

# Plant extracts as nutrient enhancers

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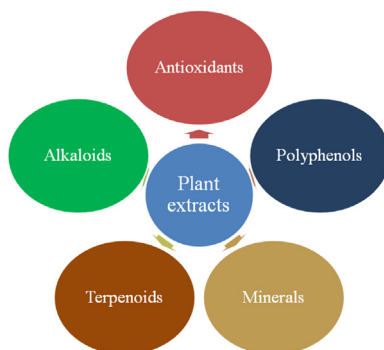
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## 7.1 Introduction

The plant extracts represented by the medicinal, spice, and aromatic plants participate in the daily health and food actions through its numerous active principles and biocomplexes extracted from different methods and processes involving different solvents, allowing the study of the extracts in the condition of raw or purified drug, starting from nature or green plants or from dehydrated plants (Moreira et al., 2005; Passos et al., 2009). The plant extracts are used in the pharmaceutical and cosmetic industries, due to their medicinal and aromatic properties, and some species are used in cooking (Barbieri and Stumpf, 2005; Handa, 2008; Mir et al., 2019). These are primary raw material for folk medicine. The plant extracts contain several vitamins, minerals, antioxidants (AOX), polyphenols, alkaloids, and terpenes (Fig. 7.1).

Plant extracts are an important source of phytonutrients that are beneficial to human health as they have been used since ancient time in traditional drugs (Cunningham, 2015; Loizzo, 2016). These phytochemicals such as vitamins, minerals, polyphenols, AOX, alkaloids, and terpenes possess antioxidant activity (Wong and Chye., 2009), antibacterial (Nair et al., 2005), antifungal (Khan and Wassilew, 1987), antidiabetic (Kumar et al., 2008a; Singh and Gupta, 2007), antiinflammatory (Kumar et al., 2008b), antiarthritic (Kumar et al., 2008c), and radio-protective activities (Jagetia et al., 2005). Owing to these properties, they are largely used for medicinal purpose. Besides, they are important to regulate certain physiological and cellular processes.

The use of plant extracts are becoming more popular in the food industry due to the presence of certain bioactive compounds such as polyphenols, carotenoids, flavonoids, and several other secondary metabolites, which have AOX-like activities against low-density lipoproteins and DNA oxidative changes (Kiokias et al., 2018; Proestos and Varzakas, 2017; Proestos, 2020; Tonthubthimthong et al., 2001). Nevertheless, these bioactive compounds involve in many physiological functions like growth, cell enlargement, tissues formation, and other defense activities. These are extracted synthetically and widely used in food industry to develop functional foods. Plant extracts have been used in cosmetics, pharmaceuticals, and more recently in nutraceutical industries. However, characterization and proper identification of individual compounds are necessary to develop de novo products.

**FIGURE 7.1**

Plants extracts and inherent bioactive constituents.

The phytochemical investigation of a plant may involve the following steps: authentication and extraction of the plant material, separation and isolation of the constituents of interest, characterization of the isolated compounds, and quantitative evaluation (Evans, 2008). Extraction, isolation, purification, and characterization again become tedious job and vary from plant to plant and part. Certain extraction methods such as using solvents, microwave-assisted extraction, ultrasonic extraction have been identified (Altemimi et al., 2017). More recently developed instruments like high performance liquid chromatography (HPLC), Mass spectroscopy, nuclear magnetic resonance, UV–visible infrared technique, etc. can identify the isolated compound (Altemimi et al., 2017). However, more epidemiological studies are needed to validate the strong mechanism and functioning of these bioactive compounds in human health. This chapter provides an overview of inherent bioactive compounds in plant extracts and their role in human health.

## 7.2 Plant extracts as sources of vitamins

Plant-derived vitamins are of great interest because of their impact on human health. They are essential for metabolism because of their redox chemistry and role as enzymatic cofactors, not only in animals but also in plants. Several vitamins have strong antioxidant potential, including both water-soluble (vitamins B and C) and lipid-soluble (vitamins A, E and K) compounds. As one of the seven major nutrients, vitamins play important roles in the body. Vitamins are involved in the processes of normal metabolism and cell regulation, and they are necessary for growth and development, thus they are chemicals that we all need to stay healthy (Glavinic et al., 2017; Khayat et al., 2017). There are thirteen vitamins that are recognized as playing roles in human nutrition (Eggersdorfer et al., 2012). Based on their solubility, these vitamins can be divided into fat-soluble vitamins and water-soluble vitamins. The former contains vitamin A, D, E, and K, while the latter group includes the B-complex and C vitamins. A number of biological functions in the body have been associated with the fat-soluble vitamins (Lounder et al., 2017). Once the amount of vitamins cannot meet the body's needs, the vitamins must be supplied from the diet.

