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Biosynthesis of bacterial macromolecules: A Review

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Abstract

The mechanisms of biosynthesis of bacterial macromolecules are presented. Bacterial macromolecules are large molecules that are formed by the polymerization of smaller molecules called monomers. They are essential for life and are synthesized from repeated linking of smaller organic molecules. The biosynthesis of bacterial macromolecules involves the combination of monomers to form polymers through dehydration synthesis and the input of energy which is obtained through various metabolic pathways.

Considering all life forms on Earth, from the smallest prokaryote to the largest eukaryote, there are four major classes of organic macromolecules that are always found and are essential to life. These molecules are carbohydrates, lipids, proteins and nucleic acids. All of these major macromolecule classes are similar, in that, they are large polymers that are assembled from small repeating monomer subunits. The monomer units for carbohydrates are sugar residues, whereas, the monomers for lipids are fatty acids and glycerol, for proteins are amino acids and for building the nucleic acids, DNA and RNA, are the nucleotide bases. They are a vital energy source for the organisms, provide structural support to many organisms, serve as receptors for cellular recognition, structural components of cell membranes, support growth, maintenance, transport of nutrients, storage cellular signalling and expression of genetic information, respectively.

Understanding the biosynthesis of bacterial macromolecules not only deepens the comprehension of biology, provides insights into disease mechanisms and potential therapeutic target, but also opens doors for applications in biotechnology, medicine, and the development of novel treatments of bacterial diseases.

Keywords: Bacteria, Biosynthesis, Macromolecules, Medicine, Monomers

Introduction

Smaller organic molecules are regularly joined to form larger molecules known as macromolecules, sometimes known as polymers. They are essential to existence. Biosynthesis, a multi-step, enzyme-catalyzed process that combines monomers to create polymers by dehydration synthesis and the input of energy received through multiple metabolic routes, is the mechanism by which microbial macromolecules are formed [27]. More complicated products are created from substrates [2]. The elements needed for biosynthesis include precursor molecules, favorable conditions, genetic information, regulatory molecules, chemical energy (like ATP), and catalytic enzymes that may need coenzymes (like NADH and NADPH). These constituents give rise to monomers, which function as the building blocks of macromolecules [3,29]. The four primary classes of biological macromolecules are nucleic acids, lipids, proteins, and carbohydrates. These polymers are essential to the structure and function of microorganisms [29]. The four primary classes of biological macromolecules, which are known to be essential parts of the cell and to carry out a wide variety of intricately related functions, make up the majority of a cell's dry mass [2,27]. Biological macromolecules are made of carbon and have hydrogen as their border since they are organic. In addition, they could include oxygen, nitrogen, and other elements. In order to speed up the synthesis of new molecules, adenosine triphosphate, or ATP, is usually required as an energy input for several biosynthetic processes [27, 28, 20,].

1.2 Dehydration Synthesis

Monomers are the fundamental organic molecules that combine to generate macromolecules, as was previously mentioned. It is known that during the process, water molecules are released as a byproduct and that these monomers may make covalent bonds with one another to create larger molecules, frequently referred to as polymers or macromolecules. The term "dehydration synthesis" describes this process, which is "to put together while losing water."

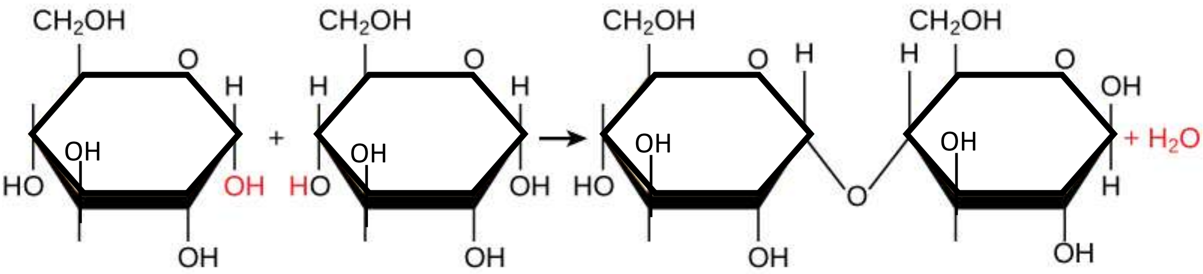


Figure 1.1 In the dehydration synthesis reaction above, two glucose molecules link to form the disaccharide maltose. In the process, it forms a water molecule (Source: openstax.org; synthesis-of-biological-macromolecules)

A process known as dehydration synthesis leads to the production of a water molecule (Figure 1.1). Through this method, the hydroxyl groups of two monomers contact with each other's hydrogen to create covalent bonds and an electron exchange. This chain of repeating monomers, however, becomes a polymer as more join. A heterogeneous collection of macromolecules can be made by combining various types of distinct monomers in a variety of ways. For instance, the building elements of cellulose, starch, and glycogen are glucose monomers.

