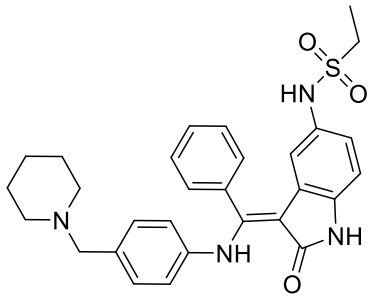
Product data sheet

MedKoo Cat#: 201466 Name: Hesperadin CAS#: 422513-13-1 (free base) Chemical Formula: $C_{29}H_{32}N_4O_3S$ Exact Mass: 516.21951 Molecular Weight: 516.65	
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:

Hesperadin is an inhibitor of human Aurora B, which can prevent the phosphorylation of substrate with IC(50) of 40 nM. Growth of cultured bloodstream forms was also sensitive to Hesperadin (IC(50) of 50 nM). Hesperadin blocked nuclear division and cytokinesis but not other aspects of the cell cycle. Consequently, growth arrested cells accumulated multiple kinetoplasts, flagella and nucleoli, similar to the effects of RNAi-dependent knockdown of TbAUK1 in cultured bloodstream forms cells. Molecular models predicted high-affinity binding of Hesperadin to both conserved and novel sites in TbAUK1. Collectively, these data demonstrate that cell cycle progression is essential for infections with T. brucei and that parasite Aurora kinases can be targeted with small-molecule inhibitors.

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	100	193.55

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.94 mL	9.68 mL	19.36 mL
5 mM	0.39 mL	1.94 mL	3.87 mL
10 mM	0.19 mL	0.97 mL	1.94 mL
50 mM	0.04 mL	0.19 mL	0.39 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. Jetton N, Rothberg KG, Hubbard JG, Wise J, Li Y, Ball HL, Ruben L. The cell cycle as a therapeutic target against Trypanosoma brucei: Hesperadin inhibits Aurora kinase-1 and blocks mitotic progression in bloodstream forms. Mol Microbiol. 2009 Apr;72(2):442-58. doi: 10.1111/j.1365-2958.2009.06657.x. Epub 2009 Mar 6. PMID: 19320832; PMCID: PMC2697958.

In vivo study

1. Wu X, Wu J, Hu W, Wang Q, Liu H, Chu Z, Lv K, Xu Y. MST4 Kinase Inhibitor Hesperadin Attenuates Autophagy and Behavioral Disorder via the MST4/AKT Pathway in Intracerebral Hemorrhage Mice. Behav Neurol. 2020 Feb 3;2020:2476861. doi: 10.1155/2020/2476861. PMID: 32089749; PMCID: PMC7023841.

7. Bioactivity

Biological target:

Hesperadin is an ATP competitive indolinone inhibitor of Aurora A and B. Hesperadin inhibits Aurora B with an IC50 of 250 nM.

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In vitro activity

After 24 hr exposure of BF cultures to 100 nM Hesperadin, cells contained a multi-lobed nucleus, numerous kDNA and numerous flagella (Fig. 6C, panels c-d); a pattern that phenocopied the loss of TbAUK1 with RNAi. The changes in cell population were quantified (Fig. 6B, right panel). In a wild-type BF population, approximately 60% of cells are in the 1N1K configuration, defined by a single nucleus (N) and a single kinetoplast (K). Within 24 hr of TbAUK1 depletion with RNAi, 1N1K cells declined to 8% of the population, while cells with the unusual configuration of more than 3K and an indeterminate number of nuclei (XN; K>3) increased to 81% of the population. After 24 hr exposure to 200 nM Hesperadin, cells with a 1N1K configuration dropped to 28% of the population, while cells with XN; K>3 increased to 25% of the population. Within 48 hr, cells with a XN; K>3 configuration increased to 48% of the population (Fig. 6C, right panel).

Reference: Mol Microbiol. 2009 Apr;72(2):442-58. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/19320832/

In vivo activity

It was confirmed that hesperadin administration for ICH mice significantly improved edema and alleviated neurological deficits at 12 h after ICH compared to the ICH group. MST4 expression in ICH mice treated with hesperadin was significantly lower than ICH mice, which proved the potential of hesperadin as an MST4 inhibitor. It was found that hesperadin is neuroprotective, which could ameliorate brain edema and behavioral deficits after experimental ICH in mice. In this study, hesperadin was confirmed to show a neuroprotective effect and can improve brain edema and neurofunction deficits in ICH mice.

Reference: Behav Neurol. 2020 Feb 3;2020:2476861. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32089749/