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Active components of tea (*Camellia sinensis*) extracts and their beneficial application on human health

Componentes activos de los extractos de té (*Camellia sinensis*) y su aplicación beneficiosa en la salud humana

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ABSTRACT

Tea is one of the most frequently consumed beverages across the world and is popular for its classic brew, flavour and wide range of health benefits. The variation in aroma, taste and colour of different kind of teas are caused by the manufacturing process popularly known as fermentation and essentially determine the quality and acceptance of tea flushes. A variety of volatile components such as terpenoids, alcohols, carbonyl compounds, etc. are reported to contribute to the signature tea aromas whereas the non-volatile polyphenolic components (mainly catechins, flavonols, theaflavins, thearubigins), amino acids and xanthines are responsible for the characteristic taste and colour of tea infusions. The nutritional value of tea is mostly gained from the tea polyphenols and amino acids that are reported to possess a broad spectrum of bioactivities, including anti-oxidant properties, reduction of various cancers, inhibition of inflammation and protective effects against diabetes, hyperlipidemia and obesity. Global tea research has generated much *in vitro* and *in vivo* data rationally correlating tea polyphenols with their preventive and therapeutic properties against human diseases like cancer, metabolic and cardiovascular diseases etc. Recently, number of studies also suggests that tea polyphenols have the potential to treat or prevent COVID-19 disease. In the current review, we focus on the chemistry behind the signature fragrance, taste and colour of variety of tea and their beneficial account as antioxidant and therapeutic effectiveness against many diseases such as lowering of blood pressure, diabetes, inflammation, anticancer properties and most interestingly against COVID-19 pandemic.
Keywords: Tea chemistry, polyphenols, catechins, theaflavins, health benefits, COVID-19.

RESUMEN

El té es una de las bebidas más consumidas en todo el mundo y es popular por su infusión clásica, su sabor y su amplia gama de beneficios para la salud. La variación en el aroma, el sabor y el color de los diferentes tipos de té son causados por el proceso de fabricación conocido popularmente como fermentación y determinan

esencialmente la calidad y la aceptación de los lavados de té. Se informa que una variedad de componentes volátiles, como terpenoides, alcoholes, compuestos de carbonilo, etc., contribuyen a los aromas característicos del té, mientras que los componentes polifenólicos no volátiles (principalmente catequinas, flavonoles, teaflavinas, tearubiginas), aminoácidos y xantinas son responsables de el sabor y color característicos de las infusiones de té. El valor nutricional del té se obtiene principalmente de los polifenoles y aminoácidos del té que, según se informa, poseen un amplio espectro de bioactividades, incluidas propiedades antioxidantes, reducción de varios tipos de cáncer, inhibición de la inflamación y efectos protectores contra la diabetes, la hiperlipidemia y la obesidad. La investigación global del té ha generado muchos datos in vitro e in vivo que correlacionan racionalmente los polifenoles del té con sus propiedades preventivas y terapéuticas contra enfermedades humanas como el cáncer, enfermedades metabólicas y cardiovasculares, etc. Recientemente, varios estudios también sugieren que los polifenoles del té tienen el potencial de tratar o prevenir la enfermedad COVID-19. En la revisión actual, nos enfocamos en la química detrás de la fragancia, el sabor y el color característicos de la variedad de té y su cuenta beneficiosa como antioxidante y efectividad terapéutica contra muchas enfermedades como la reducción de la presión arterial, diabetes, inflamación, propiedades anticancerígenas y, lo que es más interesante, contra la pandemia de COVID-19.
Palabras clave: química del té, polifenoles, catequinas, teaflavinas, beneficios para la salud, COVID-19.

INTRODUCTION

The tea plant, scientifically known as *Camellia sinensis* is indigenous to South-Eastern Asia, however is currently cultivated in more than thirty countries round the globe. The consumption and popularity of tea as a global beverage is next to water and relies on its pleasant flavour, mildly stimulating effects which people find appealing and stress busting. The fresh tea leaves are generally used for tea production and are harvested by manual or mechanical plucking. According to the extent of fermentation, tea is generally classified into three basic types: non-fermented green tea, semi-fermented oolong tea and fully fermented black tea (Jiang *et al.*, 2015). Green and black tea account for about 20% and 78% of global tea consumption respectively, whereas just about 2% is consumed as oolong tea (Jiang *et al.*, 2015).

Early research on tea can be traced back over 170 years; however, advancement on a more scientific basis has been accomplished by the tremendous development of modern analytical techniques (Drynan *et al.*, 2010, Tao *et al.*, 2016). Scientific progress reveals that more than 600 volatile and non-volatile components are responsible for essential aroma as well as taste and colour of tea (Harbowy and Balentine, 1997, Drynan *et al.*, 2010). Several key secondary metabolites, such as tea polyphenols, theanine and caffeine present in tea infusion not only contribute to its unique tastes and tea quality (Khan and Mukhtar, 2013), but also have significant health promoting effects. The health benefits of tea consumption are reported to consist of anti-oxidant (Bhutia *et al.*, 2015), cancer prevention (Pan *et al.*, 2016, Ju *et al.*, 2007), reduced occurrence of heart disease (Sharangi, 2009), antidiabetic (Hameed *et al.*, 2015) etc. Recent studies also reveal that tea polyphenols significantly interact with the binding sites present on SARS-CoV-2 virus and thus may be potentially useful as prophylaxis and treatment of COVID-19 (Park *et al.*, 2021, Jang *et al.*, 2020). In this context, the study on chemical components responsible for the aroma, taste and colour of tea infusion and their correlation with the bioactivity and therapeutic applications are of great importance. Herein, the present review will focus on the chemical insight of a cup of tea responsible for its signature fragrance, appearance and taste and its therapeutic effectiveness against many diseases such as lowering of blood pressure, diabetes, inflammation, anticancer properties and antiviral effect against COVID-19 disease. We carried out an updated bibliographic research on the principal databases (based on PubMed and Web of Science) of the articles reported in the literature in the last decade.