1.3 Hydrolysis

Placing water molecules across monomers causes a chemical reaction that involves the breakdown of the covalent connections between the monomers and the water molecules (Figure 1.2). Polymers break down into monomers during the hydrolysis process, and these monomers split into two parts: one part gets a hydrogen atom (H+), while the other part gets a hydroxyl molecule (OH-). This chemical process is similar to how water gets photolyzed.

Figure 1.2 In the dehydration synthesis reaction above, two glucose molecules link to form the disaccharide maltose. In the process, it forms a water molecule (Source: openstax.org; synthesis-of-biological-macromolecules)

It is crucial to understand that some enzymes catalyze both the dehydration and hydrolysis processes. While the dehydration reaction involves the creation of new bonds and consumes energy, the hydrolysis reaction involves the breakdown of molecules. Even while monomer and polymer reactions are similar for most macromolecules, it is important to note that each reaction is distinct for each class. The way the digestive system's catalytic enzymes—amylase, sucrose, lactase, lipase, and nuclease—hydrolyze the food particles we ingest into smaller molecules is a typical illustration of this process. This makes it easier for the cells in our bodies' digestive tract to absorb nutrients.

1.4 Importance of Biosynthesis

• Biosynthesis is necessary for the growth, development, and reproduction of organisms. It permits cells to produce energy, carry out particular functions, and build and mend structures [15].
• By the process of biosynthesis, bacterial cells may generate lipids, proteins, carbohydrates, nucleic acids, and other essential compounds from simpler starting components. Numerous different macromolecules are necessary for the development, reproduction, and maintenance of bacterial cells.
• Modern biology requires a grasp of biosynthesis, which has applications in biotechnology, agriculture, and medicine. The complexity of biosynthesis is still being explored and clarified by researchers in order to comprehend biological processes and develop new applications [15].
• The ability of bacteria to manufacture poisons or antibiotics to help them survive in a competitive situation is one of the key advantages of biosynthesis; it lets them better adapt to their surroundings and struggle for resources.

2 BIOSYNTHESIS OF CARBOHYDRATE

It is well known that a carbohydrate molecule has an atom ratio of 1:2:1 for carbon, hydrogen, and oxygen. It is a crucial component of peptidoglycan, which is the primary structural support of the bacterial cell wall and provides the cell with its hard structure, and serves as an energy source for the cells. It also encourages adhesion, motility, and biofilm formation in a variety of bacterial cells. Monosaccharides, disaccharides, and polysaccharides are the three main subtypes of carbohydrates.

2.2 Monosaccharides

These are known as simple sugars, the most common of which being glucose. They are known to include three to seven carbon atoms and can be either an aldehyde or a ketone. Nonetheless, depending on how many carbons they contain, the sugars can be categorized as trioses (3 carbons), pentoses (5 carbons), or hexoses (6 carbons). Fructose, found in sucrose and fruits, and galactose, a component of lactose and also found in milk, are the two monosaccharides that have the same chemical formula but vary physically and chemically due to the arrangement of their functional groups (Figure 2.1). Glucose, a notable monosaccharide, is created in plants through the reaction of carbon dioxide and water. Both humans and bacteria use it as an energy source to produce adenosine triphosphate (ATP) during cellular respiration.

