

# Cannabinoid

**Overview:** Cannabinoid receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Cannabinoid Receptors; see Howlett *et al.*, 2002) are activated by endogenous ligands that include *N*-arachidonoyl ethanolamine (anandamide), *N*-homo- $\gamma$ -linolenoyl ethanolamine, *N*-docosatetra-7,10,13,16-enoyl ethanolamine and 2-arachidonoyl glycerol. Potency determinations are complicated by the possibility of differential susceptibility of endogenous ligands to enzymatic conversion (see Alexander and Kendall, 2007). Both CB<sub>1</sub> and CB<sub>2</sub> receptors may be labelled with [<sup>3</sup>H]-CP55940 (0.6 nM; Showalter *et al.*, 1996) and [<sup>3</sup>H]-WIN55212-2 (2–12 nM; Slipetz *et al.*, 1995; Song and Bonner, 1996).

Further cannabinoid-like receptors have been described, including GPR55 (ENSG00000135898), which appears to respond to a wide spectrum of cannabinoid agonists and antagonists (see Brown, 2007; Pertwee, 2007; Ryberg *et al.*, 2007). GPR18 has been described to be a 7-transmembrane receptor for *N*-arachidonoyl glycine (Kohno *et al.*, 2006), while GPR119 responds to fatty acid ethanolamides (*N*-oleoyl ethanolamine > *N*-palmitoyl ethanolamine > anandamide; Overton *et al.*, 2006). Synthetic agonists for this receptor include PSN375963 and PSN632408 (Overton *et al.*, 2006). Other pharmacological targets for cannabinoids have also been proposed (see Baker *et al.*, 2006; Begg *et al.*, 2005; Pertwee, 2005a).

Nomenclature	CB <sub>1</sub>	CB <sub>2</sub>
Ensembl ID	ENSG00000118432	ENSG00000162562
Principal transduction	G <sub>i/o</sub>	G <sub>i/o</sub>
Selective agonists	ACEA (Hillard <i>et al.</i> , 1999), ACPA (Hillard <i>et al.</i> , 1999), methanandamide (Khanolkar <i>et al.</i> , 1996), O1812 (Di Marzo <i>et al.</i> , 2001)	HU308 (Hanus <i>et al.</i> , 1999), JWH133 (Huffman <i>et al.</i> , 1999; Pertwee, 2000), L759633 (Ross <i>et al.</i> , 1999), L759656 (Ross <i>et al.</i> , 1999), AM1241 (Ibrahim <i>et al.</i> , 2003)
Selective antagonists	AM251 (8.1, Lan <i>et al.</i> , 1999a), AM281 (7.9, Lan <i>et al.</i> , 1999b) rimonabant (7.9, Showalter <i>et al.</i> , 1996), LY320135 (6.9, Felder <i>et al.</i> , 1998)	SR144528 (9.2, Rinaldi-Carmona <i>et al.</i> , 1998), AM630 (7.5, Ross <i>et al.</i> , 1999)
Probes	[ <sup>3</sup> H]-rimonabant (0.6 nM, Rinaldi-Carmona <i>et al.</i> , 1996)	—

Anandamide is also an agonist at vanilloid receptors (TRPV1) and PPARs (see O'Sullivan, 2007; Zygmunt *et al.*, 1999). There is evidence for an allosteric site on the CB<sub>1</sub> receptor (Price *et al.*, 2005). All of the compounds listed as antagonists behave as inverse agonists in some bioassay systems (see Pertwee, 2005a, b).

**Abbreviations:** ACEA, arachidonoyl-2-chloroethylamide; ACPA, arachidonoylcyclopropylamide; **AM1241**, (2-iodo-5-nitro-phenyl)-[1-(1-methyl-piperidin-2-ylmethyl)-1*H*-indol-3-yl]-methanone; **AM251**, *N*-(piperidin-1-yl)-5-(4-iodophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxamide; **AM281**, 1-(2,4-dichlorophenyl)-5-(4-iodophenyl)-4-methyl-*N*-4-morpholinyl-1*H*-pyrazole-3-carboxamide; **AM630**, 6-iodopravadoline; **CP55940**, (1*R*,3*R*,4*R*)-3-[2-hydroxy-4-(1,1-dimethylheptyl) phenyl]-4-(3-hydroxypropyl)cyclohexan-1-ol; **HU308**, {4-[4-(1,1-dimethylheptyl)-2,6-dimethoxy-phenyl]-6,6-dimethyl-bicyclo[3.1.1]hept-2-en-2-yl}-methanol; **JWH133**, (3-(1,1-dimethylbutyl)-6,6,9-trimethyl-6a,7,10,10a-tetrahydro-6*H*-benzo[*c*]chromene; **L759633**, (6*a*,10*a*)-3-(1,1-dimethylheptyl)-1-methoxy-6,6,9-trimethyl-6a,7,10,10a-tetrahydro-6*H*-benzo[*c*]chromene; **L759656**, (6*a*,10*a*)-3-(1,1-dimethylheptyl)-1-methoxy-6,6-dimethyl-9-methylene-6a,7,8,9,10,10a-hexahydro-6*H*-benzo[*c*]chromene; **LY320135**, (6-methoxy-2-[4-methoxyphenyl]benzo[*b*]thien-3-yl)(4-cyanophenyl)methanone; **methanandamide**, (*R*)-(+)-arachidonoyl-1'-hydroxy-2'-propylamide; **O1812**, (*R*)-(20-cyano-16,16-dimethyl-docosa-*cis*-5,8,11,14-tetraenoyl)-1'-hydroxy-2'-propylamide; **PSN375963**, 4-(5-[4-butylcyclohexyl]-1,2,4-oxadiazol-3-yl)pyridine; **PSN632408**, 4-([3-(4-pyridinyl)-1,2,4-oxadiazol-5-yl]methoxy)-1-piperidinecarboxylic acid, 1,1-dimethylethyl ester; **rimonabant**, *N*-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1*H*-pyrazole-3-carboxamide hydrochloride, also known as SR141716A; **SR144528**, *N*-([1*S*]-endo-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl)-5-(4-chloro-3-methylphenyl)-1-(4-methylbenzyl)-pyrazole-3-carboxamide; **WIN55212-2**, (*R*)-(+)-[2,3-dihydro-5-methyl-3-(4-morpholinylmethyl)-pyrrolo-[1,2,3-*de*]-1,4-benzoxazin-6-yl]-1-naphthalenylmethanone mesylate

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## Citation Information

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