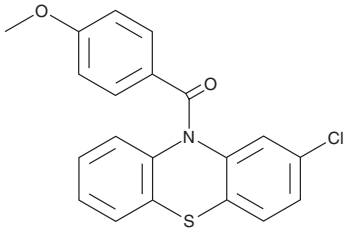
PRODUCT INFORMATION

iHAP1

Item No. 33530

CAS Registry No.:	105925-39-1
Formal Name:	(2-chloro-10H-phenothiazin-10-yl) (4-methoxyphenyl)-methanone
Synonyms:	Improved Heterocyclic Activator of PP2A 1, Tubulin Inhibitor 6
MF:	$C_{20}H_{14}ClNO_2S$
FW:	367.8
Purity:	≥98%
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

iHAP1 is supplied as a crystalline solid. A stock solution may be made by dissolving the iHAP1 in the solvent of choice, which should be purged with an inert gas. iHAP1 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of iHAP1 in these solvents is approximately 1 and 5 mg/ml, respectively.

iHAP1 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, iHAP1 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. iHAP1 has a solubility of approximately 0.33 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

iHAP1 is an inhibitor of tubulin polymerization (IC_{50} = 0.87 µM in a cell-free assay) that was originally identified as an activator of a heterotrimeric protein phosphatase 2A (PP2A) complex containing the PP2A-B56ε regulatory B subunit in a study that has since been retracted.[1-3] It does not bind to protein phosphatase 2 regulatory subunit 1A (PPP2R1A) when used at a concentration of 20 µM nor activate PP2A-B55α, PP2A-B56α, or PP2A-B56ε in a cell-free dephosphorylation assay at 10 µM.[4] iHAP1 inhibits the proliferation of K562 leukemia cells (IC_{50} = 0.84 µM) and induces apoptosis in HeLa cells when used at a concentration of 0.5 µM.[2,4] iHAP1 also inhibits acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) with IC_{50} values of 5.9 and 5.3 µM, respectively.[5]

References

1. Prinz, H., Chamasmani, B., Vogel, K., *et al.* *N*-benzoylated phenoxazines and phenothiazines: Synthesis, antiproliferative activity, and inhibition of tubulin polymerization. *J. Med. Chem.* **54(12)**, 4247-4263 (2011).
2. Morita, K., He, S., Nowak, R.P., *et al.* Allosteric activators of protein phosphatase 2A display broad antitumor activity mediated by dephosphorylation of MYBL2. *Cell* **181(3)**, 702-715 (2020).
3. Morita, K., He, S., Nowak, R.P., *et al.* Retraction Notice to: Allosteric activators of protein phosphatase 2A display broad antitumor activity mediated by dephosphorylation of MYBL2. *Cell* **185(16)**, 3058 (2022).
4. Vit, G., Duro, J., Rajendraprasad, G., *et al.* Chemogenetic profiling reveals PP2A-independent cytotoxicity of proposed PP2A activators iHAP1 and DT-061. *EMBO J.* **41(14)**, e110611 (2022).
5. Tin, G., Mohamed, T., Gondora, N., *et al.* Tricyclic phenothiazine and phenoselenazine derivatives as potential multi-targeting agents to treat Alzheimer's disease. *Med. Chem. Comm.* **6**, 1930-1941 (2015).

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