CGP77675 hydrate

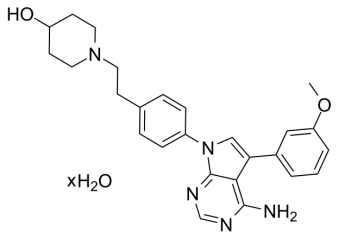
Cat. No.: HY-W062835A

Molecular Formula: $C_{26}H_{29}N_5O_2.xH_2O$

Target: Src

Pathway: Protein Tyrosine Kinase/RTK

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CGP77675 hydrate is an orally active and potent inhibitor of Src family kinases. CGP77675 hydrate inhibits phosphorylation of peptide substrates and autophosphorylation of purified Src (IC_{50}s of 5-20 and 40 nM, respectively),and also inhibits Src, EGFR, KDR, v-Abl, and Lck with IC_{50}s of 0.02, 0.15, 1.0, 0.31, and 0.29 μM, respectively. Anticancer activity[1].

IC_{50} & Target

IC50: 0.02 μM (Src), 0.15 μM (EGFR), 1.0 μM (KDR), 0.31 μM (v-Abl), 0.29 μM (Lck)[1]

In Vitro

CGP77675 hydrate dose dependently inhibits phosphorylation of poly-Glu-Tyr with an IC_{50} value of 5.5 nM, and of the optimal Src substrate (OSS) peptide with an IC_{50} value of 16.7 nM. These IC_{50} values are similar to the value obtained with chicken Src (20 nM)[1].

CGP77675 hydrate inhibits the parathyroid hormone-induced bone resorption in rat fetal long bone cultures with an IC_{50} of 0.8 μM[1].

CGP77675 hydrate (0.04-10 μM; 2 hours) potently inhibits tyrosine phosphorylation of the Src substrates Fak and paxillin, but has much less effect on Src (IC_{50} values 0.2, 0.5, and 5.7μM) in IC8.1 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MC3T3-E1 cells
Concentration:	0.2, 1, and 5 μM
Incubation Time:	3 days
Result:	Did not influence cell viability for up to 3 days of treatment.

Western Blot Analysis[1]

Cell Line:	Src-overexpressing IC8.1 cells
Concentration:	0.04, 0.2, 1, 5, and 10 μM
Incubation Time:	2 hours
Result:	Dose dependently inhibited phosphorylation of Fak and paxillin, but not of Src.

In Vivo

CGP77675 hydrate (1, 5, and 25 mg/kg; injected s.c.; twice a day) inhibits IL-1β-induced hypercalcemia in Mice[1].

CGP77675 hydrate (10 and 50 mg/kg; administered orally; twice a day for 6 weeks) partially prevents bone loss and rescues bone microarchitectural features in young ovx rats[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male mice (Tif:MAGf; Novartis Animal Farm) of 25-30 g body[1]
Dosage:	1, 5, and 25 mg/kg
Administration:	Injected s.c.; twice a day
Result:	Prevented IL-1β-induced hypercalcemia in mice without affecting serum amyloid protein levels.

Animal Model:	Eight-week-old (175-209 g) female rats of the Sprague-Dawley-derived strain Tif:RAlf[1]
Dosage:	10 and 50 mg/kg
Administration:	Administered orally; twice a day for 6 weeks
Result:	Partly prevented bone loss.

REFERENCES

[1]. Missbach M, et al. A novel inhibitor of the tyrosine kinase Src suppresses phosphorylation of its major cellularsubstrates and reduces bone resorption in vitro and in rodent models in vivo. Bone. 1999 May;24(5):437-49.

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