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YELLOW CAMELLIAS: A REVIEW OF CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES

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Abstract

To date, 69 species of yellow Camellia have been found in South China and Vietnam, and they have attracted substantial attention from scientists. Chemical and biological studies have only been carried out on a few species, with the main focus on the Chinese species Camellia nitidissima, but have shown that the main active ingredients of these yellow camellia species include flavonoids, phenolic compounds, saponins, triterpenoids, phytosterols, essential oils, amino acids, and polysaccharides. Many pharmacological studies have proved that the total extracts, fractions, and isolated substances from yellow camellia species possess antioxidant, anticancer, hypolipidemic, hypoglycemic, antiallergic, hepatoprotective, neuroprotective, anxiolytic, and antidepressant activities. This review systematically summarizes recent research results in order to provide a comprehensive and up-to-date understanding of the chemical composition and biological activities of yellow camellia species, creating a basis for research of the yellow camellia species in Vietnam and development of new products from this source.

Keywords: Biological activity; Chemical constituents; Yellow camellias.

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1. INTRODUCTION

Yellow camellia is the common name for the species of the genus *Camellia* L. with yellow flowers belonging to the family Theaceae and distributed in southern China and Vietnam. Worldwide, the genus *Camellia* consists of about 300 accepted species. In all, 97 species are distributed in China, of which 76 are endemic, and about 30 species have yellow flowers (Ming & Bartholomew, 2007; Phạm, 1991; Tran, 2002; Sealy, 1958). According to Le et al. (2020), the genus *Camellia* in Vietnam contains 95 species and 2 varieties, including 46 species of yellow camellias. Recently, Tran et al. (2019) listed 52 species of yellow camellia that have been described in Vietnam and South China, among which 40 species are native to Vietnam. Summarizing all the recent reports on yellow camellias (Le, 2017; Le et al., 2020; Le & Luong, 2016; Quach, Luong et al., 2021; Quach, Doudkin et al., 2021; Tran, 2003; Tran & Luong, 2012), a total of 69 yellow camellias species have been described to date, of which 56 species are found in Vietnam.

Some species of yellow camellias have been used medicinally in China for thousands of years. *C. nitidissima* is considered a particularly precious medicinal plant for the treatment of malignant tumors, jaundice hepatitis, liver cirrhosis, infections of the urinary system, nephritis, hypertension, irregular menstruation, dysentery, diarrhea, and sores (He, Li et al., 2018). Recently, the chemical composition and biological effects of yellow camellia species have attracted the attention of Chinese scientists. Their research results have shown that yellow camellias contain many bioactive components, including flavonoids, saponins, polysaccharides, amino acids, and volatile compounds. Yellow camellias possess remarkable antioxidant and anticancer effects (Dai et al., 2016; He, Li et al. 2019; Hou et al., 2018; Qi et al., 2016) and hypoglycemic, hypolipidemic, antibacterial, antiallergic, and antidepressant activities (He et al., 2015; He et al., 2017; He, Sai et al. 2018; Lee & Yen, 2006; Lin et al., 2013; Song et al., 2011). In the past ten years, these results have motivated many Vietnamese scientists to research yellow camellias in Vietnam as a way to develop new products for community health (Hoàng et al., 2016; Huỳnh et al., 2019; Nguyen, Pham et al., 2018; Nguyễn et al., 2019; Phạm et al., 2019; Trần, 2018; Trần et al., 2017). However, despite the large number of yellow camellia species in Vietnam, there have been few studies of their composition and biological activity and no review article in this research area. Therefore, this paper summarizes the published research results on the chemical composition and biological effects of yellow camellia species to provide an overview of these species and to give direction for exploring the potential of yellow camellias from local sources for drug development in Vietnam.

2. METHODS

A search for literature on the chemical constituents and biological effects of compounds and extracts from yellow camellias was performed using Web of Science, Pubmed, ScienceDirect, ResearchGate, and Google Scholar, updated to July 2021. The search used the keywords: “yellow camellia,” the scientific names of 69 yellow camellia species, “chemistry,” “biological activity,” “medicinal plants,” and “natural products.” The references found were then studied in detail.

3. CHEMICAL CONSTITUENTS OF YELLOW CAMELLIAS

Of the yellow camellias, the most well-studied species is *C. nitidissima*, followed by *C. chrysantha* and *C. euphlebia*. The main focus has been on the leaf and flower parts. Chemical studies of these species have shown that they contain major classes of substances similar to *C. sinensis*, including phenolic compounds, flavonoids, saponins, polysaccharides, amino acids, and essential oils.

3.1. Phenolic composition

Phenolic compounds are considered the main constituents of all *Camellia* species and have received the most research attention (Nguyen et al., 2018; Song et al., 2011; Wan et al., 2011; Wang et al., 2017; J. B. Wei et al., 2015; Yang et al., 2017; Yang et al., 2018).

The content of the main phenolic classes has been evaluated by many studies and is summarized in Table 1. The most common method to quantify total polyphenols is the colorimetric method using Folin-Ciocalteu reagent (Lin et al., 2013; Trần et al., 2017). The research results presented in other units of measurement were converted to milligrams of gallic acid equivalent (GAE) per gram. The content of total polyphenols in leaves has been studied more than other plant parts, and the results show significant differences between species. The total flavonoids were often higher in flowers than in leaves of the same species (Tang et al., 2009; Trần, 2018). Among 14 yellow camellia species in China, the new leaves of *C. pingguoensis* contained the highest amount of total flavonoids (220.11 mg/g), while the lowest total flavonoid content was found in one-year-old leaves of *C. tunghinensis* (15.18 mg/g) (Huang et al., 2011).

Song et al. (2011) investigated the phenolic profile of six yellow camellia species (*C. nitidissima, C. chrysantha, C. microcarpa, C. tunghinensis, C. impressinervis*, and *C. euphlebia*) by high performance liquid chromatography (HPLC) and liquid chromatography – mass spectrometry (LC-MS) and found that yellow camellia leaves contained more diverse phenolic compounds than common tea leaves (*C. sinensis*), including ellagitannins, proanthocyanidins, derivatives of apigenin, kaempferol, quercetin, taxifolin deoxyhexose, glucosyl isorhamnetin, platphyllosides, and (epi)catechin-(epi)afezelechin polymers. These compounds were imperceptible in green tea leaves, which were reported to be very rich in catechins, including catechin, epicatechin (EC), epicatechin gallate (ECG), gallocatechin (GC), epigallocatechin (EGC), and epigallocatechin gallate (EGCG) (Oliveira et al., 2016).

Total catechins and total polyphenol content of the leaves from six species of yellow camellia, including *C. nitidissima, C. nitidissima* var. *microcarpa, C. impressinervis, C. murauchii, C. euphlebia*, and *C. tunghinensis*, were defined by Lin et al. (2013). The results show that total catechins varied from 297.56 μg/g to 1071.52 μg/g and that *C. murauchii* contained the highest level of total catechins, while *C. nitidissima* var. *microcarpa* possessed the lowest content. Among the substances quantified, namely EC, ECG, GC, EGC, EGCG, catechin, catechin gallate (CG), gallocatechin gallate (GCG), and ECG, EGCG accounted for the largest content, while GC was not detectable

in all leaf samples of the six yellow camellia species. The total polyphenol content, determined by Folin−Ciocalteu assay, varied from 10.30 mg to 5.87 mg gallic acid equivalent/g on the basis of fresh leaf weight. The total phenols of *C. nitidissima* leaf ethanol extract was 281.04 mg gallic acid equivalent/g (Wang et al., 2018). The 70% ethanol extract from *C. nitidissima* leaves of different development periods, including new, one-year-old, and two-year-old leaves, contained 101.45 mg/g, 30.79 mg/g, and 22.9 mg/g total flavonoid, respectively (Huang et al., 2011).

