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Plant Food By-Products

Industrial Relevance for Food Additives and Nutraceuticals

J. Fernando Ayala-Zavala, PhD
Gustavo González-Aguilar, PhD
Mohammed Wasim Siddiqui, PhD
Editors

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CONTENTS

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CHAPTER 4

PLANT TISSUES AS A SOURCE OF NUTRACEUTICAL COMPOUNDS: FRUIT SEEDS, LEAVES, FLOWERS, AND STEMS

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CONTENTS

ABSTRACT

Plants have a huge role in human health and nutrition since ancient time, when man started to build sedentary societies. Man started to domesticate plants to use them as food, and eventually realized that some plant tissues had beneficial properties against diverse illness and problems they faced at the time. Nowadays, scientific research had exhaustively studied thousands of different plant tissues, from fruit seeds to flowers and stems. Scientific data now have identified that most of the chemical compounds in plants, also known as phytochemicals, involved in the color and texture of diverse plant tissues are responsible for many of the benefits that its consumption may bring to humans. In that sense, the diverse colors, shapes, and textures of plant tissues may be key points to consider at the time of looking for the right phytochemical to use in food products. The growing demand on economic and healthy food products leads the food industry to the exploitation and development of novel functional foods and nutraceutical products. In order that as the content of phytochemicals such as polyphenols, dietary fiber, carotenoids, free fatty acids, and vitamins in plant tissues may vary from one species to another, it is essential to analyze the common origin of each phytochemical compound from one plant tissue to another. Hence, this chapter summarizes the most common phytochemicals considered as nutraceutical compounds, its related health benefits, and the diverse plant tissues where we could find a specific type of phytochemical.

4.1 INTRODUCTION

Scientific research has confirmed and explained through the pass of time the huge role of plant tissues to human health. Even when ancient civilizations already had found cures and relief in plants, nowadays, science has established and identified the main chemical compounds (phytochemicals) responsible for its benefits within to manipulate or even extract these compounds (Brekhman, 2013). With the upswing of the functional foods, and the growing demand that are getting these days, food industry must be at the edge of food science limits, trying to surpass the frontier of conventional foods to develop new food products able to relief illness or contribute to enhance human health as possible. Ever since man realized that plant tissues contain beneficial compounds to human health, it started looking for ways to extract and isolate these compounds (Wang and Weller, 2006). Nowadays, science has optimized some of the phytochemical extraction methods, and the novel techniques includes ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), and accelerated solvent extraction (Gupta et al., 2012).

Likewise, scientific data reveal specific plant tissues where we can find abundance of specific types of phytochemicals, either as fiber in grains or polyphenols in flowers and fruits. The plant tissue where a phytochemical or nutraceutical compound is embedded, especially the components comprised over the different plant tissues, is first barrier to consider before its extraction and isolation. The chemistry nature of the desired phytochemical compound is also essential prior to the selection of the most adequate method for its extraction. In that sense, the current chapter describes the most common phytochemical compounds used as nutraceuticals, as well as their health-related benefits, their occurrence in plant tissues, and examples of phytochemical extraction methods.

4.2 NUTRACEUTICALS POTENTIAL IN HEALTH PROMOTION

Belief in the medicinal power of foods is not a recent, it has been widely accepted for years; almost 2500 years ago, Hippocrates said: “let food be thy medicine and medicine be thy food.” Herbal medicine, along with all other plant components, has been used for healing since the beginning of human civilization; however, with modern medicine, most herbal products were left unused and many of them were forgotten by western or traditional medicine. Nowadays, natural medicine is steadily gaining interest all over the world again. Moreover, consumers are aware of the health benefits of selected foods and their components. However, if the consumers recognize the benefits of plant components for their health, it is essential that they received factual and reliable information to make informed decisions about the merits or risks associated with changing dietary habits.

In certain countries, functional foods and nutraceuticals are used interchangeably; however, in all cases, the main focus is on improving health and reducing disease risk through, mainly, prevention (Shahidi, 2009). The term “Nutraceuticals” is a hybrid word with an intended double implication of “nutrition” and “pharmaceutical” (Chaturvedi et al., 2011; Das et al., 2012). It commonly refers to a nontoxic extract supplement that has scientifically proven health benefits for both disease treatment and prevention. It should not be mistaken with the term functional foods, which refers to foods with relevant effects on well-being and health or result in a reduction in disease (Dillard and German, 2000). Nutraceuticals has now been amalgamated in a new category under natural health products that promote health, that not only include nutraceuticals but also encompass herbal and other natural products.

The short-term goal of functional foods, nutraceuticals, and dietary supplements is to improve the quality of life and enhance health status, while its long-term goal is to increase lifespan while maintaining health. Due to the high and increasing incidents of cancer and heart disease in industrialized countries, governments have been making concerted efforts to raise public awareness about the advantages of eating a healthy diet. Indeed, numerous epidemiological studies have already documented an inverse association between fruit and vegetable consumption and chronic diseases. Hence, in some countries as a measure taken by the government, public programs to promote healthy eating are trying to increase people awareness in the diverse benefits of healthy eating, and in some cases, even promoting the intake of food with special purpose (functional foods).

However, the current lifestyle of the modern man, difficult the administration of their own time, which in most cases results in reducing the time spent for eating or food preparation. Therefore, as food industry realized of the economic impact of these modern lifestyles, the production of ready-to-eat foods comes to solve this problem, and likewise, the development of nutraceutical products seems like an attractive choice to most consumers. Nutraceuticals covers most of the therapeutics areas such as anti-arthritic, cold and cough, sleeping disorders, digestion and prevention of certain cancers, osteoporosis, blood pressure, cholesterol control, pain killers, depression, and diabetes (Chaturvedi et al., 2011; Das et al., 2012; Delzenne et al., 2013). A new paradigm has been presented by researchers in the field, with more emphasis in the nutritional aspects of the diet; and in agreement with the new lifestyle adopted today, which has changed the basic food habits (Das et al., 2012). Because prevention is a more effective strategy than treatment for chronic diseases, a constant supply of phytochemical-containing products with desirable health benefits beyond basic nutrition is essential to furnish the defensive mechanism to reduce the risk of chronic diseases in humans (Chu et al., 2002). The importance of this approach on health-care cost is enormous (Shahidi, 2009).

However, over the years, people's diet habits are based on a high consumption of fast food and processed meals (ready-to-eat), leading to a number of diseases caused due to improper nutrition. The prevalence of obesity and type 2 diabetes is rapidly increasing, becoming a major challenge for health-care professionals (Devalaraja et al., 2011). Obesity is now recognized as a global issue. It is a major problem affluent societies are facing as well as the rest of the world, since reduced activity and lack of exercise may lead to obesity with the consequence of a host of diseases and the so-called metabolic syndrome (Shahidi, 2009). Likewise, heart disease continues to be a primary cause of death in most of the developing countries worldwide, followed by cancer, osteoporosis, arthritis, and many others (Das et al., 2012). It is well established that a correction of lifestyle, such as the intake of a healthy and low energy diet along with increased physical activity is the most effective preventive therapy to ameliorate the prevalence of obesity and diabetes in society. It was suggested that in addition to standard prescribed therapies, the addition of dietary supplements to the diet could be used to manage obesity and diabetes (Devalaraja et al., 2011).

There has been a boom in the sale of nutraceuticals due to the adverse effects of traditional pharmaceuticals, increase tendency of patients to self-medication, and the growing aging of the population associated to increase in certain chronic diseases (Chaturvedi et al., 2011). Pharmaceutical and nutritional industries are conscious of the monetary success taking advantage of the more health-seeking consumers. Phytochemicals are likely to form the basis of nutraceuticals and the uses of plants as a source of them represents an enormous opportunity for growth and expansion, see Table 4.1. Leaves, stems, seeds, flowers, and fruits of plants have numerous natural compounds that have been associated to reducing the risk of coronary heart disease, diabetes, tumor incidence, cancer, blood pressure, reduces the rate of cholesterol and fat absorption, delaying gastrointestinal emptying, and providing gastrointestinal health. Recent studies have demonstrated that the phytochemicals in plants are primarily located in the outermost layers and/or skin and thus, in some cases, their extraction would lead to products that are less beneficial to health (Shahidi, 2009).

Food components used as nutraceuticals are often dietary fiber (DF), prebiotics, probiotics, polyunsaturated fatty acids (PUFAs), antioxidants, and other different types of herbal/natural foods (Das et al., 2012). There are several nutraceuticals available in the market from the food or the pharmaceutical industry, the herbal and dietary supplement market, or from the newly pharmaceutical/agribusiness/nutrition associations. Several commercial nutraceuticals are available, some as isolated nutrients, herbal-based products, genetically engineered or "designer" foods and processed products such as cereals, soups, and beverage (Fig. 4.1). Hence, it is essential to know the type of phytochemical that we can extract from the different plant tissue, as well as the health benefits that we can get from their diverse chemical structures. Likewise, nutraceutical products must be exhaustively studied, with a complete characterization of the phytochemicals comprised in the product, as well as a series of research about the effects of the phytochemical

TABLE 4.1 Phytochemical Compounds of Common Use as Nutraceuticals.

Plant tissue	Name	Terpenoids	Phenolic compounds	N- and S-based compounds	Carbohydrates	Fatty acids	Minerals	References
Fruits	*Malus domestica*	NR	Epicatechin Catechin Clorogenic acid Quercetin	NR	Starch Rafinose Sucrose Xylose	NR	NR	Krawitzky et al. (2014), Feng et al. (2014a)
	Hylocereus polyrhizus	NR	NR	Beta-cyanins	Pectin	NR	NR	Gengatharan et al. (2015), Muhammad et al. (2014)
	Punica granatum	NR	Punicalagins Rutin quercetin, gallic acid Ellagic acid	NR	NR	NR	NR	Middha et al. (2013)
	Ribes nigrum and *R. rubrum*	NR	Cyanidin Delphinidin *p*-Coumaroylqunic acid Myricetin, quercetin Kaempferol	NR	NR	NR	NR	Aneta et al. (2013)
	Mangifera indica L.	Lupeol β-Carotene, *cis*- and *trans*-violaxanthin	Maguiferin Quercetin Gallic acid Vanillic acid Clorogenic acid Protocatechuic acid Ellagic acid	NR	NR	NR	NR	Dorta et al. (2014), Low et al. (2015), Palafox-Carlos et al. (2012), Ruiz-Montañez et al. (2014)

TABLE 4.1 *(Continued)*

Plant tissue	Name	Terpenoids	Phenolic compounds	N- and S-based compounds	Carbohydrates	Fatty acids	Minerals	References
Seeds	*Hylocereus* spp.	NR	NR	NR	NR	Palmitic Oleic Linoleic	NR	Liaotrakoon et al. (2013)
	Phoenix dactylifera L.	β-Carotene Leuteina Echinenone	Coumaric, sinapic and dihydrocinamic acids, apigenin, naringenin and catechin	NR	NR	NR	NR	Habib et al. (2013), Mess-aoudi et al. (2013)
	Paulllinia cupana	NR	Procyanidin A, B, C Epicatechin Catechin	Caffeine and theobromine	NR	Linoleic Linolenic Oleic Palmitic Stearic	Ca P Mg	Hamerski et al. (2013), Schimpl et al. (2014)
	Vitis vinifera L.	NR	Gallic acid Catechin Epicatechin Quercetin *Trans*-resveratrol	NR	NR	Linoleic Oleic Palmitic Stearic	NR	Dang et al. (2014), Fernandes et al. (2013)
	Psidium guajava L.	NR	NR	NR	Starch Pectin Fructose	Lauric Myristic Palmitic Oleic Stearic Linoleic	Ca Mg Fe Zn Na K P Mn	Uchôa-Thomaz et al. (2014)

TABLE 4.1 *(Continued)*

Plant tissue	Name	Terpenoids	Phenolic compounds	N- and S-based compounds	Carbohydrates	Fatty acids	Minerals	References
Leaves	*Vitis vinifera* L.	NR	Catechin, epicatechin, quercetin, kampferol, *cis*- and *trans*-resvera-trol, apigenin	NR	NR	NR	NR	Katalinic et al. (2013)
	Paullinia cupana	NR	NR	Theobromine Theophylline Caffeine	NR	NR	NR	Schimpl et al. (2014)
	Olea europaea	NR	Hydroxytyrosol Oleuropein Luteolin apigenin	NR	Arabinose Galactose Glucose Mannose xylose	NR	NR	Romero-García et al. (2016)
	Diospyros kaki L.	NR	Gallic acid Hydroxytyrosol Hydroxybenzoic acid Vanillic acid Caffeic acid *p*-Coumaric acid Sinapic acid Catechin Gallocatechin Naringenin Apigein Kaempferol Quercetin	NR	NR	NR	NR	Martínez-Las Heras et al. (2016)

TABLE 4.1 *(Continued)*

Plant tissue	Name	Terpenoids	Phenolic compounds	N- and S-based compounds	Carbohydrates	Fatty acids	Minerals	References
	Rosmarinus officinalis	Rosmanol Carnosol Carnosic acid Rosmadial Epirosmanol	Siringic acid Gallocatechin Nepetrin Hesperidin Rosmarinic acid	NR	NR	NR	NR	Borrás-Linares et al. (2014)
Flowers	*Calluna vulgaris*	α-Amyrin Lupeol Uvaol Ursolic acid Friedelin Taraxasterol	NR	NR	NR	NR	NR	Szakiel et al. (2013)
	*Musa × paradisia*ca	NR	Gallic acid Quinic acid Shikimic acid	NR	Glycerol D-Mannitol D-Sorbitol Sucrose Xylitol	Lauric Linoleic Myristic Oleic Palmitic Stearic	NR	Acharya et al. (2016)
	Nymphaea spp.	NR	Quercetin 3-*O*-rhamnoside Quercetin 7-*O*-galactoside Naringenin 7-*O*-galactoside Kaempferol 3-*O*-glucosyl	NR	NR	NR	NR	Yin et al. (2015)

TABLE 4.1 *(Continued)*

Plant tissue	Name	Terpenoids	Phenolic compounds	N- and S-based compounds	Carbohydrates	Fatty acids	Minerals	References
Stems	*Paullinia cupana*	NR	NR	Theobromine and theophylline	NR	NR	NR	Schimpl et al. (2014)
	Rhus verniciflua	NR	Gallic acid Fustin Fisetin Sulfuretin Quercetin	NR	NR	NR	NR	Kim et al. (2013)
	Panax ginseng	Saponins	NR	NR	NR	NR	NR	Ma et al. (2015)
	Vitis vinifera L.	β-Myrcene β-Ocimene α-Pinene Limonene	Gallic acid Catechin Epicatechin Procyanidin b3 and b2 Epicatechin gallate *Trans*-resveratrol Quercetin Kaempferol Caffeic acid Syringic acid Rutin	NR	NR	NR	NR	Apostolou et al. (2013), Matarese et al. (2014)
	Pinus ponderosa	Limonene α-Pinene Myrcene Camphene Linalool	NR	NR	NR	NR	NR	Keefover-Ring et al. (2016)

NR, Not reported.

intake to human health. In that sense, once characterized the type and the amount of phytochemicals added to a nutraceutical product, the in vitro and in vivo evaluation of isolated and combined compounds must assure that the nutraceutical product is safe for human consumption.

<table>
<tr><td colspan="3"><u>Nutraceuticals</u>: product obtained from foods that have extra health benefits added to their nutritional value.</td></tr>
<tr><td colspan="2">Dietary supplements</td><td>Functional Food Ingredients</td></tr>
<tr><td colspan="2">Vitamins
Minerals
Amino acids
Herbal extracts</td><td>Vitamins
Fats
Carbohydrates
Amino acids
Fiber</td></tr>
<tr><td>Examples</td><td colspan="2">Fortified cereals (containing minerals, vitamins or extra fiber)
Supplemented beverages (containing vitamins, antioxidants, soluble fiber and minerals)
Energy drinks (with herbal extracts)
Reducing cholesterol beverages (containing fiber, antioxidants)</td></tr>
</table>

FIGURE 4.1 Nutraceuticals, their classification, and commercial presentation.

