COFFEE: THE RATIONALE BEHIND 4 CENTURIES OF CONSUMPTION

Sherweit H. El-Ahmady and **Mohamed L. Ashour**
Pharmacognosy Department, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt

Keywords: coffee, coffea arabica, coffea canephora, coffea liberica, rubiaceae, caffeine, chlorogenic acid, robusta, cafestol, kahweol.

Contents

Summary

Coffee is one of the most widely consumed beverages worldwide. The Arabs were the first to cultivate coffee during the 14th century and by the 17th century; it was introduced into the New World and established as the new commodity crop. Coffee seeds were initially chewed as a masticatory stimulant in ancient times. Since then, the dried coffee beans are roasted and ground then brewed to make the popular coffee beverage, which is mostly consumed for its addictive stimulant alkaloid, caffeine. In addition to caffeine, coffee constitutes a complex mixture of compounds, including carbohydrates, lipids, nitrogenous compounds, vitamins, minerals, alkaloids, melanoidins and phenolics. Studies have shown the beverage to exhibit various health promoting biological activities including antioxidant, antimicrobial, anti-inflammatory, anti-obesity, hepatoprotective, anticancer as well as important effects on the cardiovascular, digestive, and nervous systems. In this chapter, we present an overview of the origin of coffee, its history, chemical constituents, health benefits and economic as well as cultural impact on society. The information presented is mainly in regards to *Coffea arabica*, the more widely cultivated coffee species worldwide but brief reference is also made to other species when relevant.

1. Origin and History

The beverage, coffee, is produced from the processing of roasted coffee beans, which are the seeds of the cherry fruit growing on coffee trees. Coffee is mainly produced

from the *Coffea* species: *C. arabica, C. canephora* var. robusta and *C. liberica* producing Arabica, Robusta and Liberian (Liberica) coffees respectively. *C. arabica* accounts for 75% of the world's coffee production, originating from Ethiopia but growing in Brazil, Colombia, Mexico, Ethiopia, El Salvador, Costa Rica, Honduras, Indonesia, Guatemala, Ivory Coast, Angola, Jamaica, Uganda, India, Philippines, Cameroon and Vietnam. It is also cultivated in Angola, Cambodia, China, Puerto Rico, the Virgin Islands, Papua New Guinea, Guam, Samoa and Australia. Coffee produced from *C. arabica* is finer and more expensive than Robusta coffee due to critical growing conditions and demands of particular care and attention. The Arabica coffee is also commonly referred to as Abyssinian Coffee, Brazilian coffee or green coffee. These trees are more prone to disease than *C. canephora* and growing on high rise steep locations makes accessibility difficult. *C. canephora* is indigenous to tropical West and Central Africa (Benin, Burkina Faso, Cote d'Ivoire, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo), eastwards to Uganda and north to south from Cameroon to northern Angola. It is also distributed in Brazil as well as parts of Southeast Asia, including Indonesia and Vietnam. It is commonly known as Robusta coffee, also referred to as Congo coffee, and represents a third of the global coffee production. These trees are much easier to maintain; withstand higher temperatures than Arabica and are cultivated at lower altitudes. Robusta beans produce a coffee which has a distinctive taste and about 50-60% more caffeine than Arabica. The Robusta variety is primarily used in blends, for instant coffees and in espresso blends as fillers to enhance the coffee body and provide the formation of 'crema' while the gourmet coffee market is mostly produced from the Arabica variety. In recent years, Vietnam has become the world's leading exporter of Robusta coffee. As for *C. liberica*, it is indigenous to tropical West Africa where it is distributed in the same areas as *C. canephora* and currently this species is mainly cultivated in Malaysia, Indonesia, Philippines West Africa, Bioko island (Fernando Po), São Tomé, Surinam and Guyana. It is also grown in Mauritius, India, Sri Lanka, Thailand, Vietnam, Taiwan, and Timor. The Liberica coffee, commonly known as Monrovia coffee, is inferior in quality and less popular than Arabica or Robusta, but it is more popularly consumed in Southeast Asia.

