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Medicinal Properties of Arabica coffee (*Coffea arabica*) Oil: An Overview

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Abstract

Coffee is one of the massive tropical crops in developing countries and historically understudied in subjects of crop nutrition and administration. Arabian coffee (*Coffea arabica*) plant belongs to the genus *Coffea* in the Rubiaceae family. It is known as the most widely recognized *Coffea* species created comprehensively summing up to over 75% of the all-out *Coffea* creation. Its compounds are a complex mixture of different chemicals that have many health benefits. The usage of various parts of a coffee plant, along with its oil is verified for the manufacturing of ancient medicines that helped in curing a number of ailments. These traditional uses were scientifically proven by many studies including psychoactive responses, neurological and metabolic disorders. Coffee oil consists mainly of triglycerol and fatty acids along with antioxidants. It also possesses some biologically active fatty acids that are anti-cancerous, anti-inflammatory, anti-bacterial, anti-diabetic and anti-atherosclerotic in nature. This paper provides the medicinal properties and scientific review of Arabica coffee oil.

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SCAN ME

Introduction

Medicinal plants have played an important role in the treatment of several diseases. Medicinal plants are said to be ideal for the human body as it yields fewer side effects than synthetic drugs [1]. There is an immense perspective for discovering new drugs with the help of natural plant extracts as they demonstrate exceptional chemical diversity [2]. Isolating natural components from plants is the key process for discovering drugs [3]. These isolated components are biologically active and are anti-cancerous, anti-microbial, and anti-diarrheal in nature. They also have analgesic, antioxidant and wound healing properties [4]. Thus, the procedure for extracting biologically active components plays a primary and crucial role in the investigation of medicinal plants [4]. Coffee is one of the most popular and widely consumed beverages all over the globe. It is cultivated throughout the world and has marked its place as a major tropical crop in most of the developing countries. Despite being a popular crop, it was not studied much previously. In the botanical nomenclature, coffee comes under the family *Rubiaceae*. The genus *Coffea* consists of about 103 species which are bifurcated into two subgenera named *Coffea* and *Baracoffea*. The subgenus *Coffea* includes those species which are used in the production of coffee [5]. Amongst all the other species, *Coffea arabica* (arabica coffee) and *Coffea canephora* (robusta coffee) are mostly used for economic and commercial purposes [6]. However, *Coffea Arabica* alone comprises about 75–80% of the total coffee production throughout the world [7]. The total world coffee production, export, and consumption from 2006 to 2015 were demonstrated in Table 1 [107]. Figure 1 represents the plant species *Coffea Arabica*. Coffee is produced in around 80 countries of the world [8]. The major coffee producer and exporter throughout the world are Brazil (35%), Vietnam (15%), Indonesia (8%), Columbia (6%), India (4%), Ethiopia (4%), Honduras (4%), Costa Rica (1%) and others (23%) [9,10]. The Arabian coffee originated in Ethiopia (Africa), which is close to Saudi Arabia, therefore its growth pattern is clearly visible around the southern Arabian regions [11]. A wide range of bioactive components such as phenolic compounds and terpenoids are present in coffee in the form of concentrated hydrophobic liquids (called essential oils) that are obtained from aromatic compounds. These essential oils have the potential to work as an antimicrobial and antioxidant agent that can be used as a natural preservative for perishable foods [12]. The oils obtained from green coffee possess a considerable amount of fatty acids such as palmitic, oleic, linoleic and stearic acids and found a firm place in both cosmetic and nutraceutical industries [13]. Due to the presence of triglycerides and free fatty acids, the green coffee oil provides some cosmetic benefits such as retaining skin moisture and acting as a potent anti-aging component. Along with the secondary metabolites, these fatty components are also a reason for the attraction of cosmetic industries towards green coffee [14]. Also, coffee has a sumptuous history of medicinal benefits which are now backed by the ever-increasing number of scientific researches. Various parts of a coffee plant are used for treating influenza, anemia, edema, asthenia and rage. It is also found that coffee can cure hepatitis and liver dysfunctions. When applied externally, it can prevent nervous shock. It is used as a stimulant for lethargy and intoxication. Coffee also worked as an antitussive agent in common cold and lung disease. It acts as a cardiotonic, neurotonic and also works wonders for asthmas [15]. Coffee oil possesses many biologically active components that act as anticancer, anti-inflammatory, antibacterial, antidiabetic, and antiatherosclerotic agent [16, 17].

Crop Year	Quantity (in 1,000 60-kg bags)		
	Production	Export	Consumption (Importing Countries)
2006	128,728	91,745	75,093
2007	119,996	96,302	75,964
2008	129,566	97,599	75,715
2009	123,276	96,242	74,211
2010	134,246	97,067	76,552
2011	140,617	104,435	76,447
2012	144,960	110,914	76,949
2013	146,506	110,501	79,467
2014	142,278	114,766	80,627
2015	143,306	112,722	81,188

Table 1: Total World Coffee Production, Export, and Consumption from 2006 to 2015 [107].

Figure. 1: The plant Coffea Arabica (Hada Mountain in Aseer region, Southwest of The Kingdom of Saudi Arabia).

Methods

Literature search strategy and selection criteria

Google Web, Google scholar and PubMed were used to obtain data for this review paper. Research papers consulted for this review were those published over last 10 to 25 years.

Discussion

Botanical History

Haarer [18], Wrigley [19] and Pendergrast [20] presented the historian's account on the geographical distribution of Arabian coffee. They described its migration from the genetically diverse centre of Ethiopia to Yemen during the 6th century. From Yemen, it travelled to South-east Asia, India, East Africa and Latin America between the 17th to 19th centuries. Many researchers reported the origin of Typica and Bourbon genetic bases. They indicated the origin of genetic base Typica from a distinct plant grown in Amsterdam which was brought there from Java in the year 1706. The genetic base Bourbon was reported to have its origin in the coffee trees which were presented to La Reunion (formerly known as Bourbon Island) from a Yemenian city Mocha during 1715 t0 1718. After that, the coffee plant stretched swiftly from America to Indonesia with the help of self-fertilized seeds which extensively reduces genetic diversity [21]. *C. arabica* originates as an understory plant in the rainforests of a reduced territory in the cold areas of Ethiopian highlands. It is autogamous and the only allotetraploid *Coffea* species (others are diploid): $2n = 4X = 44$. It is most probable that this species recently originates from a distinct hybridization occurring in-between two diploid species, i.e *C.canephora* and *Coffea eugenioides* [22]. The fact that the cultivation of Arabica coffee has continuously been done from the past 4-5 centuries in the mountainous slopes and constricted valleys of Yemen and Saudi Arabia at an altitude of about 1200-1800 meters is of significant consideration [23]. The allotetraploid nature of the Arabica coffee genome is considered as an attribute that allows it to adapt remarkably through a vast range of environmental diversity of intertropical areas, despite being originated from a genetically restricted population source [24].

Genus and Family

Coffee, along with its whole tribe, genus *Coffea* and over 124 species belong to the family Rubiaceae [25].

Botanical Features

The leaves are attached to a short petiole. At the early stage, they are light bronze or tan in color which changes to dim green when fully grown. The leaves are dull from underneath and shiny on the upper side. Only two species, named as *Coffea Arabica* L (referred to as Arabica Coffee) and *Coffea canephora* P (commonly known as Robusta Coffee) lead in the worldwide commercial production of coffee. Except *C. arabica*, all the other species of coffee are diploid in nature ($2n = 2x = 22$) and are usually self-incompatible. *C. arabica* is self-fertile, has a tetraploid genome ($2n = 4x = 44$) and originated from hybridization between *C. canephora* (as paternal primogenitor) and *C. eugenioides* (as maternal primogenitor) that occurred spontaneously [26].

