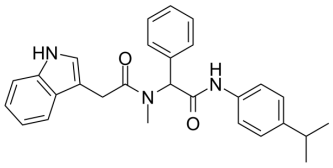
PG01

Cat. No.:	HY-103369
CAS No.:	853138-65-5
Molecular Formula:	$C_{28}H_{29}N_3O_2$
Molecular Weight:	439.55
Target:	CFTR
Pathway:	Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	PG01 is a potent CFTR Cl^- channel potentiator. PG01 can correct gating defects of CFTR mutants, is effective on b>E193K, G970R and G551D (CFTR mutants) with K_d values of 0.22 μM, 0.45 μM and 1.94 μM, respectively. PG01 is also effective on Δ F508 (K_a of 0.3 μM). PG01 increases ΔF508-CFTR Cl^- current after adding Forskolin[1][2].
IC_{50} & Target	CFTR[1]
In Vitro	PG01 itself does not activate ΔF508-CFTR, produces substantial ΔF508-CFTR Cl^- current after the addition of 0.5 and 2 μM Forskolin. PG01 at 100 nM strongly stimulates channel activity with multiple channel openings observed. The apparent K_d for PG01 for G551D-CFTR activation is 1 μM, approximately 100-fold better than that of genistein. The potency for activation G1349D-CFTR by PG01 is even better at 40 nM. PG01 produces large currents in both G551D- and G1349D-CFTR expressing cells. The currents are sensitive to CFTRinh-172 and are not seen in nontransfected cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pharmacokinetic analysis of PG01 in rats is done by serial measurements of plasma concentrations after single bolus infusions (5 mg/kg). PG01 pharmacokinetics fitted a two-compartment model with half-times of ⊠5 min and 130 min with volume of distribution 4 L. Microsome metabolism studies and rat pharmacokinetic analysis suggests significantly more rapid metabolism of PG01 than SF-03[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Pedemonte N, et al. Phenylglycine and sulfonamide correctors of defective delta F508 and G551D cystic fibrosis transmembrane conductance regulator chloride-channel gating. Mol Pharmacol. 2005 May;67(5):1797-807.

[2]. Caputo A, et al. Mutation-specific potency and efficacy of cystic fibrosis transmembrane conductance regulator chloride channel potentiators. J Pharmacol Exp Ther. 2009 Sep;330(3):783-91.

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

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