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产品名称：(R) - CR8
CAS 号：294646-77-8
产品货号：S87699

生物活性：

Description

(R)-CR8 是 Roscovitine 的第二代类似物，是一种有效的 CDK1/2/5/7/9 抑制剂。(R)-CR8 抑制 CDK1/cyclin B (IC50=0.09 μM)、CDK2/cyclin A (0.072 μM)、CDK2/cyclin E (0.041 μM)、CDK5/p25 (0.11 μM)、CDK7/cyclin H (1.1 μM)、CDK9/cyclin T (0.18 μM) 和 CK1δ/ε (0.4 μM)。(R)-CR8 诱导细胞凋亡并具有神经保护作用。(R)-CR8 作为一种分子胶降解剂来消耗细胞周期蛋白 K。

IC50 & Target[1]

Cdk1/cyclin B	cdk2/cyclin A	CDK2/cyclin E	Cdk5/p25	CDK7/cyclin H	CDK9/Cyclin T	CK1δ/ε
0.09 μM (IC50)	0.072 μM (IC50)	0.041 μM (IC50)	0.11 μM (IC50)	1.1 μM (IC50)	0.18 μM (IC50)	0.4 μM (IC50)

Cellular Effect

Cell Line	Type	Value	Description
G-361	IC_{50}	0.503 μM	Cytotoxicity against human G361 cells assessed as reduction in ce viability after 72 hrs by calcein AM staining based fluorescence as
HCT-116	IC_{50}	0.35 μM	Cytotoxicity against human HCT116 cells assessed as reduction in cell viability after 72 hrs by calcein AM staining based fluorescen assay
HEK293	IC_{50}	0.56 μM	Antiproliferative activity against HEK293 cells assessed as surviva after 48 hrs by MTS reduction assay
HT	GI_{50}	0.263 μM	Antiproliferative activity against human HT cells measured after 7 hrs by calcein AM dye-based fluorescence assay
K562	IC_{50}	0.175 μM	Cytotoxicity against human K562 cells assessed as reduction in ce viability after 72 hrs by calcein AM staining based fluorescence as
MCF7	IC_{50}	0.16 μM	Cytotoxicity against human MCF7 cells assessed as reduction in c viability after 72 hrs by calcein AM staining based fluorescence as
Sf9	IC_{50}	0.062 μM	Inhibition of His-tagged CDK2/Cyclin-E1 (unknown origin) expressed in baculovirus infected Sf9 insect cells using histone H1 substrate measured in presence of [gamma-33P]ATP
Sf9	IC_{50}	0.062 μM	Inhibition of CDK2/Cyclin E (unknown origin) expressed in sf9 ce using histone H1 as substrate in presence of [gamma33P]-ATP
Sf9	IC_{50}	0.225 μM	Inhibition of recombinant human full-length N-terminal GST-His6 fused CDK5 (M1 to P292 residues)/N-terminal His6-tagged p25 (A104 to R307 residues) expressed in baculovirus infected Sf9 ins cells using histone H1 as substrate measured in presence of [g
Sf9	IC_{50}	0.272 μM	Inhibition of recombinant human N-terminal GST-His6-fused CDI (M1 to F372 residues)/N-terminal His6-tagged cyclin T1 (M1 to K residues) expressed in baculovirus infected Sf9 insect cells using (YSPTSPS)2KK as substrate measured in presence of [gamma-3
Sf9	IC_{50}	0.787 μM	Inhibition of His-tagged CDK1/Cyclin-B1 (unknown origin) expressed in baculovirus infected Sf9 insect cells using histone H1 substrate measured in presence of [gamma-33P]ATP
Sf9	IC_{50}	1.769 μM	Inhibition of recombinant human N-terminal GST-His6-fused CDI

