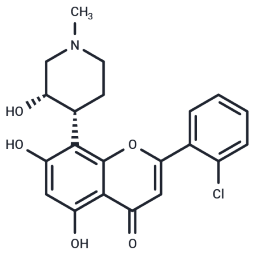
# Data Sheet (Cat.No.T6837)

TargetMol

## Flavopiridol

### Chemical Properties



CAS No. : 146426-40-6

Formula: C21H20ClNO5

Molecular Weight: 401.84

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

### Biological Description

| | |
|---|---|
| Description | Flavopiridol (Alvocidib) (Alvocidib) competes with ATP to inhibit CDKs including CDK1, CDK2, CDK4 and CDK6 with IC50 of ~ 40 nM. It is 7.5-fold more selective for CDK1, 2, 4, 6 versus CDK7. Flavopiridol is initially found to inhibit EGFR and PKA. Phase 1/2. |
| Targets(IC50) | Apoptosis,HIV Protease,CDK,Autophagy |
| In vitro | Flavopiridol displays less activity against unrelated kinases such as MAP, PAK, PKC, and EGFR with IC50 of >14 μM. Flavopiridol significantly inhibits the colony growth of HCT116, A2780, PC3, and Mia PaCa-2 cells with IC50 of 13 nM, 15 nM, 10 nM and 36 nM, respecitively. [1] Flavopiridol also potently inhibits the activity of Glycogen synthase kinase-3 (GSK-3) with an IC50 of 280 nm. [2] Compared with other CDKs, Flavopiridol inhibits the activity of CDK7 less potently with IC50 of 875 nM. Flavopiridol (0.5 μM) inhibits both pSer807/811 Rb and pThr199 NPM, whereas mild changes are observed at pThr821 Rb. Flavopiridol also decreases the overall RNA polymerase II level, as well as the phosphorylation of RNA polymerase II on the CTD repeats at Ser2 Ser5. [3] As a broad spectrum CDK inhibitor, Flavopiridol can inhibit cell cycle progression in either G1 or G2. Flavopiridol (0.3 μM) induces G1 arrest in either MCF-7 or MDA-MB-468 cells by inhibition of the CDK4 or CDK2 kinase activity. [4] Flavopiridol exhibits potent cytotoxicity against a wide variety of tumor cell lines with IC50 values ranging form 16 nM for LNCAP to 130 nM for K562. [5] |
| In vivo | Administration of Flavopiridol at 7.5 mg/kg for 7 days displays slight antitumor activity against P388 murine leukemia, resulting in %T/C value of 110, and active against the human A2780 ovarian carcinoma implanted sc in nude mice, producing 1.5 log cell kill (LCK). [5] Flavopiridol treatment at 1-2.5 mg/kg for 10 days significantly suppresses collagen-induced arthritis in mice in a dose-dependent manner, by inhibiting synovial hyperplasia and joint destruction, whereas serum concentrations of anti-collagen type II (CII) Abs and proliferative responses to CII are maintained. [6] In the p21-intact Hct116 xenografts in nude mice, administration of CPT-11 (100 mg/kg) followed by Flavopiridol (3 mg/kg) 7 and 16 hours later significantly inhibits tumor regression by 86% and 82%, respectively, displaying >2 fold inhibition compared with CPT-11 alone by 40 %. The combination produces ~30% complete response rate (CR) in contrast to CPT-11 alone where no CR is found. [7] |
| Kinase Assay | CDK kinase assay: For CDK1/cyclin B1 kinase assay, kinase reactions consist of 100 ng of baculovirus expressed GST-CDK1/cyclin B1 (human) complex, 1 μg histone HI, 0.2 μCi [γ-33P]ATP, 25 μM ATP in 50 μL kinase buffer (50 mM Tris, pH 8.0, 10 mM MgCl2, 1 mM EGTA, |