The first introduction of coffee is thought to be in the old region of Kefa, currently a part of Ethiopia. As legend goes, sometime around 850 A.D. in Abyssinia, current-day Northern Ethiopia, a goat herder named Kaldi noticed that his goats were strangely highly active after eating red berries from a small, broad-leaved shrub. These red berries were coffee cherries covering the green coffee bean, the seed of the coffee tree. The legend goes on to tell of an abbot in a local monastery concerned with a lack of alertness of monks during early morning prayers, decided to try the beans after hearing of its effect on the goats. This is speculated to be the reason for the presence of coffee trees in monastery gardens across the Arab world. Interestingly, prior to drinking of the coffee beverage, consumption of coffee was described as a high-energy snack made from a mix of the beans and fat during long journeys like those made by slaves brought from East Africa to Arabia between the 1st and 5th centuries A.D. The discarding of the snacks along the way, led to the growing of coffee trees especially in the region of Mocha, a port in current-day Yemen. So, 'Mocha', a label for fine modern day coffee was actually the name of the major area for coffee cultivation and the ancient port from which it was exported to the rest of the world. The circumstances of the transition from

beans in a ball of fat to today's 'roast and ground' coffee drink remains unclear, however the drink gained popularity in the Muslim world as an acceptable, nonalcoholic drink that was also suitably invigorating before prayer. The coffee drink spread to Aden in Yemen, onwards to Mecca and from the Arabian Peninsula to Persia, Egypt, Syria and Turkey. The appearance of the first public coffee houses 'kahveh khaneh' marked the growing popularity of coffee. The coffee houses became a place people frequented for all kinds of social activity as listening to music, watching performers, playing chess and keeping current on the news of the day. Coffee houses also became centers of all kinds of information exchange from poetry to science, so that the coffee houses were often referred to as 'Schools of the Wise.' Coffee's popularity grew among the devoted Muslims to an extent where the religious advocates and rulers feared its inclination to becoming an overindulgence. In the 16th century, drinking coffee was first prohibited in many of the Muslim territories including Mecca, and restrictions were applied, the strictest being in Turkey, in 1656, where consumption of the banned beverage was punishable by drowning. The word for coffee originally was through its Turkish form 'kahveh'.

Coffee was first introduced to Europe through travelers. One of the initial accounts was by Leonhard Rauwolf, the town physician of Augsburg who, in 1582, in his published journal of his tales of his travels in the Far East, describes coffee as a very good black drink called 'Chaube' that was used in treating stomach illness. The Christians first perceived the drink as 'devil's brew' or the 'bitter invention of Satan' offended by the black color and in retaliation for Muslims banning Christ's sanctified beverage – wine. Later on, Pope Clement 'baptized' the drink and coffee slowly spread from the Middle East to Europe. Coffee was consumed in the late 1600s in public places and the first coffee house was located in Oxford in 1650 at 'the Angel at the parish of St. Peter in the East'. By the mid-17th century, there were over 300 coffee houses in London. However, women were not allowed in these coffee houses and were confined to socializing at home over coffee parties where they would entertain their friends. These coffee houses were dwellings where people gathered for discussions and even individual houses became known for different areas of knowledge. Booths in coffee houses were made available for doctors to meet patients and businessmen to meet for commerce. Many businesses grew out of these specialized coffee houses. Lloyd's of London, for example, came into existence at the Edward Lloyd's Coffee House. The first advertisement for coffee appeared in 1657 in a London paper and through pamphlets, books and advertisements, health claims were made on coffee, both positive and negative. With the birth of the industrial revolution, caffeinated beverages grew in popularity in an effort to replace the more prevalent alcoholic drinks posing a challenge to the operation of complex machinery. Another commodity that played a role in the increasingly widespread of coffee acceptance was sugar, imported from India in the 14th century and made available to the public in the 18th century. The bitterness of tea and coffee made it a convenient vehicle for the consumption of large quantities of sugar by factory workers as a source of energy. By the mid-1600s, coffee had reached the New World (America) and coffee houses rapidly spread in New Amsterdam (current New York). It was not until "The Boston Tea Party" in 1773, that the Americans changed their tea preference to coffee after the colonists revolted against a heavy tax on tea imposed by King George. Till this day, the dominant hot drink in the United Kingdom, still remains tea while coffee is the hot drink of choice in Germany and Sweden and the national drink in

the United States. Though the Arabs tried hard to maintain the coffee monopoly within Arabia, the Dutch succeeded in obtaining some coffee seedlings and grew plantations in the islands of South East Asia (current Indonesia) while the coffee trees throughout the Caribbean, South and Central America originated from the French. Coffee seeds were carried to new lands and plantations were established worldwide and by the end of the 18th century, coffee had become one of the world's most profitable export crops.

