上海源叶生物科技有限公司
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产品名称：RA-9
CAS 号： 919091-63-7
产品货号：S89411

生物活性：

Description

RA-9 是一种高效选择性蛋白酶体相关 DUBs 抑制剂，具有良好的毒性和抗癌活性。RA-9 阻断泛素依赖性蛋白降解而不影响 20S 蛋白酶体蛋白水解活性。RA-9 选择性诱导卵巢癌细胞株和供体原代培养细胞凋亡。RA-9 诱导卵巢癌细胞内质网应激反应。

Cellular Effect

Cell Line	Type	Value	Description
A549	IC_{50}	0.4 μM	Cytotoxicity against human A549 cells after 72 hrs by MTT assay
CCRF-CEM	IC_{50}	0.81 μM	Antiproliferative activity against human CEM cells assessed as cell growth inhibition
CCRF-CEM	IC_{50}	4.47 μM	Cytotoxicity against CEM T-lymphocytes.
CCRF-CEM	IC_{50}	4.47 μM	Cytotoxicity against human CEM cells
HL-60	CC_{50}	3.6 μM	Cytotoxicity against human HL60 cells in presence of RPMI1640 containing 10% fetal bovine serum by trypan blue exclusion test
HSC-2	CC_{50}	0.9 μM	Cytotoxicity against human HSC2 by MTT method
HSC-4	CC_{50}	6.1 μM	Cytotoxicity against human HSC4 cells by MTT method
HepG2	IC_{50}	356 ng/mL	Antimalarial activity against liver stage Plasmodium berghei ANKA sporozoites infected in human HepG2 cells after 48 hrs by luciferase reporter gene assay
HepG2	IC_{50}	> 2000 ng/mL	Cytotoxicity against human HepG2 cells after 48 hrs by MTT assay
L1210	IC_{50}	0.81 μM	Antiproliferative activity against mouse L1210 cells assessed as cell growth inhibition
L1210	IC_{50}	214 μM	Inhibitory effect on the biosyntheses of protein in murine L1210 cells.
L1210	IC_{50}	228 μM	Inhibitory effect on the biosyntheses of DNA in murine L1210 cells.
L1210	IC_{50}	276 μM	Inhibitory effect on the biosyntheses of RNA in murine L1210 cells.
L1210	IC_{50}	32.09 μM	Cytotoxicity against mouse L1210 cells
L1210	IC_{50}	32.9 μM	Cytotoxicity against murine L1210 cells.
MOLT-4	IC_{50}	8.28 μM	Cytotoxicity against human Molt4/C8 cells
P388	IC_{50}	0.2 μM	Cytotoxicity against murine P388 cells.
P388	IC_{50}	0.81 μM	Antiproliferative activity against mouse P388 cells assessed as cell growth inhibition
PC-3	IC_{50}	1.54 μM	Cytotoxicity against human PC3 cells after 72 hrs by MTT assay
SK-OV-3	IC_{50}	2.5 μM	Cytotoxicity against human Scov3 cells after 72 hrs by MTT assay

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	U-87MG ATCC	IC_{50}	7.15 μM	Cytotoxicity against human U87MG cells after 48 hrs by resazurin assay

In Vitro

RA-9 (10-30 μM；48 小时) 抑制卵巢癌细胞系和原代培养物的生长[1]。

RA-9 (1.25-5 μM；18 小时) 导致卵巢癌细胞中的细胞周期停滞和半胱天冬酶介导的细胞凋亡[1]。

RA-9 (5 μM；0-24 小时) 诱导卵巢癌细胞中的内质网应激反应[1]。

RA-9 (5 μM；超过 24 小时) 处理结果与时间依赖性的 PARP 切割形成的积累早在 8 小时就很明显[1]。

Cell Viability Assay[1]

Cell Line:	Cisplatin-sensitive ovarian cancer cell lines TOV-21G and ES-2, Cisplatin-resistant ovarian cancer cell lines HEY and OVCAR-3, primary ovarian cancer cells
Concentration:	10, 20, 30 μM
Incubation Time:	48 hours
Result:	Compromised the viability of ovarian cancer cells in a dose-dependent fashion.

Cell Cycle Analysis[1]

Cell Line:	ES-2 cells
Concentration:	1.25, 5 μM
Incubation Time:	18 hours
Result:	Resulted in a dose-dependent increase in the fraction of ES-2 cells in the G2-M cell cycle phase.

Western Blot Analysis[1]

Cell Line:	ES-2, SKOV-3 and TOV-21G ovarian cancer cells
Concentration:	5 μM
Incubation Time:	0-24 h
Result:	Caused a time-dependent increase in the steady levels of the early ER-stress marker GRP-78, as well as the late ER-stress markers IRE1-α and Ero1L-α.

In Vivo

RA-9 (5 mg/kg；腹腔注射；服用一天，停药两天) 在卵巢癌小鼠模型中抑制体内人卵巢癌细胞生长并延长存活期[1].

Animal Model:	Six-week-old female immunodeficient (NCr nu/nu) mice[1]
Dosage:	5 mg/kg
Administration:	I.p; one-day on, two-days off
Result:	Significant reduction in tumor burden at day 12.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 : 4.17 mg/mL (11.41 mM; 超声助溶 (<80°C); 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7372 mL	13.6859 mL	27.3718 mL
	5 mM	0.5474 mL	2.7372 mL	5.4744 mL
	10 mM	0.2737 mL	1.3686 mL	2.7372 mL

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	*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°C, 2 years; -20°C, 1 year。-80°C 储存时，请在 2 年内使用， -20°C 储存时，请在 1 年内使用。
参考文献	[1]. Coughlin K, et al. Small-molecule RA-9 inhibits proteasome-associated DUBs and ovarian cancer in vitro and in vivo via exacerbating unfolded protein responses. Clin Cancer Res. 2014;20(12):3174-3186.