

REVIEW

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Tea beyond the cup: a comprehensive review of *Camellia sinensis* (L.) O. Kuntze

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Abstract

Background Tea or *Camellia sinensis* (L.) O. Kuntze is the most consumed beverage after water. Its consumption has been considered a health promoting habit since historical times which has now been scientifically proven for its immense beneficial characteristics to human health. Tea is enriched with polyphenolic compounds which exhibit antioxidant activity.

Objective The objective is to summarize the phytochemistry, ethnomedicinal uses and pharmacological uses of the *C. sinensis* along with the identification of the research gaps. The present study is also focused on draining the attention of researchers toward this household beverage for its better utilization in pharmaceutical preparations.

Methods All the relevant data and information on *C. sinensis* has been compiled from various search data bases such as PubMed, Springer, NCBI (National Center for Biotechnology Information), Science direct, Google scholar, etc.

Results This review article highlights the various forms and formulations of *C. sinensis* leaves and the pharmacological effects of active constituents present in it. Phytochemical studies of the plant reveal the presence of about 4000 different alkaloids, flavonoids, phenolics, minerals and vitamins, etc. Catechins (epigallocatechin gallate) are the main constituent of this plant, which act as an antioxidant, anticancer, cognition enhancer and used in the treatment of cardiovascular disorders, neurodegenerative disorders and microbial disease. Apart from this, plant possesses antidiabetic, antidepressant, antibacterial and many more other activities. The other important phytoconstituents of the plant are caffeine, theophylline, theobromine, theaflavins and thearubigins.

Conclusion *C. sinensis* is a valuable medicinal plant and can be studied further for its unrevealed phytoconstituents and pharmacological actions. Active phytoconstituents of tea have been extensively studied through in-vitro, in-vivo and clinical protocols for various pharmacological actions whereas the mechanisms of few phytoconstituents still need to be explored and studied in depth. Hence, it is concluded that plant's constituents need to be studied more to reveal their mechanism focusing on bioavailability and pharmacokinetics along with their utilization in the prevention of human diseases.

Clinical trial number Not applicable.

Keywords Tea, *Camellia sinensis*, Catechin, Ethnomedicinal plants

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Introduction

Camellia sinensis (L.) O. Kuntze (Common name - Tea, Family- Theaceae) is one of the most consumed beverages which is native to Southeast Asia, specifically Southern China, North India, Myanmar and Cambodia [1]. It is grown in over 30 nations worldwide [2, 3] with India alone accounting for 96% of global tea production. 78% of the total area of northeast India is under tea production, with Assam, West Bengal, Tamil Nadu, and Kerala being the leading tea producers. The tea comes from Darjeeling, Assam, and the Nilgiris is highly renowned for its quality all over the world. Assam is the only region in the world with its own variety of tea i.e. *C. assamica* with malty sweetness and an earthy flavor [4]. Young leaves contain maximum number of constituents therefore picked as young shoots. These leaves are processed differently like fermented (black tea), partially fermented (oolong tea), non-fermented (green tea, white tea) and due to these different process methods, all tea variables differ in color and taste. Black tea is popular in Western culture, whereas green tea is popular in Japan and China, and oolong tea is only drunk in China and Taiwan. Traditionally tea is used as a household medicine to treat the diseases like diarrhea, typhoid, headache, digestive disorders, depression, fatigue, etc. [5–9]. Tea leaves, as well as beverages prepared from its leaves, possess a high amount of polyphenols especially flavanols known as catechins which are responsible for beneficial effects on human health [10, 11]. According to previous research, tea contains over 4000 bioactive substances, of which 33% are polyphenols, with catechins being the most common. Other phytoconstituents present in tea are alkaloids, carbohydrates, amino acids, proteins, volatile organic compounds, and trace elements. Green tea has more antioxidant activity than black tea due to its higher phenolic content [11]. More than 30 countries now produce a variety of teas, not only because it is a relaxing beverage but also because it has health benefits that have been scientifically proved [12]. Tea is pharmacologically reported for treating various diseases like cancer, microbial diseases, depression, diabetes, etc [13–19]. Tea can also be found in variety of pharmaceuticals and cosmetics [1, 6, 20]. This review is a compendium of all the information that is currently available about this plant, related to its traditional uses, phytochemistry, pharmacological and cosmeceutical uses. The gaps in knowledge and information about this ethnomedicinal plant is also identified and highlighted so that future research can be conducted. Furthermore, the present review also focuses on attracting the attention of researchers and people

about health promoting benefits of this plant for its better utilization in the future.

Although there has been plenty of research regarding *Camellia sinensis*, there are still a number of knowledge gaps. There is a paucity of data that addresses the comparative pharmacokinetics and bioavailability of its polyphenols in varying types of tea, despite them being of the same family. Also, there is limited information on the long-term clinical outcomes of teaching that people consume regularly. Phytochemical differences between geographic, processing and season of harvest should be explored further. Moreover, the molecular basis of its beneficial effects and especially its therapeutic effect is not well understood in chronic diseases. Another relatively under-explored area is the potential of tea bioactives in active drug targeting and interactions with other drugs in a synergistic manner.

Materials and methods

A thorough literature review on *C. sinensis* was carried out up to March, 2023 from databases like PubMed, Springer, NCBI (National Center for Biotechnology Information), and Google scholar for the collection of detailed information about common names, geographical distribution, botanical information, phytochemistry, ethnopharmacology, pharmacological uses, and various *C. sinensis* (Fig. 1). The literature search was conducted using various keywords like “*Camellia sinensis*”, “traditional properties of *Camellia sinensis*”, “pharmacological properties of *Camellia sinensis*”, “medicinal uses of *Camellia sinensis*”, “phytochemistry of *Camellia sinensis*”.

Botanical description

Tea (Fig. 2A) is a 30 feet evergreen angiosperm, dicot shrub or tree which is heavily branched with grey coloured bark [1, 2]. Leaves (Fig. 2B) are dark green in colour having characteristic and aromatic odour with slightly bitter taste. Leaves are blunt at the apex with a tapering base and short serrate margin. Young tea leaves are hairy whereas matured ones are glabrous. Tea flowers (Fig. 2C) are fragrant, 2.5–4 cm in diameter, white, pink, or red in color and found in solitary/clusters of two or four, drooping downwards. Flower consists of numerous stamens, yellow anther and have brownish red capsule. Fruits (Fig. 2D) are brown in colour, small in size, flattened, smooth, rounded, three-celled capsule with little nut-sized seed inside each [21–23].

C. sinensis is taxonomically included in the kingdom *Plantae*, class *Magnoliopsida*, order *Theales*, family *Theaceae* and genus *Camellia* [1]. The various vernacular

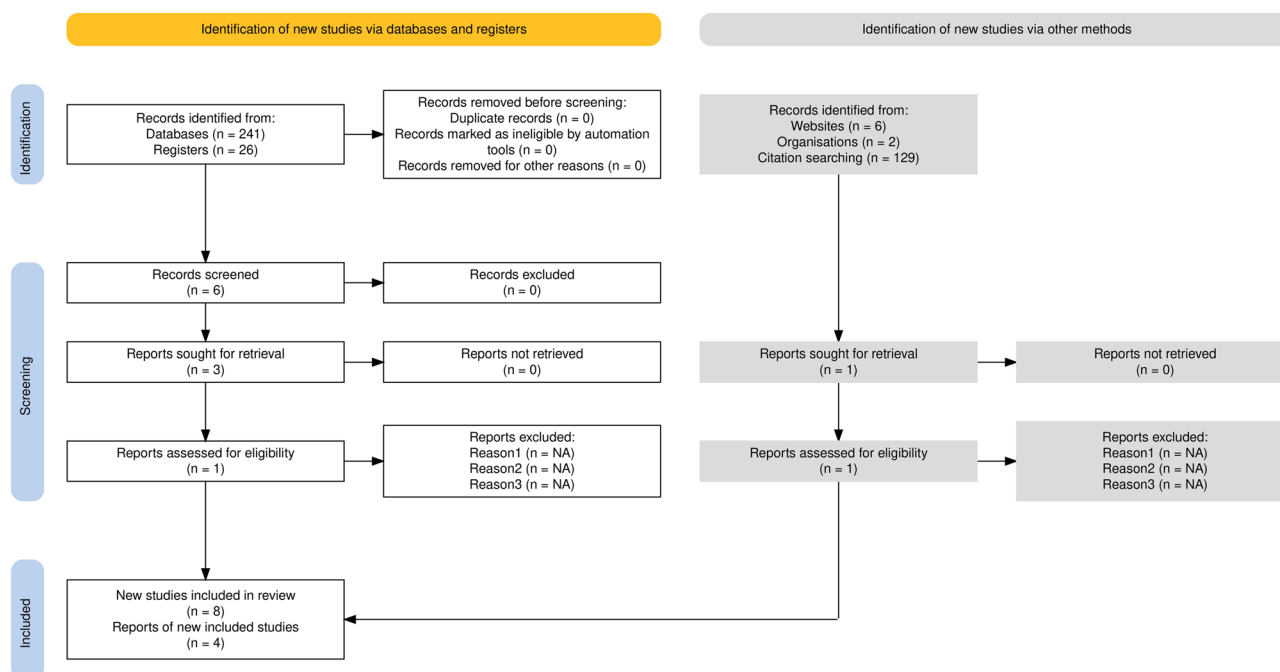


Fig. 1 Systematic review flow diagrams undoubtedly facilitate rapid comprehension of basic review methodology databases like PubMed, Springer, NCBI (National Center for Biotechnology Information), and Google scholar

names of the plants are listed in Table 1. The synonyms of *C. sinensis* include *C. thea*, *Thea sinensis*, *C. taliensis*, *C. crassicolumma*, *C. gymnogyna* and *C. tachangensis* [21, 26]. Genus *Camellia* is divided into 12 sub-generic sections and has more than 200 species [27]

Geographical distribution of *Camellia sinensis*

Tea plant is native to Southeast Asia specifically Southern China, Northern India, Myanmar and Cambodia [1]. It is grown mainly in tropical and subtropical regions between latitudes 41° N and 16° S with adequate rainfall, good drainage and slightly acidic soil [28, 29]. China, India, Kenya, Sri Lanka, Turkey, Indonesia, Vietnam, Japan, Iran and Argentina are the largest producers/cultivators of tea (Fig. 3).

Traditional uses

In traditional Indian and Chinese systems of medicine, tea is used as a stimulant, diuretic, astringent, for headache, body ache, pain, digestion, depression, detoxifier, for relief of fatigue (energizer), to improve heart health and in weakness, whereas in Japan it is called as the undisputed cause of health and longevity [6–9]. It is used traditionally to treat flatulence, regulate body temperature and blood sugar level and also promote digestion

and mental functioning [8]. Green tea is used in treating diseases like diarrhea and typhoid since ancient times [5].

Phytoconstituents of *Camellia sinensis*

There are about 4000 bioactive compounds reported in tea and one third of them are polyphenols which are responsible for its distinctive taste, color and health benefits [1, 30]. The phytoconstituents in tea and its different beverages vary with climate, season, horticulture practices and age of the leaf [1]. Fresh tea leaves are a rich source of water soluble polyphenols, specifically flavanols, flavanol gallate and flavanol glycosides [2] whereas, chlorophyll, carotenoids, lipid and amino acids present in leaves are responsible for the aroma of tea [1].

All tea variants are made from the same plant species but differ in their appearance, taste and constituents due to their respective process methods while manufacturing [31]. The level of caffeine and catechins in different tea preparations varies because of the manufacturing process. Caffeine concentration decreases in the following order: black tea > oolong tea > green tea > fresh tea leaves, whereas EGCG or catechins concentration decreases in the following order: green tea > oolong tea > fresh tea leaves > black tea [9]. Black tea is produced from fresh green leaves by enzymatic browning processes using

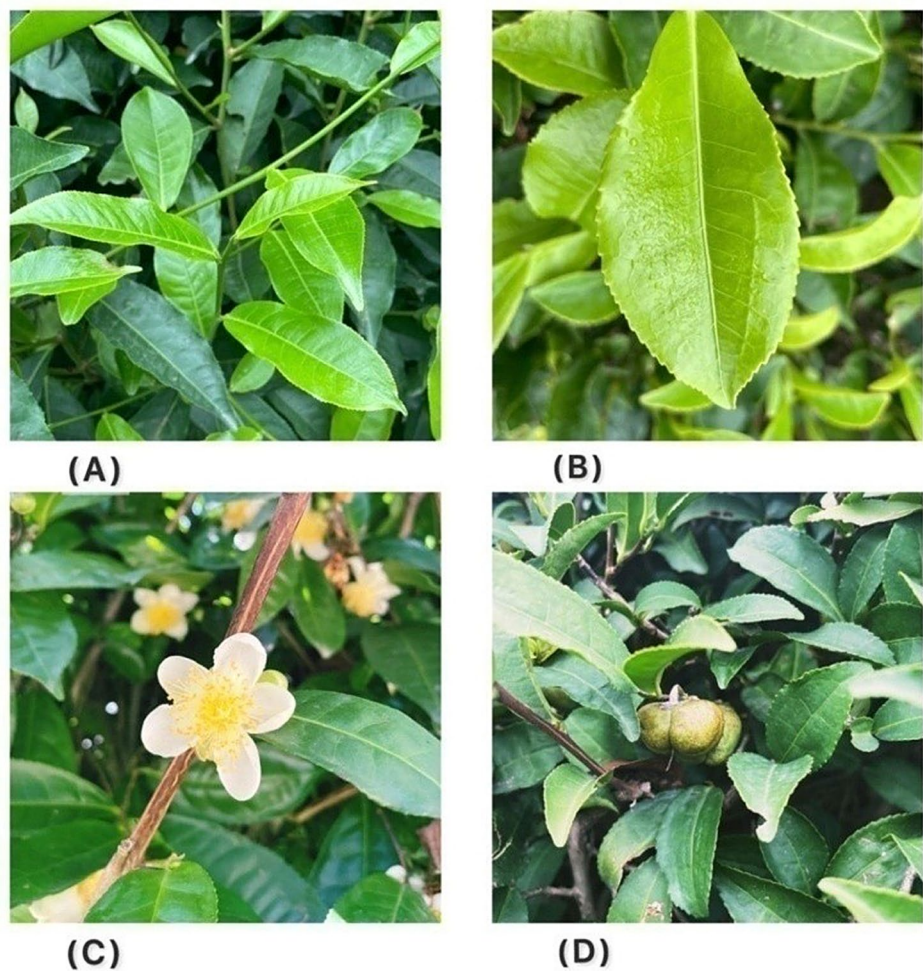
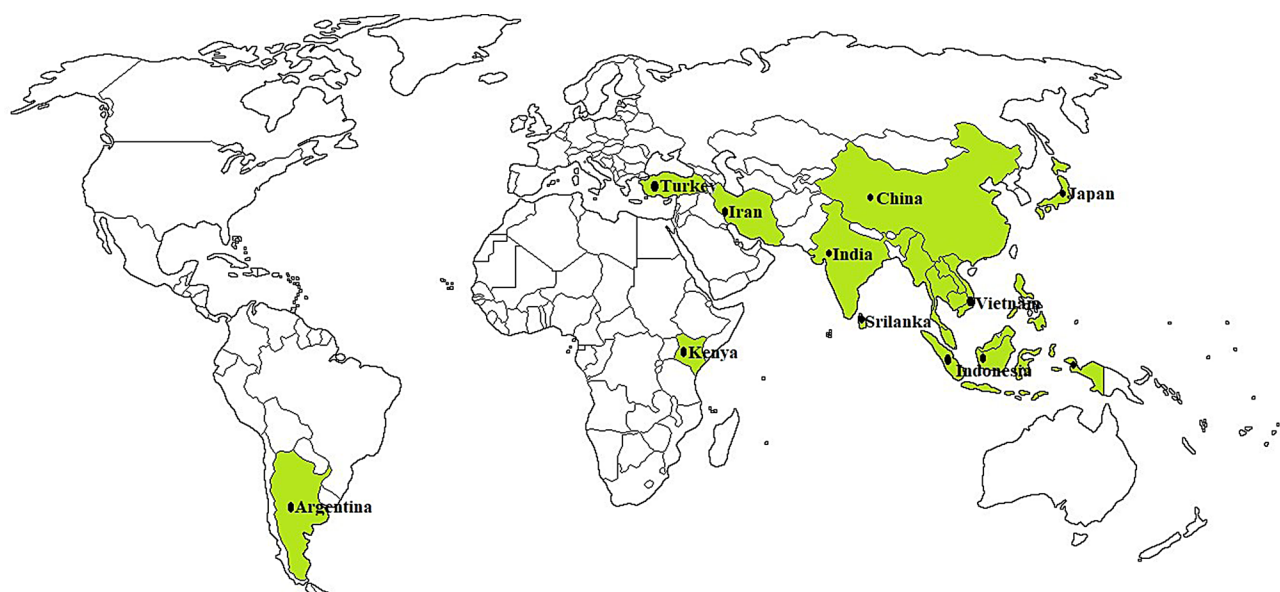
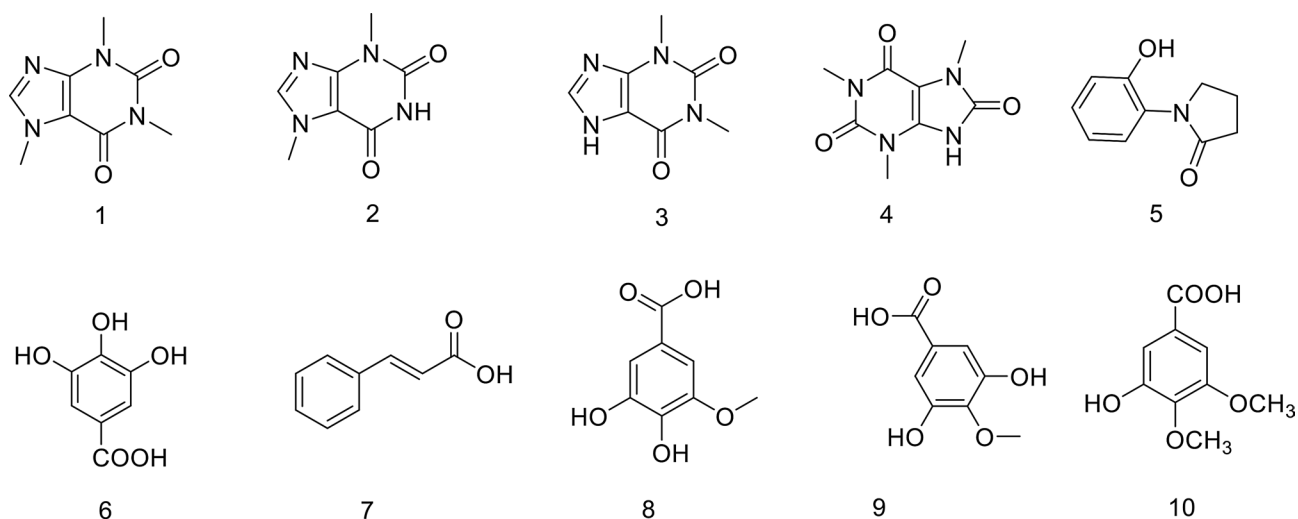


Fig. 2 Fresh tea buds (A), leaf (B), white flowers (C) and fruit (D) of *Camellia sinensis*

Table 1 Vernacular names of <i>Camellia sinensis</i>				
Sr. no	Place/Region/Country	Vernacular name	Language	References
1.	India	Chai	Hindi	[23]
2.	China	Cha	Chinese	
3.	Russia	Chai	Russian	
4.	Africa	Itye	African language	
5.	Italy	Te	Italian	[24]
6.	England & United States	Tea	English	
7.	Japan	Chanoki	Japanese	
8.	Arab	Shai	Arabic language	[25]

polyphenol oxidase enzyme and coupled chemical oxidation of the flavanols and flavanol gallates whereas to a lesser extent flavanols (specifically myricetin) glycosides and non-flavanoid theagallin. These transformational changes produce a wide range of pigments which include brownish thearubigins (major polyphenols of black tea and beverages), red-orange theaflavins (contribute taste) and bright red-orange (color of black tea) and theaflavic

acid. Theaflavins (dimeric) and thearubigins (oligomeric) are formed due to the enzymatic oxidation of flavon-3-ols (catechin in monomeric form) during the fermentation process. In the fermentation process, caffeine content remain constant [2, 10]. Green tea is less fermented tea and contains the highest quantity of catechins because processes involved in the production preserve these natural polyphenolic compounds and caffeine in the least quantity [1, 2, 4]. In Oolong tea high numbers of antioxidants are present which protect healthy skin cells and slow down the aging process [31]. White tea is the least processed type of tea and has the highest catechin content (antioxidants) and low level of caffeine content than any other type of tea variant [1, 4, 31]. White tea is one of the most costly teas for consumers and the most profitable for growers due to the maximum proportion of polyphenols in the bud [4]. The polyphenolic content of any particular type of tea depends upon the type of tea (i.e. fermented, semi-fermented and non-fermented) and type of preparation (i.e. quantity and brew timing). Polyphenolic content specifically catechin is less in black

**Fig. 3** Largest tea producing parts of the world**Fig. 4** Structures of alkaloids and phenolic compounds isolated from tea

tea (caffeine content is more) whereas more in any other less or least fermented tea. Hot brewed tea contains the highest concentration of polyphenols whereas less or least in instant preparations even the addition of milk or water reduces the polyphenolic content. So, nowadays there are fixed size tea bags that maintain the required concentrations of these active compounds. The addition of milk does not directly interfere with polyphenols (catechins) but may interfere with their antioxidant potential depending upon its fat content and volume added [10, 30, 32].

