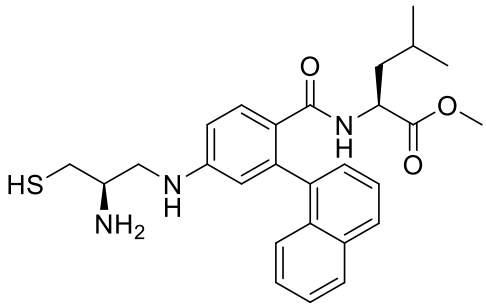
Product data sheet

MedKoo Cat#: 206801 Name: GGTI-298 free base CAS#: 180977-44-0 (free base) Chemical Formula: $C_{27}H_{33}N_3O_3S$ Exact Mass: 479.22426 Molecular Weight: 479.63422	
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:

GGTI-298 is a potent geranylgeranyltransferase-I (GGTase-I) inhibitor with potential antitumor actrivity. GGTI-298 disrupts MAP kinase activation and G(1)-S transition in Ki-Ras-overexpressing transformed adrenocortical cells. GGTI-298 induces hypophosphorylation of retinoblastoma and partner switching of cyclin-dependent kinase inhibitors. A potential mechanism for GGTI-298 antitumor activity. GGTI-298 arrests human tumor cells in G0/G1 and induces p21(WAF1/CIP1/SDI1) in a p53-independent manner. GGTI-298 induces G0-G1 block and apoptosis whereas FTI-277 causes G2-M enrichment in A549 cells.

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	100.0	208.49

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.08 mL	10.42 mL	20.85 mL
5 mM	0.42 mL	2.08 mL	4.17 mL
10 mM	0.21 mL	1.04 mL	2.08 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Chen S, Fu L, Raja SM, Yue P, Khuri FR, Sun SY. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis. Mol Cancer. 2010 Jan 29;9:23. doi: 10.1186/1476-4598-9-23. PMID: 20113484; PMCID: PMC2824632.
2. Vogt A, Sun J, Qian Y, Hamilton AD, Sebti SM. The geranylgeranyltransferase-I inhibitor GGTI-298 arrests human tumor cells in G0/G1 and induces p21(WAF1/CIP1/SDI1) in a p53-independent manner. J Biol Chem. 1997 Oct 24;272(43):27224-9. doi: 10.1074/jbc.272.43.27224. PMID: 9341167.

In vivo study

1. Lau CP, Wong KC, Huang L, Li G, Tsui SK, Kumta SM. A mouse model of luciferase-transfected stromal cells of giant cell tumor of bone. Connect Tissue Res. 2015 Nov;56(6):493-503. doi: 10.3109/03008207.2015.1075519. Epub 2015 Sep 1. PMID: 26327464.

7. Bioactivity

Biological target:

Product data sheet

GGTI298 is a CAAZ peptidomimetic geranylgeranyltransferase I (GGTase I) inhibitor, strongly inhibiting the processing of geranylgeranylated Rap1A with little effect on processing of farnesylated Ha-Ras, with IC_{50} values of 3 and > 20 μM in vivo, respectively.

In vitro activity

GGTI-298 was previously shown to induce G1 arrest and apoptosis in A549 lung cancer cells. The effects of GGTI-298 were examined on cell growth and induction of apoptosis in a panel of human NSCLC cell lines. After a 3-day exposure, GGTI-298 exhibited concentration-dependent effects on decreasing the cell numbers of 6 NSCLC cell lines tested, with IC50s ranging between 2 to 10 μM, indicating that GGTI-298 effectively inhibits the growth of human NSCLC cells. Among these cell lines, the H226 cell line was the least sensitive to GGTI-298 (Fig. 1A). By Annexin V staining, an increase was detected in the number of apoptotic cells as well as necrotic cells in the four tested cell lines (i.e., A549, Calu-1, H157 and H226) exposed to GGTI-298 for 48 h, demonstrating that GGTI-298 induces cell death, particularly apoptotic cell death. Similarly, the least apoptotic cells were detected in H226 cells treated with GGTI-298, indicating that H226 cells were less sensitive to GGTI-298-induced apoptosis (Fig. 1B). In agreement with previous reports, it was found that GGTI-298 also induced G1 arrest in these NSCLC cell lines (data not shown).

Reference: Mol Cancer. 2010 Jan 29;9:23. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/20113484/

In vivo activity

Eight mice per group were treated with either 0.9% saline (Control) or GGTI-298 (1.16 mg/kg) at day 3 post cell transplantation, to determine the effects of in both the subcutaneous and intraoessous models. Tumor growth under the dorsal skin and in the tibiae were monitored by BLI twice per week from day 3 (before drug administration) to day 35 (Figure 5A). The dorsal skin and the tibia samples were harvested on day 35 post cell transplantation to double check the presence of the Luc-G33 cells and the histological changes of the cells if any. GGTI-298 single treatment resulted in no significant reduction in tumor cell viability in the subcutaneous model (Figure 5B).

Reference: Connect Tissue Res. 2015 Nov;56(6):493-503. https://www.tandfonline.com/doi/full/10.3109/03008207.2015.1075519

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.