RG-12525

Cat. No.: HY-101676

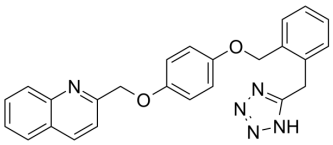
CAS No.: 120128-20-3

Molecular Formula: $C_{25}H_{21}N_5O_2$

Molecular Weight: 423.47

Target: Leukotriene Receptor; PPAR; Cytochrome P450

Pathway: GPCR/G Protein; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor



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 : 25 mg/mL (59.04 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3614 mL	11.8072 mL	23.6144 mL
	5 mM	0.4723 mL	2.3614 mL	4.7229 mL
	10 mM	0.2361 mL	1.1807 mL	2.3614 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: ≥ 2.08 mg/mL (4.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.91 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

RG-12525 is a a specific, competitive and orally effective antagonist of the peptidoleukotrienes, LTC4, LTD4 and LTE4, inhibiting LTC4-, LTD4- and LTE4-inducd guinea pig parenchymal strips contractions, with IC_{50}s of 2.6 nM, 2.5 nM and 7 nM, respectively; RG-12525 is also a peroxisome proliferator-activated receptor gamma (PPAR-gamma) agonist with IC_{50} of appr 60 nM and a potent inhibitor of CYP3A4, with a K_i value of 0.5 μM.

IC_{50} & Target

IC50: appr 60 nM (PPAR-γ)[2]

In Vitro

RG 12525 competitively inhibits ^{3}H-LTD4 binding to lung membranes (K_i = 3.0 +/- 0.3 nM) and competitively antagonizes the spasmogenic activity of LTC4, LTD4 and LTE4 on lung strips (KB values = 3 nM) with greater than 8000 fold selectivity[1]. RG

	12525 (2.5 μM or 25 μM) inhibits the microsomal activity of CYP2C9 and -3A4, but does not significantly inhibit CYP1A2,-2A6, -2C19, or -2D6. RG 12525 (25 μM) also causes a substantial amount of inhibition at the 5 and 10 μM midazolam concentrations [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	RG 12525 orally inhibits LTD4 induced wheal formation (ED_{50} = 5 mg/kg with a $t_{1/2}$ = 10 hrs at 9 mg/kg), LTD4 induces bronchoconstriction (ED_{50} = 0.6 mg/kg), and anaphylactic death (ED_{50} = 2.2 mg/kg with a $t_{1/2}$ = 7 hrs at 10 mg/kg) and antigen induces bronchoconstriction (ED_{50} = 0.6 mg/kg)[1]. RG 12525 inhibits antigen-induced mortality in the systemic anaphylaxis model with an ED_{50} (95% confidence interval) = 2.2 (0.8-6.4) mg/kg. RG 12525 also protects against LTD4-induced bronchoconstriction in a model measuring changes in pulmonary function with an ED_{50} = 0.6 (0.4-1.0) mg/kg[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Van Inwegen RG, et al. Antagonism of peptidoleukotrienes and inhibition of systemic anaphylaxis by RG 12525 in guinea pigs. Life Sci. 1989;44(12):799-807.

[2]. Fayer JL, et al. Lack of correlation between in vitro inhibition of CYP3A-mediated metabolism by a PPAR-gamma agonist and its effect on the clinical pharmacokinetics of midazolam, an in vivo probe of CYP3A activity. J Clin Pharmacol. 2001 Mar;41(3):305-16

[3]. Carnathan GW, et al. The effect of RG 12525 on leukotriene D4-mediated pulmonary responses in guinea pigs. Agents Actions. 1989 Jun;27(3-4):316-8.

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