4.3 PHYTOCHEMICALS AND ITS ROLE IN HUMAN HEALTH

Plants are an important source of phytochemicals (biologically active substances) that present antioxidant, anticarcinogenic, and antimutagenic properties (Ajila et al., 2008; Cavalcanti et al., 2011; Chiva-Blanch and Visioli, 2012). It has been suggested that including fruits and vegetables in the diet has a beneficial effect on health due to the reduction of incidence of heart disease, cancer, and some neurodegenerative disorders (Cavalcanti et al., 2011). Phytochemicals quantity and quality can vary significantly according to different intrinsic and extrinsic factors, such as plant genetics and cultivar, soil composition and growing conditions, maturity state, and part of the plant, among others (Faller and Fialho, 2010). For example, a stressful environment for plants can lead to the induction of secondary metabolism and the subsequent increment in the production of phytochemicals, especially those modulated by enzymatic activity (Reyes et al., 2007). Moreover, those phytochemicals can be used immediately to counteract the cause of the stress (as a free-radical scavenging agent against an oxidative stressful environment) or relocated elsewhere in the plant for later use.

Oxidative stress results from either a decrease of natural cell antioxidant capacity or an increased amount of reactive oxygen species (ROS) in organisms. If the balance between oxidants and antioxidants in the body is shifted by the overproduction of free radicals, it will lead to oxidative stress and DNA damage. When left unrepaired, it can cause base mutation, single- and double-strand breaks, DNA cross-linking, and chromosomal breakage and rearrangement (Contreras-Calderón et al., 2011; Chu et al., 2002; Chun et al., 2005). The development of chronic diseases, like metabolic syndrome, rheumatoide arthritis, cardiovascular diseases, cancer, arteriosclerosis, hypertension, neurodegenerative diseases, and aging process and type II diabetes, among others, involves the production of high quantities of free radicals which leads to oxidative stress in the tissues (Cavalcanti et al., 2011; Contreras-Calderón et al., 2011; Chu et al., 2002; Moure et al., 2001). An increment in the consumption of fruits and vegetables has been associated with lower risk of chronic diseases, because in addition to its vitamin and mineral composition, it will also contain other compounds with protective effects, in particular antioxidants (Contreras-Calderón et al., 2011; Chu et al., 2002; Chun et al., 2005; Faller and Fialho, 2010).

The protection that phytochemicals provided against these illnesses and syndromes has been attributed to the presence of several antioxidant compounds, like vitamin C, vitamin E, tocopherols, carotenes, and polyphenolic compounds (Chu et al., 2002). In vivo evidence of the formation of oxidized low-density lipoprotein includes the presence of excessive ROS production in the bloodstream (where they circulate as negatively charged). Moreover, their circulating levels have been positively correlated with the progression of carotid lesions and many epidemiological studies have correlated a high dietary intake of antioxidants (e.g., tocopherols, carotenoids, flavonoids, and polyphenols) with a lower incidence of cardiovascular diseases (Chiva-Blanch and Visioli, 2012; Chun et al., 2005).

Antioxidants have several roles on lipid oxidation, such as binding metal ions, scavenging radicals, and decomposing peroxides. Often, more than one mechanism is involved, which in some cases may lead to synergism or antagonic effects. Even if this is the most accepted theory on the action mechanism of fruits and vegetables in health, it is necessary take into consideration that including more vegetables in the diet can also be healthy due to the reduction in the intake of other potentially noxious foods, such as those rich in animal protein and saturated fats (Chiva-Blanch and Visioli, 2012). Plants also contain polyunsaturated fats, fiber, and vitamins that can interact with antioxidants to increases its health benefits, resulting in an overall effect which is difficult to ascertain to individual components. It is also suggested that through overlapping or complementary effects, the complex mixture of phytochemicals in fruits and vegetables provides a better protective effect on health than single phytochemicals (Contreras-Calderón et al., 2011; Chu et al., 2002).

4.3.1 NITROGEN AND SULFUR-BASED COMPOUNDS

Among nitrogen-containing compounds, glucosinolates and *S*-methylcystine sulfoxide are the major sulfur compounds present in vegetables (Manchali et al., 2012). Glucosinolates (thioglucoside-*N*-hydroxysulphates) constitute a homogeneous class of naturally occurring thiosaccharidic compounds mainly found in the botanical order *Brassicales* (Prakash and Gupta, 2012). More than 120 glucosinolates and its precursors have been identified in plants, which are known for their fungicidal, bactericidal, nematocidal, and allelopathic properties. Many recent studies are focusing in the iso-thiocyanates, one of the hydrolyzed products of glucosinolates, due to their role in the organism and its anticarcinogenic activity (Prakash and Gupta, 2012).

4.3.2 ANTIOXIDANT VITAMINS

Vitamins like vitamin C, vitamin E, and carotenoids are collectively known as antioxidant vitamins, due to their biological activity associated to the prevention of oxidative stress, which leads to several degenerative diseases and most of their protective action is related to their free-radical scavenging activity (Das et al., 2012). These vitamins are present in fresh fruits and vegetables. The human body cannot synthesize lipid- and water-soluble vitamins, such as vitamins E and C and must be derived from food (Chiva-Blanch and Visioli, 2012). The carotenoids are also present in fruits and vegetables; they are usually responsible for the color of the tissues (yellow, red, and orange in particular). Several carotenes have vitamin A activity; however, these molecules are now being studied intensively from a different point of view as phytochemical compounds with anticancer properties (Moure et al., 2001). Vitamin C or ascorbic acid can exert its antioxidant action by donating hydrogen atoms to lipid radicals, quenching singlet oxygen radicals and removing molecular oxygen from the medium.

Vitamin E is an essential, fat soluble nutrient that functions as an antioxidant in the human body, and foods and supplements must provide it (Sen et al., 2006). At present, vitamin E represents a generic term for all chemical compounds having the biological activity of RRR-α-tocopherol, which includes α-, β-, γ-, and δ-tocopherol; and α-, β-, γ-, and δ-tocotrienol. The tocopherols are saturated forms of vitamin E, whereas the tocotrienols are unsaturated and possess an isoprenoid side chain (Aggarwal et al., 2010). Some evidence suggests that human tissues can convert tocotrienols to tocopherols. Tocotrienols are the primary form of vitamin E in the seed endosperm of most monocots, including agronomically important cereal grains such as wheat, rice, and barley; it is especially found in palm oil (up to 800 mg/kg), mainly consisting of γ-tocotrienol and α-tocotrienol (Sen et al., 2010). Tocopherols occur ubiquitously in plant tissues and are the exclusive form of vitamin E in leaves of plants and seeds of most plants. In contrast, tocotrienols are considerably less widespread in the plant kingdom, being only found in significant amounts in nonphotosynthetic tissues and organs, like in seeds and fruits.

In the human body, vitamin E may exert functions beyond its antioxidant property (Sen et al., 2010). Deficiency of this vitamin is known to cause severe degenerative diseases such as ataxia, Duchenne muscular dystrophy-like muscle degeneration, and infertility (Aggarwal et al., 2010). Several studies showed that vitamin E has a neuroprotective effect, reduces Apo B levels in hypercholesterolemic subjects, modulates the normal growth of the mammary glands, has anticancer, anti-inflamatory, antihypertensile, anti-aging, anti-angiogenic, and antioxidant effect, increases immune function, and reduces serum triglycerides (Sen et al., 2006). Moreover, vitamin E and selenium has a synergistic role against lipid peroxidation (Das et al., 2012).

Carotenoids are widely distributed in plants, especially in their leaves, flowers, and fruits and are responsible for the yellow, orange, and red color of their tissues. Carotenoids are intracellular products and are usually located in the membranes of chloroplasts, mitochondria, or endoplasmatic reticulum due to their hydrophobic nature. Their function in the plant is strongly related to photosynthesis and regulation of the membranes fluidity, and they play an essential role in the protection of the tissues against excessive light and photooxidative stress (Chun et al., 2005; Jaswir et al., 2011). Carotenoids are structurally classified as carotenes (like α-carotene, β-carotene, and lycopene) and xanthophylls (like lutein, zeaxanthin, fucoxanthin, and astaxanthin).

They are essential nutrients; animals cannot produce carotenoids and must obtain them from the ingestion of vegetables. There are more than 700 known carotenoids from plants, lycopene, α-carotene, β-carotene, lutein, and zeaxanthin are the most abundant in human plasma (Aizawa and Inakuma, 2007). One of the main characteristics of carotenoids that made them important for the human diet is their provitamin A activity (Yeum and Russell, 2002). However, only three of them have a significant provitamin A activity in humans: α-carotene, β-carotene, and β-cryptoxanthin which are converted to vitamin A or retinol in the body (Jaswir et al., 2011). In turn, vitamin A is responsible of preventing eye diseases, such as night blindness. Carotenoids in general, can also act as antioxidants and reduce oxidative stress by scavenging ROS generated during photooxidative stress, via electron transfer, hydrogen transfer, or forming resonance-stabilized carbon-centered radicals (against lipid peroxyl radicals for example). Several studies have suggested the positive effect of carotenoids in cancer prevention, risk reduction of cardiovascular diseases, age-related macular degeneration and cataract formation, enhancement of the immune system, maintaining bone health, and preventing osteoporosis (Chang et al., 2010; Das et al., 2012; Jaswir et al., 2011).

4.3.3 DIETARY FIBER

Increasing attention has been given to the beneficial effects on humans of the consumption of the nondigestible components of vegetable foods, commonly known as DF. The term "dietary fiber" is used to refer to the edible parts of plants that are resistant to hydrolysis by digestive enzymes in humans (Nawirska and Kwaśniewska, 2005). It is a mixture of carbohydrate polymers, composed of resistant starch, cellulose, hemicellulose, pectin, and inulin, also associated with lignin, gums, waxes, cutin, polyphenols, resistant protein, and alginates, among others (Elleuch et al., 2011). It is widely known that DF obtained from different sources behaves differently during their transit through the gastrointestinal tract, depending on their chemical composition and physicochemical characteristics (Figuerola et al., 2005).

Although these components are not as active biologically as polyphenolic compounds or vitamins, they have a significant effect in the metabolism (Contreras-Calderón et al., 2011; Chun et al., 2005). Published reports indicate numerous health benefits associated with an increased intake of DF, including reduced risk of coronary heart disease, diabetes, obesity, and some forms of cancer (Elleuch et al., 2011; González-Centeno et al., 2010). DF exerts a buffering effect in the gastrointestinal tract, increases the fecal bulk, and stimulates the intestinal activity, stimulates colonic fermentation, improvement of gastrointestinal function, regulates postprandial insulin response, and reduces total and low-density cholesterol (Elleuch et al., 2011; Mildner-Szkudlarz et al., 2013).

DF also has a positive effect on the desirable microbiota of the intestine by creating a favorable environment for their growth. DF in general but hemicellulose and pectins in particular, have the ability to sorb harmful substances or to bind mineral components and heavy metals. Polyphenolic compounds are often associated with the food matrix and, as consequence, only a small part of them can be absorbed in the small intestine, reducing their bioavailability (Hervert-Hernández et al., 2011). These polyphenolic compounds can exert their biological activity once they reach the colon by interaction with the colonic microbiota as fermentable substrates (Saura-Calixto et al., 2007).

DF is a complex group of phytochemicals with different chemical and physical properties, often related to the source of the mix or the extraction methodology and are usually classified as water soluble (SDF) or water insoluble (IDF). The average daily requirement of total DF is 25 g/day for women younger than 50, 21 g/day for women older than 50; 38 g/day for men younger than 50, and 30 g/day for men older than 50 (Elleuch et al., 2011). In addition, most nutritionists suggest that 20–30% of daily DF intake should come from SDF, with a suggested proportion of SDF to IDF of 1:3 or 1:4. Maintaining that proportion is helpful in reducing the risk of heart diseases, level of cholesterol, triglycerides, and glucose in blood (Mildner-Szkudlarz et al., 2013). Moreover, the SDF/IDF ratio is also important for maintaining its functional properties (Figuerola et al., 2005). Therefore, the content of DF in food products and nutraceuticals can also have desirable effects on the texture for its gelling, emulsifying, and stabilizing properties (Abdul-Hamid and Luan, 2000).

DF derived from fruits and vegetables have a considerably higher proportion of SDF than those obtained from cereals (González-Centeno et al., 2010). The ideal DF extract should be as concentrated as possible, be bland in taste, color, and odor; have a balanced composition and adequate amount of associated bioactive compounds; have a good shelf life; be compatible with food processing; and have the expected physiological effects (Figuerola et al., 2005). DF concentrates can be used in various applications in the food industry with excellent results, such as nutraceuticals.

Due to all these characteristics, DF has an important role in both prevention and treatment of obesity, atherosclerosis, coronary heart diseases, large intestine cancer, and diabetes (Nawirska and Kwaśniewska, 2005). Dietary supplementation with DF could be effective in protecting against oxidative damage in the tissues due to lipid peroxidation by improving the antioxidant defense systems (Mildner-Szkudlarz et al., 2013). An increase in the level of DF in the daily diet has been recommended and because of this, it would be interesting to investigate different foods that can supply DF, like fruits and different parts of the plants. Fiber extraction and concentration could help to overcome the fiber deficit in the diet. Supplementation with DF can result in fitness-promoting foods, low in calories, cholesterol, and fat.

4.3.4 POLYUNSATURATED FATTY ACIDS

PUFAs are very important in the human diet for several body's function and need to be included in the diet since mammals are unable to synthetize them. There are two major classes of PUFAs: omega-3 and omega-6. Among omega-3, α-linolenic acid (ALA), eicosapentanoic acid (EPA), docosahexanoic acid (DHA) are the most abundant and therefore the most popular ones for the nutraceuticals industry. While EPA and DHA are found mainly in fatty fishes, ALA is often obtained from soybean, canola, walnuts, or other types of seeds. For the other major class, omega-6 the most common ones are linoleic acid (LA), γ-linolenic acid and arachidonic acid. LA is often obtained from vegetable oils like corn, safflower, soybean, and sunflower, among others. FDA recommends a maximum of 3 g/day intake of EPA and DHA omega-3 fatty acids, with no more than 2 g/day from a dietary supplement (Das et al., 2012). Several clinical studies have focused in the health benefits of PUFAs, suggesting that their main effects are in the prevention of cardiovascular diseases. Omega-3-oils in particular, have also shown positive effects in asthma, depression, diabetes, and also to be beneficial at various stages of life. It has been stated that a minimum intake of selenium per day or u3 fatty acids from marine oils would reduce the burden on health care tremendously as nearly one-third of all diseases are life-style related (Shahidi, 2009).

4.3.5 PREBIOTICS

Prebiotics are food components that beneficially affect the host by selectively altering the composition or metabolism of the gut microbiota (Das et al., 2012). Most of them are indigestible polysaccharides, in particular fructose-based oligosaccharides. These components can be naturally present in food or added. Vegetables like chicory roots, banana, tomato, alliums are rich in fructo-oligosaccharides (Das et al., 2012). Other oligosaccharides often considered as prebiotic are raffinose and stachyose, commonly found in beans and peas.

