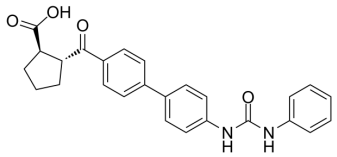
A 922500

Cat. No.:	HY-10038
CAS No.:	959122-11-3
Molecular Formula:	$C_{26}H_{24}N_2O_4$
Molecular Weight:	428.48
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 : ≥ 50 mg/mL (116.69 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3338 mL	11.6692 mL	23.3383 mL
	5 mM	0.4668 mL	2.3338 mL	4.6677 mL
	10 mM	0.2334 mL	1.1669 mL	2.3338 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 6.67 mg/mL (15.57 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A 922500 (DGAT-1 Inhibitor 4a) is a potent, selective, and orally bioavailable diacylglycerol acyltransferase 1 (DGAT-1) inhibitor with IC_{50}s of 9 and 22 nM against human and mouse DGAT-1, respectively.

IC_{50} & Target

IC50: 9 nM (human DGAT-1), 22 nM (mouse DGAT-1)[1]

In Vitro

A 922500 (A-922500) demonstrates excellent selectivity over other acyltransferases, including DGAT-2 (IC_{50}=53 μM) and the phylogenetic family members acyl coenzyme A cholesterol acyltransferase-1 and -2 (IC_{50}=296 μM) [1].

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

In Vivo	DGAT-1 inhibitor A 922500 (A-922500) reduces serum triglyceride levels from baseline at all doses tested; however, this is only statistically significant at the 3 mg/kg dose, which lowers serum triglycerides by 53%. Similarly, the 3 mg/kg dose of A 922500 significantly reduces serum FFA concentrations by 55% and total cholesterol by 25%. DGAT-1 inhibition has no significant effect on body weight at any dose tested. Although A 922500 dpes not significantly affect LDL-cholesterol or HDL-cholesterol individually, the serum LDL/HDL-cholesterol ratio is significantly improved by A 922500 at 0.3 and 3 mg/kg. Similar to the dyslipidemic hamster, treatment with 3 mg/kg A 922500 significantly reduces serum triglyceride concentrations (39%). FFA levels significantly increase over the 14-day period in vehicle-treated animals. This increase is inhibited in a dose-dependent manner by A 922500 such that FFA concentrations are 32% lower after 14 days of treatment with the DGAT-1 inhibitor at 3 mg/kg, compared with the vehicle group ($p < 0.05$). HDL-cholesterol is significantly increased from baseline levels by A 922500 at 0.3 and 3 mg/kg; however, this is only significantly increased compared with vehicle at the 3 mg/kg dose. Body weight significantly increases over the 2-week period in vehicle-treated rats, and this is not affected by A 922500. LDL-cholesterol is significantly reduced in the vehicle treated group. DGAT-1 inhibition does not further reduce LDL-cholesterol and has no effect on total cholesterol[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice and Hamsters[1] Thirteen-week-old male Golden Syrian hamsters (n=40), initially weighing approximately 140 g, are used. Ten-week-old Male Zucker fatty rats (n=32), weighing between 270 and 330 g, are used. After collection of baseline lipid profiles, hyperlipidemic hamsters (n=10/group) and Zucker fatty rats (n=8/group) are administered vehicle [20:80 (v/v), polyethylene glycol/hydroxypropyl-β-cyclodextrin (10% w/v)] or DGAT-1 inhibitor A 922500 (A-922500) at 0.03, 0.3, and 3 mg/kg, once daily by oral gavage. The dosing volume is 5 mL/kg. Serum lipid profiles are then measured 3 h after the dose on day 7 and day 14. Hamsters continue to be fed a high-fat diet with 10% fructose in the drinking water throughout the treatment period. Zucker fatty rats remain on standard rodent diet throughout the study. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2020 Aug 4;32(2):229-242.e8.
- Nat Commun. 2020 Jun 11;11(1):2967.
- Mol Cell. 2022 Jun 15;S1097-2765(22)00539-1.
- Hepatology. 2016 Apr;63(4):1272-86.
- Redox Biol. 30 August 2022, 102452.

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REFERENCES

[1]. King AJ, et al. Diacylglycerol acyltransferase 1 inhibition lowers serum triglycerides in the Zucker fatty rat and the hyperlipidemic hamster. J Pharmacol Exp Ther. 2009 Aug;330(2):526-31.

Caution: Product has not been fully validated for medical applications. For research use only.

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