2. Taxonomy and Botanical Features

The genus *Coffea*, a member of the *Rubiaceae* family, the *Ixoroideae* subfamily, tribe of *Coffeeae* DC. comprises around 104 species. The species *Coffea arabica* L. and *Coffea canephora* Pierre ex A. Froehner are the most commonly cultivated species of this genus and account for 99% of the coffee drink produced worldwide. According to taxonomists, all species of *Coffea* originated from the intertropical forests of Africa (41 species), Madagascar and the Comoros (59 species) and the Mascarenes (3 species) where each location has 100% endemicity for its *Coffea* species. The wide distribution of *C. canephora* and *C. liberica* is probably attributed to the naturalization of these species for commercial production. New species are still being discovered and described, an example is the caffeine-free species; *Coffea charrieriana* Stoff. , recently discovered in Cameroon (2008). In Africa, *Coffea* species are distributed in a diversity of forest types, but primarily found in humid, evergreen forests. The highest number of varieties of *Coffea* species are distributed in Cameroon, Tanzania and Madagascar. The major varieties of *C. arabica* include Bourbon, Typica, Caturra, Mundo Novo, Tico, San Ramon, Jamaican Blue Mountain while Robusta is the prevalent variety of *C. canephora*.

Figure 1. *Coffee arabica* tree

Figure 2. Berries on the coffee tree

The trees of *C. arabica* are glabrous shrubs or small evergreen trees, growing up to 5 m tall when unpruned with an open-branching system. These trees can grow for 20-30 years. Leaves are opposite, dark green, glossy, oblong elliptic to broadly elliptic, 7-20 cm long by 2.5-6.5 cm wide with 7-10 pairs of lateral veins, an acuminate or acute apex, an acute base, and a simple entire, slightly undulating margin. Petioles are short and stipules deltoid and acute. Flowers are white fragrant, stellate in outline, and form axillary clusters of 2-9 flowers. A single flower is 1.0-1.5 cm across, with a small cupulated calyx, a tubular corolla 10 mm long with 5 segments, 5-7 mm long. Each flower has 5 stamens with 7-8 mm long anthers and the ovary is usually 2-loculed with a bifid stigma. The fruit is an ovoid, ellipsoid to oblong fleshy berry, 10-18 mm long, green maturing to red in color turning black on drying. The fruit contains two ellipsoidal seeds which are 8-12.5 mm long, flattened on one side with a medial straight or s-shaped groove and enclosed in two membranes, the outer one is called the 'parchment' and the inner one is known as the 'silver skin'.

3. Production and Processing

Optimum conditions for coffee cultivation are cool, mildly humid climate, usually grown at high altitudes of 1,300-1,500 m in the tropics and subtropics. Studies have shown that trees of *Coffea* species not only thrive in shade but also may lead to improved bean yield, size and weight in addition to beverage quality. The beans of shade grown plants were found to constitute a higher percentage of caffeine and fat

whereas sucrose, chlorogenic acid and trigonelline were highest in beans of sun-grown plants which explains the higher bitterness and astringency of the beverage produced from the latter beans.

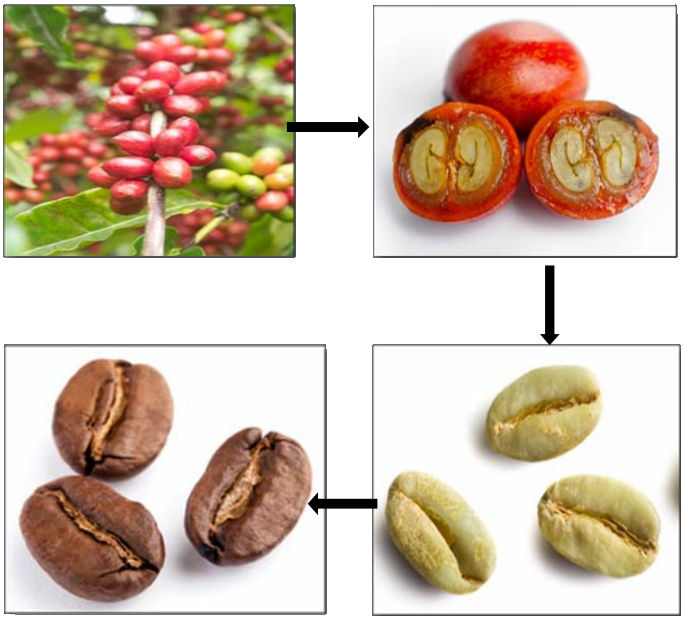


Figure 3. Coffee berries to roasted coffee beans

Obtaining the coffee beans from the harvested cherry fruit involves one of the two methods, the wet method that requires ample amounts of water, used for *C. arabica*, and the dry process used mainly for *C. robusta*. In the wet process, the cherries are soaked and fermented in water to remove the pulp prior to drying while in the dry process, the freshly picked or mechanically harvested cherries are sun dried for 2-3 weeks, followed by mechanical removal of the dried husk. The commercial beans are roasted at air temperatures reaching 230°C for a few minutes, or 180°C for up to approximately 20 minutes. Due to the internal temperature and pressure, numerous chemical reactions occur in this substantial and exothermic pyrolysis resulting in 3-5% of dry weight for a light roast to 5-8% for a medium roast and 8-14% for a dark roast. The grinding and subsequent extraction of the roasted beans yields concentrated liquor that is converted to powder, either by spray drying or by freeze drying. The percentage of solids extracted varies according to equipment, coffee particle size and the charge of coffee relative to water. The yield of solubles is controlled by different legislations in different territories but an average cup of coffee contains approximately 1-2% solids by weight. Green beans may be decaffeinated either by supercritical carbon dioxide or organic solvent.

4. Phytochemicals in Coffee

Phytochemical investigations were carried out on both coffee leaves and beans since the early 1920's. Majority of studies suggest the most common known xanthine type alkaloid to be caffeine, the name driven from the name of the bean. Moreover, detailed literature survey in both chemical abstracts (www.scifinder.org) and dictionary of natural products (http://dnp.chemnetbase.com) showed that chlorogenic acids esters,

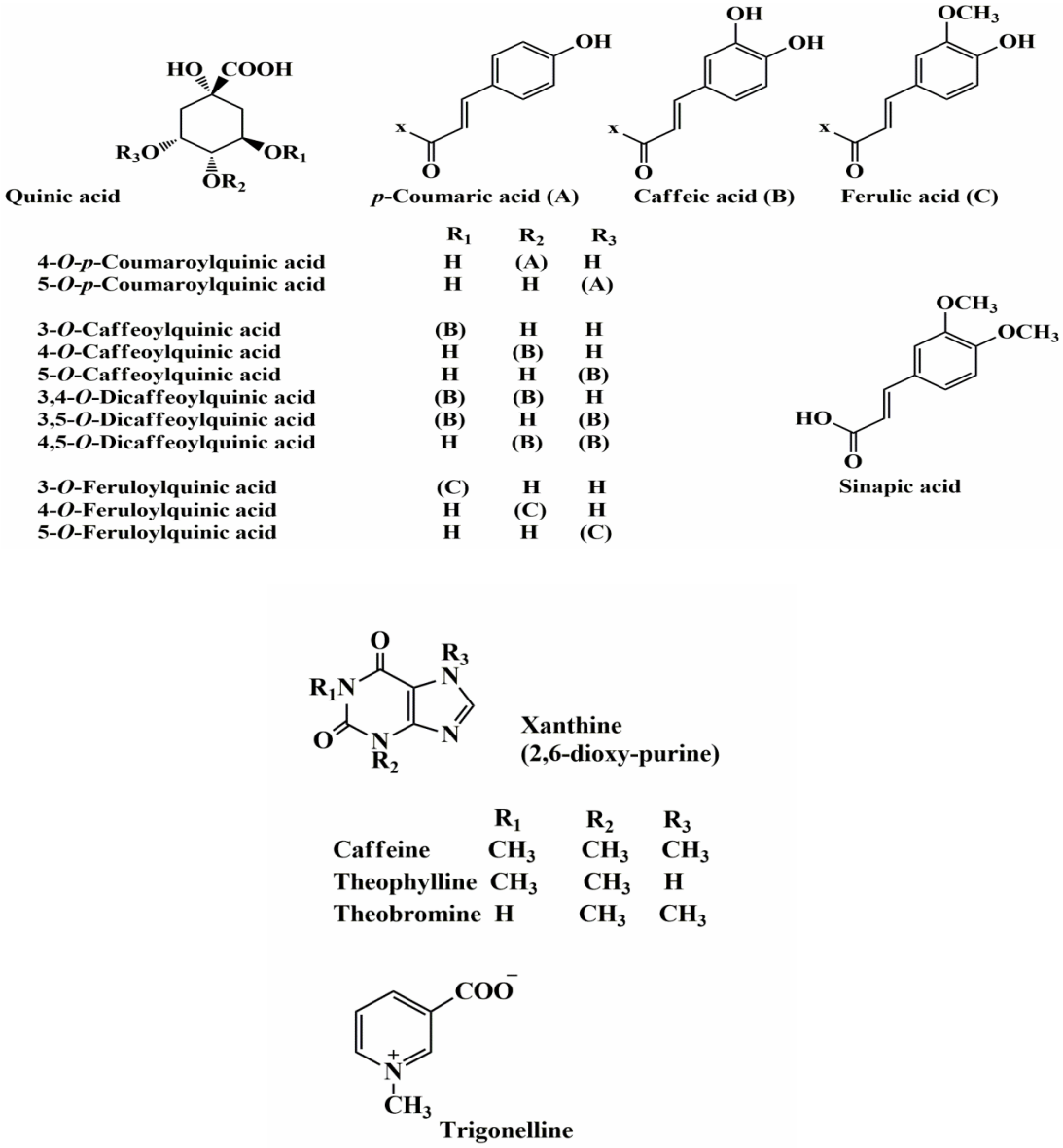
flavonoids, volatile aldehydes, tannins, lignans and anthocyanins are reported. In the following section, light is shed on the most relevant compounds isolated from coffee and their chemical structure in order to help the reader better understand the diversity in chemical constituents found in this daily consumed beverage.