The total polyphenol content in the leaf samples of 16 yellow camellia species that grow naturally in Vietnam ranged from 52.2 mg to 301.1 mg gallic acid equivalent/g with the highest values belonging to *C. cuongiana* (301.1 mg/g), *C. capitata* (253.7 mg/g), and *C. dalatensis* (239.6 mg/g) (Ngô et al., 2016; Trần et al., 2017).

Table 1. Total content of main phytochemical classes in yellow camellia species

Species	Plant parts	Total polyphenols (mg GAE/g)	Total flavonoids (mg/g)	Total catechins (μg/g)	References
C. perpetua	Leaf	70.1	7.8		Tang et al. (2009)
C. chrysanthoides	Leaf	75.7	8.2		Tang et al. (2009)
S. murauchii	Leaf	10.30		1071.52	Lin et al. (2013)
S. impressinervis	Leaf	80.85	7.89		Song et al. (2011)
	Leaf	9.70		345.50	Lin et al. (2013)
	Leaf	131.9	11.2		Tang et al. (2009)
S. euphlebia	Leaf	43.83	1.43		Song et al. (2011)
	Leaf	9.70		488.92	Lin et al. (2013)
S. microcarpa	Leaf	34.19	1.99		Song et al. (2011)
S. nitidissima	Leaf	25.87	0.75		Song et al. (2011)
	Leaf	8.36		362.89	Lin et al. (2013)
	Leaf	281.04			Wang et al. (2018)
	Flower	65.6	217.6		Tang et al. (2009)
	Leaf	39.5	9.3		Tang et al. (2009)
	Seed	58.8	68.5		Tang et al. (2009)
C. nitidissima var. *microcarpa*	Leaf	8.61		297.56	Lin et al. (2013)
S. tunghinensis	Leaf	11.42	1.12		Song et al. (2011)
		5.87		469.54	Lin et al. (2013)
S. chrysantha	Leaf	23.49	1.09		Song et al. (2011)
	Leaf	44.2	85.0		Lin et al. (2010)
	Leaf		76.1		Trần (2018)
	Flower		157.8		Trần (2018)

Table 1. Total content of main phytochemical classes in yellow camellia species (cont.)

Species	Plant parts	Total polyphenols (mg GAE/g)	Total flavonoids (mg/g)	Total catechins (μg/g)	References
C. dalatensis	Leaf	239.6			Trần et al. (2017)
C. vidalii	Leaf	117.3			
C. thuongiana	Leaf	93.4			
C. inusitata	Leaf	60.0			
C. dilinhensis	Leaf	80.4			
C. ninhii	Leaf	52.2			
C. dormoyana	Leaf	181.3			
C. capitata	Leaf	253.7			
C. langbianensis	Leaf	79.2			
C. piquetiana	Leaf	125.8			

Flavonoids, phenolic acids, tannins, and other phenolic compounds have been isolated from the leaves and flowers of yellow camellias. The structures of these compounds are shown in Figures 1 and 2.

