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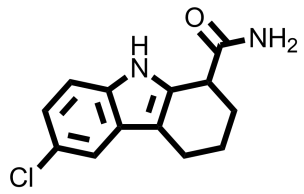
SIRT1 Inhibitor – EX-527

Chemical Name: 6-Chloro-2,3,4,9-tetrahydro-1H-carb-azole-1-carboxamide



Molecular Weight:	248.71
Formula:	$C_{13}H_{13}ClN_2O$
Purity:	≥98%
CAS#:	49843-98-3
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 month -20 °C 1 year

Biological Activity:

EX-527 is a highly potent and selective inhibitor of SIRT1 with an IC_{50} ~98 nM. It does not inhibit histone deacetylase (HDAC) or other sirtuin deacetylase family members (IC_{50} ~20-100 µM). EX-527 has been used to investigate the relationship between SIRT1-mediated deacetylation of p53, p53 activity, and cell survival following DNA damage, as well as many other biological processes involving SIRT1.

How to Use:

In vitro: EX-527 was used at 1-10 µM in vitro and in cellular assays.

In vivo: EX-527 was administered by intracerebroventricular injection to rats at 5-10 µg to increase hypothalamic acetyl-p53 levels by inhibiting hypothalamic SIRT1 activity (formulation: dissolved in DMSO in a total volume of 5 µL).

Reference:

1. Napper AD, et al. Discovery of indoles as potent and selective inhibitors of the deacetylase SIRT1. (2005) J Med Chem. 48(25):8045-54.
2. Solomon JM, et al. Inhibition of SIRT1 catalytic activity increases p53 acetylation but does not alter cell survival following DNA damage. (2006) Mol Cell Biol. 26(1):28-38.
3. Peck B, et al. SIRT inhibitors induce cell death and p53 acetylation through targeting both SIRT1 and SIRT2. (2010) Mol Cancer Ther. 9(4):844-55.
4. Velásquez DA, et al. The central Sirtuin 1/p53 pathway is essential for the orexigenic action of ghrelin. (2011) Diabetes. 60(4):1177-85.
5. Peled T, et al. Nicotinamide, a SIRT1 inhibitor, inhibits differentiation and facilitates expansion of hematopoietic progenitor cells with enhanced bone marrow homing and engraftment. (2012) Exp Hematol. 40(4):342-55.
6. Zhao X, et al. The 2.5 Å crystal structure of the SIRT1 catalytic domain bound to nicotinamide adenine dinucleotide (NAD+) and an indole (EX527 analogue) reveals a novel mechanism of histone deacetylase inhibition. (2013) J Med Chem. 56(3):963-9.