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NOMENCLATURE GUIDELINES FOR AUTHORS

With effect from January 2005

The Nomenclature Working Party (NWP) of the Editorial Board of the British Journal of Pharmacology has consulted many acknowledged experts in an effort to clarify and standardise receptor and other nomenclature systems for use by Editors until a complete set of recommendations from the International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR) is published.

The NWP is unanimous in its view that with rare exceptions, the Journal should use spellings, names and abbreviations that have been chosen by international bodies convened for the purpose.

For receptor nomenclature, with few exceptions, the Journal generally follows the guidelines laid down in three sources, the BJP Guide to Receptors and Channels, the IUPHAR Receptor Compendia and the reports of NC-IUPHAR Sub Committees published in *Pharmacological Reviews*.

1 *Definition of receptors and subtypes*

Receptors and their subtypes are defined in terms of structural information where available, affinity and selectivity of antagonists and thereafter by agonist selectivity.

2 *Format of receptor names*

(a) Editors will permit with reluctance new nomenclature systems in papers accepted for publication if, and only if, there are compelling reasons to introduce a new terminology (or modify an accepted one). The criteria upon which the new receptor type or subtype are defined must be given, together with adequate explanations of the relationship between the previous nomenclature (fully referenced) and the proposed one.

N.B. The new nomenclature should not appear in the Title, Short Title or Keywords, unless qualified by the adjective putative (e.g.... mediated by the putative imidazoline I_2 receptor).

(b) Only well-established and universally accepted subtype names will be acceptable without any reference to the originator of these terms. In cases of controversy concerning further subdivision of the subtype, full referencing must be given.

(c) When receptors are expressed from DNA or RNA that has been introduced into cells and these receptors display a dissimilar pharmacological profile to the native receptors, or have not been characterised pharmacologically, they should be denoted by use of lower case, *e.g.* 5-ht$_5$ for expressed receptors and 5-HT$_7$ for native receptors. The stoichiometry of the expressed receptor should be indicated, where appropriate, e.g. for an adult muscle nicotinic acetylcholine receptor, it might be $(\alpha_1)2\beta_1\gamma\delta$.

(d) Receptor subtypes should normally be designated by means of a subscript numeral or capital letter. Some double subscripts (i.e. numeral plus letter) are acceptable.

(e) Greek letters and Roman numerals should be avoided in any new nomenclature. The name should not include the letter 'R' or 'r' as an abbreviation for receptor.

(f) Mammalian systems are the basis of receptor classifications with primacy given to humans. Therefore non-mammalian species should be clearly indicated, e.g. *Torpedo* nicotinic acetylcholine receptor, turkey β adrenoceptor, locust GABA receptor.

3 *Types of receptor*

The NWP accepts that there are additional receptors to those described below which can be considered to be well characterised. In many cases, however, their existence has been confirmed only in cloning studies and it is as yet unclear how they relate to similar subdivisions proposed on the grounds of differences in agonist and antagonist potencies in various tissues. Italics should be used if the receptor has not been cloned. Lower case should be used to describe cloned receptors for which endogenous expression has not been described. It is incorrect to refer to any receptor, using the suffix 'ergic' (*e.g.*, cholinergic, adrenergic). See Section 5 for the correct use of such terms. For individual ion channels, nomenclature, where known, is given in the Journals Guide to Receptors and Channels.

4 *Naming of ion channels*

Ion channels are typically described by an abbreviation of the ion permeating the channel (e.g. K^+ channel, Na^+ channel, Cl^- channel. Ca^{2+} channel etc.)

Ionic currents are referred to by either the full description of the current (e.g. Ca^{2+} -activated K^+ current) or as an abbreviation using the prefix *I* followed by the atomic species carrying the current as a subscript (e.g. I_{Na}, I_{Ca},) Where it is important to specify the activator of the current, this may be added to the atomic species subscript in parenthesis (*e.g.* $I_{K(Ca)}$) for a calcium-activated potassium current or $I_{K(V)}$ for a voltage-activated potassium current).

When a pharmacological agent is used to describe a current, it must be fully defined in the text.

When, for example, a system has two currents carried by the same ionic species and activated by similar means but with (for example) different kinetics, the distinguishing factor may be added to the subscript or as a hyphen after the abbreviation (*e.g.* '$I_{K(Ca,slow)}$' or '$I_{K(Ca)}$-slow', which would refer to a kinetically slow calcium-activated potassium current).

