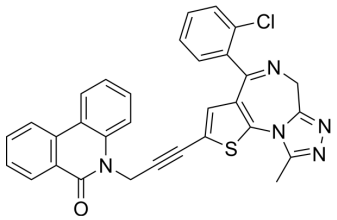
Ro-24-4736

Cat. No.:	HY-19097
CAS No.:	125030-71-9
Molecular Formula:	$C_{31}H_{20}ClN_5OS$
Molecular Weight:	546.04
Target:	Platelet-activating Factor Receptor (PAFR)
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Ro 24-4736 is a potent, selective, p.o.-active platelet-activating factor (PAF) antagonist with a long duration of action. Ro-24-4736 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.
IC_{50} & Target	PAF[1]
In Vitro	Ro 24-4736 competes with [^{3}H]PAF for its receptor site on dog platelets with an IC_{50} of 9.8±1.0 nM and selectively inhibits PAF-induced aggregation of guinea pig, dog and human platelets with concentration dependence[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ro 24-4736 dose-dependently inhibits in vivo bronchoconstriction (ID50 of 0.006-mg/kg p.o.) and ex vivo platelet aggregation (ID_{50} of 0.004 mg/kg p.o.) induced by PAF in guinea pigs. Time course studies show complete blockade of PAF-induced platelet aggregation (ex vivo) up to 8 hr after a single p.o. dose of 0.03 mg/kg as well as a long duration of action in vivo (30 hr). The in vivo PAF antagonistic activity is specific because, even at high p.o. doses (up to 10 mg/kg), Ro 24-4736 shows no inhibitory activity toward the bronchoconstrictor effects of leukotriene D4 or histamine. In comparison with other PAF antagonists evaluated in this guinea pig model, Ro 24-4736 is markedly superior in terms of p.o. potency, bioavailability and p.o. duration of action. Studies are also performed with Ro 24-4736 in additional in vivo models. When administered p.o. to sensitized guinea pigs, the drug attenuates inhaled antigen-induced airway hyper-reactivity without effect on bronchoalveolar lavage leukocyte accumulation[1]. Ro 24-4736 is a new platelet activating factor antagonist. The tissue distribution of the ^{14}C-label in male rats following a single intravenous dose of 1.0 mg/kg of 14C-Ro 24-4736 indicats appreciable uptake by the liver, kidney, heart and gastrointestinal tract. Peak plasma and tissue concentrations are seen at 5 minutes after dosing except for the small intestine (4 hrs) and abdominal fat, stomach and large intestine (4 hrs). At 48 hours, only 3.5% of the dose is present in the tissues, and 6.1% in the lumen of the gastrointestinal tracts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Crowley HJ, et al. Pharmacology of a potent platelet-activating factor antagonist: Ro 24-4736. J Pharmacol Exp Ther. 1991 Oct;259(1):78-85.

[2]. Anastasi EM, et al. Disposition and metabolism of Ro 24-4736 in the rat. Life Sci. 1994;54(26):PL483-90.

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

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