Elacridar

Cat. No.: HY-50879
CAS No.: 143664-11-3
Molecular Formula: C₃₄H₃₃N₃O₅
Molecular Weight: 563.64
Target: BCRP; P-glycoprotein
Pathway: Membrane Transporter/Ion Channel
Storage:
- Powder: -20°C 3 years, 4°C 2 years
- In solvent: -80°C 6 months, -20°C 1 month

Solvent & Solubility

In Vitro
DMSO: 12.5 mg/mL (22.18 mM; Need ultrasonic)
H₂O: < 0.1 mg/mL (insoluble)

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.22 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Elacridar is a potent P-glycoprotein (Pgp) and BCRP inhibitor.

IC₅₀ & Target
P-glycoprotein (Pgp), BCRP[1]

In Vitro
Elacridar inhibits P-glycoprotein (P-gp) labeling by [³H]azidopine with an IC₅₀ of 0.16 μM[2]. In Caki-1 and ACHN cells, elacridar (2.5 μM) significantly inhibits the cell growth. The P-glycoprotein activity is found to be inhibited by elacridar. The combination of elacridar and sunitinib lead to a significant reduction in ABC Sub-family B Member 2 (ABCG2) expression in 786-O cells[3].
In Vivo
Oral co-administration of elacridar (100 mg/kg, p.o.) and crizotinib increases the plasma and brain concentrations and brain-to-plasma ratios of crizotinib in wild-type mice, equaling the levels in Abcb1a/1b; Abcg2-/- mice. In Friend leukemia virus strain B mice, the brain-to-plasm partition coefficient (Kp, brain) of elacridar is 0.82, 0.43, and 4.31 after intravenous (2.5 mg/kg), intraperitoneal (100 mg/kg), and oral (100 mg/kg) treatment, respectively. In Mrp4(-/-) mice, elacridar fully inhibits P-gp mediated transport of topotecan, without significant effects on Bcrp1-mediated transport.

PROTOCOL

Kinase Assay
10 µL of unlabeled cell membrane suspension (at 0.4 mg of protein/mL) are aliquoted into each well in 96-well plates. 5 µL of GF120918 are then added to each well. The plate is incubated 25 min at 25°C in the dark. 5 µL of tritiated azidopine (1.8 TBq/mmol) (0.6 µM in HCl 0.2 mM) are added to each well. After 25 min of incubation at 25°C in the dark, samples are simultaneously irradiated for 2 min at 254 nm at 0°C with a thin layer chromatography-designed UV lamp directly in contact with the plate. Samples are solubilized in sodium dodecyl sulfate-polyacrylamide gel electrophoresis sample buffer but not heated. After separation on a 7.5% polyacrylamide gel, the gel is treated for fluorography with Amplify and exposed during 3 days onto a photosensitive film. The fluorography is analysed using a Camag thin layer chromatography Scanner II densitometer.

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

Cell Assay
3.0×10^3 cells per well are seeded in a 96-well plate. After 24 h incubation, an optimum concentration gradient of elacridar is added to each well. After culturing for 48 h, cell viability is assessed using the proliferation reagent, MTT. Control cells are treated with the vehicle only, 0.1% DMSO. After this final incubation, the medium is aspirated and precipitated formazan crystals are dissolved in DMSO (100 µL/well). The absorbance of each well is measured at 540 nm, and a reference wavelength of 650 nm is read with a multiskan JX microplate reader. Cell viability is calculated as percentage of the control value.

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Animal Administration
Mice are fasted for 3 hr before oral administration of either elacridar (100 mg/kg) or elacridar vehicle. Two hours later, crizotinib (5 mg/kg) is administered to mice orally. Blood and brains are isolated 4 hr after crizotinib oral administration, and processed as described above. The brain concentrations are corrected for the amount of drug in the brain vasculature. Elacridar hydrochloride is dissolved in dimethyl sulfoxide (106 mg/mL) in order to get 100 mg pure elacridar per 1 mL of dimethyl sulfoxide. The stock solution is further diluted with a mixture of Polysorbate 80, ethanol and water [20:13:67 (v/v/v)] to yield a concentration of 10 mg/mL pure elacridar.

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CUSTOMER VALIDATION

- EJNMMI Res. 2015 Mar 17;5:11.

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REFERENCES


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