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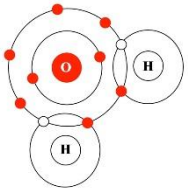
Abanico Veterinario. January-December 2025; 16:1-28. http://dx.doi.org/10.21929/abavet2025.12
Literature review. Received: 24/09/2025. Accepted:13/12/2025. Published: 28/12/2025. Code: e2025-37.
https://www.youtube.com/watch?v=StvkPpXwnog



Comprehensive analysis of medical biochemistry: molecular interactions and pathways in metabolism

Análisis integral de la bioquímica médica: interacciones moleculares y vías en el metabolismo

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ABSTRACT

Biochemistry bridges biology and chemistry, serving as the molecular foundation of life. This review aims to provide a thorough understanding of fundamental biochemical concepts, key metabolic pathways, and their relevance to health and disease management. It begins with an overview of atomic structure and the variety of biochemical reactions that occur within cells to synthesize molecules. The discussion then focuses on water and biochemical bonds, highlighting how molecular flexibility of monosaccharides, amino acids, fatty acids, and nucleotides facilitates rapid reactions and meets the body's energy and structural needs. The review explores carbohydrate metabolism, covering glycogenesis and the pentose phosphate pathway, illustrating how cells utilize sugars. It extends to crucial biomolecules such as DNA and RNA, explaining how cells translate genetic information and synthesize lipids. The review details how cells break down dietary and stored carbohydrates and lipids to release energy essential for various physiological functions. Biomedical research advances integrate deeper understanding of biochemical principles, integrating structural chemistry, enzymology, and cellular biology to support clinical problem-solving skills to maintain its utility in medical education and practice.

Keywords: Biochemistry, carbohydrates, proteins, lipids, DNA, RNA.

RESUMEN

La bioquímica es la unión de la biología y la química, sirviendo como la base molecular de la vida. Esta revisión tiene como objetivo proporcionar una comprensión profunda de los conceptos bioquímicos fundamentales, las principales vías metabólicas y su relevancia para la gestión de la salud y las enfermedades. Comienza con una visión general de la estructura atómica y la variedad de reacciones bioquímicas que ocurren dentro de las células para sintetizar moléculas. Luego, la discusión se centra en el agua y los enlaces bioquímicos, destacando cómo la flexibilidad molecular de los monosacáridos, aminoácidos, ácidos grasos y nucleótidos facilita reacciones rápidas y satisface las necesidades energéticas y estructurales del cuerpo. La revisión explora el metabolismo de los carbohidratos, abarcando

la glucogénesis y la vía de las pentosas fosfato, ilustrando cómo las células utilizan los azúcares. Se extiende a biomoléculas cruciales como el ADN y ARN, explicando cómo las células traducen la información genética y sintetizan lípidos. La revisión detalla cómo las células descomponen los carbohidratos y lípidos de la dieta y almacenados para liberar energía esencial para diversas funciones fisiológicas. Los avances en la investigación biomédica integran una comprensión más profunda de los principios bioquímicos, combinando química estructural, enzimología y biología celular para apoyar el desarrollo de habilidades de resolución de problemas clínicos, manteniendo así su utilidad en la educación y práctica médica.
Palabras clave: Bioquímica, carbohidratos, proteínas, lípidos, ADN, ARN.

ABBREVIATIONS

$^1O_2$	atomic oxygen		
aa	amino acid	N^{3-}	nitride ion
ADP	diphosphate adenosine	NAD+	nicotinamide adenine dinucleotide phosphates in their oxidized form
ATP	adenosine triphosphate		
C=O	carbonyl group	$NADPH/H^+$	nicotinamide adenine dinucleotide phosphate in reduced form
C16:0	palmitic		
$C_3H_3O_3$	pyruvate	NEFAs	non-esterified fatty acids
$C_3H_8O_3$	glycerol	NH_2	amino group
$C_6H_{11}O_9P$	glucose-6-phosphate	NH_3	ammonia
$C_6H_{12}O_6$	glucose	O_2	dioxygen
Ca^{2+}	calcium	OH	hydroxyl group
CO_2	carbon dioxide	PCR	polymerase chain reaction
$COCH_3$	acetyl group	pH	potential of hydrogen
COOH	carboxyl group	PO_3^{2-}	phosphate group
DNA	deoxyribonucleic acid	PP*i*	inorganic pyrophosphate
H^-	hydride ion	RNA	ribonucleic acid
H^+	hydrogen ion	ROS	reactive oxygen species
H_2CO_3	carbonic	tau	T subunit
H_2O	water	tRNA	transfer ribonucleic acid
Hb	haemoglobin	UDP	uridine diphosphate
HCO_3^-	hydrogen carbonate	UDP-glucose	uridine diphosphate glucose
mRNA	messenger ribonucleic acid	UTP	uridine triphosphate

INTRODUCTION

The present review offers a concise survey of aspects of biochemistry most relevant to the study of medicine and provides the reader with the most current and pertinent information. All topics are organized under five major sections. Figures follow each section to assist the study and facilitate retention of the information. Section I includes an atom, the law of conservation of matter, chemical reaction, protons, electrons, the law of electrostatics, anion, cation, oxidation-reduction, the CPK (Corey-Pauling-Koltun) system as a colour convention to distinguish the atoms of the principal chemical elements to create molecular models, and the octet rule. Section II considers the water (**H_2O**), polarity, cohesion, dioxygen (**O_2**), carbon dioxide (**CO_2**), H-bond, covalent bond, ionic bond, hydrophobic interaction, and van der Waals forces. Section III discusses monomers, polymers, polymerization, monosaccharides, *O*-glycosidic bond, hydroxyl group (**OH**), glucose (**$C_6H_{12}O_6$**), amino acid (**aa**), peptide bond, amino group (**NH_2**), carboxyl group (**COOH**), fatty acid, ester bond, triglyceride, nucleotide, phosphodiester bond, phosphate group (**PO_3^{2-}**), and potential of hydrogen (**pH**). Section IV outlines the amylases,

hydrolysis, glycogenogenesis, pentose phosphate pathway, and nicotinamide adenine dinucleotide phosphate in reduced form (**NADPH+H$^+$**). Section V includes a deoxyribonucleic acid (**DNA**), replication, DNA gyrase, DNA helicase, DNA primase, and DNA polymerases I, II, and III. Section VI considers the ribonucleic acid (**RNA**), rough endoplasmic reticulum, ribosomes, A site or aminoacyl, P site or peptidyl, proteogenesis, messenger ribonucleic acid (**mRNA**), transfer ribonucleic acid (**tRNA**), and protein translation. Section VII discusses lipogenesis, acetyl-Coenzyme A, fatty acids, triacylglycerols, glycosylation, and exocytosis. Section VIII includes glycogenolysis, glucagon, lipolysis, non-esterified fatty acids (**NEFAs**), pyruvate (**$C_3H_3O_3$**), and acetyl-Coenzyme A. Section IX considers the Krebs cycle, oxidative decarboxylation, and adenosine triphosphate (**ATP**). Biochemistry significantly contributes to cell biology, physiology, immunology, microbiology, pharmacology, toxicology, and epidemiology. These close relationships emphasize that life, as we know it, depends on biochemical reactions and processes.

