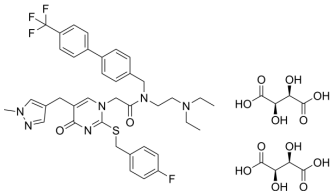
SB-435495 ditartrate

Cat. No.:	HY-19415B
CAS No.:	304694-43-7
Molecular Formula:	$C_{46}H_{52}F_4N_6O_{14}S$
Molecular Weight:	1021
Target:	Phospholipase
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	SB-435495 ditartrate is a potent, selective, reversible, non-covalent and orally active Lp-PLA_2 inhibitor with an IC_{50} of 0.06 nM[1][3].
IC_{50} & Target	Lp-PLA2 0.06 nM (IC_{50})
In Vitro	SB-435495 ditartrate inhibits CYP450 3A4 with an IC_{50} of 10 μM and the black membrane permeability is 0.017 cm/h[1]. SB-435495 (5 μM; 24 h) ditartrate significantly inhibits the expression of Lp-PLA_2 protein, while increases the expression levels of AMPKα and phosphorylated-AMPKα (T172) in oxLDL-exposed HUVECs[2]. SB-435495 (5 μM; 24-72 h) ditartrate significantly increases cell viability and NO expression, significantly decreases ET-1 expression in the oxLDL-exposed HUVECs[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SB-435495 (10 mg/kg; p.o.; once) ditartrate inhibits plasma Lp-PLA_2 in the WHHL rabbit[1]. SB-435495 (10 mg/kg; i.p.; daily for 28 days) ditartrate effectively suppresses blood–retinal barrier (BRB) breakdown in

Western Blot Analysis[2]

Cell Line:	oxLDL-exposed human umbilical vein endothelial cells
Concentration:	5 μM
Incubation Time:	24 h
Result:	The expression of Lp-PLA_2 protein was significantly inhibited. Increased the expression levels of AMPKα and phosphorylated-AMPKα (T172).

Cell Viability Assay[2]

Cell Line:	oxLDL-exposed human umbilical vein endothelial cells
Concentration:	5 μM
Incubation Time:	24, 48 and 72 h
Result:	Significantly increased cell viability.

Streptozotocin (HY-13753)-diabetic Brown Norway rats[3].

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

Animal Model:	WHHL rabbit[1]
Dosage:	10 mg/kg
Administration:	Oral, once
Result:	Inhibited plasma Lp-PLA_2 in the WHHL rabbit.

REFERENCES

[1]. Blackie JA, et al. The discovery of SB-435495. A potent, orally active inhibitor of lipoprotein-associated phospholipase A(2) for evaluation in man. Bioorg Med Chem Lett. 2002 Sep 16;12(18):2603-6.

[2]. Yang L, et al. AMP-activated protein kinase mediates the effects of lipoprotein-associated phospholipase A2 on endothelial dysfunction in atherosclerosis. Exp Ther Med. 2017 Apr;13(4):1622-1629.

[3]. Canning P, et al. Lipoprotein-associated phospholipase A2 (Lp-PLA2) as a therapeutic target to prevent retinal vasopermeability during diabetes. Proc Natl Acad Sci U S A. 2016 Jun 28;113(26):7213-8.

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