It has been reported that vitamin B1 (thiamin) is lost in food due to leaching and blenching on increased temperature (Serafini et al., 2002). According to a German study fruits and vegetables loses 31% of thiamin due to over cooking about 9% loss is by microwave treatment (Aurea & Samuel, 1998; Hertog et al., 1993). Plant extracts are the key material for traditional drug preparation and folk medicines. These extracts contain many vitamins and other phytochemicals which have therapeutic uses. Sunarić et al. (2020) isolated thiamine and riboflavin from different wild plant extracts with HPLC fluorescence detection. They reported that riboflavin concentration was ranged from 0.84–20.4 µg/g of dry extract whereas thiamine level was 0.06–0.67 µg/g. the highest riboflavin content was reported in wild garlic extract followed by rose-hip extract. Thiamine content was higher in elderberry extract. Datta et al. (2019) determined water-soluble vitamins in different edible plants and their extracts. They found that vitamin B group was the dominant in all species and B1, B2, B6 and B9 were present in all the extracts. They also reported that Vitamin B5 was not detected in any edible plant whereas ascorbic acid was reported to be available in *Asystasia gangetica*, *Oldenlandia corymbosa* with maximum value in *Achyranthes aspera* (151.75 mg/100 g dry plant material). Similarly, *Ipomoea aquatica* had highest vitamin B1, B6 and B9. Ascorbic acid is well known for its AOX properties and its anti infection properties. It reported that *Dryopteris cochleata* leaf extract showed higher ascorbic acid acetone and ethylacetate extracts (157.37 and 156.04 µg/mL, respectively) (Kathirvel & Sujatha, 2016).

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### 7.3 Plant extracts as sources of minerals

Mineral elements also are needed in minute quantities for the proper functioning of the human system, health growth, and development (Igwenyi et al., 2014). Naturally grown herbs and plants also have plenty of macro and trace elements, which are extremely valuable for our body and good health. They play an important role in cell metabolism and antioxidant system (Stern et al., 2007). It has been well documented that intake of minerals such as Ca, Mg, K, Fe, etc. reduce the risk of stroke, hypertension and also involved in oxygen transport system as an enzyme cofactor (Bongoni, et al., 2013; Janz et al., 2013; Larsson et al., 2008). Plant minerals such as selenium, copper, Zn, and Mn are well known for their antioxidant functions (Nikmaram et al., 2018). Calcium is one of the mineral believed to be an important factor governing fruit storage quality (Lechaudel et al., 2005). Ca is the main constituent of the skeleton and is important for regulating many vital cellular activities such as nerve and muscle function, hormonal actions, blood clotting, and cellular mortality (Yagi et al., 2013). Calcium is essential for healthy bones, teeth and blood (Charles, 1992). Phosphorous maintain blood sugar level, normal heart contraction dependent on phosphorous (Linder, 1991) also important for normal cell growth and repair. It helps in the process of ossification of bones by getting deposited in the form of calcium phosphate (Indrayan et al., 2005). Iron is the most well known in biological system. It performs a wide range of biological functions. Iron occupies a unique role in the metabolic process. The role of iron in the body is clearly associated with hemoglobin and the transfer of oxygen from lungs to the tissue cells (Janz et al., 2013; Prajna & Rama, 2015).

Xu et al. (2008) investigated that prolonged time of extraction and temperature could yield more minerals than the phenols and AOX in Pokan and Satsuma mandarin. They also reported

that K was the chief mineral presented in the citrus peel extracts followed by Ca and Mg and Satsuma mandarin contained higher minerals element than the Ponkan peel extract. [Monisha and Ragavan \(2015\)](#) estimated mineral content in polyherbal extracts of various plants and revealed that Fe (4.6 mg/g), P (3.4 mg/g), Ca (2.0 mg/g), and K (1.15 mg/g) were present in the extract. [Staszowska-Karkut and Materska \(2020\)](#) reported mineral content in berry plants extracts and found that minerals such as potassium (K), calcium (Ca), magnesium (Mg), phosphorus (P), sodium (Na), and iron (Fe) copper (Cu), zinc (Zn), manganese (Mn), and boron (B) are present in the leaf extracts. Black currant leaf extract produced highest Ca content followed by Mg, P and Fe when compared with raspberry and Aronia extracts. Raspberry extracts was richest in K, B, and Na whereas Aronia in Mn. [Nour et al. \(2014\)](#) found that time of harvesting greatly influences the level of minerals and they found maximum mineral content (especially Ca) in the month of June in raspberry extract. It has been also documented that leaves contain more amount of minerals than the fruits ([Janz et al., 2013](#)). [Guenane et al. \(2020\)](#) studied the mineral content from the Algerian medicinal plants and remarkably reported the high amounts of K, Ca, Na, and Mg. The lowest content of Na that is  $7168.46 \pm 216.03$  mg/kg was in *Marrubium vulgare* and maximum concentration was estimated at  $24,395.16 \pm 34.41$  mg/kg in *Malva parviflora*. The calcium contents varied between  $3362.38 \pm 442.00$ – $110,354.91 \pm 3446.46$  mg/kg, the highest calcium content was obtained for *M. parviflora* ( $110,354.91 \pm 3446.46$  mg/kg), followed by *Artemisia absinthium* ( $50,200.38 \pm 2529.01$  mg/kg) and *Scorzonena undulata* ( $49,648.51 \pm 3311.26$  mg/kg).

