

Product Data Sheet

Product Name: Aldoxorubicin

Cat. No.: GC14858

Chemical Properties

Cas. No. 1361644-26-9

Chemical Name N-[(Z)-[1-[(2S,4S)-4-[(2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyloxan-2-yl]oxy-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-3,4-dihydro-1H-tetracen-2-yl]-2-hydroxyethylidene]amino]-6-(2,5-dioxopyrrol-1-yl)hexanamide

SMILES [H][C@@]1(O[C@H]2C[C@@](/C(CO)=N/NC(CCCCCN3C(C=CC3=O)=O)=O)(O)CC(C2=C4O)=C(O)C5=C4C(C6=C(OC)C=CC=C6C5=O)=O)O[C@@H](C)[C@@H](O)[C@@H](N)C1

Formula C₃₇H₄₂N₄O₁₃

M.Wt 750.75

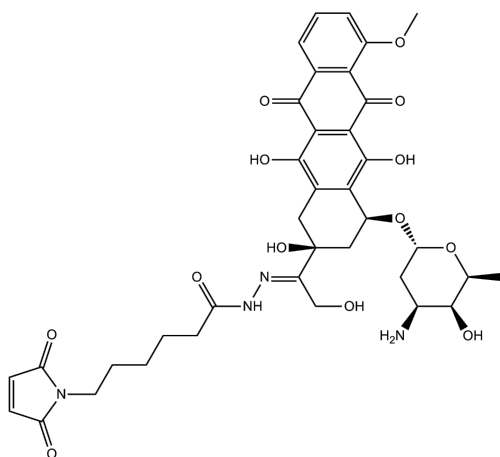
Solubility DMSO : 75 mg/mL (99.90 mM)

Storage -80°C, stored under nitrogen, unstable in solution, ready to use.

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

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Cell experiment [1]:

Cell lines human multiple myeloma cell lines RPMI8226 and U266

Preparation Method The human multiple myeloma cell lines RPMI8226 and U266 were maintained in RPMI-1640 supplemented with 10% FBS, 2mmol/L L-glutamine, 100I/U/mL penicillin, 100mg/mL streptomycin, and essential amino acids in an atmosphere of 5% CO₂ at 37°C. Cells were seeded at 1×10^5 cells/100mL/well in 96-well plates in RPMI-1640 media with FBS for 24 hours before treatment. Cells were cultured in the presence of Aldoxorubicin (0.27-2.16μM) for 48 hours. Next, cell viability was quantified using the CellTiter 96 AQueous Non-Radioactive Cell Proliferation Assay. Each well was treated with MTS for 1 to 4 hours, after which absorbance at 490nm was recorded using a 96-well plate reader. The quantity of formazan product as measured is directly proportional to the number of living cells.

Reaction
Conditions 0.27-2.16μM; 48h

Applications Aldoxorubicin markedly reduced multiple myeloma cell growth.

Animal experiment [2]:

Animal models Foxn1 nude male mice

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Preparation Method

Glioblastoma Multiforme tumors were induced in 80 Foxn1 nude male mice, 6 weeks-old, by implantation of 3×10^5 U87MG-luc cells in the right lobe of the brain. One week after tumor implantation, 64 animals were randomly assigned to four groups (16 mice/group) to be treated with different drugs, as follow:
 Group 1 (vehicle): weekly intravenous (IV) administration of physiologic solution, i.e., 7, 14, 21, 28, 35 days. Group 2: daily oral (OS) administration of temozolomide(TMZ) 0.9mg/kg, from day 7 to day 35. Group 3: weekly administration of Aldoxorubicin 16mg/kg, IV, i.e., 7, 14, 21, 28, 35 days. Group 4: TMZ-Aldoxorubicin combination for up five weeks. At the end of treatments (day 42, one week after the last injection), 32 animals were sacrificed by CO₂ inhalation; the remaining mice (8 animals/group) were observed for mortality until the 90th day of the study. BW measurements were carried out 2 times a week and BLI imaging acquisition were performed at day 0 (immediately after tumor implantation), at day 3 and then weekly until the end of the experiment (day 90). A BW loss $\geq 15\%$ has been considered as sign of suffering, involving the mouse sacrifice.

