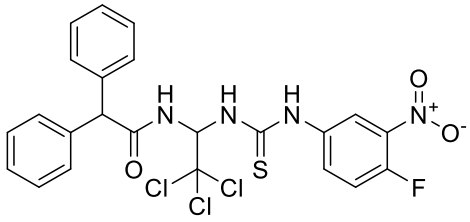
Product data sheet

MedKoo Cat#: 406386 Name: CGK733 CAS#: 905973-89-9 Chemical Formula: $C_{23}H_{18}Cl_3FN_4O_3S$ Exact Mass: 554.01492 Molecular Weight: 555.84	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

CGK733 is an ATM inhibitor and ATR inhibitor, which significantly enhanced taxol-induced cytotoxicity in HBV-positive HepG2.2.15 cells. The mechanism lies in CGK733 triggers the formation of multinucleated cells thus promotes the premature mitotic exit of taxol-induced mitotic-damaged cells through multinucleation and mitotic catastrophe in HBV-positive HepG2.2.15 cells. These results suggest that CGK733 could potentially reverse the taxol resistance in HBV-positive HCC cells and may suggest a novel strategy to treat HBV-infected HCC patients.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	100	179.91

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.80 mL	9.00 mL	17.99 mL
5 mM	0.36 mL	1.80 mL	3.60 mL
10 mM	0.18 mL	0.90 mL	1.80 mL
50 mM	0.04 mL	0.18 mL	0.36 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Wang H, Zuo B, Wang H, Ren L, Yang P, Zeng M, Duan D, Liu C, Li M. CGK733 enhances multinucleated cell formation and cytotoxicity induced by taxol in Chk1-deficient HBV-positive hepatocellular carcinoma cells. Biochem Biophys Res Commun. 2012 May 25;422(1):103-8. doi: 10.1016/j.bbrc.2012.04.115. Epub 2012 Apr 30. PMID: 22564734.

2. Alao JP, Sunnerhagen P. The ATM and ATR inhibitors CGK733 and caffeine suppress cyclin D1 levels and inhibit cell proliferation. Radiat Oncol. 2009 Nov 10;4:51. doi: 10.1186/1748-717X-4-51. PMID: 19903334; PMCID: PMC2777912.

In vivo study

1. Williams TM, Nyati S, Ross BD, Rehemtulla A. Molecular imaging of the ATM kinase activity. Int J Radiat Oncol Biol Phys. 2013 Aug 1;86(5):969-77. doi: 10.1016/j.ijrobp.2013.04.028. Epub 2013 May 29. PMID: 23726004; PMCID: PMC3710537.

7. Bioactivity

Biological target:

CGK 733 is a potent and selective inhibitor of ATM/ATR with IC50 of ~200 nM.

Product data sheet

In vitro activity

CGK733, a small molecule inhibitor reportedly targeting the kinase activities of ATM and ATR, significantly enhanced taxol-induced cytotoxicity in HBV-positive HepG2.2.15 cells. The mechanism lies in CGK733 triggers the formation of multinucleated cells thus promotes the premature mitotic exit of taxol-induced mitotic-damaged cells through multinucleation and mitotic catastrophe in HBV-positive HepG2.2.15 cells. These results suggest that CGK733 could potentially reverse the taxol resistance in HBV-positive HCC cells and may suggest a novel strategy to treat HBV-infected HCC patients.

Reference: Biochem Biophys Res Commun. 2012 May 25;422(1):103-8. https://linkinghub.elsevier.com/retrieve/pii/S0006-291X(12)00797-8

In vivo activity

In order to confirm the functionality of ATM reporter in vivo, D54-ATMR tumors were established in nude mice and treated with DMSO (control), CGK733 or KU-55933 (both 25 mg/kg) and monitored bioluminescence over time. We observed significant increases in reporter activation in a time-dependent fashion in response to both KU-55933 and CGK733 treatment (Fig. 6A, 6B). There was an immediate increase in reporter activation 1 hour after injection, which was sustained and maximal at 4 hours. However, KU-55933 was markedly more effective in inducing reporter activation compared to CGK733 given at the same dose and method of administration. With KU-55933 treatment, reporter activation increased 9.0-fold at 1 and 4 hours, before dropping down to 4.2-fold at 8 hours after injection. The differences were statistically significant at all time-points compared to vehicle treated mice. CGK733 also induced increases in reporter activity over control mice, with 2.4-fold, 3.1-fold, and 1.3-fold changes observed at 1, 4, and 8 hours, respectively. Although both the 1 hour and 4 hour treatment with CGK733 treatment were significantly different from control mice, the 8 hour values returned to near control levels. The observed persistent inhibition of ATM in-vivo compared to the in vitro data is likely due to the drug being injected in the peritoneum, which is slowly and continually absorbed into the bloodstream over hours, thus creating prolonged ATM inhibition in tumors.

Reference: Int J Radiat Oncol Biol Phys. 2013 Aug 1;86(5):969-77. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23726004/