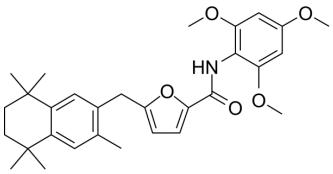
AG-045572

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



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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