

Editorial

Words derived from the noun *peptide*

Abstract: Modifications of the noun *peptide* are explored and clarified; a few are condemned. Copyright © 2006 European Peptide Society and John Wiley & Sons, Ltd.

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When preparing my recent Editorial [1] on abbreviations and symbolism in peptide science, I stumbled on the word *eupeptide* in two IUPAC-IUB sources [2,3]. It is explained in the first of these [2] that amide bonds between the α -functions of two α -amino acids are 'sometimes called eupeptide bonds'. I was rather startled by this and wondered how it could be that in a career of 40 years thinking, reading, and writing (preaching, even) about peptides, this word had never entered my vocabulary.

So I fell to pondering puzzling, redundant, and ambiguous derivatives of the noun *peptide*. It sprang by back-formation from Emil Fischer's *dipeptid*, *tripeptid*, and *polypeptid* (1902–1903). *The New Shorter OED* [4] definition is:

Any compound in which two or more amino-acids are linked together in a linear sequence, the carboxyl group of each acid being joined to the amino group of the next.

The commonest use of the word by far is for assemblies of α -amino acid residues which are drawn from those commonly found in simple proteins and linked only through their α -functions. But it is also applied to cases incorporating any amino acid, other types of component, or other sorts of linkage. The sole limitation of the definition is that at least two amino acids must be present, linked amide-wise through a *peptide bond* or a *peptide linkage*. On its own, the word *peptide* gives no clue to the origin, function, structural subtlety, properties, or molecular size. Since these aspects are what we are all concerned with, it invites elaboration.

Modifications of the form *prefixopeptide* are common; the form *prefixapeptide* is occasional. In most cases, the prefix gives at least the gist of the meaning of the composite word, e.g. *lipopeptide*, *glycopeptide*, *nucleopeptide*, *metallopeptide*, *chromopeptide*, *gonadopeptide*, *adrenopeptide*, *azapeptide*, etc. Over 50 of them are in use. But without context, the exact meaning of many of them is not obvious and some are enigmatic. New modifications should not be lightly introduced. Adjectival qualification or use of the word *peptide*, e.g. *toxic peptide* or *peptide toxin*, is generally clear, and when a neologism is being considered, it is worth asking whether existing language will provide the need.

Prefixed indication of molecular size is also common, e.g. *polypeptide* (q.v.) and *oligopeptide* (q.v.), despite the lack of consensus on where the one becomes the other on the **mer*-scale. *Micropeptide* and *nanopeptide* (not infrequently misprinted from *nonapeptide*, so bradykinin and oxytocin have both been called nanopeptides) are no less vague and do not deserve currency. *Macropeptide* (q.v.) is not a general antonym to *micropeptide* but has a limited meaning in dairy science. *Superpeptide* has been used for very high molecular weight peptides, peptides of around 30 residues, and in journalistic hyperbole; it is to be avoided. Precision has traditionally been introduced with the prefixes *di-*, *tri-*, *tetra-*, *penta-*, etc.; but beyond say 10 residues it is better to abandon this pseudoclassical practice and use e.g. *24-mer* etc. rather than *tetracosapeptide* (q.v.) etc.

Modification by suffix is less prolific, and the commonest examples *peptidase* and *peptidolysis* (*peptolysis* is a rare alternative which should not be used) are so familiar and clearly understood that they need no comment.

Below are some notes on words which have at one time or another puzzled me. The online trawling for this exercise was all done in July 2005. I have confined myself to single words derived from Fischer's German root *peptid*; this root was derived in turn from the Greek word *peptos* (cooked, digested), which has also spawned a number of words which have nothing to do with peptide science: *peptic* (pertaining to digestion), *dyspeptic* (bad-tempered; having indigestion), *eupeptic* (easily digested, having a good digestion), *peptize* (in colloid science, rubber and petroleum technology: formation and stabilization of a sol).

Allopeptide

In immunology: a peptide from a different individual (Greek *allos*, other) of the same species.

Apopeptide

The free peptide component of a bioactive peptide: cofactor complex, the cofactor having been removed (Greek *apo-*, away from).

Carbopeptoid

An oligomer in which carbohydrate units are linked through amide bonds.

Conopeptide

A peptide toxin from the marine snail genus *Conus*.

Cropeptide : cropeptide W

In cosmetic and toiletry formulations: a hydrolysis product of wheat which is used in lotions, shampoos, etc. and which is said to have moisturising properties.

Cyclotide

Coined recently [5] from **cyclopeptide** as the class name for small proteins with cystine knots. It is already in frequent use (Google 68 hits, SciFinder 864). *Oligotide*, which might have been thought to have been derived similarly, belongs to an allied field. It comes from **oligodeoxyribonucleotide**. Cyclosporin A appeared once in SciFinder as a 'cyclic oligotide'; however, it was perhaps a mistake.

Depsipeptide

A peptide in which a position in the molecule which might have been occupied by an amino acid residue is taken by a hydroxy acid residue.

A *depside* is a member of a class of naturally occurring phenolic natural products found in lichens. The word is derived from the Greek word *depsein*, meaning 'to make supple, to tan'. Whether this has anything to do with the etymology of *depsipeptide* is obscure (were the first recognised depsipeptides found in lichens?).

Eupeptide

A peptide in which the amino acid residues are linked only through α -functions, i.e. a 'normal' or 'ordinary' peptide. SciFinder gave no hits; Google gave 212, but most of these were either IUPAC-IUB documents or dictionary definitions or allusions to the so-called '*eupeptide system*' of gastrointestinal hormones. I am not aware of any use in the real literature of peptide science.

Holopeptide

- (1) A complete peptide as opposed to fragments thereof.
- (2) A complete peptide: cofactor complex as opposed to the *apopeptide* (q.v.) component.