Alkaloids and phenolic acids

Different alkaloids (methyl xanthenes) present in tea (Fig. 4) are caffeine (1), theobromine (2), and theophylline (3).

Other alkaloids, 8-oxocaffeine (4), *N*-(2-hydroxyphenyl)-2-pyrrolidinone (5) are also reported to be present in tea (pu-erh tea). Phenolic acids present in tea are gallic acid (6) and cinnamic acid (7) [5, 10, 33, 34]. The metabolite of gallic acid such as 3-*O*-methylgallic acid (8), 4-*O*-methylgallic acid (9) [1], and 3,4-di-*O*-methylgallic acid (10) are reported to be present in urine after black tea or green tea consumption [35].

Polyphenolic compounds

Polyphenolic compounds, which are also found in red wine, fruit, and vegetables, are abundant in all teas and classified into different groups based on the number of phenol rings and their binding affinity with other

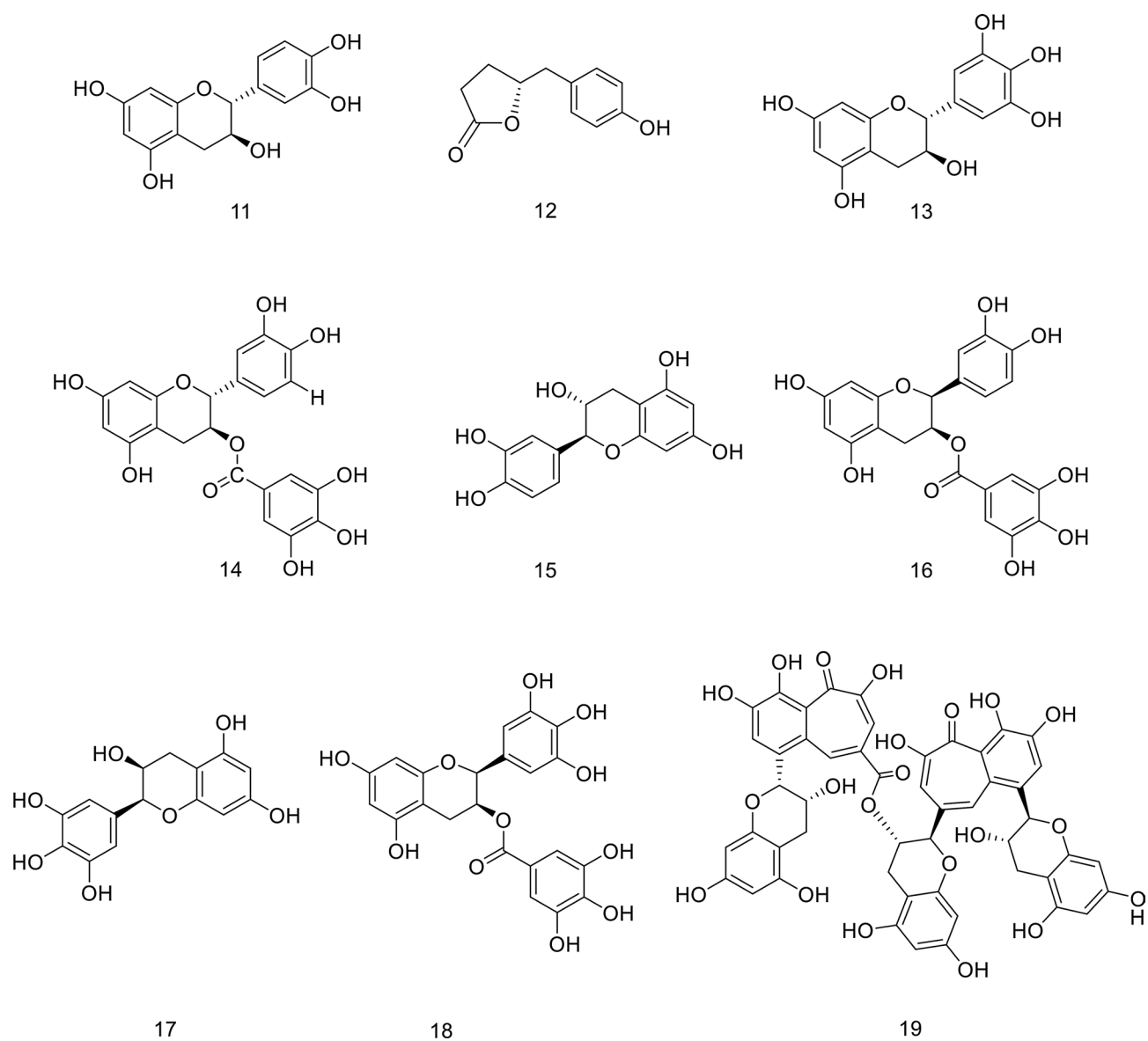
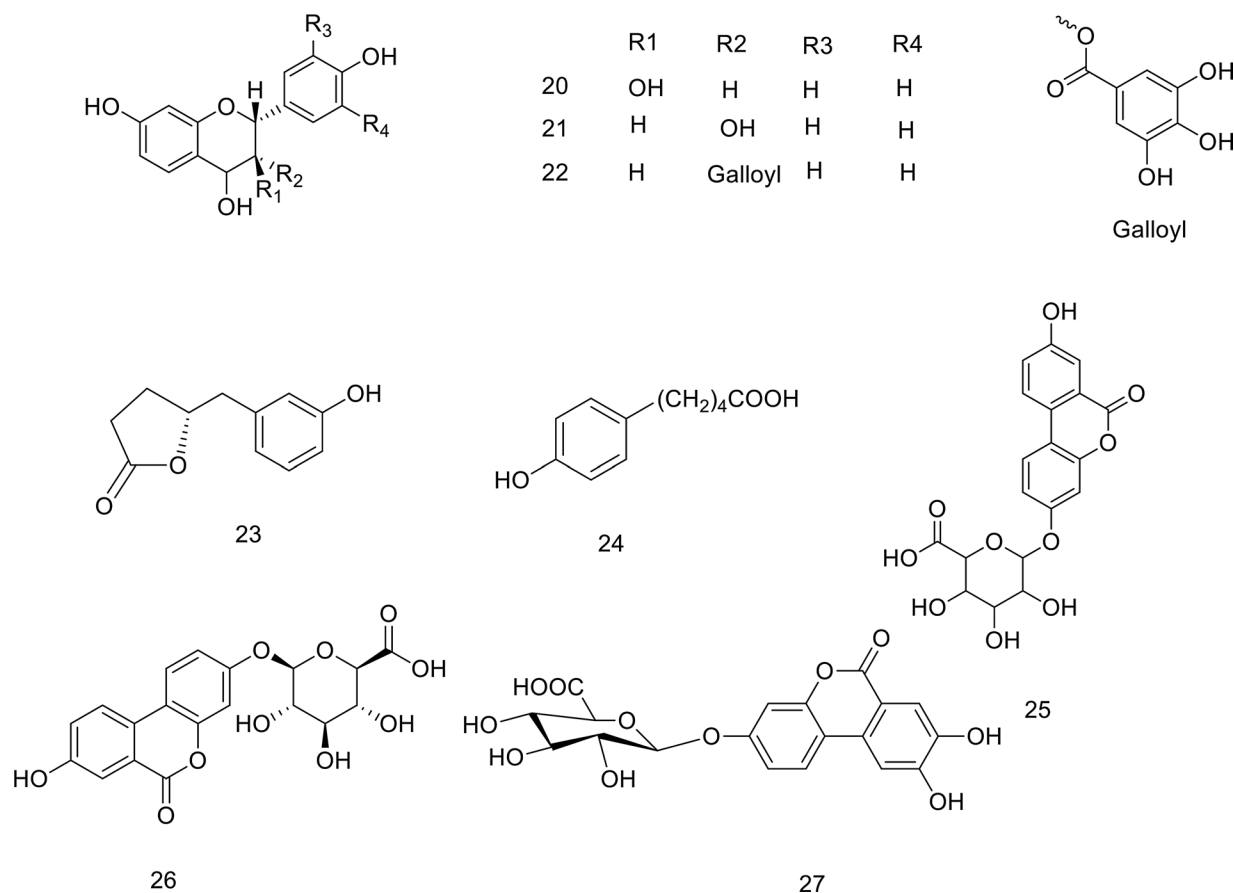


Fig. 5 Structure of catechins isolated from tea

**Fig. 5** (continued)

compounds [4, 30]. Different polyphenols present in tea are as follows:

Catechins (Fig. 5): catechin (**11**), catechin-3-O-gallate (CG) (**12**), gallocatechin (GC) (**13**), gallocatechin-3-O-gallate (GCG) (**14**), epicatechin (EC) (**15**), epicatechin-3-O-gallate (ECG) (**16**), epigallocatechin (EGC) (**17**), epigallocatechin-3-O-gallate (EGCG) (**18**), theadibenzotropolone A (**19**) [34], afzelechin (**20**), epiafzelechin (**21**) and epiafzelechin gallate (**22**) [35, 36]. 5-(hydroxyphenyl)- γ -valerolactones (**23**) and 5-(hydroxyphenyl) valeric acid (**24**) are characteristic catabolites of green tea flavan-3-ols whereas urolithin α -3-O-glucuronide (**25**), urolithin α -8-O-glucuronide (**26**) and urolithin β -glucuronide (**27**) have been detected in urine after consumption of black tea [35].

Theaflavins and thearubigins (Fig. 6): Theaflavins are dimers formed when catechins polymerize during the fermentation or semi-fermentation stages of the production of black or oolong tea, respectively [30, 33] and are theaflavin (**28**), theaflavin-3-gallate (**29**), theaflavin-3'-gallate (**30**) and theaflavin-3,3'-digallate (**31**) [2, 10]. Thearubigins (**32**) are oligomers formed when catechins polymerize during the fermentation or

semi-fermentation stages of the production of black or oolong tea, respectively [30, 33].

Other similar compounds present are theacitrins and theasinensins (Fig. 7) theacitrin A (**33**), theacitrin B (**34**) and theacitrin C (**35**), and theasinensins (theasinensin A (**36**), theasinensin B (**37**), theasinensin C (**38**), theasinensin D (**39**), theasinensin E (**40**), theasinensin F (**41**), theasinensin G (**42**), theasinensin H (**43**), dehydrotheasinensin AQ (**44**), and ethylpyrrolidinonyl theasinensin A (**45**)) [34, 37].

Other polyphenols (Fig. 8): besides the above described phytoconstituents other polyphenols present in tea are lignans (**46**), apigenin (**47**), isovitexin (**48**), vitexin (**49**), saponarin (**50**), vicenin-2 (**51**), luteolin (**52**), kaempferol (**53**), quercetine (**54**) (black tea is the major dietary source), myricetin (**55**), isoquercetin (**56**), myricitrin (**57**), rutin (**58**), kaempferitrin (**59**) [1, 9, 10, 30] theaflavic acid (**60**) [2], oolongtheanin (**61**), oolonghomobisflavan A (**62**), oolonghomobisflavan B (**63**), 8-C-ascorbyl-(-)-epigallocatechin 3-O-gallate (**64**), assamicain A (**65**), assamicain B (**66**), assamicain C (**67**), ect-pyrrolidinone A (**68**), ect-pyrrolidinone B (**69**), ect-pyrrolidinone E (**70**), ect-pyrrolidinone F (**71**), ect-pyrrolidinone I (**72**), ect-pyrrolidinone J (**73**), puerin A (**74**), puerin B (**75**), puerin C

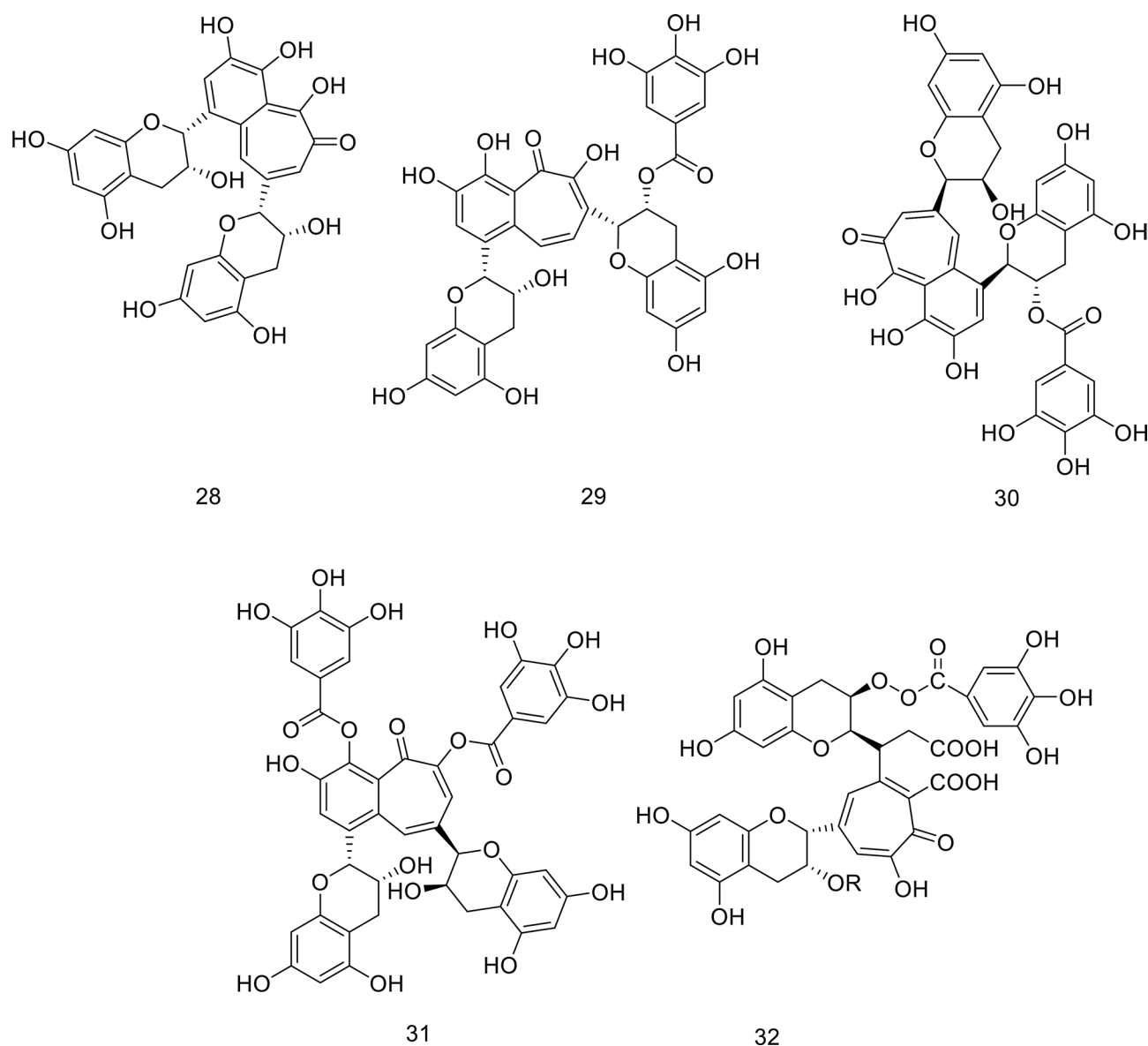


Fig. 6 Theaflavins and thearubigins isolated from tea

(76), puerin D (77), puerin E (78), puerin F (79), puerin I (80), puerin II (81), puerin III (82), puerin IV (83), puerin V (84), puerin VI (85), puerin VII (86), puerin VIII (87), (-)-epicatechin-8-C- β -D-glucopyranoside (88), myricetin-rhamnodiglucoside (89), fuzhuanin A (90) (generated during fungal fermentation process), fuzhuanin B (91), fuzhuanin C (92), fuzhuanin D (93), fuzhuanin E (94), fuzhuanin F (95) (fuzhuanin C, D, E, F are metabolites of catechins), kaempferol-3-O-rutinoside (96), epitheaflavac acid (97), epitheaflavac acid-3'-gallate (98), neotheaflavin (99), theaflavic acid (100), kaempferol 3- glucosyl-rhamnosylgalactoside (101), quercetin-3-glucosyl-rhamnosylgalactoside (102), quercetin rhamnodiglucoside (103), kaempferol rhamnodiglucoside (104), theadibenzotropolone B (105), theatribenzotropolone A (106),

epitheaflagallin 3-O-gallate (107), epitheaflagallin (108), theaflagallin (109), theaflavate A (110) (major oxidation product of ECG), theaflavate B (111), isotheaflavin-3'-O-gallate (112), neotheaflavin-3-O-gallate (113), theogallin (114) [34], bisflavanol A (115), bisflavanol B (116), bisflavanol C (117) and tricetin (118) [36].

Saponins

Different saponins (Fig. 9) like theasaponin B1 (119), isotheasaponin B1 (120), isotheasaponin B2 (121), isotheasaponin B3 (122), assamsaponin J (123) (from *C. sinensis* var. *assamica*), foliatheasaponin I (124), foliatheasaponin II (125), foliatheasaponin III (126), foliatheasaponin IV (127), foliatheasaponin V (128) and floratheasaponin A (129) are present in tea [34].