Bean

The coffee beans are tropical dicotyledonous seeds (Figure 2). The seeds are albuminous, having a copious endosperm. The embryo of the coffee seed is very small. The coffee seeds have undergone evolution to develop complicated strategies in order to preserve its nutritional content and use pericarp and pulp for encouraging its distribution by animals [27].

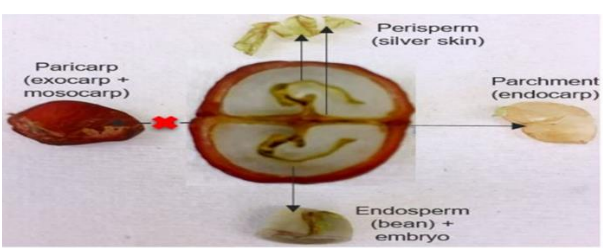

Figure 2: Tissue representatives of coffee beans used in study of Cheng *et al*. [106] (pericarp was discarded).

Leaves

The coffee leaves (Figure 3) are wax-coated and shiny. Depending on the stages of development and plant's origin, its color varies from light green to dark green to bronze. They grow in pairs on the opposite side of the main stem or branches [28]. The average lifespan of *C. arabica* leaves is about 8 months and about 7-10 months for the leaves of *C. canephora*. In accordance with the developmental phase, the leaves of the coffee plant can be divided into three types: the newly emerged young leaves and buds (fresh weight = 25 mg, length = 20 mm, width = 7 mm); fully mature and expanded second and third leaves that are positioned just below the tip (weight = 1.2 g, length = 10 to 15 cm, width = 6 cm); and the dark green colored aged leaves which are adjacent to the shoot base (weight = 1.3 g, length = 10 to 15 cm, width = 6 cm) [29].

Figure 3: Coffee leaves (Hada Mountain in Aseer region, Southwest of The Kingdom of Saudi Arabia).

Fruits

The fruit of the coffee plant is a cherry or berry and usually two coffee beans are present inside it (Figure 4). The skin of the coffee fruit is red-violet in color and conceals several parts underneath it. The parts of the coffee fruit appear in the following sequence; at first, the yellow-colored pulp is present which is followed by a yellowish parchment sheet, after that a silver-colored seed coat is present which covers the green-colored coffee bean situated at the core [30]. The pericarp comprises a green-colored, smooth, and strong outer layer in unripened fruits which changes into red-violet or deep red color after ripening. In some specific genotypes, it can also turn yellow or orange when [31]. The pericarp forms an outer covering for the mesocarp (yellowish, mushy, sweet and fibrous pulp), the pectin layer (mucilaginous sheet full of water), and the endocarp (thin parchment sheet). The coffee bean consists of a silver skin called spermoderm, followed by the endosperm and the coffee seed at last [7, 31].

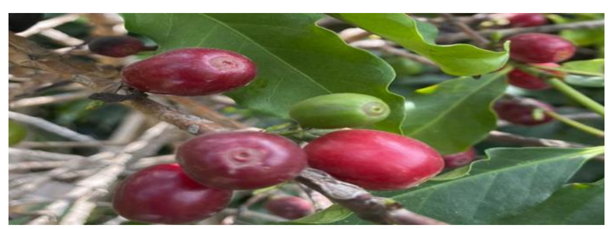

Figure 4: Coffee fruit (berry/cherry) (Hada Mountain in Aseer region, Southwest of The Kingdom of Saudi Arabia).

Flowers

The coffee flowers are pink or white in color (Figure 5). After quite a long dry spell, a rainfall even as low as 7-10 mm can trigger the flowering of the coffee plant [57]

Figure 5: Coffee flowers (Hada Mountain in Aseer region, Southwest of The Kingdom of Saudi Arabia).

Biophysical Limits

Altitude, Slope

Coffee Arabica naturally grows on high continental plateaus and tropical rain forests at an altitude of about 1000-2200 mm along with the mid-altitude areas of America and Caribbean islands; whereas, coffee Robusta naturally proliferates in lowlands and at an altitude lower than 900 mm (mid-altitude regions). The basic criterion (primary factor) for selecting land to cultivate coffee is attributed to its latitude, altitude, steepness of the slope and its exposure towards sun rays. Actually, this basic criterion (primary factor) also describes the secondary factors such as environmental conditions, fertilization and irrigation technologies, sun and shade systems, native techniques and quality parameters of harvesting policies. The association between primary factors and quality attributes of coffee was positively recognized by many researchers and called the effect of primary factors (altitude, latitude etc.) as "Terrain effect" [32]. These primary factors also affect the enzymatic action and composition of coffee which results in its different quality, aroma, taste and various other organoleptic and sensory characteristics [33]. As coffee plants are generally cultivated on slopes and steep tropical mountainous regions, so the slope's exposure towards climatic and environmental conditions also have a tendency to affect the acidic nature, typicity, aroma, bitter taste, and quality of the coffee. Usually, coffee beans harvested from the east side of the slopes have better taste, aroma, acidity, typicity and are preferred more than the ones that are grown in west-facing slopes [34].

Type of Soil

Most of the soils in the coffee farm are sand-loamy, having a pH of about 7.5 to 8 (slightly basic) [23].

Phytochemical Constituents

Major Chemical Compounds of Coffee

Compounds present in coffee are a complex blend of chemicals that provide a considerable amount of chlorogenic acids and caffeine. An important resource of cafestol and kahweol is unfiltered coffee. Cafestol and kahweol are diterpenes and are attributed to the cholesterol-increasing nature of coffee [35]. A number of populations depend upon coffee for meeting their caffeine need. Apart from that, it also holds hundreds of nutritional compounds such as carbohydrates (CHO), lipids, proteins, vitamins, minerals, alkaloids and phenolic compounds [36, 37].

Caffeine (Methylxanthine)

Caffeine is a compound that naturally occurs in coffee beans along with another 60 plant parts like tea leaves, cola nuts, cocoa beans etc. It is alkaloid in nature and its chemical name is 1, 3, 7-trimethylxanthine (Figure 6). In various physiological functions, it acts as a nonselective antagonist to adenosine receptors [38]. Caffeine is one of the most widely used psychoactive stimulating drugs all over the world. The existence of most of its biological properties is attributed to its antagonist nature against adenosine receptors specifically A1 and A2A. The caffeine content is extremely unstable, ranging from 30 mg to 350 mg per cup (150 ml) of home-made coffee [38, 39]

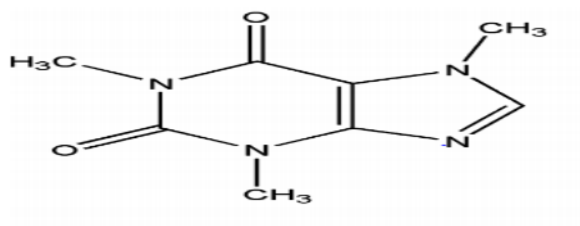

Figure 6: Caffeine (Methylxanthine) [40].

