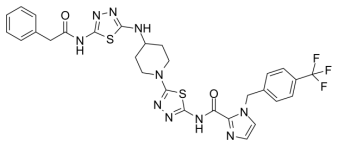
GLS1 Inhibitor-4

Cat. No.:	HY-146617
CAS No.:	2768599-97-7
Molecular Formula:	$C_{29}H_{27}F_3N_{10}O_2S_2$
Molecular Weight:	668.72
Target:	Glutaminase; Apoptosis
Pathway:	Metabolic Enzyme/Protease; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GLS1 Inhibitor-4 (compound 41e) is a potent GLS1 inhibitor with an IC_{50} of 11.86 nM. GLS1 Inhibitor-4 shows antiproliferative activity, good metabolic stability, robust GLS1 binding affinity. GLS1 Inhibitor-4 blocks the glutamine metabolism and induce the production of ROS. GLS1 Inhibitor-4 induces apoptosis and shows antitumor activity[1].

IC_{50} & Target

IC_{50}: 11.86 nM (GLS1)[1]

In Vitro

GLS1 Inhibitor-4 (compound 41e) shows antiproliferative activity with IC_{50}s of 0.051, 0.37, 0.32, 1.34 μM for HCT116 and MDA-MB-436, CT26, H22 cells, respectively[1].

GLS1 Inhibitor-4 shows good plasma and liver microsomal stability with 96% stability in Human plasma[1].

GLS1 Inhibitor-4 shows robust binding affinity with GLS1 protein, the dissociation constants (K_d) of 52 nM[1].

GLS1 Inhibitor-4 (0.1, 0.5, 1 μM) inhibits the colony formation of HCT116 cells in a dose-dependent manner[1].

GLS1 Inhibitor-4 (100, 300 nM, 12 h) reduces the concentration of a number of key metabolites downstream of glutamate within 12 h[1].

GLS1 Inhibitor-4 (30, 50, 200 nM; 6 h) increases the ROS levels in a dose-dependent manner in HCT116 cells[1].

GLS1 Inhibitor-4 (1 mmol/L; 12 h) significantly decreases the ATP production basal and maximal OCRs (oxygen consumption rates) after 12 h, suppresses the aerobic glycolysis in HCT116 cancer cells[1].

GLS1 Inhibitor-4 (30, 50, 200 nM; 24 h) induces apoptosis in a dose-dependent manner[1].

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

Apoptosis Analysis[1]

Cell Line:	HCT116 cells
Concentration:	30, 50, 200 nM
Incubation Time:	24 h
Result:	Induced approximately 28% and 95% more apoptotic cells at concentrations of 50 and 200 nM, respectively. And upregulated the expression of apoptotic protein cleaved PARP in a dose-dependent manner.

In Vivo

GLS1 Inhibitor-4 (50, 100 mg/kg; i.p.; twice a day for 21 consecutive days) shows antitumor activity in a dose-dependent manne[1].

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

Animal Model:	Six-week-old BALB/c SPF nude mice (HCT116 tumor nude mouse xenograft model)[1]
Dosage:	50, 100 mg/kg
Administration:	I.p.; twice a day for 21 consecutive days
Result:	Inhibited the tumor growth at a dose-dependent manne with the tumor growth inhibition (TGI) values of 35.5% at 50 mg/kg and 47.5% at 100 mg/kg, respectively.

REFERENCES

[1]. Xu X, et al. Discovery of novel glutaminase 1 allosteric inhibitor with 4-piperidinamine linker and aromatic heterocycles. Eur J Med Chem. 2022 Jun 5;236:114337.

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