

Product Data Sheet

Product Name: SHP099
Cat. No.: GC44887

Chemical Properties

Cas. No. 1801747-42-1

SMILES C1C=C(Cl)C(C2=NC=C(N3CCC(C)(N)CC3)N=C2N)=CC=C1

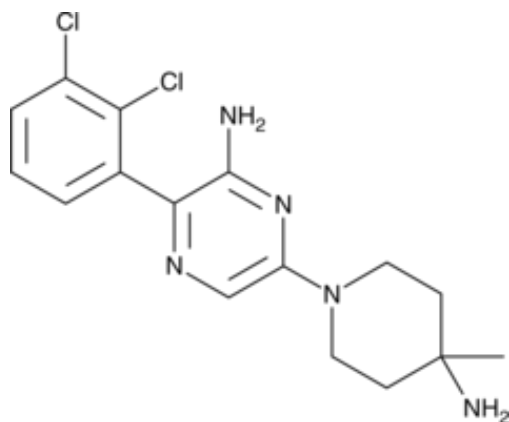
Formula C₁₆H₁₉Cl₂N₅ M.Wt 352.3

Solubility DMF: 30 mg/ml, DMSO: 30 mg/ml, DMSO: PBS (pH 7.2) (1:2): 0.33 mg/ml, Ethanol: 10 mg/ml
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 PC9 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

Preparation Method The PC9 cells were all cultured in Dulbecco's Modified Eagle Medium (DMEM) containing 10% fetal bovine serum (FBS), 100U/mL penicillin and 100mg/mL streptomycin. The cells were cultured at 37°C and 5% CO₂. 2×10^3 cells were inoculated into each well of a 96-well plate, and 200μL of the medium was added to each well. The cells were incubated with different concentrations of SHP099 (0, 0.625, 1.25, 2.5, 5, 10, and 20μM) for 24h. 50μL of MTT solution was added to the bottom of each well, and the cells were incubated for 4 hours. The absorbance was measured at 490nm using a microplate reader.

Reaction Conditions 0, 0.625, 1.25, 2.5, 5, 10, and 20μM; 24h

Applications SHP099 significantly inhibited the viability of PC9 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Female BALB/c mice

Preparation Method Female BALB/c mice (6-8 weeks old) were housed in a specific pathogen-free (SPF) facility with a 12-hour daily cycle, and had free access to food and water. CT-26 cells were inoculated subcutaneously into BALB/c mice (1×10^6). The tumor size was measured every day after inoculation, and tumor size was calculated as $0.5 \times \text{length} \times \text{width}^2$. Mice with similar tumor sizes were randomly divided into 5 groups and received PBS, 5-Fu, or SHP099. SHP099 was administered intraperitoneally at 5mg/kg daily, and anti-PD-1 antibody was administered intraperitoneally at 5mg/kg every 3 days. After 17 days, the mice were sacrificed and the tumor tissues were collected for analysis.

Dosage form 5mg/kg/day for 17 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 SHP099 treatment inhibited the tumor growth of CT-26 cell xenograft BALB/c mice, and caused the shrinking, sparse arrangement and fragmentation of tumor cells.

References:

- [1] Xia L, Yang F, Wu X, et al. SHP2 inhibition enhances the anticancer effect of Osimertinib in EGFR T790M mutant lung adenocarcinoma by blocking CXCL8 loop mediated stemness[J]. Cancer Cell International, 2021, 21(1): 337.
- [2] Zhao M, Guo W, Wu Y, et al. SHP2 inhibition triggers anti-tumor immunity and synergizes with PD-1 blockade[J]. Acta Pharmaceutica Sinica B, 2019, 9(2): 304-315.

Background

SHP099 is a highly potent, selective, orally bioavailable SHP2 inhibitor, with an IC₅₀ value of 0.071 μM [1]. SHP099 concurrently binds to the interface of the N-terminal SH2, C-terminal SH2, and protein tyrosine phosphatase domains, thus inhibiting SHP2 activity through an allosteric mechanism [2]. SHP099, widely used to inhibit the in vitro proliferation of various cancer cells, has been employed as an anti-cancer agent in mouse tumor xenograft models [3].

In vitro, SHP099 significantly inhibited the proliferation of PC9 cells and PC9GR cells within 24 hours, with IC₅₀ values of 7.536 and 8.900 μM, respectively [4]. Treatment with 20 μM SHP099 for one week significantly inhibited the phosphorylation of ERK protein in synovial mesenchymal stem cells (SMSCs), promoted the expression of SOX9 and COL2, and reduced the expression of the COL10 without affecting cell viability [5]. Treatment with 5 μM SHP099 for 3 days significantly promoted the accumulation of proteins related to induced cell death (including cleaved caspase-3) in human umbilical vein endothelial cells (HUEVCs), and reduced the decrease of pro-survival proteins (including Survivin), significantly inducing cell death [6].

In vivo, SHP099 treatment via intraperitoneal injection at 5mg/kg/day for 17 days inhibited the tumor growth of CT-26 cell xenograft BALB/c mice, without affecting body weight of mice [7]. A single intraperitoneal injection of 15mg/kg of SHP099 for 12 hours significantly inhibited the pulmonary inflammatory response in the acute lung injury mouse model and increased the survival rate of the

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

mice^[8].

References:

- [1] Wu J, Zhang H, Zhao G, et al. Allosteric inhibitors of SHP2: an updated patent review (2015-2020) [J]. Current Medicinal Chemistry, 2021, 28(19): 3825-3842.
- [2] Wang M, Li T, Ouyang Z, et al. SHP2 allosteric inhibitor TK-453 alleviates psoriasis-like skin inflammation in mice via inhibition of IL-23/Th17 axis[J]. Iscience, 2022, 25(4).
- [3] Sang Y, Hou Y, Cheng R, et al. Targeting PDGFR α -activated glioblastoma through specific inhibition of SHP-2-mediated signaling[J]. Neuro-oncology, 2019, 21(11): 1423-1435.
- [4] Xia L, Yang F, Wu X, et al. SHP2 inhibition enhances the anticancer effect of Osimertinib in EGFR T790M mutant lung adenocarcinoma by blocking CXCL8 loop mediated stemness[J]. Cancer Cell International, 2021, 21(1): 337.
- [5] Sun Z, Xu X, Lv Z, et al. Intraarticular injection of SHP2 inhibitor SHP099 promotes the repair of rabbit full-thickness cartilage defect[J]. Journal of Orthopaedic Translation, 2022, 32: 112-120.
- [6] Wang Y, Salvucci O, Ohnuki H, et al. Targeting the SHP2 phosphatase promotes vascular damage and inhibition of tumor growth[J]. EMBO Molecular Medicine, 2021, 13(7): e14089.
- [7] Zhao M, Guo W, Wu Y, et al. SHP2 inhibition triggers anti-tumor immunity and synergizes with PD-1 blockade[J]. Acta Pharmaceutica Sinica B, 2019, 9(2): 304-315.
- [8] Ye S, Zuo B, Xu L, et al. Inhibition of SHP2 by the small molecule drug SHP099 prevents lipopolysaccharide-induced acute lung injury in mice[J]. Inflammation, 2023, 46(3): 975-986.

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