Web: www.taiclone.com
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K-756

Catalog No: tcsc0035125

Available Sizes

Size: 5mg

Size: 10mg

Size: 25mg

Specifications

CAS No:
130017-40-2

Formula:
$C_{24}H_{27}N_5O_3$

Pathway:
Epigenetics;Cell Cycle/DNA Damage

Target:
PARP;PARP

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
433.5

Product Description

K-756 is a direct and selective **tankyrase** (**TNKS**) inhibitor, which inhibits the ADP-ribosylation activity of **TNKS1** and **TNKS2** with **IC $_{50}$**s of 31 and 36 nM, respectively.

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IC50 & Target: IC50: 31 nM (TNKS1), 36 nM (TNKS2)[1]

In Vitro: K-756 is a novel and selective Wnt/β-catenin pathway inhibitor targeting tankyrase (TNKS). TNKS is one of the members of the PARP family (it is also known as PARP5). K-756 binds to the induced pocket of TNKS and inhibits its enzyme activity. To study the isoform selectivity of K-756, the PARP family enzyme inhibitory activity at 10 μM is evaluated. K-756 inhibits TNKS1 and TNKS2 by 97% and 100%, respectively. In contrast, the inhibitory activity of K-756 against PARP1, PARP2, PARP3, PARP6, PARP7, and PARP11 is less than 13%. K-756 inhibits the cell growth of APC-mutant colorectal cancer COLO 320DM and SW403 cells by inhibiting the Wnt/β-catenin pathway. K-756 strongly inhibits the reporter activity in DLD-1/TCF-Luc cells with an IC_{50} of 110 nM, but does not inhibit DLD-1/mtTCF-Luc cells, even at 1,000 nM. APC-mutant colorectal cancer cell line COLO 320DM and SW403 cells are treated with K-756 and after 144 hours, cell growth inhibition is measured by an XTT assay. The application of K-756 inhibits the cell growth of COLO 320DM with a GI_{50} of 780 nM. K-756 also inhibits SW403 with a GI_{50} of 270 nM[1].

In Vivo: DLD-1/TCF-Luc cell xenografts are created in SCID mice. Vehicle (0.5% MC400) or K-756 is administered orally once a day for 3 days at 100, 200, and 400 mg/kg. The Wnt/β-catenin signal inhibition in the tumor is detected by measuring *FGF20* and *LGR5* and luciferase activity. The expression of *FGF20* and reporter activity are significantly decreased at doses of 100 mg/kg and above at 3-day administration. The expression of *LGR5* is significantly decreased at doses of 200 mg/kg and above at 3-day administration. The maximum inhibitory activity is reached with the administration of K-756 at a dose of 400 mg/kg at 3-day administration. The Wnt/β-catenin signal inhibition at a dose of 400 mg/kg is observed from 1-day administration[1].