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Review Article

A Review of the Phytochemistry, Pharmacology and Properties of Black Tea in Health

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ABSTRACT

Black tea (*Camellia sinensis* L.) is renowned for distinct organoleptic properties attributed to the post-fermentation process. Several studies have shown that the plant contains various chemical components, including theabrownins, thearubigins, theaflavins, TPs-2, TPs-1, Kaempferol, Quercetin, Myricetin, Arginine, Alanine, and GABA. Other compounds present include Theanine, Epigallocatechin gallate (EGCG), Epigallocatechin Gallate Derivative (EGCGD), Gallocatechin, and Gallic acid. These compounds are presumable responsible for the numerous health advantages of black tea, including anti-oxidant, anti-obesity, anti-cholesterol, and anti-diabetic qualities. The plant has also attracted significant attention globally due to the diverse range of bioactive chemicals, each of which has a distinct pharmacological impact. Therefore, this review aimed to offer additional details regarding the pharmacological effects, advantages, and mechanism of action for black tea in humans.

***Keywords*:** Black tea, Chemical Composition, Pharmacological Effects, Health Benefits

Introduction

Black tea (*Camellia sinensis* L.), a member of the Theaceae family, is a popular beverage valued for both the unique flavor and medicinal properties.[1] In addition, it is the world second most popular non-alcoholic beverage after water, with more than 1.38 billion servings produced worldwide in 2017.[1,2] Approximately 78% of the world tea consumption is composed of this beverage, while the remaining 20% and less than 2% are made up of green and yellow/oolong teas, respectively.[3,4] Several studies showed that this enormous consumption volume had a significant effect on public health.[5] A substantial proportion, ranging from 70%-80% of all tea produced worldwide was dedicated to black tea.[6] The polyphenols present in the beverage are acquired through the fermentation of four catechins using enzymes. In response to perceived health benefits, production has grown by an annual rate of 3.0%, while green tea increased by 5.4% in the last decade. The extensive history of the beverage showed that consumption and associated cultural practices had spread from China, rising to become a crucial trading commodity in the 18th and 19th centuries. The continuous increase in tea consumption has led to the development of several processing techniques to produce various products.[6] To yield a diverse range of products black tea is often subjected to various processing methods. Based on the degree of fermentation, the plant produces six different types of beverage products namely unfermented green, lightly fermented white, semi-fermented oolong, fully-fermented black, and post-fermented (yellow and dark) teas.[7]

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Asia, the Middle East, and the European Union are regions where tea is widely consumed. Although green tea is preferred in Japan, China, India, and some parts of the Middle East and North Africa, black tea is primarily used in Western and some Asian countries. This beverage is classified as a post-fermented variety and has distinct organoleptic qualities compared to other types. Furthermore, the production entails a unique stacking fermentation facilitated by microorganisms. The exclusive sensory properties and potential health advantages associated with black tea have contributed to the growing popularity among individuals.[8]

The components of black tea include methylxanthines (caffeine), amino acids (theanine), phenolic acids (CGA, GA, CA, as well as TRs), carbohydrates, lipids, proteins, β-carotene, volatile compounds (fluoride), and trace amounts of vitamins C, K, and A, as well as folate.[10] Several studies have shown that chemical composition serves as a determinant of quality, with variation observed at different fermentation stages.[9] Numerous variables, including temperature, relative humidity, pH level, and duration, as well as oxygen availability during fermentation, have been shown to improve the quality.[10] Two to three tender samples of leaves taken from tea plant shoots contain 10–30% phenolic compounds, such as epicatechin gallate (ECG), epicatechin gallate (EGCG), as well as epicatechin (EC), along with other catechins.[11] Peroxidases (PPO) and polyphenol oxidase (POD) content are frequently impacted by the procedures of rolling, withering, fermentation, drying, maceration, oxidative polymerization, as well as condensation. Moreover, quinones are created when phenolic compounds such as catechins experience oxidation. Quinones are further oxidized and condensed to produce other polymerization products such as theaflavin (TF), thearubigin (TR), and theabrownin (TB).[12] The black color, flavor, aroma, quality, as well as medicinal properties of tea are all attributed to the three main products, namely TF, TB, and TR.[7] According to reports, the two main polyphenols, thearugigin and theaflavin have important roles as potential antioxidants in several areas, including the prevention of cancer,[5] antibacterial effects,[13] reduced risk of type 2 diabetes and stroke,[14] antiproliferative,[15] anticancer,[15] as well as anti-cariogenic activities.[16] The compounds can also lower blood cholesterol,[17] delay aging,[18] reduce cardiovascular diseases,[17] as well as prevent α-amylase and α-glucosidase from working.[10] Therefore, this review aimed to provide more information on the active substance content, pharmacological effects, and benefits of black tea for the public.

Method

This review adhered to the PRISMA guidelines regarding study selection and eligibility criteria (Figure 1). Additionally, a thorough PubMed and Scopus search for publications was conducted before December 2022. The keywords used in the search included tea, black tea, and *Camellia sinensis*. These keywords were paired with terms such as efficacy, chemical compositions, pharmacological effects, and clinical trials. The studies acquired were all published in English. Using the reference lists from the original publications, previous meta-analyses, and review articles, more manual searches were carried out. Included studies had to meet four requirements namely (1) be adult-focused, (2) use black tea as the sole active treatment intervention, (3) use parallel or crossover designs in randomized controlled trials, and (4) provide data that might be used to identify the active ingredients in black tea. Analytical parameters were summarized to provide a comprehensive reference comprising the recent results in this field that could be used to create fresh procedures and enhance recently published methods.