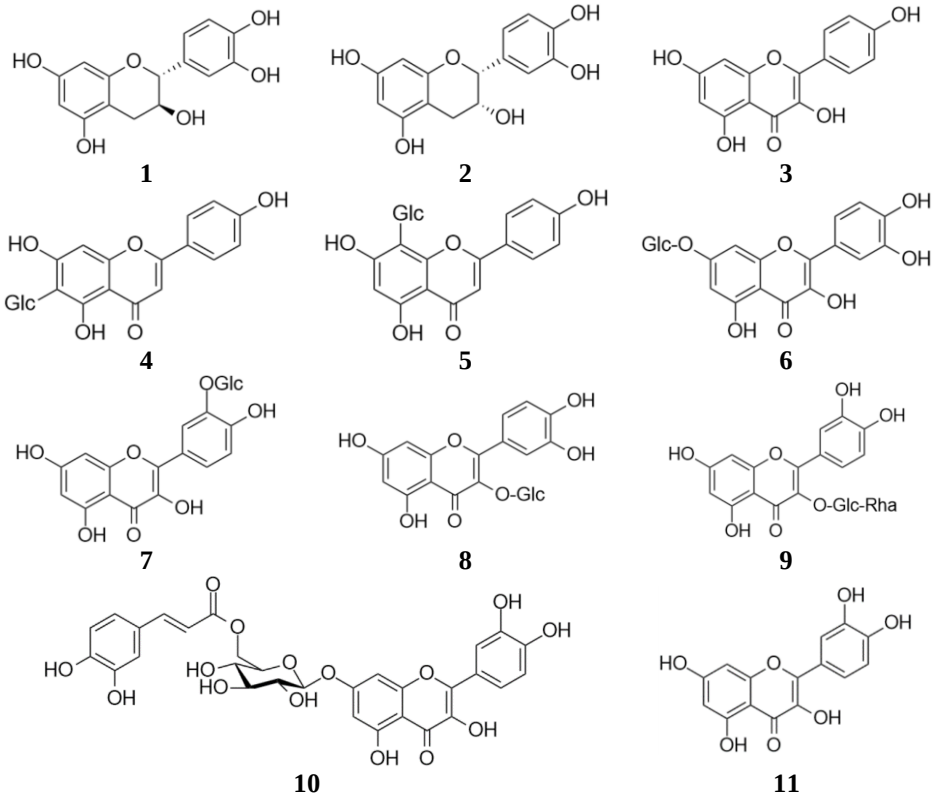


Figure 1. Structures of flavonoids isolated and identified in yellow camellias

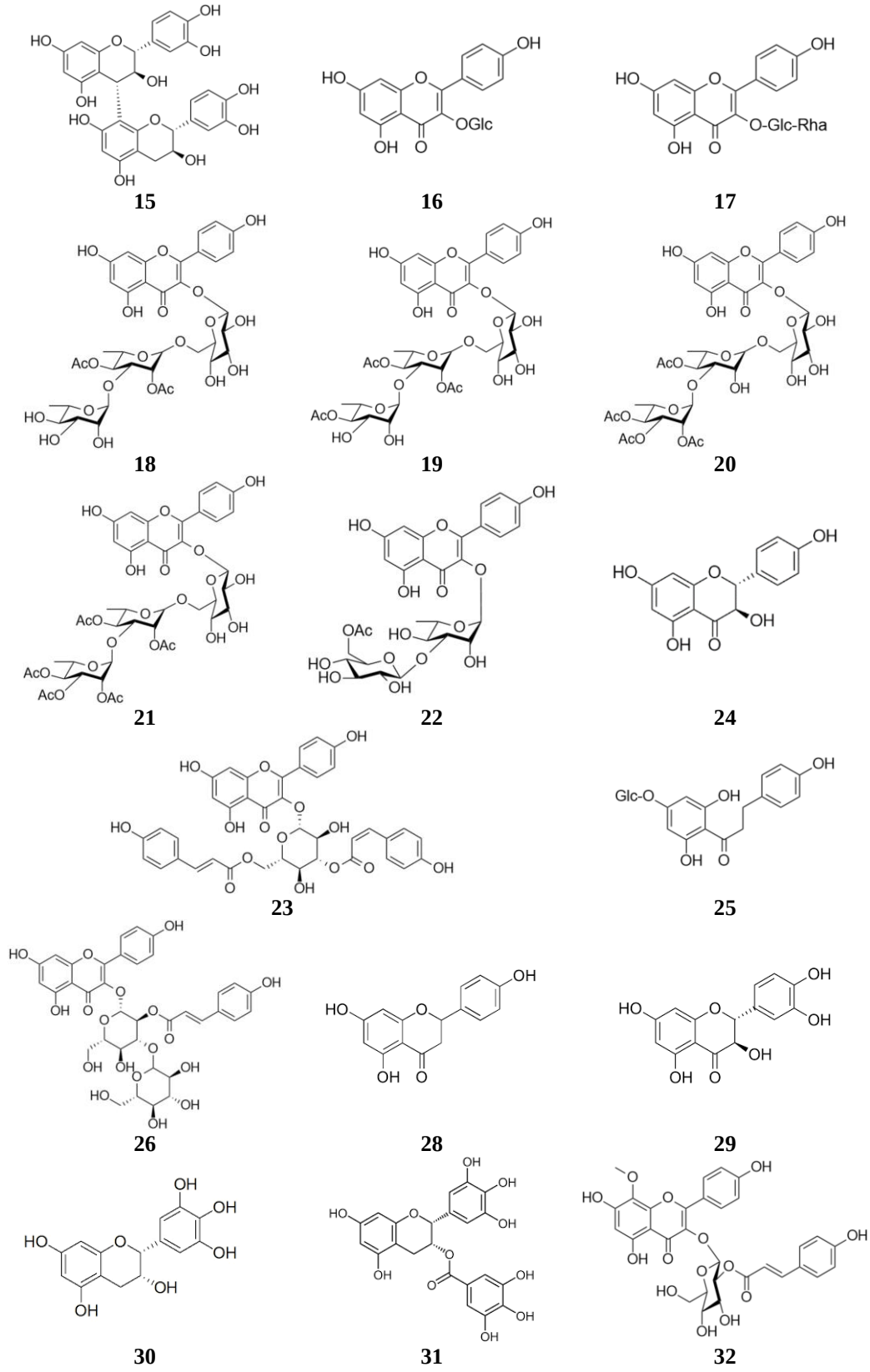


Figure 1. Structures of flavonoids isolated and identified in yellow camellias (cont.)

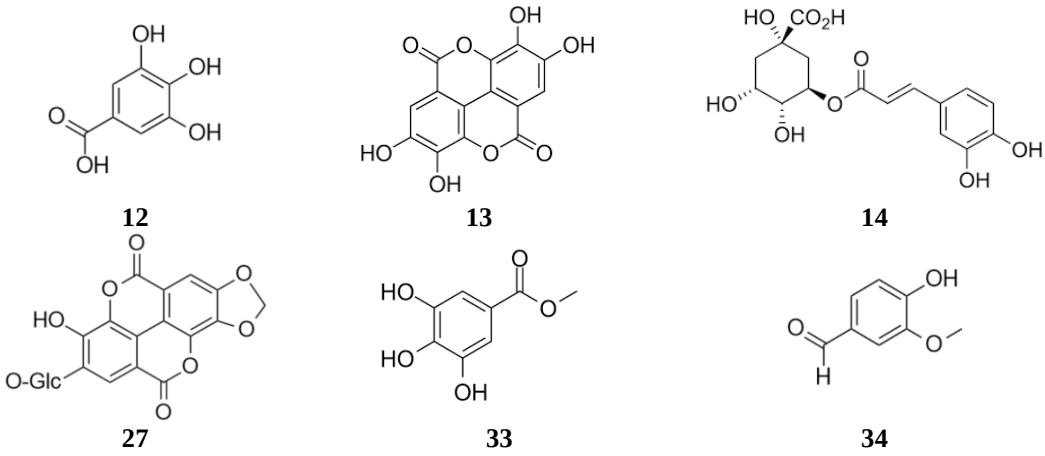


Figure 2. Structures of phenolic compounds isolated from yellow camellias

Catechin (**1**), epicatechin (**2**), kaempferol (**3**), isovitexin (**4**), vitexin (**5**), and quercetin-7-O-β-D-glucopyranoside (**6**) were identified and quantified in the leaves of *C. chrysantha* using the LC-ESI-MS method. The catechin and epicatechin content accounted for the largest amounts and varied from 32.23 μg/g to 44.89 μg/g and from 36.93 μg/g to 55.56 μg/g, respectively (J. B. Wei et al., 2015). Besides vitexin and quercetin-7-O-β-D-glucopyranoside, three other flavonoid glycosides, quercetin-3'-O-β-D-glucopyranoside (**7**), quercetin-3-O-β-D-glucopyranoside (**8**), and quercetin-3-O-rutinose (**9**), were isolated from the ethyl acetate and water-soluble fractions of the flowers of *C. chrysantha* collected in Vietnam (Nguyen et al., 2018).

Four flavonoids were isolated from the flowers of *C. nitidissima*, including quercetin 7-O-(6''-O-E-caffeoyl)-β-D-glucopyranoside (**10**), quercetin (**11**), quercetin 7-O-β-D-glucopyranoside, and quercetin 3-O-β-D-glucopyranoside, the first of which was shown to inhibit proliferation and induce apoptosis of human lymphoma U937 cells (Peng, Yu, et al., 2012). Catechin, gallic acid (**12**), ellagic acid (**13**), quercetin, kaempferol, and chlorogenic acid (**14**) were identified in *C. nitidissima* flower dichloromethane extract by HPLC Triple TOF MS/MS analysis. All six identified compounds exhibited inhibitory activities on swimming motility, swarming motility, and pyocyanin production, among which the strongest effects belonged to ellagic acid with IC_{50} values of 0.020 ± 0.003 mg/mL, 0.024 ± 0.008 mg/mL, and 0.067 ± 0.002 mg/mL, respectively (Yang et al., 2017). Twelve flavonoids were isolated and elucidated from *C. nitidissima* flowers by Yang et al. (2018), including catechin, catechin-4-α,8-catechin (**15**), quercetin, isoquercetin, kaempferol, kaempferol 3-O-β-D-glucopyranosyl (**16**), kaempferol-3-O-β-D-rutinoside (**17**), kaempferol 3-O-[α-L-rhamnopyranosyl-(1→3)-2,4-di-O-acetyl-α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside (**18**), kaempferol 3-O-[4-O-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-O-acetyl-α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside (**19**), kaempferol 3-O-[2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl-(1→3)-4-O-acetyl-α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside (**20**), kaempferol 3-O-[2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-O-acetyl-α-L-rhamnopyranosyl -(1→6)]-β-D-glucopyranosid (**21**), and multiflorin C (**22**). In addition, 21 phenolic

compounds in the ethanolic extract fraction of *C. nitidissima* flowers were identified by HPLC Triple TOF MS/MS (Yang et al., 2018). Moreover, 3-cinnamoyltribuloside (**23**), a kaempferol derivative, was isolated from the flowers of *C. nitidissima* and shown to be a potent inhibitor against NO production and iNOS mRNA expression associated with RAW 264.7 cell-activated lipopolysaccharide as well as the expression of a wide range of inflammatory cytokines, including TNF-α, IL-1β, and IL-6, both at the mRNA level and the protein level (Wang et al., 2020).

From the leaves of *C. nitidissima*, aromadendrin (**24**), catechin, phlorizin 4'-O-β-D-glucopyranoside (**25**), and kaempferol-3-O-[2-O-(trans-p-coumaroyl)-3-O-α-D-glucopyranosyl]-α-D-glucopyranoside (**26**) were isolated and identified (Hou et al., 2018; Qi et al., 2016). Additionally, a molecular network guided HPLC-UV-FLD method was performed to identify compounds with global antioxidant activity in *C. nitidissima* that indicated antioxidant ingredients including gallic acid, catechin, salicylic acid, and okicamelliaside (**27**) as a new antioxidant ingredient (Cheng, Hou et al., 2021). This ellagic acid glucoside was isolated from leaves of *Camellia japonica* and proven to be 12,000 times more potent than ketotifen fumarate, an antihistaminic drug, in inhibiting the degranulation of RBL-2H3 cells (Kuba-Miyara et al., 2012; Onodera et al., 2010). It also displayed antitumor activity by selectively inhibiting the formation of HSP90-CDC37 protein complex (Cheng, Liu et al., 2021).