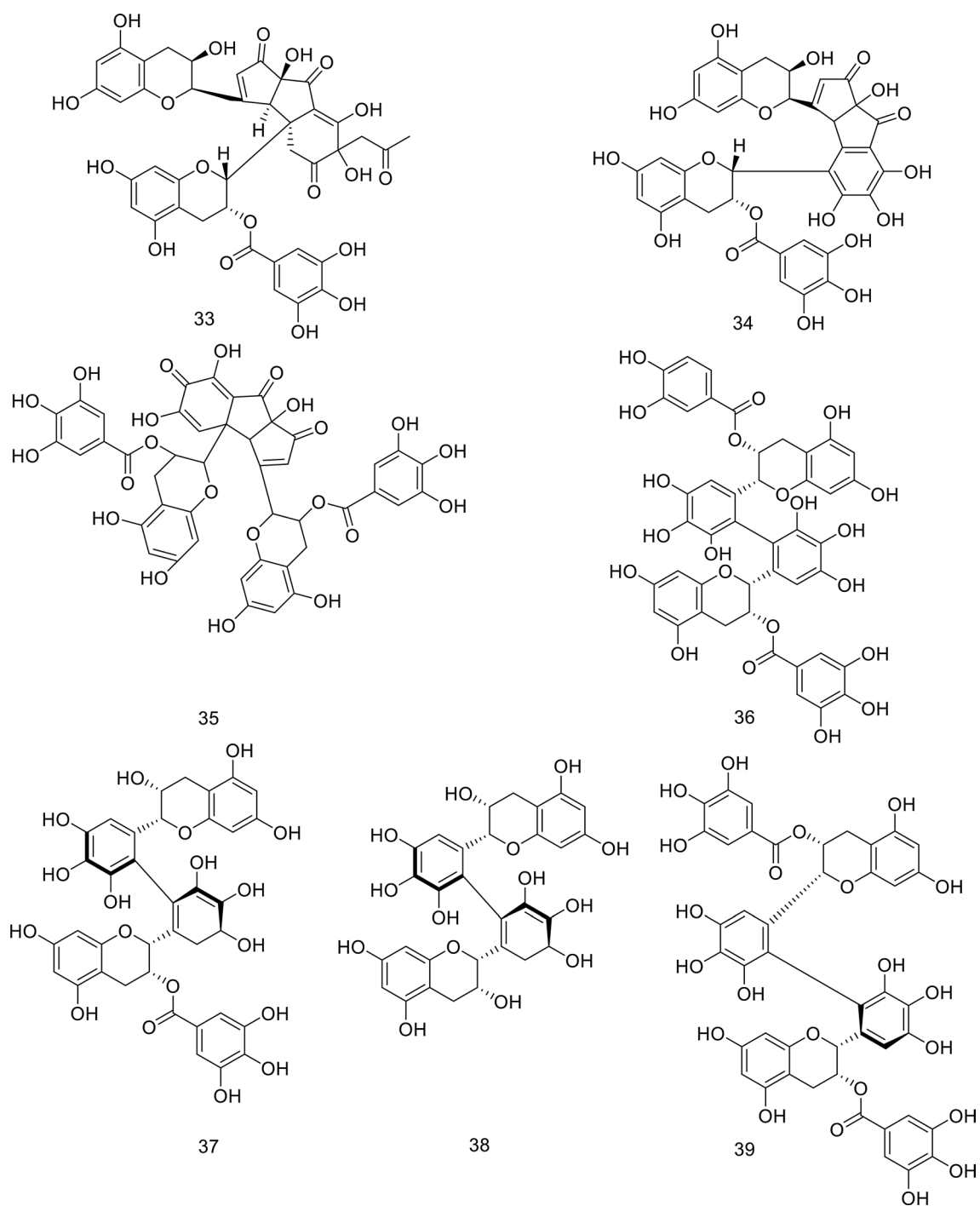
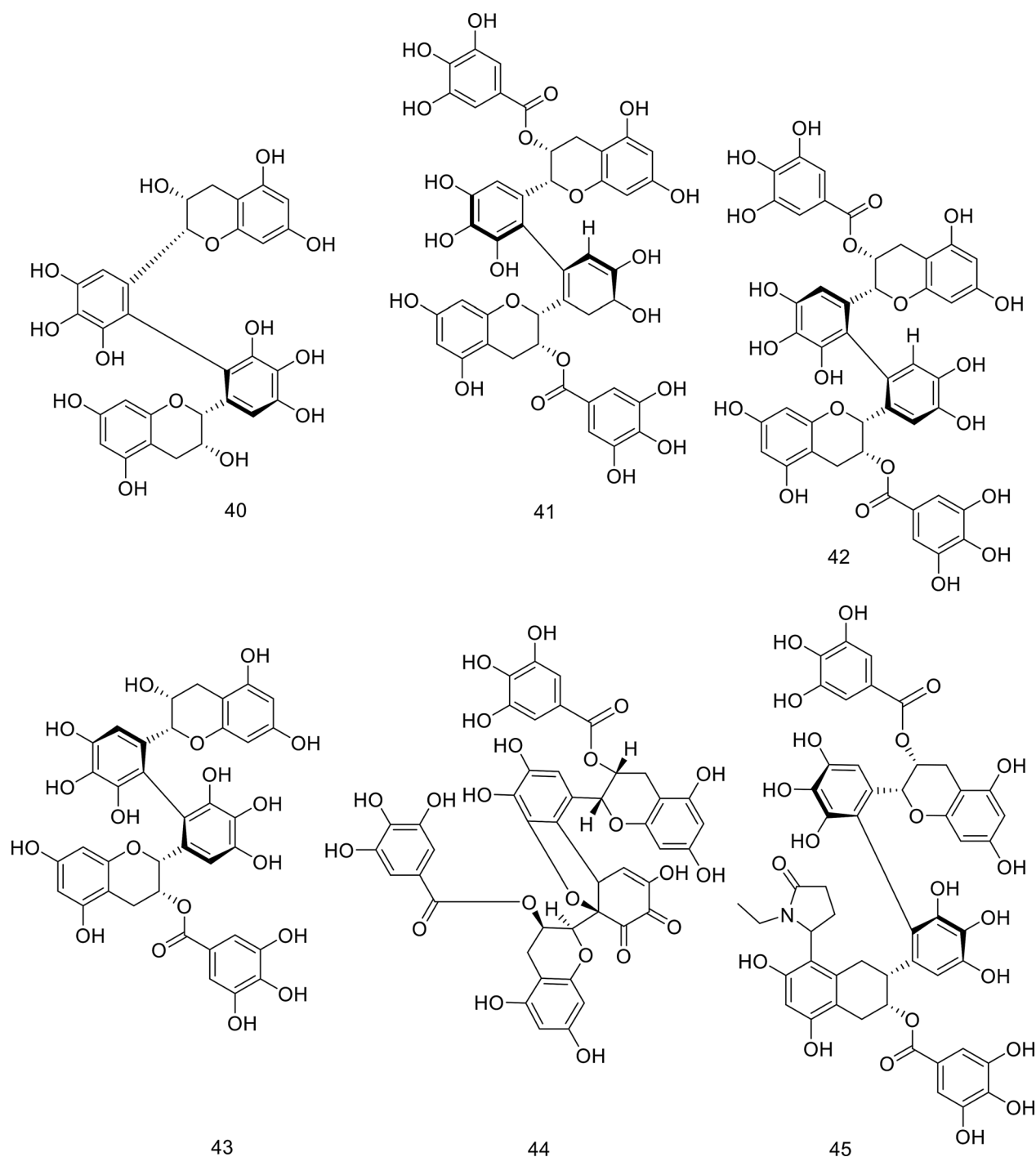


Fig. 7 Structure of theacitrins and theasinensins compounds isolated from tea

**Fig. 7** (continued)

Simple phenolics

Simple phenolics compounds present in tea (Fig. 10), teadenol A (**130**) and teadenol B (**131**) were reported in tea when fermented with *Aspergillus* species. Other phenolics compounds reported in tea are teasperol (**132**), teasperin (**133**) [34].

Amino acids, vitamins, nutrients and trace minerals

Tea also contains various amino acids, vitamins, nutrients and trace minerals (Fig. 11). Amino acids such as L-theanine (**134**) (main source of tea flavor), glutamic acid (**135**), tryptophan (**136**), aspartic acid (**137**), arginine (**138**) [5, 10, 30], glycine (**139**), serine (**140**), tyrosine (**141**), valine (**142**), leucine (**143**), threonine (**144**), lysine (**145**) [5, 38] and GABA (γ -aminobutyric acid)

(146) are present in tea and degradation of these amino acids while brewing responsible for its aroma [1]. L-theanine and GABA are non-protein amino acid which is mainly present in white tea than in any other type of tea [39]. Different vitamins like vitamin E (147), vitamin K (148), vitamin A (149), vitamin C (150) and B vitamins (vitamin B1 (151), vitamin B2 (152), vitamin B3 (153), vitamin B5 (154), vitamin B6 (155), vitamin B7 (156), vitamin B9 (157), vitamin B12 (158) are present in tea [1]. Tea contains nutrients and minerals like carbohydrates cellulose (159), glucose (160), pectin (161), fructose (162) and sucrose (163) [5], zinc (164), manganese (165), iron (166), magnesium (167), silver (168), copper (169), titanium (170), aluminium (171), bromine (172), bromium (173), sodium (174), potassium (175), nickel (176), chromium (177), fluoride (178), phosphorus (179), chromium (180), lead (181), cobalt (182) [1, 10, 30], molybdenum (183), selenium (184), cobalt (185), strontium (186), fluorine (187) and calcium (188) [5].

Miscellaneous constituents

Other compounds like tannins, polyamines, polysaccharides etc have also been isolated from this plant (Fig. 12). Tannins like strictinin (189) [35], polyamines like spermidine (190), spermine (191) [39] and polysaccharides like galactose (192), arabinose (193), rhamnose (194), xylose (195), galacturonic acid (196), mannose (197), ribose (198) and glucuronic acid (199) are present in tea plant [30]. Chlorogenic acid (200), coumarylquinic acid (201), chlorophyll (202), leutin (203), zeaxanthine (204) [1, 10], stigmasterol (205) [5], caffeic acid (206)

[40], coumaric acid (207), ferulic acid (208), ellagic acid (209) [41], assamaicin A (210) [35], norisoprenoid (211), 2,2',6,6'-tetrahydroxydiphenyl (212), salicylic acid (213), amelliaone A (214), amelliaone B (215), amelliaone C (216), amelliaone D (217) and amelliaone E (218) [34] are also present in tea.

Pharmacological activities

Tea and its various forms are considered a dietary source of biologically active constituents with a wide range of pharmacological activities, and long-term consumption of tea rich in phytoconstituents offers protection against the development of cancers, cardiovascular diseases, osteoporosis, diabetes, and neurodegenerative diseases, according to epidemiological studies and meta-analysis [30, 31]. Oxidative damage is the main cause of several diseases. The key molecules involved in the pharmacological activities of tea are polyphenols which are the most powerful antioxidants among other plant polyphenols and their pharmacological significance decrease sequentially: EGCG (epigallocatechin-3-O-gallate) > EGC (epigallocatechin) > ECG (epicatechin-3-O-gallate) > EC (epicatechin). According to some laboratory tests, EGCG is 20 times more active than vitamin C and 30 times more active than vitamin E and even at the cellular level EGCG is the most biologically active polyphenol. Tea also contains some other active molecules like caffeine, theaflavins, thearubigins, vitamins (E, A, K), and theanine which are mainly responsible for its biological activities. Concentrations of these active ingredients vary in different tea preparations and activities

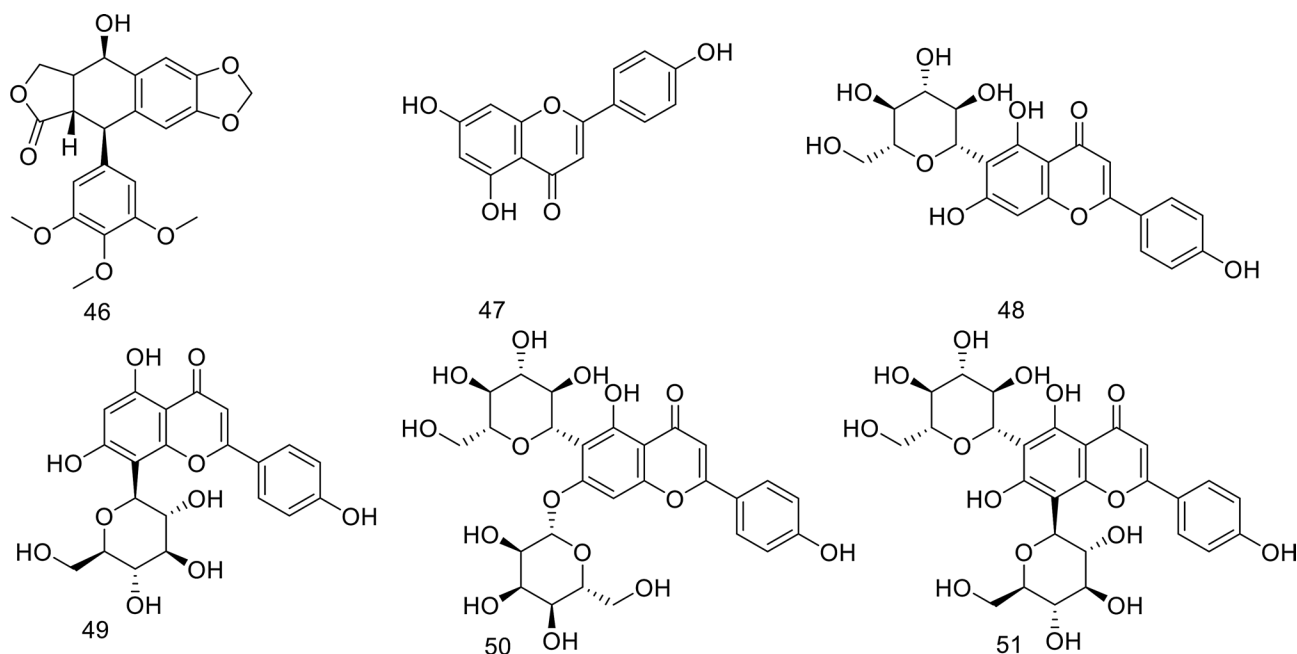
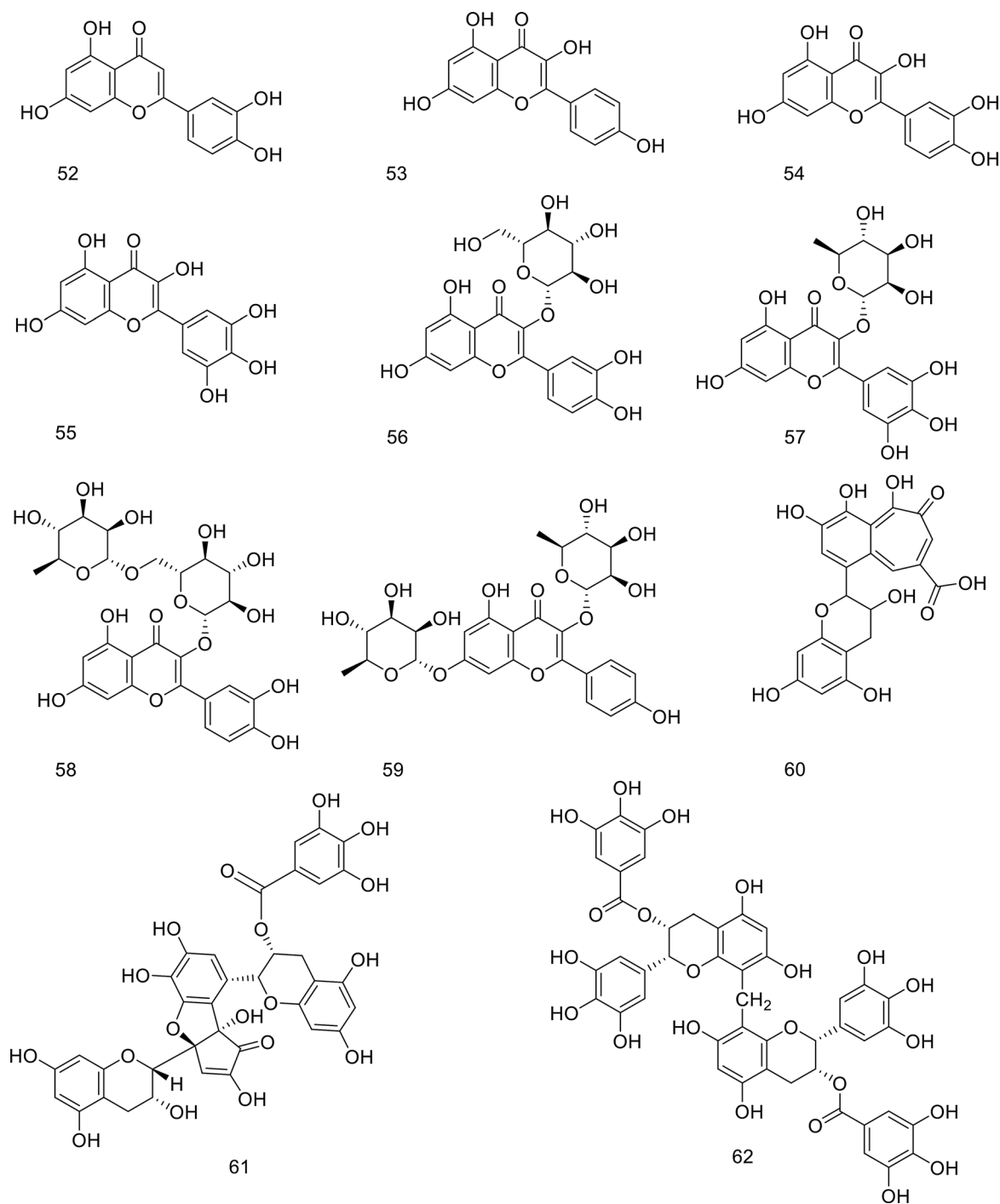
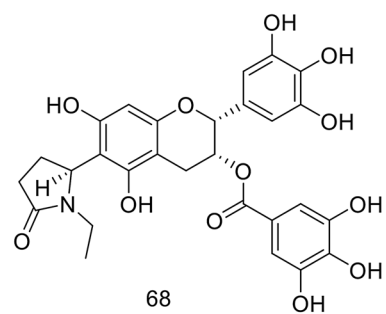
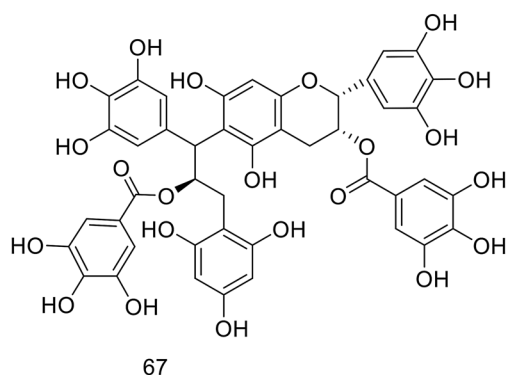
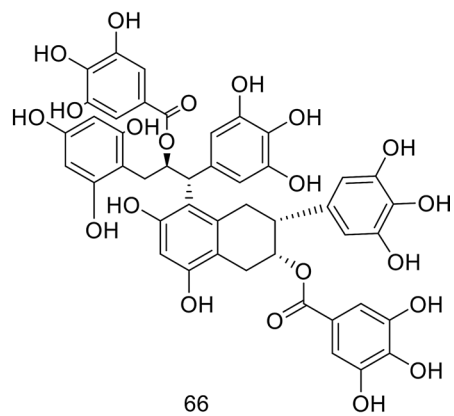
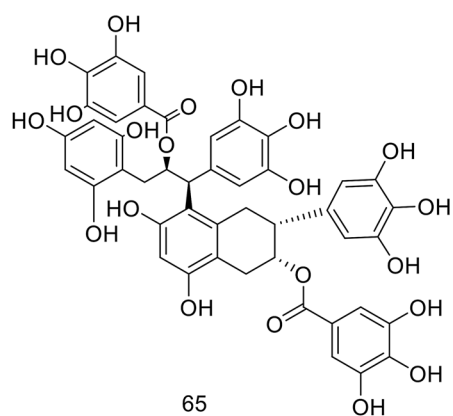
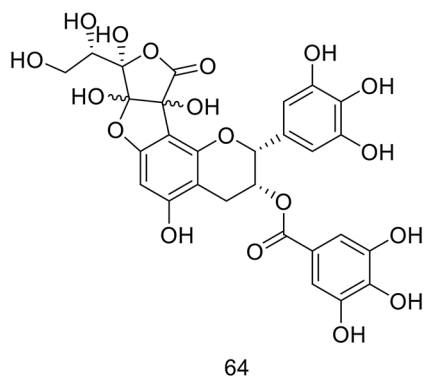
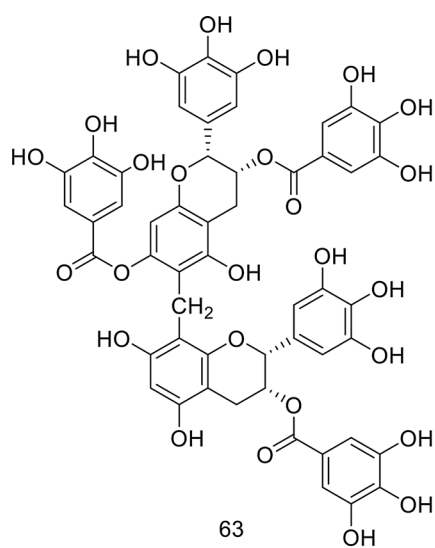
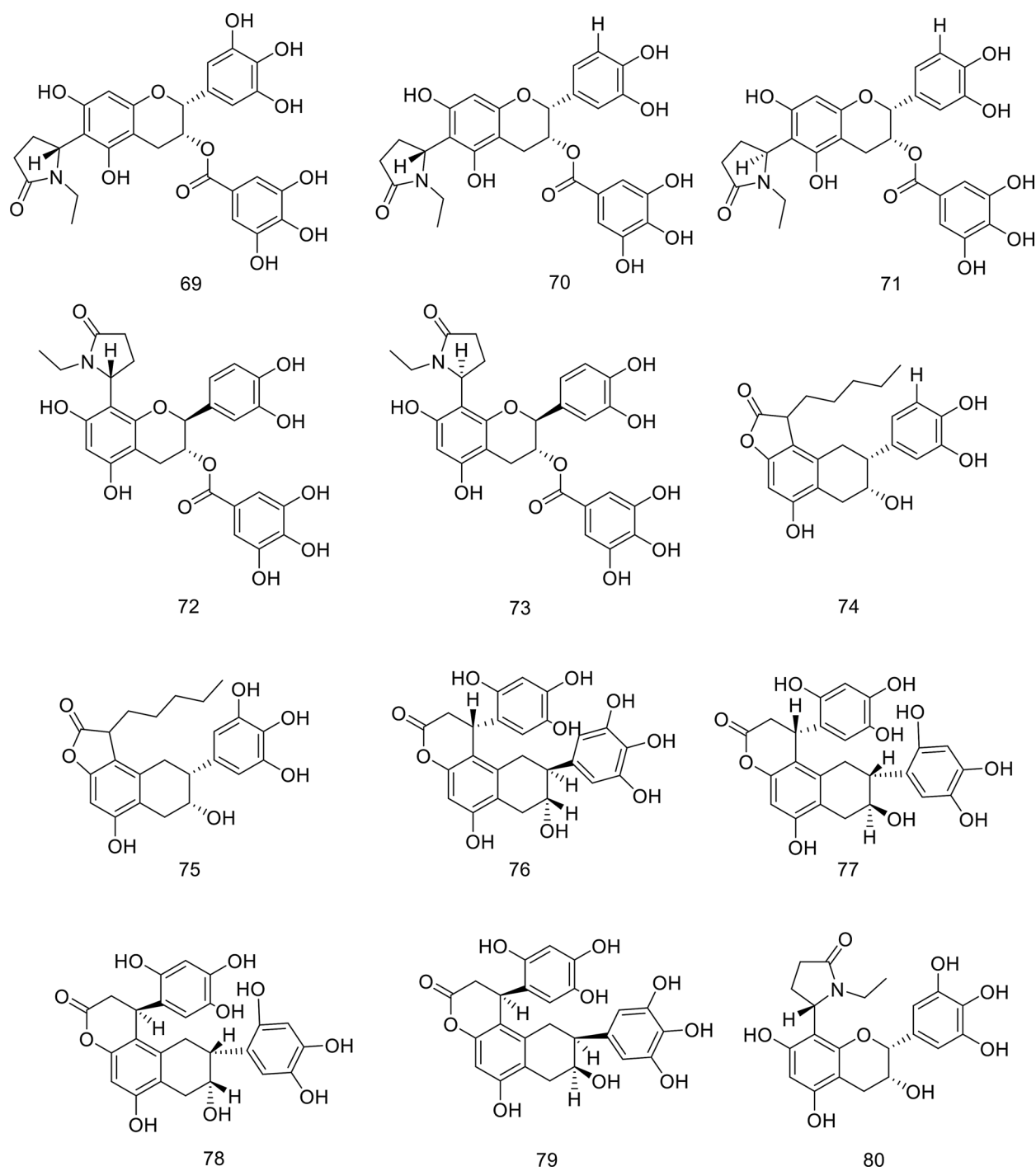
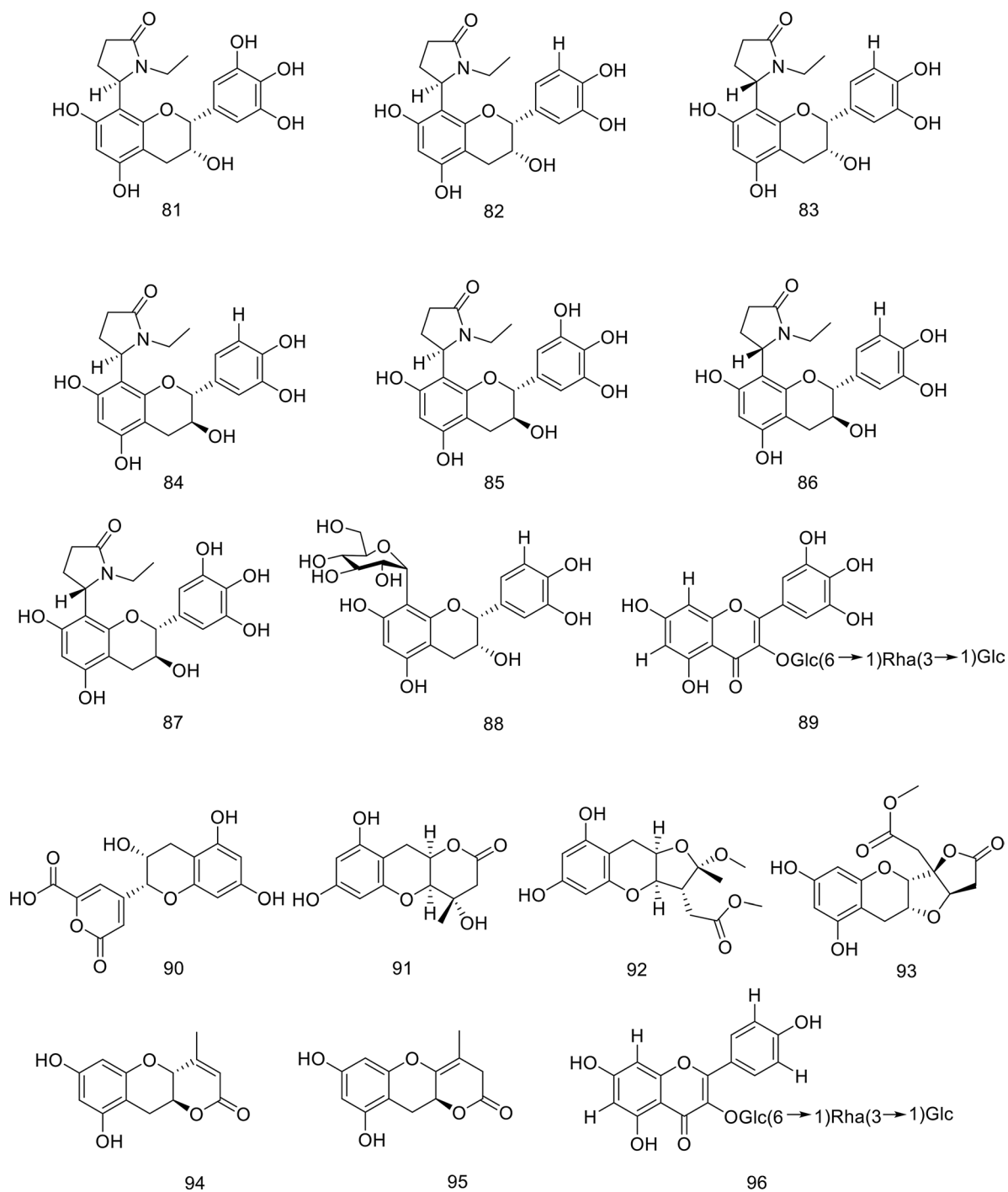