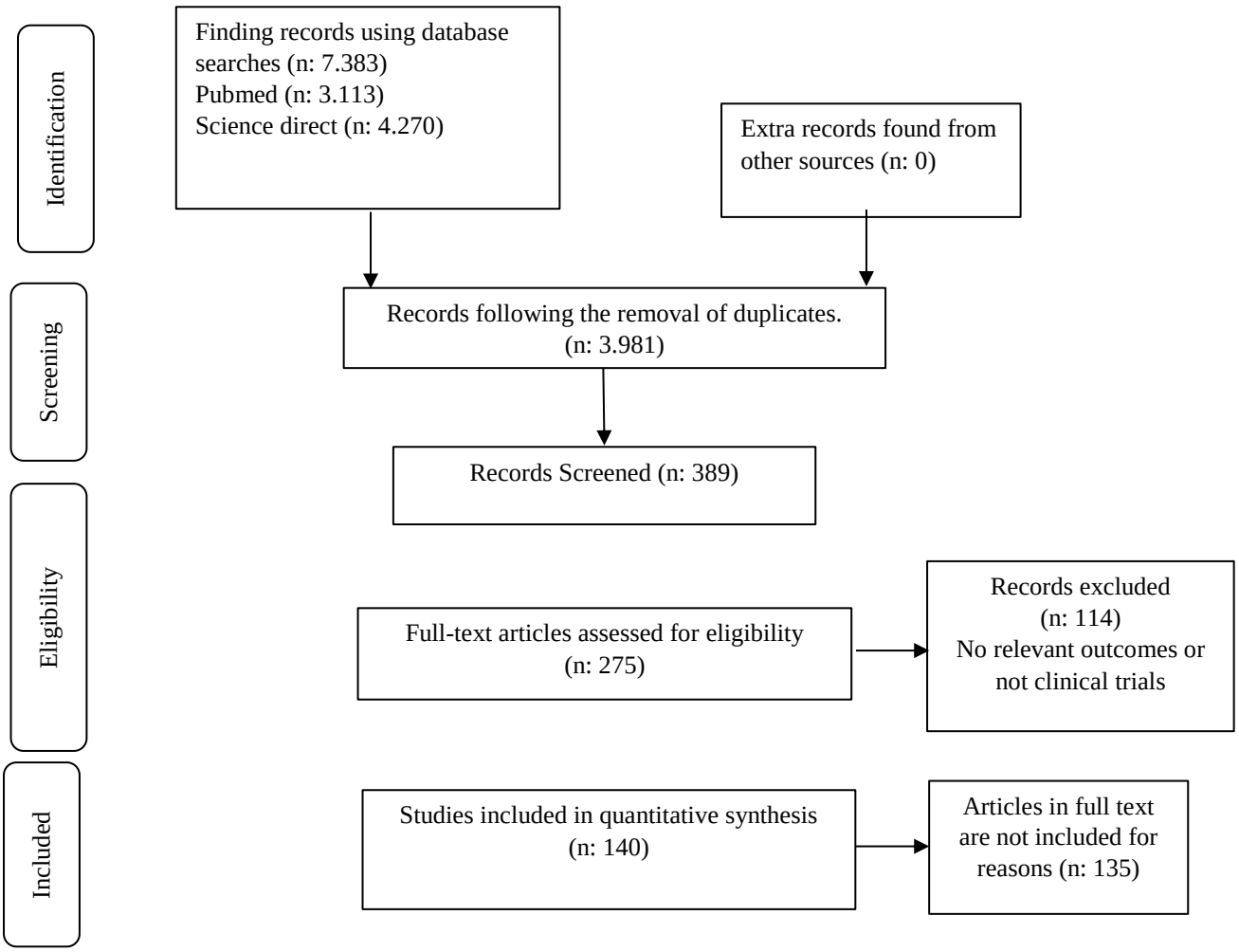

Figure 1: Diagram of the PRISMA flow used in the study selection process.

Chemical Composition

Black tea has numerous compounds, including flavonoids, phenolic acids, caffeine, and amino acids.[4,19] Furthermore, these compounds could be divided into six groups, namely pigments, polysaccharides, flavonol, amino acid, catechin-related compounds, terpenoids, and alkaloids, as shown in Table 1.

Pigments

Theaflavin, thearubigin, and theabrownin were pigments produced through the oxidation of catechins during stacking fermentation and were found to be abundant in black tea, with TB being the most prevalent and beneficial. Furthermore, black tea contains approximately 1% and 0.1-0.2% of TR and TF, respectively.[20] Using a special submerged fermentation technique with the fungus *Aspergillus niger* or *Aspergillus tubingensis*, black tea products with a high concentration of tuberculosis were produced.[21]

Theabrownin (TB)

Theabrownin is highly soluble in water and among the most abundant as well as active pigments in black tea.[22] Based on physicochemical and pharmacological qualities, this compound had better characteristics compared to TF and TR.[23] Previous results showed that despite being a family of macromolecules derived from a variety of many components, including, amino acids caffeine, proteins, as well as polyphenols, carbohydrates very few studied have described chemical makeup of tuberculosis (TB).[24]

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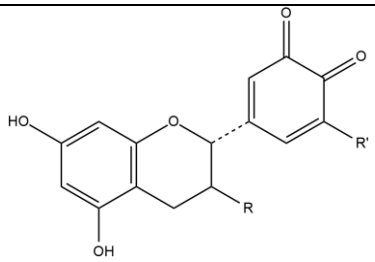
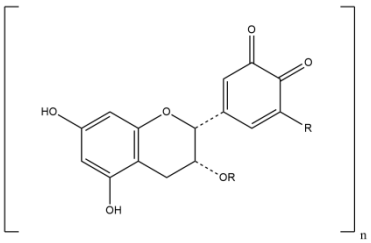
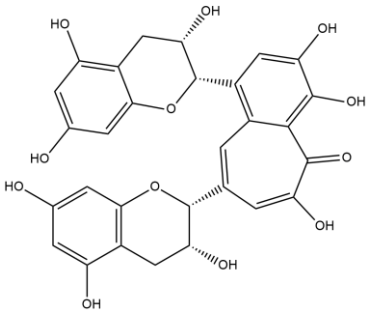
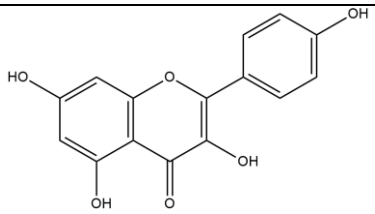
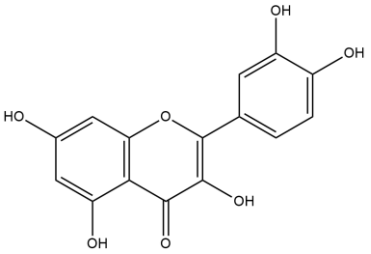
Table 1: Chemical components of black tea

