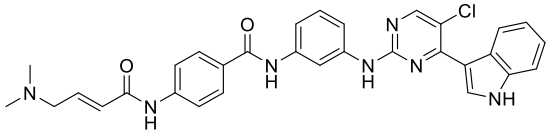
Product data sheet

MedKoo Cat#: 406560 Name: THZ1 CAS#: 1604810-83-4 (free base) Chemical Formula: $C_{31}H_{28}ClN_7O_2$ Exact Mass: 565.1993 Molecular Weight: 566.05	
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:

THZ1 is a selective CDK7 inhibitor that preferentially diminishes transcription in cancer cells. THZ1 has the unprecedented ability to target a remote cysteine residue located outside of the canonical kinase domain, providing an unanticipated means of achieving selectivity for CDK7. Cancer cell-line profiling indicates that a subset of cancer cell lines, including human T-cell acute lymphoblastic leukaemia (T-ALL), have exceptional sensitivity to THZ1. Cyclin-dependent kinases (CDKs) are involved in temporal control of the cell cycle and transcription and play central roles in cancer development and metastasis.

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	62.5	110.41
DMF	30.0	53.0
DMF:PBS (pH 7.2) (1:2)	0.3	0.53

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.77 mL	8.83 mL	17.67 mL
5 mM	0.35 mL	1.77 mL	3.53 mL
10 mM	0.18 mL	0.88 mL	1.77 mL
50 mM	0.04 mL	0.18 mL	0.35 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. Abudureheman T, Xia J, Li MH, Zhou H, Zheng WW, Zhou N, Shi RY, Zhu JM, Yang LT, Chen L, Zheng L, Xue K, Qing K, Duan CW. CDK7 Inhibitor THZ1 Induces the Cell Apoptosis of B-Cell Acute Lymphocytic Leukemia by Perturbing Cellular Metabolism. Front Oncol. 2021 Apr 6;11:663360. doi: 10.3389/fonc.2021.663360. PMID: 33889549; PMCID: PMC8056175.
2. Attia YM, Shouman SA, Salama SA, Ivan C, Elsayed AM, Amero P, Rodriguez-Aguayo C, Lopez-Berestein G. Blockade of CDK7 Reverses Endocrine Therapy Resistance in Breast Cancer. Int J Mol Sci. 2020 Apr 23;21(8):2974. doi: 10.3390/ijms21082974. PMID: 32340192; PMCID: PMC7215326.

In vivo study

1. Wei Y, Li C, Bian H, Qian W, Jin K, Xu T, Guo X, Lu X, Su F. Targeting CDK7 suppresses super enhancer-linked inflammatory genes and alleviates CAR T cell-induced cytokine release syndrome. Mol Cancer. 2021 Jan 4;20(1):5. doi: 10.1186/s12943-020-01301-7. PMID: 33397398; PMCID: PMC7780220.

2. Kuo KL, Lin WC, Liu SH, Hsu FS, Kuo Y, Liao SM, Yang SP, Wang ZH, Hsu CH, Huang KH. THZ1, a covalent CDK7 inhibitor, enhances gemcitabine-induced cytotoxicity via suppression of Bcl-2 in urothelial carcinoma. Am J Cancer Res. 2021 Jan 1;11(1):171-180. PMID: 33520367; PMCID: PMC7840706.

7. Bioactivity

Biological target:

THZ1 is a covalent CDK7 inhibitor with an IC50 of 3.2 nM and also inhibits the closely related kinases CDK12 and CDK13 and downregulates MYC expression.

In vitro activity

In the present study, THZ1 arrested the cell cycle of B-ALL cells in vitro in a low concentration, while inducing the apoptosis of B-ALL cells in vitro in a high concentration by activating the apoptotic pathways. In addition, RNA-SEQ results revealed that THZ1 disrupted the cellular metabolic pathways of B-ALL cells. Moreover, THZ1 suppressed the cellular metabolism and blocked the production of cellular metabolic intermediates in B-ALL cells. Mechanistically, THZ1 inhibited the cellular metabolism of B-ALL by downregulating the expression of c-MYC-mediated metabolic enzymes, such as HK1, PFKP, PKM2, and LDHA.

Reference: Front Oncol. 2021; 11: 663360. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8056175/

In vivo activity

The brisk elevation of peritoneal CD11b+CD86+ cells, which was already distinct 12 h after LPS injection, was almost halved in mice pretreated with THZ1 (Fig. 2e, Fig. S2C). This phenomenon was further supported by the distribution and response of peritoneal macrophages, which changed markedly in pretreated mice with the decreased percentage of CD11b+F4/80+ macrophages (mean ± SD, LPS, 70.36 ± 6.284; THZ1+LPS, 43.32 ± 11.96) and inhibited transcription of inflammatory genes (Fig. 2f, g, Fig. S2C). A slight increase in CD11b+Ly6C+ monocytes (mean ± SD, LPS, 4.494 ± 3.192; THZ1+LPS, 15.53 ± 10.10) might be a secondary consequence of reduced macrophages. Collectively, the decrease and dysfunction of macrophages support the feasibility for controlling the magnitude of CRS and rescuing mice by blocking CDK7.

Reference: Mol Cancer. 2021; 20: 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7780220/

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.