Chapter 1

Introduction to Biochemistry

Carl Neuberg coined the word "biochemistry" in 1903. Biochemistry is the study of the chemistry of life and living processes in general. Biochemistry is involved in every element of life, including conception, growth, reproduction, ageing, and death. Every movement of life, in fact, is filled with hundreds of biological reactions. Biochemistry is the most inventive and rapidly evolving field of medicine. This is demonstrated by the fact that biochemistry researchers have received the majority of Nobel Prizes in Medicine and Physiology over the years.

Origin of Biochemistry: the discovery that a cell-free yeast can ferment sugar-initiated biochemistry.

The discovery of yeast's capacity to transform carbohydrates to ethyl alcohol predates recorded history. This process, however, did not directly lead to the study of biochemistry until the early twentieth century. Despite extensive research into winemaking, Louis Pasteur, a prominent French scientist, maintained that fermentation was possible only in imperfect cells. The Büchner brothers, who discovered that fertilization could take place in cellular parts in 1899, pointed out his mistake. These findings are due to the storage of yeast extracted from a concentrated sugar solution plant that was added as a preservative. In the early years of the 20th century, these discoveries resulted in a rapid and very fruitful experiment that led to the study of biochemistry. This study found important functions of inorganic phosphate, ADP, ATP, and NADH, as well as phosphorylated sugars and chemical processes and enzymes that convert glucose into pyruvate or ethanol and -CO_2 (fermentation). After research in the 1930s and 1940s, scientists discovered the intermediate cycles of citric acid and urea biosynthesis, as well as the important roles of cofactors found in vitamins or "coenzymes" such as thiamine pyrophosphate, riboflavin, and, finally, coenzyme A, coenzyme Q, and cobamide coenzymes. The 1950s described the biosynthesis processes of pentoses and the breakdown of amino acids and lipids, as well as how complex carbohydrates are created and broken down into simple sugars.

Scope of Biochemistry in Pharmacy

For health-care practitioners, particularly physicians, learning and maintaining good health, as well as comprehending and effectively treating diseases, are two major concerns. Both of these basic difficulties are impacted by biochemistry, and the link between biochemistry and medicine is a two-way street. Many features of health and sickness have been emphasized by biochemical research, and the study of many aspects of health and disease has opened up new branches of biochemistry. Archibald Garrod, an English physician, investigated persons with the relatively unusual disorders of alkaptonuria, albinism, cystinuria, and pentosuria in the early 1900s and concluded that they were genetically determined. These are known as inborn metabolic errors, according to Garrod. His discoveries established the framework for the study of human biochemical genetics to expand. A more current example is the research of the genetic and molecular roots of familial hypercholesterolemia, a disorder that causes atherosclerosis at an early age. This enabled a broader knowledge of cell receptors and methods of absorption, not just of cholesterol, but of how other chemicals cross cell membranes, in addition to clarifying different genetic defects responsible for this sickness. The identification of oncogenes and tumour suppressor genes in cancer cells has moved emphasis to the molecular pathways that govern normal cell growth. These examples highlight how disease study may lead to new disciplines of fundamental biochemical research. Science supplies a platform for physicians and other health-care and biology professionals that impact practise, motivates curiosity, and fosters the use of scientific approaches for lifelong learning. The area of medicine will have a logical basis capable of tolerating and responding to new findings as long as medical treatment is firmly established in biochemistry and other fundamental sciences (Figure 1.1). Nutrition and Preventive Medicine are touched by biochemical research. Health is described by the World Health Organization (WHO) as a condition of "complete physical, mental, and social well-being." A healthy diet must include a range of chemicals, the most essential of which being vitamins and particular amino acids as well as fatty acids, minerals, and water. Nutrition is strongly reliant on biochemical knowledge, and biochemistry and nutrition have a number of similarities.

