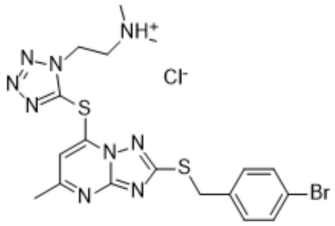
WS-384

Cat. No.:	HY-161470
Molecular Formula:	$C_{18}H_{21}BrClN_9S_2$
Molecular Weight:	542.91
Target:	Histone Demethylase; E1/E2/E3 Enzyme; DNA/RNA Synthesis; Caspase; Apoptosis
Pathway:	Epigenetics; Metabolic Enzyme/Protease; Cell Cycle/DNA Damage; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	WS-384 is a dual LSD1 and DCN1-UBC12 protein-protein interaction inhibitor with oral activity, with IC_{50} values of 338.79 nM and 14.81 nM, respectively. WS-384 possesses anticancer activity and can cause cell cycle arrest, DNA damage, and induce apoptosis. WS-384 can be used in the research of non-small cell lung cancer (NSCLC)[1].
IC_{50} & Target	IC50: 338.79 nM (LSD1)[1]. IC50: 14.81 nM (DCN1-UBC12 Protein-protein interaction)[1].
In Vitro	WS-384 (1-32 μM; 24-72 h) inhibits the growth of A549 and H1975 cells in a time- and dose-dependent manner, with an IC_{50} ranging from 2.15 to 6.67 μM, demonstrating anticancer activity[1]. WS-384 (1-8 μM; 48 h) enhances the expression levels of p21 gene and protein in A549 and H1975 cells by inhibiting the neddylation of cullin 1 and reducing the H3K4 demethylation at the CDKN1A promoter, thus inducing cell cycle arrest at the G2/M phase and apoptosis. Additionally, WS-384 (1-8 μM; 48 h) can also cause DNA damage[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	A549, H1975
Concentration:	1 μM, 2 μM, 4 μM, 8 μM (A549); 0.5 μM, 1 μM, 2 μM, 4 μM (H1975)
Incubation Time:	48 h
Result:	Increased the apoptosis rate in a concentration-dependent manner, with the apoptosis rate of A549 cells reaching 44.9% at a concentration of 8 μM and the apoptosis rate of H1975 cells reaching 36.42% at a concentration of 4 μM.

Western Blot Analysis[1]

Cell Line:	A549, H1975
Concentration:	2 μM, 4 μM, 8 μM (A549); 1 μM, 2 μM, 4 μM (H1975)
Incubation Time:	48 h

Result:	Blocked the neddylation of cullin1 and cullin3 but had no effect on the neddylation of other cullin members (cullin2, cullin4A, and cullin5). Increased the proteins expression of cleaved caspase 3, cleaved caspase 7, cleaved caspase 9, and cleaved PARP. Decreased the protein expression of p-CDC2, cyclin B1. CDK4 and CDK6. Increased the protein expression γ-H2AX (a marker protein of DNA damage).

In Vivo

WS-384 (25-50 mg/kg; p.o.; once daily for 36 consecutive days) effectively inhibits the growth of NSCLC tumors in the BALB/c nude mouse xenograft model with low toxicity[1].

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Animal Model:	BALB/c nude mice xenograft model[1].
Dosage:	25 mg/kg; 50 mg/kg;
Administration:	Oral gavage (p.o.); Once daily for 36 consecutive days
Result:	Significantly reduced tumor weight and volume in mice in the 50 mg/kg group. Had no significant toxic effects on the heart, liver, spleen, lungs, and kidneys.

REFERENCES

[1]. Li A, et al. Discovery of WS-384, a first-in-class dual LSD1 and DCN1-UBC12 protein-protein interaction inhibitor for the treatment of non-small cell lung cancer. Biomed Pharmacother. 2024;173:116240.

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