Peptides

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Resources

- This lecture
- Campbell and Farrell’s Biochemistry, Chapters 3 (pp.72-78) and 4
Formation of a polypeptide
Definitions and concepts

- A residue: each amino acid in a (poly)peptide
- Dipeptide, tripeptide, tetrapeptide, etc.
- Oligopeptide (peptide): a short chain of 20-30 amino acids
- Polypeptide: a longer peptide with no particular structure
- Protein: a polypeptide chains with an organized 3D structures
- The average molecular weight of an amino acid residue is about 110
  - The molecular weights of most proteins are between 5500 and 220,000 (calculate how many amino acids)
- We refer to the mass of a polypeptide in units of Daltons
  - A 10,000-MW protein has a mass of 10,000 Daltons (Da) or 10 kilodaltons (kDa)
Peptide bond

Chemically, it is called an amide bond.

A condensation reaction
Features of the peptide bond

- Resonance structure makes peptide bond
  - Zigzag structure
  - Double bond
  - Planar, charged, Rigid, Un-rotatable
- Hydrogen bonding
  - Except proline
Backbone, orientation and directionality

\( \alpha \)-amide N, the \( \alpha \)-C, and the \( \alpha \) carbonyl C atom

Peptide bonds

Direction
Except for proline

- Steric hindrance between the functional groups attached to the C$\alpha$ atoms will be greater in the cis configuration.
- In proline, both cis and trans conformations have about equivalent energies.
- Proline is thus found in the cis configuration more frequently than other amino acid residues.
Examples of functional and exceptional peptides
Carnosine (β-alanyl-L-histidin)e

- A dipeptide of β-alanine and histidine
- The amino group is bonded to the β-carbon of alanine
- It is highly concentrated in muscle and brain tissues
  - Protection of cells from ROS (radical oxygen species) and peroxides
  - Contraction of muscle
Glutathione

(γ-glutamyl-L-cysteinylglycine)
Function of glutathione

- It scavenges oxidizing agents by reacting with them.
- Two molecules of the reduced glutathione molecules form the oxidized form of glutathione by forming a disulfide bond between the —SH groups of the two cysteine residues.
Enkephalins

Two pentapeptides found in the brain known as enkephalins, and function as analgesics (pain relievers). They differ only in their C-terminal amino acids:

- Met-enkephalin: Tyr-Gly-Gly-Phe-Met
- Leu-enkephalin: Tyr-Gly-Gly-Phe-Leu

The aromatic side chains of tyrosine and phenylalanine play a role in their activities.
Enkephalins and morphine

There are similarities between the three-dimensional structures of opiates, such as morphine, and enkephalins.
Oxytocin and vasopressin

- Hormones with cyclic structures due to S-S link between Cys.
- Both have amide group at the C-terminus.
- Both contain nine residues, but:
  - **Oxytocin** has isoleucine and leucine.
  - **Vasopressin** has phenylalanine and arginine.
- Oxytocin regulates contraction of uterine muscle (labor contraction).
- Vasopressin regulates contraction of smooth muscle, increases water retention, and increases blood pressure.
Vasopressin

Practice: what is the primary structure?

Note: the structure ends with NH2
Gramicidin S and tyrocidine A

They are cyclic decapeptides formed by the peptide bonds.
They are produced by the bacterium Bacillus brevis and act as antibiotics.
Both contain D- and L-amino acids.
Both contain the amino acid ornithine (Orn), which does not occur in proteins.
Aspartame

L-Aspartyl-L-phenylalanine (methyl ester)

- Adiprotein that is 200 times sweeter than sugar.
- If a D-amino acid is substituted for either amino acid or for both of them, the resulting derivative is bitter rather than sweet.
Phenylketonuria (PKU)

PKU is a hereditary “inborn error of metabolism” caused by defective enzyme, phenylalanine hydroxylase.

It causes accumulation of phenylpyruvate, which causes mental retardation.

Sources of phenylalanine such as aspartame must be limited.

A substitute for aspartame, known as alatame, contains alanine rather than phenylalanine.