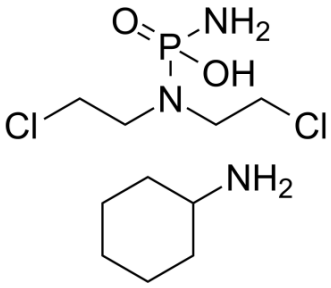
Phosphoramide mustard (cyclohexanamine)

Cat. No.:	HY-137316A
CAS No.:	1566-15-0
Molecular Formula:	$C_{10}H_{24}Cl_2N_3O_2P$
Molecular Weight:	320.2
Target:	DNA Alkylator/Crosslinker; Drug Metabolite
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	-20°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



BIOLOGICAL ACTIVITY

Description

Phosphoramide mustard cyclohexanamine is the major metabolite for Cyclophosphamide (HY-17420), with anticancer activitiy. Phosphoramide mustard cyclohexanamine induces DNA adduct formation in ovarian granulosa cells, induces DNA damage and elicits the ovarian DNA repair response[1][2].

In Vitro

Phosphoramide mustard cyclohexanamine causes cytotoxicity through forming cross-linked DNA adducts which inhibit DNA strand separation during replication[1].
Phosphoramide mustard cyclohexanamine destroys rapidly dividing cells by forming NOR-G-OH, NOR-G and G-NOR-G adducts with DNA, potentially leading to DNA damage[1].
Phosphoramide mustard cyclohexanamine (3-6 μM; 48 hours) reduces cell viability in rat spontaneously immortalized granulosa cells (SIGCs)[1].
Phosphoramide mustard cyclohexanamine (3-6 μM; 24-48 hours) induces DNA adduct formation[1].
Phosphoramide mustard cyclohexanamine (3-6 μM; 24-48 hours) induces ovarian DNA damage in rat ovaries[1].
Phosphoramide mustard cyclohexanamine increases DNA damage responses (DDR) gene (Atm, Parp1, Prkdc, Xrcc6, Brca1, Rad51) mRNA expression level[1].
Phosphoramide mustard cyclohexanamine (3-6 μM; 24-48 hours) increased DDR proteins[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	SIGCs
Concentration:	0.5 μM, 1 μM, 3 μM, 6 μM
Incubation Time:	48 hours
Result:	Reduced cell viability at concentrations of 3 μM and higher.

RT-PCR[1]

Cell Line:	SIGCs
Concentration:	3 μM, 6 μM
Incubation Time:	24 hours, 48 hours

Result:	Increased DDR gene mRNA expression levels.

Western Blot Analysis[1]

Cell Line:	SIGCs
Concentration:	3 μM, 6 μM
Incubation Time:	24 hours, 48 hours
Result:	Generally increased DDR proteins.

In Vivo

Phosphoramide mustard cyclohexanamine (2.1-20.7 mg/kg; i.p.; daily; for 5 days) inhibits subcutaneous tumor growth in rats[2].

Phosphoramide mustard cyclohexanamine (86.0 mg/kg; i.v.) has a plasma disappearance half-life of 15.1 minutes[2].

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Animal Model:	Rat, subcutaneously implanted Walker 256 carcinosarcoma tumor[2]
Dosage:	2.1 mg/kg, 4.8 mg/kg, 10.4 mg/kg, 20.7 mg/kg
Administration:	Intraperitoneal injection, once daily, for 5 consecutive days
Result:	Required to produce 50% inhibition of subcutaneous tumor growth with dose of 12 mg/kg.

Animal Model:	Rats[2]
Dosage:	86.0 mg/kg (Pharmacokinetic Analysis)
Administration:	Intravenous injection
Result:	Had a disappearance half-life of 15.1 minutes in plasma.

REFERENCES

[1]. Shanthi Ganesan, et al. Phosphoramide mustard exposure induces DNA adduct formation and the DNA damage repair response in rat ovarian granulosa cells. Toxicol Appl Pharmacol. 2015 Feb 1; 282(3): 252–258.

[2]. S Genka, et al. Brain and plasma pharmacokinetics and anticancer activities of cyclophosphamide and phosphoramide mustard in the rat. Cancer Chemother Pharmacol. 1990;27(1):1-7.

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