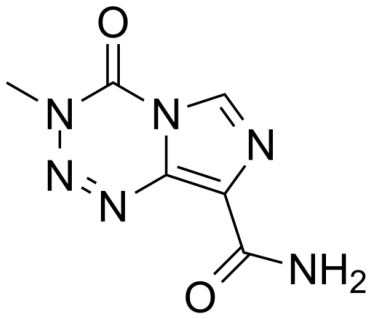
Data Sheet

Product Name:	Temozolomide
Cat. No.:	CS-0943
CAS No.:	85622-93-1
Molecular Formula:	C6H6N6O2
Molecular Weight:	194.15
Target:	Apoptosis; Autophagy; DNA Alkylator/Crosslinker
Pathway:	Apoptosis; Autophagy; Cell Cycle/DNA Damage
Solubility:	H2O : 2.86 mg/mL (14.73 mM; Need ultrasonic); DMSO : 20.83 mg/mL (107.29 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Temozolomide (NSC 362856; CCRG 81045) is an oral **DNA alkylating** agent used to treat some brain cancers. IC50 & Target: DNA alkylator[1] **In Vitro:** Temozolomide (TZM) is a methylating agent that crosses the blood-brain barrier and is indicated for malignant gliomas and metastatic melanomas. Temozolomide is effective against tumor cells that are characterized by low levels of O^6-alkylguanine DNA alkyltransferase (OGAT) and a functional mismatch repair system (MR)[1]. Determination of the IC_{50} for Temozolomide (TZM) in different cell lines gave values ranging from 14.1 to 234.6 μM that fell into two clearly differentiated groups: cell lines with low IC_{50} values (<50 μM), which include A172 (14.1±1.1 μM) and LN229 cells (14.5±1.1 μM), and those with high IC_{50} values (>100 μM), which include SF268 (147.2±2.1 μM) and SK-N-SH cells (234.6±2.3 μM)[2]. **In Vivo:** Temozolomide (TZM), as a single agent, does not significantly increase mdian survival time (MST) with respect to control. Noteworthy, intracranial injection of NU1025, immediately before the administration of 100 or 200 mg/kg Temozolomide, significantly increases lifespans with respect to controls or to groups treated with Temozolomide only. When Temozolomide is fractionated, the increase in lifespan (ILS) obtained with this schedule is higher than that observed when NU1025 is combined with a single injection of Temozolomide (statistical comparison of survival curves: NU1025 intracranially+Temozolomide 100 mg/kg×2 vs NU1025+Temozolomide 200 mg/kg; P=0.023)[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Temozolomide (TZM) is prepared in DMSO and stored, and then diluted with appropriate medium before use[1].[1]The murine lymphoma cell line L5178Y of DBA/2 (H-2^d/H-2^d) origin is cultured in RPMI-1640 containing 10% fetal calf serum and antibiotics. Inhibition of PARP is obtained by treating cells (10^5 cells/mL) with 8-hydroxy-2-methylquinazolin-4[^{3}H]-1 (NU1025), at a concentration (25 μM) that abrogates PARP activity. Cells are then exposed to Temozolomide (7.5-125 μM) and are cultured for 3 days. Cell growth is evaluated by counting viable cells in quadruplicate, and apoptosis is assessed by flow cytometry analysis of DNA content. Long-term survival is analyzed by colony-formation assay[1]. **Animal Administration:** Temozolomide (TZM) is dissolved in DMSO (40 mg/mL), diluted in saline (5 mg/mL) (Mice)[1].[1]Mice[1]

Male B6D2F1 (C57BL/6×DBA/2) mice are anesthetized with ketamine (100 mg/kg) and xylazine (5 mg/kg) in 0.9% NaCl solution (10 mL/kg intraperitoneally). L5178Y cells (10^4 in 0.03 mL RPMI-1640) are then injected intracranially, through the center-middle area of the frontal bone to a 2-mm depth, using a 0.1-mL glass microsyringe and a 27-gauge disposable needle. To evaluate tumor cell growth, brains are fixed in 10% phosphate-buffered formaldehyde, and histologic sections (5 μm) are cut along the axial plane, stained with hematoxylin-eosin, and analyzed by light microscopy. Temozolomide is dissolved in DMSO (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. Because cytotoxicity induced by Temozolomide and PARP inhibitors can be improved by fractionated modality of treatment, in selected groups a total dose of 200 mg/kg Temozolomide is divided in 2 doses of 100 mg/kg given on days 2 and 3.

References:

[1]. 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.

[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.

CAIndexNames:

Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo-

SMILES:

O=C(C1=C(N2C=N1)N=NN(C)C2=O)N

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