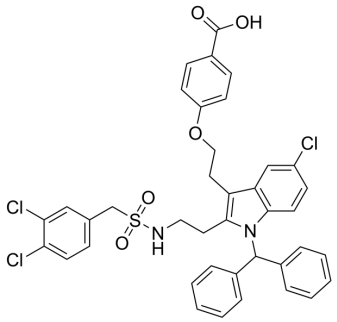
Ecopladib

Cat. No.:	HY-U00037
CAS No.:	381683-92-7
Molecular Formula:	$C_{39}H_{33}Cl_3N_2O_5S$
Molecular Weight:	748.11
Target:	Phospholipase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	Ecopladib is a sub-micromolar inhibitor of cytosolic phospholipase A2α (cPLA2α), with IC_{50}s of 0.15 μM and 0.11 μM in the GLU micelle and rat whole blood assays, respectively.
IC_{50} & Target	IC50: 0.15 μM (cPLA2α, in GLU micelle), 0.11 μM (cPLA2α, rat blood)[1]
In Vitro	Ecopladib inhibits cPLA2α in the PAPE liposome assay at 73% at a concentration of 37 nM, while it inhibits sPLA2 at 16% at 1 μM. Ecopladib inhibits the production of prostaglandins (PGF2α) and leukotrienes (LTB4 and LTC4/D4/E4) with comparable IC_{50}s of 20−30 nM. Ecopladib is inactive against COX-1 and COX-2 at 20 μM, which is nearly 100 times the IC_{50} in the MC-9 cells. Ecopladib inhibit 12- and 15-HETE, which are derived from arachidonic acid via the 12- and 15-lipoxygenase pathways and the IC_{50}s are -0.3 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ecopladib is orally efficacious in this model and displays an ED_{50} of 8 mg/kg, demonstrating that it can inhibit COX-2 derived PGE2 formation in vivo. Ecopladib is orally efficacious at reducing carrageenan-induced paw swelling: from dose−response studies, it is determined that the ED_{50} is 40 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Male Sprague−Dawley rats are anesthetized, and 10−20 mL of filtered air is injected subcutaneously under the dorsal skin to form a pouch. Three and six days later, the pouches are reinflated with 10−15 mL of sterile air. On the seventh day, the test compound is dissolved in vehicle (55.5% Phosal 53 MCT, 5.6% Tween 80, 16.7% Labrasol, and 22.2% propylene carbonate) to give 37.5 mg of test compound per mL of vehicle. This test compound in vehicle is diluted with water to the appropriate concentration and dosed at 4 mL/kg. Vehicle treated animals receives the same amount of vehicle as the animals treated with the highest dose of compound. Two hours later, 2 mL of a 1% solution of carrageenan (Viscarin carrageenan type GP-209NF) in saline is injected into the pouch. Six hours after the carrageenan injection, the rats are individually sacrificed and the contents of the pouch are harvested. The amount of fluid recovered is measured. An aliquot of the exudate is centrifuged at 6500 rpm for 10 min, and 300 μL of each supernatant is precipitated with MeOH (800 μL) precooled to 0°C. The samples are well vortexed and are kept at −80°C overnight. The samples are centrifuged again and assayed for PGE2 to

locate the PGE2 production within the linear range of the PGE2 standard curve. To minimize the difference in binding environments for the standards and samples, the standard curve is generated in a 1% solution of carrageenan that is mixed with assay buffer to the same dilution as the samples. The approximate ED_{50} value is extrapolated from the dose−response curve.

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

REFERENCES

[1]. Lee KL, et al. Discovery of Ecopladib, an indole inhibitor of cytosolic phospholipase A2alpha. J Med Chem. 2007 Mar 22;50(6):1380-400. Epub 2007 Feb 17.

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