GRA Ex-25

Cat. No.: HY-50675

CAS No.: 307983-31-9

Molecular Formula: $C_{29}H_{36}F_3N_3O_5$

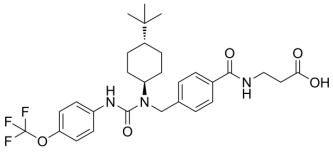
Molecular Weight: 563.61

Target: GCGR

Pathway: GPCR/G Protein

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (56.78 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7743 mL	8.8714 mL	17.7428 mL
5 mM	0.3549 mL	1.7743 mL	3.5486 mL
10 mM	0.1774 mL	0.8871 mL	1.7743 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 (4.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.69 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GRA Ex-25 is an inhibitor of glucagon receptor, with IC_{50} of 56 and 55 nM for rat and human glucagon receptors, respectively.

IC_{50} & Target

IC50: 56 nM (rat glucagon receptor), 55 nM (human glucagon receptor)[2]

In Vitro

GRA Ex-25 binds a human glucagon receptor (h-GlucRbind) with K_i of 63 nM and a moderate glucagon induced adenylate cyclase inhibition (h-GlucRcyclase) with K_i of 254 nM under our assay conditions[1]. GRA Ex-25 has similar affinity to the rat

	and human glucagon receptors (IC_{50}=56 and 55 nM, respectively)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GRA Ex-25 (3 mg/kg, i.v.) significantly reduces blood glucose caused by exogenous administration of glucagon in rat model. GRA Ex-25 is able to inhibit the rise in blood glucose levels elicited by exogenous administered glucagon, most likely because of the direct inhibition of glucagon stimulated hepatic glucose output[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Non-fasted male Sprague Dawley rats (200 g) are maintained in the anaesthetized state during the test by s.c. administration of a 1:1 mixture of Hypnorm (fentanyl, 0.05 mg/mL and fluanizone, 2.5 mg/mL) and Dormicum (Midazolam, 1.25 mg/mL). Acatheter is inserted in a jugular vein for administration of compounds. Approximately 60 min after initiation of anesthesia, test compounds (0, 1, 3, 10 and 30 mg/kg) and glucagon (3 μg/kg) are administered in 5 min intervals, respectively. Samples for determination of blood glucose concentrations are taken from the tail tip 25 and 5 min prior to administration of the compound to represent average basal values and again 10 min after administration of glucagon (time for peak response of glucagon). The results are expressed as delta values calculated as the value obtained 10 min after alucagon administration minus the average of the two basal values. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kurukulasuriya R, et al. Biaryl amide glucagon receptor antagonists. Bioorg Med Chem Lett. 2004 May 3;14(9):2047-50.

[2]. Kurukulasuriya R, et al. Biaryl amide glucagon receptor antagonists. Bioorg Med Chem Lett. 2004 May 3;14(9):2047-50.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA