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The Role and Biochemical Significance of Plant Secondary Metabolites

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ABSTRACT

Natural products can be reproduced in labs by chemical processes since they adeptly replicate the complex bioactive molecules found in nature. This encompasses a synthesis of several repeats of one-pot synthetic methods to produce natural products or analogous structures, together with subsequent biological assays of the structure and the increasing pharmacological activity of the drug. Chemical synthesis is crucial for addressing the constraints posed by the limited availability of natural resources and their sustainable harvesting, in comparison to natural production. It also facilitates the creation of structural analogues that have enhanced biological activity or pharmacokinetic properties. This presentation highlights the significance of the chemical synthesis process in drug discovery, including medicinal chemistry and the development of novel therapeutics.

Keywords: Chemical synthesis; terpenoids; flavonoids; alkaloids; lignins.

5.1 INTRODUCTION

A wide range of organic chemicals are produced by plants, most of which don't seem to have a direct role in growth and development. These chemicals, which are commonly called secondary metabolites, are frequently distributed differently among specific taxonomic groups in the kingdom of plants. More and more are shedding light on their roles, many of which are still unclear. All plants contain acyl lipids, nucleotides, amino acids, and organic acids, which all play vital and typically obvious metabolic roles [1,2]. Natural products are known for their intricate chemical structures and biosynthetic processes, but most plant biologists have historically paid little attention to them since they are thought to be physiologically

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irrelevant. However, since the 1850s, organic chemists have been deeply intrigued by these novel phytochemicals and have thoroughly examined their chemical characteristics. Natural product studies sparked the development of synthetic procedures, spectroscopic approaches to structure elucidation, and separation techniques that are now the cornerstones of modern organic chemistry. Natural goods' enormous value as dyes, polymers, fibres, glues, oils, waxes, flavouring agents, fragrances, and medications spurred interest in them rather than just academically. The current focus of this field is the search for new drugs, antibiotics, herbicides, and insecticides due to the recognition of the biological properties of a wide range of natural products. Interestingly, a reevaluation of the potential roles these compounds may play in plants, particularly in the context of ecological interactions, has been spurred by this growing appreciation of the highly diverse biological effects produced by natural products. Many of these compounds, as this chapter illustrates, have now been demonstrated to have important adaptive significance in defense against microbial infection and herbivory, as well as acting as allelopathic agents (allelochemicals that influence competition among plant species) and attractants for pollinators and animals that disperse seeds. Since these ecological roles have a significant impact on plant survival, we believe it is appropriate to refer to secondary plant metabolites that predominantly affect other species by the less derogatory term "plant natural products" [3].

5.2 TERPENOIDS

Terpenoids are a class of natural compounds derived from plants that have the largest structural variation. Since the original members of the family were isolated from turpentine, or "terpentin" as it is known in German, the term "terpenoid," or "terpene," originates from this fact. Based on the isopentane skeleton, branching five-carbon units are repeatedly fused to form terpenoids. Because many terpenoid substances can be thermally decomposed to produce the alkene gas isoprene as a byproduct and because isoprene can polymerise in multiples of five carbons to generate numerous terpenoid skeletons under the right chemical conditions, these monomers are commonly referred to as isoprene units. For these reasons, terpenoids are sometimes referred to as isoprenoids, despite the fact that isoprene is not the biological precursor of this family of metabolites, a fact that has been known by researchers for well over a century [4].

5.2.1 Biosynthesis of terpenoids

While the groups of enzymes involved in terpenoid biosynthesis are similar in plants, animals, and microbes, there are notable distinctions across these processes. Specifically, compared to mammals or microbes, plants generate a far greater variety of terpenoids. This is evident in the intricate structure of plant terpenoid biosynthesis, which occurs at the tissue, cellular, subcellular, and genetic levels. Anatomically highly specialized structures are nearly often linked to the creation of significant quantities of terpenoid natural products, as well as their subsequent storage, emission, or secretion [5]. Terpenoid essential oils are produced, stored, and released by the glandular trichomes and secretory cavities of leaves as well as the glandular epiderms of flower petals. These oils are significant because they promote insect pollination. Conifer species create and collect protective resin made of rosin (diterpenoid resin acids) and turpentine (monoterpene olefins) in their resin ducts and blisters. Rubber and other specific triterpenes and polyterpenes are produced by laticifers, and specialized epidermis forms and excrete triterpenoid surface waxes. By removing natural products from delicate metabolic processes, these unique structures guard against autotoxicity. Since the majority of these structures lack photosynthesis, they are dependent on nearby cells to provide the carbon and energy required for terpenoid biosynthesis [6].