Homopeptide

A peptide comprising only identical amino acid residues. Note that when the prefix *homo-* is applied to amino acids, it indicates carbon chain extension, as in a homologous series.

Isopeptide

A peptide in which there are inter-residue amide bonds between side chains.

Macropeptide

In dairy science: a product of milk coagulation, usually appearing as 'casein macropeptide'.

Oligopeptide

A peptide comprising a few amino acid residues.

Peptidaceous

Derived by analogy with *proteinaceous*: an infrequently used and redundant alternative to *peptidic* (q.v.).

Peptidal

An infrequently used and redundant alternative to *peptidic* (q.v.).

Peptidergic

In neuroscience: liberating, stimulated by, or involving a peptide or peptides. Derived by analogy with *adrenergic*, *cholinergic* etc.

Peptidic

Pertaining to or having the nature or composition of the peptide class. Often encountered in the negative form *nonpeptidic*.

Peptidoid

Online dictionaries gave two slightly different definitions:

- (1) 'A condensation product of two amino acids involving at least one condensing group other than the α -carboxyl or α -amino group; e.g. glutathione' [6].
- (2) 'A compound formed by the condensation of two amino acids, with the linkage involving at least one group that is not a carboxyl or an amino group' [7]. This sense was apparently meant by one Google hit alluding to lysinoalanine, *N*^ε-(2-amino,2-carboxyethyl)-lysine.

A third, adjectival, sense, 'peptide-like' may have been intended by one of the two SciFinder hits, in which a tripeptide derivative was called a 'peptidoid agonist'. This sense follows the usual meaning in English of the suffix *-oid* (e.g. *humanoid*, *spheroid*).

Most of the 14 Google hits were about the word, rather than examples of its use. It is a superfluous and confusing absurdity which ought to be eschewed.

Peptidome

Derived by analogy with *proteome*: all the peptides in a cell or tissue.

Peptidomimetic

A molecule, usually a synthetic drug candidate, which is designed to resemble a bioactive peptide in functionality, and/or overall shape, so that it can interact at that peptide's receptors, but which has structural features which diverge widely from those of the peptide, such as *pseudopeptide* (q.v.) *bonds* or conformational constraints. Peptidomimetics can also be found in natural sources; morphine is one such natural peptidomimetic.

Peptidose

This word gave 19 Google hits, but is not, as might be thought, some kind of carbohydrate: it was invariably a misprint for *peptidase*.

Peptidyl

In chemical nomenclature: an acyl group derived from a C-terminal carboxyl group of a peptide.

The *New Shorter OED* [3] defines this term beginning 'a radical...', an unfortunate use of the word *radical* in its archaic chemical sense, in which it meant a group or substituent.

Peptoid

A peptide analogue in which one or more of the proteinogenic amino acid residues has been replaced by the isomer in which the side chain has been relocated from C α to N α , e.g. in which leucine (C α -isobutylglycine) is replaced by N α -isobutylglycine. Hence *dipeptoid*, *tripeptoid*, *polypeptoid*, *peptoidic*. The term *retropeptoid* has been used [8] in sense 2 below of *retropeptide* (q.v.), i.e. for an analogue with simple reversal of the amino acid residue sequence, in this case of the N-alkylglycines, in the parent.

Note that in some local accents (e.g. the pleasant brogue of the Republic of Ireland) *side* becomes 'soid', *tide* 'toid', and *inside* 'insoide', so *peptide* is at risk of being heard as 'peptoid'.

The term *carbopeptoid* (q.v.) is unconnected with the usual meaning of *peptoid*.

Peptolide

Obsolete; a synonym for *depsipeptide* (q.v.).

Polypeptide

A peptide comprising many amino acid residues; formerly any such peptide, but in most cases either *peptide* or *protein* is now used. But the term finds current and appropriate use in *sequential polypeptides*, i.e. peptides with repeating amino acid sequences, e.g. the collagen model H-(GlyGlyPro) $_n$ -OH.

Propeptide

A biosynthetic precursor of a bioactive peptide. The use of the prefix *pro-* here is potentially confusing, as in ordinary English it means 'deputising for' or 'in favor of' as well as 'coming before'. *Prepeptide* is a less-used synonym; a *prepropeptide* is a biosynthetic precursor of a biosynthetic precursor.

Pseudopeptide

A synonym for a *peptidomimetic* (q.v.), but this use is becoming obsolete, like *peptide surrogate*. The adjectival use *pseudopeptide bond* remains current; in symbolic representation ψ , **psi**, is used to indicate a **pseudopeptide**, e.g. the analogue obtained by reduction of the peptide bond in GlyGly is represented Gly ψ [CH $_2$ NH]Gly.

Retropeptide

(1) A peptide analogue in which one or more peptide bonds -CONH- is replaced by -NHCO-. If in

addition the configurations of the α -chiral centers are inverted, then the combination term *retro-inverso peptide* is used.

(2) A peptide analogue in which the sequence of the amino acid residues in the parent peptide is reversed, e.g. [9].

Clearly, there is scope for confusion here, and care is necessary.

Teloepptide

A peptide corresponding to a part of a terminal (Greek *telos*, end) region of a protein.

It is an ironic consequence of using Greek for word design that the term for a peptide from within (Greek *endon*) a sequence, as opposed to from an *end*, is **endopeptide** (commonly found as *endopeptidase*, antonym *exoepetidase*).

Tetracosapeptide

A peptide of 24 amino acid residues, i.e. a 24-mer. Hence *tetracosactide*, *tetracosactrin*, β -corticotropin-(1-24)-peptide.

Xenopeptide

In immunology: a peptide from another species (Greek *xenos*, stranger).

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