In recent years, there has been increased attention focused on the bacteria that colonize the gut, which in ideal conditions live in symbiosis with the host. Gut microbiota is complex system, with self-regulating mechanisms that can offer protection to the host by acting as a barrier against pathogens. However, these activities could be reduced during illness, stress, or aging, or by antibiotic treatment. It can also be diminished if disbiosis (change in the microbiota composition) occurs due to changes in the host diet (Macfarlane and Macfarlane, 2013). Experiments performed in a murine system colonized with the human gut microbiota reveals that changes in the diet composition (from high carbohydrates to western diet) allows a rapid switch of the microbial community. Those data suggest that the gut microbiota composition/activity associated with nutritional imbalance might contribute to obesity and related disorders (Delzenne et al., 2013). The prebiotic consumption generally promotes the *Lactobacillus* and *Bifidobacteria* growth in the gut, thus helping in metabolism. The health benefits of the prebiotics include improved lactose tolerance, antitumor properties, neutralization of toxins, and stimulation of intestinal immune system, reduction of constipation, blood lipids, and blood cholesterol levels.

4.3.6 PHENOLIC COMPOUNDS

One of the most studied phytochemicals are phenolic compounds (PC), also known as polyphenols, a group of secondary metabolites with diverse chemical structures and many functions. These compounds are usually produced during plant growth and development and/or as a response to various forms of environmental stress (Anastasiadi et al., 2010), via the shikimic acid pathway and/or phenylpropanoid metabolism (Anastasiadi et al., 2012). Phenolic compounds are one of the most abundant phytochemicals, with consumption of about a 1 g/day, which is 10 times higher than average vitamin C intake (Chun et al., 2005; Scalbert et al., 2005). PC are widely distributed, therefore they are present in fruits, vegetables, cereals, legumes, leaves, grains, seeds, flowers, and stems foods, being present not only in fruits and vegetables but also in foods (Cavalcanti et al., 2011; Faller and Fialho, 2010; Scalbert et al., 2005). Despite their wide distribution in plants, the health benefits of including PC in the diet have been taken into consideration in the mid-1990s. Before that, the most widely studied antioxidants were vitamins, carotenoids, and minerals. Currently, the contribution of PC to the prevention of cardiovascular diseases, cancers, osteoporosis, neurodegenerative diseases, and diabetes mellitus has been repeatedly proved (Anastasiadi et al., 2010; Cavalcanti et al., 2011; Scalbert et al., 2005).

Several studies on animals have shown that including PC in their diet reduces the incidence of cancer, cardiovascular diseases, neurodegenerative diseases, diabetes, and osteoporosis (Anastasiadi et al., 2010). However, most of these studies made on the prevention of diseases by PC that are carried out in vitro or with animal testing, often use doses much higher than those present on a normal diet (Scalbert et al., 2005). To elucidate the significance of polyphenols in human health, it is essential to know the amount of polyphenols consumed in the diet and their bioavailability (Saura-Calixto et al., 2007). Most of the studies advocating the use of antioxidants suggest that intake should be well above the general levels of consumption, shifting the focus from dietary consumption to pharmacological treatment or nutraceuticals production (Chiva-Blanch and Visioli, 2012).

Other major difficulty in the study of the effects of PC in human health is the large number of them found in plants and the differences in their chemical structures. It is also necessary to consider the differences in their bioaccessibility and bioavailability, mainly due to the interaction with other components in the matrix of the tissue plant and the digestion process (Saura-Calixto et al., 2007). Food going through the human gastrointestinal tract is digested in the stomach (strong acid environment), small intestine (mild basic environment), and then colon (neutral pH), all with different enzymes present (Chu et al., 2002). Phenolic compounds are present in vegetables in two forms: free or bound, with a different resistance to digestion. Bound PC may resist the stomach and small intestine conditions and reach the colon intact, where they are released and exert bioactivity. In most published research, only free phenolics are determined on the basis of the solvent-soluble extraction, as consequence total phenolic contents and their antioxidant activities are often underestimated by not including bound phenolics (Saura-Calixto et al., 2007). Moreover, their health benefit resides in their ability to reach the colon unaffected by the gastric and small intestine digestion.

While there are several studies showing increased plasma antioxidant capacity following the intake of polyphenol-rich food items, many investigators suggest that polyphenols' bioavailability is too low to produce a significant effect on the antioxidant metabolism (Chiva-Blanch and Visioli, 2012). As a consequence, research on phytochemicals in general has expanded and is now focusing on different bioactive compounds instead of only paying attention to antioxidants. Several products are presented as a result, to complement the increase on the diet of fruits and vegetables, including functional foods, designer foods, and nutraceuticals.

Synthetic antioxidants are being replaced for natural ones, not only based on its functionality (such as solubility both in oil and water solvents, emulsification properties) but also associated to its additional health benefits. Many of them are obtained from spices or herbs and have some limitations in its practical applications in spite of their high antioxidant capacity due to its sensorial impact, especially for their flavor (Moure et al., 2001). More research is needed to find new sources of natural antioxidants that can be freely used in the food, pharmacological and nutraceuticals industries with reduced sensorial impact. However, natural phytochemical substances also need safety testing; its application should be thoroughly confirmed before nutraceuticals are developed from them. Moreover, it should also be taken into account that in food-related systems, antioxidant activity means chain-breaking inhibition of lipid peroxidation, whereas in in vivo systems, free radicals can damage proteins, DNA, and other small molecules (Moure et al., 2001). As PC are one of the most studied nutraceutical compounds due to their high abundance in most of the plant tissues, and besides that these molecules due to their diverse chemical structures has been related to several health benefits, the following section describes the most common methods of PC extraction from plants.

4.4 TECHNIQUES FOR EXTRACTION OF PHENOLIC COMPOUNDS FROM PLANTS

One of the most important step for the analysis of PC derived from plant materials is extraction, which is influenced by the PC chemical nature (molecular structure, polarity, concentration, number of aromatic rings, and hydroxyl groups), the extraction method employed, sample particle size, time and condition of storage, as well as presence of interfering substances. According to the chemical nature, plant phenolics vary from simple to highly polymerized substances that may also be present as complexes with carbohydrates, protein, and other types of cell plant components. Therefore, phenolic extracts from plant materials are always a mixture of different classes of phenolics that include varying proportions of flavonoids, phenolic acid, tannins, lignins, and simple phenols.

The analysis of polyphenols can be realized through determination of total phenolic content or quantifying an individual phenolic or a specific class of phenolic using spectrophotometry, gas chromatography, high-performance liquid chromatography (HPLC), or capillary electrophoresis methods. However, PC must first be extracted from different plant tissues and, the ideal extraction method must provide high extraction rates and should be nondestructive and time saving (Rombaut et al., 2014). In addition, optimization and standardization of extraction parameters for these phytochemical are important to retain their antioxidant properties.

Several extraction techniques have previously been reported to extract PC from plant materials, generally, are carried out using the conventional method, employ solvents assisted by mechanical agitation, pressing, or heating system, although, more recently, modern methods have been used, including SFE, UAE, MAE, subcritical water extraction (SWE), and high hydrostatic pressure processing.

4.4.1 CONVENTIONAL

The most common technique to extract phenolics from plant materials involves the use of organic and inorganic solvents. Isolation and identification analysis of plants polyphenols are mostly dependent on the extraction solvent and technique used and, generally, solvent-type effect is related with polarity of the solvents and the solubility of target compounds in them, though solubility of PC is governed by the type of solvent, degree of polymerization of phenolics, as well as, interaction of this compounds with other food compounds and formation of insoluble complexes (Naczk and Shahidi, 2004; Turkmen et al., 2006).

Complete extraction of phenolic compounds is a crucial step which is specific to the food matrix. Several factors may contribute to the optimization of phenolics extraction including solvent-to-sample ratio, extraction time and temperature, number of extraction, solvent type, pH of the aqueous solvent, ratio of water in the solvent system, besides state, cultivar, and particle size of the material (González-Montelongo et al., 2010; Khoddami et al., 2013; Tuncel and Yılmaz, 2015). The most frequently used solvents for the extraction of phenolics in plant material are methanol, ethanol, acetone, water, ethyl acetate, propanol, and their combinations. However, the choice of extraction solvent will influence the yields of phenolics extracted, seeing that the extraction of PC from a sample is directly related to the compatibility of the compounds with the solvent system according to the "like dissolves like" principle (Tuncel and Yılmaz, 2015).

A high yield of phenolics can be extracted from sorghum leaf using water (Agbangnan et al., 2012), although the use of water as the only solvent yields to an extract with a high content of impurities (e.g., organic acids, sugars, soluble proteins) along with polar compounds which could interfere in the identification and quantification (Hijazi et al., 2013). From lychee flowers, to the highest extraction yield of antioxidant components (phenols, flavonoids, and condensed tannins), acetone was required (Liu et al., 2009). In another example, an investigation into the effect of different solvents on extraction of phenolics from *Limnophila aromatic* showed that 50% aqueous acetone extract was more efficient than the pure solvent which may be facilitated the extraction of all PC soluble in both water and organic solvent (Do et al., 2014). Study reports that the application of water combined with other organic solvents makes it a moderately polar medium ensuring the optimal conditions for extraction. Besides, using water in combination with alcohols leads to an increase in swelling of plant materials and the contact surface area between the plant matrix and the solvent finally improves the extraction yield (Hijazi et al., 2013).

In general, the different properties of the phenolic components of the plant materials could concern these differences. For extraction of the total phenolics from black currant leaves, aqueous acetone was found to be more effective than methanol and water (Tabart et al., 2007). According to the authors, acetone and methanol have distinct specificities in the extraction of PC and this is due to polarity of the solvent and solubility of phenolics in them. In contrast, no significant differences between ethanol and methanol were observed in terms of extraction efficiency ($p > 0.05$) in research aiming to optimize the extraction of PC in feijoa fruit (Tuncel and Yılmaz, 2015).

Two other important parameters that affect the extraction yield of PC, in addition to selecting of extraction solvent, are temperature and time of extraction. It has been reported that high temperatures improve the efficiency of extraction, due to the enhanced diffusion rate and solubility of phytochemicals in solvents, and thus reduce the extraction time to reach maximum polyphenol content recovery. Dorta et al. (2012) demonstrated that the optimum extraction of phytochemical (flavonoids, tannins, and proanthocyanins) from mango peel and seed was between 50°C and 70°C for 60 min. Investigation into the effects of the phenolics extraction conditions from *Morinda* *citrifolia* showed that the optimized condition was at 65°C for 80 min (Thoo et al., 2010). Extraction of phenolics from grape stems was most efficient at 84.2°C during 23.4 min for red variety and at 95°C during 23 min for white variety (Dominguez-Perles et al., 2014). Tuncel and Yılmaz (2015) demonstrated that increasing temperature from 25°C to 40°C significantly increased the amount of PC extracted from feijoa fruit. Increased temperature could also negatively affect the phenolic extraction since this condition may not be suitable for all kinds of PC leading to their degradation or loss by volatilization or reaction with other components of plant material. Thus, only samples with higher proportions of thermally stable polyphenols are more appropriate to extract under elevated temperature (Thoo et al., 2010).

The solvent-to-sample ratio and the number of replicate extractions performed for each sample also affect the recovery of phenolics (Khoddami et al., 2013). Extraction amount of total phenolics increased almost linearly by increasing solvent ratio, so the higher the solvent ratio higher is the total amount of solids obtained due to the mass transfer principles (Al-Farsi and Lee, 2008). These authors reported that a 60:1 ratio of solvent to sample in a two-stage procedure is sufficient to extract most phenolics from plant tissues. Tuncel and Yılmaz (2015) founded that a 60:1 ratio of solvent to sample was most efficient to extraction of PC in feijoa fruit. Particle size also can influence phenolic extraction from plant materials. Tabart et al. (2007) showed that the use of lyophilized material (black currant leaves and buds) allowed a better extraction of phenolics antioxidants due to a better grinding of the tissues and thus a reduced particle size in the simple and degradation of some phenolics and antioxidants in undried plant material.

Conventional extraction is usually performed using reflux, cold maceration, Soxhlet, and simple distillation techniques. These methods have been used for many decades. However, conventional extraction techniques use large quantities of toxic organic solvents, are labor intense, require long extraction times, possess low selectivity and/or low extraction yields, and can result in the exposure of extracts to excessive heat, light, and oxygen (Hossain et al., 2011).

4.4.2 NONCONVENTIONAL

An efficient extraction process should maximize the recovery of target compounds with minimal degradation, resulting in an extract with high antioxidant activity using environmentally friendly technologies and low-cost raw materials (Santos et al., 2010). In this context, recently novel methods for phenolic antioxidant extraction have been employed including UAE, MAE, SFE, and SWE. These extraction methods presenting advantages when compared to conventional methods because they decreasing solvent consumption, shortening extraction time, due to the possibility of working at elevated temperatures or pressures in inert atmosphere, and giving higher yield than the conventional methods of extraction; furthermore, they can be carried out in the absence of light and oxygen (Nayak et al., 2015; Wang and Weller, 2006).

4.4.2.1 ULTRASOUND-ASSISTED EXTRACTION

UAE is an efficient extraction method and might be a potential means to extract bioactive compounds. The sonication is characterized by the production of sound waves that create cavitation bubbles near the sample tissue which releasing cell contents and extraction efficiency can be enhanced through acoustic cavitation and mechanical effects. Acoustic cavitations can disrupt cell walls facilitating solvent penetration into the plant material and allowing the intracellular content to be released, whereas mechanical effects caused by ultrasound could also be the agitation of the solvent used for extraction, thus increasing the surface contact area between the solvent and the targeted compounds by allowing greater penetration of the solvent into the sample matrix (Corbin et al., 2015).

Probe and bath systems are the two most common ways of applying ultrasound waves to the sample, and the PC extraction from plant material can be carried out using both static and dynamic modes. Whereas in a static system, there is a closed-vessel extraction for which no continuous transfer of solvent occurs, in a dynamic system extraction, solvent is supplied continuously, which allows efficient adsorption of analytes and their effective transfer from the extraction vessel (Khoddami et al., 2013). It is important to regard that in the UAE method, extract recovery is influenced not only by sonication time, temperature, and solvent selection but also by wave frequency and ultrasonic-wave distribution (Wang and Weller, 2006).

Compared to conventional methods, UAE is one of the most simple, inexpensive extraction systems and can be operated rapidly using a range of solvents. As a method to extract PC of flaxseed, UAE showed to be very efficient for the reduction of mucilage entrapment of these phenolics, thus, allowing a high extraction yield (Corbin et al., 2015). Good yield was also possible to reach using UAE of bioactive compounds (anthocyanins and phenolics) from jaboticaba peels which was shown to be a more efficient extraction method than the sophisticated extraction systems such as high pressure CO_2-assisted extraction (Rodrigues et al., 2015).

4.4.2.2 MICROWAVE-ASSISTED EXTRACTION

MAE is an alternative process that uses microwave energy to extract compounds from materials and appears to be one of the best nonconventional methods to extract PC from plant due to the special microwave/matter interactions and the vary rapid extraction time (Setyaningsih et al., 2015). Microwaves are nonionizing radiation ranging in frequency from 300 MHz to 300 GHz. The effect of microwaves is strictly related to the conversion of electromagnetic energy to heat, which is based on the direct effect of microwaves by ionic polarization and dipolar rotation on molecules with dipoles. Therefore, when microwave radiation is applied in materials or solvents, the time variation of the wave electric field leads to dipolar rotation that is due to the alignment on the electric field of molecules possessing a dipole moment and this produces molecular friction and collisions with consequent liberation of thermal energy into the medium results in fast dielectric heating.