Atom and molecular interactions

In the early days of Biochemistry, Antoine-Laurent de Lavoisier was considered the father of modern Chemistry for his studies on i) the law of conservation of matter, ii) O_2 and its vital role in respiration, iv) oxidation, v) heat and combustion, and vi) photosynthesis (Beretta, 2024). Also, Lavoisier is one of the 72 scientists whose name is inscribed on the Eiffel Tower (Kambas, 2025). His law of conservation of matter states that matter is neither created nor destroyed; it only transforms (Klein, 2015). Therefore, during every chemical reaction, the total number of atoms before and after the reaction remains constant (Ragab, 2025). The amount of matter consumed by the reactants equals the amount of matter in the products obtained (the total number of protons, neutrons, and electrons remains constant) (Sunte, 2025).

A chemical reaction occurs when atoms collide, displacing electrons (Chen *et al.*, 2020). This changes the chemical identity of the substances involved in the collision by breaking previously existing bonds between the atoms and forming new ones (Alkorta *et al.*, 2020). In other words, it involves rearranging the bonds between atoms, giving rise to new products (Li & Zuo, 2020). Also, stoichiometry calculates the quantitative relationships between reactants and products during a chemical reaction (Sardans *et al.*, 2021). The atom is the smallest unit of matter (ten billionths of a meter) (Prescod, 2024). Each atom consists of a nucleus, consisting of one or more protons (positive electrical charge) and typically a similar number of neutrons (made up of three quarks, whose combined charges are zero) (L'Annunziata, 2022). The nucleus accounts for 99.94% of the atom's total mass (Ragab, 2025). The electrons are rotating in orbitals around it, with a negative electrical charge and equivalent to 0.06% of the atom's total mass (Bailey, 2022a; El-Shorbagy *et al.*, 2025).

Charles-Augustin de Coulomb: formulated the law of electrostatics (Coulomb's law) (Lacasse, 2023). He established that this force causes attraction between protons and electrons (Popova & Popov, 2021). The force is repulsive if the charges are of the same sign (+ +,- -) (El-Shorbagy *et al.*, 2025). The force is attractive if the charges are of different signs (+,-) (Hren *et al.*, 2021). Therefore, an electrically neutral atom has equal protons and electrons (Popova & Popov, 2021). An ion is a particle that has more or fewer electrons than protons (Sibley, 2021), so it has an overall negative or positive charge, and its number of protons does not change (L'Annunziata, 2022). The ionization process occurs when electrons are gained or lost from an electrically neutral atom (Hren *et al.*, 2021; Bailey, 2022a). When one or more electrons are added (gained), a negatively charged ion (anion) is formed (El-Shorbagy *et al.*, 2025). When one or more electrons are removed (lost), a positively charged ion (cation) is formed (Sibley, 2021).

Therefore, two chemical reactions occur: i) oxidation when an atom (loses) one or more electrons from its outer orbital and acquires a positive charge (cation) (Sies *et al.*, 2024); when an atom (loses) one or more electrons from its outer orbital and acquires a positive charge (cation) (Li *et al.*, 2020); and ii) reduction, when an atom (gains) one or more electrons in its outer orbital and acquires a negative charge anion (Bailey, 2022a) (Figure 1).

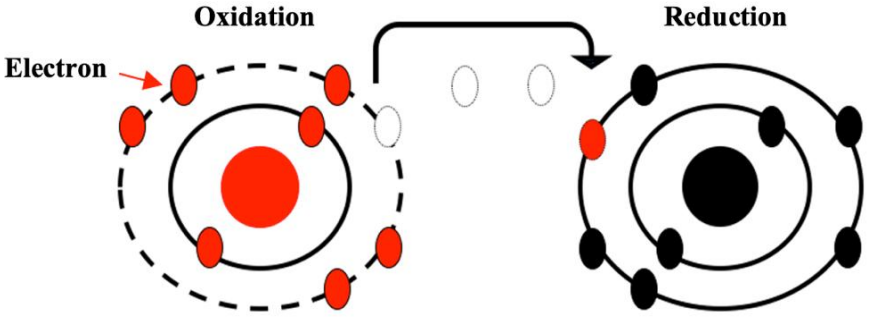

Figure 1. Oxidation and reduction

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The principal chemical elements for life are carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulphur (Helmut, 2021a). Robert Corey, Linus Pauling, and Walter Koltun established the CPK system as a colour convention to distinguish the atoms of the principal chemical elements to create molecular models (Grice & Jones, 2024). They identified carbon as black, hydrogen as white, oxygen as red, nitrogen as blue, phosphorus as orange, and sulphur as yellow (Turner, 2016). A molecule is two or more atoms chemically bonded together, and its valency indicates the number of bonds an atom forms (Hargittai, 2023). E.g., in ammonia ($\mathbf{NH_3}$), the nitride ion ($\mathbf{N^{3-}}$) has a valency of three,

since it has three free electrons in its outer orbital to form three bonds (Spatolisano *et al.*, 2023). Hydrogen has one valence since only one electron forms a bond (Suno & Ohno, 2024).

Gilbert Newton Lewis formulated the octet rule (Gutiérrez, 2023). It establishes that atoms bond to each other (losing or accepting one or more electrons) to complete their outer orbital (valence shell) in order to achieve stability (L'Annunziata, 2022). An atom is stable with eight electrons in its valence shell (Brown, 2023). This is why elements always form bonds for stability (Cui & Harshman, 2022). The hydrogen ion ($\mathbf{H^+}$) or hydride ion ($\mathbf{H^-}$), depending on whether it is a cation or an anion, respectively (Suno & Ohno, 2024)," is the exception to the rule, as it achieves stability with two electrons in its outer orbital (Brown, 2023).

Molecules and biochemical bonds

A chemical reaction involves a molecular transformation that alters both the energy and the composition of the system (Beretta, 2024). These changes are described by the state functions enthalpy, entropy, and Gibbs free energy (Sardans *et al.*, 2021). Enthalpy represents the heat exchanged at constant pressure, and its variation allows us to determine whether the reaction absorbs heat (endothermic) or releases it (exothermic) (Hargittai, 2023). Entropy measures the extent to which energy is dispersed and the degree of disorder in the system, while Gibbs free energy integrates both concepts to assess the spontaneity of a process under constant temperature and pressure (El-Shorbagy *et al.*, 2025). Based on these principles, reactions can be classified as reversible or irreversible (Bailey, 2022a). A reversible reaction proceeds in both directions (from reactants to products and from products to reactants) until it reaches dynamic equilibrium (Hargittai, 2023). In contrast, a reaction is considered practically irreversible when it proceeds almost completely toward the products, which often occurs when one of the products is removed from the system (Sardans *et al.*, 2021).

