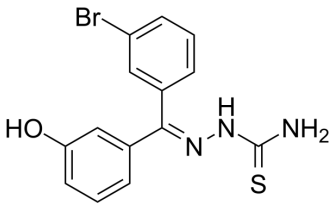
KGP94

Cat. No.:	HY-118762
CAS No.:	1131456-28-4
Molecular Formula:	$C_{14}H_{12}BrN_3OS$
Molecular Weight:	350.23
Target:	Cathepsin
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (285.53 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8553 mL	14.2763 mL	28.5527 mL
5 mM	0.5711 mL	2.8553 mL	5.7105 mL
10 mM	0.2855 mL	1.4276 mL	2.8553 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.14 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KGP94 is a selective inhibitor of cathepsin L with an IC_{50} of 189 nM[1]. KGP94 inhibits migration and invasion of metastatic carcinoma and shows low cytotoxicity (GI_{50}=26.9 μM) against various human cell lines[2].

IC_{50} & Target

189 nM (cathepsin L)[1]

In Vitro

KGP94 (10 or 20 μM, 24 h) reduces expression of M2 (macrophage) markers (Arginase-1 and CD206) and cells invasion of primary bone marrow-derived macrophages or Raw264.7[3].

KGP94 (25 μM, 24 h) impairs the incasive capacities of both prostate and breat cancer cells by 53% and 88%, respectively[4].

KGP94 (25 μM, 24 h) suppresses secreted CTSL activity by 94% and 92% in PC-3ML and MDA-MB-231, repsectively[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Invasion Assay[4]

Cell Line:	PC-3ML, MDA-MB-231
Concentration:	10 μM, 25 μM
Incubation Time:	24 hours
Result:	Attenuated migration and invasion of prostate and breast cancer cells.

In Vivo

KGP94 (i.p.; 20 mg/kg; once daily for 3 days) exhibits anti-metastatic and anti-bone resorptive efficacy in a prostate cancer bone metastasis model[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NCR nu/nu male mice[5]
Dosage:	20 mg/kg
Administration:	Intraperitoneal injection; once daily for 3 days
Result:	Reduced 65% in metastatic tumor burden and 58% in tumor angiogenesis, improved survival of bone metastases bearing mice.

REFERENCES

[1]. Parker EN, et al. Synthesis and biological evaluation of a water-soluble phosphate prodrug salt and structural analogues of KGP94, a lead inhibitor of cathepsin L. Bioorg Med Chem Lett. 2017 Mar 1. 27(5):1304-1310.

[2]. Munikishore R, et al. An efficient and concise synthesis of a selective small molecule non-peptide inhibitor of cathepsin L: KGP94. Bioorg Chem. 2021 Nov. 116:105317.

[3]. Dykes SS, et al. Cathepsin L secretion by host and neoplastic cells potentiates invasion. Oncotarget. 2019 Sep 17. 10(53):5560-5568.

[4]. Sudhan DR, et al. Cathepsin L inhibition by the small molecule KGP94 suppresses tumor microenvironment enhanced metastasis associated cell functions of prostate and breast cancer cells. Clin Exp Metastasis. 2013 Oct. 30(7):891-902.

[5]. Sudhan DR, et al. Cathepsin L inactivation leads to multimodal inhibition of prostate cancer cell dissemination in a preclinical bone metastasis model. Int J Cancer. 2016 Jun 1;138(11):2665-77.

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