PKM2/PDK1-IN-1

Cat. No.: HY-149275

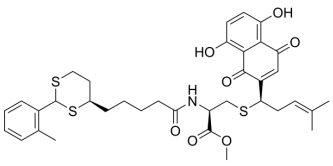
Molecular Formula: $C_{36}H_{43}NO_7S_3$

Molecular Weight: 697.92

Target: Akt; EGFR; Apoptosis; Pyruvate Kinase; PDK-1

Pathway: PI3K/Akt/mTOR; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Apoptosis; Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PKM2/PDK1-IN-1, one of shikonin thioether derivatives, is a dual inhibitor of PKM2/PDK1. PKM2/PDK1-IN-1 inhibits the proliferation of NSCLC cells, and induces apoptosis. PKM2/PDK1-IN-1 induces intercellular ROS production, and regulates the apoptotic proteins, to involves in mitochondrial and death receptor pathway[1].

IC_{50} & Target

PKM2, PDK-1[1]

In Vitro

PKM2/PDK1-IN-1 (compound E5) (0.5-4 μM; 24 h) shows a synergistic anticancer effects with Gefitinib (HY-50895)[1].
PKM2/PDK1-IN-1 (0.5 μM; 24 h) regulates the apoptotic proteins of both mitochondrial and death receptor pathway[1].
PKM2/PDK1-IN-1 (0.5 μM, 1 μM; 24 h) causes the mitochondria transmembrane potential (ΔΨm) dissipation and intracellular ROS accumulation in lung cancer cells[1].
PKM2/PDK1-IN-1 (1 μM, 2 μM; 24 h) inhibits PDK1 and enhances the downstream PDH activity in H1975 cells[1].
PKM2/PDK1-IN-1 inhibits intracellular NADPH concentration and increases ATP production of H1975 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	H1975 cells
Concentration:	0.5 μM, 1 μM, 2 μM, 4 μM24 h; with 2.5-20 μM Gefitinib
Incubation Time:	24 h
Result:	Synergistically induced cell apoptosis.

Western Blot Analysis[1]

Cell Line:	H1975 cells
Concentration:	0.5 μM
Incubation Time:	24 h; with 10 μM Gefitinib
Result:	Increased the protein levels of Cleaved Caspase-9, -3, and Cytochrome c. Deceased the protein levels of p-AKT, p-EGFR, Bcl-2.

In Vivo

PKM2/PDK1-IN-1 (compound E5) (2.4 mg/kg, 4.8 mg/kg; 6 times in 2 days) suppress the growth of H1975 xenograft tumor in

nude mice in vivo with low toxic side effects[1].

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

Animal Model:	Nude mice with H1975 xenograft tumor (6-week-old)[1]
Dosage:	4.8 mg/kg; dispersed in 20% DMSO
Administration:	IP; every two days for a total of 6 times, for 11 days
Result:	Inhibited tumor growth.

Animal Model:	For acute toxicity in ICR mice (8-week-old)[1]
Dosage:	2.4, 4.8, 9.6, 19.2, 38.4 mg/kg; dissolved in 20% DMSO
Administration:	IP; singel dose; observed for 14 days
Result:	Exhibited little side effect in mice.

REFERENCES

[1]. Lin H, et al. PKM2/PDK1 dual-targeted shikonin derivatives restore the sensitivity of EGFR-mutated NSCLC cells to gefitinib by remodeling glucose metabolism. Eur J Med Chem. 2023 Mar 5;249:115166.

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