Rapacuronium bromide

Cat. No.: HY-16423

CAS No.: 156137-99-4

Molecular Formula: $C_{37}H_{61}BrN_2O_4$

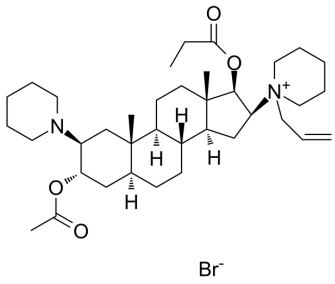
Molecular Weight: 677.8

Target: mAChR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 125 mg/mL (184.42 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.4754 mL	7.3768 mL	14.7536 mL
5 mM	0.2951 mL	1.4754 mL	2.9507 mL
10 mM	0.1475 mL	0.7377 mL	1.4754 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 (3.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.07 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rapacuronium bromide (Org 9487), a non-depolarizing neuromuscular blocker, is an allosteric modulator of muscarinic acetylcholine receptor (mAChR)[1].

IC_{50} & Target

Muscarinic receptor[1]

In Vitro

Rapacuronium binds to all muscarinic receptor subtypes at physiologically relevant concentrations and displays micromolar affinity and slight selectivity towards M_2 receptor. Rapacuronium exhibits complex effects on the kinetics of ACh binding and subsequent receptor activation estimated from stimulation of [^{35}S]GTPγS binding. Rapacuronium alone

	concentration dependently lowers [^{35}S]GTPγS binding to membranes with a maximal effect of approximately 25% at odd-numbered subtypes and 15% at even-numbered subtypes, with EC_{50} ranging from 28 μM at M_2 receptors to 76 μM at M_3 receptors. While the EC_{50} values of Rapacuronium in inhibiting [^{35}S]GTPγS binding at individual subtypes correlated with affinities measured in binding experiments with [^{3}H]ACh (R^2 = 0.76) they are lower (4- to 12-fold) at all subtypes. Measurements of ACh-stimulated [^{35}S]GTPγS binding in the presence of 0.1, 1 and 10 μM Rapacuronium shows differential effects of Rapacuronium on receptor activation by an orthosteric agonist at individual receptor subtypes. At even-numbered subtypes 1 μM and 10 μM Rapacuronium significantly increases ACh EC_{50}, with lowering of E_{MAX} at 10 μM Rapacuronium. At this subtype 0.1 and 1 μM Rapacuronium causes a significant 2-fold decrease in ACh EC_{50} and approximately 60% and 35% increase in E_{MAX}, respectively. Rapacuronium at 10 μM increases ACh EC_{50} by about 3-fold without a significant change in E_{MAX}. Rapacuronium (0.1 - 10 μM) has no effect on ACh efficacy at the M_1 and M_5 subtypes but decreases the EC_{50} of ACh in stimulating [^{35}S]GTPγS binding by 1.5- and 4-fold, respectively, at concentrations of 0.1 and 1 μM. However, this effect is not evident at 10 μM Rapacuronium[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Time course of the neuromuscular effects of Rapacuronium following the administration of the 2×ED_{90} doses to rats and guinea-pigs with ED_{90} of 5953±199 and 187±16 μg/kg in rat and guinea pig, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	For determination of [^{35}S]GTPγS binding to G-proteins in membranes a final concentration of 200 pM (M_1, M_3 and M_5 receptors) or 500 pM (M_2 and M_4 receptors) of [^{35}S]GTPγS is used. Incubation medium is supplemented with 5 μM (M_1, M_3 and M_5 receptors) or 50 μM (M_2 and M_4 receptors) GDP. Nonspecific binding is determined in the presence of 1 μM unlabeled GTPγS. When effects of Rapacuronium on ACh-stimulated [^{35}S]GTPγS binding is measured Rapacuronium is added to membranes 60 min prior to ACh and [^{35}S]GTPγS. Incubation with [^{35}S]GTPγS is carried out for 20 min and free ligand is removed by filtration as described above. Filtration and washing with ice-cold water lasted for 9 s (wash-aspirate button time). After filtration filters are dried in vacuum for 1 h while heated at 80°C and then solid scintillator Meltilex A is melted on filters (105°C, 90 s) using a hot plate. After cooling the filters are counted using a Wallac Microbeta scintillation counter[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Jakubík J, et al. Divergence of allosteric effects of Rapacuronium on binding and function of muscarinic receptors. BMC Pharmacol. 2009 Dec 28;9:15.

[2]. Vizi ES, et al. A new short-acting non-depolarizing muscle relaxant (SZ1677) without cardiovascular side-effects. Acta Anaesthesiol Scand. 2003 Mar;47(3):291-300.

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