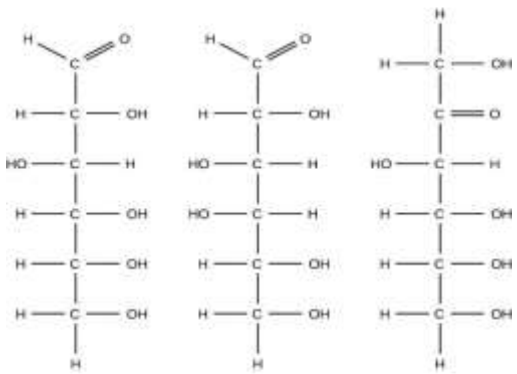
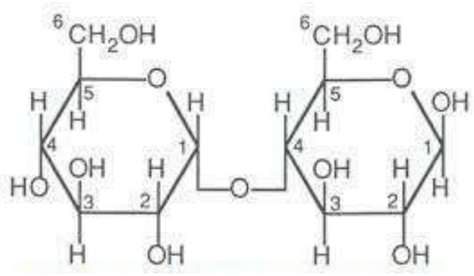


Figure 2.1 Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical formula ($C_6H_{12}O_6$) but a different atom arrangement. (Source: openstax.org; synthesis-of-biological-macromolecules)

2.3 Disaccharides

During a dehydration event, the hydrogen hydroxyl groups of two monosaccharides combine to form disaccharides, which release water molecules and form a covalent connection (Figure 2.2). The monomers glucose and galactose make up lactose, a typical disaccharide found in milk (Figure 2.3). Other disaccharides include maltose and sucrose, the two most common disaccharides composed of glucose and fructose monomers.



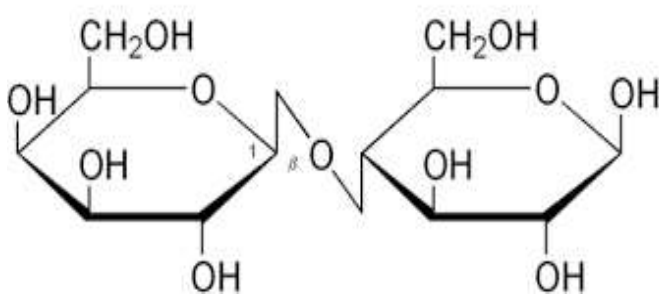


Fig 2.2 Maltose (Showing the covalent bonds between the two monosaccharides)

Fig 2.3 lactose formed from the monomers of glucose and galactose.

(Source: openstax.org; synthesis-of-biological-macromolecules)

2.4 Polysaccharides

This is a lengthy chain made up of glycosidic linkages that connect several branches or unbranched monosaccharide sequences. Figure 2.4 lists starch, chitin, cellulose, and glycogen as the primary examples. Plants store excess glucose as starch in a variety of locations, such as their seeds and roots. The majority of the extra glucose that is stored in humans and other vertebrates as glycogen is made up of glucose monomers. The most prevalent natural biopolymer, cellulose, makes up the majority of plant cell walls. By giving the cell shape and increasing its rigidity, cellulose gives the cell structural support [13, 14, 18, 21, 25, 25].

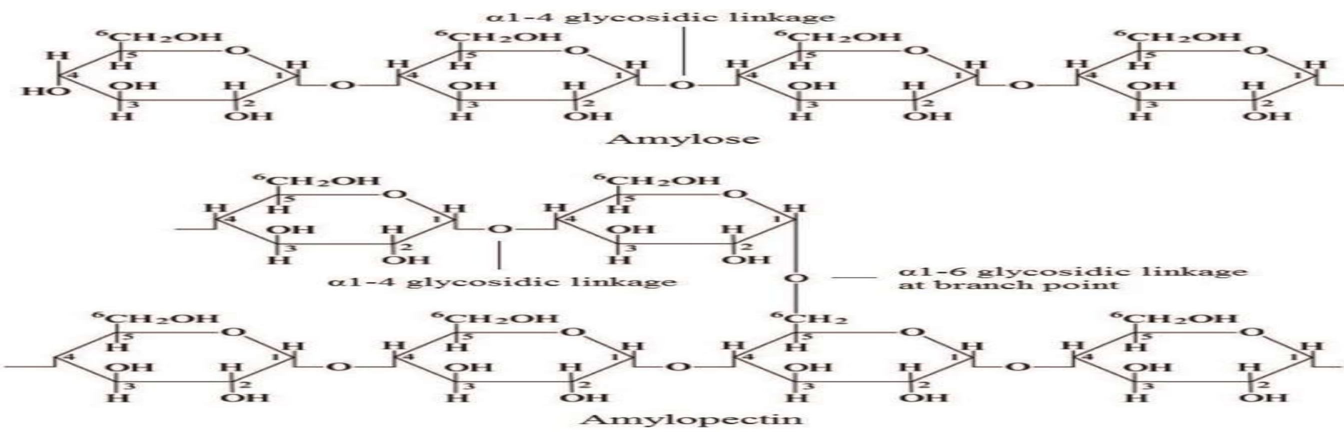


Figure 2.4 Amylose and amylopectin are two different starch forms. Unbranched glucose monomer chains comprise amylose by α 1-4 glycosidic linkages. Branched glucose monomer chains comprise amylopectin by α 1-4 and α 1-6 glycosidic linkages. Because of the way the subunits are joined, the glucose chains have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more highly branched. (Source: openstax.org; synthesis-of-biological-macromolecules).

Gluconeogenesis is another term for the production of carbohydrates (Figure 2.5). The process of gluconeogenesis converts pyruvate and other non-carbohydrate precursors, including as amino acids, lactate, glycerol, and phosphoenolpyruvate (PEP), into glucose [13]. On the other hand, two molecules of ATP and NADH are produced during the glycolysis process, which converts glucose into pyruvate. Phosphoenol pyruvate is created by hydrolyzing one guanosine triphosphate molecule and decarboxylating oxaloacetate (PEP). This reaction is a rate-limiting step in the gluconeogenic pathway (Figure 2.6). The gluconeogenesis process is broken down as follows:

2.4.1. Starting materials

The elements required for the synthesis of carbohydrates may vary depending on the organism and the specific pathway that is taken. But the following are some common antecedents:

• Pyruvate: The citric acid cycle and other metabolic activities, such the breakdown of glucose (glycolysis), typically create this three-carbon molecule.

• Lactate: Muscle cells produce this molecule during vigorous exercise, which the liver uses to revert to pyruvate for the production of gluconeogenesis.

• Amino acids: By dissolving certain amino acids and using their carbon skeletons, glucose can be produced.

• Glycerol: A lipid-containing molecule that may be converted into pyruvate to aid in the gluconeogenic process.

2.4.2 Gluconeogenesis pathway

There are eleven enzymatic stages in the primary gluconeogenesis pathway, which is located in the liver. These actions may be roughly divided into three phases:

• Step 1: Pyruvate is converted to phosphoenolpyruvate (PEP). This crucial stage necessitates the hydrolysis of a phosphate group and the energy intake of ATP.

• Step 2: Fructose 1,6-bisphosphate is created from PEP. Phosphate groups are added and carbon atoms are rearranged via a sequence of enzyme processes.

• Step 3: Fructose 1,6-bisphosphate is

converted to glucose. This stage produces glucose by a series of enzymatic reactions that remove phosphate groups at the end.

2.4.3 Regulation of gluconeogenesis

The body's requirement for glucose strictly controls the pace of gluconeogenesis. Hormones such as glucagon tell the liver to promote gluconeogenesis when blood sugar levels are low. On the other hand, insulin tells the liver to stop gluconeogenesis and store glucose as glycogen when blood sugar levels are high.

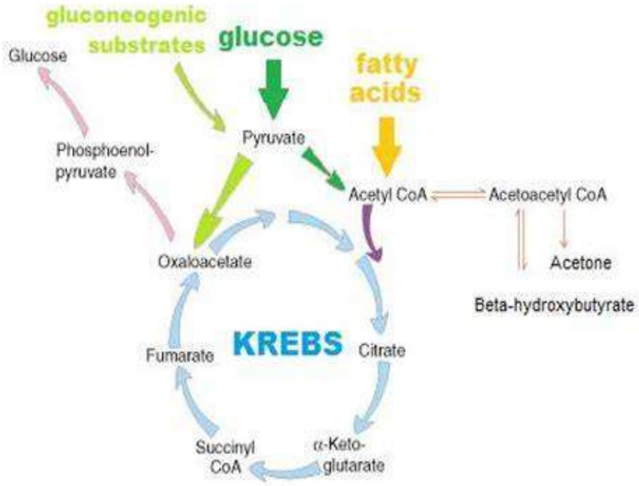


Fig 2.6 summary of gluconeogenesis pathway. (Source: Wiley et al., 2017a).

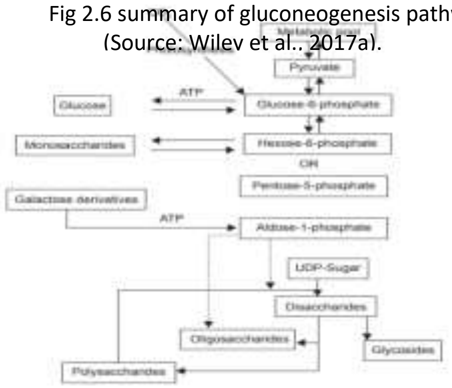


Figure 2.5 Carbohydrate biosynthesis. (Source: https://www.ncbi.nlm.nih.gov/)

3 BIOSYNTHESIS OF PROTEIN

One of the most important features of proteins is that they are made up of polymers of amino acids arranged in a linear sequence. Proteins can be classified as either enzymes or hormones based on their kinds and activities. Enzymes are protein catalysts linked to biochemical activities and made up of complex and conjugated proteins, whereas hormones are small protein chemical-signaling molecules generated by the endocrine cells with the intention of influencing or regulating specific physiologic

Proteins are also known as polypeptides because they are thought of as polymers made up of amino acids joined by peptide bonds. An amino acid is defined as having a core carbon bonded to a side chain, an amino group, and a carboxyl group. Transamination of precursor metabolites results in the formation of some amino acids. Normally, proteins are made up of 20 amino acids. The side chains of amino acids vary and can be charged (positively or negatively charged), polar, or non-polar. The "Central dogma of Molecular Biology," which states that DNA produces RNA and RNA generates proteins, is followed in the synthesis of proteins. The four main phases of ribosome-mediated protein synthesis are recycling, elongation, termination, and initiation [30].

Transcription and translation are the two steps in the production of proteins (Figure 3.1). The nucleus uses four steps—recycling, termination, extension, and activation—to transfer genetic information from DNA to mRNA. We call this procedure transcribing. Conversely, translation is the process by which the ribosome mRNA's instructions and information are read by the tRNA, which arranges the amino acids in the correct sequence, and the rRNA, which enables the amino acids to link together to create polypeptide chains. The mRNA is transported to the cytoplasm after synthesis, where it contains ribosome-specific instructions. The final protein is produced by processing a second polypeptide chain [10, 30].

3.2 Transcription

An enzyme known as an RNA polymerase, which is known to assemble nucleotides into an RNA strand using a strand of DNA as a template, creates an RNA copy of a gene's DNA sequence during the transcription stage. This copy, known as the messenger RNA molecule (mRNA), travels from the nucleus into the cytoplasm to regulate the production of proteins. Three phases comprise transcription: start, extension, and termination [19].

A. Initiation: Transcription begins when the RNA polymerase binds to a promoter, which is a particular nucleotide sequence found at the start of a gene. After joining the DNA strands, RNA polymerase breaks them apart and produces the single-stranded template needed for transcription.

B. Elongation: A single DNA strand, referred to as the template strand, serves as a template for RNA polymerase. As the polymerase reads this template base by base, it matches each nucleic acid (A, C, G, or U) with its corresponding base on the strand that codes for DNA. In order to generate mRNA molecules, this process yields complementary nucleotides that range in length from 5 to 3. The information on the RNA transcript is identical to that on the non-template DNA strand (coding), but uracil (U) is used in place of thymin.

C. Termination: Certain triplet codes (UAA, UAG, or UGA), also known as termination signals or stop signals, trigger enzymes to finish transcription and release the mRNA transcript from the polymerase when RNA polymerase gets close to the end of the gene.

3.3 Translation

Translation which is commonly described as the process of synthesizing a chain of amino acids called a polypeptide [1]. And translation occurs in the cytoplasm.

A. **Initiation**: The Initiation stage starts when a ribosome attaches itself to an mRNA transcript. Translation cannot start before the start codon 5'AUG is recognised. This codon deals with methionine, which is nearly always the first amino acid in a polypeptide chain. At the5' cap of mRNA, the small 23s ribosomal subunit binds. The larger 46s subunit then binds itself to complete the initiation complex.

B. **Elongation:** The ribosome, which has two tRNA binding sites—the P site, which preserves the peptide chain, and the A site, which accepts the tRNA—assists in the process of binding amino acids together to form lengthy chains of polypeptides. While aminoacyl-tRNA, which is complementary to the next codon, binds to the A site using energy produced by GTP hydrolysis, methionine-tRNA is located at the P site. The peptide's development has started at the A site, where methionine travels from the P site to bond with a fresh amino acid. The tRNA molecule in the P site exits the ribosome since it is no longer linked to an amino acid [1]. The ribosome then uses the energy produced by the hydrolysis of GTP to move along the mRNA molecule to the subsequent codon. The cycle continues when the expanding peptide is at the P site and the A site is free to bind the subsequent aminoacyl tRNA. Methionine at the N terminal and the last amino acid at the C terminal represent the building blocks of the polypeptide chain.

