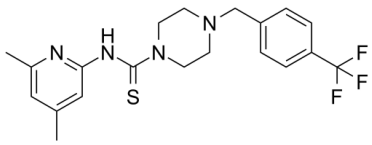
Data Sheet

Product Name:	NCT-503
Cat. No.:	CS-6987
CAS No.:	1916571-90-8
Molecular Formula:	C20H23F3N4S
Molecular Weight:	408.48
Target:	Others
Pathway:	Others
Solubility:	DMSO : 50 mg/mL (122.41 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

NCT-503 is a phosphoglycerate dehydrogenase (**PHGDH**) inhibitor with an **IC_{50}** of 2.5 μM. IC50 & Target: IC50: 2.5 μM (PHGDH)[1] **In Vitro:** Human phosphoglycerate dehydrogenase (PHGDH) catalyzes the first, rate-limiting step in the canonical glucose-derived serine synthesis pathway. NCT-503, a PHGDH inhibitor, inhibits serine synthesis from 3-phosphoglycerate in cells (IC_{50}=2.5 μM). NCT-503 is inactive against a panel of other dehydrogenases and shows minimal cross-reactivity in a panel of 168 GPCRs. Competition studies of NCT-503 against 3-phosphoglycerate (3-PG) and the co-substrate NAD^+ reveal a non-competitive mode of inhibition with respect to both 3-PG and NAD^+. NCT-503 has EC_{50}s of 8–16 μM for the PHGDH-dependent cell lines, a 6- to 10-fold higher EC_{50} for MDA-MB-231 cells, and no toxicity towards other PHGDH-independent cell lines[1]. **In Vivo:** NCT-503 exhibits favorable absorption, distribution, metabolism and excretion (ADME) properties. NCT-503 has good exposure, half-life (2.5 hr) and C_{max} (20 μM in plasma) following intraperitoneal administration with significant partitioning into the liver and brain. NCT-503 treatment reduces the growth and weight of PHGDH-dependent MDA-MB-468 xenografts but does not affect the growth or weight of PHGDH-independent MDA-MB-231 xenografts[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: NCT-503 is prepared in DMSO.[1]MDA-MB-468, BT-20, MT-3 cells are seeded in white 96-well plates allowed to attach for 24 hours. Cells are treated with NCT-503 for four days. Cell viability is assessed with Cell Titer-Glo and luminescence measured with a plate reader[1]. **Animal Administration:** NCT-503 is prepared in a vehicle of 5% ethanol, 35% PEG 300, and 60% of an aqueous 30% hydroxypropyl-β-cyclodextrin. [1]Mouse: Chronic catheters are surgically implanted into the jugular veins of normal or tumor bearing animals 3–4 days prior to infusions. Following administration of either vehicle or NCT-503 at 30 mg/kg, a constant infusion of U-^{13}C-glucose (30 mg/kg/min) is administered for a 3-hour duration. Animals are terminally anesthetized with sodium pentobarbital and all tissues are fully harvested in less than 5 minutes to preserve the metabolic state. Tumors and adjacent lung tissue are carefully dissected and rapidly frozen for analysis[1].

References:

[1]. Pacold ME, et al. A PHGDH inhibitor reveals coordination of serine synthesis and one-carbon unit fate. Nat Chem Biol. 2016 Jun;12(6):452-8.

CAIndexNames:

1-Piperazinecarbothioamide, N-(4,6-dimethyl-2-pyridinyl)-4-[[4-(trifluoromethyl)phenyl]methyl]-

SMILES:

S=C(N1CCN(CC2=CC=C(C(F)(F)F)C=C2)CC1)NC3=NC(C)=CC(C)=C3

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

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