

Product Data Sheet

Product Name: Zoledronic Acid (hydrate)

Cat. No.: GC45187

Chemical Properties

Cas. No. 165800-06-6

SMILES OP(C(O)(P(O)(O)=O)CN1C=NC=C1)(O)=O.O

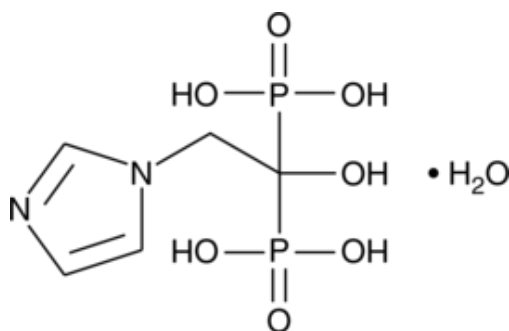
Formula C5H10N2O7P2·H2O M.Wt 290.1

Solubility PBS (pH 7.2): 1.6 mg/ml 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 Mia PaCa-2 cells

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

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Preparation Method	Mia PaCa-2 cells were grown in RPMI-1640 media supplemented with 10% fetal bovine serum in 5% CO ₂ at 37°C. The exponentially growing Mia PaCa-2 cells were seeded into 96-well microplates at a density of 3×10 ³ cells/well for 24h. Afterwards, an equal volume of medium containing various concentrations of Zoledronic Acid (0, 3, 5, 10, and 30μM) was added to each well. At the end of the incubation period (24, 48, and 72h at 37°C), cell viability was analyzed.
Reaction Conditions	0, 3, 5, 10, and 30μM; 24, 48, and 72h
Applications	Zoledronic Acid treatment significantly reduced the cell viability of Mia PaCa-2 cells in a dose and time-dependent manner.

Animal experiment [2]:

Animal models	Athymic nude mice
Preparation Method	Athymic nude mice, 4-5 weeks old, were maintained under a 12-h light and 12-h dark cycle at a temperature of 24 C±1°C and humidity of 50%±10%, free with water and diet. TC71 cells in the log-growth phase were harvested and resuspended in cold Hank's balanced salt solution at 2×10 ⁵ cells/ml. Mice were housed for 1 week before experiments were begun, then 2×10 ⁵ TC71 cells were injected into the right tibia under anesthesia. Four days after tumor cell injection, the mice were divided into groups and treated with Zoledronic acid alone (200μg/kg; s.c.; twice weekly), or paclitaxel alone (6mg/kg; i.p.; once a week). Mice in the control group were treated with phosphate-buffered saline (PBS). The tumor size was measured after 5 weeks.
Dosage form	200μg/kg; twice weekly for 5 weeks; s.c.

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Applications Zoledronic acid treatment reduced the tumor growth in mice with TC71 xenografts.

References:

- [1] Elsayed M, Kobayashi D, Kubota T, et al. Synergistic antiproliferative effects of zoledronic acid and fluvastatin on human pancreatic cancer cell lines: an in vitro study[J]. Biological and Pharmaceutical Bulletin, 2016, 39(8): 1238-1246.
- [2] Zhou Z, Guan H, Duan X, et al. Zoledronic acid inhibits primary bone tumor growth in Ewing sarcoma[J]. Cancer, 2005, 104(8): 1713-1720.

Background

Zoledronic Acid (hydrate), a parenteral bisphosphonate, is an inhibitor of osteoclast-mediated bone resorption [1]. Zoledronic Acid acts primarily by inhibiting the mevalonate pathway in osteoclasts via farnesyl diphosphate synthase inhibition, resulting in the prevention of downstream protein prenylation, with subsequent inhibition of osteoclast-mediated bone resorption and osteoclast formation and the induction of osteoclast apoptosis [2]. Zoledronic Acid has been widely used as an immunomodulator to inhibit the auxiliary functions of regulatory T cells (Tregs) in order to reduce the invasiveness of cancer[3].

In vitro, Zoledronic Acid treatment for 72 hours significantly inhibited Mia PaCa-2 cells and Suit-2 cells, with IC₅₀ values of 2.4μM and 11μM, respectively [4]. Treatment with 10 μM Zoledronic Acid for 72 hours significantly inhibited the proliferation of HT1080 cells, inducing cell cycle arrest, nuclear fragmentation, and the formation of apoptotic bodies[5]. Treatment with 50μM Zoledronic Acid for 48 hours significantly induced apoptosis in BxPC-3 cells, resulting in decreased levels of p21^{ras} and Raf-1, and downregulation of the terminal enzymes ERK/MAP kinase and pKB/Akt pathways[6].

In vivo, Zoledronic Acid treatment via subcutaneous injection at a dose of 1mg/kg dose twice a week for 6 weeks significantly inhibited lung metastasis in the osteosarcoma-bearing mice and improved the survival rate of the mice [7]. Subcutaneous injection of a 200μg/kg dose of Zoledronic Acid twice a week for 5 weeks significantly inhibited tumor growth in the TC71 xenograft mouse model and reduced the formation of osteoclasts in the tumors[8].

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- [1] Dhillon S. Zoledronic acid (Reclast®, Aclasta®): a review in osteoporosis[J]. *Drugs*, 2016, 76(17): 1683-1697.
- [2] Deeks E D, Perry C M. Zoledronic acid: a review of its use in the treatment of osteoporosis[J]. *Drugs & aging*, 2008, 25(11): 963-986.
- [3] Liu H, Wang S H, Chen S C, et al. Zoledronic acid blocks the interaction between breast cancer cells and regulatory T-cells[J]. *BMC cancer*, 2019, 19(1): 176.
- [4] Elsayed M, Kobayashi D, Kubota T, et al. Synergistic antiproliferative effects of zoledronic acid and fluvastatin on human pancreatic cancer cell lines: an in vitro study[J]. *Biological and Pharmaceutical Bulletin*, 2016, 39(8): 1238-1246.
- [5] Koto K, Murata H, Kimura S, et al. Zoledronic acid inhibits proliferation of human fibrosarcoma cells with induction of apoptosis, and shows combined effects with other anticancer agents[J]. *Oncology reports*, 2010, 24(1): 233-239.
- [6] Tassone P, Tagliaferri P, Viscomi C, et al. Zoledronic acid induces antiproliferative and apoptotic effects in human pancreatic cancer cells in vitro[J]. *British journal of cancer*, 2003, 88(12): 1971-1978.
- [7] Ory B, Heymann M F, Kamijo A, et al. Zoledronic acid suppresses lung metastases and prolongs overall survival of osteosarcoma-bearing mice[J]. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, 2005, 104(11): 2522-2529.
- [8] Zhou Z, Guan H, Duan X, et al. Zoledronic acid inhibits primary bone tumor growth in Ewing sarcoma[J]. *Cancer*, 2005, 104(8): 1713-1720.

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