Examples of some commonly used abbreviations are shown below:

Sodium current: $I_{Na(V)}$
Potassium currents: $I_{K(V)}$, $I_{K(Ca)}$, $I_{K(A)}$, $I_{K(IR)}$
Chloride currents: $I_{Cl(Ca)}$, $I_{Cl(cAMP)}$, $I_{Cl(swell)}$
Calcium currents: $I_{Ca(L)}$, $I_{Ca(T)}$, $I_{Ca(N)}$

5 *Naming of nerve fibres*

Many nerve fibres are now known to release more than one transmitter, and future work may show that this is, in fact, the general rule. In that case, the concept of the same transmitter being released either at different developmental stages or under various experimental conditions would no longer hold, and single adjectives that imply this (e.g. cholinergic, noradrenergic) would become inappropriate when applied to nerve fibres, as distinct from transmitter functions. For the present, those nerve fibres that are known to function by releasing more than one identified transmitter may be described accordingly; for example, cholinergic-peptidergic (in alphabetical order, the order implying no priority of function). N.B. The suffix 'ergic' should continue to be applied only to nerve fibres and to the transmission event, in accordance with Dale's intentions. For example 'cholinergic' indicates that the nerve fibre, or the transmission, functions through the release of a choline-like substance. The suffix should not be used loosely to mean 'pertaining to'. Hence the expression 'cholinergic receptor' (rather than acetylcholine receptor) is incorrect. Transmission events involving nitric oxide may be referred to as *nitrergic*.

Nerve fibres that release noradrenaline are to be described as noradrenergic. The term adrenergic should be reserved for nerve fibres known to release adrenaline. Where the identity of the catecholamine is uncertain catecholaminergic should be used. The adjective to be applied to nerve fibres that release dopamine as a transmitter is dopaminergic (not DAergic).

NANC is an acceptable abbreviation of non-adrenergic, non-cholinergic for peripheral efferent nerve fibres when the identity of the transmitter(s) is unknown.

Glutamatergic, not glutaminergic, should be used to describe nerve fibres releasing glutamate. In referring to peptide-releasing nerve fibres (e.g. those that may release substance P or vasoactive intestinal peptide) the nomenclature to be used is peptidergic (X), e.g. peptidergic (SP).

The terms 5-hydroxytryptamine (5-HT) and 5-hydroxytryptaminergic (i.e. nerves releasing 5-hydroxytryptamine) are preferred to those of serotonin and serotoninergic.

The term 5-HTergic is not acceptable.

The term purinergic defines transmission mediated by ATP.

6 *Terms used to describe agonist and antagonist action*

The following terms can be used without full definition where appropriate, other terms may be used but must be accompanied by a full definition.

Terms used to describe affinity and potency

(a) *EC_{50}* The concentration of an agonist that produces 50% of the maximal response for that agonist *in vitro*. The agonist may be stimulatory or inhibitory. When EC_{50} values are determined in the presence of other agonists or antagonists the concentration of the latter should be stated. Related terms, e.g. EC_{25}, are acceptable if accompanied by a full definition.

(b) *IC_{50}* This term may be used in the following ways.

(i) The concentration of antagonist that reduces the response to a sub-maximal concentration of agonist by 50%; the concentration of agonist should be stated.
(ii) The concentration of competing agonist or antagonist that inhibits the binding of a radioligand by 50%; the concentration of radioligand should be stated.

(c) *ED_{50}* This term may be used in the following ways.

(i) The dose of an agonist or antagonist that produces 50% of the maximal possible effect of that agonist or antagonist *in vivo*.
(ii) The dose of drug that produces the effect under investigation in 50% of the population.

(d) *K* The equilibrium dissociation constant (mol l^{-1}), for ligand receptor interactions. The reciprocal is called the affinity constant or association equilibrium constant. When necessary for clarity, subscripts (letters or numerals, or a combination of both) may be added but these must be clearly explained when first used.

(e) n_H The Hill coefficient.

(f) *pA_2* The negative logarithm to base 10 of the concentration of an antagonist that makes it necessary to double the molar concentration of agonist needed to elicit a given submaximal response. Note that the definition is empirical and does not pre-suppose the mechanism of antagonism. The pA_2 value can be determined from a Schild plot with unconstrained slopes, but only provides an estimate of the pK_B if the antagonism has been shown to meet all of the criteria of competition.

(g) *pD_2* The negative logarithm to base 10 of the EC_{50}

(h) *pIC_{50}* The negative logarithm to base 10 of the IC_{50}.

(i) *pK* The negative logarithm to base 10 of K (with or without subscripts as appropriate: see under K above).

