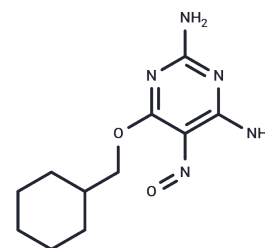


NU6027

Chemical Properties

CAS No. : 220036-08-8
 Formula: C₁₁H₁₇N₅O₂
 Molecular Weight: 251.29
 Appearance: no data available
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year



Biological Description

Description	NU6027 is a potent ATR/CDK inhibitor, inhibits CDK1/2, ATR and DNA-PK with K_i of 2.5 μ M/1.3 μ M, 0.4 μ M and 2.2 μ M, enter cells more readily than the 6-aminopurine-based inhibitors.
Targets(IC ₅₀)	ATM/ATR,CDK,DNA-PK
In vitro	NU6027 is soaked into crystals of monomeric CDK2 and the structure refined to a resolution of 1.85 Å. NU6027 (100 μ M) inhibits growth of human tumor cells with mean GI ₅₀ of 10 μ M. NU6027 causes a reduction in the number of cells in S-phase but not G1 or G2/M in MCF7 cells. [1] NU6027 is a potent inhibitor of cellular ATR activity with IC ₅₀ of 6.7 μ M in MCF7 cells and 2.8 μ M in GM847KD cells, and enhances hydroxyurea and cisplatin cytotoxicity in an ATR-dependent manner. NU6027 (10 μ M) inhibits CDK2-mediated pRbT821 by 42% and pCHK1S345 by 70%. NU6027 significantly potentiates sensitivity of cisplatin (1.4-fold at 4 μ M and 8.7-fold at 10 μ M), doxorubicin (1.3-fold at 4 μ M and 2.5-fold at 10 μ M), camptothecin (1.4-fold at 4 μ M and 2-fold at 10 μ M) and hydroxyurea (1.8-fold at 4 μ M) against MCF7 cells. NU6027 also potentiates 2 Gy IR in a concentration-dependent manner and the cytotoxicity of camptothecin and temozolomide (a DNA methylating agent) at concentrations above and below their LC ₅₀ . NU6027 (10 μ M) attenuates G2/M arrest following DNA damage, inhibits RAD51 focus formation and increases the cytotoxicity of the major classes of DNA-damaging anticancer cytotoxic therapy but not the antimitotic, paclitaxel in MCF7 cells. NU6027 (4 μ M) is synthetically lethal when DNA single-strand break repair is impaired either through poly(ADP-ribose) polymerase (PARP) inhibition or defects in XRCC1 in MCF7 cells. [3] NU6027 (4 μ M) increases the proportion of cell in early apoptosis to 7.5% after 48 hours treatment in EM-C11 cells compared to 1.73% in untreated cells. NU6027 (10 μ M) treatment reduces survival in XRCC1 deficient OVCAR-4 cells compared to proficient cells. NU6027 enhances cytotoxicity of cisplatin in XRCC1 deficient OVCAR-3 cells compared to XRCC1 proficient cells. NU6027 enhances Cisplatin induced DSB accumulation in XRCC1 deficient OVCAR-3 cells. [4]
Kinase Assay	Enzyme Inhibition Studies: Inhibition of cyclin B1/CDK1 is assayed using enzyme prepared from starfish oocytes. Inhibition of cyclinA3/CDK2 is determined using a similar assay and an assay buffer comprised of 50 mM Tris-HCl pH 7.5 containing 5 mM MgCl ₂ . The final ATP concentration in both CDK assays is 12.5 μ M, and the IC ₅₀ concentration for NU6027 is the concentration required to inhibit enzyme activity by 50% under the assay conditions used. To determine the K_m for ATP for cyclin B1/CDK1 and cyclin A3/CDK2, and K_i values for NU6027, assays are performed in the absence of

	NU6027 and at two fixed NU6027 concentrations (5 μ M and 10 μ M), with ATP concentrations ranging from 6.25 μ M to 800 μ M. Data are fitted to the Michaelis-Menten equation using unweighted nonlinear least squares regression.
Cell Research	The growth inhibitory activity of the NU6027 is evaluated in the NCI in vitro cell line panel using the standard 48 hours exposure assay and NU6027 concentrations ranging from 10^{-9} to 10^{-4} M. Relationships between the profile of cell growth inhibition produced by NU6027 and that of standard anticancer agents, and the established CDK inhibitors olomoucine and flavopiridol, is investigated using the COMPARE algorithm. (Only for Reference)

Solubility Information

Solubility	H ₂ O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 3 mg/mL (11.94 mM), Sonication is recommended. DMSO: 5.5 mg/mL (21.89 mM), Sonication is recommended. (< 1 mg/mL refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.9795 mL	19.8973 mL	39.7947 mL
5 mM	0.7959 mL	3.9795 mL	7.9589 mL
10 mM	0.3979 mL	1.9897 mL	3.9795 mL
50 mM	0.0796 mL	0.3979 mL	0.7959 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.

Reference

- Arris CE, et al. J Med Chem, 2000, 43(15), 2797-2804.
 Charrier JD, et al. J Med Chem, 2011, 54(7), 2320-2330.
 Peasland A, et al. Br J Cancer, 2011, 105(3), 372-381.
 Sultana R, et al. PLoS One, 2013, 8(2), e57098.

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