上海源叶生物科技有限公司
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产品名称：AZD-7648
CAS 号：2230820-11-6
产品货号：S88606

生物活性：

Description	AZD-7648 是一种具有选择性的口服有效 DNA-PK 抑制剂，IC50 值为 0.6 nM, AZD-7648 诱导细胞凋亡 (apoptosis)，具有抗肿瘤活性。

IC50 & Target[1]	PI3Kγ	ATM	DNA-PKcs
	1.37 μM (IC50)	17.93 μM (IC50)	91.3 nM (IC_{50})

Cellular Effect

Cell Line	Type	Value	Description
A549	IC_{50}	0.091 μM	Inhibition of DNA-PK in human A549 cells assessed as reduction in irradiation-induced autophosphorylation at S2056 residue preincubated for 1 hr followed by 8 Gy irradiation and measured after 1 hr by ELISA
B16-F10	IC_{50}	11.4 μM	Synergistic antiproliferative activity against mouse B16-F10 cells assessed as reduction in cell viability incubated for 48 hrs in presence of doxorubicin by CCK-8 assay
B16-F10	IC_{50}	33.6 μM	Antiproliferative activity against mouse B16-F10 cells assessed as reduction in cell viability incubated for 48 hrs by CCK-8 assay
CHO	IC_{50}	> 198 μM	Inhibition of human ERG stably expressed in CHO cells at -90 mV holding potential by electrophysiological assay
CT26	IC_{50}	18.8 μM	Antiproliferative activity against mouse CT26 cells assessed as reduction in cell viability incubated for 48 hrs by CCK-8 assay
CT26	IC_{50}	6.74 μM	Synergistic antiproliferative activity against mouse CT26 cells assessed as reduction in cell viability incubated for 48 hrs in presence of doxorubicin by CCK-8 assay
HCT-116	IC_{50}	19.5 μM	Antiproliferative activity against human HCT-116 cells assessed as inhibition of cell growth incubated for 48 hrs in presence of 100 nM doxorubicin by MTT assay
HCT-116	IC_{50}	35.3 μM	Antiproliferative activity against human HCT-116 cells assessed as inhibition of cell growth incubated for 48 hrs by MTT assay
HCT-116	IC_{50}	38.08 nM	Inhibition of colony formation in human HCT-116 cells preincubated with compound for 1 hr followed by exposure to 2 Gy gamma irradiation and measured after 7 days by crystal violet staining based chemiluminescence assay
HT-29	IC_{50}	17.9 μM	Inhibition of ATM in human HT-29 cells assessed as reduction in irradiation-induced autophosphorylation at Ser1981 residue preincubated for 1 hr followed by 6 Gy irradiation and measured after 1 hr by Hoechst staining-based imaging analysis
HT-29	IC_{50}	> 29 μM	Inhibition of ATR in human HT-29 cells assessed as

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				reduction in 4NQO-induced CHK1 phosphorylation at S345 residue preincubated for 1 hr followed by 4NQO addition and measured after 1 hr by Hoechst staining-based imaging analysis
	HeLa	IC_{50}	0.6 nM	Inhibition of human HeLa cell-derived full length DNA-PK catalytic subunit using fluorescein-EPPLSQEAFADLWKK as substrate preincubated for 30 mins followed by substrate addition and measured after 40 mins TR-FRET assay
	Jurkat	IC_{50}	0.09 μM	Synergistic antiproliferative activity against human Jurkat cells assessed as reduction in cell viability incubated for 48 hrs in presence of doxorubicin by CCK-8 assay
	Jurkat	IC_{50}	12.3 μM	Antiproliferative activity against human Jurkat cells assessed as reduction in cell viability incubated for 48 hrs by CCK-8 assay
	MDA-MB-231	IC_{50}	> 30 μM	Inhibition of mTOR/PI3Kalpha in human MDA-MB-231 cells assessed as reduction in AKT phosphorylation at S473 residue measured after 2 hrs by Hoechst staining-based imaging analysis
	MDA-MB-468	IC_{50}	> 30 μM	Inhibition of PI3Kbeta in human MDA-MB-468 cells assessed as reduction in AKT phosphorylation at T208 residue measured after 2 hrs by QuantaBlu substrate based fluorescence assay

In Vitro

AZD7648 (0-30 μM) 是一种有效的放射增敏剂[1]。

AZD7648 (3 μM) 可增加对 Doxorubicin 的敏感性[1]。

AZD7648 (0.6 μM) 增强 PARP 抑制剂 Olaparib 的活性[1].

Cell Cycle Analysis[1]

Cell Line:	IR (ionizing radiation)-treated A549 cells or A549 cells
Concentration:	0-30 μM
Incubation Time:	48 h
Result:	Arrested cell cycle at G2/M phase.

Western Blot Analysis[1]

Cell Line:	IR (ionizing radiation)-treated A549 cells or OAW42 cells treated with Doxorubicin
Concentration:	0.03, 0.1, 0.3, 1, 3, 10 and 30 μM for A549; 3 μM for OAW42
Incubation Time:	1 h for A549; 0.5, 2, 4, 8 and 16 h for OAW42
Result:	Potently inhibited DNA-PKcs autophosphorylation at Ser2056. Downregulated pDNA-PKcs Ser2056, γH2AX Ser139 and pRPA32 Ser4/Ser8 phosphorylation at early time points (at 30 min, 2 h and 4 h). Resulted in increased levels of γH2AX and the apoptosis marker cleaved PARP1 compared with doxorubicin treatment alone at later time points (8 and 16 h).

In Vivo

AZD-7648（100 mg/kg；口服；每天一次，连续 5 天）可抑制肿瘤生长并抑制肿瘤消退[1]。

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Animal Model:	Nude mice, A549 xenografts and NCI-H1299 xenografts[1]
Dosage:	100 mg/kg
Administration:	Oral administration, once daily for 5 days
Result:	Induced tumour growth inhibition in combination with IR in A549 xenografts and induced tumour regression in combination with IR in NCI-H1299 xenografts.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：5.83 mg/mL (15.33 mM; 超声助溶 (<60°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	2.6288 mL	13.1441 mL	26.2881 mL
	5 mM	0.5258 mL	2.6288 mL	5.2576 mL
	10 mM	0.2629 mL	1.3144 mL	2.6288 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°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

动物实验：

以下溶解方案，请直接配制工作液。建议现用现配，在短期内尽快用完。 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。

方案 一

请依序添加每种溶剂： 0.5% HPMC/0.1% Tween-80 in Saline water

Solubility: 10 mg/mL (26.29 mM); 悬浊液; 超声助溶。

参考文献

[1]. Fok JHL, et al. AZD7648 is a potent and selective DNA-PK inhibitor that enhances radiation, chemotherapy and olaparib activity. Nat Commun. 2019 Nov 7;10(1):5065.

完整储备液配制表：

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, 6 months; -20° C, 1 month。-80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	2.6288 mL	13.1441 mL	26.2881 mL	65.7203 mL
	5 mM	0.5258 mL	2.6288 mL	5.2576 mL	13.1441 mL
	10 mM	0.2629 mL	1.3144 mL	2.6288 mL	6.5720 mL
	15 mM	0.1753 mL	0.8763 mL	1.7525 mL	4.3814 mL