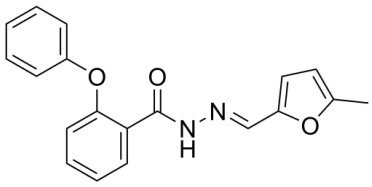
Data Sheet

Product Name:	PNU-74654
Cat. No.:	CS-6211
CAS No.:	113906-27-7
Molecular Formula:	$C_{19}H_{16}N_2O_3$
Molecular Weight:	320.34
Target:	Apoptosis; Wnt; β-catenin
Pathway:	Apoptosis; Stem Cell/Wnt
Solubility:	DMSO : ≥ 30 mg/mL



BIOLOGICAL ACTIVITY:

PNU-74654 is an inhibitor of **Wnt/β-catenin** pathway with an **IC_{50}** of 129.8 μM in NCI-H295 cell. IC50 & 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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

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.

CAIndexNames:

Benzoic acid, 2-phenoxy-, 2-[(5-methyl-2-furanyl)methylene]hydrazide

SMILES:

O=C(N/N=C/C1=CC=C(C)O1)C2=CC=CC=C2OC3=CC=CC=C3

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

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