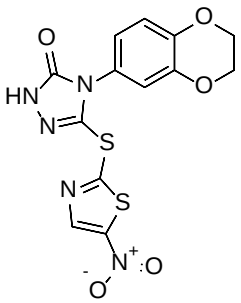
Product data sheet

MedKoo Cat#: 530628 Name: BI-78D3 CAS#: 883065-90-5 Chemical Formula: $C_{13}H_9N_5O_5S_2$ Exact Mass: 379.0045 Molecular Weight: 379.37	
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:
BI-78D3, also known as JNK Inhibitor X, is a potent JNK inhibitor. BI-78D3 dose-dependently inhibits the phosphorylation of JNK substrates both in vitro and in cell. BI-78D3 not only blocks JNK dependent Con A-induced liver damage but also restores insulin sensitivity in mouse models of type 2 diabetes.

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
DMF	33.0	86.99
DMSO	67.74	178.56
DMSO:PBS (pH 7.2) (1:1)	0.50	177.93
Ethanol	1.40	3.69

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.64 mL	13.18 mL	26.36 mL
5 mM	0.53 mL	2.64 mL	5.27 mL
10 mM	0.26 mL	1.32 mL	2.64 mL
50 mM	0.05 mL	0.26 mL	0.53 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. Kaoud TS, Johnson WH, Ebelt ND, Piserchio A, Zamora-Olivares D, Van Ravenstein SX, Pridgen JR, Edupuganti R, Sammons R, Cano M, Warthaka M, Harger M, Tavares CDJ, Park J, Radwan MF, Ren P, Anslyn EV, Tsai KY, Ghose R, Dalby KN. Modulating multi-functional ERK complexes by covalent targeting of a recruitment site in vivo. Nat Commun. 2019 Nov 19;10(1):5232. doi: 10.1038/s41467-019-12996-8. PMID: 31745079; PMCID: PMC6863825.

In vivo study

1. Kaoud TS, Johnson WH, Ebelt ND, Piserchio A, Zamora-Olivares D, Van Ravenstein SX, Pridgen JR, Edupuganti R, Sammons R, Cano M, Warthaka M, Harger M, Tavares CDJ, Park J, Radwan MF, Ren P, Anslyn EV, Tsai KY, Ghose R, Dalby KN. Modulating multi-functional ERK complexes by covalent targeting of a recruitment site in vivo. Nat Commun. 2019 Nov 19;10(1):5232. doi: 10.1038/s41467-019-12996-8. PMID: 31745079; PMCID: PMC6863825.

7. Bioactivity
Biological target:

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BI-78D3 inhibits the JNK kinase activity with an IC50 of 280 nM.

In vitro activity

As the ERK pathway regulates cell survival and proliferation1, the proliferation potential of cells following incubation with BI-78D3, with drug washout, was evaluated by monitoring their approach to confluence. Dose-dependent suppression of cell growth (IC50 ~ 3.5 μM) was noted when measured over 90 h (Fig. 4d). A similar treatment abrogated the formation of anchorage-dependent and anchorage-independent colonies (Fig. 4e). Cell cycle analysis revealed that treatment with BI-78D3 (6 μM), followed by washout for 24 and 48 h induced G1 arrest (Supplementary Fig. 17). Annexin V (Fig. 4f) and caspase3/7 assays (Fig. 4g) revealed significant dose-dependent induction of apoptosis 72 h after treatment, which is also evidenced by a significant induction of a sub-G1 population (Supplementary Fig. 18). Similar results were observed when BI-78D3 was not washed out.

Reference: Nat Commun. 2019 Nov 19;10(1):5232. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6863825/

In vivo activity

The effect of BI-78D3 on the growth of a BRAF-mutant xenograft model established from the human melanoma cell line A375 was evaluated. Inbred, athymic nude mice were injected with 1 × 106 A375 cells into the right flank. When tumors reached an average volume of 150 mm3, mice were randomized into two groups of ten mice each. One group was treated daily with an intraperitoneal injection of vehicle (2.5% ethanol, 5% Tween-80, 1× PBS), and the other group with 15 mg kg−1 BI-78D3 suspended in the vehicle. Tumor volumes were measured daily until tumors reached a maximum diameter of 1 cm. The tumor measurements of these mice were analyzed for tumor growth comparison (Fig. 5a) where BI-78D3 (15 mg kg−1 daily) caused potent tumor growth suppression after 10 days of treatment. BI-78D3 was tolerated by the mice, as measured by morbidity, lethality, and loss in body weight (Supplementary Fig. 23).

Reference: Nat Commun. 2019 Nov 19;10(1):5232. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6863825/