All the plant parts have nutritional qualities, which when used in the right proportions could be of tremendous benefit to the body. Mineral analysis conducted by [Imelouane et al. \(2011\)](#) showed that the *Thymus vulgaris* contained calcium (313,044 mg/kg), magnesium (53,873 mg/kg), potassium (279,491 mg/kg), iron (27,095 mg/kg), zinc (415.33 mg/kg), and manganese (731.41 mg/kg). [Ponmari and Balasubiramanian \(2017\)](#) studied five medicinally important plants such as *Glycyrrhiza glabra* (L.), *Gymnema sylvestre* (R.Br.), *Solanum trilobatum* (L.), *Alpinia calcarata* (Rox.), and *Centella asiatica* (L) and revealed that all the medicinal plants possess the highest Mg and lowest Zn content was observed in all the five studied plants except *Alpinia calcarata*. Mineral content in *Astragalus* spp. extracts have been estimated to differentiate the composition at different growth stages. They have reported higher iron content at vegetative stage 65.29 and 30.19 mg Fe/100 g, in *Astragalus glycyphyllos* and *Astragalus cicer*, respectively, whereas Fe concentration in flowering plants amounted to 21.72 and 14.94 mg/100 g. The study suggests that at early phenological stages of the plants extract contain higher macro and micro-mineral contents ([Butkutė et al., 2018](#)). Sugar maple tree bark extracts showed higher mineral content (K, Ca, Mg, P, Na, Fe, and Cu) and lower Zn and Mn level than the red maple bark extract ([Bhatta et al., 2018](#)). [Biel et al. \(2020\)](#) evaluated mineral profile of globe artichoke leaf extracts and revealed that extract contained K (506.3 mg/100 g DM), P (414 mg/100 g DM), Ca (386.9 mg Ca/100 g DM), Mg in descending order, whereas Zn, Fe, Cr, and Mn were prominent among micronutrients. Due to these, artichoke extract is increasing in demand globally. The content of mineral elements in plants depends to a high degree on the soils abundance, cultivation techniques, soil fertility, nutritional status and extraction ([Kruczek, 2005](#); [Xu et al., 2008](#)). Plant extract contains abundant minerals in sufficient quantity and can be used directly as infusion of as food additives.

## 7.4 Plant extracts as sources of antioxidants

The plants and their products are found throughout human history as herbal supplements as botanicals, nutraceuticals, and drugs (Ekor, 2014). In whole population of the world, about 60%–80% of the population still relies on conventional medicine for the healing of familiar diseases (Ravishankar & Shukla, 2007). Folklore medicine are as a source of primary health care and the chief reason for the use of folk medicine is the accessibility, affordability and cultural beliefs (Tag et al., 2012). Plants have been found of great importance due to their medicinal and nutritional properties with a primary source of bioactive compounds. The use of synthetic and natural food AOX regularly in medicine and foods particularly those having fats and oils to shield the food from oxidation. Butylated hydroxytoluene and butylated hydroxyanisole are the synthetic and natural food AOX which have been used extensively in cosmetic, food and therapeutic industries. But, owing to their instability at high temperatures, high volatility, synthetic antioxidant's carcinogenic behavior, users' inclinations led to shift in the consideration of producers or manufacturers from man-made to natural AOX (Papas, 1999). A variety of medicinal plants extracts have been reported to reveal antioxidant activity, including *Allium sativum*, *Zingiber officinale*, *Crocus sativus*, *Dodonaea viscosa*, *Barleria noctiflora*, *Anacardium occidentale*, *Datura fastuosa*, *Caesalpinia bonducella*, and many more. Numerous AOX identified as active oxygen scavengers or free radicals, obtained naturally from the plant sources are used in food, cosmetic and remedial purposes proved to be brilliant alternatives for man-made AOX because of their inexpensiveness, and have no any harmful effect on human body.

To defy the detrimental effects of reactive oxygen species (ROS), plants have a powerfully built enzymatic and nonenzymatic scavenging pathway. Enzymes included are catalase, superoxide dismutase, ascorbate peroxidase, glutathione reductase, glutathione-S-transferase, dehydroascorbate reductase, monodehydroascorbate reductase, peroxidases, and glutathione peroxidase. Nonenzymatic compounds include glutathione, carotenoids, tocopherols, and ascorbate (AsA). There are unambiguous, well-synchronized ROS generating and scavenging systems present in different organelles of the plant cells. Lesser levels of ROS comparatively act as signaling essences that arouses abiotic stress tolerance by altering the expression of resistant genes. In plants, elevated levels of AOX have been accounted to demonstrate better resistance to different types of environmental stresses (Hasanuzzaman et al., 2012).

Plant produces many nonnutritive secondary metabolites, which have AOX-like effects. AOX are the compounds that protect human against several diseases by scavenging free radical activity. They also protect cell membrane and macromolecules by same mechanism (Wu et al., 2017a). Studies have been investigated that plant extracts like curcumin and ellagic acid are used as food supplements and have antimicrobial activities thus prevent the metabolism of aflatoxin B1 (AFB1) and increase the activity of glutathione-S-transferase involved in the detoxification of xenobiotics (Makhuvele et al., 2020). Plant extracts and flower extracts of *Astragalus* spp. contained AOX level ranges from 7.52 to 35.64  $\mu\text{mol/g}$  (Butkutė et al., 2018). They also showed the highest antioxidant capacity in flower extracts followed by leaves and stem extracts. *A. cicer* extracts had higher 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity than the *A. glycyphyllos* (Butkutė et al., 2018). Several studies showed that the extracts of different spice plants highly effective against food born diseases causing bacteria's (Prashanth et al., 2001; Mahfuzul Hoque et al., 2007; Negi