Compound Group	Chemical Name	Chemical Structure	Reference
Pigments	Theabrownin		44–46
	Thearubigin		44–46
	Theaflavin		44–46
Polysaccarides	Tea Polysacarides-1	n/a	38,45
	Tea Polysacarides-2	n/a	38,45
Flavonol	Kaempferol		44–47
	Quercetin		44–46

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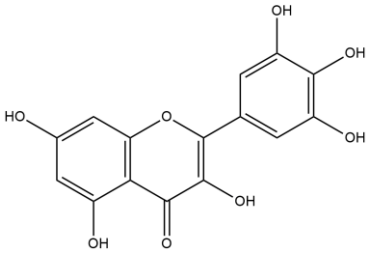
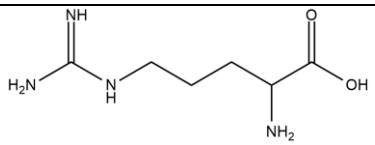
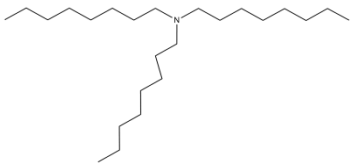
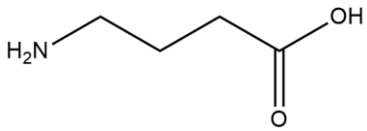
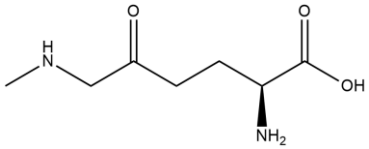
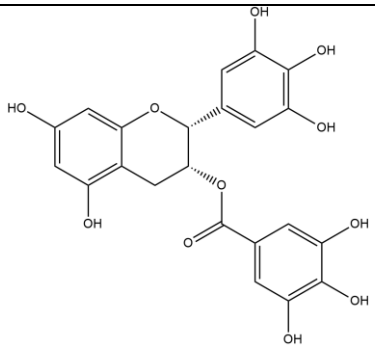
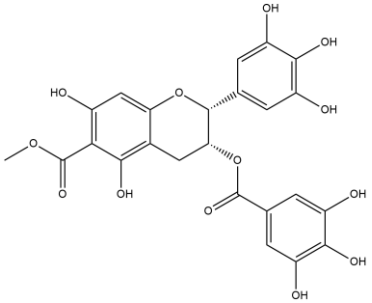
	Myricetin		44–46
Amino acid	Arginine		44–46
	Alamine		44–46
	GABA		44–46
	Theanine		44–46
Catechin-Related Polyphenols	EGCG		44–46
	EGCGD		44–46

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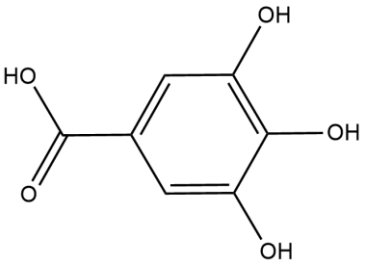
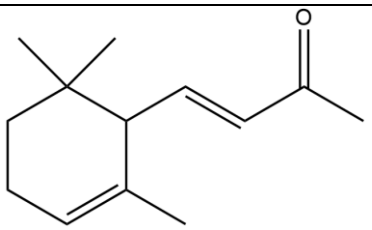
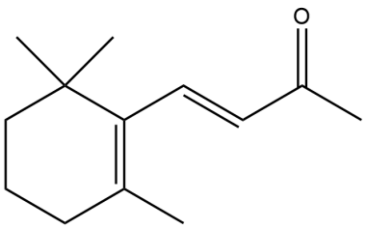
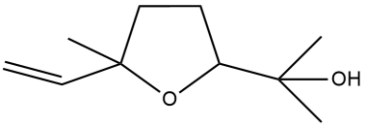
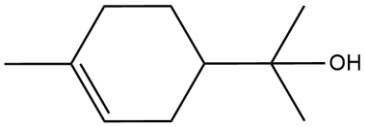
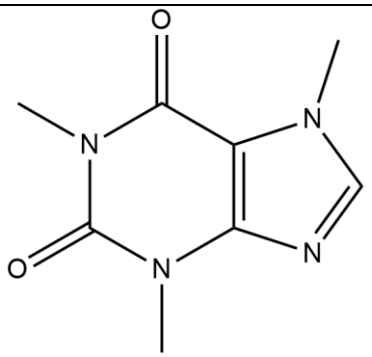
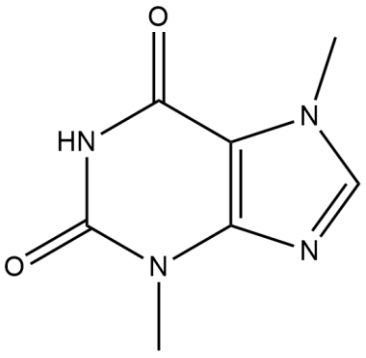
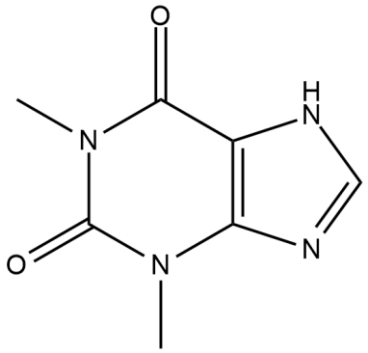
	Gallic acid		44–46
Terpenoids	*α*-Ionone		44–46
	β-Ionone		44–46
	Linalool oxides		44–46
	α-Terpineol		44–46
Alkaloids	Caffeine		44–46
	Theobromine		44–46