Terms used to describe the mode of antagonism

(a) *Competitive antagonism* In competitive antagonism the binding of agonist and antagonist is mutually exclusive. This may be because the agonist and antagonist compete for the same binding site or combine with adjacent sites that overlap. A third possibility is that different sites are

involved but they influence the receptor macromolecule in such a way that agonist and antagonist molecules cannot be bound at the same time.

(b) *Irreversible competitive antagonism* Used to describe antagonists that bind irreversibly.

(c) *Non-competitive antagonism* Agonist and antagonist can be bound simultaneously; antagonist binding reduces or prevents the action of the agonist.

(d) *Un-competitive antagonism* Antagonist binding is dependent upon prior agonist activation (*e.g.* open channel blockade).

(e) *Irreversible non-competitive antagonism* Used to describe non-competitive antagonists that bind irreversibly.

For a more detailed account of the terms used to describe agonist and antagonist action see Neubig, R.R., (2003) *Pharmacol. Rev.,* **55**, 597–606.

7 *Guidance on statistical analysis of data*

Given that populations of data with a Gaussian (normal) distribution on a logarithmic scale (e.g. pD_2, pEC_{50}, etc.) will show a skewed distribution once converted to a natural scale, parametric analysis is only appropriate on the logarithmic scale for such data. Thus, the expression of EC_{50} and ED_{50} values (derived from log concentration-or log dose-response curves) as means $\pm$ s.e.mean is inappropriate. However, pD_2 or pIC_{50} values may be reported as means $\pm$ s.e.mean.

8 *Enzymes*

The International Union of Biochemistry and Molecular Biology Enzyme Commission (EC) number and full name (Enzyme Nomenclature 1992, Academic Press, San Diego and London) must be quoted when first mentioned in text. Subsequently the accepted trivial name is used. Trivial names may be used in the title. The following abbreviations may be used; cyclo-oxygenase (COX-1 and COX-2), guanylyl cyclase (GC), monoamine oxidase (MAO-A and MAO-B), nitric oxide synthase (eNOS, nNOS and iNOS), phosphodiesterase (PDE1 to PDE11), catechol-O-methyl transferase (COMT), adenylyl cyclase (AC), acetylcholinesterase (AChE), acetyl coenzyme A (AcetylCoA), adenosine triphosphatase (ATPase), angiotensin converting enzyme (ACE), choline acetyltransferase (ChAT), coenzyme A (CoA), deoxyribonuclease (DNAse), GABA transaminase (GABA-T), glutamic acid decarboxylase (GAD), lipoxygenase (LOX), phenylethanolamine N-methyltransferase (PNMT), phospholipase (PLA_2, PLC, PLD), protein kinase (PKA, PKB, PKC, PKG), tyrosine hydroxylase (TH), tyrosine kinase (TK), ribonuclease (RNase)

9 *Transporters*

Transporters should be defined in full at first mention.

10 *Other nomenclature requirements*

(a) *Racemates* Authors must state unambiguously in the Methods section of papers which isomers were used, e.g. (+)- or (−)-propranolol, and must bring to the attention of the reader the composite character of drugs that are mixtures of stereoisomers. Furthermore, the implications of the composite nature of such drugs studied for the interpretation of the data measured and the conclusions drawn must be made explicit. Capital R and S refer to the absolute configurations of chiral centres and should be used where necessary.

(b) *Purines* This term should not be used as a synonym for purine nucleotides or nucleosides.

(c) *Eicosanoids* The system of nomenclature to be used for eicosanoids is that published in *Methods in Enzymology* (1990) **187**, 1–9. In manuscripts, the first use of the full chemical name of any eicosanoid should indicate double bond geometry when this is known.

(d) *Cell lines* Cell type, range of passage number, species and source should be defined.

(e) *Molecular biology* Abbreviations pertaining to molecular biological techniques need to be defined or presented in such a way that they can be recognised by the non-specialist.

(f) *Tension* Tension is force and should be calibrated in Newtons, ($1\ \text{Newton} = 1\ \text{kg ms}^{-1}$) or in kg weight, g weight, or mg weight etc. It should not be calibrated in units of mass (e.g. kg). (See Miller D.J. (1988) *Trends Pharmacol. Sci.,* **9**, 124–125).

(g) *Ions* When referring to ions, the charge should be indicated, *e.g.* Na^+, Ca^{2+}, $3Na^+/Ca^{2+}$ exchange, etc.

(h) *Inhibitors of nitric oxide synthase (NOS)* Commonly used inhibitors of NOS and their appropriate abbreviations include L-N^G-mono-methylarginine (L-NMMA), L-N^G-nitroarginine (L-NOARG), and L-N^G-nitroarginine methyl ester (L-NAME).