et al., 2003). The study conducted by Bhatta et al. (2018) reported that red maple bark extracts showed higher antioxidant activity than that of sugar maple bark extracts. A study by Biel et al. (2020) was conducted to find out AOX activity of globe artichoke plant extracts. The study revealed that the ABTS++ assay showed higher antioxidant and very high radical scavenging capacity (79.74%) with AOX capacity at 1060.8 Trolox/1 g DM. Some researchers investigated AOX properties of *Bletilla striata* plant extracts and its polysaccharides in vitro and demonstrated that it has definite DPPH radical, hydroxyl radical, and superoxide anion systems ultrasonic microwave synergistic extraction had higher DPPH and hydroxyl radical activity (Cai et al., 2016; Qu et al., 2016). Extracts from *Kadsura* spp. had shown rich AOX value and key enzyme inhibition properties, thus fruits and other parts extracts could be utilized in food application (Sritalahareuthai et al., 2020). It has been reported that content of AOX positively correlated with the extraction temperature and elevated extraction temperature helps in forming browning compounds as a result of Maillard reaction, thus the level of AOX increases (Anese, Nicoli, et al., 1999; Anese, Manzocco, et al., 1999; Ju & Howard, 2005; Nicoli et al., 1997; O'Brien et al., 1989). Similarly, higher AOX were observed in grape skin extracts when value determined at higher temperature (Ju & Howard, 2005). Datta et al. (2019) performed a study on six medicinal herbs extracts to differentiate the AOX value from various solvent extraction methods and revealed that 70% hydroethanol was proved to better in terms of higher AOX yield followed by methanol. They also reported that Maximum DPPH radical scavenging ability was observed *A. ganjetica* (39.14%) and *A. aspera* (28.051%) whereas FRAP micromole Trolox equivalent (TE)/g was higher in *A. aspera* than the *A. ganjetica*.

## 7.5 Plant extracts as sources of polyphenols

Polyphenols are important secondary metabolites in plants, which have strong free radical scavenging capacity. Owing to their structural arrangement especially (–OH) group makes them antimicrobial in nature (Gyawali & Ibrahim, 2014). Fruits peel, leaves, bark, and root extracts are rich source of polyphenols and contain in a wide range. Phenolic compounds from the natural extracts gained significance importance due to their antioxidant potential and effective against different diseases. Medicinal herbs, tea, coffee, artichoke, leafy vegetables and many fruit plant extracts contain the strong polyphenolic content and its derivatives. Many of them are still in practice as folk medicines in different parts of the world. However, these are more common in rural areas due to their food supplement and primary medicine. Besides, these play crucial role in plant developmental processes and help to plant cope during adverse climatic conditions especially during stresses. Flavonoids are indispensable component found in variety of plants, fruits, vegetables, herbs and their extracts. Current trends and research outcomes on flavonoids suggest that they exert their important role in functioning of lowering down the coronary heart diseases, cardiovascular mortality rate and have great potential to modulate key cellular enzymatic functions (Panche et al., 2016). Tannins are polyphenolics compounds and are classified into hydrolysable and condensed type on the basis of their biological activity and functions. Tannins possess antioxidant value, free radical scavenging activity, antiulcerogenic activities, and antimicrobial and gastroprotective properties (Amarowicz et al., 2004; Ho et al., 2001; Koleckar et al., 2008). Condensed tannins are more



common and abundant in plants and they represent value of common commercial tannin. Several tannins are found in vegetables and are being used as folk medicine. Rubus is another common source of ellagitannin. Some of the tannin like tannic acid and gallic acid is allowed to add in food products as a food additive. Plant phenols are classes of variable organized natural products that are well known to have important antimicrobial and antioxidant activities for their beneficial effects on health (Prashith et al., 2010; Sahu & Mahato, 1994). The primary metabolite is also a precursor to bioactive compounds used as medicinal drugs (Ebi & Ofoefule, 2000). In general, the bioavailability of polyphenols, or the quantity of polyphenols that are consumed unchanged, determines their biological function. After being absorbed, polyphenols could also pass through the gastrointestinal system, thereby affecting the intestinal micro biota. This can have two consequences: first, the active form of polyphenols is modified; Second, the composition of the intestinal micro biota is changed, which is likely to inhibit pathogenic bacteria and enrich beneficial bacteria. Therefore polyphenols have a significant influence on human health (Abbas et al., 2017).

The phloroglucinol and pyrogallol compounds isolated along with ferulic, vanillic, p-coumaric, and caffeic acids constitute the antioxidant activity of the plant (Mazumder et al., 2003). Shikimic acid, gallic acid, B-sitosterol, tannic acid, chebulic acid triethyl ester, gallic acid ethylester, and ellagicethaedioic acid has been confirmed to be in *Terminalia chebula* (Ates & Erdourul, 2003). There are several components in the Terminalia plant, such as tannins, flavonoids, sterols, amino acids, fructose, resin, and fixed oils. Compounds such as anthraquinones, 4, 2, 4 chebulyl-glucopyranose, terpinene, and terpineneol are also found (Srivastav et al., 2010). They can be divided into several groups. Phenols and phenolic acids vary from having several substitutions and hydroxylations to becoming a basic phenol ring with a single substitution such as cinnamic and caffeic acids. The site and degree of hydroxylation are shown to interact with the toxicity of the secondary metabolite. The further oxidized the structure is, the metabolite appears to be more inhibitory (Cowan, 1999). Phenolic inhibition pathways involve inhibiting enzymes. This inhibition is suggested to take place by reactions to the proteins with sulfhydryl groups (Coppo & Marchese, 2014; Cowan, 1999).

It was observed that ethanolic extracts of *Syrian propolis* extracts contain several active compounds including phenolic acids and phenolic aldehydes as well as flavonoids and quinones (Harfouch et al., 2016). The existence of five phenolic compounds, including phenolic acids, cinnamic acid and p-coumaric acid, was confirmed by phytochemical screening using HPLC and ferulic acid as well as catechin and sinapic acid in *Allium ampeloprasum* var. porrumethanolic leaf extract by (Alamri & Moustafa, 2012). The studies confirmed the antibacterial activities in almost all types of polyphenols which were extracted as solvent extraction.

