Simvastatin

Cat. No.: HY-17502

CAS No.: 79902-63-9

Molecular Formula: $C_{25}H_{38}O_5$

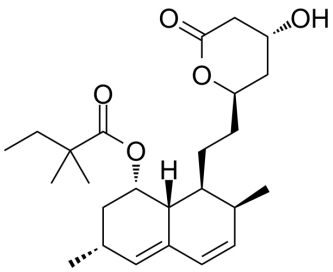
Molecular Weight: 418.57

Target: HMG-CoA Reductase (HMGCR); Autophagy; Mitophagy; Apoptosis; Ferroptosis

Pathway: Metabolic Enzyme/Protease; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 100 mg/mL (238.91 mM; Need ultrasonic)

DMSO : ≥ 50 mg/mL (119.45 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3891 mL	11.9454 mL	23.8909 mL
	5 mM	0.4778 mL	2.3891 mL	4.7782 mL
	10 mM	0.2389 mL	1.1945 mL	2.3891 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: 10 mg/mL (23.89 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 (5.97 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.97 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution
5. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution
6. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Simvastatin (MK 733) is a competitive inhibitor of HMG-CoA reductase with a K_i of 0.2 nM.
IC_{50} & Target	Ki: 0.2 nM (HMG-CoA reductase)[1]

In Vitro

Simvastatin is an inactive drug precursor that has no drug activity itself and must be metabolized into its hydroxy acid form in the liver to function. In vitro experiments, it can be activated by sodium hydroxide (NaOH).

Simvastatin suppresses cholesterol synthesis in mouse L-M cell, rat H4II E cell, and human Hep G2 cell with IC_{50}s of 19.3 nM, 13.3 nM and 15.6 nM, respectively[1].

Simvastatin causes a dose-dependent increase in serine 473 phosphorylation of Akt within 30 minutes, with maximal phosphorylation occurring at 1.0 μM[2].

Simvastatin (1.0 μM) enhances phosphorylation of the endogenous Akt substrate endothelial nitric oxide synthase (eNOS), inhibits serum-free media undergo apoptosis and accelerates vascular structure formation[2].

Simvastatin shows anti-inflammatory effects, reduces anti-CD3/anti-CD28 antibody-stimulated proliferation of PB-derived mononuclear cells and synovial fluid cells from rheumatoid arthritis blood, as well as IFN-γ release at 10 μM[3].

Simvastatin (10 μM) also blocks cell-mediated macrophage TNF-γ release induced via cognate interactions by appr 30%[3].

Simvastatin (5 μM) significantly reduces the expression of ABCA1 in astrocytes and neuroblastoma cells, the expression of apolipoprotein E in astrocytes, and increases cyclin-dependent kinase 5 and glycogen synthase kinase 3β expression in SK-N-SH cells[7].

Simvastatin has the ability to inhibit exosome release[10].

Simvastatin (32 and 64 μM; 24, 48, and 72 h) inhibits tumor cell growth, arrests in the G0/G1 phase[11].

Simvastatin (32 and 64 μM; 48 h) induces apoptosis in HepG2 and Huh7 cells[11].

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

Cell Proliferation Assay[11]

Cell Line:	HepG2 and Huh7 cells
Concentration:	32 and 64 μM
Incubation Time:	24, 48, and 72 hours
Result:	Inhibited tumor cell growth as compared to controls (ctrl, $p<0.05$).

Apoptosis Analysis[11]

Cell Line:	HepG2 and Huh7 cells
Concentration:	32 and 64 μM
Incubation Time:	48 hours
Result:	Increased early apoptosis from 9.2% in non-treated ctrl cells to 18.2% (32 μM) and 19.8% (64 μM), respectively, increased late apoptosis from 35.0% in ctrl cells to 56.9% (32 μM) and 48.0% (64 μM), respectively, in HepG2 cells.

Cell Cycle Analysis[11]

Cell Line:	HepG2 and Huh7 cells
Concentration:	32 and 64 μM
Incubation Time:	24, 48, and 72 hours
Result:	Exhibited downregulation of CDK1, CDK2, CDK4 and cyclins D1 and E as compared to ctrl tumor cells.

In Vivo	Simvastatin suppresses the conversion of radiolabeled acetate to cholesterol with an IC_{50} of 0.2 mg/kg via p.o.

administration[1].Simvastatin (4 mg/day, p.o. for 13 weeks) returns the cholesterol-induced increases in total cholesterol, LDL-cholesterol and HDL-cholesterol to normal level in rabbits fed an atherogenci cholesterol-rich diet[4].
Simvastatin (6 mg/kg) increases LDL receptor-dependent binding and the number of hepatic LDL receptors in rabbits fed a diet containing 0.25% cholesterol[5].
Simvastatin (20 mg/kg/day) causes a 1.3-fold less macrophage content in lesions, and 2-fold less vascular cell adhesion molecule-1, interleukin-1beta, and tissue factor expression, companied by a 2.1-fold increases in lesional smooth muscle cell and collagen content in cynomolgus monkeys fed an atherogenic diet[6].
Simvastatin (oral gavage; 15 and 30 mg/kg; once daily; 14 d) treatment attenuats oxidative damage, TNF-a and IL-6 levels, and restores itochondrial enzyme complex activities[12].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male wistar rats with oxidative damage by Intrastriatal 6-OHDA administration[12]
Dosage:	15 and 30 mg/kg
Administration:	Oral gavage; 15 and 30 mg/kg; once daily; 14 days
Result:	Attenuated oxidative damage (reduced MDA, nitrite levels and restoration of reduced GSH) , attenuated TNF-a and IL-6 levels, and restored itochondrial enzyme complex activities as compared to 6-OHDA group.

CUSTOMER VALIDATION

- Blood. 2021 Oct 8;blood.2021012327.
- J Exp Med. 2021 Sep 6;218(9):e20202637.
- Chem Eng J. 478, 15 December 2023, 147465
- Chem Eng J. 2022: 141111.
- Biomaterials. 2020 Aug;250:119963.

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[2]. Anil Kumar, et al. Neuroprotective potential of atorvastatin and simvastatin (HMG-CoA reductase inhibitors) against 6-hydroxydopamine (6-OHDA) induced Parkinson-like symptoms. Brain Res. 2012 Aug 30;1471:13-22.

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