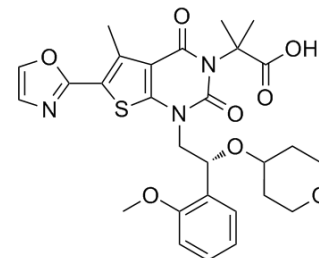


## Firsocostat

<b>Cat. No.:</b>	HY-16901		
<b>CAS No.:</b>	1434635-54-7		
<b>Molecular Formula:</b>	C <sub>28</sub> H <sub>31</sub> N <sub>3</sub> O <sub>8</sub> S		
<b>Molecular Weight:</b>	569.63		
<b>Target:</b>	Acetyl-CoA Carboxylase		
<b>Pathway:</b>	Metabolic Enzyme/Protease		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 50 mg/mL (87.78 mM)  
 \* "≥" means soluble, but saturation unknown.

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	1.7555 mL	8.7776 mL	17.5553 mL
5 mM	0.3511 mL	1.7555 mL	3.5111 mL
10 mM	0.1756 mL	0.8778 mL	1.7555 mL

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

#### In Vivo

1. Add each solvent one by one: 1% DMSO >> 99% saline  
 Solubility: 0.5 mg/mL (0.88 mM); Suspended solution; Need ultrasonic

### BIOLOGICAL ACTIVITY

#### Description

Firsocostat (ND-630; GS-0976; NDI-010976) is an acetyl-CoA carboxylase (ACC) inhibitor; inhibits human ACC1 and ACC2 with IC<sub>50</sub> values of 2.1 and 6.1 nM, respectively.

#### IC<sub>50</sub> & Target

IC<sub>50</sub>: 2.1 nM (hACC1); 6.1 nM (hACC2)<sup>[1]</sup>

#### In Vitro

Firsocostat (ND-630) inhibits hACC1 (IC<sub>50</sub>=2.1±0.2 nM) and hACC2 (IC<sub>50</sub>=6.1±0.8 nM). Inhibition is reversible and highly specific for ACC. Firsocostat inhibits ACC activity by interacting within the phosphopeptide-acceptor and dimerization site of the enzyme to prevent dimerization. Firsocostat inhibits fatty acid synthesis with an EC<sub>50</sub> of 66 nM in HepG2 cells without altering the total cell number, cellular protein concentration, and incorporation of acetate into cholesterol<sup>[1]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## In Vivo

Chronical administration of Firsocostat (ND-630) to rats with diet-induced obesity reduces hepatic steatosis, improves insulin sensitivity, reduces weight gain without affecting food intake, and favorably affects dyslipidemia. Chronical administration of Firsocostat Zucker diabetic fatty rats, Firsocostat reduces hepatic steatosis, improves glucose-stimulated insulin secretion, and reduces hemoglobin A1c (0.9% reduction). Firsocostat exhibits an aqueous solubility of 594  $\mu$ M and human and rat plasma protein binding of 98.5% and 98.6%, respectively. Pharmacokinetic evaluation of Firsocostat in male Sprague-Dawley rats [i.v. 3 mg/kg; orally (p.o.) 10 mg/kg] yields a plasma  $t_{1/2}$  of 4.5 h, bioavailability of 37%, clearance of 33 mL/min/kg, volume of distribution of 1.9 L/kg, oral time of maximum plasma concentration of 0.25 h<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Animal Administration <sup>[1]</sup>

Rats: Firsocostat is prepared in aqueous saline solution containing 1% Tween 80 and 0.5% methyl cellulose. Eight-week-old male ZDF rats are given either vehicle or Firsocostat (0.5, 1.5, 5 mg/kg) in vehicle by oral gavage b.i.d. for 37 d. Blood glucose is measured by glucometer at baseline and weekly just before dosing. Blood is collected at baseline, after 3 wk of treatment, and at the end of the study, 6 h after dosing and after a 6-h fast, for measurement of the indicated parameters. After 3 wk of treatment, animals received an oGTT (1 g/kg glucose). At the end of the study animals are killed, and liver cholesterol, triglycerides, and free fatty acids are determined<sup>[1]</sup>.

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

## CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2020 Sep 3;5(1):187.
- Cell Rep. 2021 Jul 27;36(4):109460.
- iScience. 2021, 102651.
- PeerJ. 2019 Dec 20;7:e8115.
- SLAS Discov. 2020 Aug;25(7):709-722.

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## REFERENCES

[1]. Harriman G, et al. Acetyl-CoA carboxylase inhibition by ND-630 reduces hepatic steatosis, improves insulin sensitivity, and modulates dyslipidemia in rats. Proc Natl Acad Sci U S A. 2016 Mar 29;113(13):E1796-805.

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

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