Maple bark is a rich source of phenolics compounds and has glucidase inhibitory and anticancer activities (Yuan et al., 2011, 2012). Several plant parts and their extracts have been used to characterize the content of total phenolics. A diverse value of total phenolic content (TPC) in *Annona crassiflora* has been determined from different extraction methods and different parts (Arruda et al., 2017, 2018; Arruda & Pastore, 2019). Phenolic compounds have been investigated to different AOX activities, anticancer properties, antimicrobial and antiinflammatory properties (Caleja et al., 2017). Tusevski et al. (2014) reported a TPC (15.93 mg GAE/g) in liquorice milkvetch. Similarly, Butkutė et al. (2018) reported that *A. glycyphyllos* extracts from leaves and flowers contained higher amount of phenolic compounds (25.99 and 23.71 mg GAE/g, respectively). Bark extracts from red maple tree shows significant higher amount of TPC ( $40.12 \pm 0.86$  g GAE/100 g

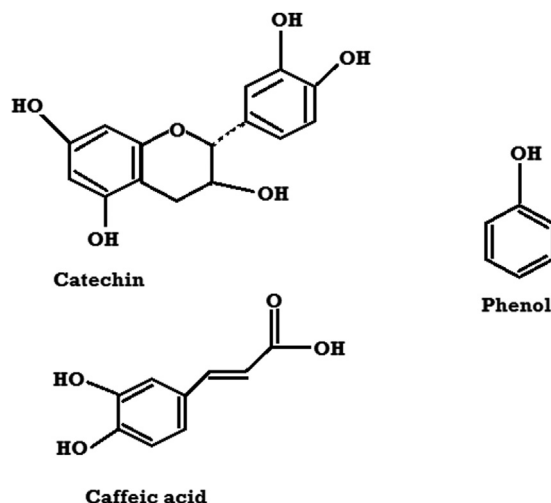
dry extract) than the white extracts. The study confirmed that the TPC in maple tree was higher than that of some tropical fruits by products in which TPC ranges from (0.37–0.46 g of GAE/100 g dry matter) (Selani et al., 2016). However, green tea leaf extract shows higher TPC (29.8 g GAE/100 g) than the white maple bark extract (Yin et al., 2012). Each and every plant has different amount of phenolic content and its composition and there are several multiple approaches used to characterization and isolation of composition. Many researchers determined the phenolic content in artichoke leaf extract and found 2795 mg CAE (chlorogenic acid equivalents)/100 g DM by Biel et al. (2020), in green globe leaf extract it varies from 8760 to 9561 mg CAE/100 g DM (Wang et al., 2003) and 3167 mg caffeic acid equivalent/100 g DM by Salata and Gruszecki (2010). Several researchers compared the different solvent extraction process (including water extract) in numerous plants and herbs extracts and found promising results when used methanol as extract solvent (Ademoyegun et al., 2013; Gouveia & Castilho, 2012). TPC from twenty five leafy vegetables was determined by Ademoyegun et al. (2013) and the highest TPC content 164.52 mg GAE/100 g DM was found in methanol extract from *Sesamum radiatum*. It is a well-established fact that polyphenols have very strong antioxidant potential as compare to carotenoids and ascorbic acids (Biel et al., 2020) thus the plant extracts derived polyphenols well recognized with numerous therapeutic uses. As mentioned earlier, the extraction procedure makes differences in the value. A study conducted by Xu et al. (2008) in that hot water extraction of total phenol acids were carried out of citrus peel extracts of ponkan and Satsuma mandarin. They reported that ferulic acid was the dominant phenolic acid in both the citrus peel extracts, however, extract of Ponkan had higher content of caffeic and p-coumaric acid. Grape extracts and seed extracts is very rich in polyphenols and had been reported to be beneficial in reducing the risk of cardiovascular diseases and type-2 diabetes. It has been reported that cinnamon extract induces the glycogen synthase and insulin receptor kinase, triggers glucose uptake with inhibitory action on glycogen synthase kinase-3 beta and dephosphorylation of the insulin receptor thus enhance insulin sensitivity (Lin et al., 2016). Coffee extract rich in chlorogenic acid that has beneficial effects on type -2 diabetes, reason being chlorogenic acid inhibits Na<sup>+</sup>-dependent glucose transporters, SGLT1 and SGLT2 by interacting with the absorption of glucose from the intestine (Bassoli et al., 2008; Greenberg et al., 2006; Johnston et al., 2005; McCarty, 2005). The study also suggests that elevated extraction time may reduce the amount of TPC and at 100°C some of phenols get destroyed (Xu et al., 2008). Tea leaves extract contains an excellent amount of polyphenols including catechin and gallic acid. Salehi et al. (2019) reviewed the phytochemical composition of berberis plant extract and reported various tannins, polyphenols, essential oils and their application in food industry. Chemical structure of some important phenolic are depicted in Fig. 7.2.

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## 7.6 Plant extracts as sources of alkaloids

Plants have always been a cornerstone for the traditional medicine systems, and they have brought continuous remedies to the mankind for thousands of years. It is observed that plants synthesize many secondary metabolites that support the plants to survive and reproduce (Jing et al., 2014). These secondary metabolites are alkaloids, phenols, steroids, glycosides, tannins, terpenoids, and phytoalexins. Among these, the most important group of secondary metabolites are the alkaloids



**FIGURE 7.2**

Chemical structure of catechin, caffeic acid, and basic phenols.

that are known to possess ample therapeutic properties (Roy, 2017). Alkaloids have strong biological effects on human as well as on animals in very small doses. They are found not only in food and drinks but also available as stimulant drugs which showed antiinflammatory, anticancer, analgesics, local anesthetic and pain relief, antimicrobial, antifungal and many other activities. Alkaloids are beneficial as ingredients for foods, supplements, pharmaceuticals, and in several other applications in human life (Kurek, 2019).