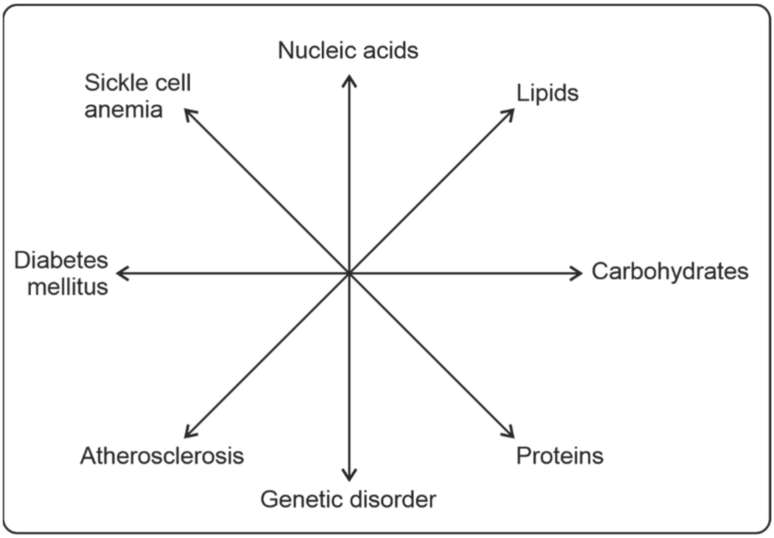

Fig. 1.1 Two-way connection of biochemistry and medicine.

Life is made up of lifeless molecules. The bacteria *Escherichia coli* has roughly 6,000 distinct chemical molecules in a single cell. Only a fraction of the 100,000 distinct kinds of molecules believed to exist in man have been identified.

Cell

Life's structural and functional unit is the cell. It can also be looked as the fundamental unit of biological activity. The contributions of Schleiden and Schwann gave rise to the idea of cell (1838). The complexity of cell structure, however, were not revealed until around 1940.

Prokaryotic and Eukaryotic Cells

The living kingdom's cells may be classified into two groups.

1. **Prokaryotes** (Greek: pro – before; karyon – nucleus) have a simple structure and lack a well-defined nucleus. Various bacteria are among them.
2. **Eukaryotes** (Greek: eu – true; karyon – nucleus) have a well-defined nucleus and more complicated structure and function than prokaryotes. Eukaryotic cells make up the higher creatures (animals and plants).

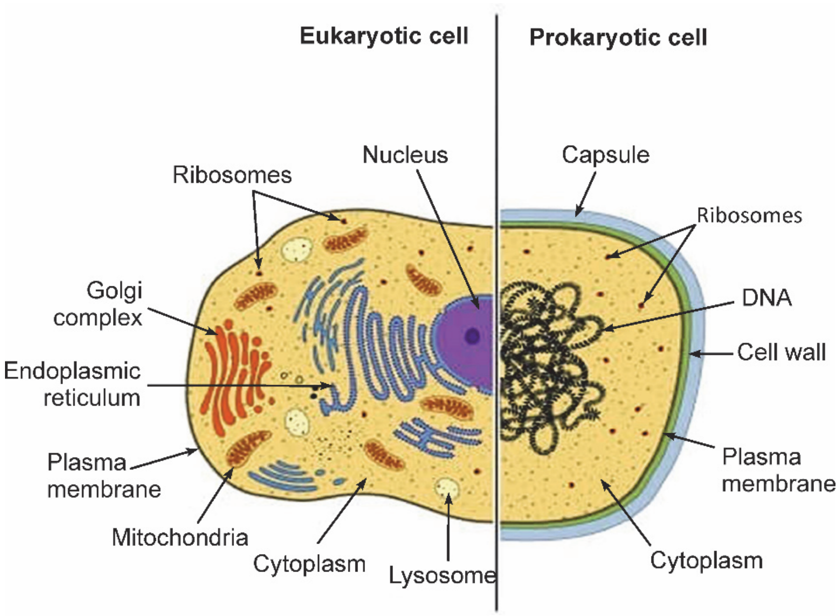

Fig. 1.2 Diagram of prokaryotic and eurkaryotic cells.

The differences between the two are shown in **Table 1.1**

Table 1.1 Differences between prokaryotic and eurkaryotic cells.

