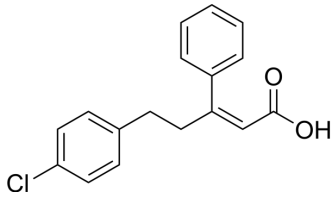
PS48

Cat. No.:	HY-15967
CAS No.:	1180676-32-7
Molecular Formula:	$C_{17}H_{15}ClO_2$
Molecular Weight:	286.75
Target:	PDK-1
Pathway:	PI3K/Akt/mTOR
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 : 100 mg/mL (348.74 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.4874 mL	17.4368 mL	34.8736 mL
5 mM	0.6975 mL	3.4874 mL	6.9747 mL
10 mM	0.3487 mL	1.7437 mL	3.4874 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: ≥ 2.5 mg/mL (8.72 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.72 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	PS48 is an activator of PDK1 with an AC_{50} of 8 μM.
IC_{50} & Target	AC50: 8 μM (PDK1)[1]
In Vitro	PS48 activates full length PDK1 (His-PDK1- FL) and PDK1 50-359[Tyr288Gly;Gln292Ala] (His-PDK1 dm) with AC_{50}s (the concentrations required to reach 50% of the maximal activation) of 7.95±0.2 and 10.0±2.0 μM, respectively. PS48 binds to

PDK150–359 with a 1:1 stoichiometry and a binding affinity in the micromolar range (K_d=10.3 μM)[1]. PDK1 activator, PS48, has the ability to reverse the cell proliferation inhibition role of triptolide (TP) in vitro. The inhibition role of TP in cell number is significantly reversed by PS48. TP significantly increases the cell proportion in G0-G1 phase and decreases the cell proportion in G2-M and S phase. However, the effect of TP on cell cycle distribution is all reversed by PS48. In addition, suppression of PDK1/Akt/mTOR pathway by TP in high glucose (HG)-treated human renal mesangial cells (HRMCs) is also reversed by PS48, as well as the expression of Ki-67 and proliferating cell nuclear antigen (PCNA)[2].

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

PROTOCOL

Kinase Assay [1]

PDK1 activity tests are performed using T308tide as a substrate for PDK1. In brief, PDK1 activity assay is performed at room temperature (22°C) in a 20 μL mix containing 50 mM Tris pH 7.5, 0.05 mg/mL BSA, 0.1% β-mercaptoethanol, 10 mM $MgCl_2$, 100 μM [γ^{32}P]ATP (5-50 cpm/pmol) , 0.003% Brij, 150-500 ng PDK1, and T308tide (from 0.1 to 1 mM). When appropriate, the PDK1 activity assay is performed in a 96 well format and 4 μL aliquots spotted on p81 phosphocellulose papers using ep motion 5070, washed in 0.01% phosphoric acid, dried, and then exposed and analysed using PhosphoImager technology. Activity measurements are performed in duplicates or triplicates with less than 10% difference between replicates. Experiments are repeated at least twice[1].

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Cell Assay [2]

Human renal mesangial cells (HRMCs) are cultured with 1640 media, containing 10% fetal bovin serum at 37 °C in 5% CO_2. Cells are cultured with D-glucose at normal (5.5 mM) or high (25 mM) concentrations in serum-free medium. D-Mannitol (25 mM) is used for a control of osmolality. TP is reconstituted in 0.01% DMSO and freshly diluted with culture medium to 10 ug/L before using. To determine the specific role of PDK1 in TP-potentiated anti-proliferation, 5 μM PS48 (MedChem Express, USA) is applied following the treatment of TP. MTT assay is used to detect cell proliferation. HRMCs are seeded at a density of 1x10^5/mL into 96-well plates. After 12, 24, 48 and 72 h incubation with different compounds, 20 uL MTT (5 mg/mL) is added to each well. Cells are then cultured for an additional 2 h and subsequently lysed using DMSO (150 uL/well). When the formazan crystals completely dissolve, the optical density (OD) is measured at 570 nm. The arithmetic mean OD of six wells for each group is calculated[2].

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CUSTOMER VALIDATION

- Redox Biol. 2021 Jan;38:101774.
- Int J Biol Sci. 2017 Sep 21;13(10):1266-1275.
- Stem Cell Res Ther. 2020 Apr 16;11(1):157.
- Virol Sin. 2021 Sep 14.
- Reprod Domest Anim. 2020 Dec;55(12):1678-1687.

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REFERENCES

[1]. Hindie V, et al. Structure and allosteric effects of low-molecular-weight activators on the protein kinase PDK1. Nat Chem Biol. 2009 Oct;5(10):758-64.

[2]. Han F, et al. Triptolide Suppresses Glomerular Mesangial Cell Proliferation in Diabetic Nephropathy Is Associated with Inhibition of PDK1/Akt/mTOR Pathway. Int J Biol Sci. 2017 Sep 21;13(10):1266-1275.

Caution: Product has not been fully validated for medical applications. For research use only.

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