Chlorogenic acids (Polyphenol)

Chlorogenic acid (CGA) is an esterified chemical compound found in coffee (Figure 7). It is a nutritionally important phenolic ester of trans-cinnamic acid and quinic acid [39, 41]. It is also called as 5-O-caffeoylquinic acid. The range of chlorogenic acid in a 200 ml cup of coffee (7-oz) is about 70 to 350 mg, out of which nearly 35-175 mg is caffeic acid [42]. Chlorogenic acid plays an important role in regulating glucose and lipid metabolism and other similar disorders, such as diabetes mellitus, cardiovascular disease (CVD), overweight and obesity, cancer, and fatty liver disease (hepatic steatosis). Besides, it is also anti-diabetic, anti-inflammatory, anti-carcinogenic and anti-obesity in nature and has the potential for providing many health benefits. It can also act as a non-pharmacological and non-invasive drug for treating and preventing some chronic diseases [43].

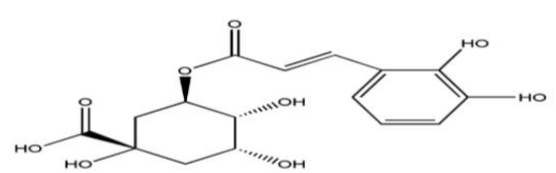

Figure 7: Chlorogenic acids (Polyphenol) [40].

Coffee Lipids (Kahweol and Cafestol)

A standard *Coffea arabica* bean contains coffee lipids named kahweol and cafestol; both of which are structurally analogous to each other (Figure 8). In one ml of coffee, the concentration of kaweol and cafestol ranges from 0.1 to 7 mg individually [44, 45]. Kahweol and cafestol are diterpenes (fat-soluble compounds) having anticarcinogenic properties. It also works against the activity of aflatoxin B1 (AFB1) in humans. It increases cholesterol levels in human blood when consumed in an unfiltered form [46, 47]. Diterpenes present in coffee (cafestol and kahweol) can produce a wide range of biochemical reactions that in turn reduce the genotoxicity of various carcinogens such as 7,12-dimethylbenz[a]anthracene (DMBA), aflatoxin B1 (AFB1), benzo[a]pyrene (BaP) and 2- amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) [46].

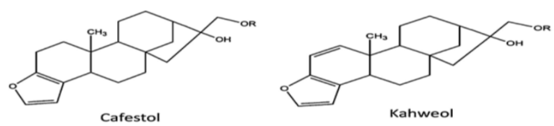

Figure 8: Coffee Lipids (Cafestol & Kahweol) [40]

Leaves

The leaves of the coffee plant contain various kinds of phytochemicals [48-51]. These are as follows:

Alkaloids: caffeine, adenine-7-glucosyl, trigonelline, 7-methylxanthine and theobromine

Flavonoids: quercetin, anthocyanins, quercetin glucoside, isoquercetin, kaempferol and rutin

Terpenoids: cafesterol, 16-O-methyl cafesterol, kahweol

Amino acids: pipecolic acid and histidine

Xanthonoids: mangiferin and isomangiferin

Phenolic acids: cafeic, ferulic, chlorogenic, p-coumaric and sinapic acids

Catechins: catechin and epicatechin.

Along with these, sucrose and tannins are also present.

Fruit

The coffee fruit has a number of bioactive compounds like chlorogenic acid, caffeine and tannins that act as eminent antioxidant agents [52].These bioactive compounds demonstrate various health benefits and have the potential to provide protection against a number of chronic diseases, like cancer, obesity and diabetes [53, 54]. In the south-western region of the country, many Saudi women mix the outer layer of the coffee fruit (locally called as Gisher) which account for about 40% of coffee fruit (Figure 4) with hot water and use the extract as a drink, in which they believe to clear their wombs from the bad blood that is attached to the womb during or after the menstrual cycle or after childbirth [109].

Flower

Emura *et al*. [55] analyzed the extract of coffee (*Coffea arabica* L.) flower with the help of Gas Chromatography-mass Spectrometry (GC-MS). The results exhibited that the coffee flowers have a considerable amount of nitrogenous aromatic compounds and derivatives of phenylethane also. The white flower has a highly recognizable scent, and could a potential source of food and beverage ingredients as it is a rich source of bioactive compounds that can play a crucial role in human health as antioxidants and help prevent cardiovascular diseases, cancers, and diabetes[110].

Beans

By mass, 7-17% of lipid is present in the beans of green coffee. Like all the other vegetable oils, the oil of coffee is also composed of free fatty acids and triacylglycerols (75%) [56]. The antioxidant nature of phenolic compounds made them most important amongst all the other biologically active components present in coffee beans. Out of many phenolic compounds, chlorogenic acids are the ones mainly accountable for the antioxidant action. These compounds inhibit the propagation of oxidative damage by scavenging the free radicals *in vitro* [58]. The generation of chlorogenic acid takes place by the process of esterification happening between quinic acid and one or more derivative of *trans*-cinnamic acid. The classification of these compounds can be done on the basis of type, position and number of residual acyl groups.Monoesters of caffeoylquinicacid (especially 5-caffeoylquinic acid) are the most commonly found chlorogenic acids in coffee [59].

Arabica Coffee Oil

Like all the other commonly used vegetable oils, the coffee oil is also composed mainly of 75% triacylglycerols and a little quantity of free fatty acid. Along with these, wax, and a small amount of sterols, phosphatides, tocopherols, ceramides and diterpenes (unsaponifiable materials) are also present [108]. The highest amount of unsaponifiable matter (nearly 13.54%) is found to be present in *Coffea Arabica* while the lowest level (0.36%) is present in *C. kapakata* [60]. Besides, the composition of fatty acids present in coffee oil extracted by green coffee beans is found to be the same after baking. Linoleic acid was found to be most dominated fatty acid with a concentration of about 39.36% to 47.80% which is followed by 29.44% to 35.55% of palmitic acid [61]. Coffee oils contain a significant amount of aromatic compounds that impart coffee its distinct flavor. This is why coffee oils are considered as a chief transporter of aroma and flavor. Calligaris *et al*. [62] extracted coffee oil and detected almost 30 volatile organic compounds in it, most of them are responsible for imparting roasted coffee its distinct and exquisite aroma. Phenolic compounds like chlorogenic acids are present in coffee seed oils which act as an antioxidant agent and are referred as biologically active secondary metabolites. Caffeine, the pharmaceutically significant methylxanthine is also present in coffee oil [62].

Coffee Bean Residue

The coffee oil and seed residue have the same chemical profile. Both of them contain phenolic compounds such as caffeine and chlorogenic acid, along with esters (5 monoacyl and 3 diacyl) of quinic acid and trans-cinnamic acid. Thus, coffee residues have immense potential to be used as a biologically active compound or as a resource for manufacturing food supplements, pharmaceutical/nutraceutical products and cosmetic goods [13]. Nurman *et al*. [63] analyzed the ground oil of Arabica coffee with the help of gas Chromatography. The results demonstrated the presence of some active compounds including methylcyclopentane(14,93%), pentadecylic acid (8,81%), cyclohexane (1,36%), linoleic acid (9,00%), 2,3 dimethylbenzofuran (1,61%), ethyl linoleate (6,36%), and 1,2-benzenedicarboxylic acid, bis (2 etylhexyl) ester (18,09%). An abundant amount of cafestol and kahweol (kaurene diterpene components) are also present in coffee oil. These compounds are related to the defense mechanism of about thirty-four plants, and also to the nutraceutical and sensory characteristics of beverages [64].