Characteristic	Prokaryotes	Eukaryotes
Size	The size is usually small (generally 1–10 µm).	The size of the cell is larger compared to prokaryotes (generally 10–100 µm).
Cell membrane	A stiff and strong cell wall surrounds the cell.	A flexible plasma membrane surrounds the cell.
Nucleus	Histones are not present; however, DNA is found as a nucleoid.	DNA is associated with histones, and the nucleus is highly defined and enclosed by a membrane.
Subcellular organelles	Absent	Organelles (mitochondria, nucleus, and lysosomes) are present inside the cell.
Energy metabolism	Mitochondria is absent and energy metabolism enzymes are linked to the membrane.	Energy-metabolizing enzymes are found in mitochondria
Cytoplasm	Organelles and cytoskeleton are absent.	Organelles and the cytoskeleton (a network of filaments and filaments) are found.

The nucleus, which is surrounded by a double membrane nuclear envelope, is the biggest cellular organelle. The outer membrane is connected to the endoplasmic reticulum membranes. The two nuclear membranes feature nuclear holes with a diameter of around 90 nm at regular intervals. These holes allow products generated in the nucleus to freely flow into the surrounding cytoplasm.

DNA, the reservoir of genetic information, is found in the nucleus. Nucleosomes are made up of eukaryotic DNA and basic proteins (histones) in a 1:1 ratio. Chromatin fibres of chromosomes are made up of nucleosomes. A single human chromosome thus has around a million nucleosomes. The number of chromosomes in a species is a distinguishing trait. Humans have 46 chromosomes in their nucleus, which are tightly packed.

The nucleolus is a compact mass found in the nucleus of eukaryotic cells.

It contains a lot of RNA, especially ribosomal RNA, which reaches the cytosol via nuclear pores.

Nucleoplasm is the term used to describe the nucleus's ground material. Enzymes like DNA polymerases and RNA polymerases are abundant.

Cell Organelles

Many membrane-bound organelles in eukaryotic cells carry out specialised biological functions which are necessary for overall growth and development of living organism. The following are the main organelles and their functions:

1. **Nucleus:** The nucleus contains more than 95 percent of the DNA. The nucleus is the cell's command center and houses all of the cell's DNA. The complicated architecture of nuclear pore complexes control protein and nucleic acid ribonucleic acids (RNAs) migration through the nuclear envelope. DNA is coiled into a thick mass called chromatin in the nucleus, which is stained darkly with dyes. The nucleolus is a second dense mass joined to the inner nuclear envelope by a thin membrane. DNA polymerases and RNA polymerases are found in the nucleoplasm of the nucleus and are involved in the synthesis of m-RNA and t-RNA.

   The main functions of nucleus are as follows:

   - The nucleus is where DNA replication and RNA transcription take place. Transcription is the primary metabolic activity of the nucleus and is the initial step in the manifestation of genetic information.

- The nucleolus is non membranous and contains enzymes such as RNA polymerase, RNAase, ATPase, and others, but not DNA polymerase. The nucleolus is where ribosomal RNA is made (r-RNA).
- Ribosome subunits are put together in nucleolus.