From the ethanol extract of *C. hakodae* flowers collected in Soc Son district, Hanoi, 10 flavonoid compounds were isolated and identified, namely quercetin, kaempferol, naringenin (**28**), taxifolin (**29**), epigallocatechin (**30**), (−)epicatechin, epigallocatechin gallate (**31**), quercetin 7-O-β-D-glucopyranoside, quercetin 3-O-β-D-glucopyranoside, and sexangularetin 3-O-(2″-O-(E)-p-coumaroyl-β-D-glucopyranoside) (**32**). The last was a new compound that was proven to exhibit weak-to-moderate cytotoxic activities against KB (IC_{50} 72.7 μg/mL), Lu (IC_{50} 90.2 μg/mL), and HepG2 (IC_{50} 192.0 μg/mL) cell lines, but was inactive against MCF7 (IC_{50} 256.0 μg/mL) (Nguyen, Tran, Pham et al., 2019).

C. cucphuongensis, a yellow camellia species discovered in Vietnam, named scientifically, and published by Tran and Rosmann (1998), was the subject of a phytochemical study. From the leaves of this species, kaempferol, methyl gallate (**33**), gallic acid, astragalin, and vanillin (**34**) were isolated and identified (Phạm et al., 2019; Trần, 2019).

By the LC/HRMS method, 46 compounds were detected in 70% ethanol extract from flowers of *C. quephongensis* collected in Que Phong, Nghe An Province, Vietnam. Five flavonoids and five phenols were identified by HRMS, including isorhamnetin, catechol, ephicatechin, rutin, quercetin 3-O-β-D-glucopyranoside, pyrogalol, gallic acid, vanillin, and piceatannol (Nguyễn et al., 2017).

3.2. Saponins

Total saponin content was determined by the colorimetric method based on coloration reaction with vanillin in the methanol extract of different plant parts from four

yellow camellia species. Among these, the leaf methanol extract from *C. nitidissima* produced the highest saponin amount (432.40 mg/g), surpassing *C. impressinervis* (362.9 mg/g), *C. chrysanthoides* (300.8 mg/g), and *C. perpetua* (359.0 mg/g) (Tang et al., 2009). The same study also showed that the saponin content of *C. nitidissima* leaves was significantly higher than from seeds (135.3 mg/g) and flowers (213.0 mg/g) (Tang et al., 2009). Wei, Ning, & Liu (2015) set up an ultrasonic-extraction process for saponins from *C. chrysantha* leaves with an extract rate of 15.16%.

Structures of saponins identified in yellow camellias are shown in Figure 3.

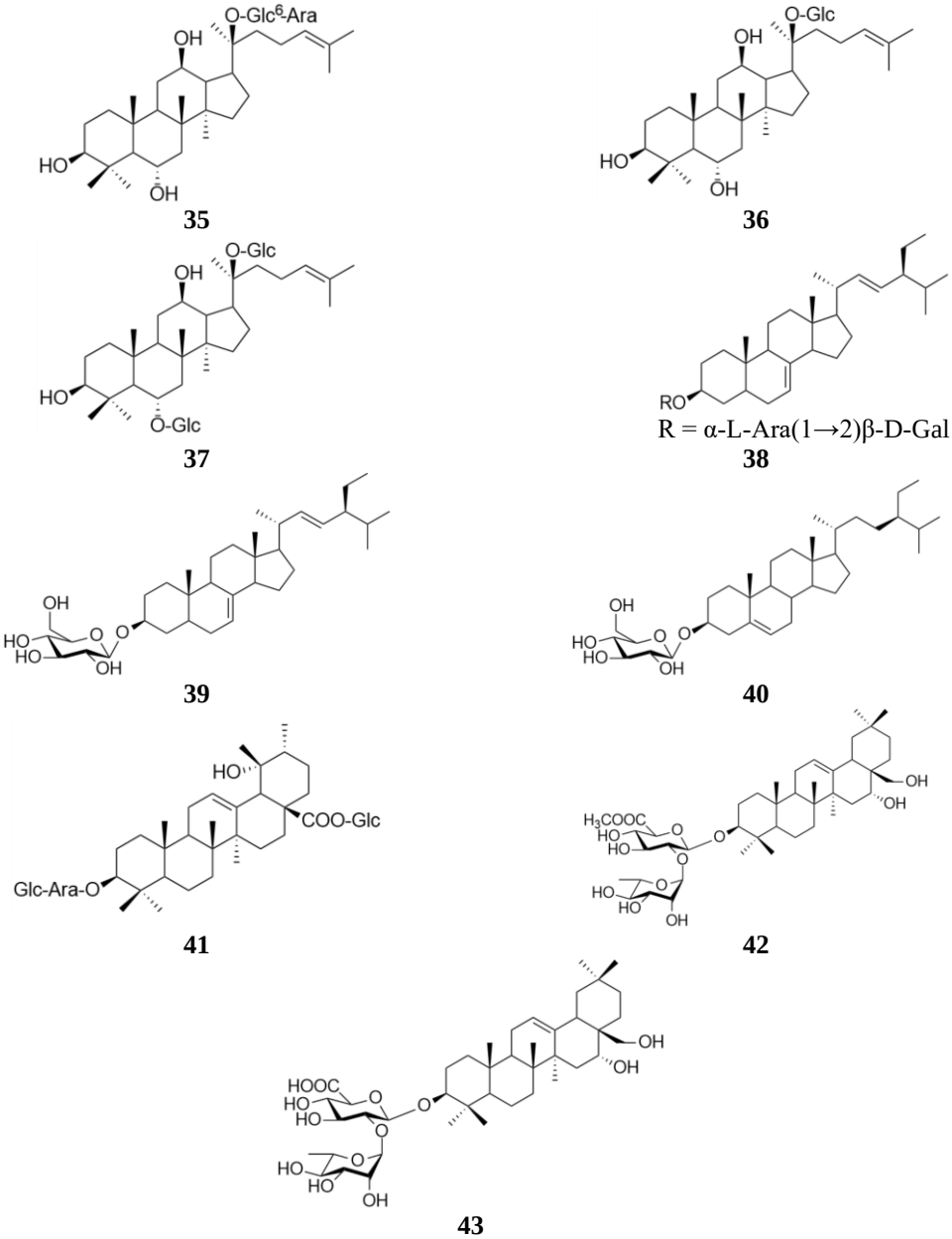


Figure 3. Structures of saponins isolated and identified in yellow camellias

From the aqueous extract of *C. nitidissima* leaves, four saponins with antioxidant activities were purified by XAD16 chromatography (Zeng, 2010). Subsequent research isolated triterpene saponin containing glucose and galactose moiety in its chemical structure, which was shown to have high antioxidant activity (Zeng, 2010). From an aqueous extract of *C. nitidissima* leaves, (20(S)-O-protopanaxatriol 20-O-α-L-arabinofuranosyl(1→6)-β-D-glucopyranoside) (**35**), (20-O-β-D-glucopyranosyl-20(S)-protopanaxatriol (**36**), and ginsenoside Rg1 (6,20-di-O-β-glucosyl-20(S)-protopanaxatriol) (**37**) were isolated and identified (Su et al., 2012). Interestingly, the three aforementioned compounds are common in the genus *Panax* but are rarely found in the genus *Camellia* (Qi et al., 2011). These triterpene saponins have antioxidant, cardioprotective, neuroprotective, and antidiabetic activities (Qi et al., 2011). This, in turn, suggests that these saponins might have a role in the pharmacology of *C. nidissima*.

