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Adrenoceptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

The nomenclature of the Adrenoceptors has been agreed by theNC-IUPHAR Subcommittee on Adrenoceptors [58], see also [180].

Adrenoceptors, α_1

α_1-Adrenoceptors are activated by the endogenous agonists (-)-adrenaline and (-)-noradrenaline. phenylephrine, methoxamine and cirazoline are agonists and prazosin and cirazoline antagonists considered selective for α_1- relative to α_2-adrenoceptors. [^{3}H]prazosin and [^{125}I]HEAT (BE2254) are relatively selective radioligands. S(+)-niguldipine also has high affinity for L-type Ca^{2+} channels. Fluorescent derivatives of prazosin (Bodipy PLprazosin- QAPB) are used to examine cellular localisation of α_1-adrenoceptors. Selective α_1-adrenoceptor agonists are used as nasal decongestants; antagonists to treat hypertension (doxazosin, prazosin) and benign prostatic hyperplasia (alfuzosin, tamsulosin). The α_1- and β_2-adrenoceptor antagonist carvedilol is used to treat congestive heart failure, although the contribution of α_1-adrenoceptor blockade to the therapeutic effect is unclear. Several anti-depressants and anti-psychotic drugs are α_1-adrenoceptor antagonists contributing to side effects such as orthostatic hypotension and extrapyramidal effects.

Adrenoceptors, α_2

α_2-Adrenoceptors are activated by (-)-adrenaline and with lower potency by (-)-noradrenaline. brimonidine and talipexole are agonists and rauwolscine and yohimbine antagonists selective for α_2- relative to α_1-adrenoceptors. [^{3}H]rauwolscine, [^{3}H]brimonidine and [^{3}H]RX821002 are relatively selective radioligands. There is species variation in the pharmacology of the α_{2A}-adrenoceptor. Multiple mutations of α_2-adrenoceptors have been described, some associated with alterations in function. Presynaptic α_2-adrenoceptors regulate many functions in the nervous system. The α_2-adrenoceptor agonists clonidine, guanabenz and brimonidine affect central baroreflex control (hypotension and bradycardia), induce hypnotic effects and analgesia, and modulate seizure activity and platelet aggregation. clonidine is an anti-hypertensive and counteracts opioid withdrawal. dexmedetomidine (also xylazine) is used as a sedative and analgesic in human and veterinary medicine with sympatholytic and anxiolytic properties. The α_2-adrenoceptor antagonist yohimbine has been used to treat erectile dysfunction and mirtazapine as an anti-depressant. The α_{2B} subtype appears to be involved in neurotransmission in the spinal cord and α_{2C} in regulating catecholamine release from adrenal chromaffin cells.

Adrenoceptors, β

β-Adrenoceptors are activated by the endogenous agonists (-)-adrenaline and (-)-noradrenaline. Isoprenaline is selective for β-adrenoceptors relative to α_1- and α_2-adrenoceptors, while propranolol (pK_i 8.2-9.2) and cyanopindolol (pK_i 10.0-11.0) are relatively β_1 and β_2 adrenoceptor-selective antagonists. (-)-noradrenaline, xamoterol and (-)-Ro 363 show selectivity for β_1- relative to β_2-adrenoceptors. Pharmacological differences exist between human and mouse β_3-adrenoceptors, and the 'rodent selective' agonists BRL 37344 and CL316243 have low efficacy at the human β_3-adrenoceptor whereas CGP 12177 and L 755507 activate human β_3-adrenoceptors [88]. β_3-Adrenoceptors are resistant to blockade by propranolol, but can be blocked by high concentrations of bupranolol. SR59230A has reasonably high affinity at β_3-adrenoceptors, but does not discriminate well between the three β- subtypes whereas L 755507 is more selective. [^{125}I]-cyanopindolol, [^{125}I]-hydroxy benzylpindolol and [^{3}H]-alprenolol are high affinity radioligands that label β_1- and β_2- adrenoceptors and β_3-adrenoceptors can be labelled with higher concentrations (nM) of [^{125}I]-cyanopindolol together with β_1- and β_2-adrenoceptor antagonists. [^{3}H]-L-748337 is a β_3-selective radioligand [474]. Fluorescent ligands such as BODIPY-TMR-CGP12177 can be used to track β-adrenoceptors at the cellular level [8]. Somewhat selective β_1-adrenoceptor agonists (denopamine, dobutamine) are used short term to treat cardiogenic shock but, chronically, reduce survival. β_1-Adrenoceptor-preferring antagonists are used to treat hypertension (atenolol, betaxolol, bisoprolol, metoprolol and nebivolol), cardiac arrhythmias (atenolol, bisoprolol, esmolol) and cardiac failure (metoprolol, nebivolol). Cardiac failure is also treated with carvedilol that blocks β_1- and β_2-adrenoceptors, as well as α_1-adrenoceptors. Short (salbutamol, terbutaline) and long (formoterol, salmeterol) acting β_2-adrenoceptor-selective agonists are powerful bronchodilators used to treat respiratory disorders. Many first generation β-adrenoceptor antagonists (propranolol) block both β_1- and β_2-adrenoceptors and there are no β_2-adrenoceptor-selective antagonists used therapeutically. The β_3-adrenoceptor agonist mirabegron is used to control overactive bladder syndrome.

Contents

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β_3-adrenoceptor

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