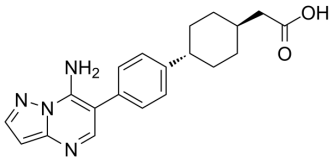
ABT-046

Cat. No.:	HY-15197
CAS No.:	1031336-60-3
Molecular Formula:	$C_{20}H_{22}N_4O_2$
Molecular Weight:	350.41
Target:	Acyltransferase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 66.67 mg/mL (190.26 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8538 mL	14.2690 mL	28.5380 mL
	5 mM	0.5708 mL	2.8538 mL	5.7076 mL
	10 mM	0.2854 mL	1.4269 mL	2.8538 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (4.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ABT-046 is a potent, selective, and orally active acyl CoA:diacylglycerol acyltransferase 1 (DGAT-1) inhibitor with IC_{50}s of both 8 nM against human and mouse DGAT-1[1].

IC_{50} & Target

IC_{50}: 8 nM (hDGAT-1 and mDGAT-1)[1]

In Vitro

ABT-046 shows no inhibition against human DGAT-2 and inhibits triglyceride formation in HeLa cells expressing human DGAT-1 with an IC_{50} of 78 nM[1].
ABT-046 exhibits high in vitro permeability values in Caco-2 cells with no evidence of active efflux (efflux ratio = 1.4 and 1.1 at 0.5 and 5 μM, respectively)[1].
ABT-046 demonstrates negligible turnover in microsome preparations from mouse and human livers[1].

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

In Vivo

ABT-046 (0.03-3 mg/kg; i.g.; once) significantly reduced postprandial triglycerides in CD-1 mice[1].
ABT-046 (0.3 mg/kg; i.g.; once) abolishes the postprandial triglyceride excursion in diet-induced obesity mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male CD-1 mice, postprandial hyperlipidemia model[1]
Dosage:	0.03, 0.3, or 3 mg/kg
Administration:	Oral gavage, single dose
Result:	Showed a dose-dependent reduction in serum triglycerides starting at 0.03 mg/kg and increasing through the higher doses (40, 60, and 90% reduction from vehicle at 0.03, 0.3, and 3.0 mg/kg, respectively). The ascending pharmacodynamics correlated well with a linear increase in plasma exposure going from 0.03 to 3 mg/kg (C_{2h} = 0.033, 0.36, and 3.10 μg/mL at 0.03, 0.3, and 3.0 mg/kg, respectively).

Animal Model:	Male C57BL/6J diet-induced obesity (DIO) mice[1]
Dosage:	0.3 mg/kg
Administration:	Oral gavage, single dose
Result:	Afforded a sustained reduction in serum triglyceride concentrations throughout the experiment.

Animal Model:	CD-1 mice and Sprague-Dawley rats[1]
Dosage:	10 mg/kg or 5 mg/kg
Administration:	Intravenous injection or oral gavage (Pharmacokinetic Analysis)
Result:	Selected Pharmacokinetic Properties of ABT-046[a][1]

	mouse (10 mg/kg)	rat (5 mg/kg)
	iv[b]	
$T_{1/2}$ (h)	4.6	3.8
V_{ss} (L/kg)	0.3	0.3
Clp (L/h/kg)	0.1	0.05
	po[b]	
$T_{1/2}$ (h)	5.1	5.6
C_{max} (μg/mL)	17.4	9.3

AUC (μg h/mL)	151	130
F (%)	78	91

[a] All values are mean values ± SEMs (n = 3 unless specified otherwise).
[b] 1% Tween-80 in water.

REFERENCES

[1]. Yeh VS, et al. Identification and preliminary characterization of a potent, safe, and orally efficacious inhibitor of Acyl-CoA: Diacylglycerol acyltransferase 1. J Med Chem. 2012 Feb 23;55(4):1751-1757.

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