Two C-27 steroidal saponins, stigmasta-7,22-diene-3-O-[α-L-arabinopyranosyl (1→2)]-β-D-galactopyranoside (**38**) and α-spinasteryl-β-D-glucopyranoside (**39**) were successively isolated from the leaves of *C. nitidissima* (Hou et al., 2018; Qi et al., 2016). In the flowers of *C. nitidissima*, a sterol glycoside daucosterol (**40**) was found (Peng, Yu et al., 2011), and ilexside II [3β-O-[β-D-glucopyranosyl-(1→2)-α-L-arabinopyranosyl]-pomolic acid-(28→1)-β-D-glucopyranosyl ester] (**41**) was identified in *C. nitidissima* leaves (Wei et al., 2014).

The leaves of *C. bugiamapensis*, a yellow camellia species from Vietnam, were investigated for phytochemical composition and bioactivity for the first time by Nguyen et al. (2017). Two new triterpene saponins, camellioside I (**42**) and camellioside J (**43**), were isolated from the methanol extract. Camellioside I inhibited NO production with an IC_{50} of 49.42 ± 1.34 μM on lipopolysaccharide-induced NO production in RAW264.7 cells.

3.3. Triterpenoid and phytosterols

Several triterpene compounds were isolated from the leaves of *C. nitidissima* and identified as 3β-acetoxy-20-lupanol (**44**), A1-barrigenol-22a-angelate (**45**), and 3β,6α, 13β-trihydroxyolean-7-one (**46**) (Hou et al., 2018; Qi et al., 2016). Among them, A1-barrigenol-22a-angelate showed inhibiting action on the lung cancer cell line EGFR-mutant, NCI-H1975 with an IC_{50} of 13.37 ± 2.05 μM at 48 h, and thus showed strong potential for antitumor drug development (Hou et al., 2018). In the flowers of *C. nitidissima*, lupeol (**47**), oleanolic acid (**48**), β-sitosterol (**49**) were found (Peng, Yu et al., 2011).

β-sitosterol, α-spinasterol (**50**), oleanic acid, β-amyrin (**51**), and olibanumol L (**52**) were isolated from *C. euphlebia* in Guangxi, China (Yan, 2013). Additionally, β-amyrin and α-amyrin (**53**) were identified as the main components in *C. euphlebia* leaves by the GC-MS method, accounting for 17.24% and 13.6% of the total liposoluble components, respectively (L. Peng et al., 2012).

From the ethanol extract of the leaves of *C. dalatensis*, an endemic yellow camellia species from Lam Dong Province, Nguyen et al. (2019) isolated and identified two phytosterols, spinasterol and stigmasterol (**54**), and one triterpene, oleanolic acid.

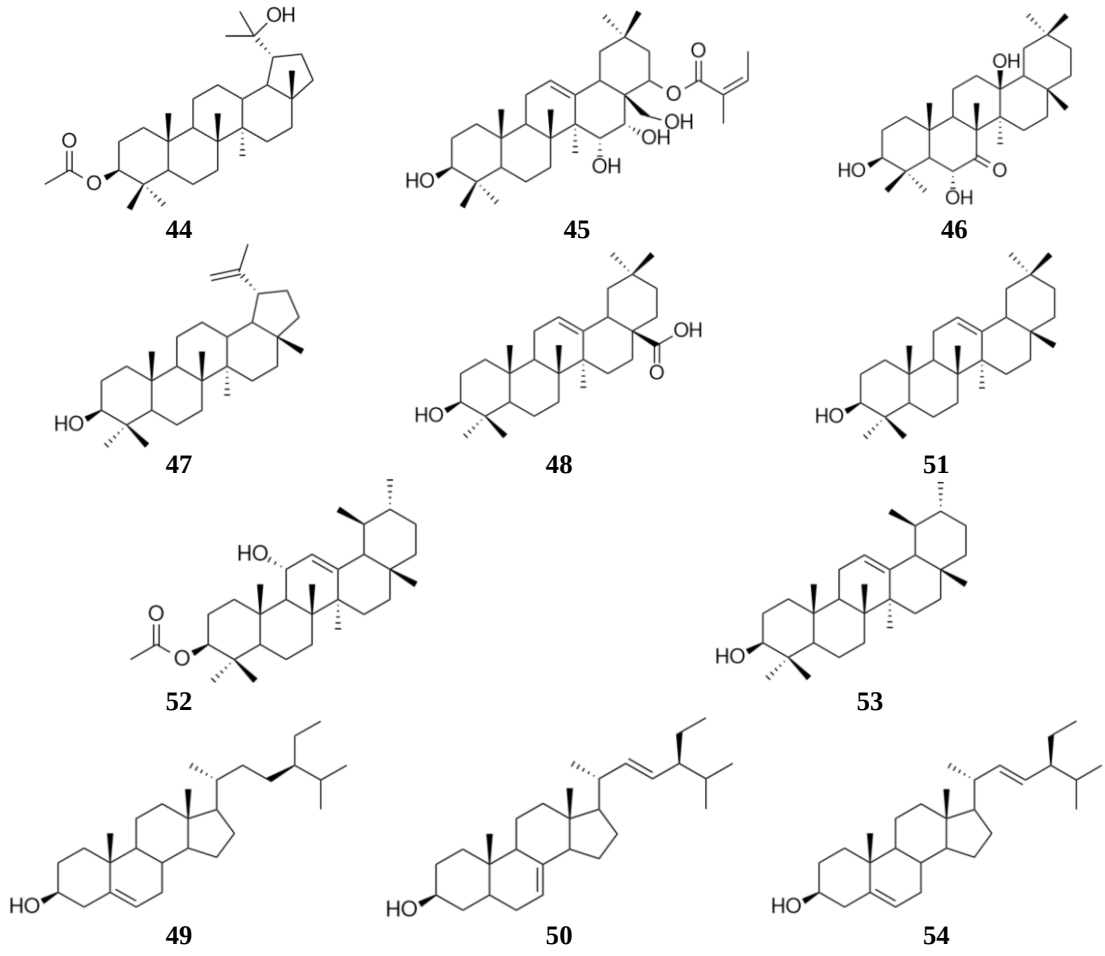


Figure 4. Structures of triterpenes and phytosterols isolated from yellow camellias