4.1. Chlorogenic and Other Organic Acid Derivatives

Coffee beans are rich sources of chlorogenic acids, (6-10% on a dry weight). More than 70 chlorogenic acids individual esters in addition to the free acids are reported in either the green or the roasted beans. Chlorogenic acids are a family of esters formed between quinic acid and either caffeic (3,4-dihydroxy-cinnamic acid), *p*-coumaric (4-hydroxy-cinnamic acid), ferulic (3-methoxy, 4-hydroxy-cinnamic acid) acid and to lesser extent sinapic (3,5-Dimethoxy-4-hydroxycinnamic acid) acid. All the chlorogenic acids in coffee have the cinnamate moiety in the trans-configuration. The main components reported in green coffee beans include the monoester caffeoyl quinic acids with the major component known as 5-*O*-caffeoylquinic acid, accounting for approximately 60% of the total chlorogenic acids in the roasted coffee beans. Also, significant amounts of 3-*O*- and 4-*O*-caffeoylquinic acid, and the three analogous 3, 4 and 5 feruloylquinic acids were reported. In addition, dicaffeoyl quinic acids derivatives such as 3,4-*O*-, 3,5-*O*- and 4,5-*O*-dicaffeoylquinic acids; feruloyl quinic acids; p- coumaroyl quinic acids and their isomers. Quinic acid is a monocarboxylic cyclic acid with four hydroxyl groups, which occurs free or bound in the chlorogenic acids of green coffee beans, upon roasting bound quinic acid is liberated producing diverse stereoisomers and quinides derivatives upon epimerisation and lactonization. In addition, cinnamoyl–amino acid, cinnamoyl-glycosides and cinnamoyl-hexose conjugates have also been reported. The relatively minor sinapic acid esters are of restricted occurrence. Those containing 3,4-dimethoxycinnamic acid or 3,4,5-trimethoxycinnamic acid are scarce, and the chlorogenic acid containing 3,5-dihydroxy-4-methoxycinnamic acid appears to be unique to coffee. The triacyl chlorogenic acids have been traced only in Robusta coffee beans. It is worth noting that the chlorogenic acids and the cinnamoyl–amino acid conjugates have been used as criteria in chemotaxonomic studies.

Besides chlorogenic and quinic acid, the major acids in green coffee are malic and citric acids. Apart from the chlorogenic acids, citric acid represents the next highest acid concentration in green beans. Analysis of the Arabica coffees gave an average of 5.6 g/kg for malic acid and 12.3 g/kg for citric acid. Additional acids such as succinic, glycolic, lactic and phosphoric acids were also detected.