The efficiency of microwave heating at a given frequency and temperature depends on the ability of the material to absorb eletromagnetic energy and to dissipate heat (Flórez et al., 2015). In addition, an increase in the extraction yield of solutes from food matrix is reached when solvents are used with a high dielectric constant and a high dissipation factor which also facilitates distribution of heat throughout the matrix. Then, polar solvents have a higher dielectric constant than nonpolar solvents and can absorb more microwave energy, which can result in a higher yield of phenolics. Application of microwave radiation induces changes at cellular level. During MAE, polar molecules absorbed efficiently the energy and the sudden heating generated cause liquid vaporization and pressure built up within the cells that drastically change the physical properties of the cell walls. In addition, the cell structure is broken down and improves the capillary–porous structure of the tissues, facilitating faster diffusion out of the solid (Flórez et al., 2015).

Seeing that different chemical substances absorb microwaves to different extents, the MAE is an efficient method for extractions and this behavior makes it possible to selectively extract target compounds from complex food matrix at a higher rate than in conventional extraction, since it is induced by highly localized heating caused by microwaves, which could be due to a synergy combination of mass and heat transfer phenomena acting in the same direction (Flórez et al., 2015; Setyaningsih et al., 2015). Furthermore, the increase of movement and collision efficiency of the molecules induced by the change in the electric field direction weakens hydrogen bonds which facilitates disruption of the solute–matrix interactions and release of target compounds.

MAE has recently received much attention due to its many advantages, including shorter extraction time, lower organic solvent requirement, and increased extraction yields. In addition, this system rapidly generates heat and this result in good quality extracts with better target compound recovery. However, the efficiency of this extraction method depends on extraction time, extraction temperature, solid–liquid ratio, and the type and composition of solvent used (Setyaningsih et al., 2015). MAE can be used for the extraction of polyphenols from plant material since these compounds are dipoles and can absorb microwave energy due to their hydroxyl groups which are distributed along its molecular structure (Khoddami et al., 2013). In addition, this alternative extraction method can be applied to extraction of heat-sensitive bioactive compounds from plant materials where rapid heating and hence shorter extraction time is desired.

Researches have been performed to determine the best operating conditions to extract different PC using this method. MAE method was used for the extraction of PC from rice grains and the highest yield was obtained applying extraction temperature 185°C, microwave power 1000 W, extraction time 20 min, solvent 100% methanol, and solvent-to-sample ratio 10:1 (Setyaningsih et al., 2015). MAE method induced high extraction selectivity of bioactive compounds from *Urtica dioica* leaves and stems and high yield of extracted compounds was obtained with microwave power 750°C, extraction time 2 min, and solvent 100% ethanol (Hijazi et al., 2013).

The MAE under optimum conditions can be considered as a powerful tool for the extraction of PC from variety of plant material.

4.4.2.3 ENZYME-ASSISTED EXTRACTION

Enzyme-assisted extraction (EAE) of bioactive compounds from plants have been widely investigated due to its advantages that including easy operation and environment friendship, becoming a potential alternative to conventional solvent based extraction methods. This method also has shown faster extraction, higher recovery, reduced solvent usage, and lower energy consumption when compared to nonenzymatic methods (Puri et al., 2012). In recent years, EAE has also been gaining attention as efficient method to enhance the release and recovery of PC from plants since enzymes can effectively work catalyzing the degradation of vegetables cell wall, favoring the release of bioactive components contained inside the cell as well as those reported to be linked to cell wall polysaccharides by hydrophobic interactions and hydrogen bonds.

It is known that the primary cell wall of plants is mainly composed of cellulose, hemicellulose, and pectin; thus cellulases, hemicellulases, and pectinases as well as others enzymes can be used to catalyze and hydrolyze the cell wall polysaccharides and therefore enabling a better release and a more efficient extraction of PC (Miron et al., 2013). Different enzymes have been employed (alone or in combination) to enhance and accelerate phenolics extraction of plant material. Pectinases were employed to extraction and release anthocyanins from saffron tepals and showed high efficiency as compared to conventional ethanol extraction (Lotfi et al., 2015). PC from thymus leaves were efficiently extracted by enzyme-assisted method with cellulase and polygalacturonase which induced increase in antioxidant capacity of the extracts (Cerda et al., 2013). In another study, extraction of antioxidant phenolics from ginger was studied, and the enzymes' pretreatment had a significant influence on the yield of 6-gingerol and the total polyphenols.

For some studies, enzyme pretreatment of raw material normally results in a reduction in extraction time, minimizes usage of solvents, and provides increased yield and quality of product. However, compared to prior research evaluating the use of enzymatic treatment for enhancement of antioxidant compounds extraction from thymus, better results were observed in this investigation when commercial enzymes were incorporated during the solvent extraction of PC and not when applied as a pretreatment process. This study suggests that the difference can be due to a long extraction time in the second case, once the enzyme was in contact with the thymus sample during the pretreatment time and during the extraction time (21 h total), which decreases the concentration of phenols in the medium because of their degradation by the same enzyme activity still present in the extract (Cerda et al., 2013).

In most studies, the enzyme incorporation increases the presence of PC and antioxidant activity. The enzymes required for extraction process can be derived from bacteria, fungi, animal organs, or vegetable/fruit extracts. However, to use enzymes most effectively for extraction applications, it is important to understand their catalytic property and mode of action, optimal operational conditions, and which enzyme or enzymes combination is appropriate for the plant material selected. In addition, the parameters impacting enzyme-assisted release of bioactives (pH, time, temperature, and concentration) need to be optimized for each specific process: enzymes normally function at an optimal temperature, however, they can still be used over a range of temperatures, providing flexibility for both cost and product quality; substrate particle size reduction prior to enzymatic treatment provides better accessibility of the enzyme to the cell to increase extraction yields significantly; in aqueous extraction, the enzymes can rupture the polysaccharide–protein colloid in the cell wall creating an emulsion that interferes with extraction, so nonaqueous systems are preferable for some materials (Puri et al., 2012).

The EAE is an attractive proposition to enhance the yields of bioactive compounds. Although further investigations are needed, in particular to synthesize of new enzymes and purification of enzymatic mixtures, helping to improve the level of released bioactives making it a viable extraction process at commercial scale.

4.4.2.4 SUBCRITICAL WATER EXTRACTION

Recently, SWE, also referred as pressurized or low-polarity water extraction, has been used as an alternative technique for the extraction of bioactive compounds. Subcritical water (SW) is defined as water at a temperature between its boiling and critical point where the pressure is regulated in such a way that water remains in its liquid (Herrero et al., 2012). The technique has been receiving much attention in the field of natural compounds extraction because SW is an efficient solvent for both polar and nonpolar compounds and its versatility as a solvent is related to the tunable polarity of water, which is directly dependent upon the temperature; when the temperature of water is increased, its polarity decreased, so the solubility of nonpolar organic increases, whereas the solubility of polar organics decreases (Carr et al., 2011). Under subcritical condition, the change in the water temperature can lead to changes in the water's dielectric constant and consequently the water polarity: under standard temperature and pressure (25°C and 101 kPa) water is a polar compound with dielectric constant of about 80, but when the temperature is increased to about 200–350°C, the dielectric constant drops to around 20–30, which is similar to the range of dielectric constants of conventional solvents usually applying in the conventional bioactive extraction process like methanol, ethanol, and acetone at room temperature (Carr et al., 2011; Duba et al., 2015; Herrero et al., 2012).

However, these solvents are often toxic and rigorous organic solvent removal is necessary due to the extract can be ingested as an ingredient food or pharmaceutical. Therefore, SW is an ideal candidate for use as solvent for the natural compounds extraction from plant material because water is ubiquitous, nontoxic, and has low disposal costs. SWE process based on the thermodynamic properties of water which are described in terms of hydrogen bonding strength and its structure. Changes in hydrogen bonding strength are reflected in the dielectric constant; at higher temperatures, the increased thermal agitation reduces the hydrogen bond strength in water and leads to a reduction in dielectric constant value which makes the water a solvent of less polarity which in turn increases the solubility of some organic compounds as polyphenols. However, the solubility of organic compounds in SW depends on several factors like chain length, type, and position of side groups, molecular weight, position of hydrogen bonding, etc. of the solute being solubilized (Carr et al., 2011).

Treatment with SWE has been shown to be sufficiently powerful to extract polyphenols from grape skins and defatted grape seeds (Duba et al., 2015). The study shown that high yields of total polyphenols were obtained for both skins and seeds. For extraction of flavonols from black tea, celery, and ginseng leaf, the effectiveness of SWE compared to that of other extraction solvents, such as ethanol, methanol, and hot water has been studied and the results indicated that SWE is a highly selective and rapid method for extraction of flavonols from plants. Therefore, SW could be an excellent alternative to organic solvent as a medium for extracting flavonols (Cheigh et al., 2015). SWE has been demonstrated to be an effective extraction method for a wide range of PC providing higher yield and reduction on extraction time by up to 50% of conventional method extraction time. In addition, SWE could be a good alternative industrial method to use for extraction of large amounts of PC without toxic organic solvent residues.

4.4.2.5 SUPERCRITICAL FLUID EXTRACTION

SFE is another environmentally friendly extraction technique which in recent years has received greater attention as an important alternative to traditional solvent extraction methods since degradation and decomposition of the active compounds is avoided operating at reduced temperatures, in absence of light and oxygen (Meneses et al., 2015). In addition, the extracts obtained by SFE are natural origin, present absence of residual organic solvent, and composition controlled by process selectivity (Paes et al., 2014). SFE method extracts soluble components from a raw material exploiting the unique properties of gases above their critical points (Mallikarjun Gouda et al., 2015). Thus, the relatively low viscosity (near to the gas) and the high diffusivity of supercritical fluids (SCF) help to penetrate the porous solid materials more efficiently than liquid solvents, thus resulting in faster and more efficient extractions (Otero-Pareja et al., 2015). SFE is usually performed in inert atmospheres, absence of light, at moderate temperatures and short time contributing to avoid oxidation, thermal degradation, and others chemical changes in bioactive compounds (Nyam et al., 2010).

In SFE method, methane, carbon dioxide, ethane, propane, ammonia, ethanol, benzene, and water are the usual SCF applied. Among them, carbon dioxide (CO_2) is the most used because is nontoxic, nonflammable, and noncorrosive, in addition to be inert to most materials, cheap, and readily available in bulk quantity with satisfied purity (Nyam et al., 2010). Thus, CO_2 is an ideal solvent which has been used to extracting of phenolics from asparagus, peach leaves, and myrtle leaves (Kazan et al., 2014; Pujol et al., 2013; Solana et al., 2015). However, CO_2 has a very limited capacity to dissolve polar and high molecular weight compounds being the addition of polar cosolvent such as methanol, ethanol, and acetone recommended to modify its polarity (Meneses et al., 2015).

4.5 PLANT TISSUE SELECTION

To date, there are at least 14 groups of plant secondary metabolites with nutraceutical potential. Alkaloids, amines, cyanogenic glycosides, terpenes, isoprenoids, tocopherols, phenylpropanoids, glucosinolates, polyacetylenes, polyketides, saponins, steroids, small peptides, and nonprotein amino acids are just few examples (Karim and Azlan, 2012). Despite that, these phytochemicals are distributed along the diverse plant tissues and may vary upon species, some of these phytochemicals are more common to occur in a specific plant tissue according to their physiological role in plants, see Figure 4.2. The selection of the most suitable source of bioactives to design effective nutraceuticals implies the selection of high-quality raw materials and a strict control of by-side contaminants (Lockwood, 2011), among other factors. This represents an everyday dilemma for agronomists, food chemists, and pharmaceutical developers, which not only have to face the problem of obtaining highly pure ingredients but also must be sensitive to the rapid changes of the functional/nutraceutical market (Siro et al., 2008). A comprehensive path to obtain nutraceutical bioactives (*NB*) is depicted in Figure 4.3, summarizing some important considerations at each stage. Anticipating that the selection of plant/tissue source (Fig. 4.3, **Stage 1**) turns out to be the critical starting point in the research and development process, in the following paragraphs, this aspect is addressed in detail.

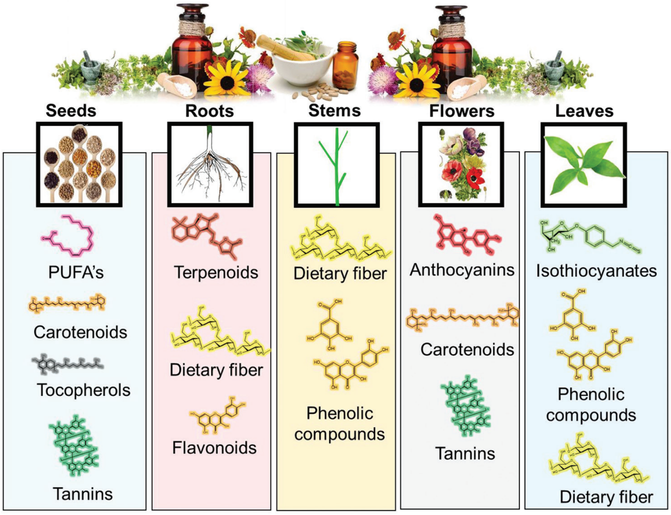


FIGURE 4.2 Common phytochemical distribution in plant tissues.

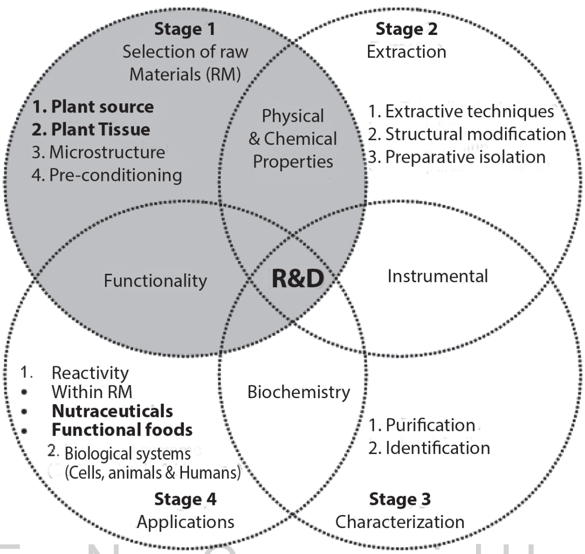


FIGURE 4.3 Research and development (R&D) of functional foods and nutraceuticals.

First, the specific chemical fingerprint of a particular plant, along with its health-promoting properties, far outstrips its taxonomy. The natural distribution of a particular *NB* in fruits, the edible usually fleshy and sweet smelling part of a plant that may or may not contain seeds, is primarily committed by their taxa-specific richness. For example, *lycopene* a linear carotenoid (Saini et al., 2015) that plays a modest role on prostate cancer (Chen et al., 2013) and cardiovascular disease (Müller et al., 2015) is found in a higher amount (>1000 times) in mature fruits of watermelon (*Cucurbitaceae*) and tomato (*Solanaceae*) as compared to mango (*Anacardiaceae*) or carrot (*Apiaceae*), though the later are richer in another carotenoid: *β-carotene*.

As if this were not enough, phylogenetically related plants also have marked differences in *NB* content. For example, the *Solanaceae* family compromises 98 genera and approximately 2700 species; *Capsicum annum* belongs to it and includes a wide variety of hot peppers with graded levels of pungency (Scoville units) associated with their *capsaicin* content, an alkaloid with a protective antioxidant effect against nonalcoholic fatty liver disease and hyperglycemic-induced endothelial disorders (McCarty et al., 2015), adipogenesis (Alcalá-Hernández et al., 2015), and cancer (Swain and Kumar Mishra, 2015). Fortunately, information on structure–function as well as plant sources for specific *NB*, is continuously deposited in several open access databases (e.g., USDA-NDB, phenol-explorer, PhytAMP, SOFA, and GMD) in such way that the selection of the richest source of a particular *NB* seems to be no longer the problem. The systematization within these databases also helps to bring together several plants and even specific tissues, with the same functional/nutraceutical action (Andrade-Cetto and Heinrich, 2005).