3.4. Monoterpenes

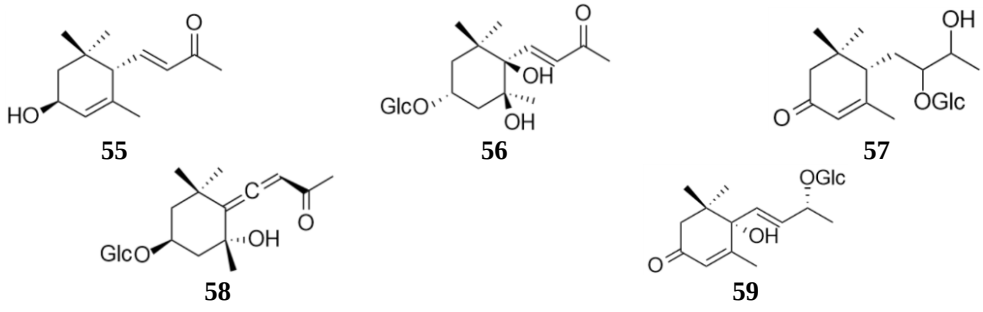


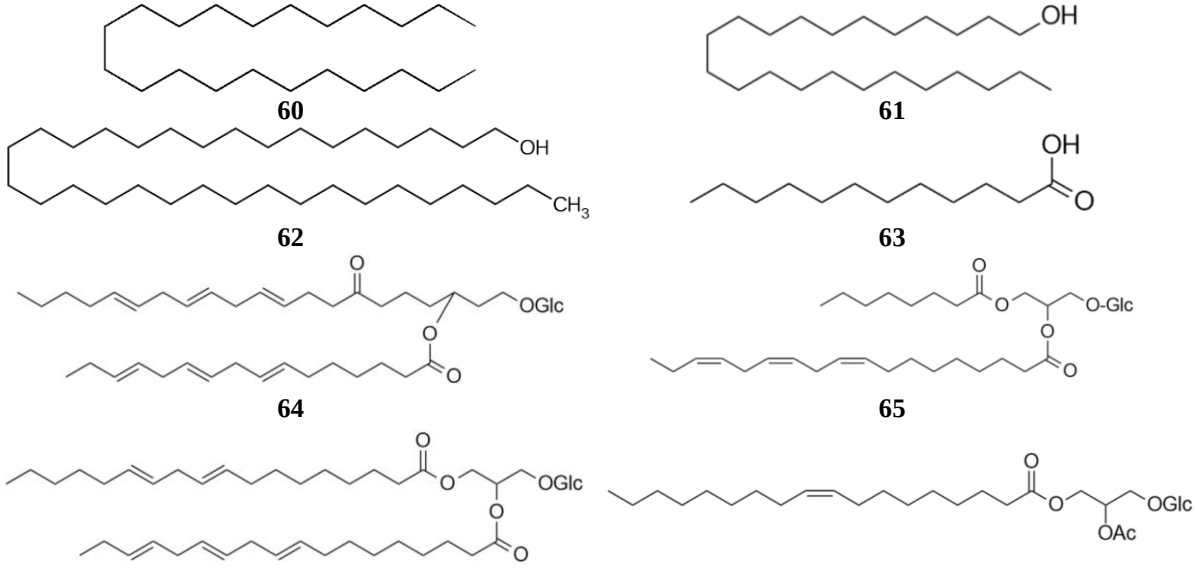
Figure 5. Structures of megastigmanes isolated from yellow camellias

Megastigmane compounds and glycosides were successively isolated from yellow camellias, including (3R,6R,7E)-3-hydroxy-4,7-megastigmadien-9-one (**55**) from the leaves of *C. nitidissima* (Hou et al., 2018; Qi et al., 2016), and camellistigoside A (**56**), camellistigoside B (**57**), icariside B1 (**58**), and (6S,9R)-roseoside (**59**) from *C. bugiamapensis* leaves (Nguyen et al., 2017).

3.5. Fatty compounds

GC-MS analysis was carried out after methyl esterification of liposoluble components from *C. euphlebia*. Twenty components were identified, among which organic acids were major chemical constituents (35.99%) with palmitic acid making up the largest part, 14.57% (L. Peng et al., 2012).

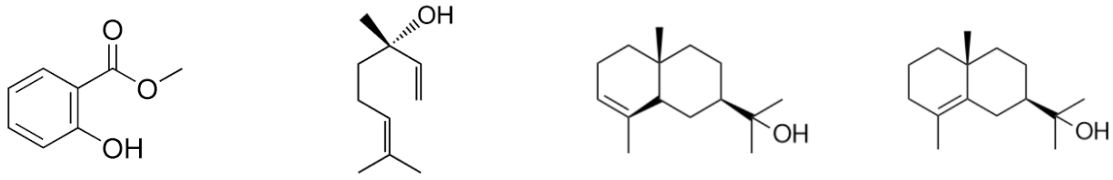
Fatty compounds isolated from yellow camellias include aliphatic hydrocarbon, acid, alcohol, ester, and glycoside derivatives, namely docosane (**60**) and 1-tricosanol (**61**) from *C. dalatensis* leaves (Nguyễn et al., 2019); n-tetratriacontanol (**62**) from *C. euphlebia* (Yan, 2013); dodecanoic acid (**63**); β-D-glucopyranoside,3-[(1-oxo-9,12,15-octadecatrienyl)oxy]- 2-[(1-oxo-9,12,15-octadecatrienyl)oxy (**64**); β-D-glucopyranoside, 2-[[(9Z,12Z,15Z)-1-oxo-9,12,15-octadecatrien-1-yl]oxy]-3-[(1-oxooctyl) oxy]propyl (**65**); β-D-Glucopyranoside,3-[(1-oxo-9,12-octadecadienyl)oxy]-2-[(1-oxo-9,12,15-octadecatrienyl)oxy]propyl (**66**); and β-D-galactopyranoside, (2S)-2-(acetyloxy) -3-[[(9Z)-1-oxo-9-octadecen-1-yl]oxy]propyl (**67**) (Hou et al., 2018; Qi et al., 2016).



60 **61** **62** **63** **64** **65** **66** **67**

Figure 6. Structures of fatty compounds isolated from yellow camellias

3.6. Essential oils



68 **69** **70** **71**

Figure 7. Structures of some volatile compounds in yellow camellias

A study of *C. nitidissima* leaves showed that methyl salicylate (**68**) was the most abundant volatile component (26.91%), followed by benzyl alcohol, cis-octahydropentalene, cis-linaloloxide, and phenylethyl alcohol at 5.92, 5.56, 4.17, and 4.01%, respectively (Huang, Chen, Wen, Li, Liu, & Wei, 2009). The GC-MS analysis of *C. nitidissima* leaf oil obtained by (Ge et al., 2019) showed the presence of methyl salicylate (6.8%) but the principal compounds were linalool (**69**) (35.8%), phytol (7.9%), and geranyl acetone (7.3%). In total, 55 constituents were identified by GC-MS in the essential oils from *C. nitidissima* leaves and 34 from flowers. While linalool was the major component in leaf oil, α-eudesmol (**70**) (34.3%), γ-eudesmol (**71**) (31.5%), and linalool (11.1%) were the most abundant in the flower oil. Both essential oils exhibited mild antioxidant activities with IC_{50} values of 164.8 and 720.3 μg/mL for DPPH assay, respectively, and no considerable antibacterial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus* (Wang et al., 2018).

Wei and Zhang (2013) found 45 volatile compounds in ether extract of *C. nitidissima* leaves and noticed distinct differences in volatile composition between this species and *C. euphlebia*, which is composed of 26 identified compounds. Phytol (58%), geranylacetone (5.6%), and n-hexanal (3.3%) were found to be the main components of the *C. euphlebia* leaf oil, while the major constituents of the oil of *C. tunghinensis* leaves were n-hexanal (17.2%), 2-pentylfuran (10.6%), phytone (7.5%), and geranyl acetone (5.0%) (Ge et al., 2019). The leaf oils of *C. euphlebia*, *C. nitidissima*, and *C. tunghinensis* exhibited moderate antioxidant effects, with IC_{50} values of 120.56–321.91 μg/mL in ABTS assays and 42.82–164.98 μg/mL in DPPH assays (Ge et al., 2019). Moreover, the oils were tested for antimicrobial activities against four microorganisms (*Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*) and showed weak antibacterial effects with MIC values of 0.625–2.5 mg/mL (Ge et al., 2019).

Additionally, Zou et al. (2015) used headspace solid phase microextraction (HS-SPME) to extract and GC-MS to determine 43 volatile compounds in *C. impressinervis* leaves. The major components identified were hexahydrofarnesyl acetone (16.24%), phytol (13.29%), α-ionone (4.82%), butylated hydroxytoluene (4.22%), β-ionone (3.41%), and 2,3-dehydro-α-ionone (3.37%).

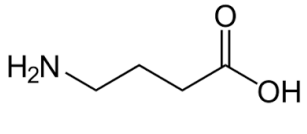
3.7. Amino acids

The total content of free amino acid in the leaves of *C. chrysantha* was 80.8 mg/100 g, in which the ratio of proline was 38.7% (Lin et al., 2010).

All eighteen kinds of protein-bound amino acids, including the seven essential amino acids, were found in *C. nitidissima* leaves. Wild and cultivated *C. nitidissima* leaves contained 51.44 mg/g and 68.55 mg/g total amino acids, respectively. Glutamate was considered the richest amino acid, accounting for 13.22% and 12.34% of the total amino acid content in wild and cultivated *C. nitidissima* leaves, respectively. The second most abundant amino acid was aspartic acid, contributing 10.50% of the total amino acid content in cultivated *C. nitidissima* leaves (Xiong et al., 2012). These two amino acids were also present in the highest amounts in leaves of other yellow camellia species, such

as *C. euphlebia, C. nitidissima* var. *microcarpa, C. impressinervis, C. murauchii*, and *C. tunghinensis* (Lin et al., 2013).

