Perifosine

Cat. No.: HY-50909

CAS No.: 157716-52-4

Molecular Formula: $C_{25}H_{52}NO_4P$

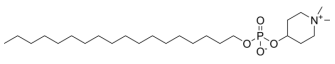
Molecular Weight: 461.66

Target: Akt; Autophagy; Apoptosis

Pathway: PI3K/Akt/mTOR; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (216.61 mM; Need ultrasonic)
DMF : < 1 mg/mL (insoluble)
DMSO : < 1 mg/mL (insoluble or slightly soluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1661 mL	10.8305 mL	21.6610 mL
	5 mM	0.4332 mL	2.1661 mL	4.3322 mL
	10 mM	0.2166 mL	1.0830 mL	2.1661 mL

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

In Vivo

1. Add each solvent one by one: PBS
Solubility: 50 mg/mL (108.30 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Perifosine is an oral Akt inhibitor which inhibits proliferation of different tumor cell lines with IC_{50}s of 0.6-8.9 μM.

IC_{50} & Target

Autophagy

In Vitro

The IC_{50} for growth of Ntv-a/LacZ cell lines is determined by MTT assay. When the cells are cultured for 48 hours in 10% FCS-supplemented media, the IC_{50} for cells with constitutively active PDGF, Ras, or Akt signaling is similar and found to be ~45 μM[1].Perifosine, a oral-bioavailable alkylphospholipid (ALK), on the cell cycle kinetics of immortalized keratinocytes (HaCaT) as well as head and neck squamous carcinoma cells. Proliferation is assessed by the incorporation of [^{3}H]thymidine into cellular DNA. Exposure to Perifosine (0.1-30 μM) for 24 h results in a dose-dependent inhibition of [^{3}H]thymidine uptake in all cell lines tested. The IC_{50}s for growth are between 0.6 and 8.9 μM, reaching IC_{80}s of ~10 μM. Perifosine blocks cell cycle

	progression of head and neck squamous carcinoma cells at G_1-S and G_2-M by inducing $p21^{WAF1}$, irrespective of p53 function, and may be exploited clinically because the majority of human malignancies harbor p53 mutations. Perifosine (20 μM) induces both G_1-S and G_2-M cell cycle arrest, together with $p21^{WAF1}$ expression in both p53 wild-type and $p53^{-/-}$ clones[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Mice are identified with tumors by bioluminescence imaging and either treated them with 100 mg/kg Temozolomide, or 30 mg/kg Perifosine, or a combination with 100 mg/kg Temozolomide and 30 mg/kg Perifosine (Temozolomide+Perifosine) for 3 to 5 days. The mice are sacrificed and tumors analyzed histologically for cell proliferation by Ki-67 immunostaining. Ki-67 staining index is significantly reduced in mice treated with either Temozolomide (Ki-67 staining index=5.5±1.2%, n=4, P=0.0019) or Perifosine (Ki-67 staining index=3.2±1.1%, n=3, P=0.001) compared with Control, demonstrating the inhibitory effect on proliferation. Most importantly, the tumors treated with Temozolomide+Perifosine have the lowest Ki-67 staining index (1.7±1.2%, n=3, P=0.0005). The additional treatment with Perifosine results in a significantly lower proliferation rate than Temozolomide alone (P=0.0087)[1]. Perifosine markedly decreases p-Akt from 10 min to 24 hours and subsequently, moderately decreased p-S6 from 1h to 24 h after injection[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	Exponentially growing cells (HN12, HN30, and HaCaT) are lysed, and 500 μg of total cellular protein are used to immunoprecipitate active cdc2 and cdk2 complexes. After capturing with gammabind G Sepharose and subsequent washes, the active immune complexes are assessed for activity in the presence of increasing concentrations of Perifosine (0.1-30 μM) or flavopiridol (300 nM) in the kinase assay buffer containing [γ-^{32}P]ATP (3000 Ci/mmol) and 0.2 mg/mL histone H1, 25 μM ATP. Reactions are incubated at 37°C for 30 min and terminated by the addition of SDS-gel loading buffer, resolved in SDS-PAGE, and dried gels are subjected to autoradiography and phosphorimaging[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cell proliferation studies by measuring the uptake of [^{3}H]thymidine is performed. Briefly, HNSCC and HaCaT cells (1-2×10^4 /well) are grown overnight in 24-well plates and exposed to either Perifosine (0.1-30 μM) or PBS (control). After treatment (24-48 h), cells are pulsed with [^{3}H]thymidine (1 μCi/well) for 4-6 h, fixed (5% trichloroacetic acid), and solubilized (0.5 M NaOH) before scintillation counting. Experiments are performed in triplicates[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Mice[1] Drug treatment of tumor-bearing mice. Image-positive Ef-luc Ntv-a mice are treated daily with i.p. administration of buffer alone as a control, or i.p. administration of 100 mg/kg Temozolomide, or oral administration of 30 mg/kg Perifosine, or a combination with Perifosine and Temozolomide for 3 to 5 days. The mean doses of the treatments are: Control, 5 (all five); Temozolomide, 3.75 (three to five); Perifosine, 3.75 (three to four); and Perifosine+Temozolomide, 3 (all three). Control buffer solution consisted of 5% DMSO and 1% Tween 80 in distilled water. Rats[3] To further determine whether the paradoxical effect of rapamycin on S6 phosphorylation is related to upstream signals of Akt-mTOR, rats are treated with Perifosine (20 mg/kg, ip, once), an Akt inhibitor, 30 min before rapamycin administration. Rats are sacrificed 1 h or 6 h after rapamycin injection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Acta Pharm Sin B. 2023 Oct;13(10):4253-4272.

- Int J Biol Sci. 2016 Mar 30;12(5):607-16.
- Front Oncol. 2021 Apr 12;11:608570.
- J Cell Biochem. 2020 Mar;121(3):2343-2353.

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REFERENCES

[1]. Momota H, et al. Perifosine inhibits multiple signaling pathways in glial progenitors and cooperates with temozolomide to arrest cell proliferation in gliomas in vivo. Cancer Res, 2005, 65(16), 7429-7435.

[2]. Vyomesh Patel, et al. Perifosine, a novel alkylphospholipid, induces p21(WAF1) expression in squamous carcinoma cells through a p53-independent pathway, leading to loss in cyclin-dependent kinase activity and cell cycle arrest. Cancer Res, 2002, 62(5), 14

[3]. Chen L, et al. Rapamycin has paradoxical effects on S6 phosphorylation in rats with and without seizures. Epilepsia. 2012 Nov;53(11):2026-33.

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