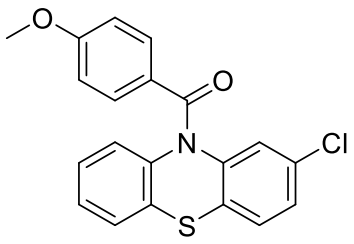
Product data sheet

MedKoo Cat#: 555876 Name: CUN25391 CAS#: 105925-39-1 Chemical Formula: $C_{20}H_{14}ClNO_2S$ Exact Mass: 367.0434 Molecular Weight: 367.847	
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:

CUN25391, also known as Tubulin inhibitor 6 or iHAP1 (Compound 14b in literature 1) is a tubulin inhibitor and a potent inhibitor of multiple cancer cell lines. CUN25391 inhibits tubulin polymerization with an IC50 of 0.87 μM. This product has not formal name. For the convenience of scientific communication, we named it by combining its Inchi key (3 letters from the first letter of each section) with the last 5 digits of its CAS number or its molecule weight if its CAS number is not available (see MedKoo Chemical Nomenclature, https://www.medkoo.com/page/naming).

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	27.0	73.56

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.72 mL	13.59 mL	27.19 mL
5 mM	0.54 mL	2.72 mL	5.44 mL
10 mM	0.27 mL	1.36 mL	2.72 mL
50 mM	0.05 mL	0.27 mL	0.54 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. Morita K, He S, Nowak RP, Wang J, Zimmerman MW, Fu C, Durbin AD, Martel MW, Prutsch N, Gray NS, Fischer ES, Look AT. Allosteric Activators of Protein Phosphatase 2A Display Broad Antitumor Activity Mediated by Dephosphorylation of MYBL2. Cell. 2020 Apr 30;181(3):702-715.e20. doi: 10.1016/j.cell.2020.03.051. Epub 2020 Apr 20. PMID: 32315619; PMCID: PMC7397863.

In vivo study

1. Morita K, He S, Nowak RP, Wang J, Zimmerman MW, Fu C, Durbin AD, Martel MW, Prutsch N, Gray NS, Fischer ES, Look AT. Allosteric Activators of Protein Phosphatase 2A Display Broad Antitumor Activity Mediated by Dephosphorylation of MYBL2. Cell. 2020 Apr 30;181(3):702-715.e20. doi: 10.1016/j.cell.2020.03.051. Epub 2020 Apr 20. PMID: 32315619; PMCID: PMC7397863.

7. Bioactivity

Biological target:

Tubulin inhibitor 6 (Compound 14b) is a potent inhibitor of tubulin polymerization with an IC50 of 0.87 μM, of multiple cancer cell lines, and of K562 cell growth with an IC50 of 840 nM.

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In vitro activity

To determine whether iHAP1 treatment induces the identical subunits to form a heterotrimeric PP2A enzyme in neuroblastoma as in T-ALL cells, Kelly cells were established that stably expressed shRNAs targeting each of the subunits of PP2A. As shown in Figures S5H and S5I, Kelly cells acquired resistance to iHAP1 treatment when the expression levels of each of the subunits PPP2R1A, PPP2CA, or PPP2R5E (B56ε) was downregulated but not when PPP2R2A (B55α) was downregulated. These results indicate that iHAP1 consistently induces formation of the heterotrimeric PP2A holoenzyme complex containing PPP2R1A, PPP2CA, and PPP2R5E (B56ε) in diverse types of human cancers and expands the robustness of our findings beyond T-ALL cells.

Reference: Cell. 2020 Apr 30; 181(3): 702–715.e20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7397863/

In vivo activity

To document the enhanced antileukemic activity of iHAP1 in vivo and verify that it does not induce movement disorders through inhibition of dopamine signaling, iHAP1 was added to water containing normal 6-day-old zebrafish embryos. iHAP1 did not affect upright swimming or coordination at concentrations up to 2 μM The anti-T-ALL activity of iHAP1 versus PPZ was tested in the transgenic zebrafish T-ALL model (Gutierrez et al., 2014; Li et al., 2019), first by adding each compound to the water of zebrafish embryos for 5 days to determine the maximum tolerated doses (MTDs) of PPZ and iHAP1 (5 μM and 2 μM, respectively). As shown in Figures 2A and 2B, iHAP1 at 2 μM induced a strikingly greater loss of GFP-labeled T-ALL cells than 5 μM PPZ, indicating increased antitumor potency in vivo, consistent with our in vitro finding that iHAP1 is ~10 fold more active than PPZ against human T-ALL cells. Additioanlly, mice treated with doses of iHAP1 as high as 80 mg/kg/day lacked evidence of neurologic toxicity or any other toxicity, consistent with our biochemical reporter assays showing that iHAP1 does not inhibit dopamine signaling through DRD2. Thus, in preclinical testing against T-ALL xenografts, iHAP1 emerged as a promising compound, showing improved antitumor activity and lack of toxicity.

Reference: Cell. 2020 Apr 30; 181(3): 702–715.e20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7397863/