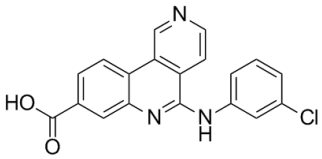
Data Sheet

Product Name:	CX–4945
Cat. No.:	HY-50855
CAS No.:	1009820-21-6
Molecular Formula:	C19H12ClN3O2
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 **IC_{50}** values of 1 nM against CK2α and CK2α'.
IC50 & Target: IC50: 1 nM (CK2α), 1 nM (CK2α')
In Vitro: CX–4945 causes cell–cycle arrest and selectively induced apoptosis in cancer cells relative to normal cells, attenuates PI3K/Akt signalingand, and the antiproliferative activity of CX–4945 is correlated with expression levels of the CK2α 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 μM CX–4945 at ATP concentrations equivalent to the K_m value for ATP for each respective human recombinant kinase. The determination of IC_{50} 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 μM. The K_i value (inhibition constant) for CX–4945 against recombinant CK2 is determined by graphing the IC_{50} 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 μL, 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 mm^3, 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 × $width^2$)/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–κB. 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.

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