FA16

Cat. No.: HY-151964

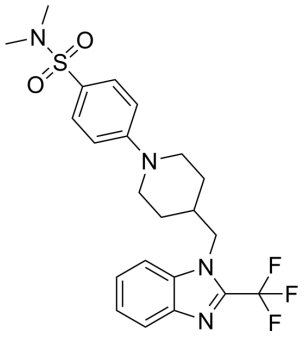
Molecular Formula: $C_{22}H_{25}F_3N_4O_2S$

Molecular Weight: 466.52

Target: Ferroptosis

Pathway: Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

FA16 is a specific ferroptosis inducer (IC_{50}=1.26 μM; HT1080 cells) with metabolic stability, is the derivate of 2-(trifluoromethyl)benzimidazole. FA16 acts by inhibiting cystine/glutamate antiporter (system X_c^-), which mediates the exchange of intracellular glutamate and extracellular cystine. FA16 significantly inhibits tumor growth in the HepG2 xenograft model[1].

In Vitro

FA16 (1 μM; 5 min) has satisfactory metabolic stability in rat and human liver microsomes[1].
FA16 (5 μM; 10 h) induces lipid ROS accumulation and inhibits glutamate release dose-dependently in HT1080 cells[1].
FA16 (5 μM; 24 h) results mitochondria shrunken with increased membrane density, which was in line with the morphological feature related to ferroptosis[1].
FA16 (10 μM; 24 h) induced cell death, which can be rescued by the ferroptosis inhibitors Fer-1, Trolox or DFO, but not by the inhibitors of apoptosis or necroptosis[1].

Parameter	Microsomal stability ($T_{1/2}$ min)	Intrinsic clearance (μL/min/ mg protein)
Human	15.6	88.6
Rat	10.4	132.8

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

Cell Viability Assay[1]

Cell Line:	Human cancer cell lines: Clear-cell renal cell carcinoma cells (786-O), breast cancer cells (MDA-MB-231), cervical cancer cells (HeLa), hepatocellular carcinoma cells (HepG2), melanoma cells (A375), and prostate cancer cells (DU145); Human normal cell lines: cardiomyocytes (AC16), colon mucosal epithelial cells (NCM460), embryonic kidney cells (293T), and hepatic cells (LO2)
Concentration:	0-10 μM
Incubation Time:	48 hours
Result:	Inhibited cell growth with IC_{50}s of 0.7 μM (786-O), 4.34 μM (MDA-MB-231), 1.91 μM (HeLa),

	1.33 μM (HepG2), 2.31 μM (A375), and 1.64 μM (DU145), respectively.
Immunofluorescence[1]	
Cell Line:	HT1080 cells
Concentration:	5 μM
Incubation Time:	10 hours
Result:	Significantly induced lipid ROS accumulation, as indicated by the great enhancement in green fluorescence intensity.
RT-PCR[1]	
Cell Line:	HT1080 cells
Concentration:	0.5 μM, 1 μM, and 5 μM
Incubation Time:	6 hours and 18 hours
Result:	Increased the system X_c^- component SLC7A11, ChaC GSHspecific γ-glutamylcyclotransferase 1 (CHAC1), but little changed GPX4.

In Vivo

FA16 (15 or 30 mg/kg; i.p.; every other for 21 d) significantly inhibits tumor growth with good safety (no weight loss) in 786-O xenograft mice model, and it induced ferroptosis in tumor tissues[1].

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Animal Model:	BALB/c nude mice bearing HepG2 tumors (s.c.)[1]
Dosage:	15 or 30 mg/kg
Administration:	Intraperitoneal injection; every other for 21 days
Result:	Significantly inhibited tumor growth with a tumor growth inhibition (TGI) value of 47.6% and 77.1% at 15 and 30 mg/ kg, respectively.

REFERENCES

[1]. Fang Y, et al. Discovery and optimization of 2-(trifluoromethyl)benzimidazole derivatives as novel ferroptosis inducers in vitro and in vivo. Eur J Med Chem. 2023 Jan 5;245(Pt 1):114905.

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

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