

Product Data Sheet

Product Name: Miltefosine

Cat. No.: GC10811

Chemical Properties

Cas. No. 58066-85-6

Chemical Name hexadecyl 2-(trimethylazaniumyl)ethyl phosphate

SMILES CCCCCCCCCCCCCCCCOP(=O)([O-])OCC[N+](C)(C)C

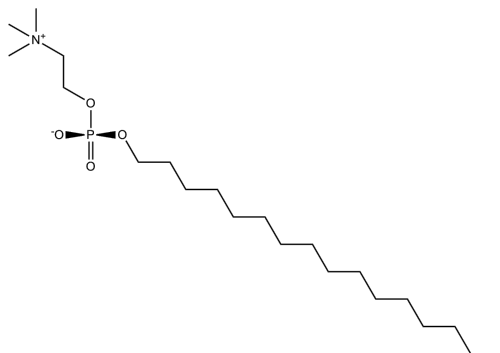
Formula $C_{21}H_{46}NO_4P$ M.Wt 407.57

Solubility $\geq 10.2\text{mg/mL}$ in Water Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines L6E9 rat skeletal muscle cell line

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation method The solubility of this compound in DMSO is limited. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

Reacting condition 10, 20, 40 or 60 µM; 15, 30, 45 or 60 mins

Applications In L6E9 rat skeletal muscle cell line, Miltefosine dose-dependently inhibited insulin-stimulated Akt/PKB phosphorylation, with 75% inhibition at 40 µM and 98% inhibition at 60 µM. Besides, Miltefosine (40 µM for 60 mins) pre-treatment also inhibited insulin-stimulated activation of PI3K, without significant effect on cell survival, cell number, protein content or cell morphology.

Animal experiment [2]:

Animal models BC-1 cell-xenografted NOD-SCID mice

Dosage form 50 mg/kg; i.p.; 5 days a week, for 20 days

Applications Compared with vehicle-treated mice, Miltefosine showed inhibition on the growth rate of tumors. By day 14 after treatment, there was an approximately 50% decrease in the average tumor volume of Miltefosine-treated mice. Immunohistochemical analyses of tumor sections from Miltefosine-treated mice displayed reduced phosphorylation of ribosomal S6 protein which correlated with the delay in tumor progression in the treatment group.

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Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

- [1]. Verma, N.K. and C.S. Dey, The anti-leishmanial drug miltefosine causes insulin resistance in skeletal muscle cells in vitro. *Diabetologia*, 2006. 49(7): p. 1656-60.
- [2]. Bhatt AP, Bhende PM, Sin SH, Roy D, Dittmer DP, Damania B. Dual inhibition of PI3K and mTOR inhibits autocrine and paracrine proliferative loops in PI3K/Akt/mTOR-addicted lymphomas. *Blood*. 2010 Jun 3;115(22):4455-63.

Background

Miltefosine is an inhibitor of PI3K/Akt signaling with IC₅₀ value of 34.6±11.7μM, 6.8±0.9 μM when tested with MCF7 and Hela-WT respectively [1].

PI3K (phosphoinositide-3-kinase) family is an important part in the growth factor super-family signaling process, and can be activated by a variety of cytokines and chemical factors. The activation of PI3K can phosphorylate and activate AKT, localizing it in the plasma membrane. The PI3K/Akt pathway is an intracellular signaling pathway which plays an important role in regulating cell cycle, such as cellular quiescence, proliferation, cancer, longevity and so forth [2, 3]. Many studies have shown that PI3K/Akt had abnormal expression in patients with cancer or virus infection.

Miltefosine is an inhibitor for PI3K/Akt signaling. When tested with macrophages infected by human HIV-1 virus, miltefosine showed significant ability to reduce the viral production via inhibiting PI3K/Akt signaling pathway [4]. In L6E9 skeletal muscle cell line, treatment of miltefosine resulted in the resistance of skeletal muscle cells via inhibiting PI3K/Akt signaling pathway [5].

References:

- [1]. Rybczynska, M., et al., *MDR1 causes resistance to the antitumour drug miltefosine. Br J Cancer*, 2001. 84(10): p. 1405-11.
- [2]. Bauer, T.M., M.R. Patel, and J.R. Infante, *Targeting PI3 kinase in cancer. Pharmacol Ther*, 2015. 146c: p. 53-60.
- [3]. Minami, A., et al., *Connection between Tumor Suppressor BRCA1 and PTEN in Damaged DNA*

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Repair. Front Oncol, 2014. 4: p. 318.

[4]. Chugh, P., et al., Akt inhibitors as an HIV-1 infected macrophage-specific anti-viral therapy. *Retrovirology*, 2008. 5(11): p. 1742-4690.

[5]. Verma, N.K. and C.S. Dey, The anti-leishmanial drug miltefosine causes insulin resistance in skeletal muscle cells in vitro. *Diabetologia*, 2006. 49(7): p. 1656-60.

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