Theophylline  44–46

Thearubigin (TR)

About 60% of the solid content in black tea is made up of thearubigin, the most abundant class of phenolics[25,26] known to possess anti-initiating qualities against cancer cells. This molecule, along with other polyphenols, is frequently called polymeric black tea polyphenols or PBPs.[27] It is responsible for providing a reddish tonality to the beverage compared to green and white tea. The beverage is often affected by TR along with other intrinsic compounds, including unoxidized polyphenols as well as TF.[26] In most cases, the synthesis of TR starts when 75% of phenolic flavan-3-ol molecules derived from catechins are converted. The presence of TR is linked to the nutraceutical qualities of tea, which improve integrity and help mitigate a variety of diseases. According to a previous study, TR is complex because of the different concentrations, which are frequently discovered erratically, for example, 20% in black tea leaf and 60% as solids in the final infusion.[28]

Thearubigin has attracted significant attention due to the ability to activate phase II enzymes by upregulating transcription in the liver and lungs following an increase in Nrf2-mediated antioxidant-responsive element binding. However, PBP extract has not been documented to affect Nrf2 or Keap1 at the transcriptional level through posttranslational changes such as phosphorylation and reduced ubiquitination. The nuclear translocation of PKC and the phosphorylation of Nrf2 by PI3-kinase, facilitated by the pretreatment of this drug, are essential for the release of Nrf2 from Keap1 and the derivative. Moreover, the anticancer implications were investigated due to the capacity to reduce carcinogen DNA adducts by deactivating phase I enzymes produced by carcinogens, including CYP450 1A1 and 1A2.[29] The hue of TR was typically a dark brown crystalline structure water soluble and acidic.[30]

Theaflavin (TF)

Theaflavin ($C_{29}H_{24}O_9$) is typically an orange-colored crystalline structure, with a molecular weight of 516.5.[30] This compound is produced when catechins in the di and tri form condensed hydroxylated B rings. Moreover, TF combines catechins from benzotropolones into the intricate structure of the hydroxy-substituted benzotropolone ring.[31] In most cases, this reaction starts with the B ring being oxidized to create quinines. Gallocatechin quinone is then added to the catechin quinone, which reduces the amount of decarboxylation.[32] Theaflavin (TF1), theaflavin-3-gallate (TF2A), theaflavin-3'-gallate (TF2B), and theaflavin-3, 3'-digallate (TF3) are the four chemicals that make up TF. In general, TF1, TF2 (including TF2A and TF2B), and TF3 have chemical formulae $C_{29}H_{24}O_{12}$, $C_{39}H_{28}O_{16}$, as well as $C_{43}H_{32}O_{20}$, respectively. The result of potassium ferricyanide oxidation of epicatechin gallate (EC) is called theaflavate A.[38] TF has been reported to have antioxidant effects,[33] and this correlated with the digallate ester's esterification of the hydroxyl ring.[34] Additionally, this compound may activate some antioxidant enzymes, including catalase (CAT), glutathione-S-transferases (GST), superoxide dismutase (SOD), and glutathione peroxidase (GPX), which would decrease lipid peroxidation.[35]

Tea Polysaccharides (TPs)

TPs are a collection of heteropolysaccharides isolated from the leaves, flowers, and seeds of tea plant. These compounds are composed of 3.5% protein, 43.1% uronic acid, as well as 44.2% neutral sugar.[36] The potential benefits include anti-tumor, aging, bacterial, anti-skin-aging, prevention of radiation damage, oxidant, coagulation, HIV, cancer, mutation, atherosclerotic, as well as inflammatory characteristics. In addition to reducing hepatotoxicity and enhancing immunity, TPs may decrease diabetes.[37,38,39] Black tea extract was treated with 40% and 70% ethanol, respectively, to precipitate the two forms of TPs, namely TPs-1 and TPs-2. Both had phagocytic effects but TPs-1 had greater effects.[38]

Flavonol

Considering flavonol occurs in plants as glycosides, it is often referred to as aglycon. Numerous investigations have reported that the quick metabolism was caused by the frequent attachment of glucose and galactose sugar moieties to aglycon.[40] Additionally, several variables, including plant variances, soil, season, light, ripeness degree, and food preparation, as well as processing, affect the compound availability and composition.[41] The process of forming phenylalanine from phenylpyruvate is an essential step in the formation of flavonol. This is achieved by combining derivatives generated from phenylalanine through the shikimic acid pathway with acetic acid. The compound absorption rate is influenced by the linked sugar moiety, necessary for absorption.[42] The boiling point ranges from 276 to 278 ºC, and the characteristic tone is yellowish. It is also only weakly soluble in water but easily soluble in hot ethanol, diethyl ether, as well as other organic solvents.[43] Flavonol, which is found in tea and other natural products, has been linked to a decrease in heart problems and is also used in antidepressant medications. Table 1 shows chemical components of black tea.