Mother Nature also distributes several *NB* in other tissues during the plant's lifetime, according to their physiological role. For example, leaves have the highest photosynthetic activity and so they are rich in *chlorophyll*, a porphyrin pigment with antioxidant and anticancer activity (İnanç, 2011). Straws, stalks, and stems, whose main function is to support for and the elevation of leaves, flowers, and fruits, are rich in *xylo-oligosaccharides* (Carvalho et al., 2013) useful to improve gut's health, while seeds (the ripened ovule of a plant, containing the embryo and the endosperm, wrapped in a protective coat) have the highest content of *fatty acids*, *phytosterols*, and *proteins*, all having a pivotal role on preventing cardiovascular diseases. Edible flowers are excellent sources of volatile *NB* secreted during specialized ant pollination (de Vega et al., 2014), with several medical applications such as antiseptic, antispasmodic, and antiparasitic actions (Mlcek and Rop, 2011). Lastly, from woody barks and fruit exocarps (e.g., shells, peels, and pods) is possible to get many *alkaloids* an PC such as c*ondensed* and *hydrolyzed tannins*, which protect the plant from predators' attack but also have and hypoglycemic effect (Olivas-Aguirre et al., 2014; Shan et al., 2005). The development of sophisticated techniques to isolate and identify *NB* from all of the above-mentioned plant tissues (Fig. 4.3, **stage 3**) has been used in *Plant Molecular Systematics* to consolidate three research lines:

Molecular and nutraceutical characterization of a single NB obtained from different plant sources.

New tools for the molecular identification of *NB* (HPLC–MS, MS, MALDI-TOF, etc.) has led to the conclusion that many nutraceutical actions are restricted to just one metabolite. For example, *Butein* and *chalconoid* isolated from stems, barks, flowers, fruits, heartwoods, and leaves of at least 30 different plants (Semwal et al., 2015) has many medical applications as an analgesic, antibiotic, antithrombotic, anticancer, and anti-inflammatory agent. Also, apigenin-7-*O*-glycoside (flavan-3-ol) isolated from olive leaves, chamomile flowers, salvia stems is either a strong hematopoietic (Samet et al., 2015) or an anti-anxiolitic (Kumar and Bhat, 2014). *Lunasin* (Fig. 4.4), a 43 amino acid peptide found in soybean, wheat, barley, rice, rye, triticale, and amaranth, has anticancer and anti-inflamatory capacity (Malaguti et al., 2014).

Identification of different NBs from distinct plant sources with a same nutraceutical action.

From folk medicine, it has been possible to gain knowledge on several plant sources (and tissues) for a specific metabolic condition or disease. For example, Mexican diabetic patients use several "phytoremedies" (Table 4.2) including those known as *tizanas* which are herbal infusions prepared with flowers, fruits, or roots from different plants but with the same medicinal purpose (Johnson et al., 2006). However, despite the accumulated empirical knowledge, very little is known about their pharmacological effectiveness and their safe intake/toxicity level. In this sense, the isolation and purification of the associated *NB* to these *tizanas* is a crucial step (Fig. 4.3, **stage 3**) to develop culturally accepted nutraceuticals, either alone or combined.

To further complicate this matter, the natural distribution of *NB* within a single plant, can differ from one tissue to another. For example, it is well known that several noncommunicable chronic diseases are associated with pro-inflammatory conditions along with an altered redox status. These conditions could be reversed by consuming plant antioxidants such as PCs. PCs are widely distributed in the plant kingdom, grouping a plethora of chemical compounds with radical scavenging capacity (RSC). Fresh-cut aromatic herbs such as coriander, mint, and parsley are believed to provide the organism with extra *NB* with RSC and anti-inflammatory capacity (Santos et al., 2014). However, a graphical adaptation of how their RSC is differently distributed from stem to leaves, as described by Al-Juhaimi et al. (2011), is shown in Figure 4.5. This same phenomenon extends to the comparison of peels and seeds vs. pulp (common edible part) of tropical fruits such as avocado, guava, mango, and pomegranate (Ayala-Zavala et al., 2011).

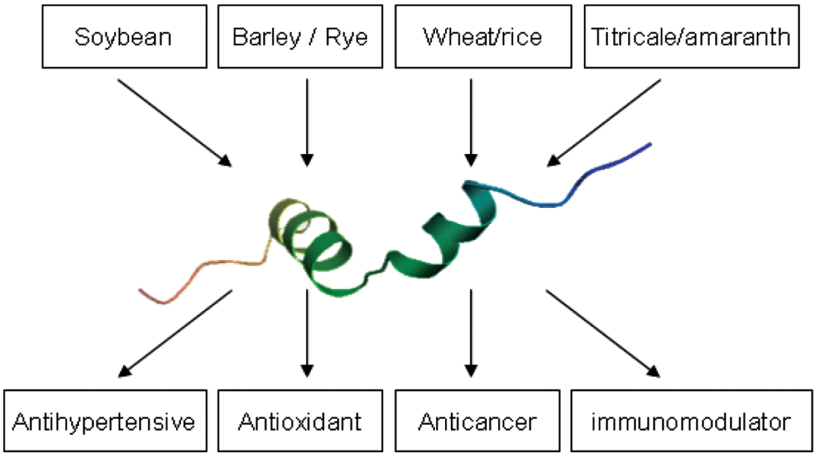


FIGURE 4.4 Lunasin: sources and nutraceutical actions.

TABLE 4.2 Mexican Plants with Hypoglycemic Effect and Related *NB*.

Common name	Family	Plant part	Associated *NB*
Maguey	*Agavaceae*	Stem	Sapogenins
Onion	*Liliaceae*	Bulb	Sulfuric derivates
Angel grass	*Asteraceae*	Leaf/stem	Terpenes
Sabila	*Liliaceae*	Stem (roasted)	Polysaccharides/flavonoids
Pineapple	*Bromeliaceae*	Fruit (juice)	Monoterpenoids/lactones
Peanut	*Fabaceae*	Seed (oil)	Sterols/flavonoids
Pingüica	*Ericaceae*	Leaves	Alkaloid/flavonoids
Beet	*Chenopodiaceae*	Stem	Alkaloids/flavonoids
Prodigiosa	*Asteraceae*	Leaf/stem	Sesquiterpenes/lactones
White zapote	*Rutaceae*	Bark	Alkaloids
Tejocote	*Rosaceae*	Root	Tannins/flavonoids
Guayacan flower	*Solanaceae*	Flower	Alkaloids

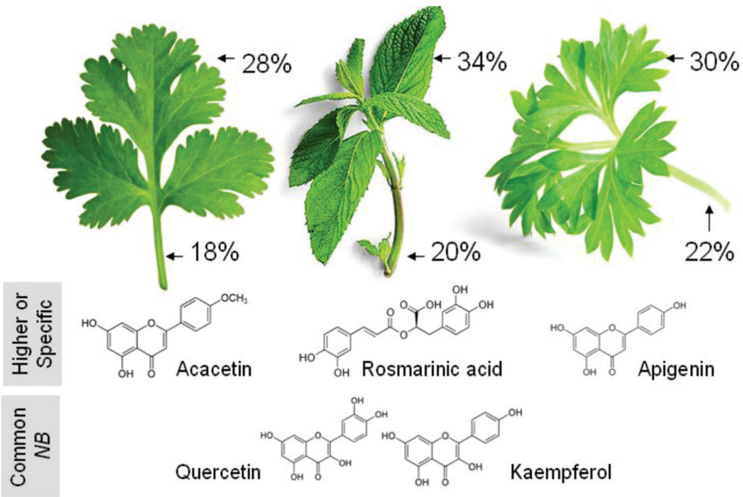


FIGURE 4.5 Selected PC and RSC activity (% DPPH inhibition) of leaf and stem extracts from culinary herbs. Coriander (left), mint (center), and parsley (right).

Generation of metabolomic data on a specific plant source with different nutraceutical applications.

The concept of "integral exploitation" commonly used in the agribusiness sector (agriculture and forestry) has been recently benefited with the second *MSP* research line. Since the 1970s, this sector realized the need to diversify the applications of several plant resources, building up a strategic partnership between primary producers and academics. As an example, several patents have been authorized on the use of tropical, semi-arid, and arid crops as potential sources of *NB* (Souto et al., 2014). Also, researchers worldwide have focused their efforts on elucidating the biological control (metabolomics) and the tissue-specific richness in *NB* of a single plant source (Ayala-Zavala et al., 2011; Patel, 2015; Sharma et al., 2015). A few examples of specific plant tissues rich in *NB*, as well as their potential use to enhance human health are summarized in Table 4.3.

For example, *bitter gourd* (*Momordica charantia* L.), has been traditionally used as a food in tropical regions such as India, Malaya, China, tropical Africa, Middle East, America. As a medicinal plant, it has been reported to possess antilipolytic, hyploglycemic, analgesic, abortifacient, antiviral, anticytotoxic, and antimutagenic properties. These preventive effects are related to the differential antioxidant capacity (as assayed FRAP) and PC content (phenolic acids) of its parts.

TABLE 4.3 Phenolic Compounds Screening and Nutraceutical Potential from Selected Plant Sources.

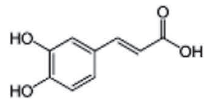
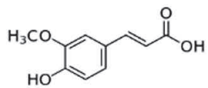
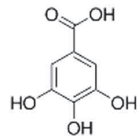
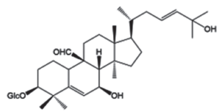
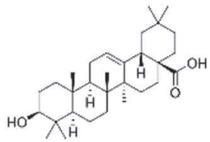
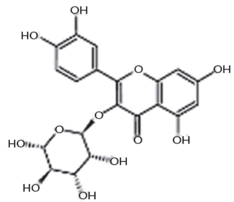
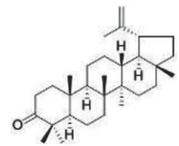
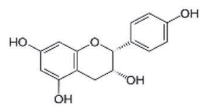
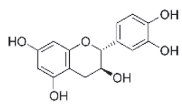
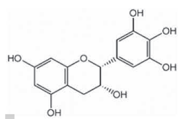
Plant	Tissue	*NB*	Structure	Action	References
Bitter gourd *Momordica charantia* L	Leaf	Caffeic acid		Hepatoprotective Neuroprotective Anti-inflammatory Cardioprotective	Kubola and Siriamornpun (2008), Tolba et al. (2013)
	Stem	Ferulic acid		Anticytotoxic Cardioprotective Hepatoprotective	Alam et al. (2013), Kubola and Siriamornpun (2008)
	Fruit (ripe)	Gallic acid		Neuroprotective Hepatoprotective Anti-inflammatory Anti-allergic Antiulcerogenic	Kubola and Siriamornpun (2008), Sen et al. (2013)
		Cucurbitane-type triterpene glycosides		Hyploglycemic Hepatoprotective Antiproliferative	Hsiao et al. (2013), Torres-Moreno et al. (2015)
Guamuchil/manila tamarind *Pithecellobium dulce* (Roxb.) *Benth*	Seed	Oleanolic acid		Antidiabetic Hypolipidemic Anti-inflammatory	Nagmoti et al. (2015), Wang et al. (2013)

TABLE 4.3 *(Continued)*

	Leaves	Quercetin		Anti-inflammatory Antibacterial Neuroprotective Hypolipidemic	Chandran and Balaji (2008), Ghosh et al. (2013), Jung et al. (2013)
	Bark	Lupenol		Anticancer Antiparasitic Antidislipidemic	Monroy and Colín (2004), Pitchai et al. (2014), Srivastava et al. (2013)
Flamboyant *Delonix regia*	Fruit	Afzelechin		Elastase (neutrophyl) inhibitory activity	Feng et al. (2014b), Huang et al. (2013), Siddiqui et al. (2014)
	Stem bark	Catechin		Antityrosinase activity Cytoprotective Antidiabetic Anti-inflammatory	Feng et al. (2014b), Gawlik-Dziki et al. (2016), Liu et al. (2014), Morel et al. (1993)
	Leaf	(Epi)-gallo-chatechin		Antioxidant Antiproliferative Anti-inflammatory	Feng et al. (2014b)

In summary, the careful selection of a primary plant source of *NB*s will determine the success or failure of the final manufactured nutraceutical. In this sense, it is crucial to select the most suitable plant tissue for a particular purpose, as well as other important factors such as ripening stage and proper extractive methods and technologies, which could hinder the quality and performance of the final *NB*.

4.6 NUTRACEUTICAL PRODUCTS IN MARKET

Nutraceuticals market is growing rapidly, the global profits for 2013 was approximately 175 billion US dollars and is expected to grow to 424 billion by 2017 (Daliri and Lee, 2015). There has been an increase in the consumption of nutraceuticals in the last decade, the United States being the largest consumer of nutraceuticals and functional foods followed by Japan and Europe, and other countries such as India, China, Russia, and Canada. The rise in the incidence of obesity, cardiovascular disease, cancer, and diabetes, along with the knowledge of reduce risk of several diseases and maintain a state of health through a diet rich in fruits and vegetables, and the need for products that offer higher bioavailability of one or more bioactive ingredients, among other factors have contributed to the growth of this industry (Zawistowski and Debasis, 2008). People's awareness in the health-related benefits of dietary supplements, and the practical presentation of most of the nutraceutical products and functional foods are key to their successful growth.

Most of the nutraceuticals products are targeting weight control, vascular health, general nutrition, and sports nutrition mainly. Nutraceuticals also focus in other health areas such as eye health, diabetes, mental health, cancer, arthritis, ageing, and sexual health and performance. Most common nutraceuticals in the market are those that contain ingredients like DF, vitamin E, PUFAs, inulin, probiotics, conjugated LA, soy and plant antioxidant (polyphenols). Nutraceuticals normally are consumed as pills, capsules, soft gels, and tinctures and can be categorized as nutrients (vitamins and minerals), botanicals (nutraceuticals made from plant parts), and dietary supplements (Dureja et al., 2003). However, nutraceuticals can be taken either as a food additive or a powder concentrate and it depends on the consumer's preference and needs.

The growing demand of consumers for nutraceuticals has increased the release of new functional products every year. Between 2008 and 2009, the United States launched 881 healthy products, followed by Italy and Japan with 325 and 314, respectively (Valls et al., 2013). There are organizations from different countries such as the Food and Drug Administration (FDA), the European Authority of Food Safety, or the Ministry of Health, Labour, and Welfare (MHLW) that are in charge to regulate this type of products and to assure that its claims are not misleading consumers. FDA is responsible for the regulation of nutraceuticals under the authority of the Federal Food, Drug, and Cosmetic Act and evaluates the safety and labeling of dietary supplements fulfill the requirements of Dietary Supplement Health and Education and FDA before marketing. The FDA does not recognize nutraceuticals as they are not legally defined, they are regulated under the same statutes as food products and not like drugs and must not have claims that says the product use is for the treatment or prevention of a specific disease. The manufacturer must notify and give information to the FDA that the new product is safe and it is under the conditions of use as stipulated in its labeling. Until now, most of the dietary supplements that are selling in the United States possess one of the three claims (nutrient content, structure/function, and health claims) (Hasler, 2008).

In Europe, the situation is similar than in the United States, nutraceuticals products are regulated by the same legislation than foods. The European Union distinguishes two types of claims. Nutrition claims: it suggests that food has particular beneficial nutritional properties due to the energy it provides or the nutrients it contains. Health claims: it implies that there exists a relationship between food or one of food constituents and health. Inside this claim exist other claims such as reduction disease risk claims which state that the consumption of a food or food constituent significantly reduces a risk factor in the development of human disease (Hasler, 2008; Verhagen et al., 2010). The MHLW enacted functional foods or Food for Specified Health Uses (FOSHU) as a regulatory system for approval of food with health claims that can be used on a label to inform consumers about their functionality (Regulations, 1996). Japan is the only country that has a specific food category besides food and medicine. Also, FOSHU is the only category of functional foods that are qualified to carry health function claims in Japan; their health benefits are aim especially to gastrointestinal health, blood pressure, dental hygiene, bone health, serum cholesterol, mineral absorption, and blood glucose (Bagchi, 2008).

To assure the future of the nutraceuticals industry, it is necessary to legally define the term nutraceutical and try to uniform the legislations of the different countries for these products. Companies should perform long-term clinical trials in animals and humans to scientifically validate the health benefit they are selling and to identify the presence of many ingredients that can harmful to the consumers. Also, health professionals and academics should work together along with manufacturers to provide scientific evidence for the development of new functional products.

4.7 CONCLUDING REMARKS

The scientific breakthroughs and constant innovation in food science and technologies are pushed by the desire of people to get healthier choices of food products that they may add to their diet at low cost. The growing demand for novel functional foods and nutraceutical products are leading scientist around the world to the continuous search of new natural sources of bioactive compounds with optimum extraction yield to the food industry, to get low cost of product manufacture. Plant tissues as product of their secondary metabolism has a great variety of phytochemicals, from PC to DF, or even carotenoids, vitamins, and amino acids. Hence, it depends on the desirable health effect of the plant tissue that should be selected for the extraction of the appropriate phytochemical to incorporate it in the nutraceutical product. In that sense, plant tissues represent a great source of bioactive compounds due to their great amount and diversity of phytochemicals. Moreover, once the phytochemical desired is on target, and the plant tissue source of this compound is found, it is essential to select a proper extraction method to achieve the optimum extraction yield of the desirable compound. However, there are plenty of plant tissues yet uncharacterized in many countries around the world, and scientists around the world must continue the contribution at least with information about the local plant tissues of their own region.

KEYWORDS

- **functional foods**
- **phytochemicals**
- **design foods**
- **functional ingredients**
- **extraction methods**

REFERENCES

Abdul-Hamid, A.; Luan, Y. S. Functional Properties of Dietary Fibre Prepared from Defatted Rice Bran. *Food Chem*. **2000,** *68* (1), 15–19.

Acharya, J.; Karak, S.; De, B. Metabolite Profile and Bioactivity of *Musa × paradisiaca* L. Flower Extracts. *J. Food Biochem*. **2016** *40* (6), 724–730.

Agbangnan, P.; Tachon, D.; Dangou, J.; Chrostowska, A.; Fouquet, E.; Sohounhloue, D. Optimization of the Extraction of Sorghum's Polyphenols for Industrial Production by Membrane Processes. *Res. J. Res. Sci*. **2012,** *1*, 1–8.

Aggarwal, B. B.; Sundaram, C.; Prasad, S.; Kannappan, R. Tocotrienols, the Vitamin E of the 21st Century: Its Potential against Cancer and Other Chronic Diseases. *Biochem. Pharmacol*. **2010,** *80* (11), 1613–1631.

Aizawa, K.; Inakuma, T. Quantitation of Carotenoids in Commonly Consumed Vegetables in Japan. *Food Sci. Technol. Res*. **2007,** *13* (3), 247–252.

Ajila, C.; Leelavathi, K.; Rao, U. P. Improvement of Dietary Fiber Content and Antioxidant Properties in Soft Dough Biscuits with the Incorporation of Mango Peel Powder. *J. Cer. Sci*. **2008,** *48* (2), 319–326.

Al-Farsi, M. A.; Lee, C. Y. Nutritional and Functional Properties of Dates: A Review. *Crit. Rev. Food Sci. Nutr*. **2008,** *48* (10), 877–887.

Al-Juhaimi, F.; Ghafoor, K. Total Phenols and Antioxidant Activities of Leaf and Stem Extracts from Coriander, Mint and Parsley Grown in Saudi Arabia. *Pak. J. Bot*. **2011,** *43* (4), 2235–2237.

Alam, M. A.; Sernia, C.; Brown, L. Ferulic Acid Improves Cardiovascular and Kidney Structure and Function in Hypertensive Rats. *J. Cardiovasc. Pharmacol*. **2013,** *61* (3), 240–249.

Alcalá-Hernández, C. F.; de la Rosa, L. A. A.; Wall-Medrano, A.; López-Díaz, J. A.; Álvarez-Parrilla, E. Avances en Terapia Farmacológica y Fitoquímica de la Adipogénesis. *Nutr. Hosp*. **2015,** *32* (n02).

Anastasiadi, M.; Pratsinis, H.; Kletsas, D.; Skaltsounis, A.-L.; Haroutounian, S. A. Bioactive Non-coloured Polyphenols Content of Grapes, Wines and Vinification By-products: Evaluation of the Antioxidant Activities of their Extracts. *Food Res. Int*. **2010,** *43* (3), 805–813.

Anastasiadi, M.; Pratsinis, H.; Kletsas, D.; Skaltsounis, A.-L.; Haroutounian, S. A. Grape Stem Extracts: Polyphenolic Content and Assessment of their In Vitro Antioxidant Properties. *LWT—Food Sci. Technol*. **2012,** *48* (2), 316–322.

Andrade-Cetto, A.; Heinrich, M. Mexican Plants with Hypoglycaemic Effect Used in the Treatment of Diabetes. *J. Ethnopharmacol*. **2005,** *99* (3), 325–348.

Aneta, W.; Jan, O.; Magdalena, M.; Joanna, W. Phenolic Profile, Antioxidant and Antiproliferative Activity of Black and Red Currants (*Ribes* spp.) from Organic and Conventional Cultivation. *Int. J. Food Sci. Technol*. **2013,** *48* (4), 715–726.

Apostolou, A.; Stagos, D.; Galitsiou, E.; Spyrou, A.; Haroutounian, S.; Portesis, N.; et al. Assessment of Polyphenolic Content, Antioxidant Activity, Protection against ROS-Induced DNA Damage and Anticancer Activity of *Vitis vinifera* Stem Extracts. *Food Chem. Toxicol*. **2013,** *61*, 60–68.

Ayala-Zavala, J.; Vega-Vega, V.; Rosas-Domínguez, C.; Palafox-Carlos, H.; Villa-Rodriguez, J.; Siddiqui, M. W.; et al. Agro-industrial Potential of Exotic Fruit Byproducts as a Source of Food Additives. *Food Res. Int*. **2011,** *44* (7), 1866–1874.

Bagchi, D. *Nutraceutical and Functional Food Regulations in the United States and around the World*; Academic Press: Cambridge, MA, 2008.

Borrás-Linares, I.; Stojanović, Z.; Quirantes-Piné, R.; Arráez-Román, D.; Švarc-Gajić, J.; Fernández-Gutiérrez, A.; Segura-Carretero, A. *Rosmarinus officinalis* Leaves as a Natural Source of Bioactive Compounds. *Int. J. Mol. Sci.* **2014,** *15* (11), 20585–20606.

Brekhman, I. I. S. K. *Man and Biologically Active Substances: The Effect of Drugs, Diet and Pollution on Health*: Elsevier: Amsterdam, 2013.

Carr, A. G.; Mammucari, R.; Foster, N. A Review of Subcritical Water as a Solvent and Its Utilisation for the Processing of Hydrophobic Organic Compounds. *Chem. Eng. J.* **2011,** *172* (1), 1–17.

Carvalho, A. F. A.; de Oliva Neto, P.; Da Silva, D. F.; Pastore, G. M. Xylo-oligosaccharides from Lignocellulosic Materials: Chemical Structure, Health Benefits and Production by Chemical and Enzymatic Hydrolysis. *Food Res. Int.* **2013,** *51* (1), 75–85.

Cavalcanti, R. N.; Veggi, P. C.; Meireles, M. A. A. Supercritical Fluid Extraction with a Modifier of Antioxidant Compounds from Jabuticaba (*Myrciaria cauliflora*) Byproducts: Economic Viability. *Proc. Food Sci.* **2011,** *1*, 1672–1678.

Cerda, A.; Martínez, M. E.; Soto, C.; Poirrier, P.; Perez-Correa, J. R.; Vergara-Salinas, J. R.; Zúñiga, M. E. The Enhancement of Antioxidant Compounds Extracted from *Thymus vulgaris* Using Enzymes and the Effect of Extracting Solvent. *Food Chem.* **2013,** *139* (1), 138–143.

Contreras-Calderón, J.; Calderón-Jaimes, L.; Guerra-Hernández, E.; García-Villanova, B. Antioxidant Capacity, Phenolic Content and Vitamin C in Pulp, Peel and Seed from 24 Exotic Fruits from Colombia. *Food Res. Int.* **2011,** *44* (7), 2047–2053.

Corbin, C.; Fidel, T.; Leclerc, E. A.; Barakzoy, E.; Sagot, N.; Falguiéres, A.; et al. Development and Validation of an Efficient Ultrasound Assisted Extraction of Phenolic Compounds from Flax (*Linum usitatissimum* L.) Seeds. *Ultrason. Sonochem.* **2015,** *26*, 176–185.

Chandran, P.; Balaji, S. Phytochemical Investigation and Pharmocological Studies of the Flowers of *Pithecellobium dulce*. *Ethnobot. Leafl.* **2008,** *12*, 245–253.

Chang, R. C.-C.; Ho, Y.-S.; Yu, M.-S.; So, K.-F. *Medicinal and Nutraceutical Uses of Wolfberry in Preventing Neurodegeneration in Alzheimer's Disease*; 2010; pp 169–185.

Chaturvedi, S.; Sharma, P.; Garg, V. K.; Bansal, M. Role of Nutraceuticals in Health Promotion. *Health* **2011,** *4*, 5.

Cheigh, C.-I.; Yoo, S.-Y.; Ko, M.-J.; Chang, P.-S.; Chung, M.-S. Extraction Characteristics of Subcritical Water Depending on the Number of Hydroxyl Group in Flavonols. *Food Chem.* **2015,** *168*, 21–26.

Chen, J.; Song, Y.; Zhang, L. Lycopene/Tomato Consumption and the Risk of Prostate Cancer: A Systematic Review and Meta-Analysis of Prospective Studies. *J. Nutr. Sci. Vitaminol.* **2013,** *59* (3), 213–223.

Chiva-Blanch, G.; Visioli, F. Polyphenols and Health: Moving beyond Antioxidants. *J. Berry Res.* **2012,** *2* (2), 63–71.

Chu, Y.-F.; Sun, J.; Wu, X.; Liu, R. H. Antioxidant and Antiproliferative Activities of Common Vegetables. *J. Agric. Food Chem.* **2002,** *50* (23), 6910–6916.

Chun, O. K.; Kim, D. O.; Smith, N.; Schroeder, D.; Han, J. T.; Lee, C. Y. Daily Consumption of Phenolics and Total Antioxidant Capacity from Fruit and Vegetables in the American Diet. *J. Sci. Food Agric.* **2005,** *85* (10), 1715–1724.

Daliri, E. B.-M.; Lee, B. H. Current Trends and Future Perspectives on Functional Foods and Nutraceuticals. *Beneficial Microorganisms in Food and Nutraceuticals*; Springer: Berlin, 2015; pp 221–244.

Dang, Y. Y.; Zhang, H.; Xiu, Z. L. Microwave-Assisted Aqueous Two-Phase Extraction of Phenolics from Grape (*Vitis vinifera*) Seed. *J. Chem. Technol. Biotechnol.* **2014,** *89* (10), 1576–1581.

Das, L.; Bhaumik, E.; Raychaudhuri, U.; Chakraborty, R. Role of Nutraceuticals in Human Health. *J. Food Sci. Technol*. **2012,** *49* (2), 173–183.

de Vega, C.; Herrera, C. M.; Dötterl, S. Floral Volatiles Play a Key Role in Specialized Ant Pollination. *Perspect. Pl. Ecol., Evol. Syst.* **2014,** *16* (1), 32–42.

Delzenne, N. M.; Neyrinck, A. M.; Cani, P. D. Gut Microbiota and Metabolic Disorders: How Prebiotic Can Work? *Br. J. Nutr.* **2013,** *109* (S2), S81–S85.

Devalaraja, S.; Jain, S.; Yadav, H. Exotic Fruits as Therapeutic Complements for Diabetes, Obesity and Metabolic Syndrome. *Food Res. Int*. **2011,** *44* (7), 1856–1865.

Dillard, C. J.; German, J. B. Phytochemicals: Nutraceuticals and Human Health. *J. Sci. Food Agric.* **2000,** *80* (12), 1744–1756.

Do, Q. D.; Angkawijaya, A. E.; Tran-Nguyen, P. L.; Huynh, L. H.; Soetaredjo, F. E.; Ismadji, S.; Ju, Y.-H. Effect of Extraction Solvent on Total Phenol Content, Total Flavonoid Content, and Antioxidant Activity of *Limnophila aromatica*. *J. Food Drug Anal*. **2014,** *22* (3), 296–302.

Dominguez-Perles, R.; Teixeira, A.; Rosa, E.; Barros, A. Assessment of (Poly)phenols in Grape (*Vitis vinifera* L.) Stems by Using Food/Pharma Industry Compatible Solvents and Response Surface Methodology. *Food Chem*. **2014,** *164*, 339–346.

Dorta, E.; González, M.; Lobo, M. G.; Sánchez-Moreno, C.; de Ancos, B. Screening of Phenolic Compounds in By-product Extracts from Mangoes (*Mangifera indica* L.) by HPLC-ESI-QTOF-MS and Multivariate Analysis for Use as a Food Ingredient. *Food Res. Int*. **2014,** *57*, 51–60.

Dorta, E.; Lobo, M. G.; Gonzalez, M. Reutilization of Mango Byproducts: Study of the Effect of Extraction Solvent and Temperature on their Antioxidant Properties. *J. Food Sci*. **2012,** *77* (1), C80-C88.

Duba, K. S.; Casazza, A. A.; Mohamed, H. B.; Perego, P.; Fiori, L. Extraction of Polyphenols from Grape Skins and Defatted Grape Seeds Using Subcritical Water: Experiments and Modeling. *Food Bioprod. Process*. **2015,** *94*, 29–38.

Dureja, H.; Kaushik, D.; Kumar, V. Developments in Nutraceuticals. *Indian J. Pharmacol.* **2003,** *35* (6), 363–372.

Elleuch, M.; Bedigian, D.; Roiseux, O.; Besbes, S.; Blecker, C.; Attia, H. Dietary Fibre and Fibre-Rich By-products of Food Processing: Characterisation, Technological Functionality and Commercial Applications: A Review. *Food Chem*. **2011,** *124* (2), 411–421.

Faller, A.; Fialho, E. Polyphenol Content and Antioxidant Capacity in Organic and Conventional Plant Foods. *J. Food Compos. Anal.* **2010,** *23* (6), 561–568.

Feng, F.; Li, M.; Ma, F.; Cheng, L. Effects of Location within the Tree Canopy on Carbohydrates, Organic Acids, Amino Acids and Phenolic Compounds in the Fruit Peel and Flesh from Three Apple (*Malus × domestica*) Cultivars. *Hortic. Res.* **2014a,** *1*, 14019.

Feng, H.-L.; Tian, L.; Chai, W.-M.; Chen, X.-X.; Shi, Y.; Gao, Y.-S.; et al. Isolation and Purification of Condensed Tannins from Flamboyant Tree and their Antioxidant and Antityrosinase Activities. *Appl. Biochem. Biotechnol.* **2014b,** *173* (1), 179–192.