Thus, among the main molecules of medical importance, H_2O stands out as a biological solvent (Nilsson & Pettersson, 2015). It is a molecule formed by two hydrogen atoms and one energetically excited singlet or atomic oxygen ($\mathbf{^1O_2}$), joined by a covalent bond (Greer, 2006). The H_2O (Figure 2) is a strongly polar molecule, as its electrons give it a diamagnetic property (it repels magnetic fields) (Tanaka, 2000). Many biological macromolecules, e.g., carbohydrates, are polar and dissolve easily in H_2O (Chandel, 2021a). Polarity is the property that facilitates the movement of electrons toward the atom with the greatest electronegativity (electric dipole) (Roussy *et al.*, 2023). The high polarity of H_2O also favours lipids (nonpolar or hydrophobic) to aggregate and stay together, forming biological barriers, e.g., cell membranes (Pratt *et al.*, 2016). The H_2O also exhibits cohesion, favoring large molecules' stability (Nilsson & Pettersson, 2015).

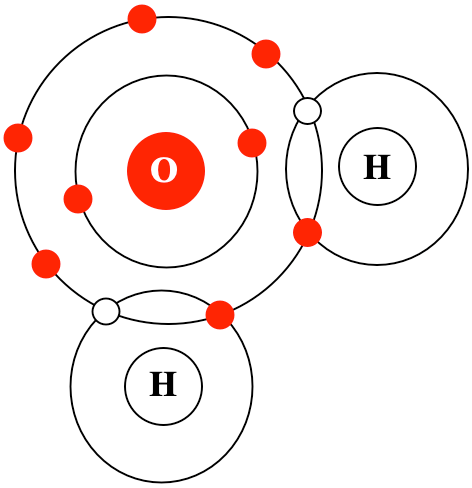

Figure 2. Water (H_2O)

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The O_2 is a molecule formed by two atoms of oxygen, $^1O_2$, joined to complete eight "octet" electrons (Figure 3), in their outer orbital or valence shell (Greer, 2006). It is an essential element for breathing, which is why we have always considered it synonymous with life, freedom, and relief, when it also makes us sick, age, and die (Sies, 2015). The latter is due to the formation of reactive oxygen species (**ROS**) (Sies *et al.*, 2022).

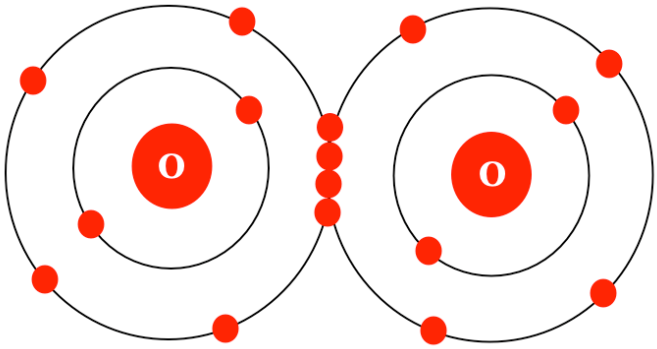

Figure 3. Dioxygen gas (O_2)

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CO_2 is a molecule formed by two atoms $^1O_2$ joined to complete eight "octet" electrons (Figure 4), in their outer orbital or valence shell with a C atom, which has four electrons in its external orbital (Sullivan *et al.*, 2021).

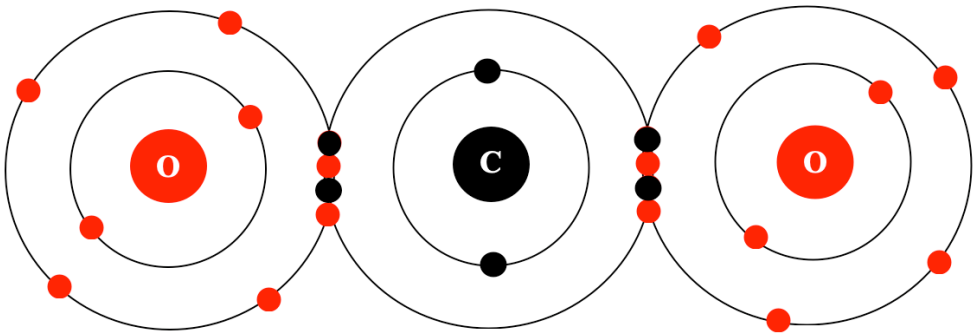

Figure 4. Carbon dioxide (CO_2)

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All these molecules are formed by biochemical bonds exchanging or sharing electrons between two or more atoms (Gawthrop *et al.*, 2015). The H-bond is a weak chemical bond formed by electromagnetic interactions between the oxide, the N^{3-}, and the hydrogen (Weiss *et al.*, 2001). A covalent bond is a strong chemical bond, where the atoms being bonded share electrons to acquire a stable configuration, to complete eight "octet" electrons in their external orbital or valence shell (Chakma & Konkolewicz, 2019). An ionic bond is a weak chemical bond between atoms, formed by electrostatic interactions (opposite charges) that allow ionization in aqueous solutions (Luxford & Bretz, 2013). Hydrophobic interaction is a weak chemical bond between atoms that forms when nonpolar (hydrophobic) molecules form tightly bonded bonds in a polar environment with H_2O interaction (Tanaka, 2000; Xiao *et al.*, 2020). They play an essential role in the stability of cell membranes (Gawthrop *et al.*, 2015). Finally, van der Waals forces are a weak chemical bond between atoms, formed by attractive forces that occur when electrons are within three to four angstroms (Castellanos *et al.*, 2022). They are important in bonding enzymes with substrates and the interactions between aa and nucleotides (Matyushov, 2022).

Monomers and polymers

Molecules of metabolic importance are classified mainly into two: i) monomers or small molecules linked by covalent bonds, and ii) polymers or macromolecules (usually organic) formed by the union of several monomers (Helmut, 2021a). Through the chemical process called polymerization, monomers are chemically grouped. Monomers are joined together individually, as are dimers, trimers, tetramers, and pentamers (Moazzen & McKellar, 2013). Monomers are joined through H-bonds, ionic bonds, hydrophobic interactions, and van der Waals forces (Gawthrop *et al.*, 2015). Therefore:

1. Monosaccharides are the monomers of polysaccharide polymers (Chandel, 2021a).
2. AAs are the monomers of protein polymers (Ling *et al.*, 2023).
3. Fatty acids are the monomers of lipid polymers (Stavila *et al.*, 2023).
4. Nucleotides are the monomers of DNA and RNA polymers (Chandel, 2021b).