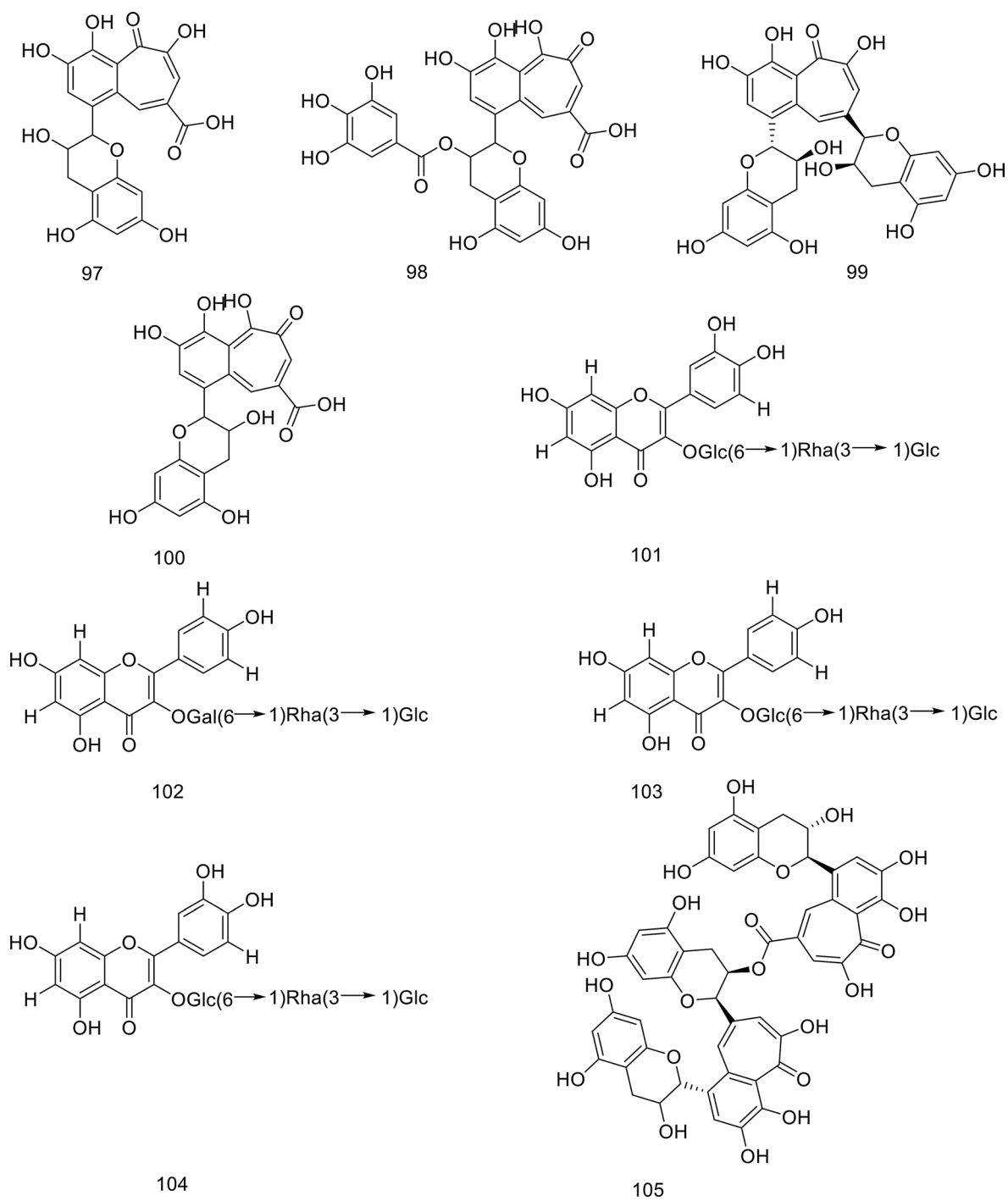
Fig. 8 Structure of different polyphenolic compounds isolated from tea

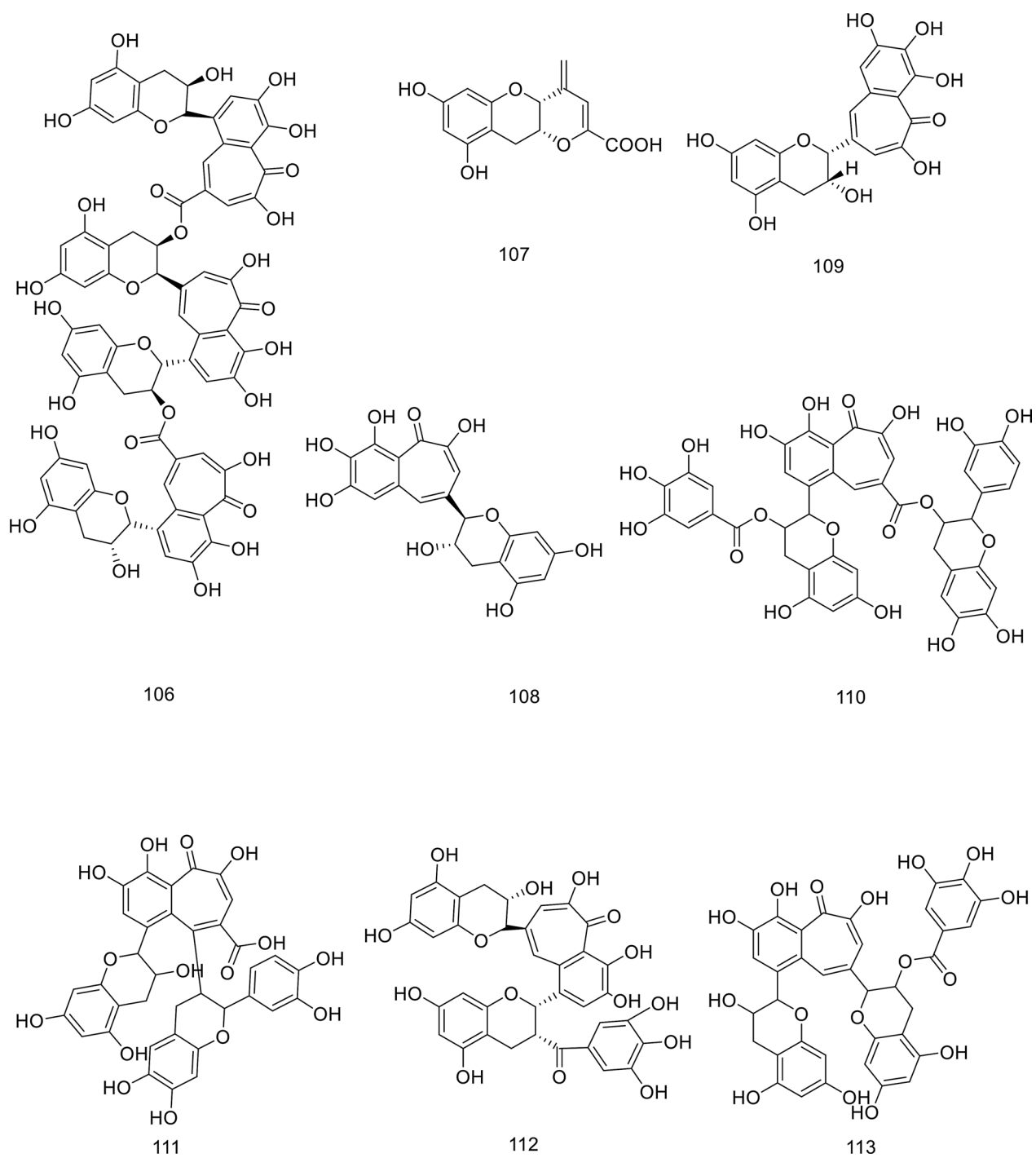
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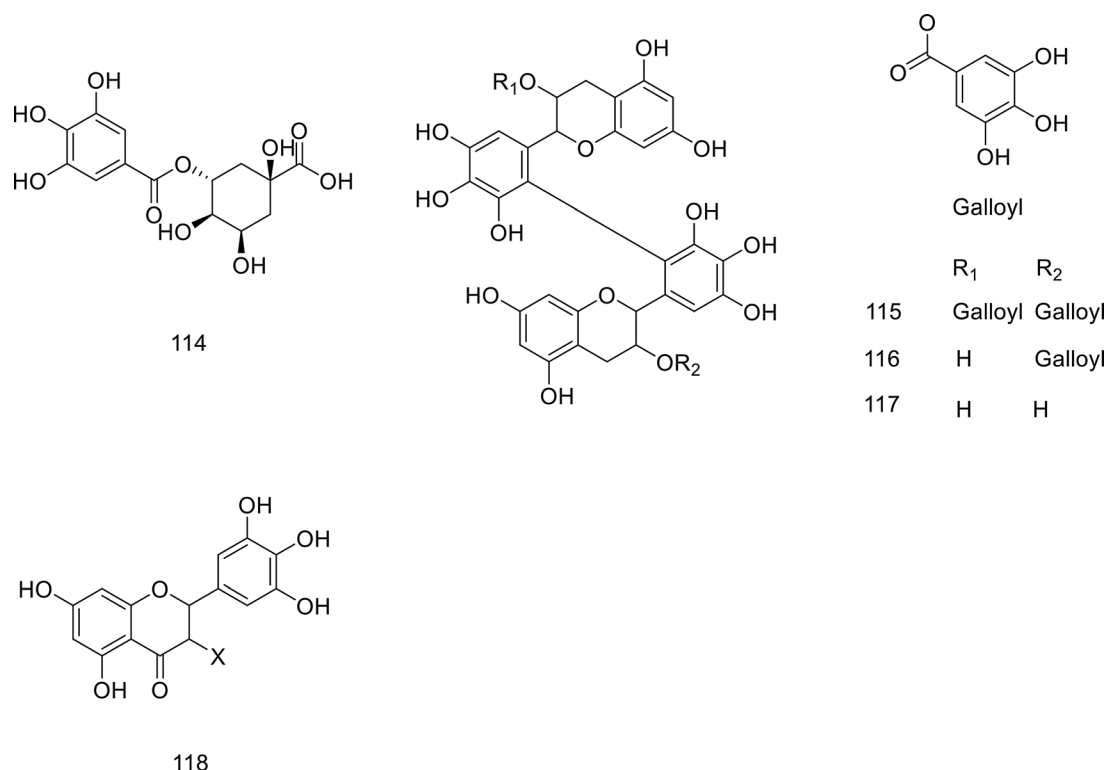
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like antioxidant activity decrease in the following order: green tea > oolong tea > black tea and according to some studies overall activities of black tea are highest than others [42, 43]. The extraction and isolation of various compounds from different plant parts of *C. sinensis* reported many pharmacological activities (Fig. 12) such as antioxidant, anticancer, antibacterial, antiviral, antiatherosclerosis, antiobesity, antihyperglycemic, hepatoprotective, antiaging, anticariogenic, antifibrinolytic, anti-inflammatory, immunomodulatory, wound healing, endometriosis, CNS diseases and respiratory diseases. Therefore, all these pharmacological studies have been thoroughly discussed in this section (Table 2) (See Fig. 13).

Antioxidant activity

Free radicals and other reactive oxygen species cause oxidative changes, and oxidative metabolism is required for cells to survive [44]. Various studies claim *C. sinensis* as one of the potential source for curing the oxidative damage.

