

## Temozolomide

## Chemical Properties

CAS No. : 85622-93-1

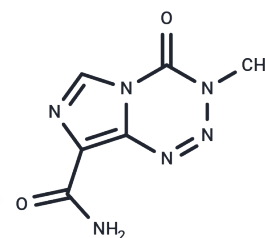
Formula: C<sub>6</sub>H<sub>6</sub>N<sub>6</sub>O<sub>2</sub>

Molecular Weight: 194.15

Store under nitrogen, Keep away from direct sunlight

Storage: Powder: -20°C for 3 years

Actual storage temperature shall be subject to the COA.



## Biological Description

Description	Temozolomide (TMZ) is a DNA alkylating agent with blood-brain barrier permeability and oral activity. Temozolomide has antitumor activity and antiangiogenic activity, and also induces apoptosis and autophagy. Temozolomide is stable under acidic conditions and hydrolyzes under neutral or slightly alkaline conditions.
Targets(IC50)	Apoptosis, Autophagy, DNA Alkylator/Crosslinker, DNA/RNA Synthesis
In vitro	<p><b>METHODS:</b> Melanoma cells SK-mel-28, MM200, IgR3, Mel-FH were treated with Temozolomide (0-500 μM) for 72 h. Cell viability was examined using MTT.</p> <p><b>RESULTS:</b> The p53 status and MGMT expression levels were correlated with the sensitivity of Temozolomide. MM200 and IgR3 (expressing wild-type p53 and low MGMT levels) showed comparable sensitivity to Temozolomide, with IC<sub>50</sub> values of 23 and 22 μM, respectively, whereas SK mel-28 and Mel-FH (mutant-type p53 and high MGMT level) were resistant with IC<sub>50</sub> values &gt;256 and &gt;247 μM. [1]</p> <p><b>METHODS:</b> Melanoma cells MM200 and IgR3 were treated with Temozolomide (100 μM) for 24-72 h. The cell cycle was examined by Flow Cytometry.</p> <p><b>RESULTS:</b> Temozolomide induced G<sub>2</sub>/M cell cycle arrest in MM200 and IgR3 cells. [1]</p> <p><b>METHODS:</b> Human glioma cells U118 were treated with Temozolomide (250-500 μM) for 3-48 h. The m5C level in DNA was measured.</p> <p><b>RESULTS:</b> The response of U118 cells to Temozolomide depends on the concentration and time of the reaction. The amount of m5C in DNA increased significantly within a short period of time after Temozolomide treatment. m5C(R) reached the highest level after 24 h of treatment with 500 μM Temozolomide. [2]</p>
In vivo	<p><b>METHODS:</b> To assay antitumor activity in vivo, Temozolomide (68 mg/kg by gavage) and AG-014699 (1 mg/kg by intraperitoneal injection) were administered intraperitoneally to CD1 nu/nu mice harboring medulloblastomas D425Med, D283Med, or D384Med once daily for five days.</p> <p><b>RESULTS:</b> AG-014699 enhanced the efficacy of Temozolomide in an in vivo model of medulloblastoma. [3]</p> <p><b>METHODS:</b> To assay antitumor activity in vivo, Temozolomide (0.9 mg/kg orally once daily) and Aldox (16 mg/kg intravenously once weekly) were administered to Foxn1 nude mice bearing human glioblastoma U87MG once daily for five weeks.</p> <p><b>RESULTS:</b> Combined treatment with Temozolomide and AldoxAldo induced significant tumor volume suppression and increased survival. [4]</p>

Cell Research	Cell lines exposed to TMZ (with or without 5-Aza or O6-BG pre-treatment) were grown in 24-well plates under standard culture conditions for 6 days. Cytotoxicity was determined using the sulphorhodamine-B (SRB) method. Briefly, the cells were fixed with 10% trichloroacetic acid for 20 min at 4°C then washed three times with water. After 24 hours, cells were stained for 30 min at room temperature with 0.4% SRB dissolved in 1% acetic acid and then washed three times with 1% acetic acid. The plates were air-dried and the dye solubilized with 300 µl/well of 10 mM Tris base (pH 10.5) for 10 min on a shaker. The optical density of each well was measured spectrophotometrically using a Titertek multiscan colorimeter at 492 nm [2].
Animal Research	TZM was dissolved in dimethyl-sulfoxide (40 mg/mL), diluted in saline (5 mg/mL), and administered intraperitoneally on day 2 after tumor injection at 100 mg/kg or 200 mg/kg, doses commonly used for in vivo preclinical studies.15-17 Because cytotoxicity induced by TZM and PARP inhibitors can be improved by fractionated modality of treatment,9 in selected groups a total dose of 200 mg/kg TZM was divided in 2 doses of 100 mg/kg given on days 2 and 3. NU1025 was dissolved in polyethylene glycol-400 (40% in saline) and was injected intracranially at the maximal deliverable dose (1 mg/mouse, 0.03 mL) or, in selected groups, intraperitoneally (0.3 mL) on day 2 after tumor challenge, 1 hour before TZM administration. Control mice were injected with drug vehicles [4].