The biochemical bond of monosaccharides is the *O*-glycosidic bond, the union between two or more monosaccharides through a condensation "dehydration" of their OH group (Xin & Weigang, 2016). As a result, a molecule of H_2O is lost, and an ether bond is formed. The $C_6H_{12}O_6$ (Figure 5) is the principal organic monosaccharide in nature (Chandel, 2021a).

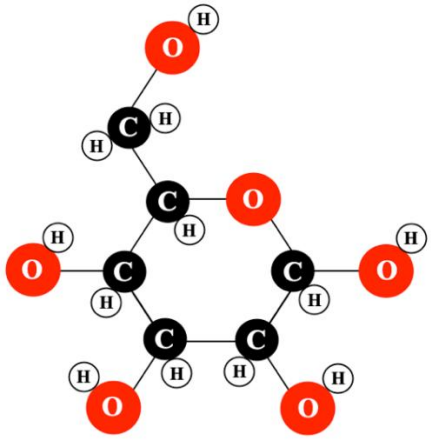

Figure 5. Glucose ($C_6H_{12}O_6$)

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It is the primary substrate for the synthesis of structural polysaccharides e.g., cellulose, and energy storage polysaccharides e.g., starch (composed of amylose and amylopectin and contained in the endosperm of seed plants) and glycogen (contained in the vacuoles of hepatocytes and in the vacuoles of myocytes) (Schombs & Gervay, 2016). The biochemical bond of aa is the peptide bond, which is the union between the NH_2 group of one aa and the COOH group of another, accompanied by the formation of a molecule of H_2O (Hansen *et al.*, 2002). This is a "dehydration" condensation, so a molecule of H_2O is lost, and a covalent bond CO-NH is formed (Nissen *et al.*, 2000) (Figure 6).

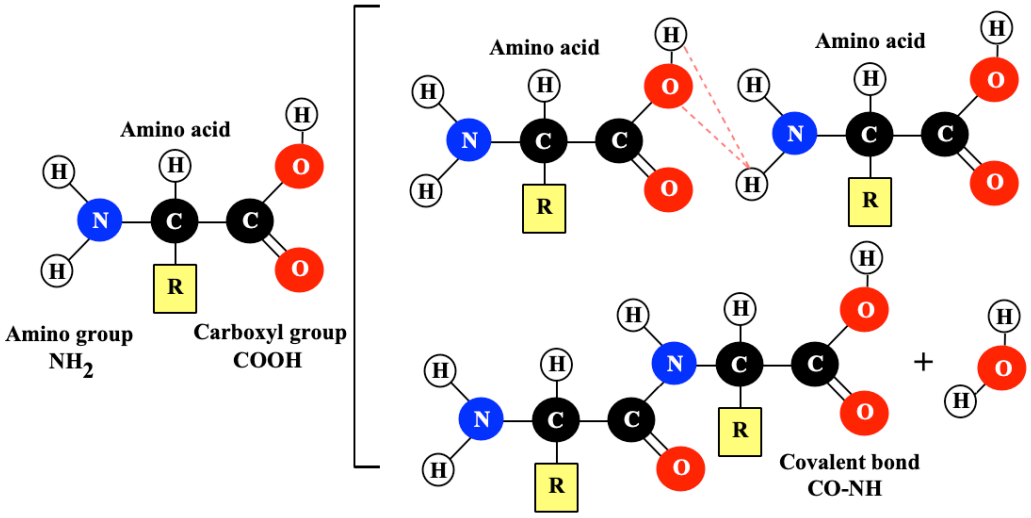

Figure 6. Amino acid, covalent bond (CO-NH)

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The biochemical bond of fatty acid is the ester bond, which is the union between the OH group of a monosaccharide, e.g., glycerol (**$C_3H_8O_3$**), and the COOH group of a fatty acid, accompanied by the formation of a molecule of H_2O (He *et al.*, 2023). This occurs through dehydration condensation, so a molecule of H_2O is lost, and a covalent bond COO-CH is formed (Nissen *et al.*, 2000). This bond prevents the polar groups from becoming accessible (Roussy *et al.*, 2023). Therefore, nonpolar (hydrophobic) and highly insoluble molecules are formed (Nilsson & Pettersson, 2015).

The biochemical bond of nucleotide is the phosphodiester bond (Figure 7), which is the union between the OH group of a five-carbon monosaccharide (aldopentose: ribose or deoxyribose) and a PO_3^{2-} group (Chandel, 2021b). The pentose was previously linked to the NH_2 group of a pyrimidine nitrogenous base: cytosine, thymine, and uracil, or a purine nitrogenous base: adenine and guanine, forming a nucleoside (Bailey, 2022b).