C. **Termination**: One of the three stop codons that reach the A site facilitates the last step of protein synthesis. The peptide and tRNA in the P site hydrolyse, releasing the polypeptide into the cytoplasm, because the tRNA molecules are unable to bind to these codons. The ribosome's big and tiny subunits prepare for the subsequent translation cycle.

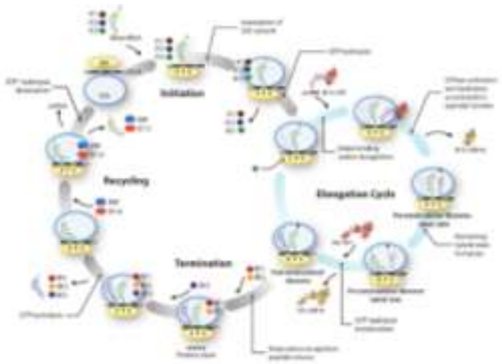


Figure 3.1 Protein synthesis process (Source: Agirrezabala & Frank (2010)

4 BIOSYNTHESIS OF NUCLEIC ACIDS (DNA & RNA)

Nucleotide bases make up nucleic acids, which are utilized to store and transmit genetic information from parent cells to progeny. Purine and pyrimidine synthesis is involved. The two kinds of cyclic nitrogenous bases with many double bonds that make up nucleotides are purines and pyrimidines. Different processes are used to synthesis these nitrogenous bases, and the final products are then joined with either ribose or deoxyribose to produce nucleotides. While pyrimidines like uracil, cytosine, and thymine have a single ring, purines like adenine and guanine are made up of two linked rings. A number of amino acids contribute to the synthesis of these nitrogenous bases, including by supplying the nitrogen needed to make pyrimidine and purine [5,16,22,23,25,30].

4.2 Purine Biosynthesis

The energetically costly de novo process from tiny molecules like carbon dioxide, amino acids, and ribose sugars, or the energetically less expensive "salvage" approach, are the two main pathways for nucleotide synthesis. The de novo pathway enzymes use 5-phosphoribosyl-1-pyrophosphate (5-PRPP) to create purine and pyrimidine nucleotides "from scratch" utilizing basic chemicals including CO2, amino acids, and tetrahydrofolate [6,24,25]. Compared to the salvage process, this nucleotide synthesis pathway requires a higher energy input [9,24]. Nucleotides can be produced from intermediates in the nucleotide degradative route through a process known as a salvage pathway.

4.2.1 Overview of the De novo pathway of Purines

The purine base is synthesized on the ribose moiety.

• PRPP synthase transforms ribose-5-phosphate (supplied by the pentose-phosphate pathway) into phosphoribosyl pyrophosphate (PRPP), a process that requires one ATP.

• Next, in the committed stage of the process, 5-phosphoribosylamine is formed by adding an α-amino group to PRPP derived from glutamine. By catalyzing this process, glutamine PRPP amidinotransferase is involved.

•Inosine 5′-monophosphate, or IMP, is created by nine distinct processes and contains the base hypoxanthine.

• Next, IMP can be converted by IMP dehydrogenase (the rate-limiting step) to GMP or by adenylosuccinate synthetase to AMP.

• It is possible to phosphorylate GMP and AMP to the triphosphate level. Nucleotide triphosphates, or ATP and GTP, are employed in energy-demanding procedures and in the creation of RNA.

Ribonucleotide reductase, which needs the protein thioredoxin, catalyzes the reduction of the ribose molecule to deoxyribose at the diphosphate level.

DNA synthesis can proceed with the utilization of dATP and dGTP following the phosphorylation of the diphosphates. Through a sequence of processes, purine bases can be recovered and transformed into free bases, nucleotides, and nucleosides. [7,8,11].