### Solubility Information

Solubility	DMSO: 30.6 mg/mL (157.61 mM),Sonication and heating are recommended. H2O: 5 mg/mL (25.75 mM),Sonication is recommended. ( < 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	PBS: 5 mg/mL (25.75 mM),Sonication is recommended. 10% DMSO+90% Saline: 2.88 mg/mL (14.83 mM),Solution. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	5.1507 mL	25.7533 mL	51.5066 mL
5 mM	1.0301 mL	5.1507 mL	10.3013 mL
10 mM	0.5151 mL	2.5753 mL	5.1507 mL
50 mM	0.103 mL	0.5151 mL	1.0301 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

- Mhaidat NM, et al. Temozolomide induces senescence but not apoptosis in human melanoma cells. *Br J Cancer*. 2007 Nov 5;97(9):1225-33.
- Wang Y, Wang X, Wang K, et al. Chronic stress accelerates glioblastoma progression via DRD2/ERK/ $\beta$ -catenin axis and Dopamine/ERK/TH positive feedback loop. *Journal of Experimental & Clinical Cancer Research*. 2023, 42(1): 1-17.
- Zhang B, Xu C, Liu J, et al. Nidogen-1 expression is associated with overall survival and temozolomide sensitivity in low-grade glioma patients. *Aging (Albany NY)*. 2021 Mar 18;13(6):9085-9107. doi: 10.18632/aging.202789. Epub 2021 Mar 18.
- Herbener V J, Burster T, Goreth A, et al. Considering the Experimental use of Temozolomide in Glioblastoma Research. *Biomedicines*. 2020, 8(6): 151
- Li F, Chen S, Yu J, et al. Interplay of m6A and histone modifications contributes to temozolomide resistance in glioblastoma. *Clinical and Translational Medicine*. 2021, 11(9): e553
- Zhang M, Ding Y, Gao M, et al. Discovery of Novel N-(Anthracen-9-ylmethyl) Benzamide Derivatives as ZNF207 Inhibitors Promising in Treating Glioma. *Journal of Medicinal Chemistry*. 2024
- Barciszewska AM, et al. A New Epigenetic Mechanism of Temozolomide Action in Glioma Cells. *PLoS One*. 2015 Aug 26;10(8):e0136669.
- Liu X, Guo C, Leng T, et al. Differential regulation of H3K9/H3K14 acetylation by small molecules drives neuron-fate-induction of glioma cell. *Cell Death & Disease*. 2023, 14(2): 142.
- Liu X, Guo Q, Gao G, et al. Exosome-transmitted circCABIN1 promotes temozolomide resistance in glioblastoma via sustaining ErbB downstream signaling. *Journal of Nanobiotechnology*. 2023, 21(1): 1-25.
- Daniel RA, et al. Central nervous system penetration and enhancement of temozolomide activity in childhood medulloblastoma models by poly(ADP-ribose) polymerase inhibitor AG-014699. *Br J Cancer*. 2010 Nov 9;103(10): 1588-96.
- Da Ros M, et al. Aldoxorubicin and Temozolomide combination in a xenograft mice model of human glioblastoma. *Oncotarget*. 2018 Oct 9;9(79):34935-34944.
- Chen Y, Guo Y, Li S, et al. Remdesivir inhibits the progression of glioblastoma by enhancing endoplasmic reticulum stress. *Biomedicine & Pharmacotherapy*. 2023, 157: 114037.
- Daniel RA, et al. Central nervous system penetration and enhancement of temozolomide activity in childhood medulloblastoma models by poly(ADP-ribose) polymerase inhibitor AG-014699.
- Dong J, Peng Y, Zhong M, et al. Implication of lncRNA ZBED3-AS1 downregulation in acquired resistance to Temozolomide and glycolysis in glioblastoma. *European Journal of Pharmacology*. 2022: 175444.
- Tong S, Hong Y, Xu Y, et al. TFR2 regulates ferroptosis and enhances temozolomide chemo-sensitization in gliomas. *Experimental Cell Research*. 2023: 113474.
- Zhang B, Xu C, Liu J, et al. Nidogen-1 expression is associated with overall survival and temozolomide sensitivity in low-grade glioma patients[J]. *Aging (Albany NY)*. 2021, 13(6): 9085.
- Herbener V J, Burster T, Goreth A, et al. Considering the Experimental use of Temozolomide in Glioblastoma Research[J]. *Biomedicines*. 2020, 8(6): 151.
- Jiao W, Zhu S, Shao J, et al. ZSTK474 Sensitizes Glioblastoma to Temozolomide by Blocking Homologous Recombination Repair. *BioMed Research International*. 2022
- Li J, Sun Y, Sun X, et al. AEG-1 silencing attenuates M2-polarization of glioma-associated microglia/macrophages and sensitizes glioma cells to temozolomide. *Scientific reports*. 2021, 11(1): 1-12.
- Wang Y, Wang X, Wang X, et al. Imipramine impedes glioma progression by inhibiting YAP as a Hippo pathway independent manner and synergizes with temozolomide. *Journal of Cellular and Molecular Medicine*. 2021

**Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins**

**This product is for Research Use Only · Not for Human or Veterinary or Therapeutic Use**

Tel: 781-999-4286 E\_mail: info@targetmol.com Address: 34 Washington Street, Wellesley Hills, MA 02481