Chapter 3
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Biosynthetic Pathways: Unlocking Nature's Medicinal Potential

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ABSTRACT

Biosynthesis refers to the synthesis of natural products that occur within biological systems. Metabolic products are categorized as primary and secondary metabolites, which serve essential functions in the growth, protection, and survival of organisms. This account focuses on the biosynthetic pathways involved in the formation of major classes of natural products, specifically alkaloids, terpenoids and polyketides. The analysis includes specific reactions catalyzed by enzymes and co-factors involved in these pathways, as well as the regulation of biosynthesis. The understanding of biosynthetic enzyme assembly of complex structures enhances appreciation for natural chemistries and is instrumental in the redesign and utilization of these systems in bioengineering and synthetic biology, facilitating the discovery of new drugs and therapeutic targets.

Keywords: Therapeutic synthesis; advancements in biosynthetic methodologies; potential for production; future outlook.

3.1 INTRODUCTION

Medicinal plants are essential in traditional Chinese medicine and contemporary pharmaceuticals, acting as crucial sources of natural compounds for plant-derived treatments and cutting-edge therapies. Nonetheless, conventional approaches to sourcing natural products have faced challenges in fulfilling the growing needs of medicinal research and development. The synthesis of these natural products is frequently intricate and may present environmental challenges. Moreover, the process of extracting natural compounds from medicinal plants presents challenges and inefficiencies, often leading to low yields [1].

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To tackle these challenges, it is essential to create innovative methods and strategies to improve the yield of natural products derived from medicinal plants. Concentrating on biosynthetic pathways, metabolic engineering, and the synthetic biology of natural products opens up avenues to tap into plentiful natural product resources. The Journal of Chinese Herbal Medicines (CHM) welcomes submissions of rigorous studies or comprehensive reviews focused on the biosynthesis of natural products [2].

Over the last ten years, a significant number of publications in CHM have concentrated on the biosynthesis and metabolic engineering of natural compounds derived from medicinal plants. Recent technological advancements, especially in multiomics and gene editing methods such as CRISPR-Cas9, have greatly enhanced our comprehension of the biosynthetic pathways and regulatory networks that play a role in the formation of natural products in these plants [3].

The forthcoming chapter "Biosynthesis of natural products" will encapsulate the latest advancements in the field of natural product biosynthesis research. The discussion will encompass areas including genetic engineering, plant cell culture engineering, metabolic engineering, and synthetic biology [4]. The review will also address the challenges linked to improving natural compounds derived from medicinal plants and emphasize progress in biosynthetic methods, exploring the possibilities for generating natural compounds from therapeutic plants.

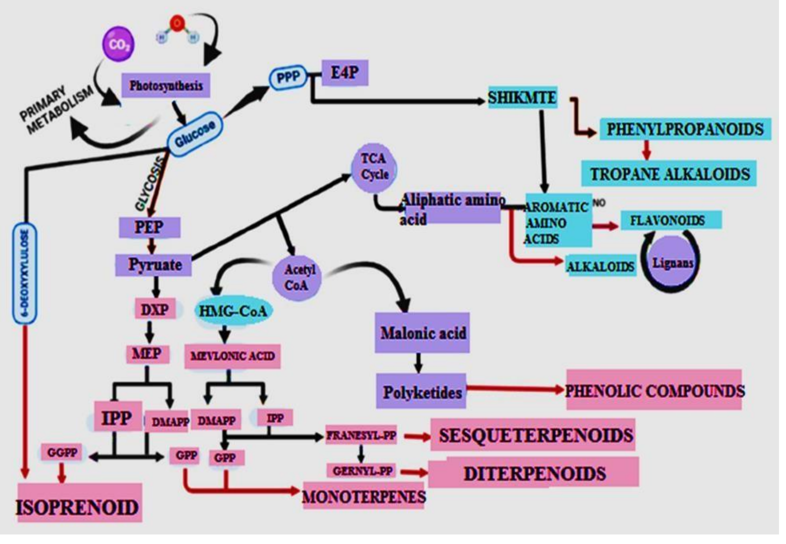

Fig. 3.1. Biosynthesis of natural products

3.2 SYNTHETIC BIOLOGY FOR THERAPEUTIC SYNTHESIS

Synthetic biology includes various definitions and is essentially defined as the endeavour to alter or improve the functions of organisms via molecular biology, allowing them to execute new tasks in a reliable way. The main goal is to generate therapeutic natural compounds with economical yields through the use of a suitable host organism. Natural products mainly result from the activities of different genes; each gene encodes an enzyme that transforms an input chemical into an output chemical. The subsequent processing of this output occurs through the next enzyme in a sequential manner, culminating in the final natural product. A pathway is formed by the collective biosynthetic genes [5].

To attain the best yields of natural products, it is essential for synthetic biologists to find a balance between the expression of pathway genes and the growth of host cells. This balancing act requires careful consideration of the stress caused by pathway gene expression, encompassing both the depletion of host resources and the buildup of detrimental intermediate products. To achieve this equilibrium and improve pathway yields, advancements in synthetic biology have introduced tools for the accurate regulation of pathway dynamics. The categorization of these tools can be divided into two primary groups [6].

The initial category encompasses methods originating from well-established domains of genetic and metabolic engineering, including basic mutation and screening, strategic modulation of gene expression in host organisms, protein engineering, directed evolution, and enhancement of growth conditions. The second category includes tools that are directly associated with synthetic biology, concentrating on the alteration of naturally occurring biological components at the DNA, RNA, and protein levels to enhance pathway efficiency [7].