4.3 Pyrimidine Synthesis

Pyrimidine synthesis is just as complicated as purine synthesis, but it's different in that pyrimidine rings are finished before ribose is joined. Aspartic acid carbonyl phosphate, a high-energy molecule made from bicarbonate and ammonia supplied by the amino acid glutamine, is the first step in the biosynthesis of pyrimidines [4,8]. These two substrates bond (condensation) to generate carbamoyl aspartate, which is then converted to the original pyrimidine product, orotic acid, via aspartate carbmoyltransferase. The ribose 5-phosphate that is joined to orotic acid to produce a nucleotide is supplied by the high-energy molecule 5-phosphoribosyl 1-pyrophosphate (PRPP). Subsequently, uridine monophosphate, uridine triphosphate, and cytidine triphosphate are produced from orotidine monophosphate. The reduction of these ribonucleotides to deoxy-forms is analogous to that of purine ribonucleotides. After this stage, the cell only needs to produce deoxythymidine monophosphate, which is the sole remaining deoxynucleotide. It is produced by methylating deoxy-uridine monophosphate with a derivative of folic acid [30]. Nucleotide polymerization yields DNA and RNA as the end products. While RNA is created through transcription, DNA is created through the process of DNA replication.

Purine and pyrimidine are joined to the deoxyribose sugars' 1'-carbon in DNA, and the bases stretch toward the center of the helix that is created by the two chains. In the middle, base pairs—one base for every 0.54 nm—are layered atop one another as a result of interactions between the bases from each strand and the other [29, 30]. Two hydrogen bonds always link the pyrimidine Thymine T of one strand with the purine adenine of the other. Three hydrogen bonds bind the purine guanine to cytosine (C). The complementary nature of the two strands in a DNA double helix is indicated by the AT-GC base pairs.

Similar to DNA, RNA is made up of the nucleotides adenine, guanine, cytosine, and uracil (rather than thymine, which is found in DNA) and the sugar ribose. RNA molecules are single-stranded in cells [12,24, 30].

5. BIOSYNTHESIS OF LIPIDS

The biological process known as "lipogenesis" produces fat, particularly when it transforms carbohydrates into fat, which may then be stored for use as a long-term energy source in times of food scarcity. Ketoacyl and isoprene groups are two different types of biochemical units/building blocks that can contribute totally or partially to the formation of biological lipids [29]. The process of creating fatty acids involves gradually adding two-carbon units—derived from acetyl CoA—to an expanding chain. One ATP molecule and two NADPH molecules must be used in order to add each of these two-carbon units [17].

The steps involved are as follows: The enzyme acetyl CoA carboxylase (ACC) catalyzes the carboxylation of acetyl-Coa to malonyl-CoA. Fatty acid synthase is primarily involved in a sequence of enzymatic processes that lengthen the fatty acid chain. Malonyl-CoA is added to the fatty acid chain that is developing in each cycle [26].

Fatty acids are bonded to either diacylglycerol or glycerol-3-phosphate during the formation of phospholipids. A significant part of biological membranes are phospholipids. They consist of a phosphate group, two fatty acid chains, and a glycerol backbone. The cytoplasmic process of phospholipid production entails attaching a phosphate group to a diacylglycerol molecule. Phospholipidserine synthase (PSS) and phosphatidylcholine synthase (PCS) are two of the enzymes that catalyse the process [17,25,26].

Sterols are a crucial part of the cell wall, and several other bacteria synthesis them using mevalonate or non-mevalonate intermediates. Many different lipids with distinct biological roles are produced when phosphorylation or glycosylation of lipids occurs. The byproducts of amino acid, fatty acid, and glycolysis production combine to form a complex membrane lipid [30].

6 CONCLUSIONS

To sum up, biosynthesis is an essential process that keeps living things operating by giving them the ability to make and preserve the wide variety of biomolecules required for existence. Its intricacy is a reflection of the complexities of biological systems, which depend heavily on accuracy and control. The energy-intensive and highly controlled processes involved in biosynthesis depend on the intake of ATP (adenosine triphosphate) and other cofactors. In order to preserve cellular homeostasis and adapt to shifting external circumstances, biosynthesis must be regulated. Numerous bacterial cell defects can result from dysregulation in the biosynthetic process. The pace and efficiency of biosynthetic processes are influenced by the availability of precursors, energy sources such as ATP and GTP, and the metabolic state of the cell. This stringent control guarantees that the cell uses its resources wisely and adjusts to shifting environmental circumstances. Knowing the complexities of biosynthesis opens up new avenues for applications in biotechnology, medicine, and the development of novel therapies and treatments for bacterial diseases. It also deepens understanding of biology, offers insights into disease mechanisms and potential therapeutic targets.

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Authors Contributions: The first author initiated the topic and encouraged co-authors to present the review in a manuscript form. All authors contributed to and read final manuscript.

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