L-368,899

Cat. No.: HY-15008

CAS No.: 148927-60-0

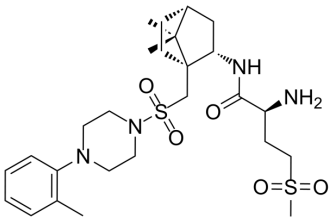
Molecular Formula: $C_{26}H_{42}N_4O_5S_2$

Molecular Weight: 554.77

Target: Oxytocin Receptor

Pathway: GPCR/G Protein

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

L-368,899 is an orally active and selective OT (oxytocin) receptor antagonist, with IC_{50}s of 8.9 and 26 nM for uterus of rat and human, respectively. L-368,899 can cross the blood-brain barrier (BBB). L-368,899 inhibits oxytocin-stimulated uterine contractions in rats and can be used in study of preterm labor[1][2][3].

IC_{50} & Target

IC50: 8.9 nM (rat uterus), 26 nM (human uterus)[3].

In Vivo

L-368,899 (0.1, 0.3, 1 mg/kg; infused i.v.; single) shows a dose-related antagonism of OT-stimulated uterine contractions with an AD_{50} value of 0.35 mg/kg in vivo[1].

L-368,899 (3, 10, 30 mg/kg; i.d.; single) inhibits the contractile effects of OT (AD_{50}= 7 mg/kg) with a long (>4 h) duration of action in vivo (AD_{50}: the dose of L-368,899 required to reduce the response to OT by 50%)[1].

L-368,899 (10 mg/kg, p.o.; single) shows bioavailability (AUC 0-6 h) of 35%[1].

L-368,899 (0.54, 1.8, 5.4 mg/kg; i.v.; single) reduces both oxytocin-induced and endogenous increases in plasma PGFM concentration[2].

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

Animal Model:	Adult female Sprague-Dawley rats (250-350 g)[1].
Dosage:	0.1, 0.3, 1 mg/kg
Administration:	Infused intravenous injection; single.
Result:	Inhibited OT-stimulated uterine contractions with an AD_{50} value of 0.35 mg/kg.

Animal Model:	Adult female Sprague-Dawley rats (250-350 g)[1].
Dosage:	3, 10, 30 mg/kg
Administration:	Intraduodenal; single.
Result:	Exhibited a antagonism of OT-stimulated uterine contractions with an AD_{50} of 7 mg/kg and duration of action more than 4 h.

Animal Model:	Adult female Sprague-Dawley rats (250-350 g)[1].
Dosage:	10 mg/kg
Administration:	Oral administration, single.
Result:	Showed orally active with bioavailability (AUC 0-6 h) of 35%.

Animal Model:	Mature Dorset cross ewes (53-57 kg; Removal of ovaries)[2].
Dosage:	0.54, 1.8, 5.4 mg/kg (3, 10 and 30 μg/kg/min for 3 h; dissolved in 0.9% saline).
Administration:	Intravenous infusion; single.
Result:	Led to a significant decrease in both the frequency (from 2.2 to 1.0 episodes/ewe) and amplitude (from 68.8 to 31.8 pg/mL) of episodes of increased plasma concentration of PGFM.

REFERENCES

[1]. Pettibone D J, et al. L-368,899, a potent orally active oxytocin antagonist for potential use in preterm labor[J]. Drug development research, 1993, 30(3): 129-142.

[2]. Mann GE, et al. Attenuation of PGF2alpha release in ewes infused with the oxytocin antagonist L-368,899. Domest Anim Endocrinol. 2003 Oct;25(3):255-62.

[3]. Williams PD, et al. 1-((7,7-Dimethyl-2(S)-(2(S)-amino-4-(methylsulfonyl)butyramido)bicyclo [2.2.1]-heptan-1(S)-yl)methyl)sulfonyl)-4-(2-methylphenyl)piperaz ine (L-368,899): an orally bioavailable, non-peptide oxytocin antagonist with potential utility for managing preterm labor. J Med Chem. 1994 Mar 4;37(5):565-71.

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