GGTI298 Trifluoroacetate

Cat. No.: HY-15871

CAS No.: 1217457-86-7

Molecular Formula: $C_{29}H_{34}F_3N_3O_5S$

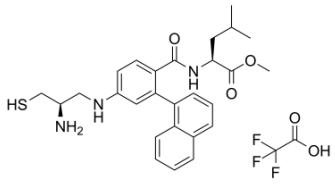
Molecular Weight: 593.66

Target: Ras; Apoptosis

Pathway: GPCR/G Protein; Apoptosis

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 : 150 mg/mL (252.67 mM; Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6845 mL	8.4223 mL	16.8447 mL
5 mM	0.3369 mL	1.6845 mL	3.3689 mL
10 mM	0.1684 mL	0.8422 mL	1.6845 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 (4.21 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.21 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GGTI298 Trifluoroacetate is a CAAZ peptidomimetic geranylgeranyltransferase I (GGTase I) inhibitor, which can inhibit Rap1A with IC_{50} of 3 μM; little effect on Ha-Ras with IC_{50} of >20 μM.

IC_{50} & Target

IC50: 3 μM (Rap1A, in vivo), > 20 μM (Ha-Ras, in vivo)[3]

In Vitro

RhoA inhibitor (GGTI298 Trifluoroacetate) significantly reduces cAMP agonist-stimulated apical K+ conductance[1].

	Knockdown of DR4 abolishes NF-κB activation, leading to sensitization of DR5-dependent apoptosis induced by the combination of GGTI298 Trifluoroacetate and TRAIL. GGTI298 Trifluoroacetate/TRAIL activates NF-κB and inhibits Akt. Knockdown of DR5, prevents GGTI298/TRAIL-induced IκBα and p-Akt reduction, suggesting that DR5 mediates reduction of I κBα and p-Akt induced by GGTI298/TRAIL. In contrast, DR4 knockdown further facilitates GGTI298/TRAIL-induced p-Akt reduction[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The vivo mouse ileal loop experiments show fluid accumulation is reduced in a dose-dependent manner by TRAM-34, GGTI298 Trifluoroacetate, or H1152 when inject together with cholera toxin into the loop[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	The given cells are lysed with reporter lysis buffer and subjected to luciferase activity assay using luciferase assay system in a luminometer. Relative luciferase activity is normalized to protein content[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cells are seeded in 96-well cell culture plates and treated the next day with the agents (including GGTI298 Trifluoroacetate). The viable cell number is determined using the sulforhodamine B assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	The ileal loop experiment is performed in 6-8-week-old mice by a modifing rabbit ileal loop assay. Following gut sterilization, the animals are kept fasted for 24 h prior to surgery and fed only water ad libitum. Anesthesia is induced by a mixture of ketamine (35 mg/kg of body weight) and xylazine (5 mg/kg of body weight). A laparotomy is performed, and the experimental loops of 5-cm length are constricted at the terminal ileum by tying with non-absorbable silk. The following fluids are instilled in each loop by means of a tuberculin syringe fitting with a disposable needle through the ligated end of the loop: pure CT (1 μg; positive control), saline (negative control), CT (1 μg)+TRAM-34 (different concentrations in μM), CT (1 μg)+ H1152 (1 μM), and CT (1 μg)+GGTI298 Trifluoroacetate (different concentrations in μM), a specific inhibitor of Rap1A. The intestine is returned to the peritoneum, and the mice are sutured and returned to their cages. After 6 h, these animals are sacrificed by cervical dislocation, and the loops are excised[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sheikh IA, et al. The Epac1 signaling pathway regulates Cl- secretion via modulation of apical KCNN4c channels in diarrhea. J Biol Chem. 2013 Jul 12;288(28):20404-15.

[2]. Chen S, et al. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis. Mol Cancer. 2010 Jan 29;9:23.

[3]. McGuire TF, et al. Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation. J Biol Chem. 1996 Nov 1;271(44):27402-7.

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