Among the above six yellow camellia species, *C. euphlebia* leaves had the highest total amino acids (11.52 mg/g). γ-Aminobutyric acid (**72**) (GABA) was found in 5 of 6 investigated species, and its content was shown to vary between 409.62 μg/mL (*C. euphlebia*) and 257.45 μg/mL (*C. nitidissima* var. *microcarpa*), with the exclusion of *C. tunghinensis*. GABA is a neurotransmitter with strong inhibitory effects, mainly on the central nervous systems of mammals, and shows antihypertensive actions. Theanine (**73**), a unique free amino acid found only in tea plants, was detected in only two of the six species, including *C. murauchii* and *C. nitidissima* var. *microcarpa* at the amounts of 6.88 μg/mL and 6.97 μg/mL, respectively. Theanine provides a majority of the signature sweet and umami taste of tea and has pharmacological effects. This amino acid is considered an index for measuring tea characteristics and quality (Lin et al., 2013).



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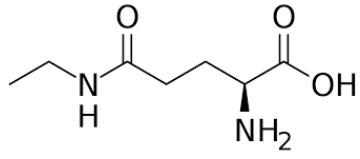

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Figure 8. Structures of nonprotein amino acids in yellow camellias

3.8. Polysaccharides

The method using phenol-sulfuric acid was used in the study by Niu et al. (2014) to quantify the polysaccharides in four *C. nitidissima* parts, with the content in aqueous extracts of flowers, bud tips, peels, and leaves being 32.88, 35.89, 30.02 and 29.48%, respectively. This result is similar to those of common green tea leaves and flowers (the aqueous extract of *C. sinensis* leaves and flowers contained 36.4 and 29.3 mg/g, respectively, while the aqueous extract of *C. oleifera* leaves contained 37.7 mg/g polysaccharides) (Feng et al., 2014; Wang et al., 2010). However, although their polysaccharide contents were similar, there were differences regarding the type and ratio composition of monosaccharides among camellia species. Subsequent research showed that the hypolipidemic polysaccharides from *C. nitidissima* leaves are comprised of six different monosaccharide compounds, namely arabinose (43.26%), galactose (27.56%), rhamnose (14.30%), glucose (10.69%), xylose (2.34%), and mannose (1.82%) (J. B. Wei et al., 2008; L. Wei et al., 2008).

The isolation of acidic protein-bound polysaccharides from *C. nitidissima* leaves resulted in neutral saccharide, galacturonic acid, and protein being found with contents of 41.9, 24.4, and 12.6%, respectively. The constituents of neutral saccharide included glucose (31%), galactose (27%), arabinose (21%), mannose (13%), rhamnose (6%), and xylose (2%) (Tian et al., 2011). The majority of crude polysaccharides were galacturonic acid and pectin substances. Furthermore, by ion-exchange and size-exclusion chromatography, Tian (2011) was able to obtain TPS3-1, a purified polysaccharide with

a molecular weight of 4.15 x 10^6 U. This polysaccharide's structure went through further analysis, including partial acidic hydrolysis, IR, and NMR. The results showed two domains that comprised TPS3-1, a smooth one containing methyl esterified polygalacturonic acid, and a hair-like one containing three types of varying chemical and structural fragments (Tian, 2011).

3.9. Other phytochemical constituents

The caffeine content in leaf samples of six yellow camellia species *C. nitidissima, C. nitidissima* var. *microcarpa, C. impressinervis, C. murauchii, C. euphlebia*, and *C. tunghinensis* from Tea Flower Manor (Ping Xi, Taipei, Taiwan) was quantified by the HPLC method and found to vary from 18.02 μg/g (*C. murauchii*) to 33.83 μg/g (*C. nitidissima*) (Lin et al., 2013). However, no caffeine was detected in the leaves of six species of yellow camellia collected from Yellow Camellia Garden (Guangxi, China) in January 2008, including C. *nitidissima, C. impressinervis, C. euphlebia, C. tunghinensis, C. microcarpa*, and *C. chrysantha* (Song et al., 2011).

Wei et al. (2014) also found in *C. nitidissima* leaves quinic acid, daucic acid, 1,3,4-tri-O-acetyl-α-acetyl-α-D-frutofuranosyl,3,6-tri-O-acetyl-α-D-glucopyranoside, dyhydroxyl-6-methyloxy-tetrahydro-2H-pyran-3-oxyl-tetrahydro-2H-pyran-3,4,5-triol, 4′H-spiro[1,3-dioxolo[4,5-c]pyran-2,3-pyran]-3a, 4,5,7(6H)-tetrayl tetraacetate, (2S,3aR, 4′S,5′S,6R,6′R,7R,7aS)-6,6′-bis[(acetyloxy)methyl]tetrahydro-4H, and (2S,3R,4R,5R,6S) -2-(2S,3R,4S,5S,6R)-4,5-dyhydroxyl-2-(5-hydroxyl-7-methyloxy-2-(4-methoxyphenyl) -4-carbonyl-4H-chromene-6)-6-(hydroxylmethyl)-tetrahydro-2H-pyran-3-oxyl)-4,5-dyhydroxyl-6-methyl-tetrahydro-2H-pyran-3-tetraylacetate.

The contents of vitamin C and vitamin E in the flowers of *C. chrysantha* were 90 mg/100 g and 520 mg/100 g, respectively (Lin et al., 2010).

3.10. Trace elements

Eighteen mineral elements, namely Na, K, Mg, Ca, Cu, Zn, Mn, Al, Fe, Ni, P, N, Cr, Co, Ge, Se, Mo, and V, have been detected in *C. nitidissima, C. euphlebia*, and *C. pubipetala* by atomic absorption spectrometry (AAS), inductively coupled plasma atomic emission spectrometry (ICP-AES), inductively coupled plasma-mass spectrometry (ICP-MS), and hydride generation-atomic fluorescence spectrometry (HG-AFS) (Chai et al., 2016; Gan, 2009; He, Li et al., 2018; Lin et al., 2010; Peng & Gan, 2009; J. B. Wei et al., 2008; Xiong et al., 2012).

Leaves of four yellow camellia species collected in Vietnam, *C. gilbertii, C. hakodae, C. hirsuta*, and *C. petelotii*, were investigated for mineral composition. V, Zn, Mn, and Se were detected in all samples (Nguyễn et al., 2007).

4. PHARMACOLOGICAL ACTIVITIES

Most recent studies of biological activities of yellow camellias focused on antioxidant and anticancer activity of total extracts, fractions, or isolated constituents from leaves and flowers of the plants. In addition, yellow camellias have been proven to possess hypolipidemic, hypoglycemic, antiallergic, immunomodulatory, hepatoprotective, neuroprotective, anxiolytic, and antidepressant activities. *C. nitidissima* and *C. euphlebia* were the subjects of the most research among yellow camellias. Furthermore, studies of acute, genetic, and subchronic toxicities of *C. nitidissima*, *C. euphlebia*, and *C. hakodae* leaf extracts suggested high safety profiles (Nguyen et al., 2020; L. Peng et al., 2011; Xia, Huang et al., 2013).

The recent results of pharmacological activities of yellow camellias are summarized in Table 2.

