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Exploration of Recent Progress of Plant Synthetic Biology for Plant Natural Products

***Abstract*: Plant natural products (PNPs) are Abundantly used in various fields which include health products, medicines, food additives, cosmetics, biofuels, flavors and other agriculture as well as industrial sectors and reservoirs of large number of compounds. With increase of the world population, it has become very difficult to satisfy our demands of daily life within the limited resources. Growing of specific plant in limited land, time and other obstacles made scientists and researchers to think an alternative way. Scientists have been continuously trying to construct infrequent plant natural products having complex structures at large scale by developing new strategies for creating cell factories artificially. Synthetic biology is a focus research area in recent trends for artificially alteration of possible biosynthetic pathway of the target molecule. Designing of synthetic biology cycle, construction of various strategies and methodology of different plant cells to modify biosynthetic pathway of secondary metabolite production is very important for synthetic biologists. This work will boost young researchers to work for betterment of the human society. The present article will discuss recent progress of synthetic biology in the field of Natural products, different strategies and methodologies of different plant species and their prospects.**

Keywords: Plant Natural products, Synthetic biology of Plant, designing way, reconstruction of metabolic pathway, strategies and methods for production of desired target products.

Plant natural products (PNPs) are reservoirs of immense number of phytochemicals which are widely used for various purposes like medicines, food additives, health products, cosmetics, renewable biofuels, flavors and other industrial sectors. Natural products having pharmacological activities are natural medicines. Source of these compounds are secondary metabolites of plants, animals and microorganisms[1-2]. Due to transformation and optimization in the journey of long evolution path, a good medicinal value has been developed[3-4]. A wide variety of chemical compounds are produced by plants which can be classified into primary (such as phytosterols, acyl lipids, nucleotides, amino acids, and organic acids) and secondary metabolites. The latter class compounds are known as natural products. The occurrences of secondary metabolites in plant kingdom are very limited but they have significant role for survivability of plants. The natural products derived from the plants have various important functionalities which include protection against pests, various diseases, UV-B damage, ecological, and other environmental stresses. These are backbones of pharmaceutical drugs, a large number of agrochemicals, food and drink industries, and other industrial biotechnology applications. It is true that plants are rich source of diversified and precious natural products. But identifying synthetic pathways for these compounds is more complicated than in microbes due to their larger and complex genomes. However, the existence of organized genes in many cases for natural products pathways is in operon-like clusters within the plant genomes. With the help of advance technology, accelerate the possibility to access the genes and enzymes of particular metabolism in plants smoothly. The plant synthetic biology may be useful for modifying the metabolic diversity of the plants and synthesizing the modified plant natural products. Extensive research on plants has become more attractive now a days for natural sources derived high value products in connection with various fields like medicines, foods, flavors, renewable fuels, cosmetics etc. But it is needless to mention that some challenges also exist. These challenges are basically very fundamental which include low abundance of secondary metabolites within plant, slow growth rate due to very complex metabolites. In addition to that, some plants are in danger of extinction, some chemical structures are so complex that they face difficulty to synthesis. Therefore, some alternative approachable needs are indeed to have high value natural products and fulfil our demands.

As it is very difficult to develop sufficient plants to satisfy our demand for these desirable compounds, researchers are seeking to manufacture those herbal products in their laboratories via expression in clean-to-subculture flowers, bacteria or yeast—so-referred to

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as heterologous hosts. For that purposes researchers are trying to develop cell factories that can produce greater than naturally made natural host. As plant natural products and their derivatives are vital resource for maturing the field of health products, medicines and food additives, synthetic biology techniques initiate new techniques for artificially construction and optimization of biosynthetic pathway of the target compounds within microbial cell at large scale.

Synthetic Biology in the Field of Natural Products: Now a day's investigation of plant natural products biosynthesis is very important for focusing on the compounds having economic significance for industrial purpose or of physiological importance (e.g., hormones). The studies have been developed from biochemical assays with cell-free extracts and isolation of the relevant enzymes to molecular biology based recombinant expression and analysis of plants genetically modified to over or under express the encoding genes. Various approach can be followed like making of artificial bio-system having unique properties[5], redesigning of system for desired purposes[6], and reconstruction for understanding biology[7]. The biosynthesis of very few plant natural products is very important. Identification of the relevant biosynthetic pathway enables access to the resulting natural product, via metabolic engineering for different classes of plant natural products like flavonoids, alkaloids, betalains, and glucosinolates and in the native plant or in microbial hosts. Emphasis should be given on microbial platforms as a highly useful tool for engineering these natural products with additional consideration given to microbial consortia. The potential to lifestyle sturdy assortments of microbes with various capability has dramatically elevated to permit a much wider scope of merchandise to be engineered in more and more green ways. These technological developments are persevering with increase at a fast tempo and coincide with new finding out concerning using plant natural products.

Synthetic Biology of Plant : The prime aims of synthetic biology are to design and modify natural systems or reconstruction of artificial biological devices and systems by applying engineering principles so that predictable behaviors are exhibited[8]. Development processes of this field can resemble automobile mechanics. For higher efficiency (top down), an older model can be tweaked or a new model can be made from scratch (bottom up). To make minimum size system, lesser number of parts and less complex structure, the top down system is applied in the existing plant. Whereas bottle up approach is applied to individual parts to form biological system artificially having potent properties[5]. Irrespective of said both approaches, ultimate aim of the synthetic biology is to redesign a desirable system for a target purpose[6] and by reconstruction to know biology greatly[7]. Biologists, engineers, scientists, and others work together for finding effective routes to combine various genetic architecture into purposeful products for real-life that are used every day. In some cases, main focus of the synthetic biologists more in engineering than biology. The prime focus of biology is on discovery of science and analysis while, focus of engineering on design, redesign and synthesis. Its extensive uses have been found in various fields like agriculture sustainability[9], improvement of human health and wellness[10], recent development of synthetic element of plant from single fraction to developed circuits, innovation of software, and incorporation of hardware tools within the engineering cycle[11]. It is different from conventional plant biotechnology that mainly relies on recombinant DNA technology and its focuses observed on recombination of preexisting heterologous genes and promoters whereas plant synthetic biology aims to combine the modules of nature differently with new innovative ways and to make new modules. It is similar to systems biology, focus of synthetic biology goes on the interactions and active behaviors of a natural or artificial system's parts[12]. Systems biology deals with the investigation of complex mechanisms of biological systems by the treatment of knowledge on the behavior of proteins, genes, biochemical networks including physiological responses within a whole system[13].

Methods for Partial Synthetic Modification of Biosynthetic Pathway of PNP in Plant Cell : It is observed to have tremendous complex metabolic pathway of plants secondary metabolites and these can be arranged in 3 dimensional grid, linear or cyclical having diversified branch. Although there are some limitations of microbial chassis e.g. very weak expression of P450 Enzymes and lesser tolerance to active products nor yielding of minimum yield. One important advantage to perform modification of metabolic pathway of PNP is due to known partial or complete biosynthetic pathway of the target PNPs, Hence, implementation of pathway is possible by overexpression, or by blocking competing reactions. There are three major genetic systems of plants. These are nuclear, plastid and mitochondrial. Due to the plant homology, plant cells synthesize specific PNP.

Zhuet al[14] reported recent progress in the modification of biosynthesis and other synthetic biology application of Plant natural products in plant cell. There, recent progress of modified biosynthesis of PNP within Plant cell of different secondary metabolites and associated methods has been introduced in tabular form. Different strategies and methods used for modification of biosynthesis of Plant Natural products in plant Cell have been well presented there[14].

Designing Way of Synthetic Biology Cycle : There are five stages for ideal designing of synthetic biology cycle. These are: conceptualization, designing, model preparation, construction, and, lastly, exploration, test, and validation[15,16–18]. Conceptualization directs the grand goals (i.e., expected features and activities of a device) of networks of synthetic gene in response to inputs and desired outputs. The targets should be formulated rationally so that production and testing be unambiguously. Basic knowledge helps synthetic biologists to construct nature's principles and modules with the help of biomimetic. After the specification of an objective, it is important to select genetic parts and strategy constructions for the actualization of the objective. In this context, use of Computer-Aided Design (CAD) helps for determination and optimization of kinetic parameters, network hierarchies, and parts selection[15]. It helps also modeling for the network analysis behaviors, sensitivity, and the promising design selection for implementation. Construction involves the fabrication, assembly of synthetic circuits and also their integration in a plant host[19]. A combination of trial-error approach with fine-tuning is needed for testing, experimental probing, and justification. Furthermore, multiple repetitions might be required to form a series of upgraded approximate solutions to eventually procure the convenient functions and properties[15]. Empowering tools to satisfy the design of plant synthetic biology cycle include various principles related to engineering for design, parts selection of component, and design and modeling of plant computational tools[19]. Standardization parts are very dependent on modularity and orthogonality and allow parts to be combined to form a complex system. The decomposition and simplification of a technical process by abstraction, decoupling, and standardization can lead to reduction of effort in the design cycle.

Conclusion

Since the historical period, secondary metabolites of plant have been used as origin of medicine. To fulfill demand in a large scale, it is needed to set up sustainable routes for availing secondary metabolites. For synthesizing PNPs within the cell of plant a perfect host is necessary where genetic transformation and metabolic process will be carried on. It is true that more than 500,000 natural products are known but their biosynthetic pathway have not yet been identified[20]. Hence, searching of these biosynthetic pathway and analysis should bring under the consideration. It is our belief that various strategies and methods will be matured for the next generation such as sequencing technology, genetic engineering technology, bioinformatics analysis, and other synthetic biology technologies. Interpretation of diversified biosynthetic pathways will be possible in the studies on medicinal plants. Although it is true that there is still a long journey to overcome the gridlock in the plant synthetic biology development, use of plant cells can be utilized as an excellent substitute for PNP production and provide a huge opportunity for future agriculture and industry. The present work will help the researchers to bring into their notice regarding way of thinking. ❐

LALAN CHANDRA MANDAL

Assistant Professor of Chemistry,
Department of Chemistry,
Krishna Chandra College,
Hetampur, Birbhum, West Bengal 731124, India
e-mail: lalan_chem@yahoo.co.in

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