In a study, epigallocatechin-3-O-gallate (EGCG) at 5 mg/kg oral dose for 30 consecutive days increased the activity of superoxide dismutase (14.49 ± 0.70), catalase 198.3 ± 9.4 and glutathione peroxidase (77.98 ± 3.59) enzymes, whereas decreased the level guanidino compounds creatinine (1.20 ± 0.09), methylguanidine (1.89 ± 0.13) and guanidinosuccinic acid (29.82 ± 2.47) in

male Wistar rats with oxidative stress induced apoptosis [45].

The antioxidant effect of green tea infusion was tested in-vivo in 10 healthy volunteers (aged 23 to 25; five women and five men) who fasted overnight. The green tea was prepared by infusing 2.5 g of dry green tea leaves for 2 min at 80 °C in 150 ml of water. Antioxidant capacity in plasma was measured after administration of 150 ml of green tea, at baseline after 60 and 120 minutes. In the second and third week, they took 300 ml (5 gm tea leaves) and 450 ml (7.5 gm tea leaves) of infusion, respectively. Green tea showed insignificant changes in antioxidant capacity at 150 ml consumption. At 300 ml, it significantly increased by 7.0% after 60 minutes and 6.2% after 120 minutes. At 450 ml, the increase was even higher, with 12.0% after 60 minutes and 12.7% after 120 minutes [46]. Hence, the total antioxidant capacity of the plasma was significantly increased by consuming 300 ml and 400 ml of green tea.

In another study, nine healthy volunteers (one male and eight females of 26 to 59 ages) took part in a 3 days study in which volunteers consumed black tea without milk. The results showed a significant increase in FRAP (ferric reducing antioxidant power) by 65% from 9:00 a.m. to 12:00 p.m. and a further increase of 76% at 3:00 p.m. [47]. This suggests that heavy consumption of black tea can enhance the circulating antioxidant potential in the body.

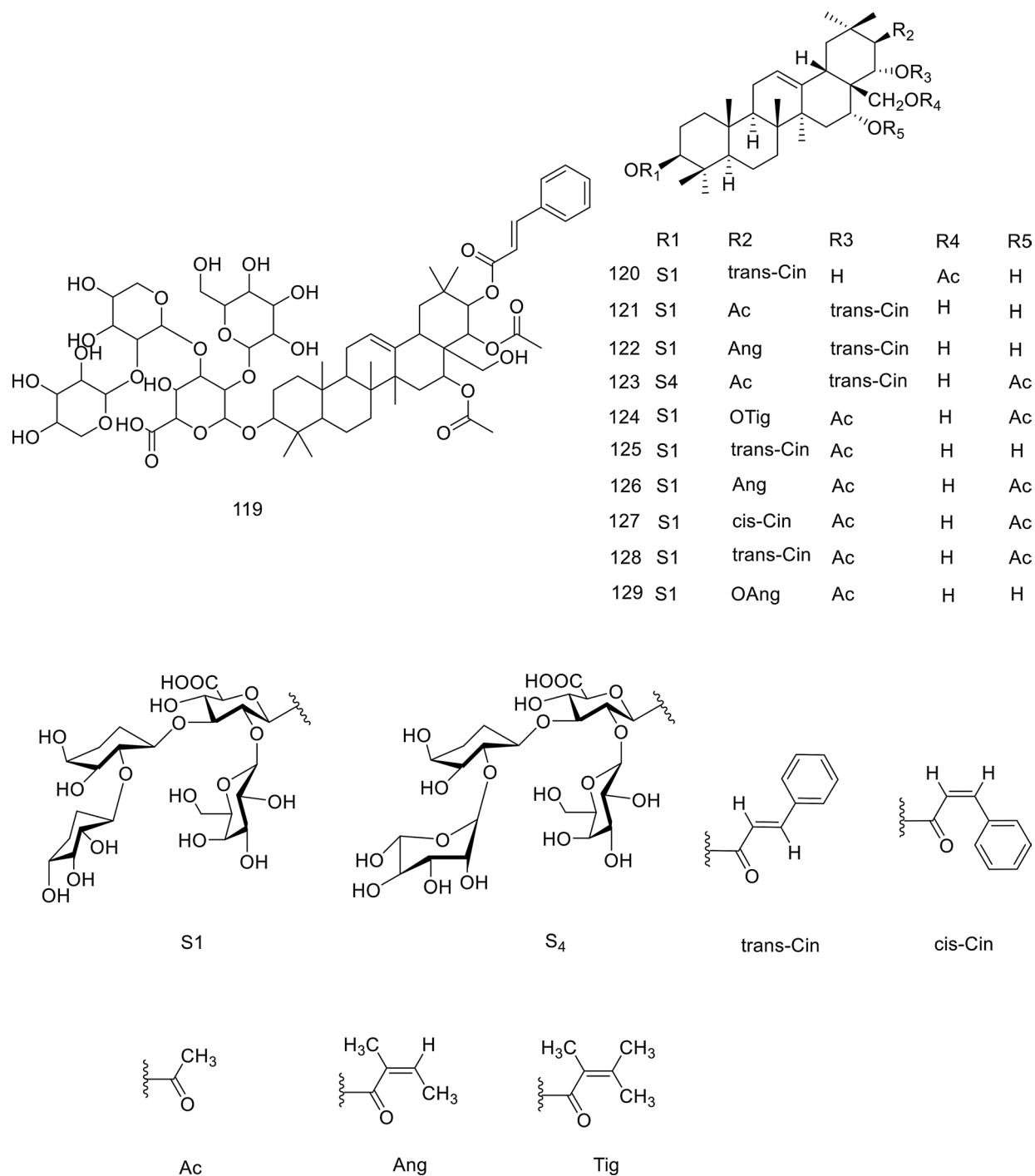


Fig. 9 Structure of different saponins isolated from tea leaves

According to Wu et al., 2011, complex of tea polyphenols with β -glucan showed antioxidant activity in Kunming mice at dose 300 mg/kg. Complex showed activity by increasing the activity of intracellular antioxidant enzymes like glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and decrease in level of malondialdehyde [48].

In another study, green tea (100 mg/kg basal pallet) administration induced immune expression, enhanced antioxidant system and cytokine gene expression in trout fish (*Oncorhynchus mykiss*). Green tea showed reduction in lipid peroxidation product, enhanced superoxide dismutase activity, increased serum bactericidal activity and total protein [49]. Green tea treatment up-regulated

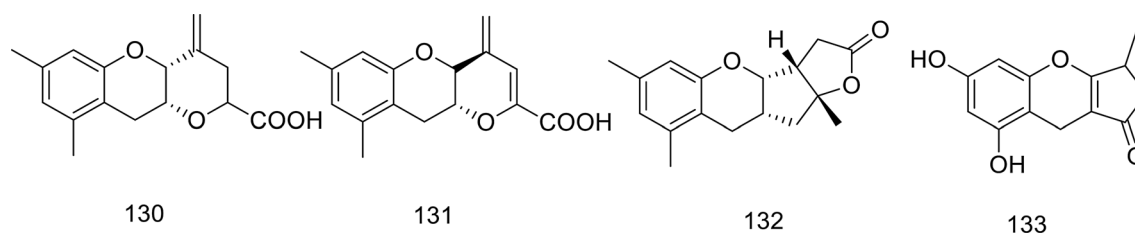


Fig. 10 Structure of different phenolics isolated from tea leaves

interleukin-1 β transcription, interleukin-6 mRNA level in the spleen and interleukin-8 transcription in the kidney and liver, while interleukin-1 β mRNA level decreased in the kidney. Moreover, green tea inhibited the production of interleukin-10, unregulated tumor necrosis factor- α transcription, and enhanced tumor necrosis factor- α (TNF- α) mRNA levels in the kidney and spleen [50]. This study suggested that green tea administration is beneficial to enhance immune and antioxidant system in trout fish.

In another study, in-vivo antioxidant activity of green tea was investigated with carbon tetrachloride induced oxidative stress in male ICR (Institute of Cancer research) mice and silymarin used as standard drug [51–55]. Oral administration of aqueous green tea extract at doses of 125, 625 and 1250 mg/kg for 8 weeks significantly reduced the levels of thiobarbituric acid-reactive substances (TBARS) and protein carbonyls in the liver by at least 28% compared with carbon tetrachloride treated mice. Moreover, green tea extract administration significantly increased the activities of catalase, GSH-Px and glutathione reductase (GSR) in the liver [56]. This study's findings demonstrated green tea's antioxidant capability against oxidative damage.

According to a study by Korir et al., 2014, tea (0.5 ml cooled tea infusion, without sugar) consumption enhanced the level of glutathione (GSH) in Swiss albino mice, GSH level was highest after 2 hours of consumption and showed 91.6% of antioxidant activity [57].

In an in-vivo study, green tea diet showed decrease in oxidative stress against PCB 126-induced oxidative stress in C57BL/6 mice. According to RNA and proteins analysis of the liver, nuclear factor (erythroid-derived 2)-like 2 proteins were up-regulated. Moreover, antioxidant enzymes and genes such as SOD1 (superoxide dismutase 1), GSR, NQO1 (NAD(P)H quinone dehydrogenase 1) and GST (glutathione S-transferase) were increased [58].

According to a study by Sadowska-Krepa et al., 2019, green tea extract (GTE) supplementation for 6 weeks to 16 men combined with a crossfit workout increased the FRAP (ferric reducing ability of plasma) level two times more (1308.1 ± 101.5) when compared with effects of placebo. GTE consumption for 6 weeks had a marginal effect on aerobic capacity and serum brain derived neurotrophic factor (BDNF) (i.e. 13.19 ± 1.9) in cross fit men, whereas

it causes a marked increase in blood antioxidant capacity [18].

In in-vivo mice model with alcohol induced acute liver injury, aqueous tea extract at 400 mg/kg decreased the level of melondialdehyde and increased the level of superoxide dismutase, glutathione peroxide and glutathione in the liver, indicating the antioxidant activity [59].

In conclusion, this study delved into the captivating realm of antioxidant activity present in various types of tea. Through meticulous analysis, we unraveled the intricate nuances of each tea's capacity to combat oxidative stress. The diverse spectrum of teas, from the robust black to the delicate green, offered distinct profiles of antioxidants, highlighting the unique contributions each can make to our well-being [60–67]. As we sip these age-old elixirs, let us savor not only their flavors but also the protective embrace of their natural antioxidants. This exploration prompts further avenues of research, beckoning us to explore the synergistic effects of blends, the impact of brewing techniques, and the potential implications for human health. As the sun sets on this study, a new dawn rises, promising an enriched understanding of teas as not just beverages, but as reservoirs of nature's vitality.

Anti-cancer activity

Cancer is a major health problem globally and is the second leading cause of death [68]. Breast cancer, colorectal cancer, prostate cancer and lung cancer are the most frequently diagnosed cancers [69]. Scientific discoveries outlined below have established that tea and its compounds hold substantial potential as anticancer agents.

Prostate cancer

According to Adhami et al., EGCG (10–40 μ mol/L) in combination with NS-398 or *N*-(2-cyclohexyloxy-4-nitrophenyl) methane sulfonamide (10 μ mol/L) resulted in enhanced cell growth inhibition, apoptosis induction, expression of Bax (Bcl-2-associated X protein), pro-caspase-6, pro-caspase-9, poly(ADP)ribose polymerase cleavage, inhibition of peroxisome proliferator activated receptor G and inhibition of nuclear factor- κ B in human prostate cancer cells viz LNCaP, PC-3 and CWR22Rr1. Whereas in in-vivo study, green tea polyphenol (0.1% in drinking water) and celecoxib (5 mg/kg) resulted in

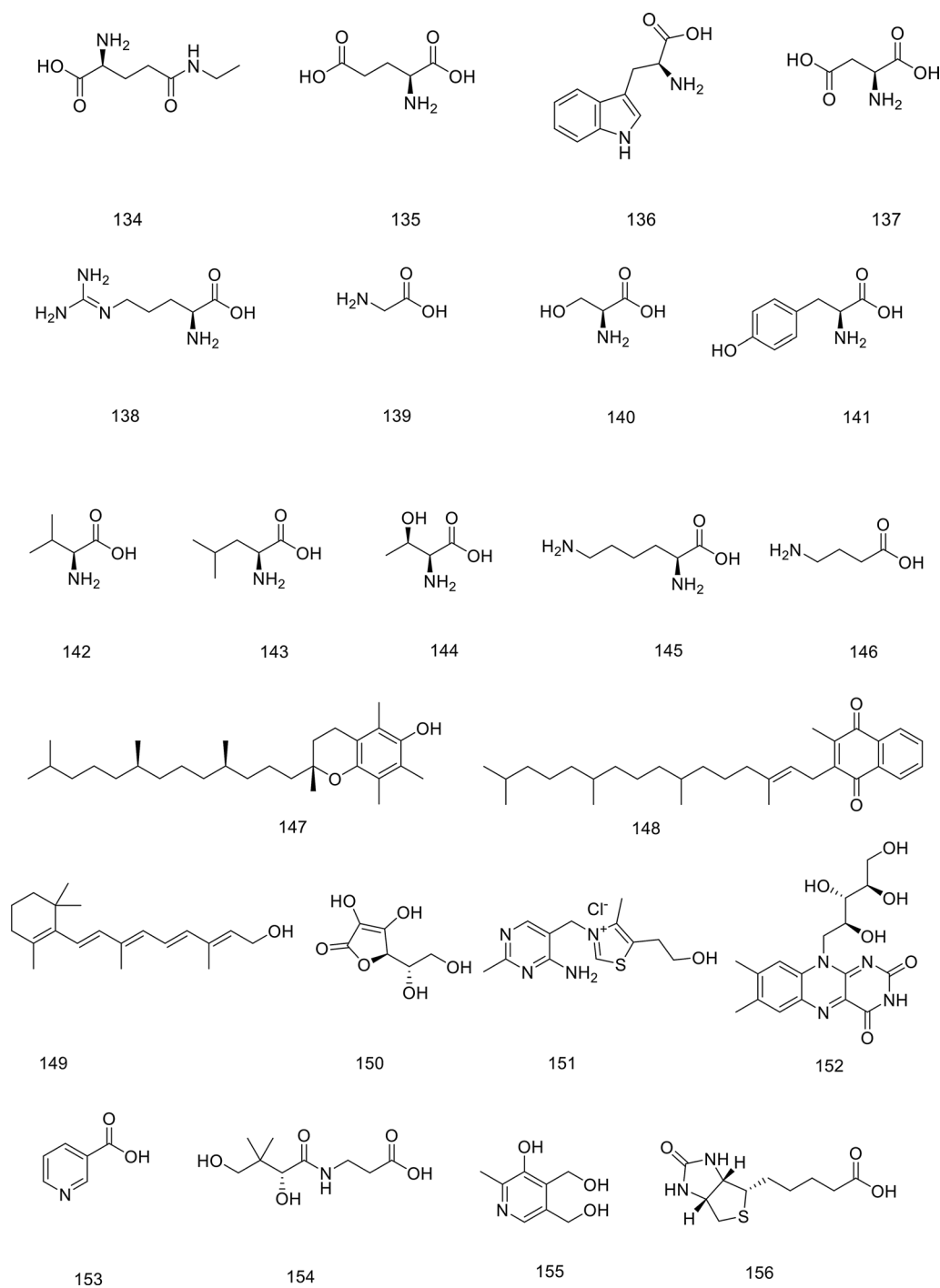


Fig. 11 Structure of amino acids, vitamins, nutrients and trace minerals isolated from tea

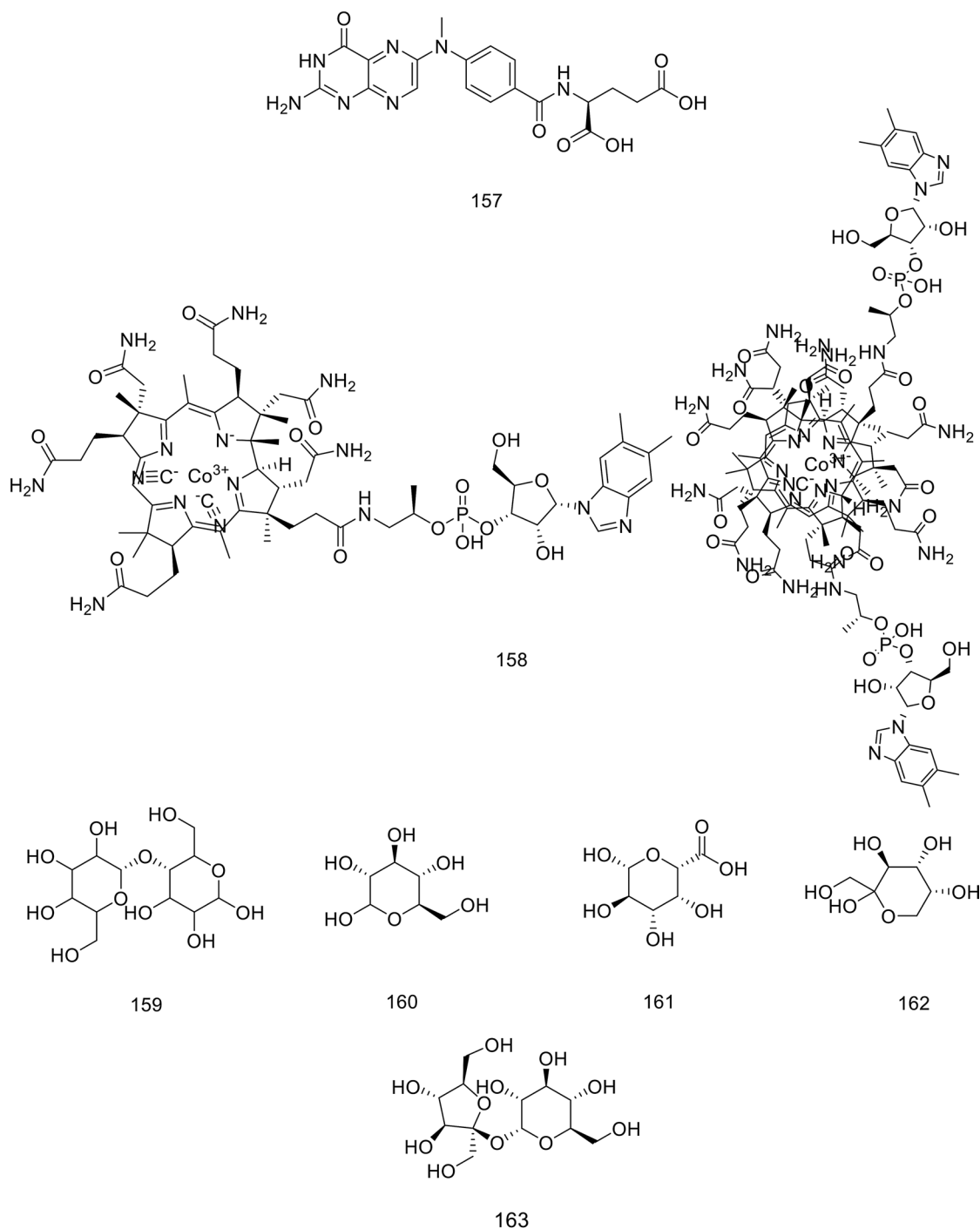


Fig. 11 (continued)

enhanced tumor growth inhibition, lowering of prostate-specific antigen levels, lowering of insulin-like growth factor-I levels and circulating levels of serum insulin-like growth factor binding protein-3 in athymic nude mice implanted with androgen-sensitive CWR22R1 cells [70].