Kaempferol

Studies have shown that kaempferol (3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-benzopyran-4-one) possesses antibacterial, anticancer, anti-inflammatory, and antioxidant properties.[48,49] Flavonoids with similar chemical structures, including rutin, quercetin, as well as kaempferol, have similar effects.[50]

Quercetin

Quercetin has the most powerful antioxidant and neuroprotective activity among polyphenolic compounds. This shows the ability to break the chain reaction of peroxidation and is also a powerful free radical scavenger.[51] Furthermore, quercetin is one of the primary contributors to the flavor of tea, specifically bitterness and astringency.[51] Several studies reported that the compound improved insulin sensitivity in tissues, regulated insulin production, and inhibited glucose absorption from the gastrointestinal tract, leading to the normalization of carbohydrate metabolism.[52] The hue of quercetin was typically pale-yellow, and the highest absorbance was measured between 360 and 380 nm [53]

Myricetin
Chemical formula of myricetin (3,30,40,5,50,7-hexahydroxyflavone) is $C_{15}H_{10}O_8$, with 318.24 molecular weight.[54] Previous studies showed that the compound has anticancer and anticancer effects along with the ability to increase insulin function while also lowering blood sugar levels.[55,56] Furthermore, it could be used to treat rheumatic diseases,[57] type 2 diabetes mellitus,[58] obesity,[59] and ulcerative colitis.[60] Myricetin is a white powder that dissolves slightly in water.[61]

Amino Acid
Free amino acids are mostly responsible for the taste and aroma of tea. The pile fermentation has a considerable impact on the amino acid profiles, leading to a sizeable reduction in the amount of overall content. All free amino acids change during the process, but in different ways.[21,62] Amino acids could reduce body weight, improve nutrient use, enhance growth performance, stimulate muscle protein synthesis, and promote muscle growth.[63]

Arginine
The bitter taste of tea is caused by arginine, which also possesses anticancer properties,[64] and strengthens theanine effects.[65] Given the crucial role in the synthesis of nitric oxide, arginine is considered an important regulator in the central nervous system.[66] This amino acid also plays an essential role in the physiological responses to stress and anxiety.[67] Despite the significantly lower levels of arginine compared to theanine, it has higher anti-stress properties.[68]

Alanine
All living things have the non-proteinogenic amino acid alanine, which is used as a precursor in cellular metabolism for coenzyme A (CoA) and pantothenic acid (vitamin B5). It also has various metabolic functions, particularly in the metabolism of fatty acids.[69] Moreover, alanine functions as a flavoring ingredient that gives tea its distinct bitter flavor. [69] This amino acid may be used as a therapeutic medication to treat type 2 diabetes and related diseases.[70]

Gamma-aminobutyric acid (GABA)
Despite not being a protein, GABA is an essential amino acid that contributes to several biological functions, including improving the therapeutic potential of plants and strengthening the ability to withstand effects of environmental stress.[71] The tricarboxylic acid cycle in black tea is responsible for both the irreversible reaction of glutamate (SSA) and -decarboxylation that leads to the synthesis of GABA as well as the degradation of polyamines by glutamate decarboxylase (GAD), GABA transaminase (GABA-T), along with succinic semi-aldehyde.[72] Moreover, GABA is the main inhibitory neurotransmitter in the brain and important for metabolism.[73] It also has anti-hypertensive and anti-stress properties, as well as increases sleep quality.[74,75]

Theanine
The most prevalent amino acid in tea, theanine also known as gamma-glutamylethylamide, 5-N-ethylglutamine, or L-theanine, is responsible for the sweet-sour taste.[76] L-theanine accounts for 50% of the total protein in plants and 1%–2% of dry weight, making it the most common amino acid.[77] This molecule has biological properties that include anti-stress and cancer. It also improves immunity, nervous attention, brain function, and resistance to Alzheimer's disease.[30,43,65]

Catechin-Related Polyphenols
The normal makeup of black tea is dominated by several components, with flavonoids having the most significant concentrations.[78] The heterocyclic oxygen carbon-oxygen ring shape as well as the location are frequently used to divide these compounds into six groups. These include flavones, flavanones, isoflavones, flavonol, and flavanols. Furthermore, anthocyanins were reported to be members of the sixth group, and flavonol was mainly composed of unoxidized catechins.[79] After fermentation, the catechins experience oxidative condensation, a process that leads to the formation of TF. These compounds, alternatively referred to as benzotropolone dimers of catechins, are significant products of the transformation. Higher molecular weight polymers known as TR are synthesized alongside TF through this intricate process of catechin condensation. These two ingredients offer black tea a unique flavor and deep hue.[44] The hue of catechin is typically a white color crystalline structure and the molecular weight is 302.24. This compound also has strong antioxidant properties, offering protection against cancer, obesity, and diabetes.[80]

EGCG
EGCG or (-)-Epigallocatechin-3-gallate is a potent antioxidant, which serves as the main component in polyphenols and the most abundant catechin in black tea. It also functions as an anti-tumor necrosis and anticholesterol agent, along with the ability to improve the capability of proteins to emulsify and protect highly unsaturated oils from oxidation.[81,82] The antioxidant activity of EGCG entails the trapping of Diphenyl-2-picrylhydrazy (DPPH) radical potential.[83]

Epigallocatechin Gallate Derivative (EGCGD)
EGCGD (2R,3R-6-methoxycarbonylgallocatechin-3-O-gallate) with $C_{24}H_{20}O_{13}$ molecular formula, is often found in the form of a brown amorphous powder with health benefits. This compound inhibits the proliferation of HCC827-Gef cells and has anti-tumor properties. Moreover, it might strengthen gefitinib effectiveness against cell lines resistant to EGFR-TKI.[84]

Gallic Acid
Black tea, lemon, grape, as well as other foods and herbs naturally contain gallic acid (3, 4, 5-trihydroxy benzoic acid), a phenolic acid.[85,86,87,89] Gallic acid-treated animals in a previous study showed lower levels of IL-6, cyclooxygenase-2, F4/80, sterol component binding transcription factor-1, as well as inductive nitric oxide synthase (NOS) in the white adipose tissue. The results suggested that by lowering adipocyte hypertrophy and inflammation caused by interactions between adipocytes and macrophages, it may be used to treat a variety of metabolic disorders, including insulin resistance and dyslipidemia. Consequently, the anti-inflammatory impact helps in overcoming difficulties associated with obesity.[90]

