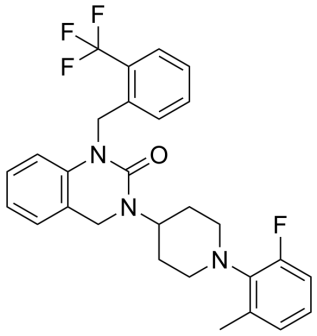
C5aR1 antagonist 1



Cat. No.:	HY-163378
CAS No.:	2365325-67-1
Molecular Formula:	$C_{28}H_{27}F_4N_3O$
Molecular Weight:	497.53
Target:	Complement System
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description	C5aR1 antagonist 1 (Compound 7e) is an orally active C5a receptor 1 (C5aR1) antagonist. C5aR1 antagonist 1 is active in DISCO and migration assays, with IC_{50} values of 38 nM and 17 nM, respectively. C5aR1 antagonist 1 can be used for the research of acute and chronic inflammatory diseases[1].
IC_{50} & Target	C5aR1
In Vitro	C5aR1 antagonist 1 (compound 7e) is a surmountable and competitive antagonist of C5aR, with the K_D value of 15 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The pharmacokinetic profile of C5aR1 antagonist 1 (compound 7e) (10/30/50 mg/kg, single administration) in vivo in rat, dog, and cynomolgus monkey indicates that the low solubility of the compound waslimiting the exposure[1]. C5aR1 antagonist 1 (1/3/10 mg/kg, administered orally 2/8/16h before blood sampling for neutrophil quantification) dose-dependent inhibits the increase of neutrophils in the blood of the neutrophilic rat model[1]. C5aR1 antagonist 1 (0/1/3/10/30 mg/kg, administered orally 2 h before blood sampling) inhibites the upregulation of CD11b of the female hC5aR1 knock-in rats by around 90%[1].

Pharmacokinetic Properties of Compound 7e[1]

Animals	Route	Dose (mg/kg)	CL mL/(min×kg)	V_{ss_obs} (L/kg)	T1/2 (h)	AUC_{0-last} (ng×h)/mL	C_{max} (ng×h)/mL	T_{max} (h)
rat	p.o.	10	39	7.1	4.1	32200	3890	2
dog	p.o.	30	2.3	7.6	1.1	14900	2530	1
monkey	p.o.	50	3500	635	2	41900	3940	4

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Animal Model:	Neutrophilia Rat Model[1]

Dosage:	1/3/10 mg/kg
Administration:	Oral gavage (p.o.), Rats were administered po with compound or vehicle at 23.5/15.5/7.5/1.5 h before hC5a iv injection.
Result:	Inhibited reactive neutrophilia induced by hC5a administration in vivo.

REFERENCES

[1]. Hubler, F., D. Renneberg, et al. "Discovery and Characterization of a New Class of C5aR1 Antagonists Showing In Vivo Activity." Journal of Medicinal Chemistry. 2024 March 04.

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