Dosage form 16mg/kg; i.v.; administered weekly for 5 weeks

Applications

Combination of Aldoxorubicin with temozolomide significantly inhibited tumor growth (with a tumor volume inhibition rate of approximately 90%) and prolonged survival (survival rate increased by 37.5% compared with the saline control group) in a U87 human glioblastoma xenograft mouse model.

References:

- [1] Sanchez E, Li M, Wang C, et al. Anti-myeloma effects of the novel anthracycline derivative INNO-206. *Clin Cancer Res.* 2012;18(14):3856-3867.
- [2] Da Ros M, Iorio AL, De Gregorio V, et al. Aldoxorubicin and Temozolomide combination in a xenograft mice model of human glioblastoma. *Oncotarget.* 2018;9(79):34935-34944.

Background

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Background

Aldoxorubicin, an albumin-binding prodrug of doxorubicin (DNA topoisomerase II inhibitor), is released from albumin under acidic conditions^[1]. Topoisomerase II is an ATP-dependent enzyme that relieves supercoiling tension by introducing double-strand DNA breaks, playing a crucial role in DNA replication, transcription, and chromosome segregation^[2]. Aldoxorubicin is widely used in the research of malignant tumors such as soft tissue sarcoma by inhibiting topoisomerase II^[3].

In vitro, treatment of L2987 human lung cancer cells with Aldoxorubicin (100nM; 48h) significantly inhibited cell proliferation^[4]. Treatment of multiple myeloma cell lines with Aldoxorubicin (0.27-2.16 μ M; 48h; PH=5 or 7) inhibited blood vessel formation and reduced multiple myeloma cell growth in a pHdependent fashion^[5].

In vivo, Aldoxorubicin (2 $\times$ 24 mg/kg), administered weekly by intravenous injection for 45 days, induced complete tumor regression in a breast cancer 3366 xenograft mouse model, significantly inhibited tumor growth in ovarian cancer A2780 and small cell lung cancer H209 xenograft mouse models, and reduced primary tumor size and inhibited metastasis in a pancreatic cancer AsPC-1 orthotopic mouse model^[6]. Combination of Aldoxorubicin (16mg/kg; i.v.; administered weekly for 5 weeks) with temozolomide (0.9mg/kg/day; orally) significantly inhibited tumor growth (with a tumor volume inhibition rate of approximately 90%) and prolonged survival (survival rate increased by 37.5% compared with the saline control group) in a U87 human glioblastoma xenograft mouse model, with no obvious drug-related adverse effects observed^[7].

References:

- [1] Rhee HK, Park HJ, Lee SK, Lee CO, Choo HY. Synthesis, cytotoxicity, and DNA topoisomerase II inhibitory activity of benzofuroquinolinediones. *Bioorg Med Chem*. 2007;15(4):1651-1658.
- [2] Swan RL, Cowell IG, Austin CA. Mechanisms to Repair Stalled Topoisomerase II-DNA Covalent Complexes. *Mol Pharmacol*. 2022;101(1):24-32.
- [3] Sachdev E, Sachdev D, Mita M. Aldoxorubicin for the treatment of soft tissue sarcoma. *Expert Opin Investig Drugs*. 2017;26(10):1175-1179.
- [4] Cranmer LD. Spotlight on aldoxorubicin (INNO-206) and its potential in the treatment of soft tissue sarcomas: evidence to date. *Onco Targets Ther*. 2019;12:2047-2062.
- [5] Sanchez E, Li M, Wang C, et al. Anti-myeloma effects of the novel anthracycline derivative INNO-206. *Clin Cancer Res*. 2012;18(14):3856-3867.

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- [6] Graeser R, Esser N, Unger H, et al. INNO-206, the (6-maleimidocaproyl hydrazone derivative of doxorubicin), shows superior antitumor efficacy compared to doxorubicin in different tumor xenograft models and in an orthotopic pancreas carcinoma model. *Invest New Drugs*. 2010;28(1):14-19.
- [7] Da Ros M, Iorio AL, De Gregorio V, et al. Aldoxorubicin and Temozolomide combination in a xenograft mice model of human glioblastoma. *Oncotarget*. 2018;9(79):34935-34944.

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