2. **Mitochondrion**: Mitochondrion is the power house of the cell. There is just one mitochondrion in certain algae, whereas there are half a million in the protozoan Chaos. The number of mitochondria in a mammalian liver cell ranging from 800 to 2500. A typical mammalian mitochondrion measures 0.2 to 0.8 μm in diameter and 0.5 to 1.0 μm in length. Mitochondrion shape changes throughout time. Mitochondria can take on a variety of forms depending on the metabolic state. Two concentric membranes surround the mitochondrion, each with distinct characteristics and biological activities. Phospholipids make up the majority of the outer mitochondrial membrane, which also contains a significant quantity of cholesterol. Porin, a protein found in abundance in the outer membrane, is also present in large quantities. Phospholipids make up the majority of the outer mitochondrial membrane, which also contains a significant quantity of cholesterol. Porin, a protein found in abundance in the outer membrane, is also present in large quantities. It is now well understood that as mitochondria transition from a resting to a respiring state, they undergo significant modifications. The inner membrane does not fold into cristae during respiration; instead, it seems to shrink, leaving a considerably larger intermembrane gap. The intermembrane gap is the area between the outer and inner membranes. Because tiny molecules may pass readily through the outer membrane, the intermembrane space has a similar ionic composition to the cytoplasm. The mitochondrial matrix is the area surrounded by the inner membrane. Matrix composition: The citric acid cycle and fatty acid oxidation enzymes are both found in the matrix. Several strands of circular DNA, ribosomes, and enzymes are also present in the matrix, which are essential for the production of the proteins encoded in the mitochondrial genome. However, the mitochondrion is not genetically self-contained, and the genes encoding the majority of mitochondrial proteins are found in nuclear DNA. The mitochondrion contains several enzymes involved in glucose, fatty acid, and nitrogen metabolism. Electron transport and oxidative phosphorylation enzymes can also be found in various parts of this cell organelle. The mitochondrion is designed to oxidise NADH (reduced NAD) and FAD quickly. H_2 (reduced FAD) is created during the glycolysis, citric acid cycle, and fatty acid oxidation processes. The energy created is captured and stored in the form of ATP for later usage in the body.

3. **Endoplasmic reticulum (ER):** Eukaryotic cells feature a variety of membrane complexes that are connected by organelles. Protein synthesis, transport, modification, storage, and secretion are all carried out by these organelles. The endoplasmic reticulum (ER) extends from the cell membrane, covers the nucleus, surrounds the mitochondria, and seems to link directly to the Golgi apparatus, varying in form, size, and quantity. Cisternae refer to these membranes and the water channels they contain.

   Endoplasmic reticulum (ER) is divided into two types:

   (i) Ergastoplasm, commonly known as rough-surfaced ER.

   They have ribosomes on them. This form of ER combines with the nuclear envelope's outer membrane near the nucleus.

   (ii) Smooth-surfaced ER: Ribosomes are not connected in smooth-surfaced ER.

   Functions: Rough ER is responsible for the generation of membrane lipids and shell proteins. These proteins are injected into the lumen of the cisternae through the ER membrane, where they are changed and transported throughout the cell.

   Smooth ER function: The smooth endoplasmic reticulum is engaged in the process. In the production of lipids, and in the modification and transport of proteins synthesised in the rough ER.

4. **Golgi complexes (also known as the Golgi apparatus):** Dictyosomes is another name for them. The Golgi complex is a unique stack of smooth-surfaced compartments or cisternae found in each eukaryotic cell. The Golgi complexes, which include flattened, fluid-filled golgi sacs, are generally tightly connected with the ER.

   A proximal or cis compartment, a middle compartment, and a distal or trans compartment make up the Golgi complex. Recent data clearly shows that the complex functions as a one-of-a-kind sorting device that accepts freshly produced proteins from the ER that all include signal or transit peptides.

5. **Lysosomes:** Lysosomes are cellular organelles that house a package of enzymes. The name lysosome comes from the Greek word Gree, which means lysis (loosening). De Duve, a Belgian biochemist, was the first to discover and characterise it as a novel organelle in 1955. The average diameter is 0.4 mm (this varies across microsomes and mitochondria). A lipoprotein membrane separates the rest of the body from them. Lysosomes are found in various quantities and varieties in all animal cells except erythrocytes. The lysosomes have a lower pH than the cytoplasm. The optimum pH for lysosomal enzymes is about 5. The enzyme acid phosphatase is utilised to identify this organelle.

6. **Peroxisomes,** also known as microbodies, are microscopic organelles found in eukaryotic cells. The particles have a diameter of around 0.5 mm. These subcellular respiratory organelles lack energy-coupled electron transport mechanisms and are most likely produced by budding from the smooth endoplasmic reticulum (SER).

   Functions: They carry out oxidation processes that create hazardous hydrogen peroxide (H_2O_2), which is eliminated by the enzyme catalase. Also, it was recently discovered that liver peroxisomes contain an extremely active -oxidative system that may oxidise long chain fatty acids (C_{16} to C_{18} or > C_{18}).