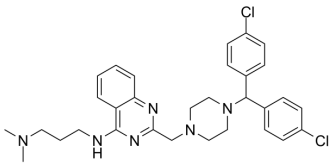
SCH529074

Cat. No.:	HY-110088
CAS No.:	922150-11-6
Molecular Formula:	$C_{31}H_{36}Cl_2N_6$
Molecular Weight:	563.56
Target:	MDM-2/p53
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (35.49 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7744 mL	8.8722 mL	17.7443 mL
	5 mM	0.3549 mL	1.7744 mL	3.5489 mL
	10 mM	0.1774 mL	0.8872 mL	1.7744 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1 mg/mL (1.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (1.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SCH529074 is a potent and orally active p53 activator. SCH529074 binds specifically and conformation-dependently to p53 DBD (DNA binding domain) with a K_i of 1-2 μM in a saturable manner. SCH529074 restores mutant p53 function and interrupts HDM2-mediated ubiquitination of wild Type p53. SCH529074 can be used for the study of non-small-cell lung carcinoma (NSCLC)[1][2].

IC_{50} & Target

Ki: 1-2 μM (p53 DBD)[2]

In Vitro

SCH529074 (2-4 μM; 24 hours) causes significant reduction in cell viability, it causes a significant decreasing to 20-25% in p53 mutant cells (H157, H1975 and H322) and to 68% in the p53 WT cell line A549 at 4 μM[1].
SCH 529074 (2 and 4 μM) induces NSCLC cells (H157, A549, HCT116 and HCT116 $p53^{-/-}$) arrested at the G0/G1 phase (59%;

72%; 66%; and 57%) compared with the control cells following low concentration (2 μM) of treatment[1].
SCH 529074 (2-4 μM; 24 hours) induces the early and late apoptotic rates at 2 μM in H1975 cells. In H157 cells, SCH 529074 treatment induces early and late apoptosis. Similarly, in A549 cells, 2 and 4 μM of SCH 529074 significantly increased early and late apoptosis. In line with that, in colon cancer cells, in HCT116 cells, 4 μM of SCH 529074 causes a significant induction of early and late apoptosis, and 4 μM of SCH 529074 significantly induces early apoptosis in HCT116 $p53^{-/-}$ cells[1].
SCH 529074 (2-6 μM; 24 hours) increases the protein levels of PUMA and p21 revealed to 4 or 6 μM in the cancer cell lines regardless of their p53 status[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	p53 mutant cells (H157, H1975 and H322) and p53 WT cell line A549
Concentration:	2 μM; 4 μM
Incubation Time:	24 hours
Result:	Inhibited cancer WT and mutant cell viability.

Cell Cycle Analysis[1]

Cell Line:	H1975, H157, A549, HCT116, HCT116 $p53^{-/-}$ cells
Concentration:	2 μM, 4 μM, 6 μM
Incubation Time:	24 hours
Result:	Induced apoptosis in all assessed NSCLC cell lines irrespective of their p53 mutational status.

Western Blot Analysis[1]

Cell Line:	H1975, H322, H157, A549, HCT116, HCT116 $p53^{-/-}$
Concentration:	2 μM, 4 μM, 6 μM
Incubation Time:	24 hours
Result:	Increased PUMA and p21 protein expression.

In Vivo

SCH529074 (oral administration; 30 or 50 mg/kg; twice daily; 4 weeks; started on day 3 until day 31) causes 79 and 43% reduction of tumor growth at 50 and 30 mg/kg doses, respectively. the degree of tumor inhibition correlates with the plasma exposure of the compound (0.26–0.55 μm at 30 mg/kg and 0.39-0.79 μm at 50 mg/kg, 2-12 h post final dosing) in human DLD-1 colorectal cancer xenograft[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female nude mice, 5–7 weeks of age, received subcutaneous inoculation of DLD-1 human colorectal carcinoma cells[2]
Dosage:	30 or 50 mg/kg
Administration:	Oral administration; twice daily; 4 weeks; started on day 3 until day 31
Result:	Inhibited tumor growth

REFERENCES

[1]. Miljana Nenkov, et al. Growth Inhibitory Role of the p53 Activator SCH 529074 in non‐small Cell Lung Cancer Cells Expressing Mutant p53. Oncol Rep. 2020 Jun;43(6):2073-2082.

[2]. Mark Demma, et al. SCH529074, a Small Molecule Activator of Mutant p53, Which Binds p53 DNA Binding Domain (DBD), Restores Growth-Suppressive Function to Mutant p53 and Interrupts HDM2-mediated Ubiquitination of Wild Type p53. J Biol Chem. 2010 Apr 2;285(

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