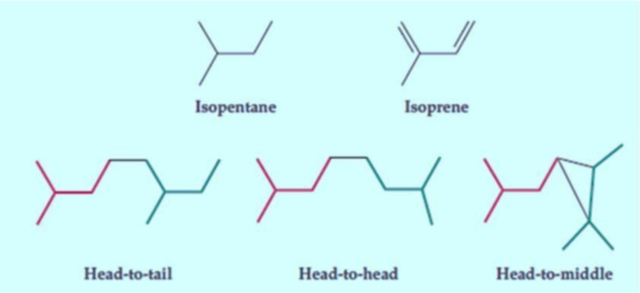

Fig. 5.1(A). Classification of terpenoids

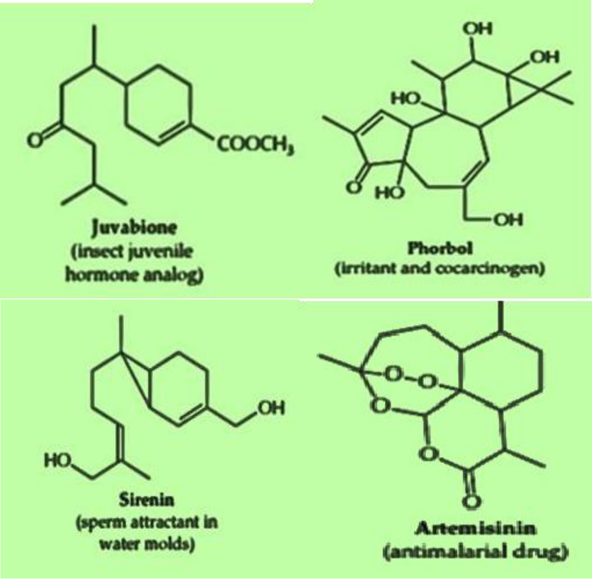

Fig. 5.1(B). Terpenoids formed by secondary transformations of parent cyclic compounds

5.3 ALKALOIDS

Plant extracts have been utilized as ingredients in poisons and potions for a large portion of human history. The opium poppy (*Papaver somniferum*) has been used for its latex in the eastern Mediterranean since at least 1400–1200 B.C. India has been using *Rauwolfia serpentina*, also known as Sarpagandha root, since around 1000 B.C. Medicinal plant extracts were utilized by the ancients as sedatives, purgatives, and antitussives to cure a variety of illnesses, such as fever, insanity, and snakebite. As the practice of using medicinal herbs extended from Arabia to Europe in the West, novel infusions and concoctions contributed to notable incidents. In 399 B.C., the philosopher Socrates ingested an extract of hemlock (*Conium maculatum*) that included coniine. Atropine-containing henbane (*Hyoscyamus*) extracts were used by Queen Cleopatra in the last century B.C. to dilate her pupils and make herself appear more attractive to her male political opponents. Opium has been the most popular medicine over the ages. It was mostly used in the form of Theriak, a mixture of wine, dried snake meat, and opium [7]. After opium's constituent parts were examined, morphine—named for the Greek mythological dream deity Morpheus—was discovered. The study of alkaloids began with German chemist Friedrich Sertürner's 1806 isolation of morphine. It was from the Arabic name al-qali, the plant from which soda was originally separated, that another pharmacist, Carl Meissner, first used the term "alkaloid" in Halle, Germany, in 1819. Originally described as basic nitrogen-containing chemicals with pharmacological activity, alkaloids are derived from plants. Several of the plants that contain alkaloids are still used as prescription medications today, serving as humanity's first "materia medica." The opium poppy's codeine, which has antitussive and analgesic properties, is one of the most well-known prescription alkaloids. Modern synthetic medications, such as the antimalarial alkaloid quinine for chloroquine derived from indole and the tropane alkaloid atropine for tropicamide, which is used to enlarge the pupil during eye tests, have also been modelled after plant alkaloids [8].

Almost every class of life, including frogs, ants, butterflies, bacteria, sponges, fungi, spiders, beetles, and mammals, has species that contain alkaloids. Alkaloids with different configurations have been separated from a range of aquatic animals. Certain species, including amphibians, have secretory glands or skin that create a variety of noxious or toxic alkaloids. Others employ plant alkaloids as a source of defense compounds, pheromones, and attractants. One example of this is the insects that are discussed below. Certain butterflies harvest alkaloidal precursors from non-food plants and process them to create defence and pheromone molecules. *Tyria jacobaea* larvae feed relentlessly on *Senecio jacobaea* until the plant is entirely stripped of its leaves [9]. The larvae maintain these alkaloids throughout their metamorphosis. Pyrolizidine alkaloids are incorporated into the reproductive biology of male Asian and American arctiid moths by sequestering them in abdominal scent organs called coremata [10].

Plant cell suspension cultures that could yield high alkaloid concentrations were not developed until the 1970s. Compared to whole-plant studies, cell culture offers several advantages as an experimental system: plant material is available yearround; cells are developed in an undifferentiated, relatively uniform state; there are no interfering microorganisms; and, most importantly, the vegetative cycle is compressed [11]. In just two weeks of incubation, plant cell cultures are able to produce a significant number of secondary products. This is in stark contrast to plant production, where the period of time required for the buildup of alkaloids can range from a single season for annual plants to several years for certain perennial species [12].

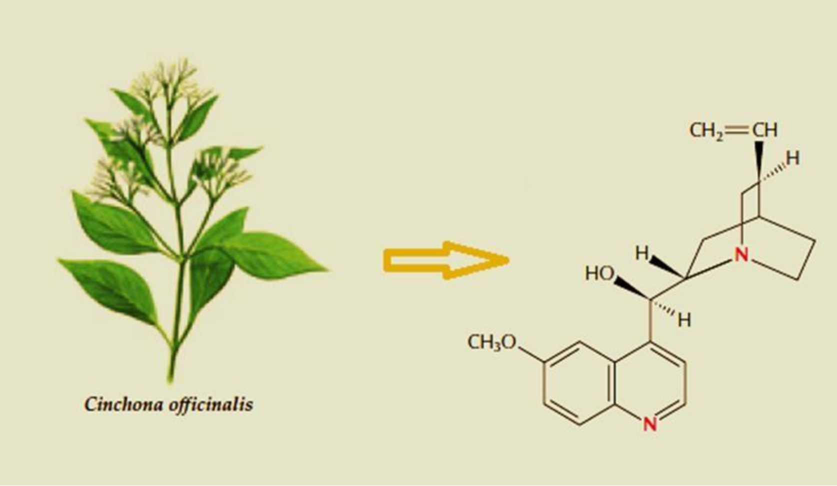

Fig. 5.1(C). An antimalarial drug Quinine isolated from *Cinchona officinalis*

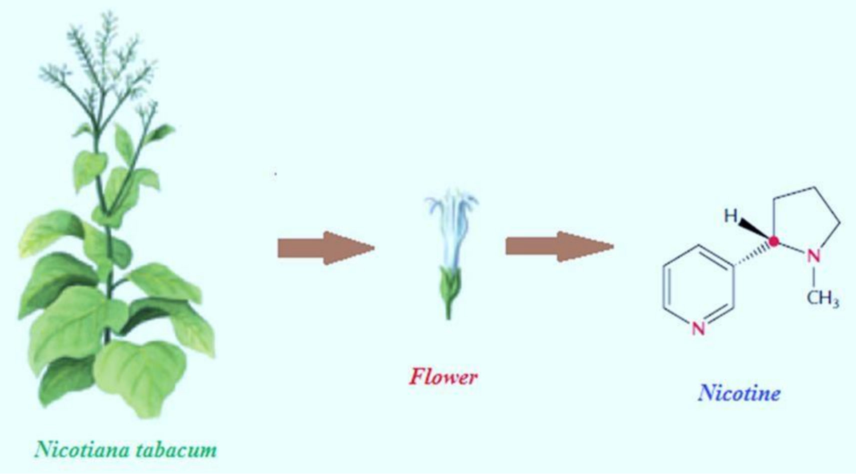

Fig. 5.1(D). Nicotine isolated from flower *Nicotiana tabacum*

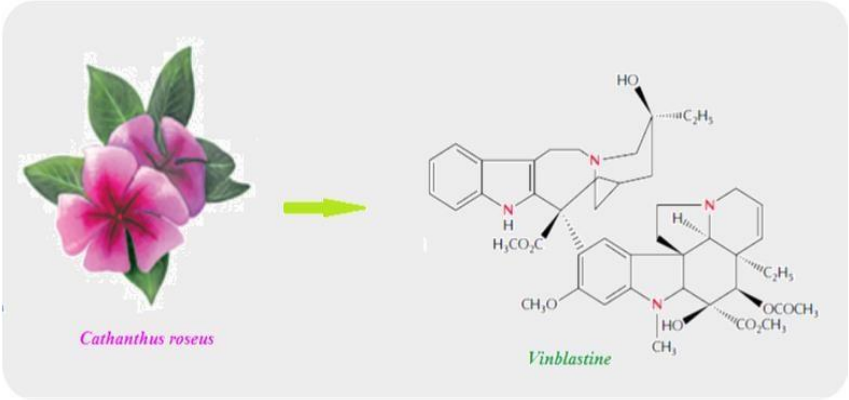

Fig. 5.1(E). Vinblastine from *Catharanthus roseus* flower.

5.3.1 Alkaloid synthesis

Alkaloids are biosynthesized by plants from basic components by use of numerous distinct enzymes. Our understanding of the synthesis of alkaloids in plants was predicated on biogenic theories until the middle of the 20th century. Routes proposed by eminent natural product chemists including Clemens Schöpf, Ernst Winterstein, Georg Trier, and Sir Robert Robinson were predicated on estimates deemed viable in the field of organic chemistry [13]. However, alkaloid biosynthesis turned into an experimental field in the 1950s when organic compounds with radioactive labels were available to test theories. These pioneering precursor-feeding studies unequivocally demonstrated that L-amino acids (such as tryptophan, tyrosine, phenylalanine, lysine, and arginine) are typically the starting point for the formation of alkaloids, either on their own or in conjunction with a steroidal, secoiridoid (such as secologanin), or other terpenoid-type moiety. These widely distributed amino acids can go from primary metabolites to substrates for extremely species-specific alkaloid metabolism in one or two conversions [14]. While the exact mechanisms by which plants produce the majority of the 12,000 known alkaloids remain unclear, a number of well-studied systems can be used as models to illustrate the kinds of building blocks and enzyme changes that have developed along the course of alkaloid biosynthesis. The first alkaloid whose production was elucidated at the enzyme level was the monoterpenoid indole alkaloid ajmalicine, which is generated from L-tryptophan. The work involved plant cell suspension cultures of the Madagascar periwinkle *C. roseus* were applied. Tryptophan decarboxylase converts the amino acid L-tryptophan to tryptamine, which is the starting point for the biosynthesis of ajmalicine and more than 1800 additional monoterpenoid indole alkaloids in plants. Next, tryptamine is stereospecifically condensed with the secoiridoid secologanin (which is produced from geraniol through many enzymatic steps) by strictosidine synthase, resulting in 3- strictosidine. Then, a variety of distinct structures can be formed by species-specific enzymatic permutations of streptosidine. The utilization of plant cell cultures to clarify the enzymatic synthesis of ajmalicine paved the way for the examination of more intricate biosynthetic pathways, including those that produce two more monoterpenoid indole alkaloids derived from L-tryptophan, namely ajmaline and vindoline [15].

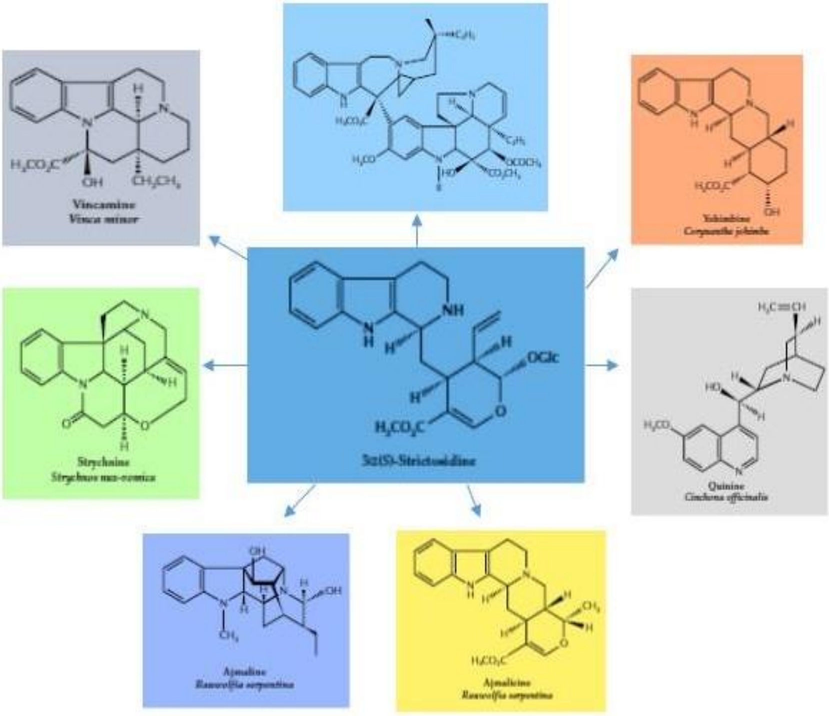

Fig. 5.1(F). Specific alkaloids isolated from natural products

5.4 BIOSYNTHESIS OF LIGNANS, LIGNINS AND SUBERIZATION

Lignans and lignins are the two main types of plant metabolites that are produced from monolignols. The majority of the metabolic flux that passes through the phenylpropanoid biosynthesis pathway is used to produce lignins, which are essential building blocks of cell walls. The processes that result in dimeric/oligomeric lignans and lignins, as well as similar complex plant polymers like those seen in suberized tissue, include free radicals. Robert Downs Haworth first used the name "lignan" in 1936 to refer to a group of dimeric phenylpropanoid (C_6C_3) metabolites that were connected by their 8-8' linkages. The term "Neolignan" which was previously used to refer to all other kinds of links, has lately been expanded to include compounds produced from allylphenol compounds, including isoeugenol. However, as long as the coupling mode (e.g., 8–8’, 8–5’) is stated, we have opted to refer to any potential phenylpropanoid (C_6C_3) coupling products in this chapter using the more convenient term lignan [16]. Remarkably, only a small number of coupling modes have been observed in nature, despite the fact that thousands of lignans are currently known to exist. Ferns, gymnosperms, and angiosperms have lignan dimers, but there are also higher oligomeric forms. Coniferyl alcohol is mostly used in the production of lignan, with minor amounts of phenylpropanoid monomers, allylphenols, and other monolignols also being utilised. Although the specific antipode, or enantiomer, can differ depending on the plant source, the majority of lignans are optically active. Delineating the biochemistry of lignan production is a relatively recent development. Work so far has mostly concentrated on producing the most prevalent 8–8’-linked lignans. Two coniferyl alcohol molecules undergo a rigorous stereoselective coupling to generate this class of natural compounds. The in vitro synthesis of (+)- pinoresinol was the first example of stereoselective regulation of phenolic coupling that was demonstrated. The general mechanism of this reaction, found in Forsythia species, is as follows: a dirigent protein (Latin: dirigere, to guide or align) orients the putative free radical substrates in such a way that random coupling cannot occur, only the formation of the 8–8’-coupled intermediate, (+)-pinoresinol, is permitted. A laccase or laccase-like enzyme catalyses a one-electron oxidation that forms the corresponding free radicals. The specific antipode, or optimal form, of pinoresinol that is produced, also differs depending on the type of plant; flax seeds, for instance, accumulate (–)-pinoresinol. Depending on the plant species, pinoresinol can subsequently go through a number of transformations after it is produced [17].

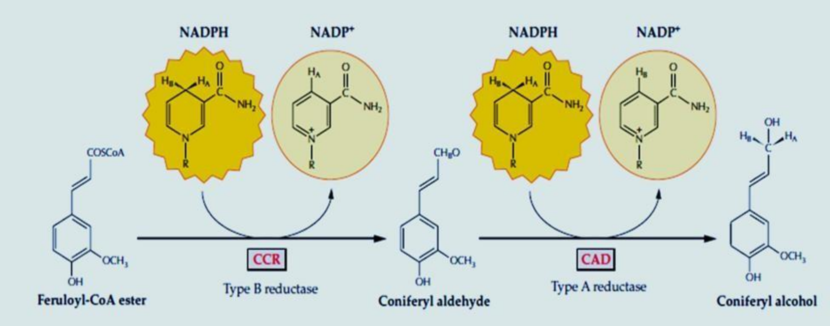

Fig. 5.1(G). Synthesis of lignana, lignins and suberization

5.5 FLAVONOIDS

The class of phenolic natural compounds known as flavonoids is vast, consisting of over 4500 distinct examples. Flavonoids can exist as monomers, dimers, and higher oligomers and are found in most plant tissues, frequently in vacuoles. Additionally, they can be discovered in different heartwoods and barks as combinations of coloured oligomeric and polymeric components [18].

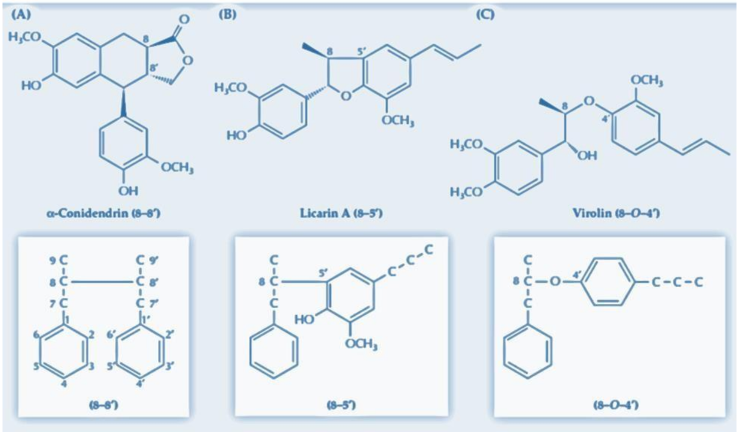

Fig. 5.1(H). Examples of lignans isolated from natural products

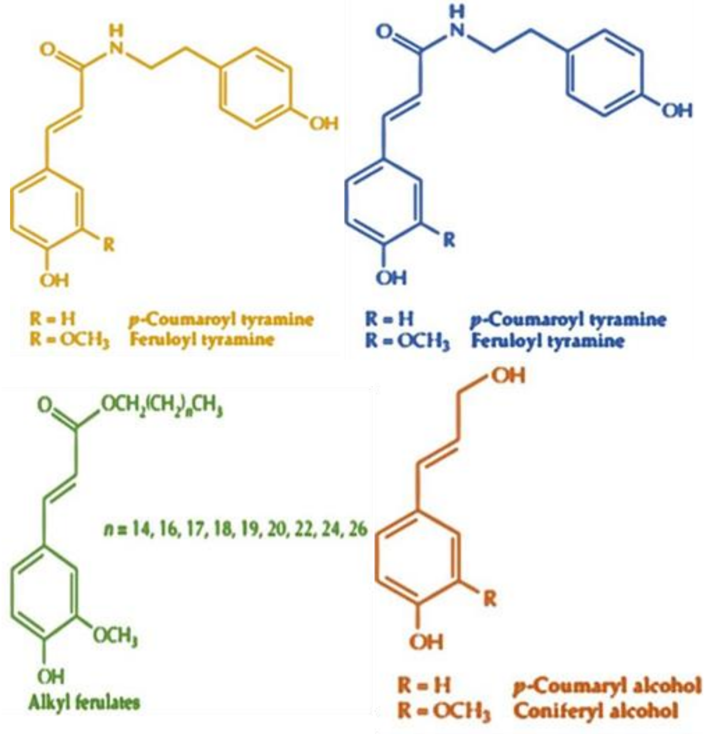

Fig. 5.1(I). Aromatic compounds derived primarily from hydroxycinnamates contain small amounts of monolignols

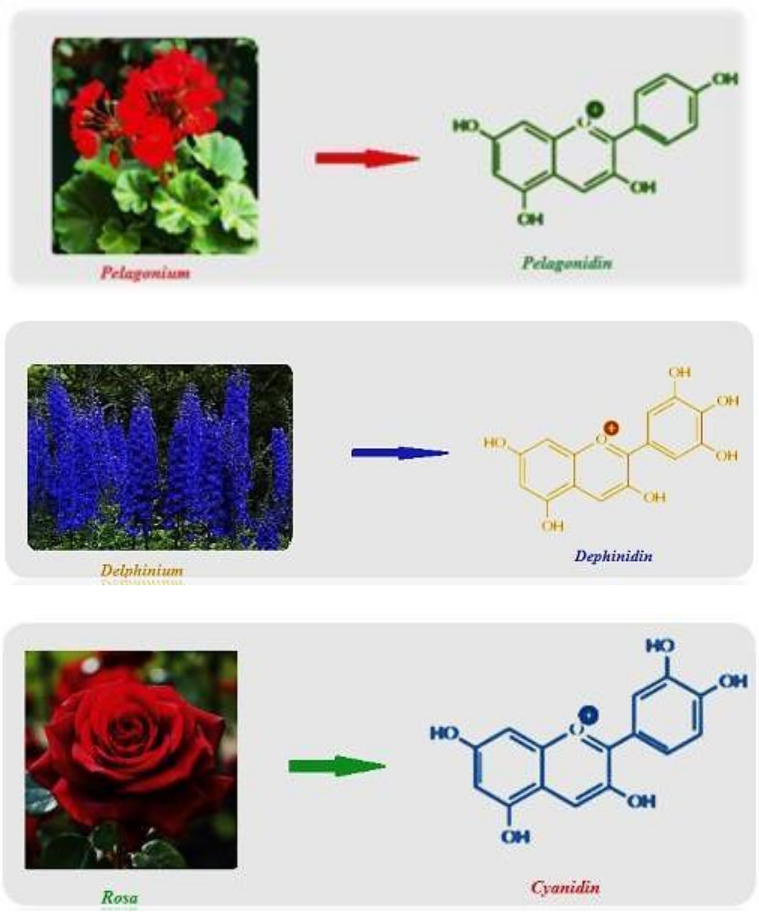

Fig. 5.1(J). Anthocyanin pigments: Pelargonidin, Delphinidin and Cyanidin, from *Pelargonium, Rosa*, and *Delphinium*

5.6 CONCLUSION

Numerous chemical molecules that are produced by plants are not directly related to the main metabolic processes of growth and development. It has only been recently that these naturally occurring compounds, also known as secondary metabolites, have been recognized in the analytical context of plants. The main roles that natural products seem to play include defense against diseases and predators, as well as a reproductive advantage through attracting pollinators and seed dispersers. They might additionally serve as poisons to give one species a competitive edge over another. Three main categories comprise the majority of natural products: phenolic chemicals (mostly phenylpropanoids), alkaloids, and terpenoids. Numerous plant terpenoids are either diverse types of attractants or poisons that prevent herbivores from feasting. Amino acids are the main building block used to create alkaloids. Many of these nitrogen-containing chemicals have pharmacologically significant effects and shield plants from a range of herbivorous predators. Plants use phenolic chemicals, which are mostly produced from byproducts of the shikimic acid pathway, for a number of crucial functions. Flavonoids, lignans, tannins, and certain basic phenolic chemicals act as defenses against infections and herbivores. Furthermore, lignins mechanically reinforce cell walls, and many flavonoid pigments serve as significant attractants. The metabolism of natural products in the majority of plant species is still unclear, despite the fact that numerous natural products and their uses have been discussed in this chapter. There is still plenty of fascinating biochemistry to learn.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Eisenreich W, Schwarz M, Cartayrade A, Arigoin D, Zenk MH, Bacher A. The deoxylulose phosphate pathway of terpenoid biosynthesis in plants and microorganisms. Chem. Biol. 1998;5:R221–R233.
2. Croteau R, Kutchan TM, Lewis NG. Natural products (secondary metabolites). Biochemistry and molecular biology of plants. 2000;24:1250-319.
3. Gershenzon J, Croteau R. Terpenoid biosynthesis: The basic pathway and formation of monoterpenes, sesquiterpenes and diterpenes. In Lipid Metabolism in Plants, Moore TS, Jr., ed. CRC Press, Boca Raton FL. 1993;339–388.
4. Rosenthal GA, Berenbaum MR eds. Herbivores: Their interactions with secondary plant metabolites, Vol. 1: The Chemical Participants, 2nd ed. Academic Press, San Diego; 1991.
5. Dixon RA. Isoflavonoids: Biochemistry, molecular biology and biological functions. In Comprehensive Natural Products Chemistry, Vol. 1, Polyketides and Other Secondary Metabolites Including Fatty Acidsand Their Derivatives, Barton DHR, Nakanishi K, Meth-Cohn O, eds.-inchief. Elsevier, Amsterdam. 1999;773–824.
6. Forkmann G, Heller W. Biosynthesis of flavonoids. In Comprehensive Natural Products Chemistry, Vol. 1, Polyketides and Other Secondary Metabolites Including Fatty Acids and Their Derivatives, Barton DHR, Nakanishi K, Meth-Cohn O, eds.-inchief. Elsevier, Amsterdam. 1999;713–748.

7. Lewis NG, Davin LB. Lignans: Biosynthesis and function. In Comprehensive Natural Products Chemistry, Vol. 1, Polyketides and Other Secondary Metabolites Including Fatty Acids and Their Derivatives, Barton DHR, Nakanishi K Meth-Cohn O, eds.-in-chief. Elsevier, Amsterdam. 1999;639–712.
8. Lewis NG, Davin LB, Sarkanen S. The nature and functions of lignins. In Comprehensive Natural Products Chemistry, Vol. 3, Carbohydrates and Their Derivatives Including Tannins, Cellulose and Related Lignins Barton DHR, Nakanishi K, Meth-Cohn O, eds.-in-chief. Elsevier, Amsterdam. 1999;617–745.
9. Bruce SO, Onyegbule FA, Ezugwu CO. Pharmacognostic, physicochemical and phytochemical evaluation of the leaves of Fadogia cienkowskii Schweinf (Rubiaceae). Journal of Pharmacognosy and Phytotherapy. 2019;11(3):52-60.
10. Okoye VO, Bruce SO, Onyegbule FA. Phytochemical screening and pharmacognostic properties of Peuraria phaseoloides leaves (roxb) benth. (fabaceae). International Journal of Public Health, Pharmacy and Pharmacology. 2020;5(2)11-24.
11. Onyegbule FA, Okoli OG, Bruce SO. *In vivo* evaluation of the antimalarial activity of the aqueous ethanol extract of monodora myristica seed in albino mice. International Journal of Science and Research (IJSR). 2019;8(6):1530-1538
12. Gutzeit HO, Ludwig-Muller J. Plant natural products: Synthesis, biological functions and practical applications, First Edition. Wiley-VCH Verlag GmbH & Co. KGaA. 2014;1- 80.
13. Hsu E. Reflections on the ‘discovery’ of the antimalarial qinghao. Br J Clin Pharmacol. 2006;61:666-670
14. White NJ. Qinghaosu (Artemisinin): The price of success. Science. 2008;320:330-334
15. Covello PS, Teoh KH, Polichuk DR, Reed DW, Nowak G. Functional genomics and the biosynthesis of artemisinin. Phytochemistry. 2007;68:1864-1871
16. Nwokeji PA, Enodiana OI, Ezenweani SR, Osaro-Itota O, Akatah HA. The Chemistry of natural product: Plant secondary metabolites. International Journal of Technology Enhancements and Emerging Engineering Research. 2016;4(8):2347-4289.
17. Smanski MJ, Zhou H, Claesen J, Shen B, Fischbach MA, Voigt CA. Microbiol. Nat. Rev. 2016;14;135-149.
18. Bhat SV, Nagasampagi BA, Sivakumar M. Chemistry of natural product. Berlin, New York. Springer. 2005;6(6):840.

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