

Product Data Sheet

Product Name: SBE 13 HCl

Cat. No.: GC14644

Chemical Properties

Cas. No. 1052532-15-6

Chemical Name N-(4-((6-chloropyridin-3-yl)methoxy)-3-methoxybenzyl)-2-(3,4-dimethoxyphenyl)ethanamine hydrochloride

SMILES COC1=C(OC)C=C(CCNCC2=CC(OC)=C(OCC3=CN=C(Cl)C=C3)C=C2)C=C1.Cl

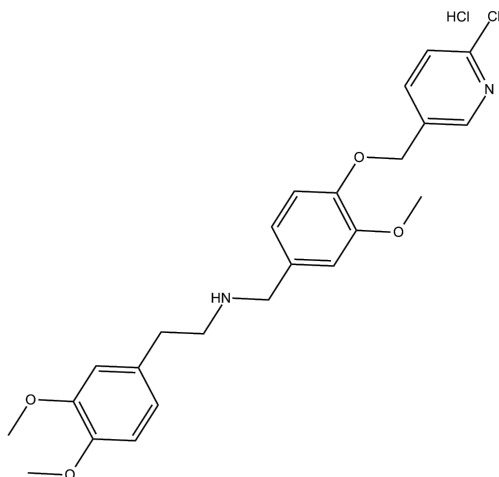
Formula $C_{24}H_{28}Cl_2N_2O_4$ M.Wt 479.4

Solubility DMF: 10 mg/ml, DMF:PBS (pH 7.2) (1:5): 0.16 mg/ml, DMSO: 1 mg/ml Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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**Kinase
experiment:**

To assay Plk1 kinase activity, cells are lysed after 13?h release in the presence of SBE13 after double thymidine block and kinase is immunoprecipitated from lysates using antibodies. In brief, for each immunoprecipitation 800?μg of total protein are incubated with Plk1 antibody cocktail (1.5?μg) for 2?h at 4°C on a rotator. Immunoprecipitated protein is collected using Protein A/G Agarose beads. Plk1 immunoprecipitates are incubated with casein (1?μg) and with [γ-32P]ATP (1?μCi) for 30?min at 37°C in kinase buffer. Products from the kinase assays are fractionated on 10?% bis-tris-polyacrylamide gels, and phosphorylated substrate is visualized by autoradiography after an exposure of 12-36?h. Equal amounts of immunoprecipitates are subjected to Western blot analysis to confirm equal loading of Plk1 protein in kinase reactions[1].

References:

- [1]. Keppner S, et al. Identification and validation of a potent type II inhibitor of inactive polo-like kinase 1. ChemMedChem. 2009 Nov;4(11):1806-9.
- [2]. Keppner S, et al. Fate of primary cells at the G /S boundary after polo-like kinase 1 inhibition by SBE13. Cell Cycle. 2011 Feb 15;10(4):708-20. Epub 2011 Feb 15.
- [3]. Keppner S, et al. Biological impact of freezing Plk1 in its inactive conformation in cancer cells. Cell Cycle. 2010 Feb 15;9(4):761-73. Epub 2010 Feb 16.

Background

The serine/threonine kinase polo-like kinase 1 (Plk1) attracts great attention in the field of cancer therapy because it exhibits generally elevated activity in cancer cells and is a negative prognostic factor for cancer patients. The importance of Plk1 activity as a measure for the aggressiveness of a tumor results from its important role in mitotic checkpoints. SBE13 is identified as a novel and potent inhibitor of inactive Plk1.

In vitro: To determine its ability to induce cell death in cancer cells, we applied kinase assays, western blot analyses, FACS can analyses, Caspase assays and immunofluorescence studies. We detected decreased cell proliferation, delayed progression through the cell cycle in lower SBE13 concentrations, a G2/M arrest using higher SBE13 concentrations followed by apoptosis, and

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abnormal mitotic figures. Notably, SBE13 did not influence activity of other kinases (Plk2, Plk3, Aurora A), indicating the selectivity of this type II Plk1 inhibitor [1].

In silico: The docking pose of SBE13 in the homology model suggests an interaction with Arg 95 of Plk1, and thus spans the whole hydrophobic pocket, which is anticipated for a type II inhibitor. Another SBE13's characteristic feature of type II inhibitors is the interaction with the hinge region and with the Asp in the Asp-Phe-Gly (DFG) motif [2].

Clinical trial: Up to now, SBE13 is still in the preclinical development stage.

Reference:

- [1] Keppner S, Proschak E, Kaufmann M, Strebhardt K, Schneider G, Sp?nkuch B. Biological impact of freezing Plk1 in its inactive conformation in cancer cells. Cell Cycle. 2010 Feb 15;9(4):761-73.
- [2] Keppner S, Proschak E, Schneider G, Sp?nkuch B. Identification and validation of a potent type II inhibitor of inactive polo-like kinase 1. ChemMedChem. 2009 Nov;4(11):1806-9.

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