Alkaloids are a group of naturally occurring chemical compounds that contain mostly basic nitrogen atom. They are also some properties with neutral (McNaught, D. & Wilkinson, 1997) and even weak acid properties (Manske, 1965). These nitrogen atoms are usually situated in a ring/cyclic structure. The word “alkaloid” is derived from a Latin word “alkali” which is used to describe any nitrogen—containing base. These alkaloids are usually organic bases and can react with acids to form salts (Roy, 2017). Morphine was the first alkaloid to be isolated from opium poppy in crystalline form by a German chemist, Friedrich Serturmer in 1804. Generally based on the structures (heterocyclic ring system), alkaloids can be classified into different classes such as indoles, quinolines, isoquinolines, pyrrolidines, pyrrolizidines, tropanes, terpenoids, and steroids. Type of alkaloids and their source are mentioned in Table 7.1.

No such classification exists, but they can be differentiated on the basis of structural pattern like indole alkaloids or precursor such as benzyloisoquinoline, tropane, pyrrolizidine, or purine alkaloids (Kennedy & Wightman, 2011). Alkaloids contributed majority of neurotoxins, and traditional psychedelics such as atropine, scopolamine, and hyoscyamine, from the belladonna (*Atropa belladonna*) plant and traditional drugs such as nicotine, caffeine, methamphetamine (ephedrine), cocaine, and opiates from a group of plants for mankind purposes (Goldman, 2001; Zenk & Juenger, 2007). It has been confirmed by various studies that plant based alkaloids are toxic to mammals except caffeine and nicotine which are widely consuming by tea, coffee and tobacco

**Table 7.1 Availability of different types of alkaloids in plant extracts.**

Name plants	Alkaloids present	References
<i>Annona crassiflora</i>	Aporphine, atherospermidine, liriodenine, stephalagine, annonine	Arruda et al. (2017); Goncalves et al. (2006); Pereira et al. (2017)
<i>Atropa belladonna</i>	Atropine, scopolamine, and hyoscyamine	Goldman (2001)
<i>Barberis vulgaris</i>	Berberine, berberrubine	Rahimi-Madiseh et al. (2017); Yu et al. (2018)
<i>Cammelia sinensis</i>	Caffeine, thearufllavin, catechine	Chen et al. (2008); Guo et al. (2008); Kennedy and Wightman (2011)
<i>Catharanthus roseus</i>	Vincristine, vinblastine	Moudi et al. (2013)
<i>Chondrodendron tomentosum</i>	Tubocurarine	Moudi et al. (2013)
<i>Cinchona officinalis</i>	Quinine	Achan et al. (2011)
<i>Cinchona pubescens</i>	Quinine, quinidine, cinchonine, acronycine, melicopine, melicopidine, and acronycidine	Moore et al. (1995); Tillequin (1997)
<i>Coffea</i> spp.	Caffeine, theobromine, theophylline	Ashihara et al. (2008); Desgagné-Penix (2017); Koyama et al. (2003)
<i>Cola acuminata</i>	Kolatine, kolateine	Ashihara et al. (2008); Desgagné-Penix (2017)
<i>Nelumbo nucifera</i>	Neferine, nuciferine, nornuciferine, <i>N</i> -methylasimilobine	Morikawa et al. (2016); Zhang et al. (2015)
<i>Nicotiana tabacum</i>	Nicotine	Kennedy and Wightman (2011); Zulak et al. (2006)
<i>Opium poppy</i>	Morphine, codeine	Hussain et al. (2018)
<i>Papaver somniferum</i>	Morphine	Hussain et al. (2018)
<i>Piper nigrum and Piper longum</i>	Piperine, piperic acid, piperlonguminine, Pellitorine, piperolein	Takooree et al. (2019)
<i>Rhizoma coptidis</i>	Berberine, palmatine, berberrubine	Chen et al. (2008); Kupeli et al. (2002); Kuo et al. (2004); Li et al. (2014)
<i>Solanum tuberosum</i>	α-Solanidine, α-solanine	Jadhav et al. (1981)
<i>Theobroma cacao</i>	Caffeine, theobromine	Zulak et al. (2006)

plants (Kennedy & Wightman, 2011). Many types of classifications have been proposed by researchers. The most popular classification among them divides the entire class of compounds into three categories (Eagleson, 1994), which are as follows:

1. True—alkaloids are compounds that is derived from amino acid and possess a heterocyclic ring with nitrogen.

For example, atropine, nicotine, etc.

2. Proto—alkaloids are compounds that are derived from amino acid and also contain a nitrogen atom which is not a part of heterocyclic ring structure.

For example, adrenaline, ephedrine, etc.

3. Pseudo—alkaloid are compounds that is not derived from amino acid.

For example, caffeine, theobromine, etc.