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				(M1 to F346 residues)/N-terminal His-tagged cyclin H (M1 to L32 residues)/N-terminal His6-tagged MAT1 (M1 to S306 residues) expressed in baculovirus infected Sf9 insect cells using (YSPTSPS
	Sf9	IC_{50}	26.09 μM	Inhibition of recombinant human N-terminal GST-fused CDK4 (S E303 residues)/cyclin D1 (Q4 to I295 residues) expressed in baculovirus infected Sf9 insect cells using RPPTLSPIPHIPR as substrate measured in presence of [gamma-33P]ATP
	SH-SY5Y	IC_{50}	0.43 μM	Antiproliferative activity against human SH-SY5Y cells assessed a survival after 48 hrs by MTS reduction assay

In Vitro

(R)-CR8 (CR8) (0.1-100 μM；48 小时) 是细胞凋亡的强效诱导剂，对 SH-SY5Y 细胞系的 IC50 为 0.49 μM[1]。

(R)-CR8 (0.25-10 μM) 诱导剂量依赖性的聚-(ADP-核糖)聚合酶 (PARP) 裂解[1]。

(R)-CR8 的 CDK 结合形式具有溶剂暴露的吡啶基部分，可诱导 CDK12-细胞周期蛋白 K 与 CUL4 衔接蛋白 DDB1 之间形成复合物，从而无需底物受体并呈递细胞周期蛋白 K 进行泛素化和降解[3]。

Apoptosis Analysis[1]

Cell Line:	SH-SY5Y cell line
Concentration:	0.1, 1, 10, 100 μM
Incubation Time:	24 hours
Result:	Reduced cell survival in a dose-dependent manner.

In Vivo

(R)-CR8 (5 mg/Kg；腹腔注射) 在 28 天的组织学评估中导致病变大小显著减小[2]。

Animal Model:	Adult (10 to 12 weeks old) male Sprague-Dawley rats (310 to 330 g)[2]
Dosage:	i.p.
Administration:	5 mg/Kg
Result:	Resulted in a significant reduction in lesion size.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：50 mg/mL (115.87 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	2.3173 mL	11.5867 mL	23.1734 mL
	5 mM	0.4635 mL	2.3173 mL	4.6347 mL
	10 mM	0.2317 mL	1.1587 mL	2.3173 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。

参考文献

[1]. Bettayeb K, et al. CR8, a potent and selective, roscovitine-derived inhibitor of cyclin-dependent kinases. Oncogene. 2008 Oct 2;27(44):5797-807.

[2]. Kabadi SV, et al. CR8, a novel inhibitor of CDK, limits microglial activation, astrocytosis, neuronal loss, and neurologic dysfunction after experimental traumatic brain injury. J Cereb Blood Flow Metab. 2014 Mar;34(3):502-13.

[3]. Słabicki M, et al. The CDK inhibitor CR8 acts as a molecular glue degrader that depletes cyclin K

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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**	2.3173 mL	11.5867 mL	23.1734 mL	57.9334 mL
	5 mM	0.4635 mL	2.3173 mL	4.6347 mL	11.5867 mL
	10 mM	0.2317 mL	1.1587 mL	2.3173 mL	5.7933 mL
	15 mM	0.1545 mL	0.7724 mL	1.5449 mL	3.8622 mL
	20 mM	0.1159 mL	0.5793 mL	1.1587 mL	2.8967 mL
	25 mM	0.0927 mL	0.4635 mL	0.9269 mL	2.3173 mL
	30 mM	0.0772 mL	0.3862 mL	0.7724 mL	1.9311 mL
	40 mM	0.0579 mL	0.2897 mL	0.5793 mL	1.4483 mL
	50 mM	0.0463 mL	0.2317 mL	0.4635 mL	1.1587 mL
	60 mM	0.0386 mL	0.1931 mL	0.3862 mL	0.9656 mL
	80 mM	0.0290 mL	0.1448 mL	0.2897 mL	0.7242 mL
	100 mM	0.0232 mL	0.1159 mL	0.2317 mL	0.5793 mL