Mefuparib hydrochloride

Cat. No.: HY-122661

CAS No.: 1449746-00-2

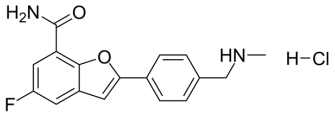
Molecular Formula: $C_{17}H_{16}ClFN_2O_2$

Molecular Weight: 334.77

Target: PARP; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

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

DMSO : 25 mg/mL (74.68 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9871 mL	14.9356 mL	29.8713 mL
	5 mM	0.5974 mL	2.9871 mL	5.9743 mL
	10 mM	0.2987 mL	1.4936 mL	2.9871 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: ≥ 2.5 mg/mL (7.47 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.47 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mefuparib hydrochloride (MPH) is an orally active, substrate-competitive and selective PARP1/2 inhibitor with IC_{50}s of 3.2 nM and 1.9 nM, respectively. Mefuparib hydrochloride induces apoptosis and possesses prominent anticancer activity in vitro and in vivo[1][2].

IC_{50} & Target

PARP1	PARP2	TNKS1	TNKS2
3.2 nM (IC_{50})	1.9 nM (IC_{50})	1.6 μM (IC_{50})	1.3 μM (IC_{50})

In Vitro

Mefuparib hydrochloride (1-10 μM; 48 hours) causes cell apoptosis[1].
Mefuparib hydrochloride (MPH; 1-10 μM; 24 hours) causes V-C8 cells into typical G2/M arrest[1].

Mefuparib hydrochloride (1-10 μM; 24 hours) causes the accumulation of DSB marked by the increased levels of γH2AX in the MDA-MB-436 (BRCA1$^{-/-}$) cells in a concentration-dependent manner[1].
Mefuparib hydrochloride exerts potent in vitro proliferation-inhibitory effects on cancer cells derived from different human tissues with an average IC_{50} of 2.16 μM (0.12 μM~3.64 μM)[1].
Mefuparib hydrochloride inhibits PARP3 (IC_{50}>10 μM), PARP6 (IC_{50}>10 μM), TNKS1 (IC_{50}=1.6 μM), TNKS2 (IC_{50}=1.3 μM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	V-C8 cells
Concentration:	1, 3, 10 μM
Incubation Time:	48 hours
Result:	Caused cell apoptosis.

Cell Cycle Analysis[1]

Cell Line:	V-C8 cells
Concentration:	1, 3, 10 μM
Incubation Time:	24 hours
Result:	Cell came into typical G2/M arrest.

Western Blot Analysis[1]

Cell Line:	MDA-MB-436 (BRCA1$^{-/-}$) cells
Concentration:	1, 10 μM
Incubation Time:	24 hours
Result:	Caused the accumulation of DSB marked by the increased levels of γH2AX in the MDA-MB-436 (BRCA1$^{-/-}$) cells in a concentration-dependent manner.

In Vivo

Mefuparib hydrochloride (MPH; 40-160 mg/kg; orally; once every other day; for 21 days) displays dose- and time-dependent killing on V-C8 xenografts accompanied by complete disappearance of some xenografts, especially in the high-dose group[1].

Mefuparib hydrochloride (160 mg/kg; orally; once every other day; for 21 days) inhibits the growth of the BR-05-0028 breast patient-derived xenograft (PDX) without obvious loss of body weight[1].
Mefuparib hydrochloride (10, 20, 40 mg/kg; oral) has a $T_{1/2}$ of 1.07-1.3 hours and a C_{max} of 116-725 ng/mL for SD rats[1].
Mefuparib hydrochloride (5, 10, 20 mg/kg; oral) has a $T_{1/2}$ of 2.16-2.7 hours and a C_{max} of 114-608 ng/mL for cynomolgus monkeys[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nude mice with V-C8 xenografts[1]
Dosage:	40, 80, 160 mg/kg
Administration:	Orally; once every other day; for 21 days
Result:	Displayed dose- and time-dependent killing on V-C8 xenografts accompanied by complete disappearance of some xenografts, especially in the high-dose group.

Animal Model:	SD rats[1]
Dosage:	10, 20, 40 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral
Result:	Had a $T_{1/2}$ of 1.07-1.3 hours and a C_{max} of 116-725 ng/mL.

REFERENCES

[1]. He JX, et al. Novel PARP1/2 inhibitor mefuparib hydrochloride elicits potent in vitro and in vivo anticancer activity, characteristic of high tissue distribution. Oncotarget. 2017 Jan 17;8(3):4156-4168.

[2]. Nie D, et al. Cancer-Cell-Membrane-Coated Nanoparticles with a Yolk-Shell Structure Augment Cancer Chemotherapy. Nano Lett. 2020 Feb 12;20(2):936-946.

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