

Product Data Sheet

Product Name: YIL 781 hydrochloride

Cat. No.: GC50049

Chemical Properties

Cas. No. 1640226-17-0

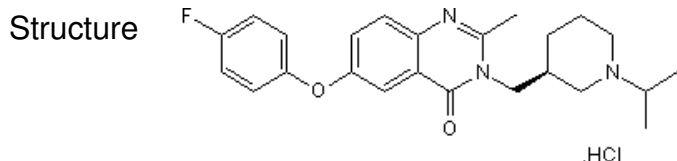
SMILES O=C2C1=CC(OC4=CC=C(F)C=C4)=CC=C1N=C(C)N2C[C@@H]3CN(C(C)C)CCC3.Cl

Formula C₂₄H₂₈FN₃O₂.HCl M.Wt 445.96

Solubility DMSO : 250 mg/mL (560.59 mM; Need ultrasonic) 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.



Protocol

Cell experiment [1]:

Cell lines HEK-293T cells

Preparation Method HEK-293T cells transfected with plasmids encoding for either GHSR1a (1.5μg) were pre-treated with selective antagonists for 10min, 1μM YIL 781 hydrochloride-GHSR1a-, and subsequently treated with the selective agonists, 200nM ghrelin -GHSR1a-. cAMP levels after 0.5μM forskolin stimulation were detected by the Lance Ultra cAMP kit and the results were expressed in % respect to levels obtained upon forskolin stimulation.

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

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Reaction
Conditions 1μM; 10min

Applications In cells expressing the GHSR1a, ghrelin induced a 25% decrease of forskolin-induced cAMP levels that was completely counteracted by YIL 781 hydrochloride (1μM), the selective GHSR1a antagonist.

Animal experiment [2]:

Animal models C57BL/6 mice

Mice were randomly divided into six groups with five mice in each group. (1) Normal group fed with a standard chow diet for 12 weeks and simultaneously injected with 0.9% normal saline daily for 2 weeks (Normal); (2) HFD group fed with HFD (45% kcal fat/17% kcal sucrose) for 12 weeks and simultaneously injected with 0.9% normal saline daily for 2 weeks; (3) Normal mice planted with gut microbiota from HFD mice group (Normal+HFDGM), received gut microbiota by intragastric administration once a week and fed with a standard chow diet for 12 weeks. The gut microbiota was isolated from fecal samples of HFD mice and cultured on agar media for 48 h. The gut microbiota from one HFD mouse was transplanted to a normal mouse. (4) High-fat diet BPH model group (BPH), fed HFD for 12 weeks and simultaneously received testosterone propionate (TP) (7.5mg/kg body weight, s.c.) daily for 2 weeks; (5) BPH with YIL 781 hydrochloride (BPH+YIL 781 hydrochloride), BPH mice were injected with YIL 781 hydrochloride, 5mg/kg body weight, i.p. daily for 1 week. Mice body weight was measured daily to adjust the dosage. Fasting blood glucose was detected and the feces were collected from mice after the last day and then the mice were sacrificed. The tissues of prostate gland were carefully harvested and weighed and then stored at -80°C for further analysis. The prostatic index (PI) (prostate weight mg/100g body weight) was analyzed.

Dosage form 5mg/kg/day; 7 days; i.p.

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Applications Ghrelin receptor antagonist YIL 781 hydrochloride showed little effect on ratio of Firmicutes to Bacteroidetes and blood ghrelin, however it significantly inhibits the prostate enlargement induced by HFD and testosterone propionate (TP).

References:

- [1] Lillo J, Lillo A, Zafra D A, et al. Identification of the ghrelin and cannabinoid CB2 receptor heteromer functionality and marked upregulation in striatal neurons from offspring of mice under a high-fat diet[J]. International journal of molecular sciences, 2021, 22(16): 8928.
- [2] Gu M, Liu C, Yang T Y, et al. High-fat diet induced gut microbiota alterations associating with Ghrelin/Jak2/Stat3 up-regulation to promote benign prostatic hyperplasia development[J]. Frontiers in cell and developmental biology, 2021, 9: 615928.

Background

YIL 781 hydrochloride is a selective ghrelin receptor (GHSR1a) antagonist with a K_i value of 17 nM^[1]. YIL 781 hydrochloride inhibits ghrelin-induced calcium response and improves glucose homeostasis in rats^[2]. Oral administration of YIL 781 hydrochloride to insulin-resistant diet-induced obesity (DIO) rats reduces blood glucose fluctuations^[3].

In vitro, pretreatment of GHSR1a-expressing HEK-293T cells with YIL 781 hydrochloride (1 μ M) for 10min completely reversed ghrelin-mediated forskolin-induced decrease in cAMP levels (approximately 25%)^[4]. Pretreatment of primary cultures of striatal neurons with YIL 781 hydrochloride (2 μ M) antagonized the GHSR1a signaling pathway induced by auxin-releasing peptide^[5].

In vivo, intraperitoneal injection of YIL 781 hydrochloride (5mg/kg/day) in mice for 1 week significantly inhibited prostate enlargement induced by a high-fat diet and testosterone propionate (TP)^[6]. YIL 781 hydrochloride (3mg/kg) reversed the effect of ulimorelin on renal sympathetic nerve activity (RSNA) in rats by intravenous injection^[7].

References:

- [1] Esler W P, Rudolph J, Claus T H, et al. Small-molecule ghrelin receptor antagonists improve glucose tolerance, suppress appetite, and promote weight loss[J]. Endocrinology, 2007, 148(11):

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5175-5185.

[2] Perdonà E, Faggioni F, Buson A, et al. Pharmacological characterization of the ghrelin receptor antagonist, GSK1614343 in rat RC-4B/C cells natively expressing GHS type 1a receptors[J]. European journal of pharmacology, 2011, 650(1): 178-183.

[3] Sangiao-Alvarellos S, Cordido F. Effect of ghrelin on glucose-insulin homeostasis: therapeutic implications[J]. International Journal of Peptides, 2010, 2010(1): 234709.

[4] Lillo J, Lillo A, Zafra D A, et al. Identification of the ghrelin and cannabinoid CB2 receptor heteromer functionality and marked upregulation in striatal neurons from offspring of mice under a high-fat diet[J]. International journal of molecular sciences, 2021, 22(16): 8928.

[5] Aguinaga D, Medrano M, Cordoní A, et al. Cocaine blocks effects of hunger hormone, ghrelin, via interaction with neuronal sigma-1 receptors[J]. Molecular neurobiology, 2019, 56(2): 1196-1210.

[6] Gu M, Liu C, Yang T Y, et al. High-fat diet induced gut microbiota alterations associating with Ghrelin/Jak2/Stat3 up-regulation to promote benign prostatic hyperplasia development[J]. Frontiers in cell and developmental biology, 2021, 9: 615928.

[7] Callaghan B, Kosari S, Pustovit R V, et al. Hypotensive effects of ghrelin receptor agonists mediated through a novel receptor[J]. British Journal of Pharmacology, 2014, 171(5): 1275-1286.

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