Coffee Oil Extraction

The oil content of green *C. arabica* coffee is nearly 15% (v/w) and extraction of the oil is done by pressing the seeds [65]. Extracting the coffee oil with organic solvents is the most common technique among all the other methods [66].During the last few years, new technologies like supercritical fluid extraction are being extensively studied at the laboratory level in order to get the maximum yield and to increase the concentration of the extracted compound [67]. Organic solvents are mostly used for extracting oil but due to environmental safety issues and increasing health risk of people, industries are being forced to discover alternate extraction techniques such as supercritical fluid extraction [68]. Extracting chemical compounds from naturally occurring materials is the most investigated function of supercritical fluids.

The advantages of supercritical fluid include flexibility for processing and retrieving the solvent after processing from the extracts, which is not possible through conventional extraction techniques [66]. Usually, the supercritical fluids extraction technique is performed with the help of carbon dioxide (CO_2) as it has a low critical temperature (32 ºC) and pressure (74 bar), non-toxic and non-flammable nature. Also, it is cheap, available in highly pure form and can easily be removed after processing the extracts [69]. Couto *et al*. [70] used supercritical carbon dioxide ($scCO_2$) at different temperatures (40, 50 and 55 ºC) and pressures (15.0, 20.0, 25.0 and 30.0 MPa) for extracting lipids with the aim of producing biodiesel. The maximum yield of about 15.4% was obtained at a pressure of 25.0 MPa and 50 °C temperature after 3 hours of extraction. Moreover, they have also calculated the effect of adding ethanol as a co-solvent. The mass ratio of ethanol to CO_2 was taken as 6.5:93.5 (w/w) at 50 °C and 20.0 MPa. A reduction in the extraction time by about 60% was observed. The total solvent requirement also decreased for achieving a yield of 12.9% when the same conditions were applied for both the methods i.e. using CO_2 alone or with co-solvent [70]. The same results were also obtained by Andrade *et al*. [71]. They studied the extraction of SCG oil with $scCO_2$ alone, and $scCO_2$ with ethanol as a co-solvent at a temperature ranging between 40, 50 and 60 °C and pressure at a range of about 10 to 30 MPa for 2.5 hours. The maximum yield obtained from SFE (supercritical fluid extraction) was 10.5 ± 0.2%, whereas the maximum yield obtained by using ethanol as a co-solvent was found to be 15 ± 2%. PLE (Pressurized Liquid Extraction) is a recent and appealing extraction technology through which highly efficient extraction can be obtained in a short duration of time and by using relatively less quantity of liquid organic solvents [72]. The major benefit of using PLE (pressurized liquid extraction) is associated with the usage of extreme temperatures which in turn increases the solubility of solute molecules in the solvent. This happens because, at high temperatures, the diffusion of solute to solvent increases and also the strong solute-matrix chemical bonds like van der Waals bonds, solute-active site interaction in the matrix, hydrogen bond and dipole-dipole interaction breaks down [72].

Another technology, i.e. gas-expanded liquid (GXL) technique uses a mixture of compressible gas disintegrated into a solvent (mostly organic). The CO_2 gas is mostly used as an expanded liquid because it has many advantages (as mentioned above) [73]. The CO_2-expanded liquid is a kind of solvent that has the properties of both the liquid and gas. The CO_2 helps in improving the mass transfer and gas solubility, whereas, the organic solvents increases the solubility of solutes (both liquid and solid) [74, 75]. Generally, CO_2-expanded fluids can be regarded as a substitute for pressurized fluids and compressed carbon dioxide which can easily be obtained just by incrementing the level of CO_2 [74]. Rodrigues *et al*. [76] applied the CO_2-expanded liquids technique for extracting *Moringa oleifera* (Drumstick tree). They successfully found the extraction yield two times higher by using an equal amount (50%) of ethanol along with CO_2 in CO_2-expanded liquids when compared with using $scCO_2$ alone. The major benefit of using CO_2-expanded liquids over $scCO_2$ lies in the fact that it works on low-pressure operations while comparing it with pressurized liquid extraction, it was again found beneficial as it uses less quantity of solvent for extraction [76,77].

Health Benefits of Arabic Coffee Consumption

Coffee consumption positively affects the psychoactive response (such as alertness, mood swings etc.), neurological disorders (like infant hyperactivity, Parkinson's and Alzheimer's diseases) and metabolic diseases (for example, diabetes, cholelithiasis, liver cirrhosis), and gonadal dysfunction [78]. In human beings, coffee drinking can help in reducing blood pressure, which can be attributed to the presence of polyphenols and chlorogenic acids in it [79]. Many researches demonstrate a fruitful connection between drinking coffee and better human health. For example, various researches suggest that coffee drinking women are less likely to develop symptomatic cholelithiasis [80].

Pharmacological Activities of Coffee

Anti-diabetic Activity

Coffee beans have many bioactive components that are widely used as antioxidants [52]. Many scientific studies pointed out the health benefits of consuming coffee such as reducing the risk of diabetes mellitus, arterial hypertension, cardiovascular diseases, obesity and even depression [81]. In recent years, around 300 million people around the globe are found to be affiliated with a serious health issue called as diabetes mellitus or type 2 diabetes [40] Consuming a moderate amount of caffeinated or decaffeinated coffee can diminish the likelihood of developing diabetes mellitus in young and middle-aged (40-60 years old) women. Other coffee constituents, except caffeine, was found to have an effect on the development of diabetes mellitus [82].

Anti-microbial Activity

The beverage coffee was intended to be used as an antioxidant agent but it also demonstrates antimicrobial activity against a wide range of microbes including fungi, gram-positive and gram-negative bacteria [83]. In a recent study, Nassar *et al.* [84] compared the antimicrobial activity of Arabica, Turkish and Brazilian coffee. They found the highest antimicrobial activity in Arabica coffee extracts when compared with the rest of the two types.

Anti-bacterial Activity

The coffee constituents such as caffeic acid, protocatechnic acid and chlorogenic acid are reported to impart antibacterial properties to coffee [85]. Many types of research have revealed the antibacterial activity of coffee against various pathogenic bacteria including *Staphylococcus aureus, Listeria monocytogenes, Enterococcus faecalis, Pseudomonas aeruginosa, Salmonella choleraesius and Escherichia coli* [83].

Anti-cancer Activity

Some studies concluded that coffee consumption has many health benefits such as 26% less probability of developing colorectal cancer [86]. Several recent studies have associated the consumption of coffee with lowered risk of developing hepatic and renal cancer too. To some extent, it is also linked to decrease the risk of premenopausal breast cancer and colorectal cancer, whereas, it does not have any relation with the cancers of the prostate, ovary and pancreas. Nevertheless, drinking coffee can help in reducing the death rate of patients suffering from liver cancer [87, 88]. Gan *et al*. [89] defined the significant association of coffee consumption with a lower risk of developing colorectal cancer if less than five cups of coffee are consumed per day. Coffee possesses bioactive compounds such as caffeine, chlorogenic acids, caffeic acid, diterpenes, trigonelline and melanoidins that have a positive effect on the human body. These bioactive compounds also have the potential to act as an anticarcinogenic agent in both animal models as well as human cell line and may protect from colorectal cancer [90].