It is worth mentioning that during roasting, there is a progressive destruction and transformation of chlorogenic acids. While approximately 8-10% of the chlorogenic acids in green beans are destroyed, some are transformed during roasting into cinnamic acid derivatives and quinic acid. Early in roasting when there is still adequate water content, isomerization (acyl migration) occurs, accompanied by some hydrolysis releasing the cinnamic acids and quinic acid. The cinnamic acids may be decarboxylated and transformed to a number of simple phenols and range of phenylindans probably via decarboxylation and cyclization of the vinylcatechol intermediate to give lactone derivatives.



	R_1	R_2	R_3
4-*O*-*p*-Coumaroylquinic acid	H	(A)	H
5-*O*-*p*-Coumaroylquinic acid	H	H	(A)
3-*O*-Caffeoylquinic acid	(B)	H	H
4-*O*-Caffeoylquinic acid	H	(B)	H
5-*O*-Caffeoylquinic acid	H	H	(B)
3,4-*O*-Dicaffeoylquinic acid	(B)	(B)	H
3,5-*O*-Dicaffeoylquinic acid	(B)	H	(B)
4,5-*O*-Dicaffeoylquinic acid	H	(B)	(B)
3-*O*-Feruloylquinic acid	(C)	H	H
4-*O*-Feruloylquinic acid	H	(C)	H
5-*O*-Feruloylquinic acid	H	H	(C)

	R_1	R_2	R_3
Caffeine	CH_3	CH_3	CH_3
Theophylline	CH_3	CH_3	H
Theobromine	H	CH_3	CH_3

Figure 4. Representation of phenolics and alkaloids isolated from different *Coffee* spp.

4.2 Methyl Xanthines and Other Alkaloids

It is widely accepted that most of the well-known central nervous system activity of coffee is associated with its content of caffeine (1-2%). This methyl xanthine derivative (3,7-dihydro-purine-2,6-dione) along with theophylline and theobromine are the major pseudo-alkaloids present in both coffee tree and beans. These are mainly combined in the green seed with chlorogenic acids and their derivative esters (above) (5-7%); which are released during roasting also causing some decomposition of chlorogenic acid to quinic acid and caffeic acid. Trigonelline (*N*-methylnicotinic acid) is present in green seeds to the extent of about 0.25-1%, and during roasting, this particular compound is converted into nicotinic acid (niacin or vitamin B_3), which is also reported in roasted *C. arabica* beans. It is important to mention that the estimated beverage consumption may provide the following amounts of caffeine per cup: coffee, 30-150 mg (average 60-80

-

-

-

Bibliography

Bond T. (2012). The Origins of Tea, Coffee and Cocoa as Beverages in *Teas, Cocoa and Coffee: Plant Secondary Metabolites and Health*. (ed. A. Crozier, H. Ashihara, F.A. Tomas-Barberan) Chichester, West Sussex, Wiley-Blackwell. [This chapter contains information on the origin and history of coffee production.]

Clarke R.J., Vitzthum O.G. (2001). *Coffee: Recent Developments*. Oxford; Malden, M.A., Blackwell Science. [This book contains an overview of coffee phytochemicals, their analyses in addition to recent trends in processing and beverage preparation].

Davis A.P., Govaerts R., Bridson S.M., Stoffelen P. (2006). An annotated taxonomic conspectus of the genus *Coffea* (Rubiaceae). *Botanical Journal of the Linnean Society* 152, 465–512. [This article presents a comprehensive review on the genus *Coffea*].

Food and Agricultural Organization (FAOSTAT). United Nations (2012) [Updated statistics on production and exports of coffee worldwide].

International Coffee Organization. http://www.ico.org [Very informative website on current and relevant sustainability projects, statistics on exports, imports, production and consumption as well as an overview of the economic situation].

Lim T. K. (2012). *Edible Medicinal and Non-medicinal Plants*. Vol. 5. Dordrecht; New York, Springer. 614-715. [This book presents detailed information of the most current literature on botany, phytochemistry and health benefits of coffee].

Lopez-Garcia E., Guallar-Castillon P., Leon-Muñoz L., Graciani A., Rodriguez-Artalejo F. (2014). Coffee Consumption and Health-related Quality of Life. *Clinical Nutrition* 33, 143-149. [A recent article on the perception of coffee and health at the consumer level].

Marcason W. (2013). What is Green Coffee Extract? *Journal of the Academy of Nutrition and Dietetics* 113(20), 364. [A recent article on the widely popular coffee extract supplement].