Table 2. Pharmacological activities of yellow camellias

Extract/Preparation	Model	Actions	References
Antioxidant activity			
C. nitidissima leaf aqueous extract	*In vitro* on ·OH and $\cdot O_2^-$	Exhibited radical scavenging activities	Qin et al. (2008)
Total polyphenols from *C. nitidissima* leaf aqueous extract	*In vitro* on ·OH, $\cdot O_2^-$, NO_2^- and DPPH·	Exhibited radical scavenging activities	Ning et al. (2010)
Flavonoid fraction from *C. nitidissima* leaf aqueous extract	*In vitro* on ·OH, $\cdot O_2^-$, and ROO·	Exhibited radical scavenging activities	Ning et al. (2011)
Saponin fraction from *C. nitidissima* leaf aqueous extract	*In vitro* on endothelial cells	Protected against damage induced by H_2O_2	Wan et al. (2011)
C. nitidissima leaf aqueous extract	*In vivo* on rats treated with D-galactose	Reduced MDA and increased SOD activity	Lu et al. (2015)
C. nitidissima flower total saponins	*In vitro* on ·OH, $\cdot O_2^-$, NO_2^- and DPPH·	Showed strong free radical scavenging activity	Cheng et al. (2016)
Anticancer			
95% ethanol seed extract of *C. nitidissima*	*In vitro* on human cervical cancer, prostate cancer, human monocytic leukemia, and breast cancer cell lines	Inhibited the proliferation of Hela S3, PC3, U937, MCF-7 cells	Han et al. (2009; Shi et al. (2009); Shi et al. (2013)
Flavonoids from *C. nitidissima* leaf extract	*In vitro* on human gastric adenocarcinoma and large cell lung cancer cell lines	Inhibited the proliferation of SGC-7901 and H460 cells	Nong et al. (2012)
Flavonoids from *C. nitidissima* leaf extract	*In vitro* on human gastric adenocarcinoma and large cell lung cancer cell lines	Inhibited the proliferation of SGC-7901 and H460 cells	Nong et al. (2012)

Table 2. Pharmacological activities of yellow camellias (cont.)

Extract/Preparation	Model	Actions	References
Ethanol leaf extract of *C. nitidissima*	*In vitro* on human nasopharyngeal carcinoma cell lines	Inhibited CNE-2 cell proliferation; raised cell morphology and rate of apoptosis; up-regulated Caspase-3 protein expression and down-regulated VEGF-C\VEGFR-3 protein	Shen (2011)
Aqueous flower extract of *C. nitidissima*	*In vitro* on human esophageal squamous carcinoma cell lines	Inhibited Eca109 cell proliferation; promoted apoptosis cell morphology	Dai et al. (2013)
95% ethanol flower extract of *C. nitidissima*	*In vitro* on human colon cancer cell lines	Inhibited the proliferation of HCT 116 cells	Yu et al. (2013)
C. nitidissima leaf powder	*In vivo* on rats with liver cancer induced by diethylnitrosamine	Decreased the number and area of γ-GT positive spots per cm^2 of the liver	Duan et al. (2006)
n-Butanol leaf extract from *C. nitidissima*	*In vitro on* gastric cancer cells	Inhibited growth and induced autophagy in human gastric cancer cells; enhanced the growth inhibition effect of paclitaxel	He, Li et al. (2019)
Hypolipidemic and anti-obesity activity			
C. nitidissima leaf aqueous extract	*In vivo* in quails fed by high fat diet	Decreased the contents of blood serum TC and TG	Huang, Chen, Wen, Li, Liang, & Wei (2009)
Polysaccharides from aqueous *C. nitidissima* leaf extract	*In vivo* in high-fat diet mice	Decreased the level of blood serum TC, TG and LDL-C	J. B. Wei et al. (2008)
Ethanol flower extract of *C. nitidissima*	*In vivo* in high-fat diet mice	Decreased TC, TG, LDL-C level, increased HDL-C serum level	Zhang (2015)
C. nitidissima leaf aqueous extract	*In silico* molecular docking	Inhibited the pancreatic lipase activity	Chen et al. (2021)
Flower extract of *C. nitidissima*	*In vivo* in rats with high-fat-diet-induced obesity	Decreased weight gain by reducing appetite and high-fat food intake	Zhang, Wu, & Qin (2020)
C. euphlebia flower aqueous extract	*In vivo* in high-fat diet mice	Decreased TC, TG, LDL-C level, increased HDL-C serum level	He et al. (2017)
Hypoglycemic activity			
70% methanol leaf extract of *C. nitidissima*	*In vivo* on alloxan-induced mice	Decreased the level of glucose in blood	Xia, Huang et al. (2013); Xia, Pan et al. (2013)

Table 2. Pharmacological activities of yellow camellias (cont.)

Extract/Preparation	Model	Actions	References
Anxiolytic activity			
C. nitidissima leaf aqueous extract	*In vivo* on light–dark box test and elevated plus-maze test	Increased light box time, entry ratio and time spent in open arm	He et al. (2015)
Aqueous extract from *C. euphlebia*	*In vivo* on light–dark box test and elevated plus-maze test	Increased light box time, the number of open arm entries	He et al. (2015)
Antidepressant activity			
C. nitidissima leaf aqueous extract	*In vivo* on forced swimming test and tail suspension test	Decreased the immobility duration in both the FST and TST	He et al. (2015)
Aqueous leaf extract of *C. euphlebia*	*In vivo* on forced swimming test and tail suspension test	Decreased immobility time in forced swimming test and tail suspension test	He, Sai et al. (2018)
Antiinflammatory activity			
Polysaccharides from aqueous *C. nitidissima* leaf extract	*In vivo* on mice treated with BCG and LPS	Decreased the liver index, spleen index, homogenate contents of TNF-α, IL-6 and NO	Zou et al. (2014)
Antiallergic activity			
95% ethanol peel *C. nitidissima* extract	*In vivo* on rats sensitized with the mixture of OVA and $Al(OH)_3$	Decreased the IgE and LT contents in the serum and EOS quantities in the whole blood	Wang et al. (2009)
Neuroprotective activity			
Ethyl acetate fraction of *C. nitidissima* leaf extract	*In vitro* on H_2O_2-induced cell injury and human neuroblastoma (SH-SY5Y) cells	Increased the cell viability of H_2O_2-treated SH-SY5Y cells and attenuated H_2O_2-induced apoptosis in SH-SY5Y cells	An et al. (2020)
Aqueous leaf extract of *C. euphlebia*	*In vitro* on corticosterone-induced neurotoxicity in differentiated PC12 cells	Showed neuroprotective effect	He, Jia, & Xu (2019); He, Wang et al. (2019)
Hepatoprotective activity			
C. nitidissima leaf 10% aqueous ethanol extract	*In vivo* on CCl_4-induced acute liver injury in SD rats	Decreased the pathological changes in liver tissues and decreased ALT, AST, MDA levels in serum and liver tissues; reduced ROS, TNF-α, interleukin-1β and IL-6 and blocked the p65 nuclear translocation	X. Zhang et al. (2020)

5. CONCLUSIONS

A review of the available scientific research on yellow camellias showed that, although 69 yellow camellia species have been discovered, studies on chemical composition and pharmacological effects have only focused on a few species, of which the most well-studied is *C. nitidissima*. Recent studies showed that the chemical composition of yellow camellias consists mainly of flavonoids, phenol compounds, and a few saponins, triterpenoids, phytosterols, essential oils, fatty compounds, polysaccharides, amino acids, and trace elements. Flavonoids, phenols, and saponins are the main active ingredients responsible for the biological effects of yellow camellias. Extracts from yellow camellia species have been shown in both *in vitro* and *in vivo* experiments to have antioxidant, anticancer, hypolipidemic, hypoglycemic, antiallergic, hepatoprotective, neuroprotective, anxiolytic, and antidepressant activities. Nevertheless, more studies need to be conducted to accurately determine the biochemical and physiological mechanisms of the therapeutic functions of the plants as well as to pinpoint bioactive compounds related to the biological activities.

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