

Product Data Sheet

Product Name: Oxatamide

Cat. No.: GC61401

Chemical Properties

Cas. No. 60607-34-3

SMILES O=C1NC2=CC=CC=C2N1CCCN3CCN(C(C4=CC=CC=C4)C5=CC=CC=C5)CC3

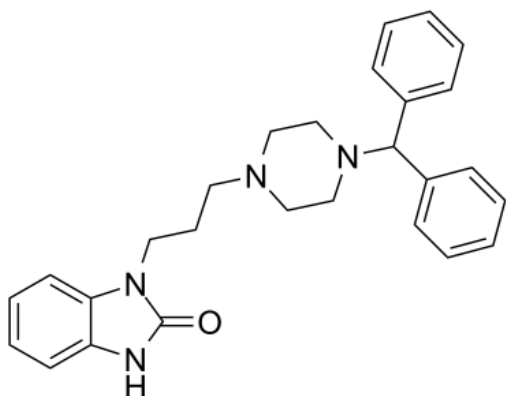
Formula $C_{27}H_{30}N_4O$ M.Wt 426.55

Solubility DMSO: 250 mg/mL (586.10 mM) 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 K562 human leukemia cells and K562 doxorubicin-resistant variant K562/DXR

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K562 and K562/DXR cells were maintained in RPMI 1640 medium supplemented with 10% fetal calf serum. The K562/DXR cell line was Preparation Method maintained in medium containing 1 μ M doxorubicin, which was washed out at least 3 days before experiments. For cytotoxicity assays, cells were incubated with various concentrations of Oxatomide (1–10 μ M; 45min) and doxorubicin.

Reaction
Conditions 11–10 μ M; 45min.

Applications Oxatomide synergistically and dose-dependently potentiated the cytotoxicity of doxorubicin in P-glycoprotein-expressing K562/DXR cells but not in the parental K562 cells. Oxatomide significantly increased the intracellular accumulation of doxorubicin in K562/DXR cells and inhibited the photolabeling of P-glycoprotein by [^{3} H]-azidopine, indicating direct interaction with and inhibition of the P-glycoprotein drug-efflux pump.

Animal experiment [2]:

Animal models Mast cell-bearing WBB6F1-+/+ mice and B6D2F1 mice

Preparation Method 30 minutes after the mice were given the Oxatomide (100mg/kg) orally, shaved on the dorsal skin and intradermally injected with a high dilution (1:128 or 1:256) of hyperimmune anti-bovine serum albumin (anti-BSA) serum to passively sensitize the skin for IgG1 antibody-mediated passive cutaneous anaphylaxis (PCA). One hour later, PCA was elicited by an intravenous injection of BSA antigen mixed with Evans blue dye.

Dosage form 100mg/kg; p.o.; single administration 30 minutes before the antigen challenge

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Applications Oxatomide nearly completely suppressed the IgG1 antibody-mediated passive cutaneous anaphylaxis (PCA) reaction in mast cell-bearing reference mice, as indicated by a significant reduction in the amount of dye extravasated at the skin reaction site.

References:

- [1] Ishikawa M, Fujita R, Furusawa S, et al. Circumvention of acquired resistance to doxorubicin in K562 human leukemia cells by oxatomide. *Biol Pharm Bull.* 2001 Oct;24(10):1185-7.
- [2] Kimura S, Watanabe A, Takeuchi M, et al, Drug susceptibility of PCA in WBB6F1-W/Wv mice. *Cell Mol Life Sci.* 1998 May;54(5):456-60.

Background

Oxatomide is an orally active H1-receptor antagonist (antihistamine)^[1-2]. Oxatomide is used in the treatment of allergic diseases such as allergic rhinitis, urticaria, and conjunctivitis^[3-4].

In vitro, Oxatomide (1-10 μ M) was incubated with P-glycoprotein-expressing doxorubicin-resistant human leukemia K562/DXR cells for 45 minutes. Oxatomide significantly reversed the multidrug resistance phenotype in K562 cells and increased the intracellular accumulation of chemotherapeutic drugs^[5]. Oxatomide (0.1–30 μ M) was used to pretreat mouse neuroblastoma N18TG2 cells, J774 macrophage cells, human myeloma RPMI8226 cells, and mouse bone marrow-derived mast cells (mBMMC) expressing functional P2X7 receptors for 1 minute, followed by stimulation with ATP (0.5–3mM) or BzATP (10–100 μ M). Oxatomide significantly inhibited P2X7 receptor-mediated calcium influx, membrane currents, mitogen-activated protein kinase (MAPK) activation, induction of inflammation-related genes, cell death (as measured by LDH release), and mast cell degranulation^[6].

In vivo, Oxatomide (1.25–5mg/kg) was orally administered 4 hours prior to challenge to sensitized male Swiss strain mice that had been infected with *Trichinella spiralis* for 30 to 40 days. Oxatomide dose-dependently and significantly prevented a lethal anaphylactic reaction induced by intravenous injection of *Trichinella* larval somatic antigens^[7]. Oxatomide (100mg/kg) was administered as a single oral dose 30 minutes before the antigen challenge to passively sensitized WBB6F1-+/+ and

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B6D2F1 mice using a high dilution (1:128) of anti-bovine serum albumin (BSA) serum. Oxatomide inhibited the passive cutaneous anaphylaxis (PCA) reaction triggered by the high-dilution antiserum^[8].

References:

- [1] Hayashi K, Yanagi M, Wood-Baker R, et al. Oxatomide for stable asthma in adults and children. Cochrane Database Syst Rev. 2003;2003(2):CD002179.
- [2] Richards DM, Brogden RN, Heel RC, et al. Oxatomide. A review of its pharmacodynamic properties and therapeutic efficacy. Drugs. 1984 Mar;27(3):210-31.
- [3] Marone G, Granata F, Spadaro G, et al. Antiinflammatory effects of oxatomide. J Investig Allergol Clin Immunol. 1999 Jul-Aug;9(4):207-14.
- [4] Yamagiwa N, Komine M, Hanaoka F, et al. Exploratory study of oxatomide derivatives with high P2X7 receptor inhibitory activity. Bioorg Med Chem Lett. 2022 Dec 1;77:129035.
- [5] Ishikawa M, Fujita R, Furusawa S, et al. Circumvention of acquired resistance to doxorubicin in K562 human leukemia cells by oxatomide. Biol Pharm Bull. 2001 Oct;24(10):1185-7.
- [6] Yoshida K, Ito M, Matsuoka I. P2X7 receptor antagonist activity of the anti-allergic agent oxatomide. Eur J Pharmacol. 2015 Nov 15;767:41-51.
- [7] De Clerck F, Van Gorp L, Vanparijs O, et al. Oxatomide protects Trichinella spiralis infected mice from lethal anaphylaxis. Agents Actions. 1978 Dec;8(6):568-71.
- [8] Kimura S, Watanabe A, Takeuchi M, et al. Drug susceptibility of PCA in WBB6F1-W/Wv mice. Cell Mol Life Sci. 1998 May;54(5):456-60.

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