Progress in Phytochemical and Bioactivities of *Coffea arabica* L.

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**Abstract**  *Coffea arabica* L. is a famous specie in genus coffee for medicinal treatment and diet with wide distribution and rich resources. It contains rich alkaloids, flavonoids and terpenes, which exhibited antioxidation, anti-inflammatory, antitumor, anti-diabetic, live protection, and neuroprotective activities. Herein, we summarized the progress in the chemical constituents and bioactivities of *C. arabica* L. to provide ideas for medicinal development prospects of *C. arabica* L.

**Keywords** *Coffea arabica* L., chemical constituents, bioactivities, progress

### Introduction

Coffee is one of the most important agricultural products in the world and is mainly distributed in Central and South America, Africa and South Asia. [1] There are 124 species in genus Coffea. Among them, *Coffea liberica*, *Coffea robusta* and *Coffea arabica* are used to make coffee beverage. [2] As the main region in China, Yunnan province occupies more than 99% of coffee planting. *Coffea arabica* Linn. (*C. arabica* L.) from Yunnan has been appraised as the world high quality coffee planting base by international coffee tasting experts. Coffee, as diuresis and stomach medicine, can be used to treat mental burnout and anorexia. Modern pharmacological studies revealed that *C. arabica* L. had the bioactivities of antioxidation, anti-inflammatory, antitumor, anti-diabetic, live protection, and neuroprotective. Up to date, a total of 152 compounds involving 5 alkaloids, 25 flavonoids, 55 terpenes, 45 phenolic acids and their derivatives, 7 sterols and 10 other compounds have been isolated from this plant. In this paper, we summarized some progresses of phytochemical and pharmacological activities of *C. arabica* L. to provide a reference for better understanding its effective substances.

### Chemical Constituents

Up to 2020, 153 compounds have been isolated from various parts of *C. arabica* L., including alkaloids, flavonoids, terpenes, sterols, phenolic acids, and other compounds.

#### Alkaloids

Alkaloids are typical constituents of genus Coffea. Up to date, five alkaloids have been isolated and identified from the seeds and the stems of *C. arabica* L. (Figure 1). These alkaloids were identified as caffeine (1), theobromine (2), theophylline (3), trigonelline (4) and nicotinic acid (5). [3,4] Among them, caffeine is the highest in *C. arabica* L. as the main active ingredient and content.

![Caffeine](https://example.com/caffeine.png)

**Figure 1** Alkaloids isolated from *C. arabica* L.

### Flavonoids

Flavonoids and their glycosides are widely present in the leaves of *C. arabica* L. They are classified into different groups including catechins, anthocyanin, myricetin, fisetin, patuletin, luteolin, apigenin and quercetin. Ratanamarn et al. [5] reported that catechin (C, 6), epicatechin (EC, 7), epicatechin gallate (ECG, 8) and epigallocatechin gallate (EGCG, 9) in fresh *C. arabica* L. leaves. Chen et al. identified delphinidin 3,5-digluco-side (10) and delphinidin 3-(6"-malonyl-glucoside) (11) in the young leaves of *C. arabica* L. [6] Besides the above mentioned constituents, flavonoids and their glycosides were also isolated from the leaves of *C. arabica* L., which were named as cyanidin-3-O-Glu (12), cyanidin-3-O-rutinoside (13), kaempferol (14), kaempferol-3-O-Glc (15), kaempferol-3-O-Glc-Hex-DeHex (16), kaempferol-3-O-Glc-Hex (17), kaempferol-3-O-Glc-(6",R-ha) (18), quercetin (19), quercitrin (20), isoqueritrin (21), rutin (22), hyperoside (23), quercetin-3-O-Glc-Hex-DeHex (24), quercetin-3-O-Glu (25), luteolin (26), patuletin (27), fisetin (28), myricetin (29) and apigenin (30). [6,7] Their structures are shown in Figure 2.