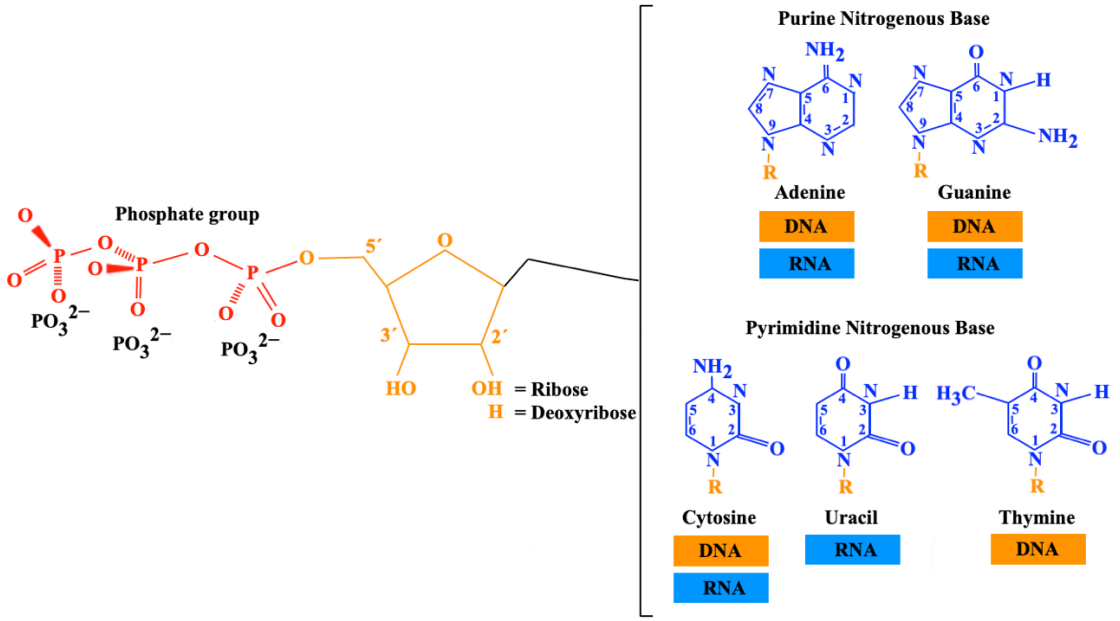

Figure 7. Nucleotide with phosphodiester bond

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The pH indicates the concentration of hydrogen present in specific solutions (Proksch, 2018). Therefore, acid dissociation is when acids release a hydrogen atom upon contact with H_2O (Nordness & Brennecke, 2020). Usually reversibly, resulting in a negatively charged ion (anion) and a positively charged ion (cation) (Yuan *et al.*, 2025). The equilibrium between hydrogen released by an acid in an aqueous medium and the hydrogen received by a conjugate base indicates how strong an acid is (Proksch, 2018). In medical practice, physiological buffers balance the presence of acidic and basic substances to maintain the pH within physiological limits (Salis & Monduzzi, 2016). Among the physiological buffers, the following stand out: i) oxygenated haemoglobin (**Hb**), which is a very efficient physiological buffer (Giardina, 2022), lowering the proportion of O_2 gaseous, and ii) the hydrogen carbonate/carbonic system, the organism can form hydrogen carbonate ($\mathbf{HCO_3^-}$) and carbonic ($\mathbf{H_2CO_3}$) anions from CO_2 gaseous (Hwee & See, 2021).

Metabolism of carbohydrates

In the cytoplasm of the eukaryotic cell, various biochemical processes take place, among which the following stand out: i) the phosphorylation of $C_6H_{12}O_6$ (Nolfi *et al.*, 2020), ii) glycogenogenesis (Pacheco *et al.*, 2021), iii) glycogenolysis-glycolysis (Panja *et al.*, 2013), and iv) the pentose phosphate pathway (TeSlaa *et al.*, 2023). Polysaccharides in food are broken down (*O*-glycosidic bond cleavage) by amylases produced in the salivary glands (particularly the parotid glands) and the pancreas (Xin & Weigang, 2016). Following this hydrolysis, the monomer $C_6H_{12}O_6$ is released (Schombs & Gervay, 2016).

The $C_6H_{12}O_6$ enters the cytoplasm to be phosphorylated (addition of PO_3^{2-} group), from adenosine triphosphate (**ATP**) (Fontecilla, 2022). This reaction is catalysed by hexokinase (Frommer *et al.*, 2003). The resulting glucose-6-phosphate (**$C_6H_{11}O_9P$**) is abundant in all cells, since the vast majority of $C_6H_{12}O_6$ that enters the cytoplasm ends up being phosphorylated, to prevent it from crossing back through the cytoplasmic membrane and diffusing into the extracellular medium (Panja *et al.*, 2013).

In glycogenogenesis or anabolism, the body must store $C_6H_{11}O_9P$ by transforming it into glycogen (Schombs & Gervay, 2016). This process occurs in the cytoplasm of myocytes and hepatocytes (Pacheco *et al.*, 2021). When $C_6H_{11}O_9P$ levels in the cytoplasm are high, phosphoglucomutase transfers the PO_3^{2-} group from carbon C6 to C1, synthesizing glucose-1-phosphate (TeSlaa *et al.*, 2023). Uridine triphosphate (**UTP**), which is generally used as a substrate in RNA synthesis due to its nitrogenous base (uracil), interacts with glucose-1-phosphate in a reaction catalysed by UDP-glucose pyrophosphorylase, forming uridine diphosphate glucose (**UDP-glucose**) and releasing an inorganic pyrophosphate (**PP*i***) (Zhang *et al.*, 2020). Insulin activates glycogen synthase 1 expressed in myocytes and/or glycogen synthase 2 expressed in hepatocytes to attach the OH group of UDP-glucose to glycogen (*O*-glycosidic bond) (Xin & Weigang, 2016), lengthening the polysaccharide and releasing the nucleotide uridine diphosphate (**UDP**) for reuse (Yamamoto *et al.*, 2011).

The pentose phosphate pathway also occurs in the cell cytoplasm and is divided into oxidative and non-oxidative phases (TeSlaa *et al.*, 2023). In the oxidative phase, $C_6H_{11}O_9P$ is dehydrogenated (losing two hydrogen), a reaction catalysed by glucose-6-phosphate dehydrogenase (Stincone *et al.*, 2015). The product is 6-phosphogluconolactone and a molecule of $NADPH/H^+$ (Xie*et al.*, 2020). The 6-phosphogluconolactone is hydrolysed (Kruger & von Schaewen, 2003). This reaction is catalysed by 6-phosphoglucolactonase, and the product is 6-phosphoglucanate (TeSlaa *et al.*, 2023). The 6-phosphoglucanate is decarboxylated (elimination of the COOH group), a reaction catalysed by 6-phosphoglucanate dehydrogenase (Stincone *et al.*, 2015). The product is ribulose-5-phosphate (ketopentose), a molecule of $NADPH/H^+$ and CO_2 (Kruger & von Schaewen, 2003; TeSlaa *et al.*, 2023). In the non-oxidative phase, depending on the metabolic state of the cell, ribulose-5-phosphate can undergo isomerization [a molecule is transformed into another that has the same atoms, but arranged differently – the carbonyl group (**C=O**) changes location] to ribose 5-phosphate (aldopentose) (Stincone *et al.*, 2015). The main functions of the pentose phosphate pathway are: i) to synthesize five-carbon monosaccharides (aldopentose-P) and ii) to generate $NADPH/H^+$ (Xie *et al.*, 2020). The $NADPH/H^+$ is the cellular reducing power unit (electron donor) most useful in biochemical reactions (Covarrubias *et al.*, 2021).

Deoxyribonucleic acid and DNA replication

The nucleus is a central organelle in eukaryotic cells, with an average diameter of 6 µm (approximately 10% of total cell volume) (Helmut, 2021b). It contains a cytoplasm-like fluid called the nucleoplasm (Caragine *et al.*, 2019). It contains most of the cell's genetic material through multiple DNA molecules known as chromatin, during the intercellular membrane (Dixon *et al.*, 2016) and chromosomes, during mitosis (Hirano, 2015). DNA is a double-stranded polymer (Figure 8), formed by nucleotides [a 5-carbon monosaccharide (aldopentose deoxyribose), a nitrogenous base: cytosine, guanine, adenine, and thymine, and a PO_3^{2-} group, linked by H-bonds (Bailey, 2022b).

