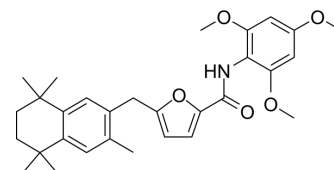


AG-045572

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)



BIOLOGICAL ACTIVITY

Description	AG-045572 is a GnRH receptor antagonist with K _s of 6.0 nM and 3.8 nM for human and rat GnRH receptor, respectively. AG-045572 is metabolized by CYP3A and ressupresses 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	<p>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].</p> <p>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].</p> <p>Pharmacokinetic Parameters of AG-045572 in Rats after Administration at 10 mg/kg i.v. and 20 mg/kg p.o.^[1]</p> <p>10 mg/kg 20 mg/kg AG-045572^[1]</p> <table border="1"> <thead> <tr> <th>Animals</th> <th>t_{1/2} (h)</th> <th>CL (L/h/kg)</th> <th>V_{ss} (L/kg)</th> <th>C_{max} (μM)</th> <th>T_{max} (h)</th> <th>F_{p.o.} (%)</th> </tr> </thead> <tbody> <tr> <td>Male</td> <td>1.4 ± 0.1</td> <td>2.2 ± 0.5</td> <td>2.1 ± 0.1</td> <td>0.61 ± 0.21</td> <td>1</td> <td>8</td> </tr> <tr> <td>Female</td> <td>1.7 ± 0.1</td> <td>1.5 ± 0.1</td> <td>2.7 ± 0.4</td> <td>2.31 ± 0.57</td> <td>1</td> <td>24</td> </tr> <tr> <td>Castrated male</td> <td>1.7 ± 0.4</td> <td>1.5 ± 0.3</td> <td>3.7 ± 1.5</td> <td>1.98 ± 0.51</td> <td>1</td> <td>23</td> </tr> <tr> <td>Pretreated male</td> <td>1.9 ± 0.2</td> <td>1.5 ± 0.2</td> <td>2.0 ± 0.6</td> <td>1.89 ± 0.41</td> <td>1</td> <td>27</td> </tr> </tbody> </table> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	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.

Caution: Product has not been fully validated for medical applications. For research use only.

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