In another study, catechin extract (30 µg/mL) and catechin extract nanoemulsion (10 µg/mL) with IC₅₀ of 15.4 g/

mL and 8.5 g/mL, respectively were able to slow the proliferation in the culture of PC-3 tumor cells. Through increased P27 expression and decreased expression of cyclin A, cyclin B, cyclin-dependent kinase 2, and cyclin-dependent kinase 1, the PC-3 cell cycle was arrested at the S phase. Additionally, by decreasing the expression of B-cell lymphoma 2 (bcl-2) and increasing the expression

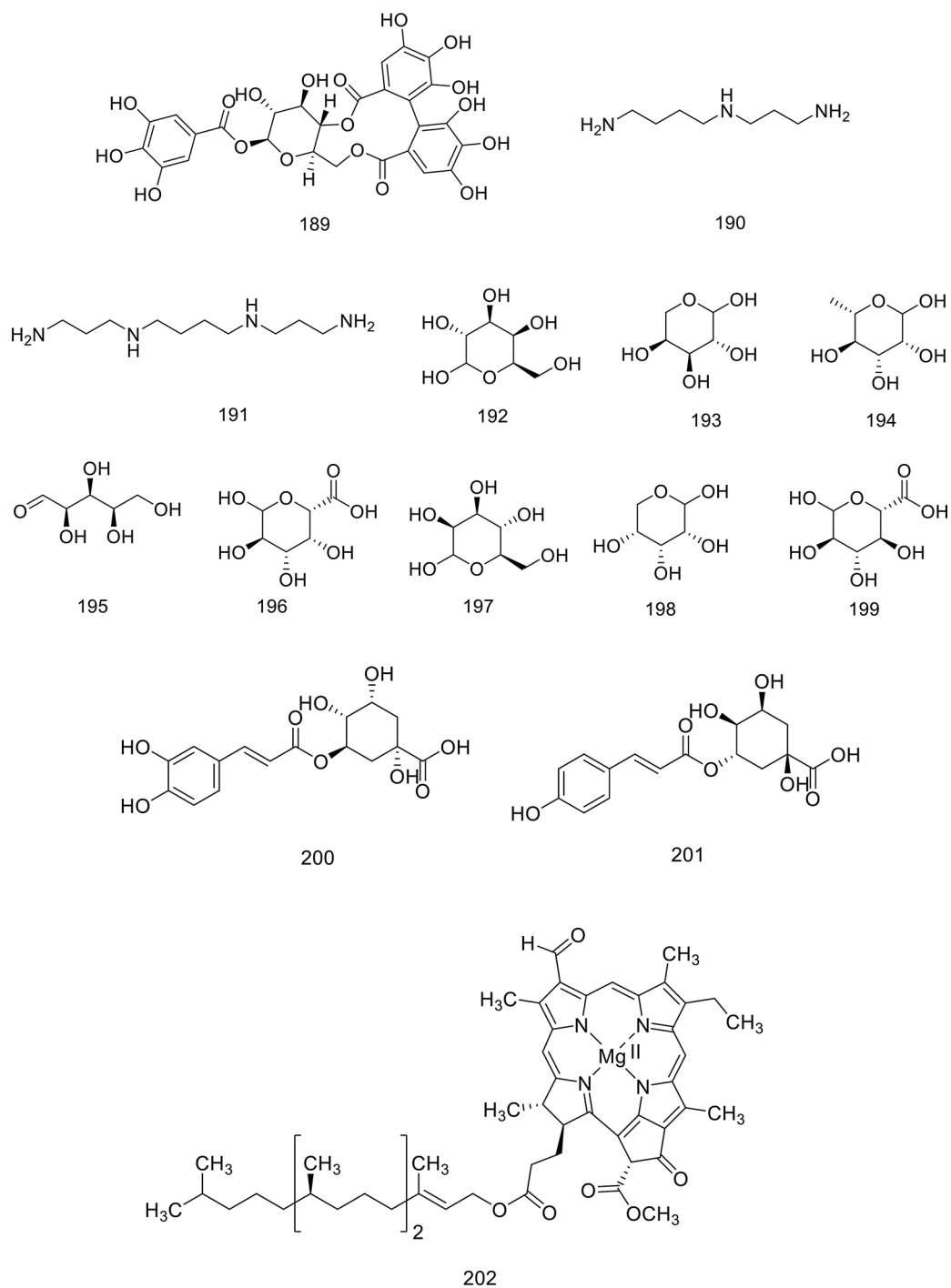
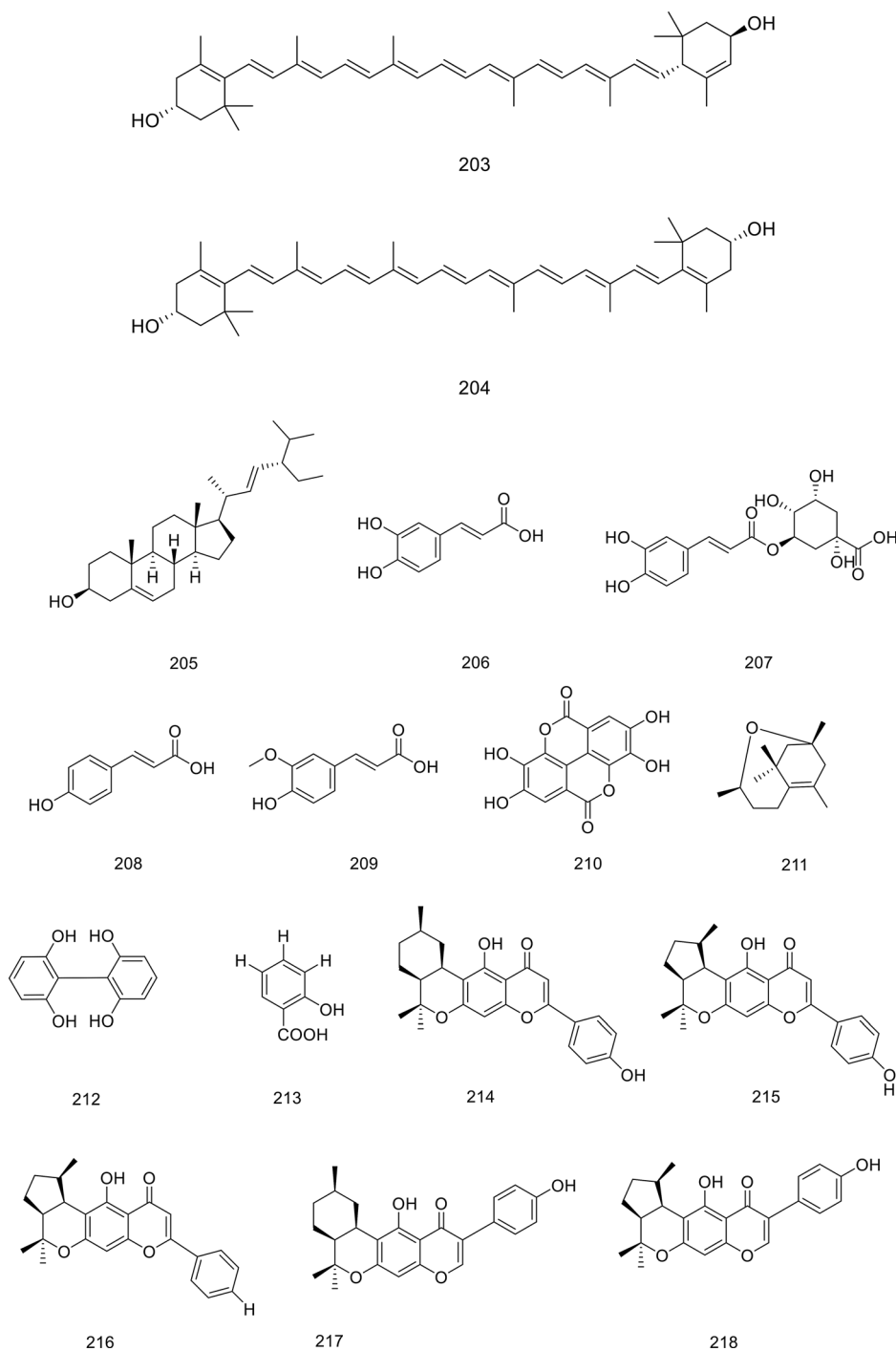


Fig. 12 Structure of tannin, polyamines, polysaccharides and other chemical constituents isolated from tea

**Fig. 12** (continued)

of cytochrome c for the activation of caspase-3, caspase-8, and caspase-9 in PC-3 cells, catechin extract and nanoemulsion were both able to cause apoptosis. Together, caspase-dependent and caspase-independent mechanisms may contribute to PC-3 cells' death [19].

From laboratory investigations to clinical glimpses, the evidence speaks resoundingly of tea's capacity to stand

against the challenges posed by prostate cancer. These insights illuminate a path of promise for future therapeutic interventions, prompting us to delve into optimized formulations, synergistic combinations, and personalized approaches for the treatment of cancer.

Table 2 Pharmacological activities on different Animals/humans/species and their observation

Pharmacological activity	Animals/humans/species used	Compound(s)/Extract	Dose/Method	Observation
Antioxidant activity	Male Wistar rats with oxidative stress	Epigallocatechin-3-O-gallate (EGCG)	5 mg/kg orally for 30 days	Increased SOD (14.49), catalase (198.3), GSH-Px (77.98); decreased creatinine, methylguanidine, and guanidinosuccinic acid levels.
Antioxidant activity	Human (10 healthy volunteers)	Green tea infusion	150–450 ml infusion (2.5–7.5 g leaves) over 3 weeks	Antioxidant capacity increased significantly at 300 ml and 450 ml doses after 60 and 120 min.
Antioxidant activity	Human (9 volunteers)	Black tea (without milk)	Daily consumption over 3 days	FRAP increased by 65% by noon and 76% by 3:00 p.m., indicating elevated antioxidant potential.
Antioxidant activity	Kunming mice	Tea polyphenols- β -glucan complex	300 mg/kg	Increased intracellular SOD and GSH-Px; reduced malondialdehyde.
Antioxidant activity	Trout fish (<i>Oncorhynchus mykiss</i>)	Green tea	100 mg/kg via basal pellet	Enhanced SOD activity, reduced lipid peroxidation, increased cytokine gene expression and TNF- α .
Antioxidant activity	Male ICR mice with CCl ₄ -induced stress	Green tea aqueous extract	125, 625, 1250 mg/kg orally for 8 weeks	Decreased TBARS and protein carbonyls; increased catalase, GSH-Px, and GSR in liver.
Antioxidant activity	Swiss albino mice	Tea infusion (no sugar)	0.5 ml	GSH peaked 2 h post-consumption; 91.6% antioxidant activity.
Antioxidant activity	C57BL/6 mice with PCB-126 oxidative stress	Green tea diet	Not specified	Upregulated Nrf2, SOD1, GSR, NQO1, and GST gene expression; antioxidant effect confirmed by RNA/protein analysis.
Antioxidant activity	Human (16 males in CrossFit program)	Green tea extract (GTE)	Supplemented for 6 weeks	FRAP doubled (1308.1 ± 101.5); mild increase in BDNF (13.19 ± 1.9); marked increase in antioxidant capacity.
Antioxidant activity	Mice with alcohol-induced liver injury	Aqueous tea extract	400 mg/kg	Reduced malondialdehyde; increased liver SOD, glutathione peroxide, and glutathione.
Prostate cancer	LNCaP, PC-3, CWR22R1 human prostate cancer cells; athymic nude mice	EGCG + NS-398/Celecoxib/Catechin nanoemulsion	EGCG (10–40 μ M), NS-398 (10 μ M); green tea polyphenols (0.1% in water); Celecoxib (5 mg/kg); Catechin extract (30 μ g/mL)	Induced apoptosis, enhanced Bax, pro-caspases, PARP cleavage, reduced PSA, IGF-1, Bcl-2; increased cytochrome c; PC-3 cells arrested at S-phase.
Breast cancer	MDA-MB-231, MCF-7, BT-474 cells; nude mice; human patients	GTP, EGCG	EGCG (50–80 μ g/ml); GTP (40–60 μ g/ml); oral dose 1 mg/0.1 ml/mouse; 400 mg EGCG in patients	Induced G1 arrest, down-regulated Cyclins D/E, CDKs, PCNA; reduced VEGF, MMP-2/9; enhanced radiotherapy-induced apoptosis; inhibited PI3K/mTOR/AKT; delayed tumor growth.
Lung cancer	4T1 cells; NCr mice	EGCG	EGCG (20–100 μ g/mL); dietary 0.1–0.5%	Inhibited proliferation, induced apoptosis via Bcl-2/Bax/caspase cascade, reduced metastasis, extended survival, and induced DNA damage in dose-dependent manner.
Colon cancer	HT29 colon cancer cells; BALB/c nude mice	EGCG	In vitro dose-dependent; 1.5 mg/day in vivo	Inhibited Erk1/2, VEGF, angiogenesis; decreased proliferation and vessel density; increased apoptosis.

Table 2 (continued)

Pharmacological activity	Animals/humans/species used	Compound(s)/Extract	Dose/Method	Observation
Hepatic cancer	BEL-7404/DOX cells; BALB/c mice	EGCG, ECG	EGCG (14 µg/ml; 40–160 mg/kg); ECG (60 µg/ml)	Inhibited HCC proliferation, MDR1 modulation, enhanced doxorubicin cytotoxicity by inhibiting P-gp and increasing drug uptake.
Skin cancer	Melanoma cell lines; nude mice (Mel 928)	EGCG; EGCG–Chitosan nanoparticles	EGCG (0.1–1 µM); 100 µg/mouse	Inhibited NF-κB, IL-1β, NLRP1, caspase-1; suppressed inflammasome activity; showed pro-apoptotic and antiproliferative effects.
Myeloma cancer	U266 myeloma cells	EGCG	10 µM	Induced apoptosis via Src inhibition, increased Akt, cGMP, and ASM activation.
Bladder cancer	SW780 bladder cancer cells; female Balb/C mice	EGCG	100 mg/kg	Reduced tumor weight (68.4%) and volume; downregulated NF-κB and MMP-9 at both mRNA and protein levels.
Anti-bacterial	Infected Mongolian gerbils	Tea catechins	70 and 100 mg/animal/day	Eradicated 10–36% <i>Helicobacter pylori</i> , reduced mucosal hemorrhage and erosion.
Anti-bacterial	Kunming male mice; <i>P. aeruginosa</i> wound model	Tea polyphenols	3.125 mg/mL	63.3% survival rate; reduction in <i>P. aeruginosa</i> colonies with increasing dose.
Anti-bacterial	In vitro (<i>S. mutans</i> and other streptococci)	EGCG	1 mg/mL	Reduced acid production (<i>S. mutans</i> : 56.3%, <i>S. sanguinis</i> : 57.0%, etc.); induced cell aggregation of streptococci (up to 72%).
Urinary tract infection	In vitro; biodistribution in mice	Polyphenon 60 nano-emulsion	4 mg/mL (vs. ciprofloxacin 10 mg/mL); radiolabeling study	Inhibited <i>E. coli</i> , <i>K. pneumoniae</i> , <i>P. mirabilis</i> ; biodistribution: 3.50% in kidney and 3.81% in bladder at 3 h.
Anti-caries	In vitro (<i>S. mutans</i>) and rat model	Sunphenon, EGCG	100 µg/mL (Sunphenon); 333.3 µg/mL (Sunphenon); 166.7 µg/mL (EGCG); 0.05% Sunphenon in diet	Reduced bacterial adhesion (83.1%), inhibited glucan synthesis (Sunphenon: 67.5%, EGCG: 90.6%); reduced caries by 40% in rats.
Anti-caries	25 human subjects	Green tea (2%)	5-minute oral rinse	Decreased <i>S. mutans</i> count in saliva and plaque; reduced gingival bleeding index.
Anti-caries	Healthy volunteers (12–18 yrs)	Aqueous green tea extract	40 mL mouth rinse for 1 minute	Reduced colony count of <i>mutans Streptococci</i> and <i>Lactobacilli</i> ; showed anticariogenic action.
Antiviral (COVID-19)	In vitro (SARS-CoV-2 infected cells)	Aqueous tea extract	100 µg/mL; IC ₅₀ = 8.9 ± 0.5 µg/mL	100% inhibition of SARS-CoV-2; thearubigins bind to 3CLpro protease and block viral replication.
Antiviral (SARS/MERS)	In vitro; lentiviral vector model	EGCG	IC ₅₀ = 1.72–2.47 µg/mL	Inhibited entry of SARS-CoV, SARS-CoV-2, and MERS; action via interference with spike receptor binding.
Antiviral (Iridovirus)	Hybrid groupers infected with SGIV (Singapore grouper iridovirus)	Green tea polyphenols	10 µL administration	Mortality reduced to 8.33% in TP-only group and 11.67% in TP+SGIV group after 7 days, indicating antiviral efficacy in aquaculture model.

Table 2 (continued)

Pharmacological activity	Animals/humans/species used	Compound(s)/Extract	Dose/Method	Observation
Antiatherosclerosis	ApoE-deficient male mice	Tea catechins	1.7 mg	Reduced plasma peroxides (20.0 ± 4.90), atheromatous areas (23%), aortic cholesterol (27%), and triglycerides (50%).
Antiatherosclerosis	ApoE-null mice with hypercholesterolemia	EGCG	10 mg/kg	Increased antioxidant capacity, reduced smooth muscle proliferation, and plaque size (55% at day 21, 73% at day 42).
CNS neurogenesis	Male Balb/C mice	EGCG	2.5 mg/kg	Increased hippocampal neurogenesis and phospho-Akt levels.
Cognition disorder	Wistar rats (doxorubicin-induced memory deficit)	Tea catechin	50, 100, 200 mg/kg	Neuroprotection via reduced oxidative stress, AChE activity, and neuroinflammation in brain.
Cognition/aging	SAMP10 mice	Green tea catechins	1–60 mg/kg	Best memory effects at 60 mg/kg; 1 mg/kg or higher prevented aging; upregulated immediate-early genes (e.g., Nr4a, Fos, Egr1, Npas4).
Antidepressant	Humans ($n=48$)	White leaf tea	Oral intake over 10 days	Lowered state-trait anxiety scores compared to placebo; effects modulated by caffeine and amino acid content.
Antidepressant	Mice	Theanine, arginine (from tea)	Not specified	Anti-stress effects reduced by aspartic acid, asparagine, and high caffeine.
Respiratory disorder	C57BL/6 mice (LPS-induced acute lung injury)	EGCG	15 mg/kg (i.p.), before and after LPS (2 mg/kg) instillation	Reduced lung injury, leukocyte count, neutrophils, MPO activity; modulated M1/M2 macrophages; decreased iNOS, TNF- α , IL-1, IL-6; increased KLF4, Arg1, Ym1; enhanced lung regeneration and reduced oxidative damage.
Anti-obesity	Wistar rats and C57BL/6N mice (diet-induced obesity)	Black tea extract and polyphenol fraction	Rats: 500, 1000 mg/kg; Mice: 1%, 5% with diet	Reduced triglycerides (rats); reduced body weight, fat mass (56.9%), and liver lipids (81.7%) in mice.
Anti-obesity	Wistar rats (high fat diet)	Green tea polyphenols (GTPs)	0.8, 1.6, 3.2 g/L with water	Reduced fat, increased adiponectin, modulated PPAR γ via ERK1/2 activation.
Anti-obesity	C57BL/6 mice (high fat diet)	Dark tea extract powder (DTP)	100, 200, 300, 400 mg/kg (oral, 12 weeks)	400 mg/kg showed greatest reduction in body weight, liver and adipose mass, triglycerides, ALT, LDL-C, inflammation, insulin, and lipogenic markers (C/EBP α , leptin, PPAR γ , FAS mRNA). Increased HDL-C and improved liver histology.
Anti-obesity	HFD-induced obesity mouse model, CIDEA reporter mice	Heat-transformed green tea + isoquercetin	100 mg/kg each (2 weeks)	Reduced body weight (3%), fat (7.09%), increased thermogenesis, energy expenditure (8.95%), improved glucose tolerance, and mitochondrial biogenesis in adipose tissue.
Antihyperglycemic	Sprague-Dawley rats	Green tea extract	0.5 g in 100 mL distilled water	Lowered glucose, insulin, triglycerides, and FFAs; enhanced glucose uptake and insulin binding in adipocytes.