Terpenoid
One of the largest groups of biochemicals is terpenoid or isoprenoid, crucial in both regulatory systems and metabolic processes.[91] According to a previous study, two pathways have been discovered for the production of this compound, namely the mevalonate and MEP pathway.[92] Terpenoid is often regarded as the primary volatile secondary component and essential to the development of tea aroma.[93]

α-Ionone
α-Ionone, with the formular $C_{13}H_{20}O$ is also called 3-buten-2-one or 4-(2,6,6-trimethyl-2-cyclohexen-1-yl). It has a taste and fragrance molecule as well as a molecular weight of 192.3.[94] Several studies showed that the compound helps to minimize the loss of collagen caused by exposure to UVB.[95]

β-Ionone
With a molecular weight of 208.30, *β*-Ionone (4-[2,6,6-trimethyl-1-cyclohexen-1-yl]-3-buten-2-one) is a cyclic terpenoid molecule. It is often produced through the oxidative degradation of carotenoids and plays a significant role in the aroma and taste creation process.[96,97] β-Ionone has significant pharmacological properties, including antileishmanial, antiinflammatory, anticancer, antifungal, chemoprotective, and antibacterial activities.[96]

Linalool oxides
Tea contains the smell component linalool (3,7-dimethyl-1,6-octadien-3-ol), a monoterpene. Free linalool oxides are less soluble and unstable compared to those found in fresh tea leaves, consisting of additional glycosides.[98] Light as an abiotic factor affects the potential to influence the production of these oxides. Furthermore, the amount of linalool present often increases along with the brightness of light.[98] Linalool has antibacterial efficacy against a range of foodborne pathogens, including Listeria monocytogene, Pseudomonas aeruginosa, Brochothrix thermosphacta, as well as P. fluorescens.[99]

α-Terpineol
α-Terpineol ($C_{10}H_{18}O$) is a volatile monoterpenoid alcohol, with antibacterial, antihypertensive, anti-inflammatory, and anticancer activities.[100]

Alkaloid
Black tea contains theophylline, theobromine, and caffeine as alkaloids. After the purine nucleus hexacyclic dinitrogenous ring was rearranged and C_2H_3NO (57 Da) was lost, fragment ions were created at m/z 124 for theophylline and theobromine and m/z 138 for caffeine. Consequently, at the m/z peak [M+H-57]+.55, these compounds showed the same ion.[46]

Caffeine
Coffee beans, cocoa beans, and kola nuts, as well as tea leaves, are among a few of the plants that naturally contain caffeine.[101] This compound may modify energy efficiency and body composition, lessen metabolic endotoxemia and inflammation in many tissues and the system, while also enhancing lipid and glucose metabolism.[102]

Theobromine
Theobromine ($C_7H_8N_4O_2$) is a purine alkaloid, responsible for the bitter flavor of tea, cocoa, and coffee. This alkaloid is considered a safer option compared to caffeine, and it causes lesser stimulation of the central nerves than other methylxanthines. The functions of the compound in shielding the surface of tooth enamel, reducing low-density lipoprotein cholesterol, preventing coughing, preserving the cardiovascular system, and raising high-density lipoprotein cholesterol levels have been showed by several studies.[103]

Theophylline
Theophylline, which has been used for decades to treat asthma and other chronic respiratory diseases with a limited therapeutic window, is a naturally occurring compound in both tea as well as cocoa beans. Additionally, even at low plasma concentrations, theophylline has significant anti-inflammatory effects in chronic obstructive lung disorders.[103]

Health Benefits
Black tea has various benefits on the body, including antioxidant, hepatoprotective, gastrointestinal protective, anti-cholesterol, anti-obesity, and anti-diabetic activities.[4] Table 2 presents effect of black tea on biochemical parameters in the human and animal models

Pharmacological Effects
Figure 2 shows the numerous biological activities and health advantages of black tea. The biological qualities are superior to those of other varieties of tea, as stated in previous studies. Furthermore, this section concisely and clearly describes the pharmacological effects.

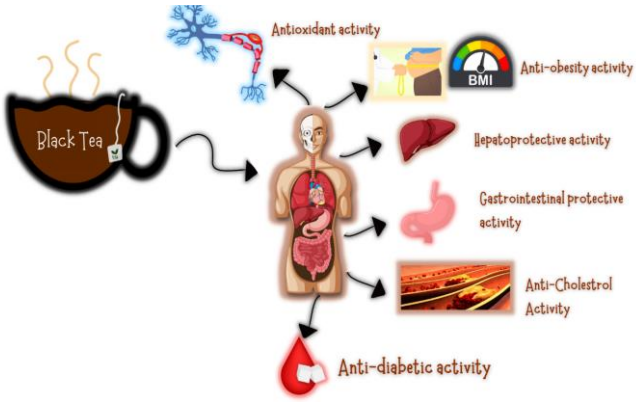


Figure 2: Biological activities and health advantages of black tea

Antioxidant Activity
The strong antioxidant activity of black tea can be attributed to the presence of compounds, such as polyphenols. Antioxidants work by combating free radicals and restoring electrons to unstable cells. Moreover, it works by counteracting the oxidative stress attributed to several metabolic and biochemical processes.[116] By lowering the amount of malondialdehyde (MDA) and raising the amounts of catalase, glutathione peroxidase, and superoxide dismutase (SOD), antioxidant mechanisms help to reduce oxidative injury. Numerous investigations stated that TF played a significant role in preventing inflammation, clastogenesis, and many forms of cancer.[102] Caffeine contained in the beverage served as a strong antioxidant agent and helped in fighting tumors, lowering blood sugar, and preventing angiogenesis.[117] Black tea primary active ingredients, TPs, TF, TR, and TB, performed several health-promoting roles, including antioxidants. [117] The high antioxidant action of polyphenols, including GA, TRs, and TFs, has also been identified. The polyphenol protection could be used to overcome FR-mediated oxidative damage. The bioactive compounds included thiadenols, polysaccharides, and flavonoids. These compounds showed potent antioxidant activity, particularly through modulating the Nrf2 pathway and enhancing the activity of antioxidant enzymes.[118]

Anti-Obesity Activity
Obesity is among the most common underlying conditions and is characterized by a BMI (Body Mass Index) of over 30.[118] This condition is often caused by poor diet, low physical activity, family history, and complications comprising increased cholesterol, blood pressure, and behavioral problems.[119] The bioactive compounds in black tea that play a role in anti-obesity activity include eurotium cristatum, TB, polysaccharides, and polyphenols. These compounds modulate the intestinal microbiota, rebalance dysbiosis,[120] modulate the composition of fungi and bacteria, as well as increase the production of acetate and butyrate.

