Rottlerin

Cat. No.: HY-18980

CAS No.: 82-08-6

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

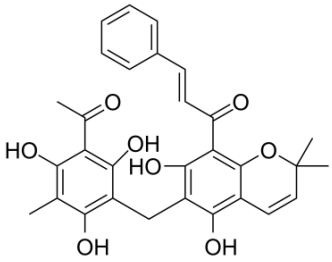
Molecular Weight: 516.54

Target: PKC; Autophagy; Apoptosis

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

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 : 2 mg/mL (3.87 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

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	---	---	---
10 mM	---	---	---

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

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].

IC_{50} & Target

PKCδ 3 μM (IC_{50}, Porcine spleen)	PKCα 30 μM (IC_{50}, baculovirus-infected Sf9 insect cells)	PKCγ 40 μM (IC_{50}, baculovirus-infected Sf9 insect cells)	PKCβ 42 μM (IC_{50}, baculovirus-infected Sf9 insect cells)
PKCη 82 μM (IC_{50}, baculovirus-	PKCζ 100 μM (IC_{50}, baculovirus-	PKCε 100 μM (IC_{50}, baculovirus-	CaM kinase III 5.3 μM (IC_{50}, EF-2 kinase

	infected Sf9 insect cells)	infected Sf9 insect cells)	infected Sf9 insect cells)	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)		

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.

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.

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