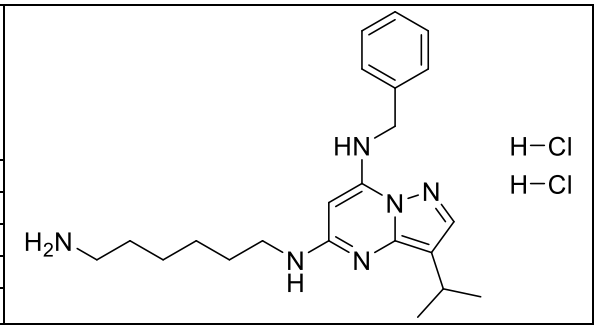
Product data sheet

MedKoo Cat#: 406179 Name: BS-181 HCl CAS#: 1883548-83-1 (2HCl) Chemical Formula: $C_{22}H_{34}Cl_2N_6$ Molecular Weight: 453.46	
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:
BS-181 is a highly selective CDK inhibitor for CDK7 with an IC(50) 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 micromol/L, with CDK2 being inhibited 35-fold less potently (IC(50) 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, and showed antitumor effects in vivo.

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	45.34	100.0
H2O	45.34	100.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.21 mL	11.03 mL	22.05 mL
5 mM	0.44 mL	2.21 mL	4.41 mL
10 mM	0.22 mL	1.10 mL	2.21 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Wang BY, Liu QY, Cao J, Chen JW, Liu ZS. Selective CDK7 inhibition with BS-181 suppresses cell proliferation and induces cell cycle arrest and apoptosis in gastric cancer. Drug Des Devel Ther. 2016 Mar 16;10:1181-9. doi: 10.2147/DDDT.S86317. PMID: 27042010; PMCID: PMC4801149.
2. Park SY, Kim KY, Jun DY, Hwang SK, Kim YH. G1 Cell Cycle Arrest and Extrinsic Apoptotic Mechanisms Underlying the Anti-Leukemic Activity of CDK7 Inhibitor BS-181. Cancers (Basel). 2020 Dec 19;12(12):3845. doi: 10.3390/cancers12123845. PMID: 33352782; PMCID: PMC7766600.

In vivo study

1. Wang BY, Liu QY, Cao J, Chen JW, Liu ZS. Selective CDK7 inhibition with BS-181 suppresses cell proliferation and induces cell cycle arrest and apoptosis in gastric cancer. Drug Des Devel Ther. 2016 Mar 16;10:1181-9. doi: 10.2147/DDDT.S86317. PMID: 27042010; PMCID: PMC4801149.
2. 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 Aug 1;69(15):6208-15. doi: 10.1158/0008-5472.CAN-09-0301. Epub 2009 Jul 28. PMID: 19638587; PMCID: PMC2875168.

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7. Bioactivity

Biological target:

BS-181 dihydrochloride is a potent and selective CDK7 inhibitor (IC50=21 nM) with activity against CDK2, CDK5 and CDK9 with IC50 values of 880 nM, 3000 nM and 4200 nM, respectively.

In vitro activity

Cell apoptosis was determined using flow cytometry. Significant increases in apoptotic cells were observed in BS-181-treated BGC823 cells compared to control ($P<0.05$, respectively; Figure 2A). Our results also showed that BS-181-induced cell apoptosis in a dose- and time-dependent manner. Additionally, caspase-3 and Bax expressions have been significantly increased, while Bcl-2 level has been reduced in cells treated with BS-181 compared to control ($P<0.05$, respectively) (Figure 2B). These results indicated that BS-181 could induce apoptosis in GC cells. Furthermore, the inhibition of CDK7 activity led to a significant reduction of key antiapoptotic protein XIAP and cell cycle regulator cyclin D1 ($P<0.05$) (Figure 2C). Thus, BS-181 may regulate cell apoptosis and cell cycle progression via downregulating XIAP and cyclin expression in BGC823 cells. In the present study, cell cycle distribution was analyzed by flow cytometry (Figure 3). Treatment of BS-181 showed an increase in cells in G0/G1, accompanied by a reduction of cell population in S and G2/M phases. These results indicated that BS-181-induced cell cycle arrest in the G0/G1 phase and delayed the progression of the cell cycle

Drug Des Devel Ther. 2016; 10: 1181–1189. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4801149/

In vivo activity

In this study, mice received intraperitoneal injection of BS-181 twice daily with 5 mg/kg/d or 10 mg/kg/d to give daily doses of 10 mg/kg or 20 mg/kg, over a period of 2 weeks. In addition, another group of 15 rats received roscovitine (20 mg/kg/d) injection for a total of 14 days. We observed that tumor growth was significantly inhibited by BS-181 in a dose-dependent manner compared to the control group ($P<0.05$, respectively) (Figure 5A). However, there was no significant difference in mice body weights between groups during a 14-day observation (Figure 5B). This indicated that there was no apparent toxicity at a daily dose of 10 mg/kg or 20 mg/kg. In addition, all animals were kept for another 30 days for survival observation. As seen in Figure 5C, eight of ten mice (80%) died in the control group, five of ten (50%) died in the roscovitine group, while six of ten (60%, 10 mg/kg/d) and three of ten (30%, 20 mg/kg/d) mice died in BS-181-treated groups. The overall difference in survival rate between rats treated with or without BS-181 was significant ($P<0.05$, respectively). Therefore, BS-181 provides potent and selective CDK7 inhibitor with the potential as an antigastric cancer agent.

Drug Des Devel Ther. 2016; 10: 1181–1189. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4801149/