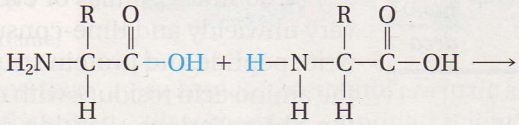
18.4 Peptides

AIMS: ***To name and describe the bond that links amino acids together. To draw complete structural formulas for simple peptides. To contrast the biological functions of some peptide hormones.***

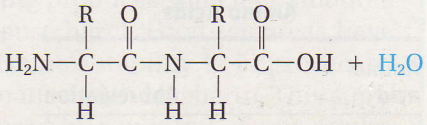
Focus

Amino acids are linked to form peptides.

A **peptide** *is any combination of amino acids in which the alpha amino group (—NH_2) of one acid is united with the alpha carboxylic group (—CO_2H) of another through an amide bond.*



Amino acid Amino acid



Peptide

The amide bonds formed in peptides always involve the alpha amino and alpha carboxylic acid groups and never those of side chains. More amino acids may be added in the same fashion to form chains such as those in Figure 18.1. *The amide bond between the carbonyl group of one amino acid and the nitrogen of the next amino acid in the peptide chain is called a* **peptide bond** *or peptide link. Amino acids that have been incorporated into peptides are called* **amino acid residues.** As more amino acid residues are added, a backbone common to all peptide molecules is formed. The amino acid residue with a free amino group at one end of the chain is the *N-terminal residue;* the residue with a free carboxylic acid at the other end of the chain is the *C-terminal residue.* The number of amino acid residues in a peptide is often indicated by a set of prefixes for peptides of up to 10

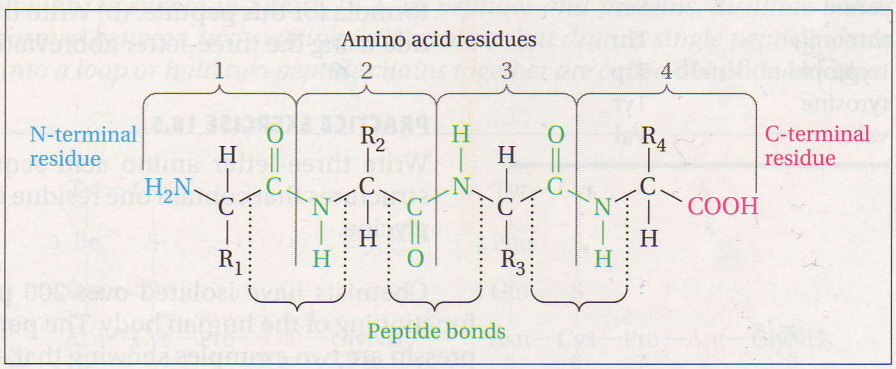


Figure 18.1
Parts of a peptide—in this case, a tetrapeptide. The peptide bonds of the zigzag backbone are shown in color. Note that the C-terminal is at the right and the N-terminal is at the left.

Table 18.1 Prefixes for Short Peptides

Residues	Prefix
2	*di-*
3	*tri-*
4	*tetra-*
5	*penta-*
6	*hexa-*
7	*hepta-*
8	*octa-*
9	*nona-*
10	*deca-*

Table 18.2 Three-Letter Abbreviations for Amino Acids

Amino acid	Abbreviation
alanine	Ala
arginine	Arg
asparagine	Asn
aspartic acid	Asp
cysteine	Cys
glutamine	Gln
glutamic acid	Glu
glycine	Gly
histidine	His
isoleucine	Ile
leucine	Leu
lysine	Lys
methionine	Met
phenylalanine	Phe
proline	Pro
serine	Ser
threonine	Thr
tryptophan	Trp
tyrosine	Tyr
valine	Val

residues, as shown in Table 18.1. *We call any peptide with more than 20 amino acid residues a* **polypeptide.** In theory, the process of adding amino acids to a peptide chain may be continued indefinitely. Names of peptides are derived from names of amino acid residues. By convention, names of peptides are always written from left to right starting with the N-terminal end; a peptide that contains N-terminal glycine, followed by a histidine, followed by C-terminal phenylalanine is named *glycyl-histidyl-phenylalanine.* The sequence is extremely important; glycyl-histidyl-phenylalanine is a different molecule from phenylalanyl-histidyl-glycine. The methyl ester of the dipeptide aspartyl phenylalanine is an artificial sweetener (see A Closer Look: Aspartame).

