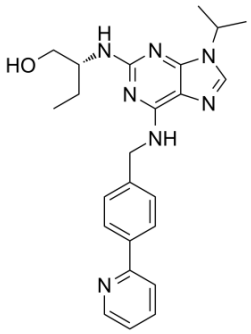
(R)-CR8



Cat. No.:	HY-18340
CAS No.:	294646-77-8
Molecular Formula:	$C_{24}H_{29}N_7O$
Molecular Weight:	431.53
Target:	CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month

BIOLOGICAL ACTIVITY

Description

(R)-CR8 (CR8), a second-generation analog of Roscovitine, is a potent CDK1/2/5/7/9 inhibitor. (R)-CR8 inhibits CDK1/cyclin B (IC_{50}=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) and CK1δ/ε (0.4 μM). (R)-CR8 induces apoptosis and has neuroprotective effect[1][2]. (R)-CR8 acts as a molecular glue degrader that depletes cyclin K[3].

IC_{50} & Target

Cdk1/cyclin B 0.09 μM (IC_{50})	cdk2/cyclin A 0.072 μM (IC_{50})	CDK2/cyclinE 0.041 μM (IC_{50})	Cdk5/p25 0.11 μM (IC_{50})
CDK7/cyclin H 1.1 μM (IC_{50})	CDK9/Cyclin T 0.18 μM (IC_{50})	CK1δ/ε 0.4 μM (IC_{50})	

In Vitro

(R)-CR8 (CR8) (0.1-100 μM; 48 hours) is a potent inducer of apoptotic cell death with an IC_{50} of 0.49 μM for SH-SY5Y cell line[1].
(R)-CR8 (0.25-10 μM) induces a dose-dependent induction of poly-(ADP-ribose)polymerase (PARP) cleavage[1].
The CDK-bound form of (R)-CR8 has a solvent-exposed pyridyl moiety that induces the formation of a complex between CDK12-cyclin K and the CUL4 adaptor protein DDB1, bypassing the requirement for a substrate receptor and presenting cyclin K for ubiquitination and degradation[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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; i.p.) results in a significant reduction in lesion size at 28 days in histological assessment[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

REFERENCES

[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 [published online ahead of print, 2020 Jun 3]. Nature. 2020;10.1038/s41586-020-2374-x.

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