Fernandes, L.; Casal, S.; Cruz, R.; Pereira, J. A.; Ramalhosa, E. Seed Oils of Ten Traditional Portuguese Grape Varieties with Interesting Chemical and Antioxidant Properties. *Food Res. Int*. **2013,** *50* (1), 161–166.

Figuerola, F.; Hurtado, M. A. L.; Estévez, A. M.; Chiffelle, I.; Asenjo, F. Fibre Concentrates from Apple Pomace and Citrus Peel as Potential Fibre Sources for Food Enrichment. *Food Chem*. **2005,** *91* (3), 395–401.

Flórez, N.; Conde, E.; Domínguez, H. Microwave Assisted Water Extraction of Plant Compounds. *J. Chem. Technol. Biotechnol.* **2015,** *90* (4), 590–607.

Gawlik-Dziki, U.; Durak, A.; Jamioł, M.; Świeca, M. Interactions between Antiradical and Anti-Inflammatory Compounds from Coffee and Coconut Affected by Gastrointestinal Digestion—In Vitro Study. *LWT—Food Sci. Technol*. **2016,** *69*, 506–514.

Gengatharan, A.; Dykes, G. A.; Choo, W. S. Betalains: Natural Plant Pigments with Potential Application in Functional Foods. *LWT—Food Sci. Technol*. **2015,** *64* (2), 645–649.

Ghosh, A.; Sarkar, S.; Mandal, A. K.; Das, N. Neuroprotective Role of Nanoencapsulated Quercetin in Combating Ischemia–Reperfusion Induced Neuronal Damage in Young and Aged Rats. *PLoS ONE* **2013,** *8* (4), e57735.

González-Centeno, M.; Rosselló, C.; Simal, S.; Garau, M.; López, F.; Femenia, A. Physico-chemical Properties of Cell Wall Materials Obtained from Ten Grape Varieties and their Byproducts: Grape Pomaces and Stems. *LWT—Food Sci. Technol*. **2010,** *43* (10), 1580–1586.

González-Montelongo, R.; Lobo, M. G.; González, M. Antioxidant Activity in Banana Peel Extracts: Testing Extraction Conditions and Related Bioactive Compounds. *Food Chem*. **2010,** *119* (3), 1030–1039.

Gupta, A.; Naraniwal, M.; Kothari, V. Modern Extraction Methods for Preparation of Bioactive Plant Extracts. *Int. J. Appl. Nat. Sci*. **2012,** *1* (1), 8–26.

Habib, H. M.; Kamal, H.; Ibrahim, W. H.; Al Dhaheri, A. S. Carotenoids, Fat Soluble Vitamins and Fatty Acid Profiles of 18 Varieties of Date Seed Oil. *Ind. Crops Prod*. **2013,** *42*, 567–572.

Hamerski, L.; Somner, G. V.; Tamaio, N. *Paullinia cupana* Kunth (Sapindaceae): A Review of Its Ethnopharmacology, Phytochemistry and Pharmacology. *J. Med. Plants Res*. **2013,** *7*, 2221–2229.

Hasler, C. M. Health Claims in the United States: An Aid to the Public or a Source of Confusion? *J. Nutr*. **2008,** *138* (6), 1216S–1220S.

Herrero, M.; Castro-Puyana, M.; Rocamora-Reverte, L.; Ferragut, J. A.; Cifuentes, A.; Ibáñez, E. Formation and Relevance of 5-Hydroxymethylfurfural in Bioactive Subcritical Water Extracts from Olive Leaves. *Food Res. Int*. **2012,** *47* (1), 31–37.

Hervert-Hernández, D.; García, O. P.; Rosado, J. L.; Goñi, I. The Contribution of Fruits and Vegetables to Dietary Intake of Polyphenols and Antioxidant Capacity in a Mexican Rural Diet: Importance of Fruit and Vegetable Variety. *Food Res. Int*. **2011,** *44* (5), 1182–1189.

Hijazi, A.; Bandar, H.; Rammal, H.; Hachem, A.; Saad, Z.; Badran, B. Techniques for the Extraction of Bioactive Compounds from Lebanese *Urtica dioica*. *Am. J. Phytomed. Clin. Therap*. **2013,** *1* (6), 507–513.

Hossain, M.; Barry-Ryan, C.; Martin-Diana, A. B.; Brunton, N. Optimisation of Accelerated Solvent Extraction of Antioxidant Compounds from Rosemary (*Rosmarinus officinalis* L.), Marjoram (*Origanum majorana* L.) and Oregano (*Origanum vulgare* L.) Using Response Surface Methodology. *Food Chem*. **2011,** *126* (1), 339–346.

Hsiao, P.-C.; Liaw, C.-C.; Hwang, S.-Y.; Cheng, H.-L.; Zhang, L.-J.; Shen, C.-C.; et al. Antiproliferative and Hypoglycemic Cucurbitane-Type Glycosides from the Fruits of *Momordica charantia*. *J. Agric. Food Chem*. **2013,** *61* (12), 2979–2986.

Huang, Y.; Chen, L.; Feng, L.; Guo, F.; Li, Y. Characterization of Total Phenolic Constituents from the Stems of *Spatholobus suberectus* Using LC-DAD-MSn and their Inhibitory Effect on Human Neutrophil Elastase Activity. *Molecules* **2013,** *18* (7), 7549–7556.

İnanç, A. L. Chlorophyll: Structural Properties, Health Benefits and Its Occurrence in Virgin Olive Oils. *Akad. Gıda* **2011,** *9* (2), 26–32.

Jaswir, I.; Noviendri, D.; Hasrini, R. F.; Octavianti, F. Carotenoids: Sources, Medicinal Properties and their Application in Food and Nutraceutical Industry. *J. Med. Plants Res*. **2011,** *5* (33), 7119–7131.

Johnson, L.; Strich, H.; Taylor, A.; Timmermann, B.; Malone, D.; Teufel-Shone, N.; et al. Use of Herbal Remedies by Diabetic Hispanic Women in the Southwestern United States. *Phytother. Res.* **2006,** *20* (4), 250–255.

Jung, C. H.; Cho, I.; Ahn, J.; Jeon, T. I.; Ha, T. Y. Quercetin Reduces High-Fat Diet-Induced Fat Accumulation in the Liver by Regulating Lipid Metabolism Genes. *Phytother. Res.* **2013,** *27* (1), 139–143.

Karim, A. A.; Azlan, A. Fruit Pod Extracts as a Source of Nutraceuticals and Pharmaceuticals. *Molecules* **2012,** *17* (10), 11931–11946.

Katalinic, V.; Mozina, S. S.; Generalic, I.; Skroza, D.; Ljubenkov, I.; Klancnik, A. Phenolic Profile, Antioxidant Capacity, and Antimicrobial Activity of Leaf Extracts from Six *Vitis vinifera* L. Varieties. *Int. J. Food Prop*. **2013,** *16* (1), 45–60.

Kazan, A.; Koyu, H.; Turu, I. C.; Yesil-Celiktas, O. Supercritical Fluid Extraction of *Prunus persica* Leaves and Utilization Possibilities as a Source of Phenolic Compounds. *J. Supercrit. Fluids* **2014,** *92*, 55–59.

Keefover-Ring, K.; Trowbridge, A.; Mason, C. J.; Raffa, K. F. Rapid Induction of Multiple Terpenoid Groups by Ponderosa Pine in Response to Bark Beetle-Associated Fungi. *J. Chem. Ecol.* **2016,** *42* (1), 1–12.

Khoddami, A.; Wilkes, M. A.; Roberts, T. H. Techniques for Analysis of Plant Phenolic Compounds. *Molecules* **2013,** *18* (2), 2328–2375.

Kim, S.-A.; Kim, S. H.; Kim, I. S.; Lee, D.; Dong, M.-S.; Na, C.-S.; et al. Simultaneous Determination of Bioactive Phenolic Compounds in the Stem Extract of *Rhus verniciflua* Stokes by High Performance Liquid Chromatography. *Food Chem*. **2013,** *141* (4), 3813–3819.

Krawitzky, M.; Arias, E.; Peiro, J.; Negueruela, A.; Val, J.; Oria, R. Determination of Color, Antioxidant Activity, and Phenolic Profile of Different Fruit Tissue of Spanish 'Verde Doncella'Apple Cultivar. *Int. J. Food Prop*. **2014,** *17* (10), 2298–2311.

Kubola, J.; Siriamornpun, S. Phenolic Contents and Antioxidant Activities of Bitter Gourd (*Momordica charantia* L.) Leaf, Stem and Fruit Fraction Extracts In Vitro. *Food Chem*. **2008,** *110* (4), 881–890.

Kumar, D.; Bhat, Z. A. Apigenin 7-Glucoside from Stachys tibetica Vatke and its Anxiolytic Effect in Rats. *Phytomedicine* **2014,** *21* (7), 1010–1014.

Liaotrakoon, W.; De Clercq, N.; Van Hoed, V.; Dewettinck, K. Dragon Fruit (*Hylocereus* spp.) Seed Oils: Their Characterization and Stability under Storage Conditions. *J. Am. Oil Chem. Soc.* **2013,** *90* (2), 207–215.

Liu, J.; Lu, J.-F.; Kan, J.; Wen, X.-Y.; Jin, C.-H. Synthesis, Characterization and In Vitro Anti-diabetic Activity of Catechin Grafted Inulin. *Int. J. Biol. Macromol*. **2014,** *64*, 76–83.

Liu, S.-C.; Lin, J.-T.; Wang, C.-K.; Chen, H.-Y.; Yang, D.-J. Antioxidant Properties of Various Solvent Extracts from Lychee (*Litchi chinenesis* Sonn.) Flowers. *Food Chem*. **2009,** *114* (2), 577–581.

Lockwood, G. B. The quality of Commercially Available Nutraceutical Supplements and Food Sources. *J. Pharm. Pharmacol.* **2011,** *63* (1), 3–10.

Lotfi, L.; Kalbasi-Ashtari, A.; Hamedi, M.; Ghorbani, F. Effects of Enzymatic Extraction on Anthocyanins Yield of Saffron Tepals (*Crocos sativus*) along with its Color Properties and Structural Stability. *J. Food Drug Anal*. **2015,** *23* (2), 210–218.

Low, D. Y.; D'Arcy, B.; Gidley, M. J. Mastication Effects on Carotenoid Bioaccessibility from Mango Fruit Tissue. *Food Res. Int*. **2015,** *67*, 238–246.

Ma, L.-Y.; Zhou, Q.-L.; Yang, X.-W. New SIRT1 Activator from Alkaline Hydrolysate of Total Saponins in the Stems–Leaves of *Panax ginseng*. *Bioorg. Med. Chem. Lett.* **2015,** *25* (22), 5321–5325.

Macfarlane, G. T.; Macfarlane, S. Manipulating the Indigenous Microbiota in Humans: Prebiotics, Probiotics, and Synbiotics. *The Human Microbiota: How Microbial Communities Affect Health and Disease*; 2013; pp 315–338.

Malaguti, M.; Dinelli, G.; Leoncini, E.; Bregola, V.; Bosi, S.; Cicero, A. F.; Hrelia, S. Bioactive Peptides in Cereals and Legumes: Agronomical, Biochemical and Clinical Aspects. *Int*. *J. Mol*. *Sci*. **2014,** *15* (11), 21120–21135.

Mallikarjun Gouda, K. G.; Udaya Sankar, K.; Sarada, R.; Ravishankar, G. Supercritical CO_2 Extraction of Functional Compounds from Spirulina and their Biological Activity. *J. Food Sci. Technol*. **2015,** *52* (6), 3627–3633.

Manchali, S.; Murthy, K. N. C.; Patil, B. S. Crucial Facts about Health Benefits of Popular Cruciferous Vegetables. *J. Funct. Foods* **2012,** *4* (1), 94–106.

Martínez-Las Heras, R.; Quifer-Rada, P.; Andrés, A.; Lamuela-Raventós, R. Polyphenolic Profile of Persimmon Leaves by High Resolution Mass Spectrometry (LC-ESI-LTQ-Orbitrap-MS). *J. Funct. Foods* **2016,** *23*, 370–377.

Matarese, F.; Cuzzola, A.; Scalabrelli, G.; D'Onofrio, C. Expression of Terpene Synthase Genes Associated with the Formation of Volatiles in Different Organs of *Vitis vinifera*. *Phytochemistry* **2014,** *105*, 12–24.

McCarty, M. F.; DiNicolantonio, J. J.; O'Keefe, J. H. Capsaicin May Have Important Potential for Promoting Vascular and Metabolic Health. *Open Heart* **2015,** *2* (1), e000262.

Meneses, M. A.; Caputo, G.; Scognamiglio, M.; Reverchon, E.; Adami, R. Antioxidant Phenolic Compounds Recovery from *Mangifera indica* L. By-products by Supercritical Antisolvent Extraction. *J. Food Eng.* **2015,** *163*, 45–53.

Messaoudi, R.; Abbeddou, S.; Mansouri, A.; Calokerinos, A. C.; Kefalas, P. Phenolic Profile and Antioxidant Activity of Date-Pits of Seven Algerian Date Palm Fruit Varieties. *Int. J. Food Prop*. **2013,** *16* (5), 1037–1047.

Middha, S. K.; Usha, T.; Pande, V. HPLC Evaluation of Phenolic Profile, Nutritive Content, and Antioxidant Capacity of Extracts Obtained from *Punica granatum* Fruit Peel. *Adv. Pharmacol. Sci.* **2013,** *2013*, Article ID 296236, 6 pages.

Mildner-Szkudlarz, S.; Bajerska, J.; Zawirska-Wojtasiak, R.; Górecka, D. White Grape Pomace as a Source of Dietary Fibre and Polyphenols and its Effect on Physical and Nutraceutical Characteristics of Wheat Biscuits. *J. Sci. Food Agric.* **2013,** *93* (2), 389–395.

Miron, T.; Herrero, M.; Ibáñez, E. Enrichment of Antioxidant Compounds from Lemon Balm (*Melissa officinalis*) by Pressurized Liquid Extraction and Enzyme-Assisted Extraction. *J. Chromatogr. A* **2013,** *1288*, 1–9.

Mlcek, J.; Rop, O. Fresh Edible Flowers of Ornamental Plants—A New Source of Nutraceutical Foods. *Trends Food Sci*. *Technol*. **2011,** *22* (10), 561–569.

Monroy, R.; Colín, H. El guamúchil Pithecellobium dulce (Roxb.) Benth, un ejemplo de uso múltiple. *Madera Bosq*. **2004,** *10* (1), 35–53.

Morel, I.; Lescoat, G.; Cogrel, P.; Sergent, O.; Pasdeloup, N.; Brissot, P.; et al. Antioxidant and Iron-Chelating Activities of the Flavonoids Catechin, Quercetin and Diosmetin on Iron-Loaded Rat Hepatocyte Cultures. *Biochem. Pharmacol*. **1993,** *45* (1), 13–19.

Moure, A.; Cruz, J. M.; Franco, D.; Domínguez, J. M.; Sineiro, J.; Domínguez, H.; et al. Natural Antioxidants from Residual Sources. *Food Chem.* **2001,** *72* (2), 145–171.

Muhammad, K.; Zahari, N. I. M.; Gannasin, S. P.; Adzahan, N. M.; Bakar, J. High Methoxyl Pectin from Dragon Fruit (*Hylocereus polyrhizus*) Peel. *Food Hydrocolloids* **2014,** *42*, 289–297.

Müller, L.; Caris-veyrat, C.; Lowe, G.; Böhm, V. Lycopene and Its Antioxidant Role in the Prevention of Cardiovascular Diseases—A Critical Review. *Crit. Rev. Food Sci. Nutr.* **2015,** *56* (11), 1868–1879.

Naczk, M.; Shahidi, F. Extraction and Analysis of Phenolics in Food. *J. Chromatogr. A* **2004,** *1054* (1), 95–111.