Antioxidant Activity

Coffee is claimed as a functional drink and as an important source of antioxidant, especially because of its higher phenolic and caffeine contents. Chemical constituents of Arabica coffee include phenolic acid and its derivatives (chlorogenic acid), alkaloids (especially caffeine), terpenoid, carbohydrate, lipid, volatile, and heterocyclic compounds [91]. Along with the distinguished stimulating effect of caffeine, various research have also signified its antioxidant potential that may happen by inhibiting the free radical-induced lipid peroxidation *in vitro* [59]. The silver skin of roasted coffee is used as a nutritional component that is rich in fiber and has antioxidative properties [31]. The evaluation of coffee revealed the increased antioxidant levels after its consumption (*in vivo*). This happened because the metabolization of dietary phenols takes place by colonial microflora which in turn increases the antioxidant activity manifolds [92]. The polyphenolic content of ground coffee was found to be 18,180 mg/g but coffee extracts obtained from Polar Regions have polyphenols in the range of 1,746 mg/g with the antioxidant activity of about 29, 04%. The phenolic content of ground coffee reaches up to 86, 23 mgGAE/g having ABTS (2, 2-azinobis-(3-ethylbenzothiazoline-6-sulfonate) antioxidant activity of about 81, 38 mmolTe/100g and 42, 12 mmolTE/100g DPPH (2, 2-diphenyl-1-picrylhydrazyl) assay when the extraction was done by using subcritical water extraction technique. The water extracts of ground coffee have polyphenols in a concentration of about 5.66 mgGAE/g along with 80.5% antioxidant activity [93, 94, 95].

Anti-viral Activity

Namba and Matsuse (2002) reported that the physiological damage occurring due to viral infections can be minimized by consuming coffee [96]. Increased coffee drink reduces death and increases treatment response to hepatitis C antiviral interferon-based therapy [97].

Anti-inflammatory Activity

Anti-inflammatory activities of green and roasted coffee beans have been previously investigated [98, 99]. Macrophages stimulated by LPS (lipopolysaccharide) secrete interleukin-6 (IL-6) which can be reduced by the anti-inflammatory action of green coffee in a dose-dependent manner [100].

Pharmacological Activities of Coffee Oil

It is proved that the melanoidins present in coffee possess antioxidant as well as metal-chelating properties [101]. A previous study by Velazquez *et al*. [102] showed that green coffee oil (*Coffea arabica* L.) has effects on collagen, elastin, and glycosaminoglycan synthesis. It also affects the transformation of beta-1 growth factor and colony-stimulating factor of granulocyte macrophage which is released *in-vitro* by the skin's fibroblast. Green coffee oil can repair the physiological balance of the skin, thus the new soft tissue can be produced.It also prevents epidermal drying by increasing mRNA aquaglyceroporins-3 expression. When the coffee is brewed, some byproducts are generated (called coffee grounds) which possess about 15% coffee oil. This oil can be employed by the cosmetic industry as a resource [103]. Along with fatty acids, the coffee grounds also have two diterpenes i.e. cafestol and kahweol.

Many types of research on mice have shown that both cafestol and kahweol can improve the CCl4-induced liver damage by inhibiting the activity of liver metabolic enzyme CYPZE1 and the formation of free radicals [104]. Much previous research suggested the use of coffee oil as a raw material for producing cosmetics as both palmitic acid and linoleic acid were found to help alleviate skin aging and swelling [108]. For example, Velazquez Pereda *et al*. [102] reported a skin treatment by using green coffee oil in a range of 3.12-25.0 mg/mL. They found that both the human derma fibroblast cells (CC-2511), as well as human skin keratin cells (HaCaT), can initiate and amplify the collagen (1.8 times), elastin (1.5 times), and glycosaminoglycans (2 times) formation. In another study, Wagemaker *et al.* [105] prepared an emulsion by using coffee oil as a raw material. They demonstrated the effectiveness of coffee oil in the treatment of ultraviolet B (280-320 nm) damaged skin by using a sun protection factor of 1.5 [14,105]. Not only linoleic and palmitic acid, different kinds of polyunsaturated fatty acids (PUFA) such as docosahexaenoic acid is also present in coffee oil. It is reported that decosahexaenoic acid is a vital compound and helps in many biological activities by acting against cancer, inflammation, pathogens, diabetes, and cardiovascular diseases [16, 17].

Conclusion

Coffee oil possesses various bioactive agents. Recently, numerous studies reported that *coffee oil* has various antioxidants that work wonderfully against diabetes, disease-causing microorganisms, cancer and inflammation. It is apparent that future studies are needed to explore not only the utilization of *coffee oil* but also its pharmacological activities and the possible application for safe and effective curing of different diseases, along with the better knowledge of the accurate mechanisms of action.

Conflict of Interest

The author declares no conflict of interest.

Author Contributions

The authors were contributed equally and have been involved in the writing of the manuscript at draft, any revision stages, and have read and approved the final version.

