

Product Data Sheet

Product Name: BS-181 HCl

Cat. No.: GC13690

Chemical Properties

Cas. No. 1397219-81-6

Chemical Name 5-N-(6-aminohexyl)-7-N-benzyl-3-propan-2-ylpyrazolo[1,5-a]pyrimidine-5,7-diamine;hydrate hydrochloride

SMILES CC(C)C1=C2N=C(C=C(N2N=C1)NCC3=CC=CC=C3)NCCCCCN.Cl

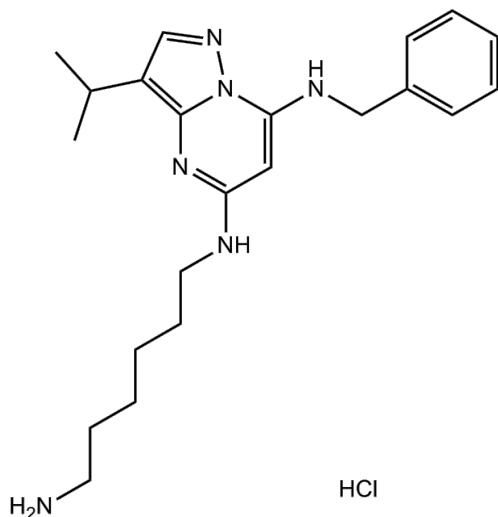
Formula $C_{22}H_{32}N_6 \cdot HCl$ M.Wt 416.99

Solubility $\geq 20.85\text{mg/mL}$ in DMSO, $\geq 6.49\text{mg/mL}$ in EtOH with ultrasonic 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

Kinase experiment [1]:

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

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In vitro kinase inhibition. Inhibition of CDK7 activity was measured by incubation of increasing amounts of BS-181 HCl with purified recombinant CDK7/CycH/MAT1 complex, followed by measurement of free ATP remaining in the reaction using a luciferase assay, luciferase activity therefore providing a measure of inhibition of CDK7 activity for the determination of IC50.

Cell experiment [1]:

Cell lines MCF-7 cells

Preparation method The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20 °C for several months.

Reaction Conditions 50 µM; 24 hrs

Applications In MCF-7 cells, BS-181 HCl inhibited the phosphorylation of CDK7 substrates, and promoted cell cycle arrest and apoptosis to inhibit the growth of cancer cell lines.

Animal experiment [1]:

Animal models Mice bearing MCF-7 xenografts

Dosage form 10 or 20 mg/kg; i.p.; b.i.d., for 2 weeks

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Applications In mice bearing MCF-7 xenografts, BS-181 HCl inhibited tumor growth in a dose-dependent manner, without apparent toxicity.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Ali S, Heathcote DA, Kroll SH, Jogalekar AS, Scheiper B, Patel H, Brackow J, Siwicka A, Fuchter MJ, Periyasamy M, Tolhurst RS, Kanneganti SK, Snyder JP, Liotta DC, Aboagye EO, Barrett AG, Coombes RC. The development of a selective cyclin-dependent kinase inhibitor that shows antitumor activity. Cancer Res. 2009;69(15):6208-15.

Background

IC50: 21 nm (CDK7)

Normal progression through the cell cycle requires the sequential action of cyclin-dependent kinases CDK1, CDK2, CDK4, and CDK6. Direct or indirect deregulation of CDK activity is a feature of almost all cancers and has led to the development of CDK inhibitors as anticancer agents. BS-181 is a highly selective CDK7 inhibitor with IC50 of 21 nM. ; >40-fold selective for CDK7 than CDK1, 2, 4, 5, 6, or 9.

In vitro: BS-181, inhibited CAK activity with an IC50 of 21 nmol/L. Testing of other CDKs as well as another 69 kinases showed that BS-181 only inhibited CDK2 at concentrations lower than 1 μ mol/L, with CDK2 being inhibited 35-fold less potently (IC50 880 nmol/L) than CDK7. In MCF-7 cells, BS-181 inhibited the phosphorylation of CDK7 substrates, promoted cell cycle arrest and apoptosis to inhibit the growth of cancer cell lines [1].

In vivo: BS-181 was stable in vivo with a plasma elimination half-life in mice of 405 minutes after i.p. administration of 10 mg/kg. The same dose of drug inhibited the growth of MCF-7 human xenografts in nude mice. BS-181 therefore provides the first example of a potent and selective CDK7 inhibitor with potential as an anticancer agent [1].

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Clinical trial: BS-181 is currently in the preclinical development and non clinical trial is ongoing.

Reference:

[1] Ali S, Heathcote DA, Kroll SH, Jogalekar AS, Scheiper B, Patel H, Brackow J, Siwicka A, Fuchter MJ, Periyasamy M, Tolhurst RS, Kanneganti SK, Snyder JP, Liotta DC, Aboagye EO, Barrett AG, Coombes RC. The development of a selective cyclin-dependent kinase inhibitor that shows antitumor activity. Cancer Res. 2009;69(15):6208-15.

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