

Adrenoceptors in GtoPdb v.2023.3

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Abstract

The nomenclature of the Adrenoceptors has been agreed by the NC-IUPHAR Subcommittee on Adrenoceptors [64, 194].

Adrenoceptors, α_1

The three α_1 -adrenoceptor subtypes α_{1A} , α_{1B} and α_{1D} are activated by the endogenous agonists (-)-adrenaline and (-)-noradrenaline. (-)-phenylephrine, methoxamine and cirazoline are agonists and prazosin and doxazosin antagonists considered selective for α_1 - relative to α_2 -adrenoceptors.

[³H]prazosin and [¹²⁵I]HEAT (BE2254) are relatively selective radioligands. S(+)-niguldipine also has high affinity for L-type Ca²⁺ channels. Fluorescent derivatives of prazosin (Bodipy FLprazosin- QAPB) are used to examine cellular localisation of α_1 -adrenoceptors. α_1 -Adrenoceptor agonists are used as nasal decongestants; antagonists to treat symptoms of benign prostatic hyperplasia (alfuzosin, doxazosin, terazosin, tamsulosin and silodosin, with the last two compounds being α_{1A} -adrenoceptor selective and claiming to relax bladder neck tone with less hypotension); and to a lesser extent hypertension (doxazosin, terazosin). 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.

Adrenoceptors, α_2

The three α_2 -adrenoceptor subtypes α_{2A} , α_{2B} and α_{2C} 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. [³H]rauwolscine, [³H]brimonidine and [³H]RX821002 are relatively selective radioligands. There are species variations 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 (relatively little used) and counteracts opioid withdrawal. dexmedetomidine (also xylazine) is increasingly used as a sedative and analgesic in human [33] and veterinary medicine and has sympatholytic and anxiolytic properties. The α_2 -adrenoceptor antagonist mirtazapine is used 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. Although subtype-selective antagonists have been developed, none are used clinically and they remain experimental tools.

Adrenoceptors, β

The three β -adrenoceptor subtypes β_1 , β_2 and β_3 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 selective antagonists for β_1 - and β_2 - relative to β_3 -adrenoceptors. (-)-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](#) (low potency) 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 between the three β - subtypes [332] whereas [L-748337](#) is more selective. [125 I]-[cyanopindolol](#), [125 I]-hydroxy benzylopindolol 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. 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 cardiac arrhythmias ([atenolol](#), [bisoprolol](#), [esmolol](#)) and cardiac failure ([metoprolol](#), [nebivolol](#)) but also in combination with other treatments to treat hypertension ([atenolol](#), [betaxolol](#), [bisoprolol](#), [metoprolol](#) and [nebivolol](#)) [528]. 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. There is evidence to suggest that β -adrenoceptor antagonists can reduce metastasis in certain types of cancer [197].

Contents

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Database links

Adrenoceptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=4>

Introduction to Adrenoceptors

<https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=4>

Receptors

α_{1A} -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=22>

α_{1B} -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=23>

α_{1D} -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=24>

α_2A -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=25>

α_2B -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=26>

α_2C -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=27>

β_1 -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=28>

β_2 -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=29>

β_3 -adrenoceptor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=30>

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