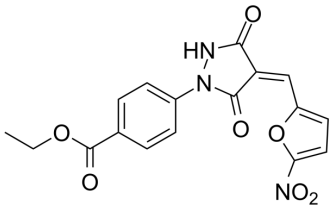
PYR-41

Cat. No.:	HY-13296
CAS No.:	418805-02-4
Molecular Formula:	$C_{17}H_{13}N_3O_7$
Molecular Weight:	371.3
Target:	E1/E2/E3 Enzyme; Apoptosis
Pathway:	Metabolic Enzyme/Protease; Apoptosis
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 : ≥ 46 mg/mL (123.89 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6932 mL	13.4662 mL	26.9324 mL
5 mM	0.5386 mL	2.6932 mL	5.3865 mL
10 mM	0.2693 mL	1.3466 mL	2.6932 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 (6.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PYR-41 is a selective and cell permeable inhibitor of ubiquitin-activating enzyme E1 with an IC_{50} of < 10 μM, with little activity at E2 and E3.

IC_{50} & Target

IC50: < 10 μM (E1)

In Vitro

PYR-41 increases total sumoylation in cells in addition to blocking ubiquitylation. PYR-41 attenuates cytokine-mediated nuclear factor-κB activation. PYR-41 also prevents the downstream ubiquitylation and proteasomal degradation of IκBα. Furthermore, PYR-41 inhibits degradation of p53 and activates the transcriptional activity of this tumor suppressor[1]. PYR-41 (50 μM) promotes accumulation of ubiquitinated proteins. PYR-41 causes a concentration-dependent (10-50 μM) decline in DUB activity in Z138 cells after 4 h. PYR-41 potently inhibits USP5 DUB activity, even at the lowest concentration (10 μM). PYR-41 potently (10-50 μM) inhibits the activity of various DUBs, determined to represent USP9x, USP5, USP14, UCH37 and

UCH-L3. Co-treatment of Z138 cells with DTT and PYR-41 completely abolishes the accumulation of ubiquitinated proteins[2].

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

PROTOCOL

Kinase Assay [1]

Rabbit or mouse E1 (apper 250 ng) is incubated with ^{32}P-ubiquitin in 1× reaction buffer [50 mM Tris (pH 7.4), 0.2 mM ATP, 0.5 mM $MgCl_2$] at room temperature for 15 min. In some experiments, the His-tagged mouse E1 is bound to TALON cobalt affinity resin before carrying out incubations and reactions. Mouse E1 and ^{32}P-ubiquitin are added to the beads in 1× reaction buffer and incubated as for E1 reactions. Samples are heated in nonreducing SDS-PAGE sample buffer and resolved by SDS-PAGE. Thioesters with ubiquitin are visualized by Storm PhosphoImager.

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

CUSTOMER VALIDATION

- Mbio. 2020 Apr 14;11(2):e00467-20.
- Cell Prolif. 2021 Jan;54(1):e12919.
- Cells. 2022 Apr 8;11(8):1265.
- Int Immunopharmacol. 2020 Oct;87:106763.
- Mol Cell Biol. 2018 Jul 16;38(15). pii: e00024-18.

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REFERENCES

[1]. Yang Y, et al. Inhibitors of ubiquitin-activating enzyme (E1), a new class of potential cancer therapeutics. Cancer Res. 2007 Oct 1;67(19):9472-81.

[2]. Kapuria V, et al. Protein cross-linking as a novel mechanism of action of a ubiquitin-activating enzyme inhibitor with anti-tumor activity. Biochem Pharmacol. 2011 Aug 15;82(4):341-9.

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