Martinez F.C., Rojas J.F., Castillo C.F. (2004). Technology Transfer in *Coffee: Growing, Processing, Sustainable Production. A Guidebook for Growers, Processors, Traders, and Researchers*. (ed. J.N. Wintgens) Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. [This book chapter contains relevant information on sustainability of coffee production using technology transfer].

National Coffee Association. http://www.ncausa.org. [This website contains information on coffee history, varieties and methods of preparation].

Rodriguez B.P., Vasquez M.M. Economic Aspects of Coffee Production in *Coffee: Growing, Processing, Sustainable Production. A Guidebook for Growers, Processors, Traders, and Researchers* (2004). (ed. J.N. Wintgens) Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. [This book chapter contains relevant information about the economic aspects, both through history and in the current time].

Ross I.A. (2005). Medicinal Plants of the World: Chemical Constituents, Traditional, and Modern Medicinal Uses Vol. 3. Totowa, N.J., Humana Press. 155-195. [A compilation of botany, chemical components and medicinal properties of *Coffea arabica*].

Saito M. (2004). Sustainable Coffee Production in *Coffee: Growing, Processing, Sustainable Production. A Guidebook for Growers, Processors, Traders, and Researchers*. (ed. J.N. Wintgens) Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim. [This book chapter contains detailed information on methods of developing sustainable coffee].

Stalmach A., Clifford M.N., Williamson G., Crozier A. (2012). Phytochemicals in Coffee and the Bioavailability of Chlorogenic Acids in *Teas, Cocoa and Coffee: Plant Secondary Metabolites and Health*. (ed. A. Crozier, H. Ashihara, F.A. Tomas-Barberan) Chichester, West Sussex, Wiley-Blackwell. [This book chapter contains a compilation of coffee constituents].

Stoffelen P., Noirot M., Couturon E., Anthony F. (2008). A new caffeine-free coffee from Cameroon. *Botanical Journal of the Linnean Society* 158, 67–72. [This article refers to the discovery of *Coffea charrieriana* in Cameroon].

Williamson G. (2012). Coffee and Health in *Teas, Cocoa and Coffee: Plant Secondary Metabolites and Health*. (ed. A. Crozier, H. Ashihara, F.A. Tomas-Barberan) Chichester, West Sussex, Wiley-Blackwell. [This book chapter contains updated literature on some of the health benefits of coffee and the metabolism of its components].

Yahin A., Yashin Y., Wang J.Y., Nemzer B. (2013). Antioxidant and Antiradical Activity of Coffee. *Antioxidants* 2, 230-245. [This article contains valuable data on the antioxidant activity of coffee varieties].

Biographical Sketches

Sherweit H. El-Ahmady is a graduate of the Faculty of Pharmacy, Cairo University, Egypt (1995). She received her MSc degree from Texas A & M University, USA, in Plant Biology (2000) and her PhD from Ain Shams University, Egypt, in Pharmaceutical Sciences – Pharmacognosy and Phytochemistry (2006). Dr. El-Ahmady has been a faculty member in Ain Shams University since 2006 where she teaches Pharmacy students and conducts research in the Department of Pharmacognosy. Her main interests include studying phytochemicals and biological activities of different medicinal plants and she has published several research papers in this field. She is also a member of the American Society of Pharmacognosy and the Egyptian Syndicate of Pharmacists. Dr. El-Ahmady is an advocate of natural medicine and encourages her students to practice healthy eating through her lectures on phytochemicals and nutrition.

Mohamed L. Ashour is a graduate of the Faculty of Pharmacy, Alexandria University, Egypt (1996). He received his MSc degree from Ain Shams University, Egypt in Pharmaceutical Sciences (Pharmacognosy) (2004) and his PhD from Heidelberg University, Germany in Pharmaceutical Biology (2010). He conducted his research as a postdoctoral fellow at Heidelberg University in (2012) after receiving the DAAD scholarship. Dr. Ashour has been a faculty member in Ain Shams University and a guest faculty member in Future University in Egypt since 2010 where he teaches Pharmacy students and continues his research in the Department of Pharmacognosy. His basic interest is secondary metabolites from plant origin where he published several research papers in the field of isolation and structure elucidation of natural products, identification of essential oils, molecular modeling and biological screening of plant extracts. He is also a member of The Society for Medicinal Plant and Natural Product Research (GA), Italo-Latin American Society of Ethnomedicine (SILAE), Egyptian Pharmaceutical Society and the Egyptian Syndicate of Pharmacists.