Structural formulas or even full word names for large peptides become very unwieldy and time-consuming to write. To simplify matters, chemists write peptide and protein structures by using three-letter abbreviations for the amino acid residues with dashes to show peptide bonds. Table 18.2 lists the abbreviations. Peptide structures written with these abbreviations always start with the N-terminal group to the left and end with the C-terminal group to the right. For example, we can write glycyl-histidyl-phenylalanine as Gly-His-Phe and phenylalanyl-histidyl-glycine as Phe-His-Gly.

EXAMPLE 18.3 Naming a peptide

Write the (a) the three-letter amino acid name and (b) the name using full abbreviations for the peptide in Figure 18.1 assuming that R_1 is methyl, R_2 is isopropyl, R_3 is methyl, and R_4 is hydrogen.

SOLUTION

(a) The full name, starting at the N-terminal end, is alanyl-valyl-alanyl-glycine.
(b) Using abbreviations: Ala-Val-Ala-Gly.

PRACTICE EXERCISE 18.4

Glutathione, a tripeptide that is widely distributed in all living tissues, is named glutamyl-cysteinyl-glycine. (a) Draw the complete structural formula for this peptide. (b) Write the amino acid sequence of the peptide using the three-letter abbreviations.

PRACTICE EXERCISE 18.5

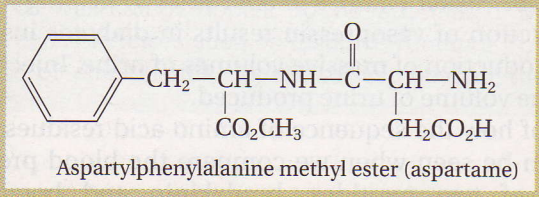
Write three-letter amino acid sequences for all possible tripeptide structures that contain one residue each of glutamic acid, cysteine, and glycine.

Chemists have isolated over 200 peptides important to the smooth functioning of the human body. The peptide hormones oxytocin and vasopressin are two examples showing that apparently minor differences in the order of amino acid residues can result in profoundly different biological actions.

A Closer Look

Aspartame

Aspartame, an artificial sweetener with the brand name NutraSweet®, is the methyl ester of the dipeptide aspartylphenylalanine.



Aspartylphenylalanine methyl ester (aspartame)

Aspartame is a substitute for sucrose and saccharin.

Aspartame is more than 50 times sweeter than sucrose. Now approved for use in more than 30 countries, this product of amino acid chemistry has found wide acceptance in the food industry as a substitute for both sucrose and saccharin (see figure). The main advantage of aspartame over saccharin is its taste, which is very similar to that of cane sugar. Its chief disadvantage is its instability. Aspartame is not recommended for the preparation of foods in which cooking temperatures exceed 150 °C. High temperatures and extremes of pH can cause aspartame in solution to hydrolyze to the unesterified dipeptide, aspartylphenylalanine and methanol, with a simultaneous loss of sweetness. Methanol is a toxic alcohol, and there is disagreement among scientists whether the breakdown of the small amounts of aspartame used for sweetening produces sufficient amounts of methanol to cause harm. Food scientists have found that aspartame's stability is improved by using it in combination with saccharin. This combination is now used in a number of soft drinks. Products that contain aspartame, however, must carry a warning label for people who suffer from the hereditary disease phenylketonuria. People who have phenylketonuria are unable to break down phenylalanine and must therefore limit its intake, as we will see in Section 26.8.

