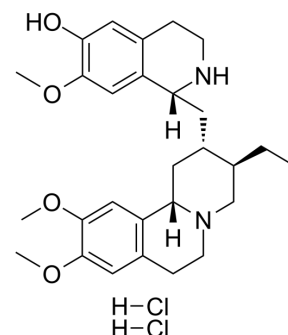


Cephaeline dihydrochloride

Cat. No.:	HY-N2260
CAS No.:	5853-29-2
Molecular Formula:	C ₂₈ H ₄₀ Cl ₂ N ₂ O ₄
Molecular Weight:	539.53
Target:	Cytochrome P450
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro	DMSO : 250 mg/mL (463.37 mM; Need ultrasonic)																			
	H ₂ O : 250 mg/mL (463.37 mM; Need ultrasonic)																			
	<table border="1"> <thead> <tr> <th rowspan="2">Solvent Concentration</th> <th colspan="3">Mass</th> </tr> <tr> <th>1 mg</th> <th>5 mg</th> <th>10 mg</th> </tr> </thead> <tbody> <tr> <td>1 mM</td> <td>1.8535 mL</td> <td>9.2673 mL</td> <td>18.5346 mL</td> </tr> <tr> <td>5 mM</td> <td>0.3707 mL</td> <td>1.8535 mL</td> <td>3.7069 mL</td> </tr> <tr> <td>10 mM</td> <td>0.1853 mL</td> <td>0.9267 mL</td> <td>1.8535 mL</td> </tr> </tbody> </table>	Solvent Concentration	Mass			1 mg	5 mg	10 mg	1 mM	1.8535 mL	9.2673 mL	18.5346 mL	5 mM	0.3707 mL	1.8535 mL	3.7069 mL	10 mM	0.1853 mL	0.9267 mL	1.8535 mL
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Please refer to the solubility information to select the appropriate solvent.																				
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (3.86 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (3.86 mM); Clear solution 																			

BIOLOGICAL ACTIVITY

Description	Cephaeline dihydrochloride is a selective CYP2D6 inhibitor with an IC ₅₀ of 121 μM.
IC₅₀ & Target	IC ₅₀ : 121 μM (CYP2D6) ^[1] Ki: 54 μM (CYP2D6) ^[1]
In Vitro	CYP2D6 reveals the highest metabolic activity for the generation of 9-O-demethylEmetine, whereas this enzyme also shows a significant metabolic activity for the generation of Cephaeline. The IC ₅₀ s of Cephaeline against CYP2C9, CYP2D6 and CYP3A4 is over 1000, 121 and 1000 μM, respectively. Further experiments are performed to determine inhibition constants (K _i) for Cephaeline on the CYP2D6 and CYP3A4 activities. Graphic analysis of Dixon plots at various Cephaeline concentrations for each of the two CYP enzyme assays yield K _i s of 54 and 355 μM for CYP2D6 and CYP3A4, respectively ^[1] .

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

PROTOCOL

Kinase Assay ^[1]

Cephaeline is dissolved in methanol to give concentrations of 0.1, 1, 10, 100 μM (only theophylline-O-demethylase activity with Cephaeline; 0.0985, June 2001 679 0.985, 9.85, 98.5 μM) ^[1].

Human liver microsomal protein is incubated with the selected marker substrates in the absence and presence of above concentrations of Cephaeline or Emetine (1-100 μM , only theophylline-O-demethylase activity with Cephaeline; 0.0985–98.5 μM , final concentration). Incubation conditions are chosen such that the product formation is linear with respect to both incubation times and protein concentrations, with substrate concentrations being at or below the K_m for each enzyme. The effects of furafylline, sulphaphenazole, tranlycypromine, quinidine, and ketoconazole, selective inhibitors of CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4, respectively, are also determined in the same microsomal samples to provide comparisons with inhibitory potentials (IC_{50}) of Cephaeline and Emetine towards the individual CYP form. The K_i s for Cephaeline and Emetine are determined by using the same pooled microsomal sample. This is achieved by varying the initial substrate concentrations (bufuralol 8, 16 and 32 μM ; testosterone 45, 90 and 180 μM) and using several inhibitor concentrations of 10, 50, and 100 μM . The K_i s are estimated by graphic analysis of Dixon plots. These values are subsequently used as initial estimates for the nonlinear least-squares regression analysis^[1].

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REFERENCES

[1]. Asano T, et al. Metabolism of ipecac alkaloids Cephaeline and Emetine by human hepatic microsomal cytochrome P450s, and their inhibitory effects on P450 enzyme activities. *Biol Pharm Bull.* 2001 Jun;24(6):678-82.

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

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