References

1. Almalki DA, Alghamdi SA, Al-Attar AM. Comparative Study on the Influence of Some Medicinal Plants on Diabetes Induced by Streptozotocin in Male Rats. Biomed Research International, (2019); 3596287: 1-11.
2. Cos P, Vlietinck AJ, Berghe DV, Maes L. Anti-infective potential of natural products: How to develop a stronger in vitro proof-of-concept. Journal of Ethnopharmacology, (2006); 106 (3): 290-302.
3. McLain KA, Miller KA, Collins WR. Introducing organic chemistry students to natural product isolation using steam distillation and liquid phase extraction of thymol, camphor and citral, monoterpenes sharing a unified biosynthetic precursor. Journal of Chemical Education, (2015); 92 (7): 1226-1228.
4. Azwanida N N. A review on the extraction methods use in medicinal plants, principle, strength and limitation. Medicinal and Aromatic Plants, (2015), 4(3): 196-202.
5. Maurin O, Davis AP, Chester M, Mvungi EF, Jaufeerally-Fakim Y, *et al*. Towards a phylogeny for coffea (rubiaceae): identifying well-supported lineages based on nuclear and plastid DNA sequences. Annals of Botany, (2007); 100(7): 1565–83.
6. Kusolwa PM, Makwinja F, Nashon J, Marianna M, Kibola A. Morphological diversity of wild coffee (*Coffea kihansiensis*) a potential coffee species for genetic improvement. Tanzania Journal of Science, (2019); 45(4): 629-649.
7. Bresciani L, Calani L, Bruni R, Brighenti F, Rio DD. Phenolic composition, caffeine content and antioxidant capacity of coffee silverskin. Food Research International, (2014); 61: 196–201.
8. Murthy PS, Naidu MM. Sustainable management of coffee industry by-products and value addition-a review. Resources, Conservation and Recycling, (2012); 66: 45–58.
9. Jenkins RW, Stageman NE, Fortune CM. Chuck CJ. Effect of the type of bean, processing, and geographical location on the biodiesel produced from waste coffee grounds. Energy Fuels, (2014); 28(2): 1166–1174.
10. Dang CH, Nguyen TD. Physicochemical characterization of robusta spent coffee ground oil for biodiesel manufacturing. Waste and Biomass Valorization, (2019); 10: 2703–2712.
11. Pohlan HAJ, Janssens MJ. Growth and production of coffee, in Soils, Plant Growth and Crop Production, ed. by W.H. Verheye EOLSS Publications, Abu Dhabi, (2010); pp. 102–134.
12. Feyzioglu G F, Tornuk F. Development of chitosan nanoparticles loaded with summer savory (Satureja hortensis L.) essential oil for antimicrobial and antioxidant delivery applications. LWT – Food Science and Technology, (2016); 70: 104-110.
13. Castro A, Oda F, Almeida M, Davanço M, Chiari B, *et al* . Green coffee seed residue: A sustainable source of antioxidant compounds. Food Chemistry, (2018), 246: 48–57.
14. Pereda MDCV, Dieamant G C, Eberlin S, Nogueira C, Colombi D, Di Stasi LC, *et al*. Effect of green *Coffea arabica* L. seed oil on extracellular matrix components and water-channel expression in in vitro and ex vivo human skin models. Journal of Cosmetic Dermatology, (2009); 8(1): 56-62.
15. Bisht S, Sisodia SS. Coffea arabica: A wonder gift to medical science. Journal of Natural Pharmaceuticals, (2010); 1 (1):58-65.
16. Klinkesorn U, Sophanodora P, Chinachoti P, McClements DJ, Decker EA. Increasing the oxidative stability of liquid and dried tuna oil-in-water emulsions with electrostatic layer-by-layer deposition technology. Journal of Agricultural and Food Chemistry, (2005); 53 (11): 4561–4566.
17. Lorente-Cebrián S, Costa AG, Navas-Carretero S, Zabala M, Laiglesia LM, *et al*. An update on the role of omega-3 fatty acids on inflammatory and degenerative diseases. Journal of Physiology and Biochemistry, (2015); 71: 341–349.
18. Haarer A E. Modern coffee production. Leonard Hill, London.1962.
19. Wrigley G. Coffee. - Tropical agriculture series, Longmans Scientific and Technical, Harlow.1988
20. Pendergrast, M. Uncommon grounds: the history of coffee and how it transformed our world. - Basic Books, Perseus Books Groups, New York.1999.
21. Anthony F, Bertrand B, Etienne H, Lashermesm P. Coffea and Psilanthus. In Wild Crop Relatives: Genomic and Breeding Resources, Plantation and Ornamental Crops. Edited by C Kole, (2011); pp; 41–60. Berlin: Springer-Verlag.
22. Lashermes P, Combes MC, Robert J, Trouslot P, D'Hont A , *et al* .Molecular characterization and origin of the *Coffea arabica* L. genome. Molecular and General Genetics MGG, (1999); 261:259–266.
23. Tounekti T, Mahdhi M, Al-Turki TA, Khemira H. Genetic Diversity Analysis of Coffee (Coffea arabica L.) Germplasm Accessions Growing in the Southwestern Saudi Arabia Using Quantitative Traits. Natural Resources, (2017); 8 (5): 321-336.
24. Chen Z J. Molecular mechanisms of polyploidy and hybrid vigor. Trends in Plant Science, (2010); 15(2):57–71.
25. Davis AP, Tosh J, Ruch N, Fay MF. Growing coffee: Psilanthus (Rubiaceae) subsumed on the basis of molecular and morphological data; implications for the size, morphology, distribution and evolutionary history of Coffea. Botanical Journal Linnean Society's, (2011); 167 (4):357–377.
26. Charrier A, Eskes AB. Botany and genetics of coffee. In:Wintgens JN (ed) Coffee: Growing, Processing, Sustainable Production A Guidebook for Growers, Processors, Traders, and Researchers. WILEY-VCH Verlag GmbH and Co. KCaA, Weinheim, Germany. 2014
27. Giovanni J, Nguyen C, Ampofo B, Zhong S, Fei Z. The Epigenome and Transcriptional Dynamics of Fruit Ripening. Annual Review of Plant Biology, (2017); 68:61–84.

