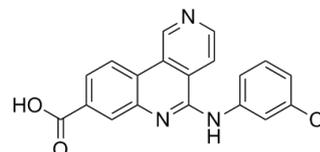


Data Sheet

Product Name:	CX-4945
Cat. No.:	HY-50855
CAS No.:	1009820-21-6
Molecular Formula:	C ₁₉ H ₁₂ CIN ₃ O ₂
Molecular Weight:	349.77
Target:	Autophagy; Casein Kinase
Pathway:	Autophagy; Cell Cycle/DNA Damage; Stem Cell/Wnt
Solubility:	DMSO: ≥ 35 mg/mL



BIOLOGICAL ACTIVITY:

CX-4945 is an orally bioavailable, highly selective and potent **CK2** inhibitor, with **IC₅₀** values of 1 nM against CK2 α and CK2 α' .

IC₅₀ & Target: IC₅₀: 1 nM (CK2 α), 1 nM (CK2 α')

In Vitro: CX-4945 causes cell-cycle arrest and selectively induced apoptosis in cancer cells relative to normal cells, attenuates PI3K/Akt signaling, and the antiproliferative activity of CX-4945 is correlated with expression levels of the CK2 α catalytic subunit, Attenuation of PI3K/Akt signaling^[1]. CX-4945 with bortezomib treatment prevents leukemic cells from engaging a functional UPR in order to buffer the bortezomib-mediated proteotoxic stress in ER lumen, and decreases pro-survival ER chaperon BIP/Grp78 expression^[2]. CX-4945 induces cytotoxicity and apoptosis, and exerts anti-proliferative effects in hematological tumors by downregulating CK2 expression and suppressing activation of CK2-mediated PI3K/Akt/mTOR signaling pathways^[3].

In Vivo: CX-4945 (25 or 75 mg/kg, p.o.) is well tolerated and demonstrated robust antitumor activity with concomitant reductions of the mechanism-based biomarker phospho-p21 (T145) in murine xenograft models^[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: ^[1]The percent inhibition of each kinase is estimated using 0.5 μ M CX-4945 at ATP concentrations equivalent to the K_m value for ATP for each respective human recombinant kinase. The determination of IC₅₀ values is done at ATP concentrations equivalent to the K_m for ATP for each kinase using 9 concentrations of CX-4945 over a range of 0.0001 to 1 μ M. The K_i value (inhibition constant) for CX-4945 against recombinant CK2 is determined by graphing the IC₅₀ values of CX-4945 determined in the presence of various concentrations of ATP against the concentration of ATP.

Cell Assay: CX-4945 is dissolved in DMSO at a concentration of 5 mM.^[1] Various cell lines are seeded at a density of 3,000 cells per well 24 hours prior to treatment, in appropriate media, and then treated with indicated concentrations of CX-4945. Suspensions cells are seeded and treated on the same day. Following 4 days of incubation, Alamar Blue (20 μ L, 10% of volume per well) is added and the cells are further incubated at 37°C for 4–5 hours. Fluorescence with excitation wavelength at 530–560 nm and emission wavelength at 590 nm is measured.

Animal Administration: ^[1]Xenografts are initiated by subcutaneous injection of BxPC-3 cells into the right hind flank region of each mouse or BT-474 cells are injected into the mammary fat pad of mice implanted with estrogen pellets. When tumors reach a designated volume of 150–200 mm³, animals are randomized and divided into groups of 9 to 10 mice per group. CX-4945 is administered by oral gavage twice daily at 25 or 75 mg/kg for 31 and 35 consecutive days for the BT-474 and BxPC-3 models, respectively. Tumor volumes and body weights are measured twice weekly. The length and width of the tumor are measured with calipers and the volume calculated using the following formula: tumor volume=(length \times width²)/2.

References:

- [1]. Siddiqui-Jain A, et al. CX-4945, an orally bioavailable selective inhibitor of protein kinase CK2, inhibits prosurvival and angiogenic signaling and exhibits antitumor efficacy. *Cancer Res.* 2010 Dec 15;70(24):10288–98.
- [2]. Buontempo F, et al. Synergistic cytotoxic effects of bortezomib and CK2 inhibitor CX-4945 in acute lymphoblastic leukemia: turning off the prosurvival ER chaperone BIP/Grp78 and turning on the pro-apoptotic NF- κ B. *Oncotarget.* 2016 Jan 12;7(2):1323–40.
- [3]. Chon HJ, et al. The casein kinase 2 inhibitor, CX-4945, as an anti-cancer drug in treatment of human hematological malignancies. *Front Pharmacol.* 2015 Mar 31;6:70.

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

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