PJ34 hydrochloride

Cat. No.: HY-13688

CAS No.: 344458-15-7

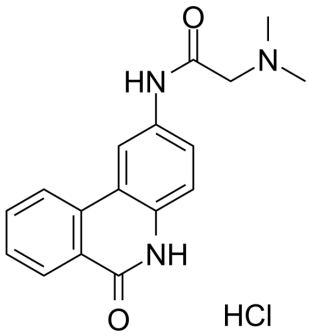
Molecular Formula: $C_{17}H_{18}ClN_3O_2$

Molecular Weight: 331.8

Target: PARP

Pathway: Cell Cycle/DNA Damage; Epigenetics

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



SOLVENT & SOLUBILITY

In Vitro

H_2O : 50 mg/mL (150.69 mM; Need ultrasonic)
DMSO : 10 mg/mL (30.14 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0139 mL	15.0693 mL	30.1386 mL
5 mM	0.6028 mL	3.0139 mL	6.0277 mL
10 mM	0.3014 mL	1.5069 mL	3.0139 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: ≥ 1 mg/mL (3.01 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (3.01 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (3.01 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PJ34 hydrochloride is an inhibitor of PARP1/2 with IC_{50} of 110 nM and 86 nM, respectively.

IC_{50} & Target

PARP	PARP-2	PARP-1
110 nM (IC_{50})	86 nM (IC_{50})	110 nM (IC_{50})

In Vitro

PJ34 inhibits the PARP enzyme activity with an IC_{50} of 110±1.9 nM. To compare the neuroprotective properties of other PARP inhibitors in PC12 cells, PJ34 is evaluated using by LDH assay. PJ34 treatment also significantly and concentration dependently attenuates cell death at a concentration ranging from 10^{-7} to 10^{-5} M[1].

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

In Vivo

To compare the potency and efficacy with other PARP inhibitors, PJ34 is evaluated at the doses of 3.2 and 10 mg/kg, respectively. PJ34 at the dose of 3.2 mg/kg significantly reduces cortical damage by 33%; however, 10 mg/kg dosing shows reversed effect (17% reduction)[1]. PJ34 (25 mg/kg) reduces the levels of TNF-α mRNA in ischemic animals by 70% and these values in treated mice do not differ from that of sham or naive animals. Treatment of ischemic mice with PJ34 reduces the level of E-selectin mRNA by 81% and that of ICAM-1 mRNA by 54%, compared to vehicle-treated ischemic mice[2].

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

PROTOCOL

Kinase Assay [1]

To assess the PARP-1 or PARP-2 inhibitory activity of FR247304, 3-AB, and PJ34, PARP activity is evaluated with minor modifications. PARP enzyme assay is carried out in a final volume of 100 µL consisting of 50 mM Tris-HCl (pH 8.0), 25 mM $MgCl_2$, 1 mM dithiothreitol, 10 µg activated salmon sperm DNA, 0.1 µCi of [adenylate-^{32}P]NAD, 0.2 units of recombinant human PARP for PARP-1 assay or 0.1 units of recombinant mouse PARP-2 for PARP-2 assay, and various concentrations of FR261529 or 3-AB. The reaction mixture is incubated at room temperature (23°C) for 15 min, and the reaction is terminated by adding 200 µL of ice-cold 20% trichloroacetic acid (TCA) and incubated at 4°C for 10 min. The precipitate is transferred onto GF/B filter and washed three times with 10% TCA solution and 70% ethanol. After the filter is dried, the radioactivity is determined by liquid scintillation counting.

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

Cell Assay [1]

PC12 cell cultured are grown in Dulbecco's modified Eagle's medium supplemented with 5% (v/v) fetal calf serum, 5% (v/v) horse serum, and a 1% (v/v) penicillin-streptomycin antibiotics mixture. Cells are grown in an atmosphere of 95% air and 5% CO_2 at 37°C. For all experiment, cells are seeded at a density of 4×10^4 cells/well in 96-well culture plates and allowed to attach overnight. For assessment of cell viability, hydrogen peroxide-induced cytotoxicity is quantified by a standard measurement of LDH release with the use of the LDH assay kit. Briefly, 6 h after hydrogen peroxide exposure, 20 µL of medium of each well is collected, and the solution prepared from LDH assay kit is added. After incubation at room temperature for 30 min, the reaction is stopped by addition of 1 N HCl, and absorbance is measured at 450 nm using a microplate reader.

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

Animal Administration [1][2]

Rats[1]

For transient focal ischemia, 9- to 10-week-old male Wistar rats (weighing 274-380 g) are used. FR247304, PJ34, or 3-AB, which is suspended with 0.5% methylcellulose, is administered at doses of 10 and 32 mg/kg for FR247304, 3.2 and 10 mg/kg for PJ34, or 32 and 100 mg/kg for 3-AB intraperitonially twice at 10 min before MCA occlusion and 10 min before recirculation. The administration volume is adjusted to 2 mL/kg.

Mice[2]

Male Swiss albino mice (27-32 g) are used. The PARP inhibitor, PJ34 (1.25, 12.5 or 25 mg/kg) is dissolved in isotonic saline (NaCl, 0.9%) and injected intraperitoneally, in a volume of 10 mL/kg, 15 min before ischemia and again 4 h after the onset of ischemia. Control ischemic mice and sham animals are given vehicle (saline). Naive animals are also included in the studies.

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

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2023 Mar 28;120(13):e2213857120.
- Part Fibre Toxicol. 2020 Jun 8;17(1):23.
- Acta Biomater. 2022 May 25;S1742-7061(22)00310-5.
- Cancer Lett. 2021 Jul 3;S0304-3835(21)00325-6.

- Free Radic Biol Med. 2021 Dec 16;S0891-5849(21)01112-6.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Iwashita A, et al. A novel and potent poly(ADP-ribose) polymerase-1 inhibitor, FR247304 (5-chloro-2-[3-(4-phenyl-3,6-dihydro-1(2H)-pyridinyl)propyl]-4(3H)-quinazolinone), attenuates neuronal damage in in vitro and in vivo models of cerebral ischemia. J Ph

[2]. Haddad M, et al. Anti-inflammatory effects of PJ34, a poly(ADP-ribose) polymerase inhibitor, in transient focal cerebral ischemia in mice. Br J Pharmacol. 2006 Sep;149(1):23-30.

[3]. Diani-Moore S, et al. NAD+ loss, a new player in AhR biology: prevention of thymus atrophy and hepatosteatosis by NAD+ repletion. Sci Rep. 2017 May 23;7(1):2268.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA