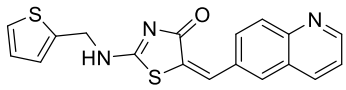
Product data sheet

MedKoo Cat#: 406182 Name: RO-3306 CAS#: 872573-93-8 Chemical Formula: $C_{18}H_{13}N_3OS_2$ Exact Mass: 351.05 Molecular Weight: 351.44	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
RO-3306 is a CDK1 inhibitor with potential anticancer activity. Treatment of growing AML cells with RO-3306 induced G2/M-phase cell cycle arrest and apoptosis in a dose- and time-dependent manner. RO-3306 downregulated expression of the antiapoptotic proteins Bcl-2 and survivin and blocked p53-mediated induction of p21 and MDM2. RO-3306 actively enhances downstream p53 signaling to promote apoptosis.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	16.26	46.27
DMSO:PBS (pH 7.2) (1:2)	0.25	0.71
DMF	20.0	56.91

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.85 mL	14.23 mL	28.45 mL
5 mM	0.57 mL	2.85 mL	5.69 mL
10 mM	0.28 mL	1.42 mL	2.85 mL
50 mM	0.06 mL	0.28 mL	0.57 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Sunada S, Saito H, Zhang D, Xu Z, Miki Y. CDK1 inhibitor controls G2/M phase transition and reverses DNA damage sensitivity. Biochem Biophys Res Commun. 2021 Apr 23;550:56-61. doi: 10.1016/j.bbrc.2021.02.117. Epub 2021 Mar 5. PMID: 33684621.
2. Kojima K, Shimanuki M, Shikami M, Andreeff M, Nakakuma H. Cyclin-dependent kinase 1 inhibitor RO-3306 enhances p53-mediated Bax activation and mitochondrial apoptosis in AML. Cancer Sci. 2009 Jun;100(6):1128-36. doi: 10.1111/j.1349-7006.2009.01150.x. Epub 2009 Mar 10. PMID: 19385969; PMCID: PMC2759356.

In vivo study

1. Ying X, Che X, Wang J, Zou G, Yu Q, Zhang X. CDK1 serves as a novel therapeutic target for endometrioid endometrial cancer. J Cancer. 2021 Feb 22;12(8):2206-2215. doi: 10.7150/jca.51139. PMID: 33758599; PMCID: PMC7974891.
2. Czaplinski S, Hugle M, Stiehl V, Fulda S. Polo-like kinase 1 inhibition sensitizes neuroblastoma cells for vinca alkaloid-induced apoptosis. Oncotarget. 2016 Feb 23;7(8):8700-11. doi: 10.18632/oncotarget.3901. PMID: 26046302; PMCID: PMC4890998.

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7. Bioactivity

Biological target:

Ro-3306 is an inhibitor of CDK1, with Kis of 20 nM, 35 nM and 340 nM for CDK1, CDK1/cyclin B1 and CDK2/cyclin E, respectively.

In vitro activity

To analyze the DNA damage and repair processes during RO-3306-induced G2 arrest, this study examined whether irradiated cells undergoing prolonged G2 arrest repaired DSBs or induced damaged DNA to enter M-phase during RO-3306 treatment. Immediate discontinuation of RO-3306 treatment (10 μM) and exchanged treatment (DMSO or 2 μM) after irradiation in HL-60 cells resulted in mitotic entry and DSB levels significantly higher in M-phase cells, compared to in non-irradiated control (Fig. 4A and B). In contrast, persistent 10 μM RO-3306 treatment for 8 h after irradiation dramatically decreased DSB levels in M-phase cells compared to the immediate release of RO-3306 treatment (Fig. 4C and D). This study showed that further DNA-PK inhibition during prolonged G2 arrest delayed DNA repair and inhibited cell proliferation (supplementary Fig. 2). The clonogenic assay demonstrated that persistent treatment with RO-3306 after irradiation resulted in higher fractions of surviving HeLa cells, supporting the resistance of cells to CDK1 inhibition (Fig. 4E). These results show that even higher dose of RO-3306 induced prolonged G2 arrest, allowing irradiated cells to repair DSBs and preventing DNA damage from being carried over into M-phase.

Reference: Biochem Biophys Res Commun. 2021 Apr 23;550:56-61.
https://www.sciencedirect.com/science/article/pii/S0006291X21003466?via%3Dihub

In vivo activity

Subcutaneous tumor xenografts developed from HEC-1-B cells in BALB/c nude mice were successfully established individually. Consistent with the in vitro results, the tumor growth of xenograft endometrial cancer grafts was significantly blocked with the treatment of RO3306 (Figure (5A-D). As early as day 4 of the treatment, there was a extremely significant difference in tumor volume between the RO3306 treatment group and the control group ($p < 0.0001$) (Figure 5A). At the end of the study, tumor volumes of endometrial cancer grafts in the RO3306 treatment group and the control group were 392.2 ± 24.34 and $689.8 \pm 104.3 mm^3$, respectively, with highly significant differences between the two groups ($p < 0.01$) (Figure 5A). As to body weight, there was no significant difference between the two groups ($p > 0.05$) (Figure 5B). The tumor weight of endometrial cancer grafts harvested at the end of the study in the RO3306 treatment group was significantly lower than that in the control group ($p < 0.05$) (Figure 5C). These data suggested that CDK1 played an important role in the growth and proliferation of endometrial cancer cells in vivo and RO3306 can serve as its targeted inhibitor for the treatment of endometrioid endometrial cancer.

Reference: J Cancer. 2021; 12(8): 2206–2215. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7974891/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.