Adrenoceptors, \(a_2\)

**Overview**: \(a_2\)-Adrenoceptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Adrenoceptors; Bylund et al., 1994) are GPCR activated by endogenous agonists with a relative potency of adrenaline > noradrenaline. UK14304 (brimonidine) and BHT920 are agonists selective for \(a_2\)-adrenoceptors relative to \(a_1\)-adrenoceptors. Rauwolscine (9:0) and yohimbine (9:0) are antagonists selective for \(a_2\)-adrenoceptors relative to \(a_1\)-adrenoceptors. \([^3H]\)-rauwolscine (1 nM), \([^3H]\)-UK14304 (5 nM) and \([^3H]\)-RX821002 (0.5 nM and 0.1 nM at \(a_2C\)) are relatively selective radioligands. There is species variation in the pharmacology of the \(a_2A\)-adrenoceptor; for example, yohimbine, rauwolscine and oxymetazoline have an ~20-fold lower affinity for rat, mouse and bovine \(a_2A\)-adrenoceptors compared to the human receptor. These \(a_2\) orthologues are sometimes referred to as \(a_2\)-adrenoceptors. Multiple mutations of \(a_2\)-adrenoceptors have been described, some of which are associated with alterations in function. The effects of classical (not subtype selective) \(a_2\)-adrenoceptor agonists such as clonidine, guanabenz and UK14304 (brimonidine) on central baroreflex control (hypotension and bradycardia), hypnotic, analgesic, seizure modulation and platelet aggregation are mediated by \(a_2A\)-adrenoceptors. The roles of \(a_2A\) and \(a_2C\)-adrenoceptors are less clear but the \(a_2D\) subtype appears to be involved in neurotransmission in the spinal cord and \(a_2C\) in regulating catecholamine release from adrenal chromaffin cells.

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>(a_{2A})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other names</td>
<td>(a_2)</td>
</tr>
<tr>
<td>Ensembl ID</td>
<td>ENSG0000150594</td>
</tr>
<tr>
<td>Principal transduction</td>
<td>(G_\text{in})</td>
</tr>
<tr>
<td>Selective agonists</td>
<td>Oxymetazoline</td>
</tr>
<tr>
<td>Selective antagonists</td>
<td>BRL44408 (8.0, Young et al., 1989)</td>
</tr>
</tbody>
</table>

Oxymetazoline is a reduced efficacy agonist. ARC239 (pK, 8:0) and prazosin (pK, 7.5) show selectivity for \(a_2A\) and \(a_2C\)-adrenoceptors over \(a_2A\)-adrenoceptors. Binding sites for imidazolines, distinct from \(a_2\)-adrenoceptors, have been identified and classified as \(I_1\), \(I_2\) and \(I_3\) sites and catecholamines have a low affinity for these sites. \(I_1\)-imidazoline receptors are involved in central inhibition of sympathetic tone, \(I_2\)-imidazoline receptors are an allosteric binding site on monoamine oxidase B, and \(I_3\)-imidazoline receptors regulate insulin secretion from pancreatic \(B\)-cells.

**Abbreviations**: ARC239, 2-(2,4-[\(O\)-methoxyphenyl]-piperazin-1-yl); BHT920, 6-allyl-2-amino-5,6,7,8-tetrahydro-4H-thiazolo-[4,5-d]-azepline; BRL44408, 2-(4,5-dihydro-1H-imidazol-2-ylmethyl)-1-methyl-1,3-dihydroisoindole; JP1302, N-[4-[4-methyl-1-piperazinyl][phenyl]-9-acridinamine dihydrochloride; MK912, (2S,12E)(-\(S\),\(S\))\(,\)3\(,\)3\(,\)dimethylspiro\((1,3,4,5,6,7,12\)b-octahydro-2H-benzo\(\gamma\)furo\(2,3-\)ajquinolinizine)\(-\)2,4\(-\)pyrimidin-2\(-\)one; RX21002, 2-(2-methoxy-1,4-benzodioxan-2-yl)-2-imidazoline; UK14304, 5-bromo-6-[2-imidazolin-2-ylamino]quinoxaline, also known as brimonidine.

For more information on related products, please visit [www.aladdin-e.com](http://www.aladdin-e.com)

**Further Reading**


**References**


(Source: BRITISH JOURNAL OF PHARMACOLOGY)