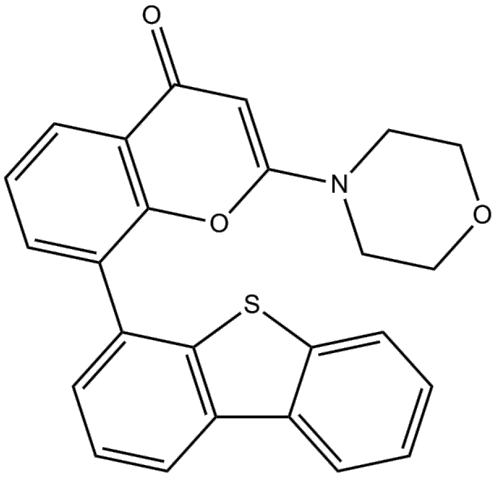
Product Data Sheet

Product Name: NU7441 (KU-57788)
Cat. No.: GC11251

Chemical Properties

Cas. No.	503468-95-9		
Chemical Name	8-dibenzothiophen-4-yl-2-morpholin-4-ylchromen-4-one		
SMILES	C1COCCN1C2=CC(=O)C3=C(O2)C(=CC=C3)C4=CC=CC5=C4SC6=CC=CC=C56		
Formula	$C_{25}H_{19}NO_3S$	M.Wt	413.49
Solubility	≥ 4.13mg/mL in DMSO, <2.48 mg/mL in EtOH, <2.56 mg/mL in Water	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	HepG2 cells
Preparation Method	HepG2 cells (4000 per well) were cultured in a 96-well plate for 24h. Once the cells completed the attachment, 0.1, 1, 5, and 10μM of NU7441 were added to the culture media. After 12h of NU7441 treatment, 10% CCK-8 solution was added into the culture media, and the incubation continued for 2h. OD450 values were determined by a spectrometer, and the results were analyzed to measure the cell growth.
Reaction Conditions	0.1, 1, 5, and 10μM;12h
Applications	NU7441 inhibits the growth of HepG2 cells in a dose- and time-dependent manner.

Animal experiment [2]:

Animal models	Female BALB/c mice

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Preparation Method	Female BALB/c mice, 6 weeks old and (18±2) g weight were divided into 4 groups equally and randomly: normal group, asthmatic group (OVA group), asthmatic mice treated with NU7441 (NU group), and asthmatic mice treated with vehicle for NU7441 (OVA+vehicle group). Mice were sensitized with 100 μL sensitization liquid [20μg ovalbumin (OVA) and 3mg $Al(OH)_3$ emulsified in saline] per mice by intraperitoneally on days 0, 7, 14, and challenged with 1% OVA aerosol for 30min from days 21. The normal group was sensitized and challenged with saline instead of OVA. NU7441 at dose of 10mg/kg or vehicle (5% DMSO) was administered intraperitoneally once a day on days 21 to days 30, 30min after OVA challenge.
Dosage form	10mg/kg/day for 10 days; i. p.
Applications	The OVA-exposed group had obvious airway inflammation characteristics, and NU7441 significantly reduced inflammatory cell infiltration and ciliary damage. In addition, NU7441 aggravated the degree of DNA damage in the airways of asthmatic mice.

References:

[1]Yang C, Wang Q, Liu X, et al. NU7441 enhances the radiosensitivity of liver cancer cells[J]. Cellular Physiology and Biochemistry, 2016, 38(5): 1897-1905.

[2]Wang Y, Lin J, Shu J, et al. Oxidative damage and DNA damage in lungs of an ovalbumin-induced asthmatic murine model[J]. Journal of Thoracic Disease, 2018, 10(8): 4819.

Background

NU7441 (KU-57788) is a highly potent and selective DNA-dependent protein kinase (DNA-PK) inhibitor with an IC_{50} of 13nM[1]. NU7441 also inhibits phosphatidylinositol 3-kinase (PI3K) and

mammalian target of rapamycin (mTOR) with IC_{50} of 5.0 and 1.7μM, respectively[2]. NU7441 is an inhibitor of the non-homologous end joining (NHEJ) pathway[3].

In vitro, NU7441 (0.1-10μM) treatment of human hepatocellular carcinoma HepG2 cells for 72h dose- and time-dependently inhibited cell proliferation, reduced cellular pDNA-PKcs (S2056) protein expression, increased G2/M phase arrest of the cell cycle and induced apoptosis[4]. NU7441 (0.5-10μM) treatment of human oral squamous cell carcinoma cell lines (HSC2 and HSC2-R cells) for 0-48h significantly enhanced 6Gy X-ray irradiation-induced apoptosis and abolished colony formation in both cell lines[5].

In vivo, NU7441 (10mg/kg/day) was treated by intraperitoneal injection for 10 days in ovalbumin-induced asthmatic mice, which aggravated the degree of DNA damage in the mouse airways, but inhibited the infiltration of inflammatory cells and the level of inflammatory cytokines in the lungs[6]. NU7441 (5mg/kg) was treated by intratracheal administration in acute lung injury (ALI) mice, which significantly reduced pulmonary edema and reduced the production of inflammatory cytokines in bronchoalveolar lavage fluid (BALF)[7].

References:
[1] Hardcastle I R, Cockcroft X, Curtin N J, et al. Discovery of potent chromen-4-one inhibitors of the DNA-dependent protein kinase (DNA-PK) using a small-molecule library approach[J]. Journal of medicinal chemistry, 2005, 48(24): 7829-7846.
[2] Ma C C, Li H, Wan R Z, et al. Developments of DNA-dependent protein kinase inhibitors as anticancer agents[J]. Mini Reviews in Medicinal Chemistry, 2014, 14(11): 884-895.
[3] Iglesias-Corral D, García-Valles P, Arroyo-Garrapucho N, et al. Chloroquine-induced DNA damage synergizes with DNA repair inhibitors causing cancer cell death[J]. Frontiers in Oncology, 2024, 14.
[4] Yang C, Wang Q, Liu X, et al. NU7441 enhances the radiosensitivity of liver cancer cells[J]. Cellular Physiology and Biochemistry, 2016, 38(5): 1897-1905.
[5] Ohuchi K, Saga R, Hasegawa K, et al. DNAPKcs phosphorylation specific inhibitor, NU7441, enhances the radiosensitivity of clinically relevant radioresistant oral squamous cell carcinoma cells[J]. Biomedical Reports, 2023, 18(4): 1-8.
[6] Wang Y, Lin J, Shu J, et al. Oxidative damage and DNA damage in lungs of an ovalbumin-induced asthmatic murine model[J]. Journal of Thoracic Disease, 2018, 10(8): 4819.

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[7] Pyakurel K, Ghonim M, Ibba S, et al. DNA-Dependent Protein Kinase Inhibition Prevents Manifestation of Acute Lung Injury in Mice, a Novel Target Associated with Th1 Type Disease[J]. The FASEB Journal, 2016, 30: 1202.4-1202.4.

Caution: Product has not been fully validated for medical applications. For research use only.
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