#### Terpenes

Terpenes are another type of characteristic constituents in *C. arabica* L. 55 terpenes include the skeletons of ent-kaurene, kahweol, villanovane diterpenoid, ent-kaurene diterpenoid glucosides, dammarane and pentacyclic triterpene. These terpenes were identified ursolic acid (31), [8] caffruene A—D (32—35), [9] cafrenuel A—B (36—37), [10] tricalyloside A—E (40—43), [11] 16α,17-dihydroxy-ent-kauren-19-αl (44), [11] 16β,17-hydroxy-ent-kauren-19-αlic acid (45), [11] 16α,17-dihydroxy-ent-kauren-19-αlic acid (46), [11] 9β,16α,17-trihydroxy-ent-kauren-19-αlic acid (47), [11] 16β,7,17-dihydroxy-ent-kauren-19-αlic methyl ester (48), [11] 16α,17-dihydroxy-9(11)-ent-kauren-19-αlic acid (49), [11] (2β,4β,15α)-15-hydroxy-2-[2-O-[3-methyl-1-oxo-buty]-β-D-glucopyranosyl]-oxy]-18-nor-ent-kauren-16-β-8-αlic acid (50), [11] cafalrocil A—H (51—58), [12] mascaroside I—II (59—60), [13] panaculoside VI (61), [13] cofaryloside I (62), [13] villanovane I (63), [13] mozambicoside (64), [13] bengalenol (65), [13] 19-norkaur-16-en-18-αlic acid (66).
acid-15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-β-D-glucopyranosyl]oxy]-[2β,4β,15α] (66),[13] 19-norak-16-ene-18-oic acid-15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-β-D-glucopyranosyl]oxy]-[2β,4β,15α] (67),[13] 19-norak-16-ene-18-oic acid-2-[[3-O-β-D-glucopyranosyl-2-O-(3-methyl-1-oxobutyl)-β-D-glucopyranosyl]oxy]-15-hydroxy-[2β,4β,15α] (68),[13] 2β,16α,17-trihydroxy-entkauran-19-oic acid (69),[13] paniculoside IV (70),[14] mascaroside III—V (71—73),[14] 20-nor-coumaroylside I—II (74—75),[14] villanovane (76),[14] tricalysine A (77),[14] 2β,6β,17-trihydroxy-entkauran-19-oic acid (78), 2-O-[2-(2-O-isovaleryl-β-D-glucopyranosyl)-4-αtracyligenin (79),[14] 2-O-[2-(2-O-isovaleryl-β-D-glucopyranosyl)-4-β-tracyligenin (80),[14] 3-O-β-D-glucopyranosyl-2-O-(2-O-isovaleryl-β-D-glucopyranosyl)-4-β-tracyligenin (81),[14] kahweol (82),[8] catesol (83),[8] 16-β-methylcatesol (84) and ent-kaurane diterpenoid (85).[8]

Their structures are shown in Figure 3.

Phenolic acids and their derivatives

Phenolic acids and their derivatives from coffee main include mono-, di-, caffeoylquinic acid and feruloylquinic acid, p-coumaroylquinic acid and their methyl esters. Asamnew et al.[15] identified 57 phenolic acids from 19 green and roasted coffee beans by UPLC (Figure 4), which were identified as vanillic acid (86), benzoic acid (87), p-hydroxybenzoic acid (88), 3-hydroxybenzoic acid (89), gentisic acid (90), protocatechueic acid (91), caffic acid (92), sinapic acid (93), p-coumaric acid (94), caftaric acid (95), 3-O-p-coumaroylquininic acid (96), 5-O-p-coumaroylquininic acid (97), 4-O-p-coumaroylquininic acid (98), 3-O-caffeoylquininic acid (99), 4-O-caffeoylquininic acid (100), 4-O-caffeoylquininic acid (101), 4-O-caffeoylquininic acid methyl ester (102), 3-O-caffeoylquininic acid methyl ester (103), 5-O-caffeoylquininic acid methyl ester (104), 3,4-di-O-caffeoylquininic acid (105), 3,4-di-O-caffeoylquininic acid (106), 4,5-di-O-caffeoylquininic acid (107), 3,4-di-O-caffeoylquininic acid methyl ester (108), 3,5-di-O-caffeoylquininic acid methyl ester (109), 4,5-di-O-caffeoylquininic acid methyl ester (110), 3,4-di-O-caffeoylquininic acid methyl ester (111), 4-O-feruloylquininic acid methyl ester (112), 5-O-feruloylquininic acid (113), 1-O-feruloylquininic acid methyl ester (114), 3-O-feruloylquininic acid methyl ester (115), 5-O-feruloylquininic acid methyl ester (116), 3-O-feruloyl-5-O-caffeoylquininic acid (117), 3-O-feruloyl-4-O-caffeoylquininic acid (118), 4-O-feruloyl-5-O-caffeoylquininic acid (119), 3-O-caffeoyl-4-O-feruloylquininic acid (120), 3-O-feruloylquininic acid (121), 4-O-caffeoyl-5-O-feruloylquininic acid (122), 3-O-feruloyl-4-O-p-coumaroylquininic acid (123), 3-O-p-coumaroyl-5-O-feruloylquininic acid (124), 4-O-p-coumaroyl-5-O-caffeoylquininic acid (125), caffeoyl-N-trypotphan (126), 5-O-caffeoyl-1,3 -quinine (127), 3-O-caffeoyl-1,5-quinine (128), 4-O-caffeoyl-1,3,3-quinine (129), 5-O-caffeoyl-1,4-quinine (130), 4-O-caffeoyl-1,5-quinine (131), 3-O-feruloyl-1,5-quinine (132), 3,4-di-O-caffeoyl-1,5-quinine (133), 4,5-di-O-caffeoyl-1,3-quinine (134), 3-O-caffeoyl-4-O-3-methylbutanoylquinic acid (135) and 3-O-caffeoyl-4-O-3-methylbutanoyl-1,5-quinine (136).
A pharmacological study on the robusta coffee plant revealed that the crude extracts and pure compounds showed a wide range of biological activities, including antioxidant activity, anti-inflammatory activity, antitumor activity, antidiabetic activity, live protection activity, and neuroprotective activity.