28. Wintgens J N. The Coffee Plant. In Coffee: Crowing, Processing, Sustuinuchle Production, ed. J. N. Wintgens, 1–24. Weinheim: Wiley-VCH Verlad GmbH and Co.2004.
29. Ashihara H, Monteiro AM, Gillies FM, Crozier A. Biosynthesis of Caffeine in Leaves of Coffee. Plant Physiolgy. (1996), 111:747-753.
30. Ghosh P, Venkatachalapathy N. Processing and drying of coffee a review. - International Journal of Engineering Research and Technology, (2014); 3(12): 784–794.
31. Esquivel P, Jiménez VM. Functional properties of coffee and coffee by-products. Food Research International, (2012); 46 (2): 488-495.
32. Barham E. (2003) Translating terroir: the global challenge of French AOC labelling. Journal of Rural Studies, (2003); 19:127–138.
33. Rodrigues CI, Maia R, Miranda M, Ribeirinho M, Nogueira JMF, *et al* . Stable isotope analysis for green coffee bean: a possible method for geographic origin discrimination. Journal of Food Composition and Analysis, (2009); 22(5): 463–471.
34. Cannell, M.G.R. Physiology of the coffee crop. In Coffee: Botany, Biochemistry and Production of Beans and Beverage. Edited by Clifford, M.N., Wilson, K, pp 108–34. London: Croom Helm.1985
35. Clark I, Landolt HP. Coffee, caffeine and sleep: a systematic review of epidemiological studies and randomized controlled trials. Sleep Medicine Reviews, (2017); 31: 70-78.
36. De Mejia EG, Ramirez-mares MV. The impact of caffeine and coffee on our health. Trends in Endocrinology and Metabolism, (2014); 25(10): 489-492.
37. Grosso G, Micek A, Godos J, Sciacca S, Pajak A, *et al*. Coffee consumption and risk of all-cause, cardiovascular, and cancer mortality in smokers and non-smokers: a dose response meta-analysis. European Journal of Epidemiology, (2016); 31: 1191–1205.
38. Nawrot P, Jordan S, Eastwood J, Rotstein J, Hugenholtz A, Feeley M. Effects of caffeine on human health. Food Additives and Contaminants, (2003); 20 (1):1-30.
39. Higdon, J.V., Frei, B. Coffee and health: a review of recent human research. Critical Reviews in Food Science and Nutrition, (2006); 46(2): 101-123.
40. Wachamo HL. Review on Health Benefit and Risk of Coffee ConsumptionWachamo. Medicinal and Aromatic Plants, (2017); 6(4): 2-12.
41. Casal S, Rebelo I. Coffee: A Dietary intervention on type 2 diabetes? Current Medicinal Chemistry, (2017); 24: 376-383.
42. Kale LB, Reddy KJ. A study on caffeine consumption and its association with stress and appetite among call centre employees in Mumbai city, India. International Journal of Community Medicine and Public Health, (2017); 4(3):835-840.
43. Tajik N, Tajik M, Mack I, Enck P. The potential effects of chlorogenic acid, the main phenolic components in coffee, on health: acomprehensive review of the literature. European Journal of Nutrition, (2017); 56: 2215–2244.
44. Ranheim T, Halvorsen B. Coffee consumption and human health beneficial or detrimental? Mechanisms for effects of coffee consumption on different risk factors for cardiovascular disease and type 2 diabetes mellitus. Molecular Nutrition and Food Research, (2005); 49: 274-284.
45. Arab L. Epidemiologic evidence on coffee and cancer. Nutrition and Cancer, (2010); 62:271-283.
46. Cavin C, Holzhaeuser D, Scharf G, Constable A, Huber W, *et al*. Cafestol and kahweol, two coffee specific diterpenes with anticarcinogenic activity. Food and Chemical Toxicology, (2002); 40(8): 1155-1163.
47. Post SM, De wit EC, Princen HM. Cafestol, the cholesterol-raising factor in boiled coffee, suppresses bile acid synthesis by downregulation of cholesterol 7α-hydroxylase and sterol 27-hydroxylase in rat hepatocytes. Arteriosclerosis, Thrombosis and Vascular Biology, (1997); 17(11): 3064–3070.
48. Campa C, Mondolot L, Rakotondravao A, Bidel LPR, Gargadennec A, *et al*. A survey of mangiferin and hydroxycinnamic acid ester accumulation in coffee (Coffea) leaves: biological implications and uses. Annals of Botany, (2012); 110(3): 595-613.
49. Júnior APD, Shimizu MM, Moura JCMSM, Catharino RR, Ramos RA, *et al*. Looking for the physiological role of anthocyanins in the leaves of coffea arabica. Photochemistry and Photobiology, (2012); 88(4): 928–937.
50. Patay E B, Nemeth T, Nemeth T S, Filep R, Vlase L, Papp N. Histological and phytochemical studies of *Coffea benghalensis* Roxb. Ex. Schult. compared with *Coffea arabica* L. Farmacia. Farmacia , (2016) ; 64(1): 125–130.
51. Ross I A. Medicinal plants of the world. New Jersey: Humana Press. 2005.
52. Mullen W, Nemzer B, Ou B, Stalmach A, Hunter J, *et al* . The antioxidant and chlorogenic acid profiles of whole coffee fruits are influenced by the extraction procedures. Journal of Agricultural and Food Chemistry, (2001); 59(8): 3754–3762.
53. Johnston KL, Clifford MN, Morgan LM. Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. The American Journal of Clinical Nutrition, (2003); 78(4): 728–733.
54. Tyszka-Czochara M, Pawel K, Marcin M. Caffeic acid expands anti-tumor effect of metformin in human metastatic cervical carcinoma HTB-34 cells: implications of AMPK activation and impairment of fatty acids de novo biosynthesis. International Journal of Molecular Sciences, (2017); 18 (2): 462-474.
55. Emura M, Nohara I, Toyoda T, Kanisawa T. The volatile constituents of the coffee flower (*Coffea arabica* L.). Flavour and Fragrance Journal, (1997); 12: 9-13.
56. Ferrari M, Ravera F, De Angelis E, Suggiliverani F, Navarini L. Interfacial prop-erties of coffee oil . Colloids and surfaces A: Physical chemical and engineering aspects, (2010); 365(1-3): 79–82.
57. Schroth G, Laderach P, Dempewolf J, Philpott S, Haggar J, *et al*. Towards a climate change adaptation strategy for coffee communities and ecosystems in the Sierra Madre de Chiapas, Mexico. Mitigation and Adaptation Strategies for Global Change, (2009); 14: 605–625.
58. Rivelli D P, Ropke C D, Silva V V, Miranda D V, Almeida R L, *et al* . Simultaneous determination of chlorogenic acid, caffeic acid and caffeine in hydroalcoholic and aqueous extracts of Ilex paraguariensis by HPLC and correlation with antioxidant capacity of the extracts by DPPH· reduction. Revista Brasileira de Ciências Farmacêuticas, (2007); 43(2): 215-222.
59. Parras P, Martínez-Tomé M, Jiménez AM, Murcia M A. Antioxidant capacity of coffees of several origins brewed following three different procedures. Food Chemistry, (2007); 102(3): 582-592.
60. Wagemaker TAL, Carvalho CRL, Maia NB, Baggio SR, Filho GO. Sun protection factor, content and composition of lipid fraction of green coffee beans. Industrial Crops and Products, (2011); 33(2): 469–473.
61. Martín MJ, Pablos F, González AG, Valdenebro MS, León-Camacho M. Fatty acid profiles as discriminant parameters for coffee varieties differentiation. Talanta, (2001); 54(2): 291–297.
62. Calligaris S, Mundari M, Gianmichele A, Barba L. Insights into the physicochemical properties of coffee oil. European Journal of Lipid Science and Technology, (2009); 111:1270–1277.
63. Nurman S, Lamona A, Nasir M. Optimization and characterization of n-hexane extracts of arabica coffee ground (*Coffea arabica* L.) fromgayo plateau as source of natural antioxidant. Journal of Physics: Conference Series, (2019); 1232: 012049.
64. Ivamoto ST, Sakuray, LM Ferreira LP, Kitzberger, CSG, *et al*. Diterpenes biochemical profile and transcriptional analysis of cytochrome P450s genes in leaves, roots, flowers, and during Coffea arabica L. fruit development. Plant Physiology and Biochemistry, (2016); 111:340-347.
65. Speer K, Kölling-Speer. Lipids In: Coffee Recent Developments. Oxford, Blackwell Science, (2001); 33-49.
66. Reverchon E, De Marco I. Supercritical fluid extraction and fractionation of natural matter. Journal of Supercritical Fluids, (2006); 38 (2): 146–166.
67. Barbosa HMA, Melo MMR, Coimbra MA, Passos CP, Silva CM. Optimiza-tion of the supercritical fluid coextraction of oil and diterpenes from spentcoffee grounds using experimental design and response surface methodology. The Journal of Supercritical Fluids, (2014); 85: 165–172.
68. Ahangari B, Sargolzaei J. Extraction of lipids from spent coffee grounds using organic solvents and supercritical carbon dioxide. Journal of Food Processing and Preservation, (2013); 37:1014–1021.
69. Pourmortazavi SM, Hajimirsadeghi SS. Supercritical fluid extraction in plant essential and volatile oil analysis. Journal of Chromatography, (2007); 1163(1-2): 2–24.
70. Couto RM, Fernandes J, da Silva MDRG, Simões PC. Supercritical fluid extraction of lipids from spent coffee grounds. Journal of Supercritical Fluids, (2009); 51: 159–166.
71. Andrade KS, Gonçalvez RT, Maraschin M, Ribeiro-Do-Valle RM, Martnez J, Ferreira SRS.Supercritical fluid extraction from spent coffee grounds andcoffee husks: antioxidant activity and effect of

