

Product Data Sheet

Product Name: Piperlongumine

Cat. No.: GC10282

Chemical Properties

Cas. No. 20069-09-4

Chemical Name 1-[(E)-3-(3,4,5-trimethoxyphenyl)prop-2-enoyl]-2,3-dihydropyridin-6-one

SMILES COC1=CC(=CC(=C1OC)OC)C=CC(=O)N2CCC=CC2=O

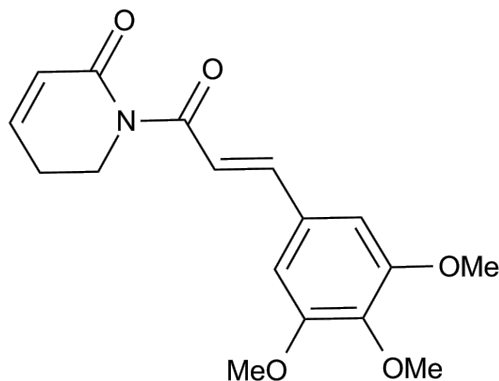
Formula $C_{17}H_{19}NO_5$ M.Wt 317.34

Solubility $\geq 10.45\text{mg/mL}$ in DMSO 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]:

Cell lines U937 cells

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

U937 cells ($2.5-5.0 \times 10^4$ cells/200 μ L of RPMI-1640 medium/well) were seeded in 96-well tissue culture plates and incubated with Piperlongumine (0-20 μ M) for 48h. MTT assay for measuring cell viability.

Reaction Conditions 0-20 μ M; 48h

Applications Piperlongumine could suppress the proliferation of U937 cells in a time- and dose-dependent manner.

Animal experiment [2]:

Animal models Nude BALB/c mice

Preparation Method Tumors were established by subcutaneous injection of 5×10^6 BxPC-3 cells into the flanks of mice. When tumors reached around 100mm³, the mice were randomly assigned to four groups: (i) control (DMSO was dissolved in 200 μ L PBS, once daily by i.p. injection); (ii) Piperlongumine (10mg/kg, once daily by i.p. injection); (iii) Gemcitabine (100mg/kg, twice weekly by i.p. injection); and (iv) Piperlongumine and Gemcitabine, following the same schedule of individual drugs. The mice were closely monitored for 24 days, then euthanized, and the tumors were removed. Each tumor was divided into two pieces: one fixed in 10% buffered formalin, and the other kept at -80°C for further analysis.

Dosage form 10mg/kg/day for 24 days; i.p.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications Piperlongumine alone can significantly inhibit tumor growth. Piperlongumine combined with Gemcitabine is more effective in reducing tumor burden.

References:

- [1]Wang H, Wang Y, Gao H, et al. Piperlongumine induces apoptosis and autophagy in leukemic cells through targeting the PI3K/Akt/mTOR and p38 signaling pathways[J]. *Oncology Letters*, 2018, 15(2): 1423-1428.
- [2]Wang Y, Wu X, Zhou Y, et al. Piperlongumine suppresses growth and sensitizes pancreatic tumors to gemcitabine in a xenograft mouse model by modulating the NF-kappa B pathway[J]. *Cancer Prevention Research*, 2016, 9(3): 234-244.

Background

Piperlongumine is a natural alkaloid compound extracted from *Piper longum L.*, which has multiple pharmacological activities, including anti-tumor, lipid metabolism regulation, anti-platelet aggregation and analgesic activities^[1, 2]. Piperlongumine directly binds to and inhibits the antioxidant enzyme glutathione S-transferase Pi 1, leading to increased ROS levels in cancer cells and inducing cell apoptosis, while having no obvious toxicity to normal cells^[3].

In vitro, treatment of leukemia U937 cells with Piperlongumine (0-20 μ M) for 48h inhibited cell proliferation in a time- and dose-dependent manner, induced cell apoptosis, increased the expression of intracellular anti-microtubule-associated protein 1A/1B-light chain 3 (LC3-I), and reduced the intracellular protein kinase B (Akt) level^[4]. Piperlongumine (0-20 μ M) treatment of prostate cancer PC-3 cells, breast cancer MCF-7 cells and renal cancer 786-O cells induced cell autophagy, reduced the phosphorylation levels of intracellular Akt effectors, GSK-3 β and TSC2, and led to increased intracellular ROS production^[5]. Piperlongumine (0-5 μ M) treatment of thyroid cancer cell lines (IHH-4, WRO, 8505c and KMH-2 cells) for 24h and 48h inhibited the growth of all cells in a dose- and time-dependent manner, significantly reduced colony formation, and induced G2/M phase arrest and apoptosis^[6].

In vivo, Piperlongumine (10mg/kg) was treated by intraperitoneal injection in BxPC-3 cell xenograft mice for 24 days, which significantly inhibited tumor growth, reduced microvascular density in

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

pancreatic tumor tissues and induced cell apoptosis, and eliminated the increase in NF- κ B activity in pancreatic tumor tissues induced by Gemcitabine^[7]. Piperlongumine (50mg/kg/day) was treated orally in aged mice for 8 weeks, which significantly improved the novel object recognition and nesting behavior of aged mice, and increased the levels of calmodulin-dependent protein kinase II α (CaMKII α) and extracellular signal-regulated kinase 1/2 (ERK1/2) in the hippocampus^[8].

References:

- [1] Piska K, Gunia-Krzyżak A, Koczurkiewicz P, et al. Piperlongumine (piplartine) as a lead compound for anticancer agents—Synthesis and properties of analogues: A mini-review[J]. European journal of medicinal chemistry, 2018, 156: 13-20.
- [2] Martha Perez Gutierrez R, Maria Neira Gonzalez A, Hoyo-Vadillo C. Alkaloids from piper: a review of its phytochemistry and pharmacology[J]. Mini Reviews in Medicinal Chemistry, 2013, 13(2): 163-193.
- [3] Chen Y J, Kuo C C, Ting L L, et al. Piperlongumine inhibits cancer stem cell properties and regulates multiple malignant phenotypes in oral cancer[J]. Oncology letters, 2018, 15(2): 1789-1798.
- [4] Wang H, Wang Y, Gao H, et al. Piperlongumine induces apoptosis and autophagy in leukemic cells through targeting the PI3K/Akt/mTOR and p38 signaling pathways[J]. Oncology Letters, 2018, 15(2): 1423-1428.
- [5] Makhov P, Golovine K, Teper E, et al. Piperlongumine promotes autophagy via inhibition of Akt/mTOR signalling and mediates cancer cell death[J]. British journal of cancer, 2014, 110(4): 899-907.
- [6] Kung F P, Lim Y P, Chao W Y, et al. Piperlongumine, a potent anticancer phytotherapeutic, induces cell cycle arrest and apoptosis in vitro and in vivo through the ROS/Akt pathway in human thyroid cancer cells[J]. Cancers, 2021, 13(17): 4266.
- [7] Wang Y, Wu X, Zhou Y, et al. Piperlongumine suppresses growth and sensitizes pancreatic tumors to gemcitabine in a xenograft mouse model by modulating the NF-kappa B pathway[J]. Cancer Prevention Research, 2016, 9(3): 234-244.
- [8] Go J, Park T S, Han G H, et al. Piperlongumine decreases cognitive impairment and improves hippocampal function in aged mice[J]. International Journal of Molecular Medicine, 2018, 42(4): 1875-1884.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA