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Green Extraction of Natural Products

Theory and Practice

Edited by
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Green Extraction of Natural Products

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Green Extraction of Natural Products

Theory and Practice

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Preface

Green extraction of natural products is a new concept that meets the challenges of the twenty-first century, protecting both environment and consumers and, at the same time, enhancing competitiveness of industries by becoming more ecologic, economic, and innovative and thereby sustainable. It is based on the discovery and designs of extraction processes which reduce energy consumption, allow use of alternative solvents and renewable natural products, and ensure a safe and high quality extract and final product. Within the green extraction approach, the concept of a "green extract" is introduced. This is an extract obtained by following processes that have the lowest possible impact on the environment (less energy and solvent consumption, etc.), and whose eventual recycling is planned for from the beginning (coproducts, biodegradability, etc.). This green extract should be the result of a whole chain of values in both senses of the term: economic and responsible, starting from production and harvesting of the plant, the transformation processes – not only solid–liquid extraction but also separation and purification – together with formulation and marketing.

This book is an attempt to advance practical objectives of "green extraction of natural products." The book has been made possible due to the collaboration between "Dechema ProcessNet – Germany" and "France Eco Extraction" associations but also because of the critical mass of international research and industrial teams who have contributed to establish a series of methodological and technological tools in the field of extraction of natural products to prevent and reduce petroleum solvents, fossil energy, and chemical wastes and hazards in extraction as a process including preparation of starting materials, drying, grinding, solid–liquid extraction, liquid–liquid extraction, separation, purification, formulation, until final packaging. Part of the contents are based on the significant amounts of materials accumulated from a Dechema training course on phytochemical process development and production held several times over the past years at the TU Clausthal with lecturers from industry and academia, some of who have contributed to this book.

This book attempts to summarize current knowledge on green extraction of natural products in terms of innovative processes, methods, alternative solvents, and product safety. It provides necessary theoretical background and details about green extraction with regard to techniques, mechanisms, protocols, industrial applications, safety precautions, and environmental impacts. This book is targeted at industry professionals as well as academicians engaged in separation and extraction engineering or natural product chemistry research, and graduate-level students. Each chapter would be complementary to other chapters and based on presentations by the reputed international researchers and professionals, addressing the latest efforts in the field.

We are convinced that this book will make a useful contribution toward the collection of accumulated knowledge in one place, and is the starting point for future collaborations in this new area of "green extraction of natural products" between research, industry, and education, covering a wide range of relevant applications: perfume, cosmetic, pharmaceutical, food ingredients, nutraceuticals, biofuel, and fine chemicals industries.

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1
Green Extraction: From Concepts to Research, Education, and Economical Opportunities

Farid Chemat, Natacha Rombaut, Anne-Sylvie Fabiano-Tixier, Jean T. Pierson, and Antoine Bily

1.1
Introduction

One of the principal aims of sustainable development of green processing is in the teaching of green chemistry in colleges, high schools, and academic laboratories of both developed and developing nations. The researchers from academia and professionals from industry have chosen not to ignore the potential consequences of green chemistry and processes and have realized that they have responsibilities in education, research, and acceptance for industrial implementation of green chemistry (analysis, extraction, synthesis, separation, etc.) [1]. They recognize that their research will affect the future of the planet with the creation of new products and processes that improve the quality of life and reduce environmental hazards [2–4]. The implementation of green chemistry technologies minimizes the use of materials that are hazardous to human health and environment [5], decreases energy and water usage, and maximizes efficiency (Figure 1.1).

Extraction of natural products has been used probably since the discovery of fire. Egyptians and Phoenicians, Jews and Arabs, Indians and Chinese, Greeks and Romans, and even the Mayans and Aztecs, all possessed innovative extraction processes (maceration, alembic distillation, etc.) used even for perfume, medicine, or food. However, during the 1990s, it was not easy to find literature concerning the dispersed efforts for greening the extraction practices. It was necessary to wait for the tremendous development of green chemistry made by the Environmental Protection Agency (EPA) and led by Paul Anastas [3], who published a series of fundamental books from 1994 trying to create a general conscience on the need for green chemistry.

Recent trends in extraction techniques have largely focused on finding solutions that minimize the use of solvent and energy, such as supercritical fluid extraction, ultrasound extraction, subcritical water extraction, controlled pressure drop process, pulse electric field, and microwave extraction. The tremendous efforts made in greening extraction processes can be evaluated through the consideration of books devoted to these aspects as can be seen in Figure 1.2. Theoretical and

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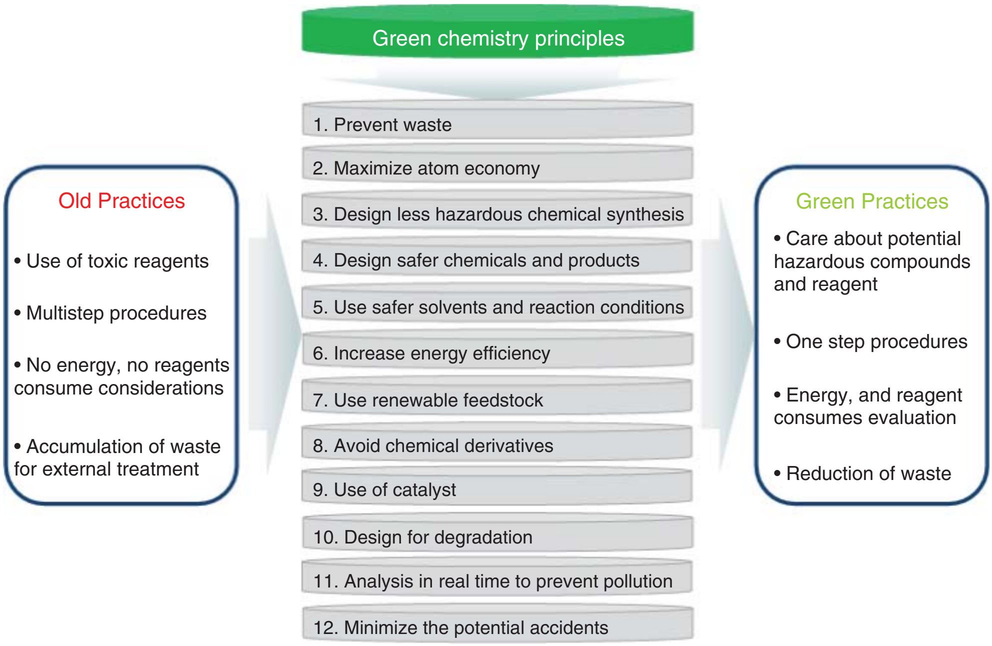
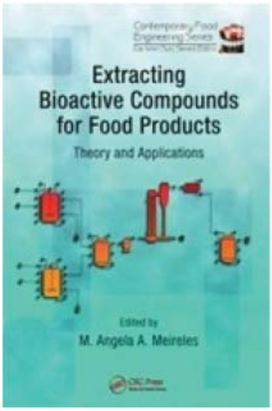


Figure 1.1 Impact of green chemistry in changing industrial and academic practices.

practical efforts are absolutely necessary to convince the members of the chemical societies about the need for such a revolution in our mentality and practice.

To meet the requirements of the market and to abide by the regulations in force, any extraction process must meet a number of quality criteria, contrary to some popular misconceptions; the "natural" state of an extract is no guarantee of its harmlessness to humans and the environment. In such a changing context, we must now switch over from a simple interest in data analysis to interest in models to a strong consideration of the environmental side effects of our practices as a consequence of the high demands of the extraction processes. This evolution or revolution in the extraction of natural products is summarized in Figure 1.3. Green extraction of natural products could be a new concept to meet the challenges of the twenty-first century, to protect both the environment and consumers, and at the same time enhance competition among industries to evolve more ecologic, economic, and innovative methods. Within the green extraction approach, the concept of the green extract is that of an extract obtained in such way as to have the lowest possible impact on the environment (lower energy and solvent consumption, etc.) and whose eventual recycling would have been planned for (coproducts, biodegradability, etc.). The green extract should be the result of a whole chain of values in both senses of the term, that is, economic and responsible, starting from the production and harvesting of the plant, the transformation process of extraction, and separation together with formulation marketing.



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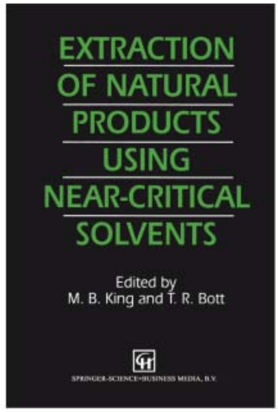

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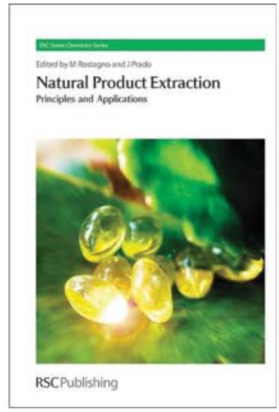

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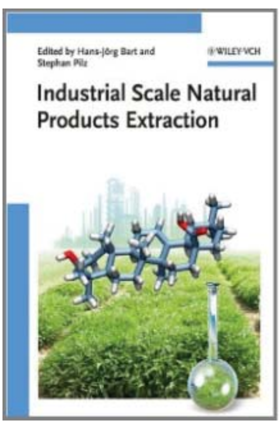

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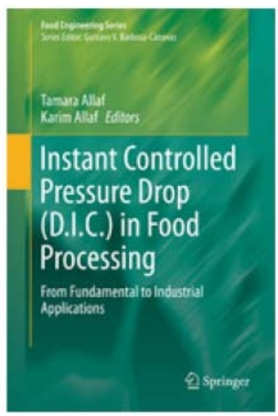

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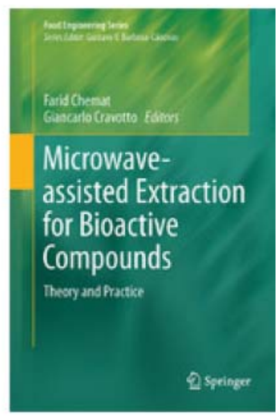

Microwave Assisted
Extraction for
Bioactive Compounds
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G. Cravotto
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Figure 1.2 Books devoted to green extraction of natural products.

Various industrial sectors, such as pharmaceutical, cosmetic, and food industries have increasing needs in natural products. They are obtained from plant or animal resources through extraction processes. In order to meet demand and fulfill regulations, the extraction processes are challenged to increase extraction efficiency (yield and selectivity toward compounds of interest), reduce or eliminate petrochemical solvents, together with moderate energy consumption. Within

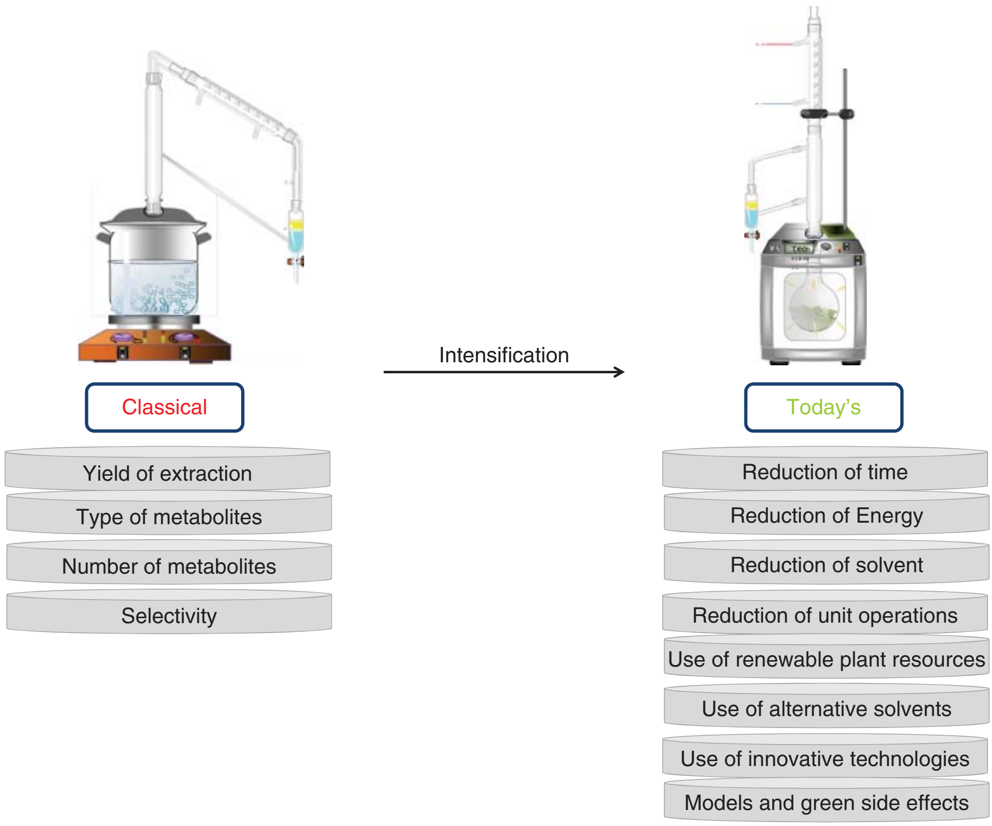

Figure 1.3 Extraction of natural products: evolution or revolution.

these constraints, green extraction has been recently introduced on the basis of green chemistry and green engineering further referring to modern "sustainable processes." In relation to green extraction of natural products, its definition has been given by Chemat *et al.* [2]: "*Green Extraction is based on the discovery and design of extraction processes which will reduce energy consumption, allows use of alternative solvents and renewable natural products, and ensure a safe and high quality extract/product.*" The listing of the six principles of green extraction of natural products should be viewed for industry and scientists as a guideline to establish an innovative and green label, charter, and standard, and as a reflection to innovate not only in process but in all aspects of solid–liquid extraction. The principles have been identified and described not as rules but more as innovative examples to follow, discovered by scientists and successfully applied by industry.

- *Principle 1:* Innovation by selection and use of varieties of renewable plant resources
- *Principle 2:* Use of alternative solvents, principally water or bio-based solvents

- *Principle 3:* Reduction in energy consumption by energy recovery, using innovative technologies
- *Principle 4:* Manufacture of coproducts instead of waste to include the bio- and agro-refining industries
- *Principle 5:* Reduction in unit operations, favoring safe, robust, and controlled processes
- *Principle 6:* Aiming for a non-denatured and biodegradable extract without contaminants.

This chapter aims at specifying the notion of natural products and illustrating how natural products can be used as ingredients in different industrial sectors. For this, we limit ourselves to compounds obtained from the plant kingdom. The biomolecule composition of a vegetable cell is usually divided into two major groups: primary and secondary metabolites. The former refers to key compounds in plant metabolism, and the latter to compounds which are involved in specific functions in the plant. Croteau *et al.* [6] introduced the term *plant natural product* to designate secondary metabolites, due to their biological activity and role in plant ecology. The expression "*natural product*" is today broadly used to designate extracts obtained from plants containing specific compounds, possessing a technological, functional, or nutritional application [7, 8]. Using the example of the orange tree as a veritable biorefinery, a few valuable metabolites are evidenced. The chemical structure and diversity of the different classes of metabolites in the plant kingdom are then reviewed. Some applications of natural products as ingredients are ultimately presented.

This chapter also presents as ultimate examples, the successful application of green extraction of natural products in academia as a vector of green teaching and research and also in industry, presenting a continuous challenge for innovation and competitiveness.

1.2
Orange Fruit is not Limited to Produce Only Juice?

The pattern from metabolites to ingredients can be illustrated through the example of the orange tree. The major industrial use of oranges is juice production. However, the known diversity of the phytochemical composition of the fruit and the orange tree allows considering the tree as a biorefinery of natural products. The following section describes the by-product valorization of orange juice production along with some examples of the phytochemicals identified in the orange tree and fruit.

With a total production of 68 million tons in 2012 [9], orange is one of the major crops in the processing industry. Out of the total production, 95% is used to manufacture orange juice. Considering that 3 kg of oranges are necessary to produce 1 l of orange juice, there is a great potential for valorization of the by-products generated [10]. Further, not only the by-products from the fruits but also the whole orange tree can be used for nutritional, pharmacological, or cosmetic purposes. In this section, the pathways for valorization of orange products are described. Different types of by-products can be generated from orange juice production: those from the orange tree and those from the orange itself. By-products generated by orange juice production are pulps, peels, and seeds [10, 11].

One of the main by-products obtained from the orange fruit is the pulp (42.5% w/w of orange waste) [9, 12]. Owing to their high fiber content, pulps are mainly used for livestock feeding. Moreover, inclusion of the pulp in cattle feed would support growth and lactation in a better way than would starch-rich supplements [13].

Accounting for 50% of the mass of the fruit, orange peels contribute to a high proportion of the by-products [11]. Peels can be processed by steam distillation [14] or by cold pressing [15] to extract essential oil. Essential oil is used in foods and beverages as a flavoring agent, in cosmetics, and in perfumes [16]. Peels also contain some valuable chemicals, for example, pectin [17], which used as a texturing agent and food stabilizer. Pectin can be incorporated in foods such as jam or jellies. Peels contain structural components such as cellulose [18] and hemicellulose. After biorefining, these molecules can be transformed into biofuels and biochemicals. The juice extracted from the peels is evaporated to give citrus molasses [19], marketed for livestock feeding [13], or is used in the fermentation process of alcohol. Further use of this by-product requires more refining as the phytochemicals in the juice contribute to a strong bitterness and dark color. As a refined product, orange peel syrup can be used as natural sweetener. Orange seeds represent a small part of the residue from orange juice production (from 0.5 to 5%). The main interest of the seeds is in their oil content (up to 40%). Extraction of orange seed oil has been performed by organic solvents [20, 21]. However, because the high oil content of the seeds, mechanical pressing could perhaps be used to recover oil.

Flowers, leaves, and the lignocellulosic biomass have found various applications. Flavoring substances such as essential oils, namely, Neroli and Petitgrain, are extracted from the flowers and leaves (less than 1% content [22]), respectively. Oils can be used in the cosmetics and food industries [23, 24]. It is noteworthy that the water distilled from flowers and leaves after the extraction of essential oils (orange blossom water and eau de brouts) can also be valorized in the same way as essential oils because of their aromatic characteristics. The lignocellulosic biomass issued from roots, twigs, and leaves can also be valorized by the production of biochemicals and/or biofuels [25, 26]. These inedible parts of the tree also contain some alkaloids, which may be used in the pharmaceutical industry.

The numerous uses of orange by-products are due to the phytochemical composition of the fruit and the tree. The following section examines the structure and localization of these natural products. The section focuses on the identification of the chemical structure of the phytochemicals of interest contained in the orange tree. Their localizations and structures are illustrated in Figures 1.4 and 1.5. The variety and structural complexity of these phytochemicals enables their

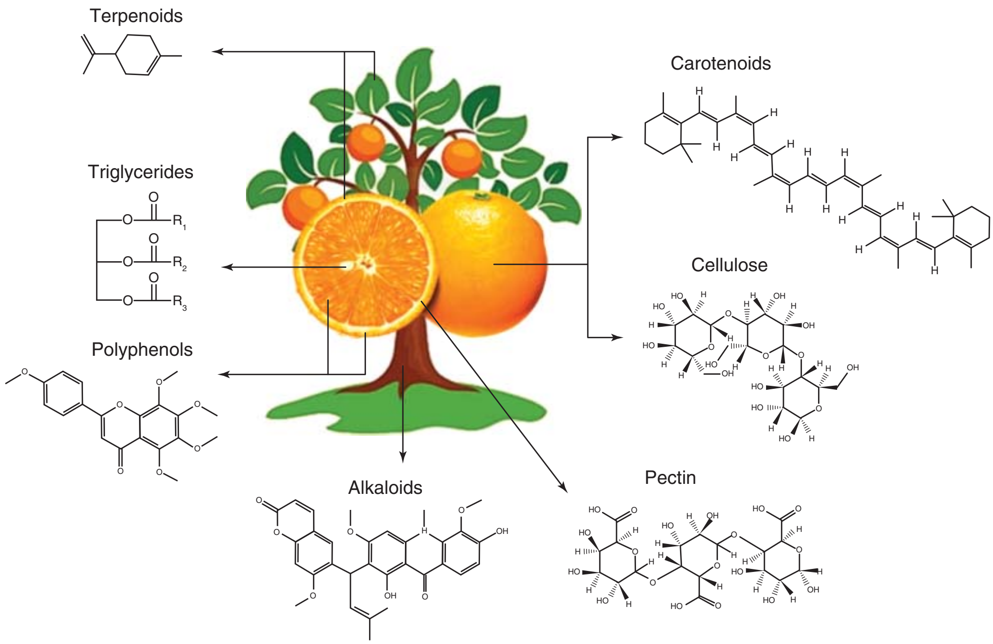

Figure 1.4 Localization and structure of phytochemicals contained in the orange tree and fruit.

classification according to their biochemical function into primary and secondary metabolites.

Two types of polymers issued from primary metabolites are constitutive of the by-products detailed in the previous section: cellulose and pectin. Cellulose, which is polymer of cellobiose, is a structural cell component [27] and, therefore, is present in the whole tree. Pectin would be located more specifically in the peel of the fruit. The lipidic fraction is mainly found in the seeds of oranges. Although seeds have a high oil content, the low amount of seeds in the orange fruit leads to an overall low lipidic fraction taking the whole tree into consideration.

Three common classes of secondary metabolites are identified in the composition of the orange tree: terpenoids, alkaloids, and polyphenols. Terpenoids are constitutive of essential oils and those found in oranges (Neroli and Petitgrain oils) have different terpenic profiles. Neroli oil is composed of linalool, limonene, beta-pinene, *trans*-beta-ocimene, linalyl acetate, and terpineol, while Petitgrain oil is mostly composed of linalyl acetate and linalool [23, 24, 28]. Orange peels also contain a terpenic fraction, which is exclusively composed of limonene. The high concentration of limonoids were identified at first in the fruits of the the Rutaceae family (e.g., *Citrus*), however those compounds were further identified in other plants [29, 30]. Carotenoids are another terpenoid class identified in the orange tree: β-cryptoxanthin, β-carotene, lycopene, and isomers of violaxanthin were detected, more specifically, in the fruit [31]. Alkaloids are located in the

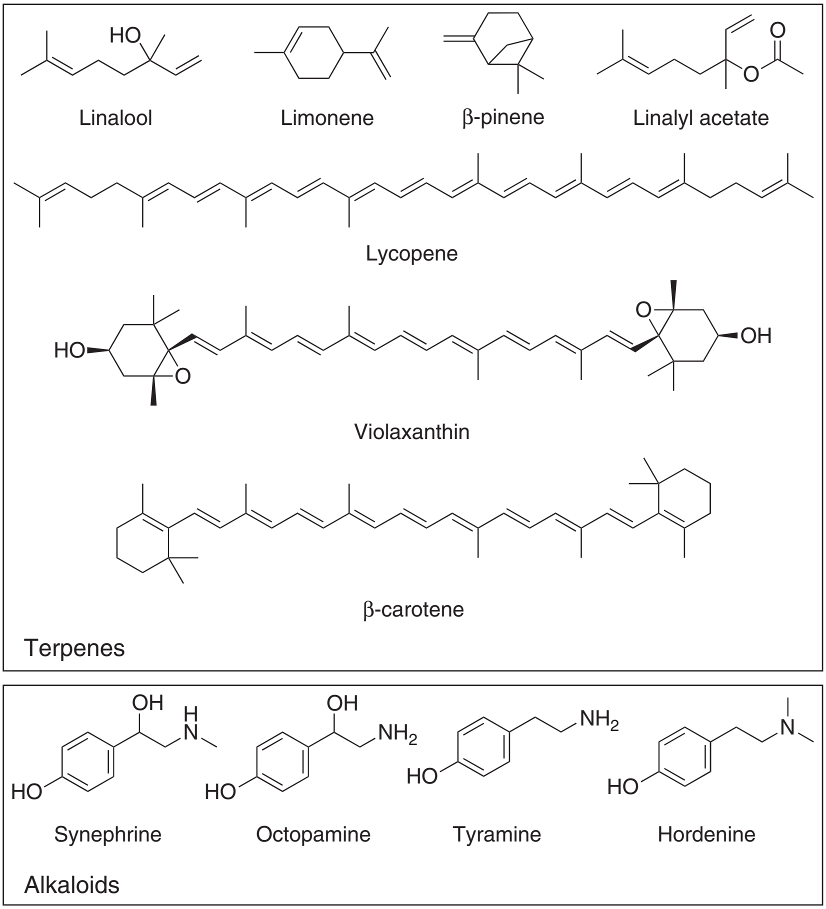

Figure 1.5 Structure of secondary metabolites (terpenes and alkaloids) contained in the orange tree.

leaves and the roots of the orange tree [32]. Owing to their biological activity, these compounds are of interest in pharmaceutical applications. Synephrine, which is an adrenergic and used for weight management, has been identified in the orange tree [33]. It is mainly isolated from citrus species and commonly found in juices. Although synephrine can be synthesized, the increasing demand for natural extract makes this alkaloid an important extraction target. Other alkaloids commonly reported from *Citrus aurantium* are octopamin, tyramine, *N*-methyltyramine, and hordenine [34]. Polyphenols are the third class of secondary metabolites found in the orange tree. Phenolic compounds identified in the orange fruit (located more specifically in peel and juice) are essentially flavanone glycosides such as nariginin, hesperidin, narirutin, and neohesperidin [35]. These polyphenols are specific of the *Citrus* family, and are of increasing interest because of their antioxidant potential. In a less specific occurrence, lignin, a structural component mostly found in the membranes of vegetable cells, is found in the whole orange tree.

This introductive example of the orange tree, through the valorization of by-products generated from orange juice production, allows us to distinguish different categories of molecules considered as natural products. The following section summarizes the categories of metabolites that can be identified in vegetables, aiming at a classification of natural products.

1.3 Chemistry of Natural Products

The term *natural product* designates any substance or chemical produced by nature. Considering vegetables, this wide definition can be restricted to any chemical vegetable component or phytochemical. In biochemistry, phytochemicals are commonly classified into two groups according to their function: primary and secondary metabolites. Primary metabolites include any compound essential to basic plant metabolism and thus survival. On the other hand, secondary metabolites are involved in ecological functions such as attractants for pollinators, in the protection against herbivorial and microbial infections, and in allelopathy (which refers to a positive or negative effect, e.g., the growth of one plant into another induced by phytochemicals). In this section, the well-known primary metabolites are briefly reviewed, focusing on secondary metabolites.

