

Product Data Sheet

Product Name: Cinaciguat

Cat. No.: GC10962

Chemical Properties

Cas. No. 329773-35-5

Chemical Name 4-[[4-carboxybutyl]-[2-[2-[[4-(2-phenylethyl)phenyl]methoxy]phenyl]ethyl]amino]methyl]benzoic acid

SMILES C1=CC=C(C=C1)CCC2=CC=C(C=C2)COC3=CC=CC=C3CCN(CCCCC(=O)O)CC4=CC=C(C=C4)C(=O)O

Formula $C_{36}H_{39}NO_5$

M.Wt 565.7

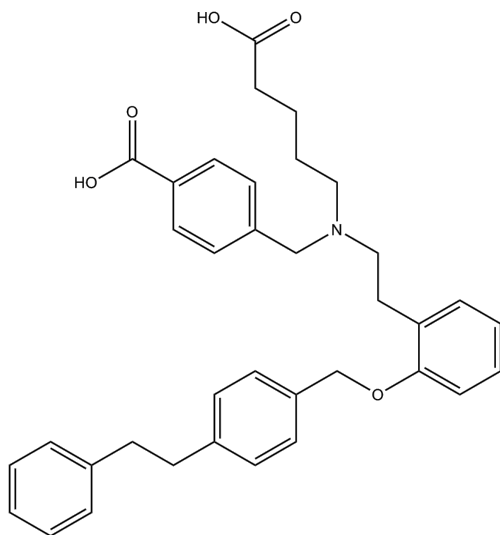
Solubility DMSO : ≥ 50 mg/mL (88.39 mM)

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

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

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Animal experiment: After confirmation of DM, rats are randomised into four groups: vehicle-treated control, cinaciguat-treated control, vehicle-treated diabetic and cinaciguat-treated diabetic groups. Animals are treated for 8 weeks with 0.5% methylcellulose vehicle or with the sGC activator cinaciguat in suspension p.o. (10 mg/kg/day), starting immediately after DM confirmation. Water bottles are filled every morning with the same amount of fresh tap water and daily water intake is measured. Animal cages are handled with care and are not moved after water bottle replacement to prevent spilling of water from the bottles. Body weight of the animals are recorded every 2 days and the dose of cinaciguat is adjusted accordingly.

References:

- [1]. Mátyás C, et al. The soluble guanylate cyclase activator cinaciguat prevents cardiac dysfunction in a rat model of type-1 diabetes mellitus. *Cardiovasc Diabetol*. 2015 Oct 31;14:145.
- [2]. Reinke Y, et al. The soluble guanylate cyclase stimulator riociguat and the soluble guanylate cyclase activator cinaciguat exert no direct effects on contractility and relaxation of cardiac myocytes from normal rats. *Format: AbstractSend to Eur J Pharmacol*
- [3]. Cosyns SM, et al. Influence of cinaciguat on gastrointestinal motility in apo-sGC mice. *Neurogastroenterol Motil*. 2014 Nov;26(11):1573-85.

Background

Cinaciguat, also known as BAY-58-2667, is a NO-independent activator for sGC with EC₅₀ of ~10 nM for heme-free/oxidized sGC. [1]

Heme-related dysfunction can lead to cardiovascular diseases with the oxidation of the heme of soluble guanylate cyclase (sGC) critically implicated in some of these cardiovascular diseases. sGC, the main nitric oxide receptor, stimulates second messenger cGMP production, however reactive oxygen species are known to scavenge NO and oxidize/inactivate the heme leading to sGC degradation. Cinaciguat binding causes a rotation of the α -helix away from the heme pocket, as this helix is normally held in place via the inhibitory His105–heme covalent bond. [2]

Cinaciguat activates sGC with EC₅₀ and K_d values in the low nanomolar range. This renders the compound the most potent NO-independent sGC activator reported to date. Furthermore, cinaciguat

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produces an additive, non-synergistic effect when combined with NO donors. Cinaciguat could also relax blood vessels with a high potency which is several orders of magnitude greater than the NO-donors sodium nitroprusside (SNP) and 3-morpho-linosydnonimin. In addition, the compound reduces coronary perfusion pressure in the rat Langendorff heart preparation and remains active in tissues made tolerant to glyceryl trinitrate. [1]

Cinaciguat could protect cardiomyocytes against ischemia/reperfusion injuries. Cinaciguat caused 63 and 41% reduction of infarct size when given before I/R and at reperfusion in rabbits, respectively. In addition, cinaciguat pretreatment caused a more robust 80% reduction in infarct size vs. 63% reduction when given at reperfusion and preserved cardiac function following I/R in mice, through cGMP-PKG-dependent generation of H₂S in the heart and cardiomyocytes.[3]

References:

- [1] Evgenov, Oleg V., et al. "NO-independent stimulators and activators of soluble guanylate cyclase: discovery and therapeutic potential." *Nature reviews Drug discovery* 5.9 (2006): 755-768.
- [2] Martin, Faye, et al. "Structure of cinaciguat (BAY 58–2667) bound to Nostoc H-NOX domain reveals insights into heme-mimetic activation of the soluble guanylyl cyclase." *Journal of Biological Chemistry* 285.29 (2010): 22651-22657.
- [3] Salloum, Fadi N., et al. "Cinaciguat, a novel activator of soluble guanylate cyclase, protects against ischemia/reperfusion injury: role of hydrogen sulfide." *American Journal of Physiology-Heart and Circulatory Physiology* 302.6 (2012): H1347-H1354.

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