Some studies have suggested that tea extracts are very rich in different alkaloids. Green and black tea leaf extract contains caffeine, catechin, theaflavin, and saponins (Chen et al., 2008; Guo et al., 2008; Vignoli et al., 2011). Caffeine concentration reported to be higher in green tea leaves (Ramdani et al., 2018). Quinine is an alkaloid obtained from the bark of *Cinchona officinalis* belonging to the family Rubiaceae. It is used as a powerful antimalarial drug (Achan et al., 2011). Colchicine is obtained from the plants of Liliaceae family, which is used for the treatment of gout (Kurek, 2019). Atropine belongs to tropane group of alkaloids that is obtained from *A. belladonna* of Solanaceae family (Kurek, 2019). Tubocurarine is an alkaloid, obtained from *Chondrodendron tomentosum* which acts as a muscle relaxant and is an ingredient of poison curare. Alkaloids vincristine and vinblastine are obtained from the pink periwinkle plant extracts, *Catharanthus roseus* belonging to family Apocynaceae (Moudi et al., 2013). Morphine is one of the most recognized alkaloids that have been used and is still intended for medical purposes. It is present in dried latex of unripe capsules of *Papaver somniferum* (Hussain et al., 2018). Codeine is a derivative of morphine from opium poppy that possesses excellent analgesic property. Morphine (10%) and codeine (0.5%) are present in opium.

Pereira et al. (2017) first time isolated and characterized the aporphine alkaloid namely stephalagine from the *A. crassiflora* peel extract. It has been reported that *Astragalus* spp. extract contains neurotoxin indolizidine alkaloid, swainsonine (Kristanc & Kreft, 2016). Similarly, Goncalves et al. (2006) characterized and isolated two alkaloids atherospermidine and liriodenine from the plant stem. Arruda et al. (2017) found alkaloid stephalagine content up to 30 mg/kg DW in *A. crassiflora*. However, annonine is another chief alkaloid present in *Annona* leaves due to geographical variations. Chen et al. (2008) analyzed the berberine (a isoquinoline alkaloid) from *Rhizoma coptidis* herb. Piperine, a well-known alkaloid from *Piper nigrum* and *Piper longum* has been using since many centuries. Berberine and berberrubine also extracted from *Barberis vulgaris* and used to cure jaundice, toothache, asthma, skin pigmentation, etc. (Rahimi-Madiseh et al., 2017; Yu et al., 2018). Zhang et al. (2015) reported that neferine alkaloid is found abundantly in *Nelumbo nucifera*. Takooree et al. (2019) reported that major alkaloids in *P. nigrum* are piperine, piperic acid, piperlonguminine, pellitorine, piperolein B, piperettine, etc. are present which show the biological activities.  $\alpha$ -Solaniidine and  $\alpha$ -solanine are major glycoalkaloids distributed in potato (Jadhav et al., 1981).

Ferré (2008) found that caffeine is a competitive antagonist in mammals of inhibitory adenosine A<sub>1</sub> and A<sub>2</sub> receptors, which leads to activation via increased dopaminergic and glutamatergic activity. It is most commonly and widely used psychoactive compound due to its stimulatory effect. Caffeine is active constituents found in many herbs and plants such as tea (*Camellia sinensis*), guarana (*Paulinia cupana*), maté (*Ilex paraguariensis*), and cocoa (*Theobroma cacao*). Tobacco plant (*Nicotiana tabacum*) produces nicotine (a pyridinealkaloid) which has insecticide and antiparasite properties (Zulak et al., 2006). Milugo et al. (2013) reported antagonistic correlation between alkaloids and saponins in *Rauvolfia caffra* plant extracts. They reported that leaf extracts containing

saponins along with alkaloids, steroids, terpenoids glycosides showed poorest AOX activity (15%) whereas without saponins these all compounds in fraction showed strongest AOX activity (42.39%). Several studies revealed that alkaloids obtained from *R. coptidis* namely berberine and palmatine have antiinflammatory activity and widely used as traditional medicine in China (Kupeli et al., 2002; Kuo et al., 2004). Li et al. (2014) had done quantitative analysis of total alkaloids and their seasonal variation in *R. coptidis* plant extracts taken in various months. The result confirmed that berberine was the chief alkaloid throughout the growing period ranged from 35.22 to 79.45 mg/g DW followed by palmatine ranged (9.92 to 23.99 mg/g DW) coptisine (17.09–41.85 mg/gDW), jateorrhizine (2.98–6.88 mg/g DW), epiberberine (7.52–21.08 mg/g DW), and columbamine (5.02–10.84 mg/g DW). In addition to that, authors also reported that season has great impact on the quantity of alkaloids and sample collected during spring season had the higher amount of total alkaloids followed by July and October (Li et al., 2014). Physiological role of alkaloids is mainly due to defense against pathogen and herbivores and equally have several medicinal benefits if intake in permissible limit. Desgagné-Penix (2017) reviewed the distribution of alkaloids in woody plants. Isah (2016) reported that a tree *Taxus brevifolia* yields an important alkaloid taxol (Paclitaxel) which has anticancerous properties. Purine alkaloids such as caffeine, theobromine and theophylline were abundantly found in coffee bean extracts, cocoa beans, kolatine, and kolatene in *Cola acuminata* and other nonwoody species like tea, gurana, etc. (Koyama et al., 2003; Ashihara et al., 2008; Desgagné-Penix, 2017). Quinoline alkaloids (quinine, quinidine, cinchonine, acronycine, melicopine, melicopidine, acronycidine, etc.) are extracted from quinine tree (*Cinchona pubescens*), species of *Acronychia*, *Sarcomelicope* and *Acronychia acidula* (Epifano et al., 2013; Moore et al., 1995; Tillequin, 1997). Mulberry and coca bush also produce tropane alkaloids (Moore et al., 1995). Pomegranate tree and fruit extracts also rich in pyridine alkaloids. *Zanthoxylum* a member of Rutaceae family produces canthin-6-one alkaloid from bark and peel extracts (Cebrián-Torrejón et al., 2012). Plant extracts of *Acacia rigidula* possess indole category of alkaloids (including bcarbolines, harmine, harmaline, elaeagnine, tryptoline, etc.) (Clement et al., 1998). A quantitative analysis with mass liquid spectroscopy has been carried out to isolate alkaloids in flower extract of *Nelumbo nucifera* (Morikawa et al., 2016). They have isolated nuciferine, nornuciferine, *N*-methyasimilobine, asimilobine, pronuciferine, and arnepavine alkaloids. Due to the structural diversity and alkalinity, their fractionation and characterization faced practical difficulties. Recent chromatographic techniques could be used for efficient quantification and characterization. Alkaloids due to their wide array and adaptability, represents a path for pharmaceutical and nutraceutical industries. Many vegetables, herbs and bitter fruits contain high amount of glycoalkaloids but need care when consuming such foods.