1.3.1 Primary Metabolites

1.3.1.1 Glucides

Glucides are metabolites mainly used for the storage and transport of energy and are located in every organ of a plant [27]. In cells, glucides are stored as starch which is a polymer of glucose. Glucides are also metabolic precursors of secondary metabolites and are constitutive of cell membranes. For instance cellulose, a macromolecule composed of a repetition of glucose moieties, is one of the main components of vegetable cell membranes. It is one of the most abundant compounds on the Earth.

Owing to their numerous functions in basic plant metabolism, glucides constitute a wide class of metabolites. The classification, chemistry, and structure of glucides are described in many biochemistry reference books [36, 37], therefore, their diversity is not reviewed in this section, but examples are given of glucides having industrial applications. Glucides are divided into two classes: oses and osides, which are polymers of oses or a combination of oses with a non-glucidic molecule, respectively [38].

Oses classically processed in industry are fructose, glucose, and oses derivatives such as polyols. One of the most-extracted oside is saccharose (e.g., isolated from sugar beet and sugar cane) [38]. The main polysaccharides which can be extracted from vegetables are fructosannes such as insulin, starch, cellulose, fibers, mucilages, and pectins [38]. These macromolecules can be used as such for food or nonfood application, or can also be chemically transformed to produce chemicals or ingredients (e.g., starch is the starting point of modified starches, dextrines, glucose syrups, glucose, and sorbitol). Fibers are a group mainly composed of cellulose, hemicellulose, pectins, and lignins; because of their indigestibility, these compounds qualified as "dietary fibers" [38]. Mucilages are highly hydrophilic colloids and can be used for their texturing properties (e.g., in pharmaceutical applications). Pectins are mostly located in fruits (apples, citrus fruits) and are structural macromolecules that constitute cell walls. They can be used for their jellifying properties [38].

1.3.1.2 **Lipids**

Similar to glucides, lipids have an energy storage function [27], and are the precursors of numerous metabolites. Lipids are a group of heterogeneous compounds (fatty acids, glycerolipids, cerides, etc.). In plants, lipids are stored in oleosomes as oils, which are mainly composed of triacylglycerols (esters of glycerol and fatty acids) [27]. Some lipid structures are illustrated in Figure 1.6.

Fatty acids are a large group composed of linear saturated and unsaturated hydrocarbonated chains with a carboxylic acid function. Commonly found saturated fatty acids range from butyric (C4) to arachidic fatty acids (C20) [39]. Longer chains exist and are synthesized through the same metabolic pathway by elongation, but are less common in the plant kingdom. Unsaturated fatty acids are classically produced by the addition of double bonds to the corresponding saturated fatty acids [8]. The number of unsaturations and their position along the carbon chain are used to classify unsaturated fatty acids. Palmitoleic (C16:1), oleic (C18:1), linoleic (C18:2), linolenic (C18:3), and arachidonic (C20:4) fatty acids are among the commonly found unsaturated fatty acids [27].

Through the combination of fatty acids with primary metabolites present in plants (e.g., glycerol), complex compounds are formed (mono-, di-, and triglycerides), such as glycolipids, glyceroglycolipids, phospholipids and phosphosphingolipids (based on sphingosine structure) [40], or aromatic polyketides such as anthraquinones [41] and naphthoquinones [42].

1.3.1.3 **Amino Acids and Proteins**

Amino acids are of great importance in metabolism, as they are the building blocks of enzymes, peptides, and structural proteins. Amino acids are also precursors of numerous secondary metabolites (alkaloids, betalains, some polyphenols, etc.) [38]. Proteins play a major role in human and animal nutrition. However, the applications as the final product or extract composed specifically of amino acids, proteins, and enzymes are quite limited, and therefore are not developed in this section.