Chloropyramine hydrochloride

Cat. No.: HY-B1305

CAS No.: 6170-42-9

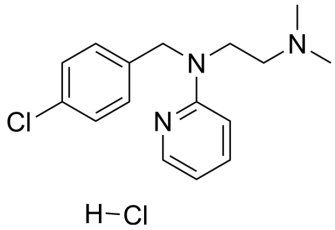
Molecular Formula: $C_{16}H_{21}Cl_2N_3$

Molecular Weight: 326.26

Target: FAK; Histamine Receptor; VEGFR

Pathway: Protein Tyrosine Kinase/RTK; GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (306.50 mM; Need ultrasonic)
DMSO : 30 mg/mL (91.95 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0650 mL	15.3252 mL	30.6504 mL
	5 mM	0.6130 mL	3.0650 mL	6.1301 mL
	10 mM	0.3065 mL	1.5325 mL	3.0650 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (153.25 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description Chloropyramine hydrochloride is a histamine receptor H1 antagonist which can also inhibit the biochemical function of VEGFR-3 and FAK.

IC_{50} & Target	H_1 Receptor	VEGFR-3

In Vitro	BT474 cells are highly sensitive to Chloropyramine hydrochloride (compound 1) treatment, whereby 1 μM concentrations cause a 40% reduction of viability after 48 h of treatment. It is found that at 1 μM concentrations of Chloropyramine hydrochloride, viability of control MCF7-pcDNA3 cells is significantly higher than the viability of MCF7-VEGFR-3 cells ($P<0.01$) and at 10 μM concentration this difference reaches twofold ($P<0.001$). In the BT474 cells treatment with Chloropyramine hydrochloride also leads to a concentration-dependent decrease of cell proliferation. When treatment with Chloropyramine hydrochloride is continued for 48 h, the breast cancer cells that overexpressed VEGFR-3 undergo apoptosis. This effect is dose-dependent, with 10 μM Chloropyramine hydrochloride inducing apoptosis in more than 60% of BT474 cells. In our model cell lines MCF7-pcDNA3 and MCF7-VEGFR-3, treatment with 10 μM Chloropyramine hydrochloride for 48 h leads to a 4-fold increase in apoptotic cell death in the cell line that overexpressed VEGFR-3 (18% versus 76 % respectively)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Chloropyramine hydrochloride causes a dramatic reduction of tumor growth in both model systems whereby the tumor size in the treated groups is approximately 20% of the tumor size in vehicle control groups. Doxorubicin administered at 3 mg/kg causes approximately 60% reduction of tumor growth, but has no effect on tumor growth at 0, 3 mg/kg. In contrast, there is a modest effect of Chloropyramine hydrochloride alone (50% reduction of tumor growth). The low-dose combination of Chloropyramine hydrochloride and doxorubicin has a prolonged anti-tumor effect (85% reduction of tumor growth) that is greater than either drug alone[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Cells are incubated in presence or absence of Chloropyramine hydrochloride and stained with anti-FAK antibody 4.47 or in combination with paxillin or VEGFR-3. Detection is done with Alexa Fluor 546 secondary antibody and for dual staining combination of Alexa Fluor 488 and Alexa Fluor 546 secondary antibody is used[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cell survival is assayed in MTS assay by measuring mitochondrial dehydrogenase activity of metabolically active cells. 5.0×10^3 (100 μL) cells are plated in 96-well plates and are allowed to attach overnight. One hundred microliters of fresh media with or without Chloropyramine hydrochloride is added to each well. Cells are treated for designated amount of time. MTS assay is performed according the manufacturers protocol[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	BT474 and MCF7-VEGFR-3 cells at a concentration of 2 to 5×10^6 cells per 200 μL are subcutaneously injected into the right flank of the 5 to 6 week old mice, 5 in each group. Treatment with Chloropyramine hydrochloride is started next day after cells injection via intraperitoneal injection (IP) once a day. Tumor size is measured thrice weekly and volume is calculated using the formula length×width$^2\times0.5$. Animals are sacrificed after 21 days of treatment or when tumor size reaches protocol end point. Tumor is excised, measured and preserved for protein and RNA preparation and cytochemistry[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kurenova EV, et al. Small molecule chloropyramine hydrochloride (C4) targets the binding site of focal adhesion kinase and vascular endothelial growth factor receptor 3 and suppresses breast cancer growth in vivo. J Med Chem. 2009 Aug 13;52(15):4716-24.

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

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