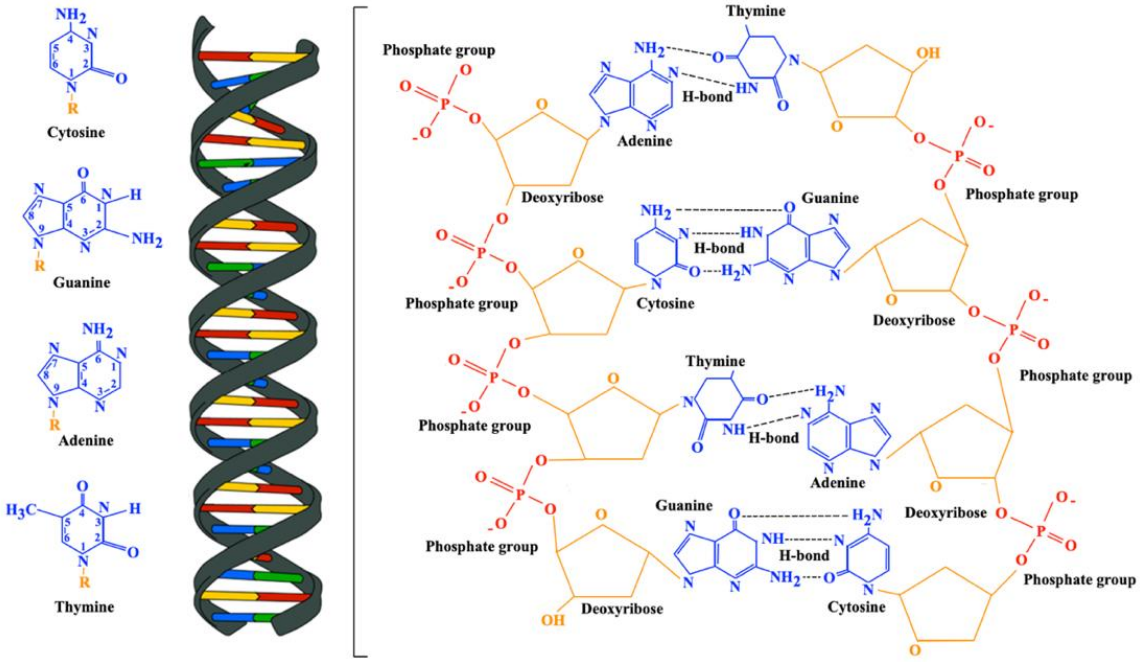

Figure 8. Deoxyribonucleic acid structure

Source Own Work

DNA replication is obtaining two identical copies or replicas of a DNA molecule (Helmut, 2021b). This process is fundamental to transferring genetic information from one generation to the next and, therefore, is the basis of inheritance (Costa & Diffley, 2022). DNA replication requires:

1. DNA gyrase or topoisomerase reduces the molecular tension in DNA caused by supercoiling (Costa & Diffley, 2022).
2. DNA helicase opens DNA like a zipper and breaks the H-bonds between nucleotides (Brosh & Matson, 2020).

3. When H-bonds are broken, replication proteins A or single-stranded deoxyribonucleic acid binding proteins are synthesized as an alternate product. These prevent the strand from rejoining (Helmut, 2021b).
4. DNA primase synthesizes small RNA fragments of about ten nucleotides, known as primers, used in the laboratory technique of polymerase chain reaction (**PCR**) (Costa & Diffley, 2022).
5. Due to their exposed OH group, primers establish a starting point for the DNA-polymerase complex to begin synthesis of the new strand (Fontana & Gahlon, 2020).
6. The T subunit (**tau**) holds two DNA-polymerase complexes together in a single DNA molecule, because in the cell, both double helix strands are duplicated simultaneously (Helmut, 2021b).
7. DNA polymerase I replaces the primers with complementary nucleotides (Yao & O'Donnell, 2021).
8. DNA polymerase II is involved in error correction (Fontana & Gahlon, 2020).
9. DNA polymerase III is responsible for chain elongation (Yao & O'Donnell, 2021).

Ribonucleic acid and proteogenesis

The rough endoplasmic reticulum and ribosomes are the organelles responsible for protein synthesis (Opron & Burton, 2018), and the synthesis of hydrolase enzymes, e.g., lipase, esterase, glycogen phosphorylase, and glucose-6-phosphatase, peptidase or protease, aminotransferase, and nuclease (Busto *et al.*, 2010). Ribosomes have an A site, aminoacyl, and P site or peptidyl (Hoffmann *et al.*, 2022). RNA is a single-stranded polymer (Figure 9), formed by ribonucleotides [a 5-carbon monosaccharide (aldopentose ribose), a nitrogenous base: cytosine, guanine, adenine, and uracil, and a PO_3^{2-} group, linked by phosphodiester bonds (Helmut, 2021c; Bailey, 2022b).