Nagmoti, D. M.; Kothavade, P. S.; Bulani, V. D.; Gawali, N. B.; Juvekar, A. R. Antidiabetic and Antihyperlipidemic Activity of *Pithecellobium dulce* (Roxb.) Benth Seeds Extract in Streptozotocin-Induced Diabetic Rats. *Eur. J. Integr. Med.* **2015,** *7* (3), 263–273.

Nawirska, A.; Kwaśniewska, M. Dietary Fibre Fractions from Fruit and Vegetable Processing Waste. *Food Chem*. **2005,** *91* (2), 221–225.

Nayak, B.; Dahmoune, F.; Moussi, K.; Remini, H.; Dairi, S.; Aoun, O.; Khodir, M. Comparison of Microwave, Ultrasound and Accelerated-Assisted Solvent Extraction for Recovery of Polyphenols from *Citrus sinensis* Peels. *Food Chem*. **2015,** *187*, 507–516.

Nyam, K. L.; Tan, C. P.; Karim, R.; Lai, O. M.; Long, K.; Man, Y. B. C. Extraction of Tocopherol-Enriched Oils from Kalahari Melon and Roselle Seeds by Supercritical Fluid Extraction (SFE-CO_2). *Food Chem*. **2010,** *119* (3), 1278–1283.

Olivas-Aguirre, F.; Wall-Medrano, A.; Gonzalez-Aguilar, G. A.; López-Díaz, J.; Alvarez-Parrilla, E.; De la Rosa, L. A.; Ramos-Jimenez, A. Hydrolyzable Tannins: Biochemistry, Nutritional & Analytical Aspects and Health Effects. *Nutr. Hosp*. **2014,** *31* (1), 55–66.

Otero-Pareja, M. J.; Casas, L.; Fernández-Ponce, M. T.; Mantell, C.; Ossa, E. J. Green Extraction of Antioxidants from Different Varieties of Red Grape Pomace. *Molecules* **2015,** *20* (6), 9686–9702.

Paes, J.; Dotta, R.; Barbero, G. F.; Martínez, J. Extraction of Phenolic Compounds and Anthocyanins from Blueberry (*Vaccinium myrtillus* L.) Residues Using Supercritical CO_2 and Pressurized Liquids. *J. Supercrit. Fluids* **2014,** *95*, 8–16.

Palafox-Carlos, H.; Yahia, E.; González-Aguilar, G. Identification and Quantification of Major Phenolic Compounds from Mango (*Mangifera indica*, cv. Ataulfo) fruit by HPLC–DAD–MS/MS-ESI and their individual contribution to the antioxidant activity during ripening. *Food Chem*. **2012,** *135* (1), 105–111.

Patel, S. *Emerging Bioresources with Nutraceutical and Pharmaceutical Prospects*: Springer, 2015.

Pitchai, D.; Roy, A.; Ignatius, C. In Vitro Evaluation of Anticancer Potentials of Lupeol Isolated from *Elephantopus scaber* L. on MCF-7 Cell Line. *J. Adv. Pharmaceut. Technol. Res*. **2014,** *5* (4), 179.

Prakash, D.; Gupta, C. Glucosinolates: The Phytochemicals of Nutraceutical Importance. *J. Complement Integr. Med.*, **2012,** *9*, Article 13.

Pujol, D.; Liu, C.; Gominho, J.; Olivella, M.; Fiol, N.; Villaescusa, I.; Pereira, H. The Chemical Composition of Exhausted Coffee Waste. *Ind. Crops Prod*. **2013,** *50*, 423–429.

Puri, M.; Sharma, D.; Barrow, C. J. Enzyme-Assisted Extraction of Bioactives from Plants. *Trends Biotechnol*. **2012,** *30* (1), 37–44.

Regulations, N. I. L. E. Ministerial Ordinance No. 41, July 1991. *Amendment to Ministerial Ordinance*; 1996, 33.

Reyes, L. F.; Villarreal, J. E.; Cisneros-Zevallos, L. The Increase in Antioxidant Capacity after Wounding Depends on the Type of Fruit or Vegetable Tissue. *Food Chem*. **2007,** *101* (3), 1254–1262.

Rodrigues, S.; Fernandes, F. A.; de Brito, E. S.; Sousa, A. D.; Narain, N. Ultrasound Extraction of Phenolics and Anthocyanins from Jabuticaba Peel. *Ind. Crops Prod*. **2015,** *69*, 400–407.

Rombaut, N.; Tixier, A. S.; Bily, A.; Chemat, F. Green Extraction Processes of Natural Products as Tools for Biorefinery. *Biofuels, Bioprod. Biorefining* **2014,** *8* (4), 530–544.

Romero-García, J. M.; Lama-Muñoz, A.; Rodríguez-Gutiérrez, G.; Moya, M.; Ruiz, E.; Fernández-Bolaños, J.; Castro, E. Obtaining Sugars and Natural Antioxidants from Olive Leaves by Steam-Explosion. *Food Chem*. **2016,** *210*, 457–465.

Ruiz-Montañez, G.; Ragazzo-Sánchez, J.; Calderón-Santoyo, M.; Velazquez-De La Cruz, G.; de León, J. R.; Navarro-Ocaña, A. Evaluation of Extraction Methods for Preparative Scale Obtention of Mangiferin and Lupeol from Mango Peels (*Mangifera indica* L.). *Food Chem*. **2014,** *159*, 267–272.

Saini, R. K.; Nile, S. H.; Park, S. W. Carotenoids from Fruits and Vegetables: Chemistry, Analysis, Occurrence, Bioavailability and Biological Activities. *Food Res. Int*. **2015,** *76*, 735–750.

Samet, I.; Villareal, M. O.; Motojima, H.; Han, J.; Sayadi, S.; Isoda, H. Olive Leaf Components Apigenin 7-Glucoside and Luteolin 7-Glucoside Direct Human Hematopoietic Stem Cell Differentiation towards Erythroid Lineage. *Differentiation* **2015,** *89* (5), 146–155.

Santos, D. T.; Veggi, P. C.; Meireles, M. A. A. Extraction of antioxidant compounds from Jabuticaba (*Myrciaria cauliflora*) Skins: Yield, Composition and Economical Evaluation. *J. Food Eng*. **2010,** *101* (1), 23–31.

Santos, J.; Herrero, M.; Mendiola, J.; Oliva-Teles, M.; Ibáñez, E.; Delerue-Matos, C.; Oliveira, M. Fresh-cut Aromatic Herbs: Nutritional Quality Stability during Shelf-Life. *LWT—Food Sci. Technol*. **2014,** *59* (1), 101–107.

Saura-Calixto, F.; Serrano, J.; Goñi, I. Intake and Bioaccessibility of Total Polyphenols in a Whole Diet. *Food Chem*. **2007,** *101* (2), 492–501.

Scalbert, A.; Johnson, I. T.; Saltmarsh, M. Polyphenols: Antioxidants and Beyond. *Am. J. Clin. Nutr.* **2005,** *81* (1), 215S–217S.

Schimpl, F. C.; Kiyota, E.; Mayer, J. L. S.; de Carvalho Gonçalves, J. F.; da Silva, J. F.; Mazzafera, P. Molecular and Biochemical Characterization of Caffeine Synthase and Purine Alkaloid Concentration in Guarana Fruit. *Phytochemistry* **2014,** *105*, 25–36.

Semwal, R. B.; Semwal, D. K.; Combrinck, S.; Viljoen, A. Butein: From Ancient Traditional Remedy to Modern Nutraceutical. *Phytochem. Lett.* **2015,** *11*, 188–201.

Sen, C. K.; Khanna, S.; Roy, S. Tocotrienols: Vitamin E beyond Tocopherols. *Life Sci.* **2006,** *78* (18), 2088–2098.

Sen, C. K.; Rink, C.; Khanna, S. Palm Oil-Derived Natural Vitamin E α-Tocotrienol in Brain Health and Disease. *J. Am. Coll. Nutr.* **2010,** *29* (sup3), 314S–323S.

Sen, S.; Asokkumar, K.; Umamaheswari, M.; Sivashanmugam, A.; Subhadradevi, V. Antiulcerogenic Effect of Gallic Acid in Rats and its Effect on Oxidant and Antioxidant Parameters in Stomach Tissue. *Indian J. Pharm. Sci.* **2013,** *75* (2), 149–155.

Setyaningsih, W.; Saputro, I.; Palma, M.; Barroso, C. Optimisation and Validation of the Microwave-Assisted Extraction of Phenolic Compounds from Rice Grains. *Food Chem*. **2015,** *169*, 141–149.

Shahidi, F. Nutraceuticals and Functional Foods: Whole versus Processed Foods. *Trends Food Sci. Technol*. **2009,** *20* (9), 376–387.

Shan, B.; Cai, Y. Z.; Sun, M.; Corke, H. Antioxidant Capacity of 26 Spice Extracts and Characterization of their Phenolic Constituents. *J. Agric. Food Chem*. **2005,** *53* (20), 7749–7759.

Sharma, S. K.; Bansal, S.; Mangal, M.; Dixit, A. K.; Gupta, R. K.; Mangal, A. Utilization of Food Processing By-products as Dietary, Functional and Novel Fibre: A Review. *Crit. Rev. Food Sci. Nutr.* (just-accepted), **2015,** *56* (10), 1647–1661.
Siddiqui, B. S.; Hasan, M.; Mairaj, F.; Mehmood, I.; Hafizur, R. M.; Hameed, A.; Shinwari, Z. K. Two New Compounds from the Aerial Parts of *Bergenia himalaica* Boriss and their Anti-Hyperglycemic Effect in Streptozotocin–Nicotinamide Induced Diabetic Rats. *J. Ethnopharmacol*. **2014,** *152* (3), 561–567.
Siro, I.; Kapolna, E.; Kapolna, B.; Lugasi, A. Functional Food. Product Development, Marketing and Consumer Acceptance—A Review. *Appetite* **2008,** *51* (3), 456–467.
Solana, M.; Boschiero, I.; Dall'Acqua, S.; Bertucco, A. A Comparison between Supercritical Fluid and Pressurized Liquid Extraction Methods for Obtaining Phenolic Compounds from *Asparagus officinalis* L. *J. Supercrit. Fluids* **2015,** *100*, 201–208.
Souto, A. A.; Campos, M. M.; Morrone, F. B.; da Silva, R. B. M.; de Sousa Maciel, I. *Composition Containing Resveratrol and/or Derivatives thereof and Plant Oil, Process for Producing Said Composition, Nutraceutical and/or Pharmaceutical Product, and Method for Enhancing the Potential of Resveratrol*. Google Patents, 2014.
Srivastava, S.; Sonkar, R.; Mishra, S. K.; Tiwari, A.; Balramnavar, V.; Mir, S.; et al. Anti-dyslipidemic and Antioxidant Effects of Novel Lupeol-Derived Chalcones. *Lipids*. **2013,** *48* (10), 1017–1027.
Swain, J.; Kumar Mishra, A. Location, Partitioning Behavior, and Interaction of Capsaicin with Lipid Bilayer Membrane: Study Using Its Intrinsic Fluorescence. *J. Phys. Chem. B* **2015,** *119* (36), 12086–12093.
Szakiel, A.; Niżyński, B.; Pączkowski, C. Triterpenoid Profile of Flower and Leaf Cuticular Waxes of Heather *Calluna vulgaris*. *Nat. Prod. Res*. **2013,** *27* (15), 1404–1407.
Tabart, J.; Kevers, C.; Sipel, A.; Pincemail, J.; Defraigne, J.-O.; Dommes, J. Optimisation of Extraction of Phenolics and Antioxidants from Black Currant Leaves and Buds and of Stability during Storage. *Food Chem*. **2007,** *105* (3), 1268–1275.
Thoo, Y. Y.; Ho, S. K.; Liang, J. Y.; Ho, C. W.; Tan, C. P. Effects of Binary Solvent Extraction System, Extraction Time and Extraction Temperature on Phenolic Antioxidants and Antioxidant Capacity from Mengkudu (*Morinda citrifolia*). *Food Chem*. **2010,** *120* (1), 290–295.
Tolba, M. F.; Azab, S. S.; Khalifa, A. E.; Abdel-Rahman, S. Z.; Abdel-Naim, A. B. Caffeic Acid Phenethyl Ester, a Promising Component of Propolis with a Plethora of Biological Activities: A Review on its Anti-inflammatory, Neuroprotective, Hepatoprotective, and Cardioprotective Effects. *IUBMB Life* **2013,** *65* (8), 699–709.
Torres-Moreno, H.; Velázquez, C.; Garibay-Escobar, A.; Curini, M.; Marcotullio, M.; Robles-Zepeda, R. Antiproliferative and Apoptosis Induction of Cucurbitacin-Type Triterpenes from *Ibervillea sonorae*. *Ind. Crops Prod*. **2015,** *77*, 895–900.
Tuncel, N. B.; Yılmaz, N. Optimizing the Extraction of Phenolics and Antioxidants from feijoa (*Feijoa sellowiana*, Myrtaceae). *J. Food Sci. Technol*. **2015,** *52* (1), 141–150.
Turkmen, N.; Sari, F.; Velioglu, Y. S. Effects of Extraction Solvents on Concentration and Antioxidant Activity of Black and Black Mate Tea Polyphenols Determined by Ferrous Tartrate and Folin–Ciocalteu Methods. *Food Chem*. **2006,** *99* (4), 835–841.
Uchôa-Thomaz, A. M. A.; Sousa, E. C.; Carioca, J. O. B.; Morais, S. M. D.; Lima, A. D.; Martins, C. G.; et al. Chemical Composition, Fatty Acid Profile and Bioactive Compounds of Guava Seeds (*Psidium guajava* L.). *Food Sci. Technol. (Campinas)* **2014,** *34* (3), 485–492.

Valls, J.; Pasamontes, N.; Pantaleón, A.; Vinaixa, S.; Vaqué, M.; Soler, A.; et al. Prospects of Functional Foods/Nutraceuticals and Markets. *Natural Products*; Springer: Berlin, 2013; pp 2491–2525.

Verhagen, H.; Vos, E.; Francl, S.; Heinonen, M.; van Loveren, H. Status of Nutrition and Health Claims in Europe. *Arch. Biochem. Biophys.* **2010,** *501* (1), 6–15.

Wang, L.; Weller, C. L. Recent Advances in Extraction of Nutraceuticals from Plants. *Trends Food Sci. Technol.* **2006,** *17* (6), 300–312. doi:http://dx.doi.org/10.1016/j.tifs.2005.12.004.

Wang, X.; Liu, R.; Zhang, W.; Zhang, X.; Liao, N.; Wang, Z.; et al. Oleanolic Acid Improves Hepatic Insulin Resistance via Antioxidant, Hypolipidemic and Anti-inflammatory Effects. *Mol. Cell. Endocrinol.* **2013,** *376* (1), 70–80.

Yeum, K.-J.; Russell, R. M. Carotenoid Bioavailability and Bioconversion. *Annu. Rev. Nutr.* **2002,** *22* (1), 483–504.

Yin, D.-D.; Yuan, R.-Y.; Wu, Q.; Li, S.-S.; Shao, S.; Xu, Y.-J.; et al. Assessment of Flavonoids and Volatile Compounds in Tea Infusions of Water Lily Flowers and their Antioxidant Activities. *Food Chem.* **2015,** *187*, 20–28.

Zawistowski, J.; Debasis, B. Regulation of Functional Foods in Selected Asian Countries in the Pacific Rim. In *Nutraceutical and Functional Food Regulations in the United States and Around the World*, first ed.; Bagchi, D.; Elsevier Inc.: USA, 2008; pp 365–401.