The difference between "metabolic engineering" and "synthetic biology" is becoming less clear in the realm of improving natural product production, with these terms frequently being used interchangeably in scholarly conversations. This review will analyses the two categories of tools previously mentioned, focusing on scenarios pertinent to the production of natural compounds that possess therapeutic potential [8].

3.3 ADVANCEMENTS IN BIOSYNTHETIC METHODOLOGIES FOR NATURAL GOODS

Over the past two decades, progress in metabolic engineering, synthetic biology, multi-omics, and systems biology has significantly improved the production of natural compounds sourced from medicinal plants. A variety of strategies have been developed to engineer the biosynthesis of these compounds in microbial systems, effectively replicating numerous biosynthetic pathways in these organisms [9]. An effective strategy in synthetic biology involves modular synthesis, which segments metabolic processes into programmable components to enhance the production of targeted natural products. Alongside conventional strains, a range of microorganisms has been engineered to serve as host cells for the production of these compounds. Techniques like metabolic engineering, utilizing genetic circuits and genome editing, have been applied to optimize intricate multistep biosynthetic pathways [10].

Furthermore, advanced screening methods employing biosensors have enabled the identification of transporters that contribute to the secretion of natural products. The insights gained from multiomics and systems biology have enhanced our comprehension of the molecular mechanisms that control the synthesis and regulation of natural products within plant cells. By integrating genomic, transcriptomic, proteomic and metabolomic data, it is possible to design and optimize these metabolic pathways more effectively [11,12].

3.4 POTENTIAL FOR PRODUCTION OF NATURAL COMPOUNDS FROM MEDICINAL FLORA

Recent advancements in biological research and sequencing technologies have markedly enhanced the efficient extraction of valuable natural products from heterologous systems through the application of metabolic engineering and synthetic biology techniques, as demonstrated by compounds such as artemisinin and paclitaxel. The field of herbal genomics has yielded an abundance of genetic resources for the exploration of natural product biosynthesis. Moreover, the recent emergence of cost-effective and readily accessible DNA synthesis has facilitated the extensive production of enzymes, thereby enhancing the construction and modification of biosynthetic pathways for these natural compounds. Machine learning has surfaced as a potent instrument for unravelling the complex molecular mechanisms that govern intricate biosynthetic pathways. In contrast to microbial chassis, plant chassis presents significant benefits in the structural modification and functional enhancement of enzymes that play a role in the biosynthesis of natural products. The implementation of these groundbreaking technologies is set to enhance the sustainable generation of natural products, thereby yielding a wealth of chemical resources for pharmaceutical research and healthcare endeavours [13].

3.5 PROSPECTIVE OUTLOOK

The creation of "synthetic cells" is a major topic of study in synthetic biology. One might imagine a future in which these artificial cells are customized to fit particular biochemical pathways and are expertly built to produce tiny chemicals. Current projects, such as the development of "modular cells," show how they can be used to synthesize different substances with genetically modified E. coli. Subcellular compartment design is just as much a component of the concept of synthetic cells as synthetic genomes. Significant progress has been achieved in the replication of viral capsids and naturally occurring bacterial microcompartments (BMCs) in the model organism *E. coli*. Although the two types of natural compartments have shown to be successful in producing small molecules, the next big idea would be to create artificial subcellular compartments from the ground up that are tailored to the precise reaction conditions of particular natural product pathways [14].

Cell-free synthetic biology is another cutting-edge strategy in synthetic biology that seeks to perform biological processes utilizing isolated cellular components rather than conventional cellular compartments. By concentrating on metabolite production, this approach enables the construction of biological systems from the bottom up without modifying already existing biological frameworks. This method's main benefit is that it eliminates the need to modify the host organisms' background genomes in order to increase yield. Additionally, because system-level parameters can be evaluated in real time, optimizing the efficiency of multi-enzyme pathways in cell-free systems is frequently simpler [15].

Improved computational techniques for characterizing biosynthetic gene clusters derived from genomic and metagenomic DNA sequences are anticipated to result from future studies into undiscovered natural products. Research on the diversity of natural products in different soil samples from around the world indicates that the range of natural products can be greatly underestimated, especially when it comes to microorganisms that are difficult to culture in a lab. It is anticipated that developments in molecular biology methods for cloning and expressing biosynthetic pathways may create new avenues for utilizing the potential of organic molecules found in "microbial dark matter." More specifically, efforts to express biosynthetic pathways in heterologous hosts will be substantially aided by efficient and reasonably priced de novo DNA synthesis techniques. Readers are referred to an upcoming review for a thorough examination of recent advances in this discipline. As the concepts for rationally redesigning biosynthetic machinery to produce new compounds with drug-like characteristics continue to be understood, synthetic biology is emerging as a key role in improving the predictability of enzyme design [16].

3.6 CONCLUSIONS

Historically, the foundation of many significant medications created over the past century has been natural chemicals. However, during the last 20 years, the pharmaceutical industry has moved away from creating medications derived from natural compounds and towards screening libraries of artificial small molecules. Despite this trend, there are still a lot of opportunities to improve and revitalize this priceless natural resource for coming generations and to develop novel therapeutic compounds that go beyond what nature can offer through the application of synthetic biology techniques covered in this study.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

No AI tool has been used to generate data and design any image. All data have been taken from well-reputed published journals and language is manually modified without using any software.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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