Black tea has various effects, including reducing obesity by inhibiting inflammation in visceral fat, decreasing inflammatory molecules, and increasing G-protein coupled receptors. It also performs a variety of biological tasks, such as combating obesity by decreasing the amount of subcutaneous adipose tissue. However, the impact was not shown in visceral adipose tissue due to adipogenesis. The anti-obesity mechanism entails modulating the synthesis of alternative bile acids driven by the gut microbiota, as well as regulating lipid metabolism. Regulating the expression of genes linked to de-novolipogenesis allowed for this outcome.[138] Black tea has a considerable ability to lower body weight and body mass index in both obese and non-obese persons, according to several epidemiological studies.[62,121]

Anti-Diabetic Activity
Diabetes mellitus (DM) is a term formed from the Greek word diabetes, implying to siphon or pass through, and the Latin word mellitus, which means sweet. It is a metabolic disorder characterized by excessively elevated blood glucose levels. There are several forms of DM, including Type 1 (T1DM), Type 2 (T2DM), gestational (GDM), neonatal, and maturity-onset diabetes of the young (MODY). The secondary varieties are caused by endocrinopathies and steroid use, according to previous studies. The two main types of DM are T1DM and T2DM, both of which are usually caused by defective insulin secretion (T1DM) and action (T2DM). Middle-aged and older people with persistent hyperglycemia are often affected by T2DM.[122] T1DM, T2DM, and gestational DM have been reported to be the three most prevalent subtypes. Insulin resistance and comparatively low insulin secretion are common in T2DM patients. Although the absolute concentration of plasma insulin (during fasting and after meals) is frequently higher, it is not sufficient to maintain a healthy glucose homeostasis "relative" to the degree of insulin resistance. Most T2DM patients experience a progressive reduction in insulin-secreting capacity over time. The majority of people with T1DM are characterized by a complete lack of beta-cell activity. Several studies reported that autoimmune death of beta cells was a frequent cause, but most instances were considered to be idiopathic. During pregnancy, women with GDM often experience glucose intolerance, with a typical onset of the condition during the third trimester of pregnancy.

Table 2: Effect of black tea on biochemical parameters in the human and animal models

Sample	Treatment	Subject	Health Benefits	Main Effects	References
Tea powder	50 mg/kg/day for 4 weeks	Males from 24-32 years old	Anticholestrol	↓Cholestrol and TG (triglycerides)	104
Extract Tea	3 gram /day for 20 weeks	Humans of the Hyperlipidemic population	Anticholesterol	↓Weight loss and fat loss ↑ Lipid profile LDL (Low Density Lipoprotein), Cholestrol and TG (triglycerides)	105
Extract Black Tea	2 gram /day	Men and women aged 20-64 years	Antidiabetic activity	↓α-glucosidase; postprandial blood glucose values polymerized polyphenol	106
Extract Black Tea	50, 100, 200, and 500 mikrogram/mL	High sugar diet-induced Caenorhabditis elegans	Anticholesterol	↓Fat accumulation	107
Infus Tea	22 days at 450 mg/kg/day	High-fat diet rat and control diet chow normal	Anticholesterol	↓ BW (body weight), adipose tissue weight, lipids ↑FFA (free fatty acid) synthesis and gene expression	108
Black tea protein extract	For 21 days, 50 and 100 mg/kg/day	Male mice	Antidiabetic type 2	↓ BW (body weight) fasting blood glucose DTPE control group ↑Blood glucose tolerance in the high-dose DTPE group	109
Black tea extract	200 mg/kg/day	Male rat	Immunoregulation	↑BW (body weight) and immune organ index; intestinal barrier function; immunoglobulins TNF-alpha (Tumor Necrosis Factor-alpha), IL (*interleukin*)-1$_\beta$, IFN	110

				(Interferon)-γ, and IgA (Immunoglobulin A,)) ↓Damage to the jejunum and large intestine	
Dry black tea leaves	A cup of black tea (250 mL, 2.5 gram tea leaves)	A volunteer	Antiobesity activity	↓ Lipase pancreas	[111]
Extract tea	400 mg/kg	Male rat	Hepatoprotective activity	↓Lipid peroxidation; FTE; serum activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP)	[112]
Black tea extract	For 28-day treatment period, 0.1 mL/10 gram	Rats	antihyperglycemic antihypoglycemic	↓ Fasting blood glucose levels ↓ Higher fasting insulin levels	[113]
Black tea Extract	Black tea (0.3 mL, ir) at oral doses of 200, 400, and 800 mg/kg/day was given to the mice in the test groups.	Mice	Hepatoprotective activity	↓ Total-superoxide dismutase (T-SOD) and reduced glutathione (GSH) levels	[114]
Black tea Extract	0.50, 1.00, and 1.50 gram/kg	Sprague-Dawley male rats	Gastroprotective against stomach damage	↑ Production of the gastric mucus lining ↓ Inflammation ↑ NO (nitric oxide) production ↓ NOS (Nitric Oxide Synthase) activity	[115]

