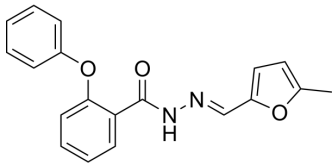
PNU-74654

Cat. No.:	HY-101130
CAS No.:	113906-27-7
Molecular Formula:	$C_{19}H_{16}N_2O_3$
Molecular Weight:	320
Target:	Wnt; β-catenin; Apoptosis
Pathway:	Stem Cell/Wnt; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (93.75 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1250 mL	15.6250 mL	31.2500 mL
5 mM	0.6250 mL	3.1250 mL	6.2500 mL
10 mM	0.3125 mL	1.5625 mL	3.1250 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 (7.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PNU-74654 is an inhibitor of Wnt/β-catenin pathway with an IC_{50} of 129.8 μM in NCI-H295 cell.

IC_{50} & Target

129.8 μM (Wnt/β-catenin, NCI-H295 cell)[1]

In Vitro

PNU-74654 binds to β-catenin with a K_D of 450 nM. The Tcf3/Tcf4-binding surface on β-catenin contains a well-defined hot spot around residues K435 and R469. The binding mode of PNU-74654 involves the two narrow pockets on either side of this hot spot[2]. In NCI-H295 cells,PNU-74654 significantly decreases cell proliferation 96 h after treatment, increases early and late apoptosis, decreases nuclear beta-catenin accumulation, impairs CTNNB1/beta-catenin expression and increases beta-catenin target genes 48 h after treatment. No effects are observed on HeLa cells. In NCI-H295 cells, PNU-74654 decreases

cortisol, testosterone and androstenedione secretion 24 and 48 h after treatment. The SF1 and CYP21A2 mRNA expression as well as the protein levels of STAR and aldosterone synthase are decreased in NCI-H295 cells after 48 h PNU-74654 treatment. In Y1 cells, PNU-74654 impairs corticosterone secretion 24 h after treatment but does not decrease cell viability[1].

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

PROTOCOL

Cell Assay [1]

The PNU-74654 compound is dissolved in DMSO at stock concentrations of 31.2 mM. For working solutions, PNU-74654 is diluted 100X in growth medium with no serum deprivation. NCI-H295 cells are plated at 200,000 cells per well in 24-well plates for gene expression, protein analysis and adrenal steroid measurements. After 48 h, cells are treated with vehicle (0.1%-0.4% DMSO) or 10, 50, 100 and 200 μM PNU-74654. After 24 and 48 h, medium supernatants are collected for adrenal steroid measurements[1].

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

CUSTOMER VALIDATION

- J Cell Physiol. 2019 Jan 26.
- Environ Toxicol. 2020 Jun;35(6):697-706.
- Stem Cells Dev. 2021 Jun 4.
- Curr Issues Mol Biol. 2022, 44(1), 222-232.
- PeerJ. 2023 Aug 18;11:e15841.

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REFERENCES

[1]. Leal LF, et al. Inhibition of the Tcf/beta-catenin complex increases apoptosis and impairs adrenocortical tumor cell proliferation and adrenal steroidogenesis. Oncotarget. 2015 Dec 15;6(40):43016-32.

[2]. Trosset JY, et al. Inhibition of protein-protein interactions: the discovery of druglike beta-catenin inhibitors by combining virtual and biophysical screening. Proteins. 2006 Jul 1;64(1):60-7.

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