| | |
|---|---|
| Kinase Assay | 0.5 mM DTT). For CDK2/cyclin E kinase assay, kinase reactions consist of 5 ng of baculovirus expressed GST-CDK2/cyclin E (human) complex, 0.5 μg GST-RB fusion protein (amino acids 776-928 of retinoblastoma protein), 0.2 μCi [γ-33P]ATP, 25 μM ATP in 50 μL kinase buffer (50 mM Hepes, pH 8.0, 10 mM MgCl2, 1 mM EGTA, 2 mM DTT). For CDK4/cyclin D1 kinase assay, kinase reactions consist of 150 ng of baculovirus expressed GST-CDK4/cyclin D1 (human), 280 ng of Stag-cyclin D1, 0.5 μg GST-RB fusion protein (amino acids 776-928 of retinoblastoma protein), 0.2 μCi [γ-33P]ATP, 25 μM ATP in 50 μL kinase buffer (50 mM Hepes, pH 8.0, 10 mM MgCl2, 1 mM EGTA, 2 mM DTT). Reactions are incubated for 45 minutes for CDK1 and CDK2, or 1 hour for CDK4 at 30 °C and stopped by the addition of cold trichloroacetic acid (TCA) to a final concentration 15%. TCA precipitates are collected onto GF/C unifilter plates using a Filtermate universal harvester and the filters are quantitated using a TopCount 96-well liquid scintillation counter. Flavopiridol is dissolved at 10 mM in dimethylformamide (DMF) and evaluated at six concentrations, each in triplicate. The final concentration of DMF in the assay = 2%. IC50 values are derived by nonlinear regression analysis and have a coefficient of variance = 16%. To assay Flavopiridol activity on CDK6, a filter-binding assay is established. The following are combined in the reaction mixture: 2 μL of CDK6 (0.7 mg/μL), 5 μL of histone H1 (6 mg/mL), 14 μL of kinase buffer (60 mM β-glycerophosphate, 30 mM p-nitrophenyl phosphate, 25 mM MOPS (pH 7.0), 5 mM EGTA, 15 mM MgCl2, 1 mM DTT, 0.1 mM Na-vanadate), 3 μL of increasing concentrations of Flavopiridol diluted in 50% DMSO, and 6 μL of 33P-ATP (1 mCi/mL) in nonradioactive ATP at 90 μM concentration (final concentration: 15 μM). The assay is initiated by the addition of 33P-ATP. The reaction is incubated for 20 minutes at 30°C. A 25 μL aliquot of the supernatant is then spotted onto Whatman P81 phosphocellulose paper. Filters are washed 5 times with 1% phosphoric acid solution. Wet filters are counted in the presence of 1 mL of scintillation fluid. Cdk9 activity is measured using 50 nM of recombinant Cdk9/cyclin T in 50 mM HEPES pH 7.5, 10 mM MgCl2, 1 mM DTT, 3 μM Na3VO4, 150 μM RNA polymerase CDT peptide and 80 μM ATP. Cdk7 assay is performed in the same buffer using 37 nM of purified kinase in the presence of 200 μM ATP and 10 μM myelin binding protein as a substrate. The potency of Flavopiridol toward CDK9 and CDK7 is determined using either a strong anion exchanger (Dowex 1-X8 resin, formate form)-based assay or a scintillation proximity assay. IC50 values are calculated from the dose-response curves. |
| Cell Research | Cells are exposed to various concentrations of Flavopiridol for 72 hours at which time the tetrazolium dye, MTS in combination with phenazine methosulfate, is added. After 3 hours, the absorbency is measured at 492 nm, which is proportional to the number of viable cells. The results are expressed as IC50 values. For cell Cycle analysis, cells are fixed in paraformaldehyde and ethanol, washed, resuspended in staining solution of TdT enzyme and FITC-dUTP, washed, stained with PI following RNase treatment, and then analyzed by flow cytometry. (Only for Reference) |

## Solubility Information

| | |
|---|---|
| Solubility | DMSO: 34 mg/mL (84.61 mM),Sonication is recommended.<br>Ethanol: 8 mg/mL (19.91 mM),Sonication is recommended.<br>H2O: < 1 mg/mL (insoluble or slightly soluble),<br>(< 1 mg/ml refers to the product slightly soluble or insoluble) |
| In vivo Formulation | 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.98 mM),Sonication is recommended.<br>*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* |

| | |
|---|---|
| In vivo Formulation | *vary and should be modified based on specific experimental conditions.* |

Preparing Stock Solutions

| | 1mg | 5mg | 10mg |
|---|---|---|---|
| 1 mM | 2.4886 mL | 12.4428 mL | 24.8855 mL |
| 5 mM | 0.4977 mL | 2.4886 mL | 4.9771 mL |
| 10 mM | 0.2489 mL | 1.2443 mL | 2.4886 mL |
| 50 mM | 0.0498 mL | 0.2489 mL | 0.4977 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

Kim KS, et al. J Med Chem, 2000, 43(22), 4126-4134.
Zhang G M, Huang S S, Ye L X, et al. Reciprocal positive regulation between BRD4 and YAP in GNAQ-mutant uveal melanoma cells confers sensitivity to BET inhibitors. Pharmacological Research. 2022: 106464.
Wang J, Luo L, Ding Q, et al. Development of a Multi-Target Strategy for the Treatment of Vitiligo via Machine Learning and Network Analysis Methods. Frontiers in pharmacology. 2021, 12.
Lu H, et al. J Med Chem, 2005, 48(3), 737-743.
Montagnoli A, et al. Nat Chem Biol, 2008, 4(6), 357-365.
Jiang L, Yu Y, Li Z, et al.BMS-265246, a Cyclin-Dependent Kinase Inhibitor, Inhibits the Infection of Herpes Simplex Virus Type 1.Viruses.2023, 15(8): 1642.
Carlson BA, et al. Cancer Res, 1996, 56(13), 2973-2978.
Kim KS, et al. J Med Chem, 2002, 45(18), 3905-3927.



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