Oxytocin and vasopressin are formed in the hypothalamus (pituitary gland) and enter the bloodstream. Each hormone is a nonapeptide (contains nine amino acid residues) with six of the amino acid residues drawn into a loop by a disulfide bond. The disulfide bond is formed by the coupling of cysteine residues in the first and sixth positions of their peptide chains, as shown in Figure 18.2. *In peptides and proteins, disulfide bonds formed between two cysteine —SH groups that draw a single peptide chain into a loop or hold two peptide chains together are called* **disulfide bridges.**

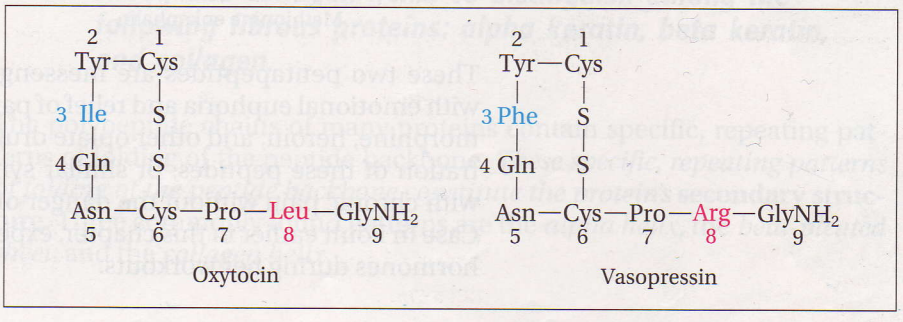
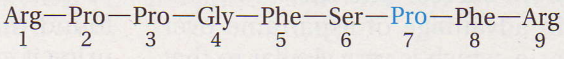


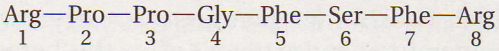
Figure 18.2
Oxytocin and vasopressin. These peptide hormones differ by two amino acid residues (shown in color). The C-terminal residues have amide functional groups rather than carboxylic acid groups.

Although the amino acid composition differs at only the third and eighth positions of their peptide chains (counting from the N-terminal end), the biological roles of these two peptides are different. Oxytocin stimulates milk ejection in females and contraction of the smooth muscle of the uterus in labor. Oxytocin has been called the "cuddle drug," because in females it stimulates sensations during lovemaking and produces feelings of relaxed satisfaction and attachment. Vasopressin is an **antidiuretic**—*it helps to maintain a proper water balance in both sexes by helping to retain water.* Defective production of vasopressin results in diabetes insipidus, characterized by the production of massive volumes of urine. Injections of the hormone control the volume of urine produced.

Another example of how the sequence of amino acid residues affects biological function can be seen when we compare the blood pressure–controlling activities of two peptides, bradykinin and boguskinin. Bradykinin is a nonapeptide formed directly in the bloodstream when a fragment is chopped from a large protein, α-2-globulin. Boguskinin is a synthetic octapeptide that lacks only the proline residue at position 7 of bradykinin.



Bradykinin



Boguskinin

Bradykinin is partially responsible for triggering pain, welt formation (as in scratches), movement of smooth muscle, and lowering of blood pressure. Blood pressure is lowered when, in response to a signal, bradykinin and related peptides relax muscles of blood vessel walls. Blood vessels dilate, or expand, and blood flows into the expanded volume, lowering blood pressure. Less than 1 μg of bradykinin lowers blood pressure in an average-sized adult. Boguskinin, on the other hand, is completely inactive—hence the name *bogus,* meaning "false."

Parts of the brain contain **enkephalins**—*peptides involved with feelings of emotion and sensation of pain.* Two major enkephalins are methionine enkephalin and leucine enkephalin, which differ in structure by only one amino acid residue:

Methionine enkephalin

Leucine enkephalin

These two pentapeptides are messengers in brain processes associated with emotional euphoria and relief of pain—the same processes affected by morphine, heroin, and other opiate drugs. Researchers hope that administration of these peptides, or similar synthetics, will bring relief to people with chronic pain without the danger of addiction. Karla, the jogger in the Case in Point earlier in this chapter, experiences the effects of these peptide hormones during her workouts.