**Antioxidation activity**

Zhang et al.[19] evaluated the antioxidant capacities of the extracts from C. arabica L. by scavenging DPPH and ABTS. The IC$_{50}$ values for scavenging DPPH free radical and ABTS were 1.082 and 1.085 mg/mL, respectively. Samuchaya et al.[18] found that the methanolic extract from leaves of C. arabica L. showed high antioxidant activity. Total antioxidant activity was significantly associated with drying and maturity, fresh young (92.93±0.51%), fresh mature (92.24±0.95%), dried young (95.01±0.44%), and dried mature (93.40±0.70%), respectively. The methanolic extract from green beans of C. arabica L. in the DPPH test showed an IC$_{50}$ value of 86.14 µg/mL.[19] The methanolic extract from green beans of C. arabica L. in the DPPH test showed an IC$_{50}$ value of 86.14 µg/mL.[19]

**Anti-inflammatory activity**

The topical anti-inflammatory activity (carrageenan-induced paw edema) of an ointment prepared using a methanolic extract from green beans of C. arabica L. histology was examined.[19]

**Antitumor activity**

According to a new study by El-Garawani, apoptotic anticancer pathway of the green and roasted C. arabica L. aqueous extracts combined with VC was examined on the cancerous MCF-7 cell line and normal human lymphocytes.[20]

**Antidiabetic activity**

Sak et al.[21] found that C. arabica L. bean and leaf extract showed a high decrease in blood glucose levels compared to the control group. Meilby et al.[22] found cafestol could increase glucose-stimulated insulin secretion in vitro and increase glucose uptake in human skeletal muscle cells. Cafestol increased insulin secretion from isolated islets by 75%—87%
Minireview

compared to the control group. Liu et al.\textsuperscript{[23]} found that trigonelline had protective efficiency on type 2 diabetes and diabetic peripheral neuropathy by decreasing blood glucose. Ginsenoside Rb1 and trigonelline could prevent the development of diabetic renal lesions by regulating the expression of miR-3550 and further associating with the Wnt/β-catenin signaling.\textsuperscript{[24]}

Live protection activity

Wiltberger et al.\textsuperscript{[25]} reported that coffee consumption is associated with a decreased risk of hepatocellular carcinoma recurrence and provides for increased survival following orthotopic liver transplantation. Multivariate analysis showed that coffee intake emerged as a major factor of hazard reduction for overall survival postoperative. Vitaglione et al.\textsuperscript{[26]} reported that coffee consumption could reduce high-fat diet-induced liver macrovesicular steatosis and serum cholesterol, alanine aminotransferase and glucose.

Neuroprotective activity

Ishida et al.\textsuperscript{[27]} found that 5-cafeoylquinic acid, one of the primary coffee polyphenols, was determined degraded Aβ fibrils.\textsuperscript{[27]} Zeitlin et al.\textsuperscript{[28]} confirmed caffeine shifted the balance between neurodegeneration and neuronal survival toward the stimulation of pro-survival cascades and inhibited pro-apoptotic pathways in the striatum and/or cortex to against AD. Using a MPTP neurotoxin model of PD, Chen et al.\textsuperscript{[29]} confirmed that caffeine might protect against PD and PD-like features by stabilizing the BBB in part. The combination of theanine plus caffeine as a neuroprotective potential effect.\textsuperscript{[30]} Trigonelline has a potential therapeutic effect on the heart tissue of colitis and a neuroprotective effect, which can improve cognition and alleviate neuronal loss.\textsuperscript{[31,32]}

Conclusion and Perspective

In summary, \textit{C. arabica} L. is widely distributed in Yunnan province in China as a high medicinal value plant. With the improvement of modern instruments and experimental techniques, many chemical constituents have been isolated from \textit{C. arabica} L. including alkaloids, flavonoids, terpenes, phenolic acids and their derivatives, sterols, flavor compounds and other compounds. The diversity of its chemical ingredients leads to a wide range of pharmacological activities such as antioxidant, anti-inflammatory, antitumor, antidiabetic, live protection, and neuroprotective activities. It should be pointed out that the researchers are mainly focused on finding compounds in \textit{C. arabica} L., but they do not conduct in-depth research on the mechanism of their action. Therefore, for more rationally and effectively to develop resources in \textit{C. arabica} L., researchers should perform further research on its chemical constituents, bioactivities and the mechanism of action in the future.

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Conflict of Interest

The authors declare no conflict of interest.

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