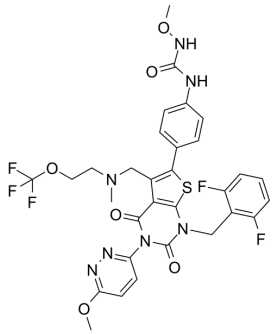
GnRH-R antagonist 1

Cat. No.:	HY-151247
CAS No.:	2826273-90-7
Molecular Formula:	$C_{31}H_{28}F_5N_7O_6S$
Molecular Weight:	721.65
Target:	GnRH Receptor
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GnRH-R antagonist 1 (compound 21a) is an orally safe and membrane-permeable GnRH-R antagonist with high binding affinity (IC_{50}=0.57 nM) and potent in vitro antagonistic activity (IC_{50}=2.18 nM). GnRH-R antagonist 1 can be used in studies of advanced prostate cancer and premature LH peaks preventing[1].

In Vitro

GnRH-R antagonist 1 has a 140-fold higher cell permeability than Relugolix and exhibits favorable stability in human and mouse microsome[1].

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

In Vivo

GnRH-R antagonist 1 (30 mg/kg; p.o.; single daily for 7 days) has a good safety profile for oral administration[1].

GnRH-R antagonist 1 (12 mg/kg; p.o.; single) shows favorable pharmacokinetic properties and high oral bioavailability with a F% value of 44.7%[1].

GnRH-R antagonist 1 (12 mg/kg; p.o.; single) inhibits circulating testosterone levels in rats (lasts for more than 24 h)[1].

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

Animal Model:	Adult Sprague-Dawley rats (200-250 g)[1].
Dosage:	30 mg/kg
Administration:	Oral administration; single daily for 7 days.
Result:	Showed no ames toxicity.

Animal Model:	Adult Sprague-Dawley rats (200-250 g)[1].
Dosage:	1 mg/kg (for i.v.); 12 mg/kg (for p.o.)
Administration:	Intravenous administration ;oral administration; single.
Result:	Exhibited clear and significnt suppressive effects on circulating testosterone levels in rats, and the suppressive effects lasted for more than 24 h. Pharmacokinetic Parameters of GnRH-R antagonist 1 in Adult Sprague-Dawley rats[1].

	IV (1 mg/kg)	PO (12 mg/kg)
T_{max} (h)	-	1.13
C_{max} (nmol/L)	3918.8	920.1
AUC_{Last} (nmol/L•h)	1374.6	7370.6
CL (L/h/kg)	1.05	-
$t_{1/2}$ (h)	2.79	4.86
F (%)	-	44.7

REFERENCES

[1]. Zou F, et al. Discovery of the thieno[2,3-d]pyrimidine-2,4-dione derivative 21a: A potent and orally bioavailable gonadotropin-releasing hormone receptor antagonist. Eur J Med Chem. 2022 Aug 18;242:114679.

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