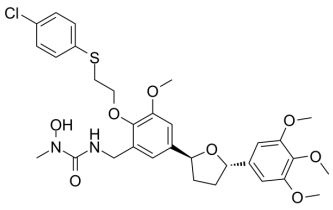
CMI-392

Cat. No.:	HY-19205A
CAS No.:	205654-37-1
Molecular Formula:	$C_{31}H_{37}ClN_2O_8S$
Molecular Weight:	633.15
Target:	Lipoxygenase
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	CMI-392 is a dual 5-lipoxygenese inhibitor and platelet-activating factor (PAF) receptor antagonist with IC_{50}s of 100 and 10 nM, respectively.	
IC_{50} & Target	5-LO 100 nM (IC_{50})	PAF 10 nM (IC_{50})
In Vivo	Topical treatment of CMI-392 in the acute and chronic TPA models result in a significant decrease of ear weight, inflammatory cell infiltration, and histological examination. The ED_{50} for PAF-induced mouse hemoconcentration and arachidonic acid-induced mouse ear edema are 2.2 and 1.8 mg/kg, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

PROTOCOL

Kinase Assay [1]	5-lipoxygenese activity in cell lysate is determined as follows: 0.1 mL reactions consisting of buffer, test compound (CMI-392 in DMSO), and an amount of cell lysate that will convert 15% of [^{14}C]AA substrate mix to oxygenated products are incubated (20 min, room temperature). A substrate mix containing [^{14}C]AA is added and incubated further (5 min, 37°C). The reaction is terminated by adding 0.2 mL of an organic extraction solution containing triphenylphosphine, followed by microcentrifugation. The organic phase (50 µL) is spotted onto silica gel TLC plates. The plates are developed in ethyl ether/acetic acid (100:0.1) (25 min, room temperature). Plates are exposed to film for 36 h. The film is developed and scanned using a densitometer, and the peak areas of AA and its products are calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Acute TPA-induced ear edema in mice is determined by topically applying TPA to the ears of mice. Mice are sacrificed after 6 h and the ear punch biopsies are weighed. Chronic TPA-induced ear edema in mice is determined by topically applying TPA once a day every 2 days for a total of 10 days. CMI-392 is topically administered twice daily on the last 3 days of the experiment. Mice are then sacrificed and the ear punch biopsies are weighed. Biopsies are homogenized and MPO content is determined via spectrophotometric assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Cai X, et al. (+/-)-trans-2-[3-methoxy-4-(4-chlorophenylthioethoxy)-5-(N-methyl-N- hydroxyureidyl)methylphenyl]-5-(3,4, 5-trimethoxyphenyl)tetrahydrofuran (CMI-392), a potent dual 5-lipoxygenase inhibitor and platelet-activating factor receptor antagonist. J Med Chem. 1998 May 21;41(11):1970-9.

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