal response to L755507, zinterol, or L748337 over basal[1].

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References:

- [1]. Sato M, et al. The beta3-adrenoceptor agonist 4-[[[(Hexylamino)carbonyl]amino]-N-[4-[2-[[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]ethyl]-phenyl]-benzenesulfonamide (L755507) and antagonist (S)-N-[4-[2-[[[3-(acetamidomethyl)phenoxy]-2-hydroxypropyl]amino]-ethyl]phenyl]benzenesulfonamide (L748337) activate different signaling pathways in Chinese hamster ovary-K1 cells stably expressing the human beta3-adrenoceptor. *Mol Pharmacol*. 2008 Nov;74(5):1417-28.
- [2]. Guoling Li, et al. Small molecules enhance CRISPR/Cas9-mediated homology-directed genome editing in primary cells. *Sci Rep*. 2017; 7: 8943.

Background

IC50: 13 nM (binding at the human $\beta 3$ adrenergic receptor) [1]

Benzenesulfonamide derivative L-755,507 is a partial agonist for the human $\beta 3$ receptor, with maximal activation 52% of that evoked by isoproterenol [2]. $\beta 3$ adrenergic receptor is a G protein-coupled receptors which can enhancement of lipolysis in adipose tissue.

In vitro: L-755,507 displays an excellent activity profile as an extremely potent human $\beta 3$ adrenergic receptor agonist ($\beta 3$ EC50 0.43 nM), with >440-fold selectivity over $\beta 1$ and $\beta 2$ binding [1]. L-755,507 is also a potent and selective $\beta 3$ partial agonist in rhesus monkeys as assessed by its affinity for the cloned β adrenergic receptors, and stimulates lipolysis in rhesus adipocytes with an EC50 = 3.9 nM [2].

In vivo: Dose rhesus monkeys with L-755,507 elicits lipolysis and metabolic rate elevation. The ED50 for glycerolemia was 0.03 mg/kg and the ED50 for tachycardia was 2.5 mg/kg, and stimulates metabolic rate by ~ 30% after acute bolus intravenous administration of 0.1 mg/kg [2].

Clinical trial: So far, no clinical study has been conducted.

References:

- [1] Parmee ER, Ok HO, Candelore MR, Tota L, Deng L, Strader CD, Wyvratt MJ, Fisher MH, Weber AE. Discovery of L-755,507: a subnanomolar human beta 3 adrenergic receptor agonist. *Bioorg Med Chem Lett*. 1998 May 5;8(9):1107-12.

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[2] Fisher MH, Amend AM, Bach TJ, Barker JM, Brady EJ, Candelore MR, Carroll D, Cascieri MA, Chiu SH, Deng L, Forrest MJ, Hegarty-Friscino B, Guan XM, Hom GJ, Hutchins JE, Kelly LJ, Mathvink RJ, Metzger JM, Miller RR, Ok HO, Parmee ER, Saperstein R, Strader CD, Stearns RA, MacIntyre DE, et al. A selective human beta3 adrenergic receptor agonist increases metabolic rate in rhesus monkeys. J Clin Invest. 1998 Jun 1;101(11):2387-93.

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