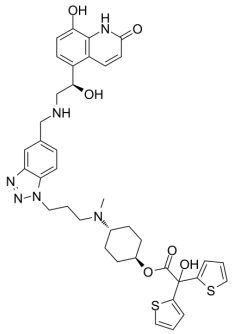
Navafenterol

Cat. No.:	HY-120802
CAS No.:	1435519-06-4
Molecular Formula:	$C_{38}H_{42}N_6O_6S_2$
Molecular Weight:	742.91
Target:	mAChR; Adrenergic Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Navafenterol (AZD-8871) is an inhaled dual-acting, potent, selective, and long-lasting M3-antagonist/β2-agonist (MABA) with long-lasting effects and favorable safety profile. The pIC_{50} is 9.5 for human M3 receptor, and the pEC_{50} is 9.5 for β2-adrenoceptor. Navafenterol can be used for the research of chronic obstructive pulmonary disease (COPD). Bronchoprotective and antisialagogue effects. Favorable cardiovascular profile[1].

In Vitro

The pIC_{50} values of Navafenterol (AZD-8871) at the human M1, M2, M3, M4, and M5 receptor are 9.9, 9.9, 9.5, 10.4, and 8.8, respectively[1].

pEC_{50} values of Navafenterol at theβ1, β2, and β3 adrenoceptor are 9.0, 9.5, and 8.7, respectively. It is selective for the β2-adrenoceptor over the β1 and β3 subtypes (3- and 6-fold, respectively)[1].

Navafenterol shows kinetic selectivity for the M3 (half-life: 4.97 hours) over the M2 receptor (half-life: 0.46 hour)[1].

Navafenterol shows dual antimuscarinic and β2-adrenoceptor functional activity in isolated guinea pig tissue (pIC_{50} in electrically stimulated trachea: 8.6; pEC_{50} in spontaneous tone isolated trachea: 8.8, respectively), which are sustained over time[1].

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

In Vivo

Navafenterol (AZD-8871) prevents acetylcholine-induced bronchoconstriction in both guinea pig and dog with minimal effects on salivation and heart rate at doses with bronchoprotective activity. Moreover, AZD8871 shows long-lasting effects in dog, with a bronchoprotective half-life longer than 24 hours. Navafenterol shows dose-proportional bronchoprotective effect, with a nonsignificantly different potency (ID_{40} of 0.40 μg/kg)[1].

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Animal Model:	Male Dunkin Hartley guinea pigs (body weight 340-600 g) bearing bronchoconstriction model[1]
Dosage:	10, 30, 100, and 300 μg/mL
Administration:	Administered by aerosol
Result:	Inhibited the bronchoconstriction in a concentration-response manner with the IC_{50} value of 2.1 μg/mL. Exhibited the antisialagogue effect with a maximal inhibition of sialorrhea of 65%±11% at 300 μg/mL and an estimated IC_{50} of 138.4 μg/mL.

Animal Model:	Male anesthetized Beagle dogs[1]
Dosage:	0.3, 1, 3, or 10 μg/kg
Administration:	Administered as nebulized liquid aerosols; the administration volume was 3 mL
Result:	Showed significant effects over 24 hours at all the doses tested (0.3-10 μg/kg). Showed long-lasting effects at 10 μg/kg, with a 79% ± 3.6% of bronchoprotection at 24 hours and a calculated half-life longer than 24 hours.

REFERENCES

[1]. Mònica Aparici, et al. Pharmacological Profile of AZD8871 (LAS191351), a Novel Inhaled Dual M3 Receptor Antagonist/ β 2-Adrenoceptor Agonist Molecule with Long-Lasting Effects and Favorable Safety Profile. J Pharmacol Exp Ther. 2019 Jul;370(1):127-136.

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