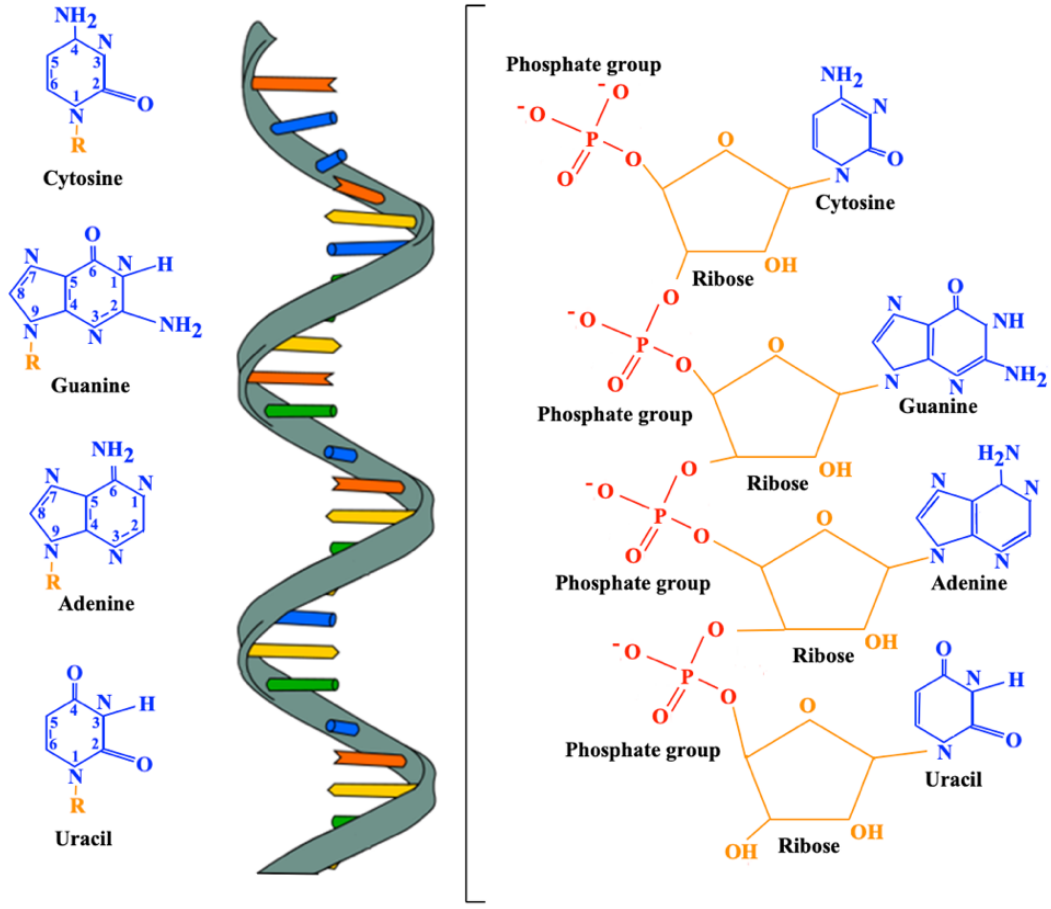

Figure 9. Ribonucleic acid structure

Source Own Work

Proteogenesis (Figure 10) begins when RNA polymerase catalyses mRNA transcription in the 5' to 3' direction (Nagao *et al.*, 2023). The mRNA carries genetic information in codons (triplet nucleotides) to the ribosomes (Komar, 2016). Polymerase III catalyses the transcription of tRNA in the 3' to 5' direction (Arimbasseri & Maraia, 2016). The tRNA transfers its anticodons to the aa to adapt them to their corresponding codon (Helmut, 2021c), following the genetic code for translating a protein.

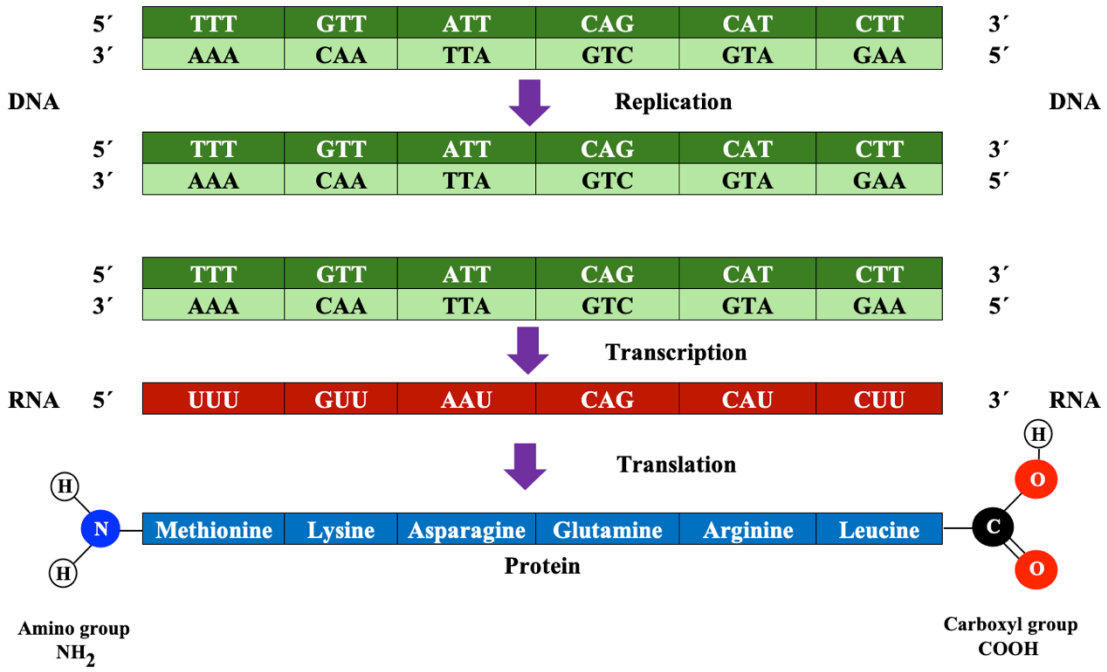

Figure 10. Replication, transcription, and protein translation

Source Own Work

Proteins are translated from the NH_2 group in the A site or aminoacyl to the COOH group in the P site or peptidyl (Nagao *et al.*, 2023). The polypeptide chain elongates via peptide bonds (Hansen *et al.*, 2002). Upon completion of protein translation, the mRNA is released and can be read by other ribosomes (Opron & Burton, 2018).

Fatty acids and lipogenesis

Lipogenesis requires the production of acetyl-Coenzyme A in the mitochondria (Cross *et al.*, 2023). However, the mitochondrial membrane is impermeable to the passage of acetyl-Coenzyme A (Nolfi *et al.*, 2020). Therefore, the tricarboxylate system and the enzymatic action of citrate synthase are also required to convert acetyl-Coenzyme A into citrate and allow its passage into the cell cytoplasm (Nematbakhsh *et al.*, 2021). Once inside the cytoplasm, citrate is transformed again into acetyl-Coenzyme A by the Liasa ATP-Citrate, obtaining oxaloacetate and diphosphate adenosine (**ADP**) (Berger & Moon, 2021). As the process for the synthesis of fatty acids is very endergonic, it accumulates energy from C, acetyl-Coenzyme to present carboxylation, a COOH group is structured in the molecule, through its junction with the HCO_3^- in a reaction catalysed by acetyl-Coenzyme to carboxylase (Jeon *et al.*, 2023).

As a result, acetyl-Coenzyme A becomes malonyl-Coenzyme with a functional COOH group (Cross *et al.*, 2023). From this moment on, lipogenesis (synthesis of fatty acids) is performed by elongation, using the protein of fatty acid synthase (Nematbakhsh *et al.*,

2021). This protein complex causes condensation, dehydration, and reduction (Berger & Moon, 2021). During the elongation, the malonyl-Coenzyme suffers a decarboxylation and groups of two carbons, to the fatty acid, always obtaining as a final product palmitic (**C16:0**) (Jeon *et al.*, 2023). Subsequently, C16:0 is released from the protein complex of fatty acid synthase and can be elongated, with the introduction of carbons, to produce other larger and/or unsaturated fatty acid molecules, with the introduction of double bonds between carbons (Jump, 2009). The synthesis of triacylglycerols begins with the esterification of three fatty acids to a $C_3H_8O_3$, inside the smooth endoplasmic reticulum (Nematbakhsh *et al.*, 2021). The Golgi apparatus is the organelle responsible for assembling and packaging proteins and lipids for their export outside the cell through regulated and constitutive exocytosis (Nakano, 2022). It is also responsible for protein glycosylation by hydrolases synthesized in the rough endoplasmic reticulum, and lipid glycosylation (Gamblin *et al.*, 2009; Hirata & Kizuka, 2021; Li *et al.*, 2022).

