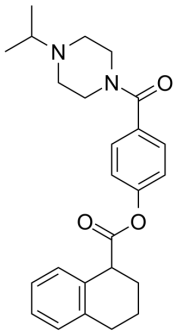
FK-448 Free base

Cat. No.:	HY-100193
CAS No.:	85858-76-0
Molecular Formula:	$C_{25}H_{30}N_2O_3$
Molecular Weight:	406.52
Target:	Proteasome
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	FK-448 Free base is an effective and specific inhibitor of chymotrypsin, with an IC_{50} of 720 nM.
IC_{50} & Target	IC50: 720 nM (Chymotrypsin)[1]
In Vitro	FK-448 Free base is an effective and specific inhibitor of chymotrypsin, with an IC_{50} of 720 nM. FK-448 Free base slightly inhibits esterolysis of Trypsin and Thrombin, with IC_{50}s of 780 and 35 μM, respectively, but shows no effects on esterolysis of plasmin, plasma kallikrein or pancreas kallikrein, with IC_{50}s of all >1 mM[1]. FK-448 moderately inhibits hydrolytic activities of cathepsin G with an IC_{50} of 15 μM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	FK-448 (20 mg/kg, i.p.) results in a decrease in the blood glucose level, and inhibits the degradation of insulin by pancreatic enzymes in rats. FK-448 (20 mg/kg, p.o.) also decreases the blood glucose level, and increases plasma IRI level in dogs[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The rates of hydrolysis of TAME by trypsin (0.5 μg/mL), plasmin (0.1 U/mL), plasma kallikrein (0.9 U/mL), pancreatic kallikrein (4 U/mL), and thrombin (6 U/mL), and that of ATEE by chymotrypsin (2 μg/mL), are determined at a substrate concentration of 10 mM. Caseinolysis of chymotrypsin is determined. The final concentration of casein is 1%. For measurement of inhibitory effects, mixtures of enzyme solution and inhibitor are preincubated at 37°C for 10 min and then the residual enzyme activity is determined. Km and Ki values are determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Rats[2] Rats are anaesthetized with ethylcarbamate (0.9 g/kg, intraperitoneally), and a front midline incision is made to expose the viscera. A hypodermic needle attached to a syringe containing the test solution is then carefully inserted into the lumen of the jejunum 2cm under the pylons. Insulin is dissolved in saline (and 0.1 M HCl if necessary) and injected at 2 mL/kg. Although most inhibitors tested are soluble in water, chymostatin is insoluble, and so it is dissolved in DMSO (final concentration, 10%). For measurement of blood glucose, samples of 0.2 mL of blood are drawn from the inferior vena cava of rats before, and 1 h after treatment or before, 0.5, 1, 1.5,2, 3 and 4 h after that, and are centrifuged at 3000 rev/min for 10 min. The plasma glucose concentration of samples is determined, and indicated as relative percents of the blood glucose

level at each period compared with that before administration (as 100%).

Dogs[2]

Enteric-coated gelatin capsules containing insulin and FK-448 are administered orally to the dogs and samples of 1 mL of blood are drawn from the median cubital vein before, and 0.5, 1, 1.5, 2, 2.5, 3, 4 and 5 h after treatment, are centrifuged at 3000 rev/min for 10min. The plasma glucose concentration of samples is also determined andindicated. Plasma IRI level is determined by double antibody radioimmunoassay using the Insulin-RIA kit[2].

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

REFERENCES

[1]. Fujii S, et al. New synthetic inhibitors of chymotrypsin. J Biochem. 1984 Feb;95(2):319-22.

[2]. Fujii S, et al. Promoting effect of the new chymotrypsin inhibitor FK-448 on the intestinal absorption of insulin in rats and dogs. J Pharm Pharmacol. 1985 Aug;37(8):545-9.

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