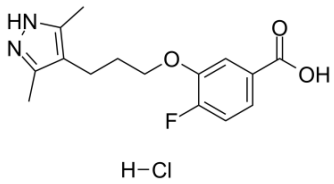
Acoramidis hydrochloride

Cat. No.:	HY-109165A
CAS No.:	2242751-53-5
Molecular Formula:	$C_{15}H_{18}ClFN_2O_3$
Molecular Weight:	328.77
Target:	Others
Pathway:	Others
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (190.10 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0416 mL	15.2082 mL	30.4164 mL
	5 mM	0.6083 mL	3.0416 mL	6.0833 mL
	10 mM	0.3042 mL	1.5208 mL	3.0416 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.33 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Acoramidis (AG10) hydrochloride is an orally active and selective kinetic stabilizer of WT and V122I-TTR (transthyretin). Acoramidis (AG10) hydrochloride is used in the study for transthyretin amyloidosis[1][2].

In Vitro

Acoramidis (AG10, 0.1-10 μM for TTR -5 μM) stabilizes V122I- and WT-TTR equally well and also exceeds their efficacy to stabilize WT and mutant TTR in whole serum[1].
Acoramidis (AG10) stimulates the mitochondrial QO2 in a concentration-dependent manner between 10 and 100 μM[3].
Acoramidis (AG10) has very minimal inhibition of two common off-targets in drug discovery, the potassium ion channel hERG (IC_{50} > 100 μM) and a number of cytochrome P450 isozymes (IC_{50} > 50 μM) (low toxicity)[1].

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

Western Blot Analysis[1].

Cell Line:	Human serum (TTR ⊠5 μM).
Concentration:	0.1 and 10 μM.
Incubation Time:	72 h.
Result:	Was significantly more effective than tafamidis in stabilizing TTR. The concentration of AG10 to 10 μM resulted in stabilization of almost all of TTR in serum.

REFERENCES

[1]. Sravan C Penchala, et al. AG10 inhibits amyloidogenesis and cellular toxicity of the familial amyloid cardiomyopathy-associated V122I transthyretin. Proc Natl Acad Sci U S A. 2013 Jun 11;110(24):9992-7.

[2]. Jonathan C Fox, et al. First-in-Human Study of AG10, a Novel, Oral, Specific, Selective, and Potent Transthyretin Stabilizer for the Treatment of Transthyretin Amyloidosis: A Phase 1 Safety, Tolerability, Pharmacokinetic, and Pharmacodynamic Study in Healthy Adult Volunteers. Clin Pharmacol Drug Dev. 2020 Jan;9(1):115-129.

[3]. Stephen P Soltoff, et al. Evidence that tyrphostins AG10 and AG18 are mitochondrial uncouplers that alter phosphorylation-dependent cell signaling. J Biol Chem. 2004 Mar 19;279(12):10910-8.

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