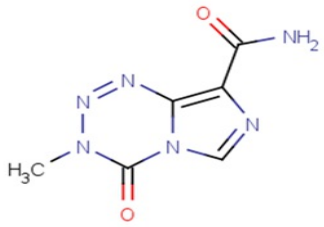
Product Name	:	Temozolomide
Catalog Number	:	T1178
CAS Number	:	85622-93-1
Molecular Formula	:	C6H6N6O2
Molecular Weight	:	194.15
Apprearence	:	Solid
Melting Point	:	212°C



Description: Temozolomide is a DNA alkylating agent interfering with DNA replication.

Storage: 2 years -80°C in solvent; 3 years -20°C powder;

Solubility	DMSO	9.7 mg/mL (50 mM)
	(< 1 mg/ml refers to the product slightly soluble or insoluble)	
Receptor (IC50)	DNA replication	

In vitro Activity

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 Activity

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 Assay

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 line: L-1210 and L-1210/BCNU cells

Animal Experiment

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

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.

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