Rottlerin

Cat. No.: HY-18980

CAS No.: 82-08-6

Molecular Formula: $C_{30}H_{28}O_8$

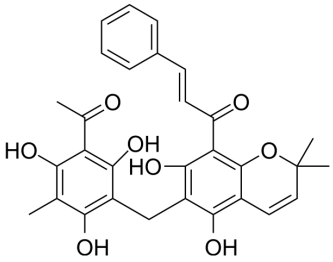
Molecular Weight: 516.54

Target: PKC; Autophagy; Apoptosis; HIV; RABV

Pathway: Epigenetics; TGF-beta/Smad; Autophagy; Apoptosis; Anti-infection

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (24.20 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9360 mL	9.6798 mL	19.3596 mL
	5 mM	0.3872 mL	1.9360 mL	3.8719 mL
	10 mM	0.1936 mL	0.9680 mL	1.9360 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 22 mg/mL (42.59 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rottlerin, a natural product purified from Mallotus Philippinensis, is a specific PKC inhibitor, with IC_{50} values for PKCδ of 3-6 μM, PKCα,β,γ of 30-42 μM, PKCε,η,ζ of 80-100 μM. Rottlerin acts as a direct mitochondrial uncoupler, and stimulates autophagy by targeting a signaling cascade upstream of mTORC1. Rottlerin induces apoptosis via caspase 3 activation[1][2][3]. Rottlerin inhibits HIV-1 integration and Rabies virus (RABV) infection[4][5].

IC_{50} & Target				
	PKCδ	PKCα	PKCγ	PKCβ
	3 μM (IC_{50}, Porcine spleen)	30 μM (IC_{50}, baculovirus-	40 μM (IC_{50}, baculovirus-	42 μM (IC_{50}, baculovirus-

		infected Sf9 insect cells)	infected Sf9 insect cells)	infected Sf9 insect cells)
	PKCη 82 μM (IC_{50}, baculovirus-infected Sf9 insect cells)	PKCζ 100 μM (IC_{50}, baculovirus-infected Sf9 insect cells)	PKCε 100 μM (IC_{50}, baculovirus-infected Sf9 insect cells)	CaM kinase III 5.3 μM (IC_{50}, EF-2 kinase activity in cytosol of murine pancreas)
	CKII 30 μM (IC_{50}, holoenzyme expressed in E.coli)	PKA 78 μM (IC_{50}, catalytic subunit from porcine heart)	HIV-1	

In Vitro

Rottlerin (20 μM, 2/6/24 hours) dramatically decreases the cyclin D-1 mRNA levels in a time-dependent manner in primary HMVEC[2].

?Rottlerin (20 μM) exhibits cell proliferation in HMVEC[2].

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

Western Blot Analysis[2]

Cell Line:	Primary HMVEC (Human Microvascular Endothelial Cell).
Concentration:	20 μM.
Incubation Time:	2, 6, 24 hours.
Result:	Dramatically decreased the cyclin D-1 mRNA levels in a time-dependent manner. After 2 h of treatment, the mRNA level was reduced to 50% of the control, to circa 40% after 6 h, and to 20% after 24 h. Consistently, a similar trend was observed in the protein levels, where the decrease was circa 50% after 2 h, 80% after 6 h, and to almost undetectable levels after 24 h.

Cell Proliferation Assay[2]

Cell Line:	Primary HMVEC (Human Microvascular Endothelial Cell).
Concentration:	20 μM.
Incubation Time:	24/48 hours.
Result:	Exhibited a strong growth inhibition, with a reduction in thymidine incorporation respect to the control cells (DMSO 0.1%) of circa 75% and 80%, respectively.

In Vivo

Rottlerin (20 mg/kg, gavage 5 days per week, once daily, for 6 weeks) inhibits AsPC-1 pancreatic tumor growth in Balb C nude mice with no toxicity[3].

?Rottlerin inhibits tumor cell proliferation, and induces apoptosis through activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase (PARP)[3].

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

Animal Model:	Balb C nude mice (4-6 weeks old) with AsPC-1 cells (2×10^6 cells mixed with Matrigel, 50:50 ratio) injection[3].
Dosage:	0 or 20 mg/kg.
Administration:	Gavage 5 days per week, once daily, for 6 weeks.
Result:	Inhibited AsPC-1 pancreatic tumor growth in Balb C nude mice and had no effecton the

	body weight of AsPC-1 tumor-bearing mice.

CUSTOMER VALIDATION

- EMBO Mol Med. 2024 Mar 12.
- Cell Commun Signal. 2024 Apr 2;22(1):210.
- Virol Sin. 2022 Aug 4;S1995-820X(22)00136-5.
- J Virol. 2021 Oct 27;JVI0134421.
- Microbiol Spectr. 2022 Aug 24;e0105622.

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REFERENCES

[1]. Gschwendt M, et al. Rottlerin, a novel protein kinase inhibitor. Biochem Biophys Res Commun. 1994 Feb 28;199(1):93-8.

[2]. Valacchi G, et al. Rottlerin exhibits antiangiogenic effects in vitro. Chem Biol Drug Des. 2011 Jun;77(6):460-70.

[3]. Minzhao Huang, et al. Rottlerin suppresses growth of human pancreatic tumors in nude mice, and pancreatic cancer cells isolated from KrasG12D mice. Cancer Letters 353 (2014) 32-40.

[4]. María Rosa López-Huertas, et al. Protein kinase Ctheta is a specific target for inhibition of the HIV type 1 replication in CD4+ T lymphocytes. J Biol Chem. 2011 Aug 5;286(31):27363-77.

[5]. Zoé Lama, et al. Kinase inhibitors tyrphostin 9 and rottlerin block early steps of rabies virus cycle. Antiviral Res. 2019 Aug;168:51-60.

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