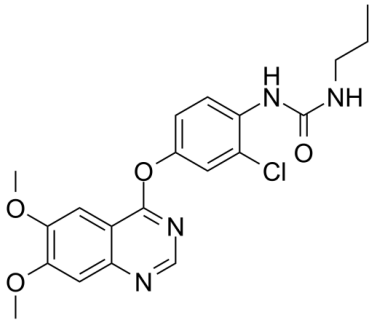
Data Sheet

Product Name:	KRN-633
Cat. No.:	CS-0220
CAS No.:	286370-15-8
Molecular Formula:	C20H21ClN4O4
Molecular Weight:	416.86
Target:	VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 8 mg/mL (19.19 mM)



BIOLOGICAL ACTIVITY:

KRN-633 is a potent **VEGFR** inhibitor with **IC_{50}**s of 170, 160 and 125 nM for VEGFR1, VEGFR2 and VEGFR3, respectively. IC50 & Target: IC50: 170 nM (VEGFR1), 160 nM (VEGFR2), 125 nM (VEGFR3)[1] **In Vitro:** KRN-633 inhibits tyrosine phosphorylation of VEGFR-1, VEGFR2, c-Kit, and PDGFR-β (IC_{50}=11.7, 1.16, 8.01, 130 nM) in human umbilical vein endothelial cells. KRN-633 also inhibits the VEGF-driven proliferation of HUVECs (IC_{50}=14.9 nM). KRN-633 suppresses capillary tube formation of endothelial cells[1]. **In Vivo:** KRN-633 inhibits tumor growth in several tumor xenograft models with diverse tissue origins, including lung, colon, and prostate, in athymic mice and rats. KRN-633 also causes the regression of some well-established tumors and those that have regrown after the cessation of treatment. KRN-633 is well tolerated and has no significant effects on body weight or the general health of the animals. Histologic analysis of tumor xenografts treated with KRN-633 reveals a reduction in the number of endothelial cells in non-necrotic areas and a decrease in vascular permeability[1].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Cell-free kinase assays are done to obtain IC_{50} values against a variety of recombinant receptor and non-RTKs. KRN-633 is tested from 0.3 nM to 10 μM. All assays are done in quadruplicate with 1 μM ATP[1]. **Cell Assay:** KRN-633 is prepared in 0.1% DMSO in medium[1].[1]A549, Ls174T, HT29, DU145, LNCap, and PC-3 cells cancer cells are cultured for 24 hours before adding KRN-633 (0.01 to 10 μM) or vehicle (0.1% DMSO in medium) and then grow for a further 96 hours. Cell viability is measured using WST-1 reagent. The percentage viability is determined relative to the untreated control[1]. **Animal Administration:** [1]Rat: Human tumor xenografts are established in the hind flank of athymic rats (BALB/cA, Jcl-nu). Rats are randomized into groups of five at the point when the tumors reach the average size indicated (162 to 657 mm^3) and are then treated with KRN-633 or vehicle, either once (qd) or twice (bid) per day, at the dosages shown. The percentage of tumor growth inhibition compared with the vehicle-treated group is calculated on the day after the last treatment (day 14)[1].

Mouse: The mice are randomized into groups of five at the point when the tumors reached the average sizes: 103 to 260 mm^3 or 500 to 667 mm^3. They are then treated with KRN-633 or vehicle, either once (qd) or twice (bid) per day, at the dosages of 10-100 mg/kg. The percentage of tumor growth inhibition (TGI) compared with the vehicle-treated group is calculated on the day after the last treatment[1].

References:

[1]. Nakamura K, et al. KRN633: A selective inhibitor of vascular endothelial growth factor receptor-2 tyrosine kinase that suppresses tumor angiogenesis and growth. Mol Cancer Ther. 2004 Dec;3(12):1639-49.

CAIndexNames:

Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-propyl-

SMILES:

ClC1=CC(OC2=NC=NC3=CC(OC)=C(C=C32)OC)=CC=C1NC(NCCC)=O

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