Table 2 (continued)

Pharmacological activity	Animals/humans/species used	Compound(s)/Extract	Dose/Method	Observation
Antihyperglycemic	CF-1 mice	EGCG	100 mg/kg (co-administered with starch)	Reduced postprandial glucose via α -amylase inhibition.
Antihyperglycemic	db/db mice	EGCG	10 g/kg	Improved glucose tolerance, insulin secretion, islet morphology; reduced ER stress markers in pancreas.
Antihyperglycemic	KK-Ay diabetic mice	Theaflavins + Theasinensin A	0.1% in diet	> 30% glucose reduction; inhibition of carbohydrate digestion and absorption.
Antihyperglycemic	Goto Kakizaki rats	Black tea aqueous extract + acarbose	1.0 mg/mL	Inhibited α -amylase; reduced plasma glucose (dose-dependent); synergistic hypoglycemic effect with acarbose.
Antihyperglycemic	ICR mice (HFD-fed)	Yellow tea infusion	1:30 w/v, 25 days	Reduced blood glucose; suppressed hepatic thioredoxin interacting protein.
Antihyperglycemic	C57BL/6 mice (HFD-induced obesity)	EGCG	25 or 75 mg/kg	Reduced glucose, insulin, liver/kidney weight, AGEs; activated Nrf2, enhanced GSH/GSSG ratio, and inhibited AGE receptor.
Hepatoprotective	Sprague–Dawley rats (lead-induced); Wistar rats (diabetic); Mice (alcohol-induced)	Aqueous green tea extract	1.5% w/v; 400 mg/kg	Reduced liver enzymes (ALT, AST, ALP), MDA, bilirubin; increased SOD, CAT, GSH, GSH-Px; antioxidant and hepatoprotective effect observed.
Anti-aging	<i>Caenorhabditis elegans</i> ; isolated murine mitochondria	EGCG and epicatechin gallate	2.5 μ M	Increased lifespan (up to 37.1 days), reduced fat, enhanced ROS defense; lifespan regulation via AMPK, SIRT1, p38 MAPK, NRF2, FOXO; transient mitochondrial inhibition followed by restoration of ATP and ROS balance.
Anticariogenic	Human (30 children, aged 12–15 years)	Water decoction of black tea	20 mL	Inhibited salivary amylase, preventing maltose release from oral debris; demonstrated anticariogenic effect.
Antifibrotic	Male ICR mice (CCl ₄ -induced hepatic fibrosis)	Aqueous green tea extract	125, 625, 1250 mg/kg	Reduced hepatic hydroxyproline levels by 18–23%; indicated antifibrotic efficacy of green tea.
Anti-inflammatory	Human corneal epithelial cells (IL-1 β challenged)	EGCG	0.3–30 μ M	Dose-dependent reduction in cytokines, MAPKs phosphorylation, NF κ B and AP-1 activity; reduced ROS and inflammation.
Immunomodulatory	Balb/C mice	EGCG	50 mg/kg	Increased regulatory T cells (Treg) in spleen and lymph nodes; suppressed T cell response; demonstrated immunomodulatory potential.
Wound healing	Male Wistar rats	70% ethanolic green tea extract + 0.6% Vaseline	Topical application for 21 days	Achieved 83% wound healing; enhanced vessel formation and reduced inflammation likely due to EGCG antioxidant activity.
Anti-Endometriosis	CMV-Luc mice (subcutaneous endometrium implantation)	Pro-EGCG	50 mg/kg	Decreased endometrial implant growth (weeks 2–4), reduced lesion size, promoted apoptosis; improved antioxidant, anti-angiogenic potential and bioavailability over native EGCG.

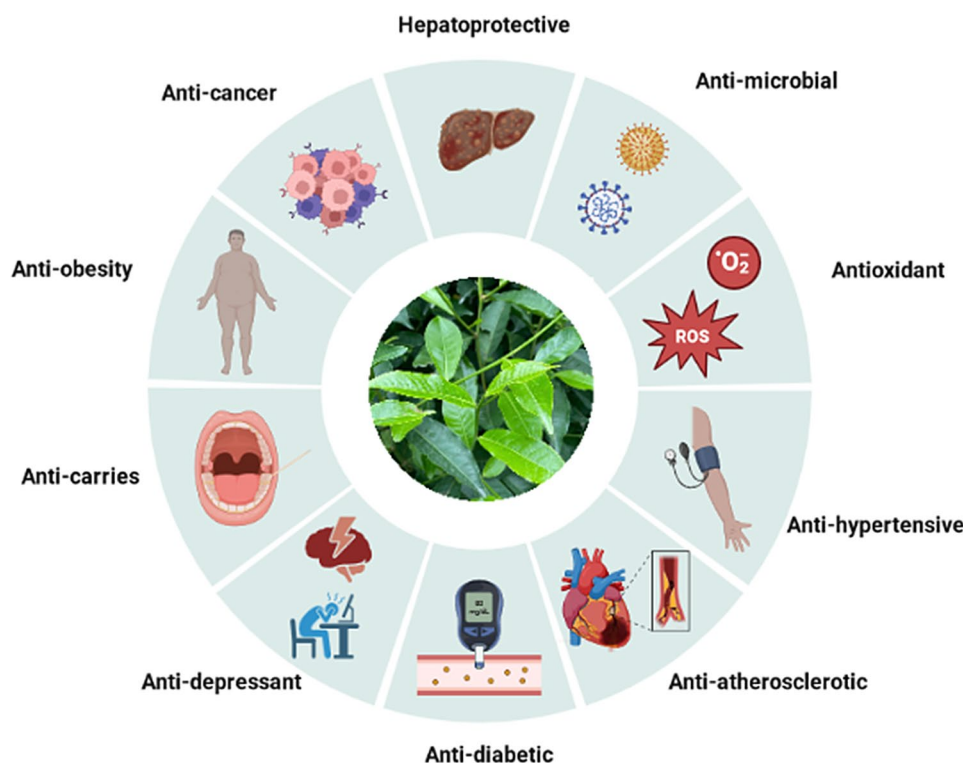


Fig. 13 Different pharmacological activities of tea and its active phytoconstituents

Breast cancer

In breast cancer MDA-MB-231 cells, green tea polyphenols (GTP, 40 µg/ml & 60 µg/ml) and epigallocatechin gallate (EGCG, 50 µg/ml and 80 µg/ml) showed cell cycle arrest at G1 phase. GTP and EGCG also down regulated the expression of Cyclin D, Cyclin E, CDK 4 (cyclin dependent kinase 4), CDK 1 (cyclin dependent kinase 1) and PCNA (proliferating cell nuclear antigen). In nude mice inoculated with MDA-MB-231 cells, GTP and EGCG showed tumor delaying activity and reduced the tumor burden. Both GTP (3 mg/mouse/day) and EGCG (at dose 1 mg/0.1 ml/mouse) were also found to induce apoptosis and inhibit the proliferation of tumor [71]. Hence it may conclude that GTP and EGCG have anti-cancer potential.

According to Tran et al., 2010, in an in-vitro model, EGCG decreases the cell proliferation and colony formation of MCF-7 breast cancer cells and specifically inhibited the expression of HSP70 (heat shock protein 70) and HSP90 (heat shock protein 90) by inhibiting their promoter activity. Whereas, in the xenograft in-vivo model, EGCG treatment at dose 10 mg/kg resulted in delayed tumor incidence and reduced tumor size as well as inhibited the expression of HSP70 and HSP90 in Balb/C mice [72]. From the above study it is concluded that EGCG can be a potential drug treatment of breast cancer.

In an in-vitro study carried out by Van Aller et al., 2011, EGCG showed anticancer activity by inhibiting

phosphoinositide-3-kinase (PI3K) and rapamycin (mTOR) in human breast tumor cell line BT-474. Moreover, EGCG inhibited cell proliferation and AKT phosphorylation [73].

In breast cancer patients under radiotherapy, EGCG at dose 400 mg showed significantly lowered in serum level of vascular endothelial growth factor, hepatocyte growth factor and decreased and reduced metalloproteinase-9 (MMP9) and metalloproteinase-2 (MMP2) activation as compared to patients with radiotherapy only. Moreover, sera from EGCG treated patients in in-vitro culture of MDA-MB-231 breast cancer cells showed suppression of cell proliferation and invasion, cell cycle arrest at G0/G1 phase and showed reduction in activation of MMP9/MMP2, Bcl-2/Bax expression, c-Met receptor, NF-κB (nuclear factor kappa B) and AKT (Akt strain transforming) phosphorylation. In MDA-MB-231 breast cancer cells, 5–10 µM EGCG showed significant of augmentation of apoptosis inducing effect of γ radiations, reduced NF-κB level and AKT phosphorylation [74]. These results indicated that, EGCG can be a therapeutic adjuvant against human metastatic breast cancer.

Hence, it may be concluded from above mentioned studies that green tea polyphenols and EGCG exhibit substantial anti-cancer activity against breast cancer cell lines. There is potential for their incorporation into appropriate dosage formats and subsequent

commercialization, enabling broader accessibility for individuals afflicted by breast cancer.

Lung cancer

In 4T1 lung cancer cells, EGCG at dose range (20–100 µg/mL) inhibited cell viability (30% to 75%), induced apoptosis and inhibited cell proliferation. It also decreased the protein expression of Bcl-2 (B cell lymphoma-2) concomitantly increased Bax, which led to release of cytochrome, which further binds with Apaf-1 (apoptotic protease activating factor-1) and ultimately led to cleavage of caspase 3 (cysteine-aspartic proteases 3) and PARP proteins (polyADP-ribose) polymerase (characteristic hallmark of apoptosis). Administration of green tea resulted in the inhibition of tumor metastasis to the lungs and an extension in the survival duration of the animals [75].

In another study, EGCG at doses of 0.1, 0.3 and 0.5% in the diet showed inhibitory activity against human lung cancer in xenograft tumors (male N Cr mice). Furthermore, EGCG showed dose dependent cell apoptosis and DNA damage [76].

From the findings of above mentioned studies it is concluded that, green tea polyphenols and EGCG has ability to prevent lung cancer and its metastasis.

Colon cancer

In in-vitro serum-deprived HT29 human colon cancer cells, EGCG inhibited Erk-1 and Erk-2 (extracellular signal regulated protein kinases-1 & 2) activation in a dose-dependent manner. EGCG also inhibited the promoter activity induced by serum starvation and increase of VEGF (vascular endothelial growth factor) expression. Whereas in in-vivo, athymic BALB/c nude mice with HT29 cells, treated with EGCG (at dose 1.5 mg/day) inhibited tumor growth (58%), microvessel density (30%), tumor cell proliferation (27%), increased tumor cell apoptosis (1.9-fold) and endothelial cell apoptosis (3-fold). EGCG also exerts anticancer effect by inhibiting angiogenesis by blocking the induction of VEGF [77]. Hence the study reveals that, EGCG can be used to inhibit Colon cancer.

Hepatic cancer

Green tea catechins (ECG and EGCG) showed antitumor activity with doxorubicin in chemoresistant hepatocellular carcinoma (HCC) in BALB/c mice model. Both ECG (60 µg/ml) and EGCG (14 µg/ml) showed inhibitory effect on HCC proliferation and identified as MDR (multidrug resistance mutation 1) modulators (specifically MDR1). EGCG (40–160 mg/kg) enhanced chemo-sensitivity and cytotoxicity of doxorubicin in BEL-7404/DOX cells by inhibiting P-gp (P-glycoprotein) pump function and thereby elevated doxorubicin intracellular concentration

[78]. From this study it is concluded that tea catechins i.e. EGC and EGCG has anticancer potential.

Skin cancer

In human metastatic melanoma cell lines, EGCG treatment inhibited melanoma cell growth at physiological doses (0.1–1 µM). It inhibited NF-κB and reduced NF-κB activity is linked with decreased IL-1β secretion from melanoma cells. EGCG is involved in the downregulation of inflammasome (involved in IL-1β secretion), NLRP1 (NLR family pyrin domain containing 1), and reduced caspase-1 activation. Furthermore, NLRP1 silencing abolishes EGCG induced inhibition of tumor cell proliferation [79].

In another study, EGCG (100 µg/mice) when encapsulated with chitosan nanoparticles, showed antiproliferative and pro-apoptotic effects in Athymic nude mice model with human melanoma Mel 928 cells [80].

Hence these studies concluded that, EGCG has anticancer potential and can be used in the treatment of skin cancer.

Myeloma cancer

Human multiple myeloma U266 cells when treated with EGCG (10 µM) showed anticancer effect. EGCG elicits phosphorylation of Src (proto-oncogene tyrosine-protein kinase Src) at Tyr 416. This leads to inhibition of Src and further induced cell death signaling, upregulation of protein kinase B (Akt) activity, increase in the level of cGMP (cyclic guanosine monophosphate) and ASM (acid sphingomyelinase) activation [81].

Bladder cancer

EGCG showed antiproliferation and antimigration activity against bladder cancer in female Balb/C mice with implanted bladder cancer SW780 cells at dose 100 mg/kg. EGCG showed activity by reducing tumor weight (68.4%) and volume. Moreover, EGCG downregulated the expression of NF-κB and MMP-9 in protein and mRNA level in SW780 cells and tumor [82].

While the studies mentioned above have primarily focused on assessing the anticancer potential of tea catechins, particularly EGCG and ECG, there remains an untapped potential within the plant's anticancer properties. Given this potential and the likelihood that the plant contains a diverse array of anticancer compounds, it becomes crucial to embark on further investigations to explore other compounds derived from this plant. By doing so, we can shed light on their potential efficacy in combating cancer. Hence above-mentioned studies intricate pathways of research on tea its anticancer potential. Understanding tea's full potential in cancer prevention and treatment is promising, calling for

continued exploration into optimal blends, concentrations, and delivery methods of bioactive tea extracts and its compounds.

Anti-bacterial activity

Bacterial infections are very common and clinical manifestation can range from mild superficial infections to systemic infections [83]. Nowadays, multidrug-resistant of anti-bacterial drugs is a global crisis that impacts humans globally [84].

In infected Mongolian gerbils, tea catechins (70 and 100 mg/animal/day) eradicated (10 to 36%) *Helicobacter pylori* which further resulted in decrease in mucosal hemorrhage and erosion [85].

Tea polyphenols inhibited *Pseudomonas aeruginosa* pathogenicity in Kunming male mice at a dosage of 3.125 mg/mL, with a survival rate of 63.3%. Moreover, in excision wound infection model *P. aeruginosa* colonies decreased with increase in concentration [86].

According to Han et al., EGCG at concentration 1 mg/ml decreased the acid production of *Streptococcus mutans* (56.3 ± 8.28) and non-mutans streptococci (*Streptococcus sanguinis* (57.0 ± 9.13), *Streptococcus gordonii* (36.4 ± 5.88) and *Streptococcus salivarius* (58.8 ± 6.88)) by inhibiting the activity of PEP-PTS (phosphoenolpyruvate-dependent phosphotransferase system). At the same concentration EGCG also caused cell aggregation of *S. mutans* (67.4 ± 7.90), non-mutans streptococci (*S. sanguinis* (72.0 ± 4.80), *S. gordonii* (63.2 ± 4.55) and *S. salivarius* (4.1 ± 1.11)) [17].

Urinary tract infection

A nano-emulsion containing 4 mg/ml of polyphenon 60 (a tea catechin) effectively hindered the growth of bacterial strains accountable for Urinary Tract Infections, namely *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. This inhibition was comparable to the effect observed with a standard drug, ciprofloxacin, at a concentration of 10 mg/ml. Biodistribution study of nano-emulsion found that the percent radio labeled polyphenon 60 (with technetium pertechnetate) per gram was found to be 3.50 ± 0.26 in kidney and 3.81 ± 0.30 in urinary bladder at 3 hours [87].

Therefore, based on this study, it can be deduced that like polyphenon 60 other tea catechins might also play a role in treating urinary tract infections. Consequently, it becomes essential to investigate their potential in this regard and create novel drug delivery dosage formulations for these compounds.

Anti-carries

Bacterial cells (*Streptococcus mutans* - is a bacterium commonly associated with dental caries, which are more commonly known as cavities or tooth decay) treated with

sunphenon (polyphenolic compound) at concentration 100 µg/mL resulted in significant decrease in bacterial attachment to saliva coated hydroxyapatite disc (83.1%). Sunphenon and EGCG inhibited water insoluble glucan synthesis from sucrose by *S. mutans* glucosyl transferase by 67.5% (at dose 333.3 µg/ml) and 90.6% (at dose 166.7 µg/ml), respectively. Whereas in rat infected with *S. mutans* and fed with cariogenic diet, when treated with 0.05% Sunphenon resulted in decrease in carries by 40% [88].

In 25 human subjects, green tea (2%) rinsing for 5 minute showed reduction in *S. mutans* count in saliva, plaque, and gingival bleeding index [89].

In another study, healthy volunteers of 12 to 18 years of age, rinsed mouth with aqueous green tea extract (40 ml) for one minute led to antimicrobial activity against mutans *Streptococci* and *Lactobacilli* by reducing colony count leading to anticariogenic action [90].

Therefore, it can be inferred that the antibacterial properties of tea polyphenols make them viable for addressing bacterial infections such as urinary tract infections and dental caries.

Antiviral activity

Viruses are group of pathogens responsible for severe life threatening diseases [91]. In the last decade numbers of antiviral agents are approved to treat viral infections like influenza, small pox, HIV etc [92].

Corona virus

Tea (100 µg/ml aqueous extract) showed potential inhibitory activity (100%) against SARS-COV-2 (severe acute respiratory syndrome corona virus 2) with an IC_{50} 8.9 ± 0.5 µg/ml. According to the study active component thearubigins bind to the cysteine 1453CLpro of protease active site and inhibit the protease activity which further helps to stop replication cycle of SARS-CoV-2 [93].

In a separate investigation, EGCG exhibited inhibitory activity against SARS-CoV, displaying an IC_{50} of 1.72 µg/ml. Furthermore, EGCG effectively impeded the entry of not only SARS-CoV-2 but also suppressed the viral infections of MERS and SARS-CoV, as evidenced by an IC_{50} of 2.47 µg/ml in an in-vitro assay involving a SARS-CoV pseudotyped lentiviral vector. Mechanistically, EGCGs inhibition was linked to its interference with the spike receptor of SARS-CoV-2 [16].

Iridovirus infection

In the context of hybrid groupers fish, the administration of green tea polyphenols (10 µL) demonstrated antiviral efficacy against Singapore grouper iridovirus (SGIV) infection. The mortality rates within the tea polyphenol (TP) treated group stood at 8.33%, while the group

treated with TP alongside SGIV injection exhibited a mortality rate of 11.67% after 7 days of treatment [94].

From the above study, it is concluded that tea has antiviral potential and can be used to treat antiviral infections like corona and iridovirus infection.

In conclusion, the remarkable antibacterial activity displayed by the tea extract and its constituent compounds underscores their potential as effective agents against bacterial infections like Urinary tract infection, dental carries, corona virus and Iridovirus infection. These findings shed light on the promising role of tea polyphenols in combating bacterial pathogens and provide a foundation for further exploration of bioactive compounds in the realm of antimicrobial therapies.

Antiatherosclerosis activity

ApoE (apolipoproteinE) deficient male mice with atherosclerosis were administered with 1.7 mg of tea catechin resulted in the reduction of plasma peroxides (20.0 ± 4.90), suggesting the improvement in oxidative state [95–97]. Atheromatous areas were attenuated (23%), reduction in aortic cholesterol (27%) and triglyceride content (0.86 ± 0.45) (50%) was noticed without change in plasma lipid level in group treated with tea catechins, which indicates the tea catechins prevents the development of atherosclerosis [14].

In another study, EGCG (10 mg/kg) increased antioxidant capacity in systemic circulation and local vascular tissue and reduced vascular smooth muscle proliferation in hypercholesterolemic apolipoprotein E-null mice with emerging and existing atherosclerotic lesions. EGCG also reduced atherosclerotic plaque size at 21 day and 42 day of treatment by 55 and 73% respectively [13].

