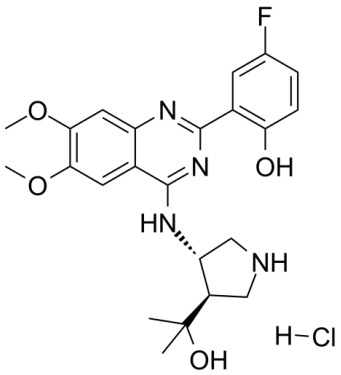
Data Sheet

Product Name:	CCT241533 (hydrochloride)
Cat. No.:	CS-1137
CAS No.:	1431697-96-9
Molecular Formula:	$C_{23}H_{28}ClFN_4O_4$
Molecular Weight:	478.9442232
Target:	Checkpoint Kinase (Chk)
Pathway:	Cell Cycle/DNA Damage
Solubility:	H2O : 33.33 mg/mL (69.59 mM; Need ultrasonic); DMSO : ≥ 100 mg/mL (208.79 mM)



BIOLOGICAL ACTIVITY:

CCT241533 hydrochloride is a potent and selective **CHK2** inhibitor with an **IC_{50}** of 3 nM and a **K_i** of 1.16 nM[1]. IC50 & Target: IC50: 3 nM (CHK2), 245 nM (CHK1)[1]

Ki: 1.16 nM (CHK2)[1] **In Vitro:** CCT241533 hydrochloride inhibits CHK2 with an IC_{50} of 3 nM and shows minimal cross reactivity against a panel of kinases at 1 μM. X-ray crystallography confirms that CCT241533 binds to CHK2 in the ATP pocket. CCT241533 blocks CHK2 activity in human tumor cell lines in response to DNA damage, as demonstrated by inhibition of CHK2 autophosphorylation at S516, band-shift mobility changes and HDMX degradation. CCT241533 does not potentiate the cytotoxicity of a selection of genotoxic agents in several cell lines. However, CCT241533 significantly potentiates the cytotoxicity of two structurally distinct PARP inhibitors. Clear induction of the pS516 CHK2 signal is seen with a PARP inhibitor alone and this activation is abolished by CCT241533. The cytotoxicity of CCT241533 in HT-29, HeLa and MCF-7, measured as the growth inhibitory IC_{50}(GI_{50}) by SRB assay, is 1.7, 2.2 and 5.1 μM, respectively[1]. CCT241533 hydrochloride is a potent CHK2 inhibitor (IC_{50}=3 nM), with selectivity (63-fold) over CHK1(IC_{50}=190 nM) and low hERG inhibition (IC_{50}=22 μM)[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: CCT241533 is dissolved in DMSO and stored, and then diluted with appropriate media before use[1].[1]HT-29, HeLa and MCF-7 cells are exposed to a fixed concentration (GI_{50}) of CCT241533 in combination with increasing concentrations of either PARP inhibitor or cytotoxic drug in a 96 hour SRB assay or 7-10 day colony forming assay. The ability of CCT241533 to enhance cell killing is expressed as a potentiation index (PI) which is the ratio of GI_{50} for the genotoxic or PARP inhibitor alone: GI_{50} for the genotoxic or PARP inhibitor in combination with a CHK2 inhibitor. Thus PI>1 indicates potentiation and PI<1 indicates protection[1].

References:

[1]. Anderson VE, et al. CCT241533 is a potent and selective inhibitor of CHK2 that potentiates the cytotoxicity of PARP inhibitors. Cancer Res. 2011 Jan 15;71(2):463-72.

[2]. Caldwell JJ, et al. Structure-based design of potent and selective 2-(quinazolin-2-yl)phenol inhibitors of checkpoint kinase 2. J Med Chem. 2011 Jan 27;54(2):580-90.

CAIndexNames:

4-fluoro-2-(4-(((3S,4R)-4-(2-hydroxypropan-2-yl)pyrrolidin-3-yl)amino)-6,7-dimethoxyquinazolin-2-yl)phenol hydrochloride

SMILES:

[H]Cl.COC1=C(OC)C=C(C(N[C@H]2[C@H](C(C)(C)O)CNC2)=NC(C3=C(O)C=CC(F)=C3)=N4)C4=C1

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

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