Protein glycosylation is the addition of a carbohydrate chain to a protein, e.g., peptidoglycan, proteoglycan, and glycoprotein (Kajihara *et al.*, 2016). Depending on the site of carbohydrate addition, there are three types of glycoproteins:

1. *N*-glycoprotein: carbohydrates are attached to the NH_2 group (Hirata & Kizuka, 2021).
2. *O*-glycoprotein: aa are attached to the OH group of monosaccharides (Li *et al.*, 2022).
3. C-glycoprotein: carbohydrates are attached to the COOH group of the aa (Gamblin *et al.*, 2009).

Lipid glycosylation is the addition of a carbohydrate chain to a lipid (Kopitz, 2017).

Regulated exocytosis is responsible for expelling molecules stored in vesicles from the Golgi apparatus, the contents of which are only released after an extracellular signalling process, e.g., calcium (**Ca^{2+}**) concentration (Nakano, 2022). Constitutive exocytosis is responsible for expelling molecules from the vesicles of the Golgi apparatus to regenerate the eukaryotic cytoplasmic membrane through a continuous process of vesicle replication, translocation, and fusion (Sugita, 2008).

Digestion of the main biological polymers

Glycogenolysis occurs in almost all tissues, especially muscle and the liver (Panja *et al.*, 2013). When $C_6H_{12}O_6$ levels in the blood are low, adrenaline (epinephrine) in the muscle and glucagon in the liver activate protein kinases, which phosphorylate (transfer of a PO_3^{2-} group) glycogen phosphorylase, which activates glycogen phosphorylase (Verberne *et al.*, 2016). Glycogen phosphorylase catalyses the transfer of an inorganic orthophosphate at C1 of glycogen (Agius, 2015). This change breaks the *O*-glycosidic bond and releases glucose-1-phosphate (Busto *et al.*, 2010). Glucose-1-phosphate is transformed into

$C_6H_{11}O_9P$. This reaction is catalysed by phosphoglucomutase, which transfers the PO_3^{2-} group from C1 to C6 (Doello & Forchhammer, 2023). Glycolysis consists of the catabolism of $C_6H_{11}O_9P$ to obtain acetyl-Coenzyme A, from $C_3H_3O_3$. The $C_3H_3O_3$ leaves the cytoplasm and enters the mitochondrial matrix, utilizing the proton-motive force generated by the respiratory chain (Nolfi *et al.*, 2020). Oxidative decarboxylation of $C_3H_3O_3$ occurs inside the mitochondria (Pacheco *et al.*, 2021). The COOH group is released as CO_2, and the remainder of the molecule undergoes dehydrogenation (oxidation), forming the acetyl group (**$COCH_3$**). This reaction is catalysed by pyruvate dehydrogenase (Wang *et al.*, 2021). Coenzyme A, ADP, and cysteine are transferred to the $COCH_3$ group, forming acetyl-Coenzyme A. Lipid catabolism in the digestive tract processes exogenous or ingested lipids from the diet. This digestive process produces the NEFAs, which are necessary for synthesizing acetyl-Coenzyme A and other biomolecules formed from them (Stich & Berlan, 2004).

The Krebs cycle

The Krebs cycle is part of cellular (mitochondrial) respiration (Chakrabarty & Chandel, 2022). The process releases the energy stored in acetyl-coenzyme A in the form of ATP (Fontecilla, 2022). Hans Adolf Krebs discovered the Krebs cycle. Acetyl-Coenzyme A gives up its $COCH_3$ group when combined with oxaloacetate to form citrate via a condensation reaction. Hydrolysis, oxidative decarboxylation, and hydration convert citrate into oxaloacetate (Nolfi *et al.*, 2020); the carbon atoms are released as CO_2 (Chakrabarty & Chandel, 2022). The cycle consumes one acetyl-Coenzyme A and three nicotinamide adenine dinucleotide phosphates in their oxidized form (**NAD^+**) per cycle (Covarrubias *et al.*, 2021). The cycle produces two CO_2 and three $NADPH/H^+$ per cycle (Chakrabarty & Chandel, 2022). For each acetyl-Coenzyme A that enters the Krebs cycle, 12 ATP are produced. For every $C_6H_{12}O_6$, two $C_3H_3O_3$ are produced, producing two acetyl-Coenzyme A. Therefore, each $C_6H_{12}O_6$ in the Krebs cycle produces four CO_2, six $NADPH+H^+$, and 24 ATP (Fontecilla, 2022).

CONCLUSIONS

This manuscript provides a concise overview of key concepts in medical biochemistry, highlighting the importance of molecular bonds, cellular metabolism, and biomolecular synthesis. It emphasizes pathways such as carbohydrate and lipid metabolism, DNA/RNA synthesis, and redox regulation, aiming to enhance understanding and diagnostic skills essential for clinical practice. offers a comprehensive overview of fundamental aspects of medical biochemistry, emphasizing the interconnectedness of atomic structure, molecular bonds, and the complexity of cellular metabolism. It highlights the significance of water and biochemical bonds in maintaining structural stability and facilitating biochemical reactions crucial for cellular function. The review underscores the pivotal roles of

carbohydrates, amino acids, fatty acids, and nucleotides in energy production, biosynthesis, and metabolic regulation. Key pathways such as glycogenogenesis, glycolysis, the pentose phosphate pathway, and lipid metabolism are explored in detail, illustrating how cells generate, store, and utilize vital biomolecules to meet physiological demands. Furthermore, the manuscript delves into molecular mechanisms of DNA and RNA synthesis, structural dynamics during protein translation, and the importance of redox biology and reactive oxygen species in maintaining cellular homeostasis. All these metabolic processes are integrated and regulated by enzymes, and energy is continuously released and consumed. These topics emphasize the complexity of biochemical regulation and its relevance to health and disease. Biomedical research advances integrate deeper understanding of biochemical principles, integrating structural chemistry, enzymology, and cellular biology to support clinical problem-solving skills to maintain its utility in medical education and practice.

Conflict of interest

The authors declare no conflict of interest. They have no known competing financial interests or personal relationships that could have appeared to influence in this chapter.

Author contribution

García-Casillas Arturo. Writing original draft.
Hernández-Rivera Juan. Review and correction.
Tirado-González Deli. Data curation and supervision.
Pérez-González Jairo. Review and correction.
Carrillo-Díaz María. Data curation and supervision.
Prado-Rebolledo Omar. Review and correction.

Funding

This research was funded by the Academic Body: UCOL-CA-11 Production Systems Agriculture, by the Network of Advances in Agricultural Research in Mexico, and the Secretariat of Science, Humanities, Technology, and Innovation (SECIHTI-Mexico).

Acknowledgements

In memory of Dra. María Guadalupe Prado-Flores.

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Errata Erratum
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