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产品名称: **Nicodicosapent**
产品别名: **Nicodicosapent**

生物活性:

Description	Nicodicosapent is a fatty acid niacin conjugate that is also an inhibitor of the sterol regulatory element binding protein (SREBP), a key regulator of cholesterol metabolism proteins such as PCSK9, HMG-CoA reductase, ATP citrate lyase, and NPC1L1.				
In Vitro	Nicodicosapent decreases the production of mature SREBP-2 protein in HepG2 cells, but does not interact with the GPR109A receptor. Nicodicosapent shows a synergistic inhibition on secreted PCSK9 and has an IC50 value of 17 μM. Nicodicosapent significantly inhibits ApoB secretion in a dose-dependent manner with IC50 of 27 μM. Nicodicosapent results in a time-dependent hydrolysis in HepG2 cells[1].				
In Vivo	Nicodicosapent (100 mg/kg po) produces high plasma levels of nicotinuric acid in the plasma. ApoE*3-Leiden mice treated with Nicodicosapent show a significant reduction in PCSK9 levels, LDL particles including VLDL and LDL cholesterol, as well as plasma triglycerides[1].				
Solvent&Solubility	In Vitro: DMSO : ≥ 100 mg/mL (222.41 mM) H₂O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.				
		Solvent Mass Concentration	1 mg	5 mg	10 mg
	Preparing	1 mM	2.2241 mL	11.1203 mL	22.2405 mL
	Stock Solutions	5 mM	0.4448 mL	2.2241 mL	4.4481 mL
		10 mM	0.2224 mL	1.1120 mL	2.2241 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。				
	储备液的保存方式和期限：-80℃，6 months; -20℃，1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。				
	In Vivo:				
	请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：				
	——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶				
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline					
Solubility: ≥ 3.75 mg/mL (8.34 mM); Clear solution					
此方案可获得 ≥ 3.75 mg/mL (8.34 mM，饱和度未知) 的澄清溶液。					
以 1 mL 工作液为例，取 100 μL 37.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀，向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。					
References	[1]. Vu CB, et al. Synthesis and Characterization of Fatty Acid Conjugates of Niacin and Salicylic Acid. J Med Chem. 2016 Feb 11;59(3):1217-31.				



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实验参考:

Animal Administration	Male Sprague-Dawley rats (n=4/treatment group) are administered with a single oral dose of either niacin (30 mg/kg) or Nicodicosapent (100 mg/kg). Compounds are formulated as an aqueous emulsion using Tween, Peceol, PEG400, and tocopherol. Nicodicosapent (170 mg) is formulated in 2.38 g of the oil mixture containing 40% Tween, 50% Peceol, 10% PEG400, and 0.2% tocopherol. The concentration of 5 in oil is 66 mg/g of oil. For oral dosing, this oil formulation is then diluted with 14.25 mL of water to form a 10 mg/mL drug emulsion and dosed as an oral gavage. Collection time points are 5, 15, and 30 min 1, 2, 4, 6, and 8 h postdose. Blood samples are collected via saphenous vein and placed in tubes containing paraoxon (10 µL of a 200 µM solution in DMSO) and stored on an ice block until centrifuged at 8000 rpm for 6 min at 2-8°C. The resulting plasma is kept frozen at -80°C until analysis. Nicodicosapent, nicotinic acid, and nicotinuric acid standard curves are generated to allow for quantitative analysis of plasma samples. Standard curves are generated by adding 10 µL of a given compound in methanol (50 µg/mL) to 50 µL of blank plasma in a 96-well microplate, resulting in the following final concentration range: 8333, 2083, 521, 130.2, 32.5, 8.1, 2.0, and 0.5 ng/mL. Then 300 µL of acetonitrile containing 100 ng/mL of an internal standard is added to each sample. The 96-well microplate is vortexed for 30 s and is then centrifuged for 45 min at 2300 g. Then 100 µL of supernatant is transferred from each sample to an empty 96-well microplate for analysis by LC/MS/MS. The instrument used is an Agilent liquid chromatograph equipped with a binary pump (1200 series), an autosampler (1200 series), and a degasser (1200 series). Mass spectrometric analysis is performed using an Agilent 6410 triple quadrupole with an ESI interface. The data acquisition and quantitation is done with Agilent Masshunter software. The column used is a Phenomenex Gemini C6 Phenyl 110A 50 mm×4.6 mm, 1.8 µm. The following mobile phase gradient is used (water = solvent A; methanol = solvent B): 0.01 min=45%A/55%B; 0.5 min=45%A/55%B; 1 min=5%A/95%B; 3.5 min=5%A/95%B; 3.51 min=45%A/55%B; 4 min=45%A/55%B.
References	[1]. Vu CB, et al. Synthesis and Characterization of Fatty Acid Conjugates of Niacin and Salicylic Acid. J Med Chem. 2016 Feb 11;59(3):1217-31.