Previous reports also showed that individuals with GDM were prone to developing T2DM. DM was also caused by diseases of the pancreas, hereditary disorders, and the overproduction of several hormones, including glucocorticoids and growth hormones. It may also result from infections, toxins, or drugs. The correct classification of DM frequently aids in selecting the best course of treatment.[123]

The antidiabetic mechanism of black tea requires the strong inhibition of glucosidase, sucrase, and maltase activity,[124] as well as facilitating the uptake of glucose cells by HepG2 cells.[125] EGCG and epicatechin-3-gallate content reportedly have an inhibiting impact (ECG).[126] The polyphenols content also has an insulinomimetic effect, which lowers blood glucose levels, while TF improves the insulin/glucose ratio and

action.[127] Black tea could control the spleen-brain axis to lower blood sugar levels. According to epidemiological studies, the antidiabetic effects include lowering blood glucose levels and insulin resistance.[128] The flavone content functions by blocking the powerful alpha glucosidases, sucrose, and maltose. In a previous study, the protein extract controlled the lymphatic brain axis to lower glucose levels and reduced Akt/GLUT4 insulin signaling pathway activity.[128]

Anti-Cholesterol Activity

Elevated serum cholesterol concentrations, particularly an increase in LDL-C, are frequently caused by hypercholesterolemia, while serum triglyceride concentrations remain within the reference range. Aside from polygenic hypercholesterolemia, some patients with mixed dyslipidemia (higher triglycerides and LDL-C) may also have obesity or metabolic syndrome.[129] The flavonoid content in black tea serves as a hypocholesterolemic agent.[130] An increased risk of atherosclerotic disease and early death was frequently associated with hypercholesterolemia.[131] Black tea had a considerable lowering effect on LDL cholesterol levels in the blood, specifically in patients at higher cardiovascular risk. However, there was no significant difference in the serum levels of total and HDL cholesterol after consuming the extract.[132] Black tea may also improve lipid profiles by reducing the level of triglyceride, cholesterol, and low-density lipoprotein.[105] Important bioactive substances that modulated the hypolipidemic impact were flavanols, flavones, acylglycosides, and metabolites. There was lipase inhibitory activity shown by tea extract and flavanols.[133] Furthermore, strong inhibitory activity was shown by several flavone acylglycosides and metabolites against 3-hydroxy-3methyl-glutaryl (HMG)-CoA reductase. This enzyme limits the rate at which hepatocytes can synthesize cholesterol.

Hepatoprotective Activity

An essential organ, the liver plays an essential role in the metabolism and removal of many toxic as well as endogenous chemicals.[134] Hepatitis B and C, alcoholic liver disease, as well as non-alcoholic fatty liver disease, are among the conditions commonly associated with liver disease. Furthermore, injury to the organ often leads to fibrosis and cirrhosis. Hepatic stellate cells are often activated following an injury and stimulated to take on the characteristics of myofibroblasts, which are fibroblast-like, contractile, and proliferative. This leads to the build-up of extracellular matrix and collagen. Cell apoptosis and diminished function occurred due to the buildup of toxic chemicals, which also damaged the liver structure.[135]

As important marker enzymes produced from hepatocytes into circulation during hepatotoxicity, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) blood levels could be used to monitor liver damage. Polysaccharides in black tea have shown a potent protective effect against hepatotoxicity, which may have been attributed to the heightened activity of liver tissue enzymatic and non-enzymatic antioxidants as well as the inhibition of peroxidation lipids. The hepatoprotective activity was achieved by strengthening the immune system enzymatic and non-enzymatic antioxidant defenses, which substantially decreased the production of free radicals. This effect could be attributed to lowering liver glutathione (GSH) and total-superoxide dismutase (T-SOD) levels.[114]

Gastrointestinal Protective Activity

Black tea protects the gastrointestinal system from stomach injury. In many cases, an imbalance between the mucosal defenses as well as aggressive elements leads to gastric mucosal damage.[136,137] Frequent exposure to HCl, pepsin, bile acids, ethanol, non-steroidal anti-inflammatory medications, and the helicobacter pylori toxin was observed in the stomach mucosa.[138,139] Furthermore, by promoting the formation of the mucous lining, decreasing inflammation, and raising NO (nitric oxide) generation through inhibition of NOS activity, the polyphenolic content of black tea offered a protective effect against stomach injury. Additionally, NO acts as a strong vasodilator by enhancing blood flow in the stomach mucosa, preventing the production of gastric acid, and enhancing the outflow of mucus and bicarbonate.[115] The caffeine content of black tea could also function as an anti-diarrhea agent by increasing intestinal permeability, reducing infection from exudative and secretory diarrhea, lowering the diarrhea index and stool levels, as well as regulating the movement of the digestive tract.[140]

Conclusion

In conclusion, black tea has been highly regarded since ancient times due to the use as herbal therapy. Moreover, the abundant composition rendered the plant a fitting option for medical therapy in the management of several ailments. The constituents include TB, TR, TF, TPs-2, TPs-1, Kaempferol, Quercetin, Myricetin, Arginine, Alanine, GABA, Theanine, EGCG, EGCGD, Gallocatechin, Gallic acid, α-Ionone, and β-Ionone, Linalool oxides, α-Terpineol, Caffeine, Theobromine, as well as Theophylline. Numerous other advantages include hepatoprotective, gastrointestinal protective, anti-obesity, anti-diabetic, anti-cholesterol, and antioxidant. Despite the potential application for various purposes due to the nutritious content, clinical product studies related to the use of black tea are still limited. This offers an opportunity for scientists to conduct studies related to the benefits of each efficacious component, potentially leading to the development and distribution of innovative products. These innovations could transform black tea from being a brewed beverage into medicinal forms, such as candies and other preparations.

Conflict of Interest

The authors declare that there is no conflict of interest.

Authors' Declaration

The authors affirm that the work presented is original, and will accept all liability for any claims about the content.

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