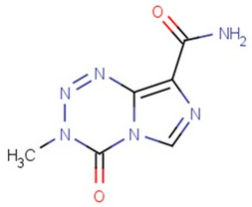
Data Sheet (Cat.No.T1178)

TargetMol
A DRUG SCREENING EXPERT

Temozolomide

Chemical Properties



CAS No.:	85622-93-1
Formula:	C6H6N6O2
Molecular Weight:	194.15
Appearance:	Solid
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	Temozolomide is a DNA alkylating agent interfering with DNA replication.
Targets(IC_{50})	DNA replication: None
In vitro	The cytotoxic/mutagenic effects of temozolomide are based on the presence of DNA O(6)-methylguanine adducts that generate base/base mismatches with cytosine and with thymine. These adducts lead to cell death, or if the cell survives, provoke somatic point mutations represented by C:G-->T:A transition in DNA helix [1]. The IC50 values for Temozolomide (TMZ) in different cell lines were ranging from 14.1 to 234.6 μM: cell lines with low IC50 values (< 50 μM), which included A172 (14.1 μM) and LN229 cells (14.5 μM), and those with high IC50 values (> 100 μM), which included SF268 (147.2 μM) and SK-N-SH cells (234.6 μM) [2]. TMZ sensitivity of both chemo-sensitive and resistant cells was enhanced significantly under hyperoxia. At the cell line-specific optimum oxygen concentration (D54-R, 80 %; U87-R, 40 %), resistant cells had the same response to TMZ as the parent chemosensitive cells under normoxia via the caspase-dependent pathway [3].
In vivo	No drug-related death occurred in mice treated with TZM (100 or 200 mg/kg) or with NU1025 ± TZM and that the maximal weight loss was 12%. Intracranial injection of NU1025, immediately before the administration of 100 or 200 mg/kg TZM, significantly increased lifespans with respect to controls or to groups treated with TZM only [4]. Co-administration of AG-014699 with temozolomide resulted in complete tumour regressions in all mice, of which three out of five were sustained throughout the experiment. The MMR-defective D283Med xenografts grew very rapidly (median time to RTV4=7 days) and showed very little response to temozolomide alone (TGD of only 2 days) with no regressions observed in any mice [5].
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 ml/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]. Cell lines: L-1210 and L-1210/BCNU cells

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]. Animal Model：DBA/2 mice with L-1210 and L-1210/BCNU cells

Solubility Information

Solubility	DMSO: 9.7 mg/mL (50 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	5.151 mL	25.753 mL	51.507 mL
5 mM	1.030 mL	5.151 mL	10.301 mL
10 mM	0.515 mL	2.575 mL	5.151 mL
50 mM	0.103 mL	0.515 mL	1.030 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Marchesi F, et al. Triazene compounds: mechanism of action and related DNA repair systems. Pharmacol Res. 2007 Oct;56(4):275-87.
2. Perazzoli G, et al. Temozolomide Resistance in Glioblastoma Cell Lines: Implication of MGMT, MMR, P-Glycoprotein and CD133 Expression. PLoS One. 2015 Oct 8;10(10):e0140131.
3. Sun S, et al. Hyperoxia resensitizes chemoresistant human glioblastoma cells to temozolomide. J Neurooncol. 2012 Sep;109(3):467-75.
4. Tentori L, et al. Combined treatment with temozolomide and poly(ADP-ribose) polymerase inhibitor enhances survival of mice bearing hematologic malignancy at the central nervous system site. Blood. 2002 Mar 15;99(6):2241-4.
5. 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.
6. 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.
7. Herbener V J, Burster T, Goreth A, et al. Considering the Experimental use of Temozolomide in Glioblastoma Research[J]. Biomedicines. 2020, 8(6): 151.

Tel:781-999-4286 E-mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481