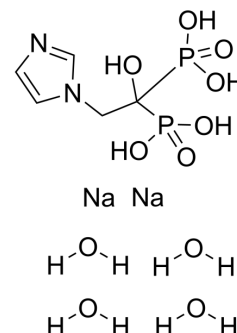


## Zoledronic acid disodium tetrahydrate

<b>Cat. No.:</b>	HY-13777B
<b>CAS No.:</b>	165800-07-7
<b>Molecular Formula:</b>	C <sub>5</sub> H <sub>18</sub> N <sub>2</sub> Na <sub>2</sub> O <sub>11</sub> P <sub>2</sub>
<b>Molecular Weight:</b>	390.13
<b>Target:</b>	Apoptosis; Autophagy; Bacterial
<b>Pathway:</b>	Apoptosis; Autophagy; Anti-infection
<b>Storage:</b>	Please store the product under the recommended conditions in the Certificate of Analysis.



### BIOLOGICAL ACTIVITY

<b>Description</b>	Zoledronic Acid (Zoledronate) disodium tetrahydrate is a third-generation bisphosphonate (BP), with potent anti-resorptive activity. Zoledronic Acid disodium tetrahydrate inhibits the differentiation and apoptosis of osteoclasts. Zoledronic Acid disodium tetrahydrate also has anti-cancer effects <sup>[1]</sup> .														
<b>In Vitro</b>	<p>Zoledronic Acid disodium tetrahydrate (0.1-1 μM; 48 hours) increases receptor activator of nuclear factor κB ligand (RANKL) and sclerostin mRNA expressions in osteocyte-like MLO-Y4 cells<sup>[2]</sup>.</p> <p>Zoledronic Acid disodium tetrahydrate increases the expression of osteoclastogenesis supporting factor from MLO-Y4 cells<sup>[2]</sup>.</p> <p>Zoledronic Acid disodium tetrahydrate enhances the RANKL expression via IL-6/ JAK2/STAT3 pathway in MLO-Y4 cells<sup>[2]</sup>.</p> <p>Zoledronic acid disodium tetrahydrate inhibits osteoclast differentiation and function through the regulation of NF-κB and JNK signalling pathways<sup>[3]</sup>.</p> <p>Zoledronic Acid disodium tetrahydrate (10-100 μM; 1-7 days) markedly reduces the viability of MC3T3-E1 cells and induces apoptosis in MC3T3-E1 cells<sup>[4]</sup>.</p> <p>Zoledronic Acid disodium tetrahydrate (10-100 μM; 4 days) inhibits cell viability due to the induction of apoptosis<sup>[4]</sup>.</p> <p>Zoledronic Acid disodium tetrahydrate exerts inhibitory effects on the differentiation and maturation of MC3T3-E1 cells at concentrations &lt;1 μM<sup>[4]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Cell Viability Assay<sup>[4]</sup></p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Cell Line:</td> <td>MC3T3-E1 cells</td> </tr> <tr> <td>Concentration:</td> <td>0.01 μM , 0.1 μM, 1 μM, 10 μM, 100 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>1 day, 3 days, 5 days, 7 days</td> </tr> <tr> <td>Result:</td> <td>Reduced cells viability at 10 μM and 100 μM.</td> </tr> </table> <p>Apoptosis Analysis<sup>[4]</sup></p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Cell Line:</td> <td>MC3T3-E1 cells</td> </tr> <tr> <td>Concentration:</td> <td>0.01 μM , 0.1 μM, 1 μM, 10 μM, 100 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>1 days, 4 days, 7 days</td> </tr> </table>	Cell Line:	MC3T3-E1 cells	Concentration:	0.01 μM , 0.1 μM, 1 μM, 10 μM, 100 μM	Incubation Time:	1 day, 3 days, 5 days, 7 days	Result:	Reduced cells viability at 10 μM and 100 μM.	Cell Line:	MC3T3-E1 cells	Concentration:	0.01 μM , 0.1 μM, 1 μM, 10 μM, 100 μM	Incubation Time:	1 days, 4 days, 7 days
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Cell Line:	MC3T3-E1 cells														
Concentration:	0.01 μM , 0.1 μM, 1 μM, 10 μM, 100 μM														
Incubation Time:	1 days, 4 days, 7 days														

Result:	Increased the number of early apoptotic cells and late apoptotic or necrotic cells at dose-dependent and time-dependent (high concentrations).
Western Blot Analysis <sup>[4]</sup>	
Cell Line:	MC3T3-E1 cells
Concentration:	0.01 $\mu$ M , 0.1 $\mu$ M, 1 $\mu$ M, 10 $\mu$ M, 100 $\mu$ M
Incubation Time:	4 days
Result:	Down-regulated the protein level of inactive caspase-3 and up-regulated the protein level of active caspase-3 at the concentrations of 10 and 100 $\mu$ M.

<b>In Vivo</b>	<p>Zoledronic Acid disodium tetrahydrate (0.05 mg/kg; i.p.; weekly; for 3 weeks) increases bone mineral density and content<sup>[5]</sup>. Zoledronic Acid disodium tetrahydrate (0.5-1 mg/kg; i.p.; weekly; for 3 weeks) inhibits both osteoclast and osteoblasts function and bone remodeling in vivo interfering with bone mechanical properties<sup>[5]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Model:	Five-week-old C57BL6 mice <sup>[5]</sup>
Dosage:	0.05 mg/kg, 0.5 mg/kg, 1 mg/kg
Administration:	Intraperitoneal injection, weekly, for 3 weeks
Result:	Inhibited both osteoclast and osteoblasts function and bone remodeling at 0.5 mg/kg and 1 mg/kg.

## CUSTOMER VALIDATION

- Oxid Med Cell Longev. 2021 Mar 31.
- Int Immunopharmacol. September 2022, 109030.
- Dis Markers. 2021 Oct 15;2021:5838582.

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## REFERENCES

- [1]. Lianwei Wang, et al. Various pathways of zoledronic acid against osteoclasts and bone cancer metastasis: a brief review. BMC Cancer. 2020; 20: 1059.
- [2]. Hyung Joon Kim, et al. Zoledronate Enhances Osteocyte-Mediated Osteoclast Differentiation by IL-6/RANKL Axis. Int J Mol Sci. 2019 Mar; 20(6): 1467.
- [3]. Xiao-Lin Huang, et al. Zoledronic acid inhibits osteoclast differentiation and function through the regulation of NF- $\kappa$ B and JNK signalling pathways. Int J Mol Med. 2019 Aug;44(2):582-592.
- [4]. XIN HUANG, et al. Dose-dependent inhibitory effects of zoledronic acid on osteoblast viability and function in vitro. Mol Med Rep. 2016 Jan; 13(1): 613-622.
- [5]. Samantha Pozzi, et al. High-dose zoledronic acid impacts bone remodeling with effects on osteoblastic lineage and bone mechanical properties. Clin Cancer Res. 2009 Sep 15;15(18):5829-39.
- [6]. Shea GKH, et al. Oral Zoledronic acid bisphosphonate for the treatment of chronic low back pain with associated Modic changes: A pilot randomized controlled trial. J

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: [tech@MedChemExpress.com](mailto:tech@MedChemExpress.com)

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA