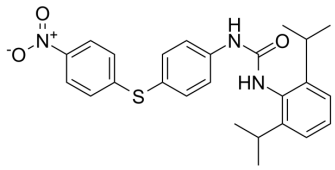
VULM 1457

Cat. No.:	HY-107571
CAS No.:	228544-65-8
Molecular Formula:	$C_{25}H_{27}N_3O_3S$
Molecular Weight:	449.57
Target:	Acyltransferase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (556.09 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2243 mL	11.1217 mL	22.2435 mL
	5 mM	0.4449 mL	2.2243 mL	4.4487 mL
	10 mM	0.2224 mL	1.1122 mL	2.2243 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

VULM 1457 is a potent inhibitor of cholesterol acyltransferase (acyl-CoA). VULM1457 significantly reduces production and secretion of adrenomedullin (AM) and down-regulates AM receptors on human hepatoblastic cells. VULM 1457 has remarkable hypolipidaemic activity and improves the overall myocardial ischaemia-reperfusion injury outcomes. VULM 1457 has the potential for the research of diabetes mellitus and hypercholesterolaemia[1][2].

IC_{50} & Target

ACAT

In Vitro

VULM1457 (0.03 and 0.1 μM) significantly down-regulates specific AM receptors on HepG2 cells, reduced AM secretion of HepG2 cells exposed to hypoxia[1].VULM1457 negatively regulates cell proliferation induced by AM[1].

Preincubation of HepG2 cells with VULM1457 (0.1 μM) significantly reduces the total number of specific [^{125}I]AM binding identified on cells at untouched affinity. Preincubation of HepG2 cells with high concentrations of VULM1457 (1.0 and 10.0 μM) significantly modifies the characteristics of binding of AM, i.e[1].

Preincubation of HepG2 cells with VULM1457 (0.1 μM) significantly reduces the specific [^{125}I]AM binding on hypoxic cells with $B_{maxHypox}$ being 127±10 and K_D 0.06±0.11 nM. Preincubation of cells with VULM1457 (0.1 μM) significantly enhances the number of cells (24.2±6 %) and higher concentrations of VULM1457 (1.0 and 10.0 μM) reduces the total number of cells. With

	the high concentrations of VULM1457 (1.0 and 10.0 μM), the reductions in [^{125}I]AM specific binding on HepG2 cells is markedly attenuated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	VULM 1457 significantly reduces atherogenic activity in animal experimental atherosclerosis[1]. VULM 1457 protect the hearts of diabetic–hypercholesterolaemic rats against ischaemia/reperfusion injury in vivo[2]. VULM 1457 (50 mg/kg/day; administered as an admixture to the fat-cholesterol diet for 5 days) significantly decreases plasma total cholesterol levels (1.7±0.1 mM vs. 2.9±0.5 mM in diabetic–hypercholesterolaemic animals). The hypolipidaemic effect of VULM 1457 is also observed in the liver of DM-HCH rats (3.9±0.2 mg/g vs. 7.4±1.0 mg/g)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Wistar rats (250-300 g body weight), fed a standard diet and tap water ad libitum[2]
Dosage:	50 mg/kg/day
Administration:	Administered as an admixture to the fat-cholesterol diet for 5 days
Result:	Improved the overall myocardial ischaemia-reperfusion injury outcomes in the diabetic-hypercholesterolaemic rats by suppressing arrhythmogenesis as well as by reducing myocardial necrosis, aside from remarkable hypolipidaemic activity.

REFERENCES

[1]. Adameová A, et al. The myocardial infarct size-limiting and antiarrhythmic effects of acyl-CoA:cholesterol acyltransferase inhibitor VULM 1457 protect the hearts of diabetic-hypercholesterolaemic rats against ischaemia/reperfusion injury both in vitro and in vivo. Eur J Pharmacol. 2007;576(1-3):114-121.

[2]. J Drímal, et al. The ACAT inhibitor VULM1457 significantly reduced production and secretion of adrenomedullin (AM) and down-regulated AM receptors on human hepatoblastic cells. Gen Physiol Biophys. 2005 Dec;24(4):397-409.

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