Sufugolix

Cat. No.: HY-100209

CAS No.: 308831-61-0

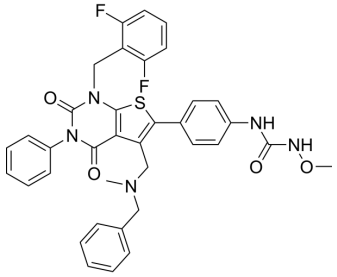
Molecular Formula: $C_{36}H_{31}F_2N_5O_4S$

Molecular Weight: 667.72

Target: GnRH Receptor

Pathway: GPCR/G Protein

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (29.95 mM; ultrasonic and warming and heat to 60°C)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4976 mL	7.4882 mL	14.9763 mL
5 mM	0.2995 mL	1.4976 mL	2.9953 mL
10 mM	0.1498 mL	0.7488 mL	1.4976 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Sufugolix (TAK-013) is a highly potent and orally available luteinizing hormone-releasing hormone (LHRH) receptor antagonist with an IC_{50} of 0.1 nM.

IC_{50} & Target

IC50: 0.1 nM (human LHRH), 0.6 nM (monkey LHRH)[1]

In Vitro

Sufugolix exhibits more than 3- and 2000-fold selectivity for the human receptor over the monkey and rat receptors, respectively. Sufugolix effectively antagonizes LHRH function on CHO cells expressing the human (IC_{50}=0.1 nM) and monkey (IC_{50}=0.6 nM) receptors. During the conformational analysis of sufugolix, using high-temperature molecular dynamics calculation, it is observed that the cis conformer of the methoxyurea is more populated than the trans conformer [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Oral administration of sufugolix causes almost complete suppression of the plasma LH levels in castrated male cynomolgus monkeys at a 30 mg/kg dose with sufficient duration of action (more than 24 h). The maximum plasma concentrations of sufugolix are 0.34 μM (reached 6 h after administration) and 0.18 μM (reached 4 h after administration) at 30 and 10 mg/kg doses, respectively[1].

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PROTOCOL

Kinase Assay [1]

The receptor-expressing CHO cells are seeded into 24-well plates at a density of 4×10^4 cells/well and cultured for 1 day. The cells are then incubated with [5,6,8,9,11,12,14,15-^{3}H]arachidonic acid (11 kBq/well) for 1 day and ished with DMEM supplemented with 20 mM HEPES and 0.2% BSA. The cells are then preincubated with the compounds (Sufugolix) at 37 °C for 60 min and the reaction is started by addition of LHRH (1 nM). After incubation at37 °C for 40 min, radioactivity in the medium is measured with a liquid scintillation counter[1].

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Animal Administration [1]

Monkeys: Sufugolix (10 or 30 mg/kg, 3 mL/kg, n=3 for each group) is suspended in 0.5% methylcellulose containing 1.2% citric acid, or 0.5% methylcellulose containing 1.2% citric acid alone (3 mL/kg, n=3), are administered orally. Blood samples (heparin-plasma) are collected from a femoral vein 24 h before administration and 0, 2, 4, 8, 24, and 48 h after administration. LH concentrations in the plasma are measured by bioassays using mouse testicular cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sasaki S, et al. Discovery of a thieno[2,3-d]pyrimidine-2,4-dione bearing a p-methoxyureidophenyl moiety at the 6-position: a highly potent and orally bioavailable non-peptide antagonist for the human luteinizing hormone-releasing hormone receptor. J Med Chem. 2003 Jan 2;46(1):113-24.

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