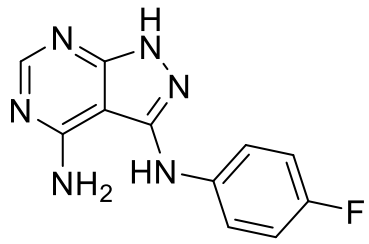
Product data sheet

MedKoo Cat#: 407307 Name: CGP-57380 CAS#: 522629-08-9 Chemical Formula: $C_{11}H_9FN_6$ Exact Mass: 244.0873 Molecular Weight: 244.2334	
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:
CGP-57380 is a selective inhibitor of MAP kinase-interacting kinase 1 (MNK1) in vitro (IC50 = 2.2 μM). MNK1 overexpression was confirmed in both primary GBMs and glioma cell lines. Inhibition of MNK1 activity in GBM cells by the small molecule CGP57380 suppressed eIF4E phosphorylation, proliferation, and colony formation whereas concomitant treatment with CGP57380 and the mTOR inhibitor rapamycin accentuated growth inhibition and cell-cycle arrest.

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	6	24.57

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	4.09 mL	20.47 mL	40.94 mL
5 mM	0.82 mL	4.09 mL	8.19 mL
10 mM	0.41 mL	2.05 mL	4.09 mL
50 mM	0.08 mL	0.41 mL	0.82 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. Lim S, Saw TY, Zhang M, Janes MR, Nacro K, Hill J, Lim AQ, Chang CT, Fruman DA, Rizzieri DA, Tan SY, Fan H, Chuah CT, Ong ST. Targeting of the MNK-eIF4E axis in blast crisis chronic myeloid leukemia inhibits leukemia stem cell function. Proc Natl Acad Sci U S A. 2013 Jun 18;110(25):E2298-307. doi: 10.1073/pnas.1301838110. Epub 2013 Jun 4. PMID: 23737503; PMCID: PMC3690864.

2. Chrestensen CA, Eschenroeder A, Ross WG, Ueda T, Watanabe-Fukunaga R, Fukunaga R, Sturgill TW. Loss of MNK function sensitizes fibroblasts to serum-withdrawal induced apoptosis. Genes Cells. 2007 Oct;12(10):1133-40. doi: 10.1111/j.1365-2443.2007.01122.x. PMID: 17903173.

In vivo study

1. Lim S, Saw TY, Zhang M, Janes MR, Nacro K, Hill J, Lim AQ, Chang CT, Fruman DA, Rizzieri DA, Tan SY, Fan H, Chuah CT, Ong ST. Targeting of the MNK-eIF4E axis in blast crisis chronic myeloid leukemia inhibits leukemia stem cell function. Proc Natl Acad Sci U S A. 2013 Jun 18;110(25):E2298-307. doi: 10.1073/pnas.1301838110. Epub 2013 Jun 4. PMID: 23737503; PMCID: PMC3690864.

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7. Bioactivity

Biological target:

CGP 57380 is a cell-permeable pyrazolo-pyrimidine compound that acts as a selective inhibitor of Mnk1 with IC50 of 2.2 μM, but has no inhibitory activity against p38, JNK1, ERK1/2, PKC, or Src-like kinases.

In vitro activity

It was found that MNK inhibition with CGP57380 decreased eIF4E phosphorylation and prevented the eIF4E mediated increase in nuclear β-catenin in K562-eIF4EWT but not K562-eIF4ES209D cells (Fig. 4 A and B). In reporter assays, CGP57380 abolished β-catenin activity in K562-eIF4EWT but not K562-eIF4ES209D cells, whereas cercosporin (a positive control for Wnt inhibition that acts directly to disrupt TCF/β-catenin complexes) eliminated activity in both cell lines (Fig. 4C). CGP57380 treatment also reduced transcript levels of several Wnt target genes (LEF1, AXIN2, and CYCLIND1) in K562-eIF4EWT but not K562-eIF4ES209D (Fig. 4D). The ability of CGP57380 to inhibit eIF4E phosphorylation and β-catenin signaling in primary BC GMPs was assessed. The primary CD34+ BC cells were sorted to obtain the HSC and GMP fractions and were treated with CGP57380 or imatinib (IM). It was found that CGP57380 effectively inhibited eIF4E phosphorylation as well as β-catenin activation, whereas IM was unable to prevent either despite inhibition of BCR-ABL1 (as readout by CrkL phosphorylation; Fig. 4 J and K).

Reference: Proc Natl Acad Sci U S A. 2013 Jun 18;110(25):E2298-307. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23737503/

In vivo activity

Findings suggested that MNK inhibition might effectively control BC CML because it extinguishes BC LSC function in vitro. To test this possibility in an in vivo BC model, the effect of CGP57380 on the ability of BC GMPs to serially transplant immunodeficient nonobese diabetic/SCID IL2Rγ-deficient mice [NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice] was investigated. In preliminary studies, it was found that a brief 48-h in vitro exposure to CGP57380 was able to delay the engraftment of BC LSCs in NSG mice, as well as reduce the leukemia cell burden in engrafted animals (Fig. S7 A and B), while leaving the normal CD34+ cell engraftment untouched (Fig. S7 C and D). These results encouraged a determination if the self-renewing capacity of BC LSCs could be targeted in vivo by small-molecule MNK inhibitors. Here, we FACS-sorted GMPs from a BC sample as previously described (6), and injected them intrafemorally into 8- to 12-wk-old female NSG mice (Fig. S8A). At 6 wk posttransplantation, engrafted mice were treated for 3 wk with DMSO, CGP57380, or dasatinib (n = 5 mice per treatment group). At the end of the treatment period, all the mice were killed, and human cells were obtained from hematopoietic tissues by using immunomagnetic beads. No difference in the percentage of CD45+ human cells in the peripheral blood or BM of each of the treatment groups was found (Fig. 6A). However, it was observed that dasatinib and CGP57380 had specific activity against committed BC progenitors, as they significantly reduced the number of colony forming units detected in BM ($P \leqslant 0.05$ and $P \leqslant 0.005$, respectively) compared with control, although the effect of CGP57380 was greater (Fig. 6B).

Reference: Proc Natl Acad Sci U S A. 2013 Jun 18;110(25):E2298-307. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23737503/