As a result, it is conceivable to conclude that tea catechins are viable candidates for the treatment of atherosclerosis. More research, other from EGCG, is needed to investigate the other tea catechins for the treatment of atherosclerosis.

CNS diseases

In male Balb/C mice, EGCG treatment showed hippocampal neurogenesis at dose 2.5 mg/kg. resulted in increase in cell survival and the hippocampal levels of phospho-Akt [98].

Cognition disorder

At 50, 100, and 200 mg/kg dosages of tea catechin, Wistar rats showed neuroprotective effects against doxorubicin-induced episodic memory deficit. Furthermore, catechin administration reduced oxidative stress, acetylcholine esterase activity, and neuroinflammation in the hippocampus and cerebral cortex [99].

Green tea (GT) catechins (60 mg/kg) were observed to inhibit the aging-related loss in brain function in senescence-accelerated mouse prone 10 (SAMP10) mice. The dosage dependency of brain function on GT-catechin indicated that consumption of 1 mg/kg or higher prevented aging and cognitive decline. The mice with the longest median longevity received 1 mg/kg GT-catechin; however, the dosage was less effective in delaying cognitive aging [100–103]. The best dose for enhancing memory acquisition was 60 mg/kg, whereas mice given 30 mg/kg or more had greater memory retention. One month after consuming GT-catechin, alterations in gene expression in the hippocampus of SAMP10 mice were examined to clarify the mechanism by which cognitive decline is prevented by GT-catechin. The findings demonstrate a considerable increase in the expression of immediate-early genes including nuclear receptor subfamily 4 (Nr4a), FBJ osteosarcoma oncogene (Fos), early growth response 1 (Egr1), neuronal PAS domain protein 4 (Npas4), and cysteine-rich protein 61 (Cyr61). These findings imply that GT-catechin prevents age-related cognitive loss by upregulating immediate-early genes that are involved in long term changes in synaptic plasticity and neuronal circuit [15].

Depression

During a study involving 48 human participants, the consumption of white leaf tea and placebo tea over a span of one week, followed by a continuation of 10 days, resulted in lowered scores on the state-trait anxiety scale in comparison to the placebo group. However, no discernible differences were observed in other stress-related indicators.

Similarly, a study conducted on mice demonstrated that the anti-stress effects of theanine, arginine, were obstructed by the presence of aspartic acid and asparagine, both of which are found in elevated levels in shaded white leaf tea. Furthermore, the beneficial anti-stress effects of shaded white leaf tea were similarly impaired in instances of elevated caffeine content [104].

In conclusion, the comprehensive exploration of tea extracts and their constituent compounds has unveiled a promising realm of potential in the realm of Central Nervous System (CNS) activity. The investigation of these natural substances has illuminated their capacity to modulate neurological functions and impact cognitive, emotional, and behavioral aspects. The diverse array of bioactive constituents within tea, such as polyphenols and catechins, have demonstrated the ability to interact with neurotransmitter systems, exhibit neuroprotective effects, and influence neural signaling pathways [105–108].

Through a combination of in-vitro and in-vivo studies, these tea-derived compounds have been linked to improved cognitive performance, stress reduction, and mood regulation. The findings underscore the potential application of tea extracts as supportive agents in addressing various CNS-related conditions, such as anxiety, depression, and neurodegenerative disorders.

However, despite the promising outcomes, it is essential to acknowledge the complexity of CNS activity and the multifaceted nature of tea compounds' interactions. Further research is necessary to delve deeper into the specific mechanisms of action, optimal dosages, and potential side effects. Additionally, clinical trials involving human subjects will be instrumental in translating these preliminary findings into practical therapeutic interventions.

Respiratory disorders

Two dosages of EGCG (15 mg/kg) were administered intraperitoneally to C57BL/6 mice with acute lung damage caused by lipopolysaccharide (LPS) 1 hour before and 3 hours after LPS instillation (2 mg/kg). In LPS-induced lung injury, EGCG therapy reduced histopathological lesions, total leukocyte count, neutrophil infiltration, wet/dry ratio, total proteins, and myeloperoxidase activity. The findings showed that EGCG inhibited LPS induced acute lung injury via modifying macrophage polarization toward the M2 phase. Additionally, in the lung microenvironment after LPS administration, EGCG decreased the expression of the proinflammatory M1 mediators iNOS (inducible nitric oxide synthase), TNF- α (tumor necrosis factor- α), IL-1 (interleukin-1), and IL-6 (interleukin-6). Additionally, it boosted the expression of genes known to enhance the M2 phenotype of macrophages, including KLF4 (kruppel like factor 4), Arg1 (arginase 1), and Ym1 (chitinase like protein 3). Moreover, EGCG reduced 8-OHdG (8-hydroxy-2'-deoxyguanosine), nitrotyrosine expression, demonstrating its capacity to prevent oxidative damage. TREM1 (triggering receptor expressed on myeloid cells 1) increased the expression of the proteins Ki67, PCNA, and Ang-1 in the lung tissue, which enhanced lung regeneration ability. These findings suggested that the protective effects of EGCG against LPS-induced acute lung injury may be explained by the reduction of the M1/M2 macrophage subtype ratio, the enhancement of KLF4, the stimulation of lung cell regeneration, and the regulation of oxidative damage in LPS-induced acute lung injury in mice [109].

Above studies concludes that the tea extracts and their compounds as adjunctive approaches to respiratory disorder management holds great potential. While more research is needed to solidify their role, the outcomes thus far suggest that these natural compounds could contribute to a comprehensive strategy for enhancing

respiratory health and improving the quality of life for individuals dealing with various respiratory challenges.

Anti-obesity activity

Black tea extract and its polymerized polyphenol fraction showed activity against diet induced obesity in male Wistar rats (500 and 1000 mg/kg) and female C57BL/6N mice (1 and 5% with diet). Black tea extract showed reduction in plasma triglyceride level in rats, whereas polyphenol fraction of black tea showed reduction in body weight, parametrial adipose tissue mass (56.9%), and liver lipid content (81.7%) in mice [110]. In high fat diet fed male Wistar rats, green tea polyphenols (GTPs) (0.8, 1.6, 3.2 g/L) when administered with water, showed reduction in fat deposits in ameliorated hypoadiponectinemia. In-vitro VAT culture, GTPs upregulates adiponectin decrease. Overall GTPs showed activity via erk1/2 activation, alleviation of PPAR γ (peroxisome proliferator activated receptor gamma) phosphorylation and increase of the PPAR γ expression [111].

The anti-obesity effect was studied in C57BL/6 mice (high-fat diet) by oral administration of dark tea extract powder (DTP) (100/200/300 mg/g) daily for 12 weeks and dose group 400 mg/kg showed significant results as compared to other dose groups. There were significant decrease in weights (21.36 ± 0.37) and this significant difference continued to the completion of administration. The weight of liver adipose tissue (0.7811 ± 0.0144) and epididymal adipose tissue (1.6086 ± 0.0859) (g), showed significant levels of absolute weight reduction. There was a significant decrease in blood ALT levels (22.33 ± 0.33). Furthermore, level of triglycerides in blood also significantly decreases (56.17 ± 1.19). There was significant increase in blood HDL-C (high density lipoprotein cholesterol) measurement (mg/dl) whereas regarding LDL-C (low density lipoprotein-cholesterol), there was a significant decrease (10.67 ± 0.33). In HFD (high fed diet) fed mice, as a result of the accumulation of lipid droplets in the liver tissue and the adipose inflammation level, liver tissues' steatosis scores significantly decreased. The adipose inflammation within the liver tissue showed significantly decreased inflammation score. Fasting blood insulin levels (ng/ml), a significant dose-dependent reduction was confirmed (2.73 ± 0.15). There was a significant decrease in C/EBP α (CAAT/enhancer binding protein alpha) protein levels (283.69 ± 45.91) in the liver tissue. With qPCR analysis, it was confirmed that leptin mRNA in the liver tissue showed a significant decrease (0.82 ± 0.03). C/EBP α analysis also showed a significant decrease in C/EBP α mRNA levels (0.44 ± 0.04). The qPCR (quantitative polymerase chain reaction) results of PPAR γ mRNA levels (0.53 ± 0.04) in the liver tissue confirmed a significant decrease. Regarding FAS (fas cell surface death receptor) mRNA, (0.60 ± 0.04) showed

a significant decrease [112]. In HFD induced obesity mouse model and CIDEA (cell death inducing DNA fragmentation factor alpha like effector A) reporter mice, heat transformed green tea extract when administered with enzymatically modified isoquercetin (100 mg/kg each) showed anti-obesity effect by activation of adipose tissue thermogenesis. The combination treatment of both increased the expression levels of brown adipocyte markers and mitochondrial proteins in adipose tissue. Moreover, two weeks of treatment led to loss of body weight (3%) and body fat (7.09%). In HFD fed mice, treatment increased energy expenditure (8.95%) and also improved glucose tolerance [113].

In conclusion, the exploration of tea extracts and their constituent compounds presents a promising avenue in the realm of anti-obesity strategies. Extensive research has unveiled their potential as supportive agents for weight management and addressing obesity-related issues. The rich composition of bioactive elements within tea, including polyphenols and catechins, demonstrates their capacity to modulate metabolic pathways, enhance thermogenesis, and regulate adipogenesis.

Antihyperglycemic activity

Green tea and its polyphenol content showed insulin sensitivity enhancing activity in Sprague-Dawley rats at dose 0.5 g with 100 mL of deionized distilled water. Green tea treatment resulted in lowering level of plasma glucose, insulin, triglyceride, and free fatty acid. Green tea also enhanced insulin stimulated glucose uptake of adipocytes and also enhanced insulin binding to adipocytes [114]. In CF-1 mice, EGCG (100 mg/kg) reduced postprandial blood glucose level when co-administered with starch. This may be due to inhibition of α -amylase (involved in starch digestion) [115]. In *db/db* mice, EGCG (10 g/kg) treatment showed antidiabetic activity. EGCG showed improvement in glucose tolerance and increased glucose-stimulated insulin secretion. Supplementation of EGCG showed reduction in the number of pathologically changed islets of Langerhans, increased size and the number of islets, and heightened pancreatic endocrine area. Moreover, EGCG also showed reduction in islet endoplasmic reticulum stress markers [116]. In diabetic male KK-Ay mice, when fed with 0.1% of theaflavins and theasinensin A showed antihyperglycemic by reducing glucose level by > 30%. There is probability that theaflavins and theasinensin A showed antihyperglycemic by suppressing glucose availability via inhibition of carbohydrate digestion and absorption [117]. Aqueous extract of black tea (1.0 mg/mL) with acarbose showed inhibition of α amylase in male GK (Goto Kakizaki) rats (non-obese type 2 diabetes mellitus). According to oral sucrose tolerance test, tea extract reduced plasma glucose level in dose dependent manner. Furthermore, tea

extract showed hypoglycemic effect and also showed synergistic effect with acarbose [118]. In HFD fed ICR mice, tea infusion (1:30 w/v) of yellow tea reduced blood glucose level on 25 days of treatment. Yellow tea suppressed HFD induced early elevation of hepatic thioredoxin interacting protein and overall showed antihyperglycemic effect [119]. In C57BL/6 with high fat diet induced obesity, EGCG showed antihyperglycemic effect. At dose 25 mg/kg or 75 mg/kg EGCG showed reduction in body weight, plasma glucose, insulin level, liver and kidney weight. Furthermore, EGCG inhibited receptor for AGE (advanced glycation end products), activated Nrf2, enhanced GSH/GSSG ratio and decreased levels of AGEs in both liver and plasma [120].

Hepatoprotective activity

Aqueous green tea extracts augmented antioxidant potential of liver on lead induced hepatotoxicity in Sprague-Dawley rats. On determination of levels of liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) and serum protein indicated the protective effects of green tea extract [121]. In diabetes induced Wistar rats, oral dose of aqueous green tea extract (1.5% w/v) reduced the level of malondialdehyde (MDA) content and serum level of ALT, AST, ALP and bilirubin whereas increased the level of glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and GSH-Px in liver, significantly [122]. In in-vivo mice model with alcohol induced acute liver injury, tea at 400 mg/kg reduced the level of alanine transaminase, aspartate transaminase, alkaline phosphatase, triacylglycerol and total bilirubin in sera, whereas decrease the level of malondialdehyde and increased the level of superoxide dismutase, glutathione peroxide and glutathione in liver, indicating the hepatoprotective effect of green tea [59].

Antiangi activity

Green tea catechins (epigallocatechin gallate and epicatechin gallate) at concentration 2.5 μ M enhanced health, lifespan and stress resistance in *Caenorhabditis elegans*. According to study lifespan increase produced by these catechins depends on AAK-2/AMPK (AMP-activated protein kinase), SIR-2.1/SIRT1 (sirtuin), PMK-1/p38 MAPK (human phosphomevalonate kinase-1/p38 mitogen activated protein kinases), SKN-1/NRF2 (nuclear factor erythroid 2-related factor 2), and DAF-16/FOXO. Over all catechins reduced fat content, enhanced ROS (reactive oxygen species) defense and improved lifespan for the long term. The maximum lifespan extended by epigallocatechin and epicatechin gallate is 35.7 ± 0.6 to 36.9 ± 0.1 days and 35.7 ± 0.6 to 37.1 ± 0.3 days respectively. In isolated murine mitochondria these catechins at 2.5 μ M hampered complex I activity after 6–12 hours

and impaired mitochondrial respiration was impaired by transient drop in ATP (adenosine triphosphate) production and temporary increase in ROS level but after 24 hours level of ATP and ROS (even dropped below control conditions) get restored [123].

Anticariogenic activity

A group of 30 children aged 12 to 15 years were administered a water decoction of black tea (20 ml). This led to the inhibition of the salivary enzyme amylase, which is responsible for impeding the release of maltose from food particles trapped within the oral cavity. This investigation demonstrated the potential anticariogenic effect of black tea [124].

Antifibrotic activity

The potential antifibrotic characteristics of aqueous green tea were examined through a study involving male ICR mice with carbon tetrachloride-induced hepatic fibrosis. The oral administration of green tea extract at doses of 125, 625, and 1250 mg/kg resulted in a noteworthy reduction ($p < 0.05$) in hydroxyproline levels, with reductions of 18, 21, and 23%, respectively. These findings signify the beneficial antifibrotic impact of tea [56].

Anti-inflammatory activity

Inflammation is a basic way in which body reacts to injury, irritation and infections. Inflammation is a non specific type of immune response and characterized by redness, heat, swelling, pain and loss of functions [125].

In Interleukin 1- β challenged human corneal epithelial cells (HCEpiC), EGCG (0.3–30 μ M) showed dose dependent reduction in cytokines release. Moreover, EGCG inhibited phosphorylation of the MAPKs p38, c-Jun N-terminal kinase, NF κ B and AP-1 (activator protein 1) transcriptional activities and also showed reduction in ROS level [126]. These all factors contribute to the reduction in inflammation.

Immunomodulatory activity

EGCG exhibited immunomodulatory effects in a Balb/C mice model when administered at a dose of 50 mg/kg. This was evidenced by an increase in the quantity and occurrence of regulatory T cells (Treg) within the spleen and lymph nodes, coupled with a suppression of T cell response [127].

Wound healing activity

Application of mixture of 70% of ethanolic extract of green tea with 0.6% Vaseline for 21 days showed wound healing effect (83%) in male Wistar rats. The antioxidant potential of EGCG present in green tea maybe responsible for wound healing effect, which is also responsible for

speeding up vessel formation on skin and anti-inflammatory activity [128].

Anti-Endometriosis activity

Prodrug of EGCG (pro-EGCG) showed activity as an anti-angiogenesis for endometriosis in CMV-Luc mice (cytomegalovirus-Luciferase) (subcutaneously planted homologous endometrium) at dose 50 mg/kg. From second to fourth week of invention, pro-EGCG significantly decreased the growth of endometrial implant. Moreover, pro-EGCG reduced lesion size, enhanced lesion apoptosis, showed better bioavailability, greater antioxidant and anti-angiogenesis capacity [129].

Limitations

The present review on *Camellia sinensis* provides extensive insight into its phytochemical and pharmacological significance; however, several limitations persist. Most of the available studies are preclinical, with limited in vivo and clinical trials to confirm the efficacy and safety of tea bioactives in humans. The variability in cultivation conditions, processing methods, and tea types influences the phytochemical composition, leading to inconsistent results across studies. Furthermore, insufficient data on the pharmacokinetics, metabolism, and bioavailability of key constituents such as catechins and theaflavins restricts their translational potential in drug development. Standardization of extraction methods and dosages is also lacking, making comparison difficult. Additionally, possible interactions of tea constituents with pharmaceutical drugs remain underexplored. Hence, more systematic, large-scale clinical investigations and mechanistic studies are essential to validate the therapeutic potential of *C. sinensis* and ensure its safe and effective incorporation into pharmaceutical formulations.

Conclusion

Being a popular drink with a variety of cultures, tea can serve as not only an invigorating beverage but a strong source of health-supportive substances. This review indicates that *Camellia sinensis* has a wide assortment of bioactive building blocks, particularly the catechin compounds such as epigallocatechin gallate (EGCG) which have high antioxidant, anti-inflammatory, anticancer, antimicrobial, and antidiabetic effects. The therapeutic value of such compounds appears feasible, as the evidence supports these findings in preclinical and clinical studies, but it is yet to be conclusive in humans. It is especially true of green tea because it is not fermented and contains more polyphenols as well as higher antioxidant activity. The prevention and management of chronic diseases like cancer, cardiovascular disorders, and diabetes may be achieved as a result of having tea as a part

of the everyday diet. In spite of the popularity of consumption and expanding scientific interest, the specific molecular pathways behind the bioactives of tea continue to be inadequately comprehended. In addition to this, its pharmacokinetics, synergies with mainstream therapies, and bioavailability are yet to be explored. On the whole, this review highlights the multifold opportunities of tea as a functional drink. The possibility of more biologically active phytochemical and therapeutic modes of action may result by further studies in applying it nutraceutically and pharmaceutically.

Abbreviations

CG	Catechin-3-O-gallate
GC	Gallic catechin
GCG	Gallic catechin-3-O-gallate
EC	Epicatechin
ECG	Epicatechin-3-O-gallate
EGC	Epigallocatechin
EGCG	Epigallocatechin-3-O-gallate
SOD	Superoxide dismutase
TBARS	Thiobarbituric acid-reactive substances
GSR	Glutathione reductase
GSH	Glutathione
GTE	Green tea extract
BDNF	Brain derived neurotrophic factor
HCC	Hepatocellular carcinoma
SGIV	Singapore grouper iridovirus
TP	The mortality rates within the tea polyphenol
GT	Green tea
CNS	Central Nervous System
LPS	Lipopolysaccharide
DTP	Dark tea extract powder
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ALP	Alkaline phosphatase
MDA	Malondialdehyde
CAT	Catalase
NCBI	National Center for Biotechnology Information
FRAP	Ferric reducing antioxidant power
ICR	Institute of Cancer research
PCNA	Proliferating cell nuclear antigen
AKT	Ak strain transforming
VEGF	Vascular endothelial growth factor
ASM	Acid sphingomyelinase
HFD	High fat diet
FAS	Fas cell surface death receptor
CIDEA	Cell death inducing DNA fragmentation factor alpha like effector A
GK	Goto Kakizaki
AGE	Advanced glycation end products
ROS	Reactive oxygen species

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Author contributions

Pankaj Kumar and Shikha Chaudhary: Collection of the information, conceptualization, planning, drafting of the manuscript and writing-review; Shubhangi Sood and Shikha Mahant: reviewing and editing; Pankaj Kalia and Rajesh Kumar: reviewing and editing; Swati Pundir: Data curation, analysis, review and editing. All authors approved the final submitted version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

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Human ethics and consent to participate

Not applicable.

Competing interests

The authors declare no competing interests.

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