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## 7.7 Plant extracts as sources of terpenes

Terpene is an isoprene-based naturally occurring compound having medicinal potential and found in plants and animals. Terpenes belong to hydrocarbon groups that consist of 5-carbon isoprene (C<sub>5</sub>H<sub>8</sub>) units as their basic building block. However, only few terpenes have been investigated for their medicinal uses (Franklin et al., 2000). Among the all, 67% potentiates belong to monoterpenes and sesquiterpenes. Terpene has activities such as antiinflammatory and also prevent inflammatory

diseases (Franklin et al., 2000). Most common plants like tea, cannabis, citrus fruits, salvia, etc. contain abundant amount of medicinal terpene. Some important terpenes like p-menthane monoterpenoids, cannabinoids, etc. synthesized through 2-C-methyl-d-erythritol-4-phosphate pathway whereas thapsigargin and artemisinin produced through the mevalonate pathway. There are some common plant terpenes which are integral part of human diet. Terpenes are diverse group of lipid-soluble compounds ubiquitously synthesized via mevalonate and deoxy-d-xylulose pathways (Rohmer, 1999). These comprise one or 5-carbon isoprene units. Likewise, terpenoids don't have separate classification system but they are classified on the basis of number of isoprene units such as hemiterpene (1 unit), monoterpene (2 units), sesquiterpene (3 units), and so on. Terpenes show the toxicity to the insects but they are less toxic to mammals (Rattan, 2010). Nowadays, recent studies showed that terpenoids are also present in our food system and contribute flavors and essential components to our diet. *Ginkgo biloba* leaf extracts have been used since long back and it reported that extracts of *G. biloba* yield species specific terpenes such as bilobalide and ginkgolides A, B, C, and J which show insecticidal, antifeedant, and antimicrobial activities (Ahn et al., 1997; Kleijnen & Knipschild, 1992; Matsumoto & Sei, 1987; Mazzanti et al., 2000). It is also reported that genus *Carissa* contains good amount of sesquiterpenes (Kirira et al., 2006; Wangteeraprasert & Likhitwitayawuid, 2009). Kumar et al. (2018) reported that bark and leaf extracts of Arjun tree contains terpenoids in ethanolic extracts. Some forest tree groups such as conifer oleoresin contains monoterpenes such as pinene and camphor; diterpenes such as taxadiene and phytane, sesquiterpenes like nerolidol (Martin et al., 2003). Several studies reported that terpenes from some forest species show antiinflammatory activities. A terpenes namely  $\alpha$ -Pinene found in coniferous and rosemary showed such effects (Cho et al., 2017). The *Mentha* plant contained several p-menthane monoterpenoids. There are two types cannabinoids from *Cannabis sativa*, that is, D9-tetrahydrocannabinol and cannabidiol reported for their psychoactive and pain relieving properties, respectively (Bergman et al., 2019). It has been reported that wormwood (*Artemisia annua* L.) a plant of Asteraceae family produced sesquiterpene endoperoxide artemisinin which is highly effecting against malarial diseases (Meshnick et al., 1996; Nosten & White, 2007). Similarly, Thapsigargin from *Thapsia garganica*, Ingenol 3-mebutate from *Euphorbia peplus* and *Euphorbia lathyris* have been isolated and used in various treatments (Siller et al., 2009). Antibacterial mode of terpenes is still unknown and unclear however, some researchers tried to elucidate the possible mechanism, that is, oxygen uptake and oxidative phosphorylation, which are crucial for microbes survival (Griffin et al., 1999). Diterpenes show its efficacy in combination therapy with antibiotics (Gupta et al., 2016). Among them, beta-carotene, phylloquinone, and tocopherols constitute pro vitamin activity while some phytosterols and essential oils provide health benefits by acting as AOX.

## 7.8 Conclusion

Plant extracts of various medicinal, fruits, and vegetable herbs are rich in phytonutrients, thus these have a great potential to cure many diseases. Vitamins and minerals are the primary nutrients present abundantly in various plant extracts and furnish various functions alone or in combination with other phytochemicals. Phenolic compounds, flavonoids, terpenes, etc. act as strong AOX and capable of scavenging free radicals thus urgent need to explore such fractions for future medicinal

purposes. Alkaloids are also becoming integral part of diet due high drug potential and therapeutic uses. Identification and characterization of these bioactive compounds may be difficult through traditional extraction processes, therefore the use of advanced methods such as ultra heat extraction, liquid chromatography, HPLC, and mass spectroscopic determination could enhance the efficacy and efficiency. The use of plant extracts for their bioactive compounds is a new era for commercial pharmaceutical and nutraceutical industries and need to be enhanced for mankind.

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