AG-045572

Cat. No.: HY-107534

CAS No.: 263847-55-8

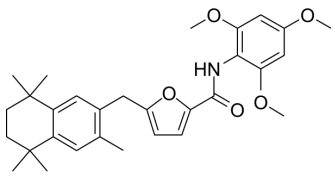
Molecular Formula: $C_{30}H_{37}NO_5$

Molecular Weight: 491.62

Target: GnRH Receptor

Pathway: GPCR/G Protein

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (203.41 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0341 mL	10.1705 mL	20.3409 mL
	5 mM	0.4068 mL	2.0341 mL	4.0682 mL
	10 mM	0.2034 mL	1.0170 mL	2.0341 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 (5.09 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.09 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AG-045572 is a GnRH receptor antagonist with K_is of 6.0 nM and 3.8 nM for human and rat GnRH receptor, respectively. AG-045572 is metabolized by CYP3A and ressuppresses testosterone[1].

In Vitro

AG-045572 (10 μM, 40 min, for human liver microsomes; 10 μM, 10 min, for male rat liver microsomes; 1 μM, 10 min, for female rat liver microsomes) is metabolized by CYP3A4 (HY-P74210) in both rats and humans with the K_m values were similar in male and female human, female rat liver microsomes, and expressed CYP3A4 and CYP3A5 (0.39, 0.27, 0.28, 0.25, and 0.26 μM, respectively), and the K_m in male rat liver microsomes was 1.5 μM, suggesting that in male and female rats AG-045572 is metabolized by different CYP3A isozymes[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

AG-045572 (10 mg/kg (i.v.) or 20 mg/kg (p.o.), one time) give to intact male rats, it showed medium $T_{1/2}$, CL and V_{ss} but oral

bioavailability was low, in female rats the bioavailability was much higher (24%), in castrated male rats the pharmacokinetics was similar to that in female rats[1].
AG-045572 (40 mg/kg, i.m. twice a day for 3 days) pretreated of intact male rats resulted in a change of its pharmacokinetics, the parameters became similar to those in female and castrated male rats[1].
Pharmacokinetic Parameters of AG-045572 in Rats after Administration at 10 mg/kg i.v. and 20 mg/kg p.o.[1]

□□□□□□10 mg/kg□□□20 mg/kg□□□AG-045572□□□□□□□□□[1]

Animals	$t_{1/2}$ (h)	CL (L/h/kg)	V_{ss} (L/kg)	C_{max} (μM)	T_{max} (h)	$F_{p.o.}$ (%)
Male	1.4 ± 0.1	2.2 ± 0.5	2.1 ± 0.1	0.61 ± 0.21	1	8
Female	1.7 ± 0.1	1.5 ± 0.1	2.7 ± 0.4	2.31 ± 0.57	1	24
Castrated male	1.7 ± 0.4	1.5 ± 0.3	3.7 ± 1.5	1.98 ± 0.51	1	23
Pretreated male	1.9 ± 0.2	1.5 ± 0.2	2.0 ± 0.6	1.89 ± 0.41	1	27

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Animal Model:	Male rats were surgically castrated via scrotal approach under halothane anesthesia and allowed 14 days post-operative recovery prior to study[1]
Dosage:	10 mg/kg, 20 mg/kg; 40 mg/kg
Administration:	administered acutely at 10 mg/kg (i.v.) or 20 mg/kg (p.o.), one time; For multiple-dose pretreatment, male rats at 40 mg/kg, i.m. twice a day for 3 days.
Result:	Showed medium $T_{1/2}$, CL and V_{ss} but oral bioavailability was low, in female rats the bioavailability was much higher (24%) Became similar to those in female and castrated male rats.

REFERENCES

[1]. Iatsimirskaia EA, et al. Effect of testosterone suppression on the pharmacokinetics of a potent gnRH receptor antagonist. Pharm Res. 2002 Feb;19(2):202-8.

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