operational variables on extract composition.Talanta, (2012); 88: 544–552.
72. Oliveira NA, Santiago HPC, Fukumasu H, Oliveira AL. Green coffee extracts rich in diterpenes e process optimization of pressurized liquid extraction using ethanol as solvent. Journal of Food Engineering, (2018); 224: 148–155.
73. Jessop PG, Subramaniam B. Gas-expanded liquids. Chemical Reviews,(2007) 107(6): 2666–2694.
74. Herrero M, Mendiola JA, Ibanez E, Turner C, Wang J. Gas expanded liquids and switchable solvents. Current Opinion in Green and Sustainable Chemistry, (2017); 5:24–30.
75. Siougkrou E, Galindo A, Adjiman CS. On the optimal design of gas-expanded liquids based on process performance. Chemical Engineering Science, (2014); 115, 19–30.
76. Rodrigues PC, Mendiola JA, Quirantes-Piné PR, Ibanez E, Segura CA. Green downstream processing using supercritical carbon dioxide, CO 2 -expanded ethanol and pressurized hot water extractions for recovering bioactive compounds from Moringa oleifera leaves. Journal of Supercritical Fluids, (2016); 116: 90–100.
77. Toda TA, Sawada MM, Rodrigues CEC. Kinetics of soybean oil extractionusing ethanol as solvent: experimental data and modeling. Food and Bioproducts Processing, (2016); 98, 1–10.
78. Dórea JG, Da costa THM. Is coffee a functional food? British Journal of Nutrition, (2005); 93 (6): 773-782.
79. Loader TB, Taylor CG, Zahradka P, Jones P J. Chlorogenic acid from coffee beans: evaluating the evidence for a blood pressure-regulating health claim. Nutrition Reviews. (2017); 75(2): 114-133.
80. Leitzmann MF, Stampfer MJ, Willett WC, Spiegelman D, Colditz GA, *et al* . Coffee intake is associated with lower risk of symptomatic gallstone disease in women. Gastroenterology, (2002); 123(6): 1823-1830.
81. O'keefe JH, Bhatti SK, Patil HR, Dinicolantonio, JJ, Lucan SC, *et al*. Effects of habitual coffee consumption on cardiometabolic disease, cardiovascular health, and all-cause mortality. Journal of the American College of Cardiology, (2013); 62(12): 1043-1051.
82. Van dam RM, Willett WC, Manson JE, Hu FB. Coffee, caffeine, and risk of type 2 diabetes. Diabetes Care. (2006), 29(2): 398-403.
83. Martınez-Tome M, Jimenez-Monreal AM, Garcıa-Jimenez L, Almela L, Garcıa-Diz, L, *et al*. Assessment of antimicrobial activity of coffee brewed in three different ways from different origins. European Food Research and Technology, (2011); 233:497–505.
84. Nassar O M, El-Sayed M H, Kobisi A A. Estimation of Total Phenolic Contents and In vitro Antioxidant and Antimicrobial Activities of the Most Common Coffee Brews Available in the Local Markets of the Northern Region of Saudi Arabia . Journal of Pharmaceutical Research International, (2019); 31(1): 1-8.
85. Dogasaki C, Shindo T, Furuhata K, Fukuyama M. Identification of chemical structure of antibacterial components against Legionella pneumophilia in a coffee beverage. Yakugaku Zasshi. (2002); 122(7):487-494.
86. Je Y, Liu W, Giovannucci E. Coffee consumption and risk of colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. International Journal of Cancer, (2009); 124:1662-1668.
87. Nkondjock, A. Coffee consumption and the risk of cancer: an overview. Cancer Letters, (2009); 277 (2): 121-125.
88. Saab S, Mallam D, Cox GA, Ton, MJ. The impact of coffee on liver diseases: a systematic review. Liver International. (2014); 34: 495-504.
89. Gan Y, Wu J, Zhang S, Li L, Cao S, *et al*. Association of coffee consumption with risk of colorectal cancer: a meta-analysis of prospective cohort studies. Oncotarget, (2017); 8(12): 18699–18711.
90. Bułdak R J, Hejmo T , Osowski M , Bułdak L , Kukla M , Polaniak R , Birkner E. The impact of coffee and its selected bioactive compounds on the development and progression of colorectal cancer *in vivo* and *in vitro*. Molecules,(2018); 23(12): 3309-3333.
91. Brezová V, Šlebodová A, Staško A. Coffee as a source of antioxidants: An EPR study. Food Chemistry, (2009); 114(3): 859-868.
92. Olthof MR, Hollman, PC, Katan, MB. Chlorogenic acid and caffeic acid are absorbed in humans. Journal of Nutrition, (2001); 131(1): 66-71.
93. Palupi N W, Praptiningsih Y. Oxidized rapioca starch as an alginate substitute for encapsulation of antioxidant from coffee residue. Agriculture and Agricultural Science Procedia, (2016); 9:304-308.
94. Xu H, Wang W, Liu X, Yuan F, Gao Y. Antioxidative phenolics obtained from spent coffee grounds (*Coffea arabica* L.) by subcritical water extraction. Industrial Crops and Products, (2015); 76: 946–954.
95. Sant'Anna V, Biondo E, Kolchinski EM, Silva LFS, Correa APF, Bach E, Brandelli A. Total Polyphenols, Antioxidant, Antimicrobial and Allelopathic Activities of Spend Coffee Ground Aqueous Extract. Waste Biomass Valorization, (2017); 8: 439–442.
96. Namba T, Matuse T. A historical study of coffee in Japanese and Asian countries: Focusing the medicinal uses in Asian traditional medicines. Yakushigaku Zasshi, (2002); 37 (1): 65-75.
97. Loy V. Health maintenance in liver disease and cirrhosis. Liver Disorders, (2017); pp 89-98.
98. Prieto MA, Vazquez JA. *In vitro* determination of the lipophilic and hydrophilic antioxidant capacity of unroasted coffee bean extracts and their synergistic and antagonistic effects. Food Research International, (2014); 62:1183-1196.
99. Naidu MM, Sulochanamma G, Sampathu SR, Srinivas P. Studies on extraction and antioxidant potential of green coffee. Food Chemistry, (2008); 107(1): 377-384.
100. Kiattisin K, Nitthikan N, Poomanee W, Leelapornpisid P, Viernstein H, *et al* . Anti-inflammatory, antioxidant activities and safety of *Coffea arabica* leaf extract for alternative cosmetic ingredient. Chiang Mai Journal of Science, (2019); 46(2): 284-294.
101. Wen X, Takenaka M, Murata M, Homma S. Antioxidative activity of a zinc-chelating substance in coffee. Bioscience, Biotechnology, and Biochemistry, (2004); 68(11): 2313–2318.
102. Velazquez PMC, Dieamant GC, Eberlin S, Nogueira C, Colombi D, *et al*. Effect of green *Coffea arabica* L. seed oil on extracellular matrix components and water-channel expression in in *vitro* and ex *vivo* human skin models.- Journal of Cosmetic Dermatology, (2009); 8(1): 56-62.
103. Yang C, Hung F, Chen B. Preparation of coffee oil-algae oil-based nanoemulsions and the study of their inhibition effect on UVA-induced skin damage in mice and melanoma cell growth. International Journal of Nanomedicine, (2017); 12: 6559–6580.
104. Choi SY, Lee KJ, Kim HG, Han EH, Chung YC, *et al*. Protective effect of the coffee diterpenes kahweol and cafestol on tert-butyl hydroperoxide-induced oxidative hapatotoxicity. Bulletin of the Korean Chemical Society, (2016); 27 (9):1386-1392.
105. Wagemaker TA, Silva SA, Leonardi GR, Campos PMM. Green *Coffee arabica* L. seed oil influences the stability and protective effects of topical formulations. Industrial Crops and Products, (2015); 63:34–40.
106. Cheng B, Furtado A, Henry R J. The coffee bean transcriptome explains the accumulation of the major bean components through ripening. Scientific Reports, (2018); (8): 11414.
107. ICO (International Coffee Organization). International Coffee Organization trade statistics. (2016). Retrieved from. http://www.ico.org/monthly_coffee_trade_stats.asp
108. Oliveira PMA, Almeida RH, Oliveira NA, Bostyn S. Enrichment of diterpenes in green coffee oil using supercritical fluid extraction-characterization and comparison with green coffee oil from pressing. Journal of Supercritical Fluids, (2014); 95: 137–145.
109. AL-Asmari KM, Zeid IMA, Al-Attar AM. Coffee Arabica in Saudi Arabia: An Overview. International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR), (2020); 10(4): 71-78.
110. Mak YW, Chuah L O, Ahmad R, Bhat, R. Antioxidant and antibacterial activities of hibiscus (Hibiscus rosa-sinensis L.) and Cassia (*Senna bicapsularis* L.) flower extracts. Journal of King Saud University-Science, (2013); 25(4):275-282.

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