BIIE-0246

Cat. No.: HY-101986

CAS No.: 246146-55-4

Molecular Formula: $C_{49}H_{57}N_{11}O_6$

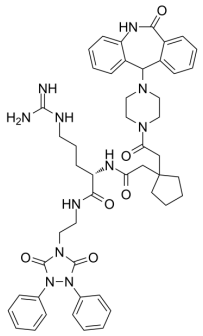
Molecular Weight: 896.05

Target: Neuropeptide Y Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (111.60 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1160 mL	5.5800 mL	11.1601 mL
	5 mM	0.2232 mL	1.1160 mL	2.2320 mL
	10 mM	0.1116 mL	0.5580 mL	1.1160 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (2.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BIIE-0246 is a potent and highly selective non-peptide neuropeptide Y (NPY) Y_2 receptor antagonist, with an IC_{50} of 15 nM.

IC_{50} & Target

NPY Y_2 receptor
15±3 nM (IC_{50})

In Vitro

Receptor binding assays in HEK 293 cells transfected with the rat Y2 receptor cDNA demonstrate that BIIE-0246 competes with high affinity (IC_{50}=15±3 nM) against specific [^{125}I]PYY_{3-36} binding sites. In contrast, BIIE-0246, at concentrations up to 10

	μM, fails to compete for significant amounts of specific [^{125}I]GR231118, [^{125}I]hPP and [^{125}I][Leu^{31}, Pro^{34}]PYY binding sites in HEK 293 cells transfected with the rat Y_1, Y_4 or Y_5 receptor cDNA, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	On chow diet, genetically obese NPY mice show increased gain in body weight and adiposity. Treatment with BIIE-0246 promotes body weight gain in both genotypes after 4.5 weeks, and already at 2 weeks. BIIE-0246 has no significant effect on fat mass gain. In DIO, BIIE-0246 has different effects on body weight and composition depending on the genotype (treatment×genotype interaction in body weight P<0.05, in fat mass P<0.001 and in lean mass P<0.05). In DIO-WT group, post hoc analysis reveals increased body weight and fat mass gain, and a tendency to decrease lean mass gain. In DIO-NPY, BIIE-0246 inhibits fat mass gain (P=0.05). Interestingly, increased cholesterol levels are detected also in WT mice treated with BIIE-0246 for 2 weeks, but not in the 4.5-week cohort. In DIO-NPY mice in both treatment groups, cholesterol levels correlate positively with body fat mass (DIO-NPY vehicle P<0.01; DIO-NPY BIIE-0246 P<0.001), but not in any other group, and the slope of the regression curve of cholesterol and fat mass is significantly decreased in BIIE-0246-treated DIO-NPY group when compared with vehicle-treated group[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] Homozygous transgenic male OE-NPYDbH and WT mice are used. The mice are housed at 21±3°C with a 12-h light/12-h dark cycle. To study the effect of Y_2-receptor antagonism in healthy conditions, standard rodent chow is fed ad libitum to OE-NPYDbH (NPY) and WT mice. To study the effect in DIO, western diet is fed for 8 weeks prior to the drug administration. Drug treatment is studied at the age of 20 weeks. Prior to treatments the mice are habituated for 2 weeks to the handling stress with daily saline injections (i.p). Mice receive 1.3 mg/kg of Y_2-receptor antagonist (BIIE-0246) or vehicle with daily IP injections. At termination, mice are fasted for 3 h and blood glucose is measured from awake animals. Mice are then anesthetized with ketamine (75 mg/kg i.p) and medetomidine (1 mg/kg i.p). Subcutaneous, epididymal, retroperitoneal and mesenteric white adipose tissue (WAT) pads, interscapular brown adipose tissue (BAT) and liver are collected and weighed [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Dumont Y, et al. BIIE0246, a potent and highly selective non-peptide neuropeptide Y Y(2) receptor antagonist. Br J Pharmacol. 2000 Mar;129(6):1075-88.

[2]. Liisa Ailanen, et al. Peripherally Administered Y2-Receptor Antagonist BIIE0246 Prevents Diet-Induced Obesity in Mice With Excess Neuropeptide Y, but Enhances Obesity in Control Mice. Front Pharmacol. 2018; 9: 319.

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