RESULTS AND DISCUSSION

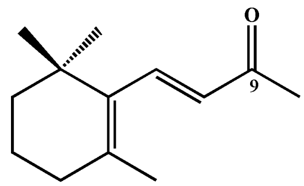
1. Aroma, taste and colour of tea: A cup of a blend of finished tea is totally different as of the infusion of fresh tea flushes in colour, taste and aroma. In fresh tea flushes, there exist a broad range of volatile as well as non-volatile compounds: volatile components primarily determine the aroma of tea flushes, whereas the non-volatile materials are responsible for the taste and colour (Harbowy and Balentine, 1997, Chaturvedula and Prakash, 2011). A series of transformation occur in the course of processing tea (finished or made tea). The three basic types of manufacturing tea are green, oolong and black tea depending principally on the extent of fermentation. Green tea endures slight or no fermentation, whether oolong tea is a product of partial fermentation. Black tea is formed as an outcome of full fermentation. The difference in colour, taste and fragrance of variety of teas are caused as a result of the manufacturing process.

1.1 Tea aroma formation: The recognition and acceptability of tea as a universal beverage depends primarily on the aroma of the tea leaves when they are brewed. A continuous and thorough research reveals that more than 600 compounds have been isolated which are responsible for characteristic aroma of tea (Harbowy and Balentine, 1997, Drynan *et al.*, 2010). Many of these compounds do not exist in fresh tea flushes and are derived from other components during processing.

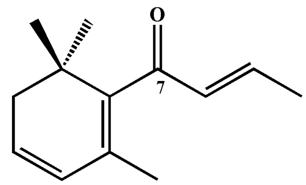
1.1.1. Carotenoid derived volatile aroma compounds: Carotenoid-derived flavour compounds are among the most potent aroma components and significantly contribute to the quality of tea (Kawakami and Kobayashi, 2000). Particularly, β- ionone (1, Fig. 1) is a significant contributor to the woody flavour of green and black tea and has a low odour threshold of 0.007 ppb in aqueous medium whereas β- damascenone (2, Fig. 1) appears as fruity flavour showing an extremely low threshold of 0.002 ppb in water (Ravichandran, 2002). Both the compounds can be produced by enzymatic fermentation course during tea manufacturing process. Enzymatic fermentation and heat drying, both the procedures are essential for the formation of β- ionone which is further oxidized to dihydroactinidiolide (3, Fig. 1) and theaspirone (4, Fig. 1), which are viewed as critical fruity and flowery aromas respectively in determining the character of black tea.

1.1.2 Fatty acid as precursor of volatile aroma compounds: Tea liquor contains large extent of volatiles, including alcohols, aldehydes, and lactones which are derived from saturated and unsaturated fatty acids.

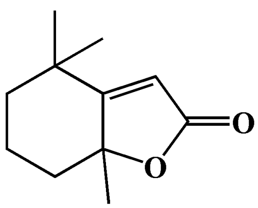
Unsaturated fatty acids such as □□□linolenic acid, linoleic acid, oleic acid and palmitoleic acid are precursors of C_6 and C_9 aldehydes and alcohols like *E*-2-hexanal (5, Fig. 2), *Z*-3-haxanol (6, Fig. 2), n-nonanal (7, Fig. 2) and n-nonanol (8, Fig. 2) which are essential contributor to the typical "fresh green" odour of tea.



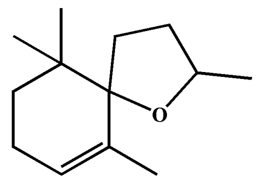
β - ionone
1



β - damascenone
2

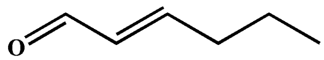


Dihydroactinidiolide
3

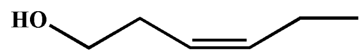


Theaspirane
4

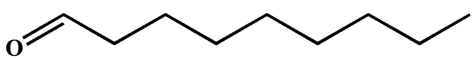
Figure 1. Carotenoid derived volatile aroma compounds



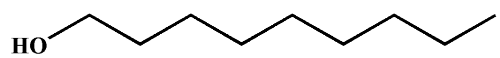
E-2-hexenal
5



Z-3-hexenol
6



n-nonanal
7



n-nonanol
8

Figure 2. Representative aldehydes and alcohols responsible for fresh green odour

1.1.3 Volatile terpene and phenylpropanoids/benzenoids aroma compounds: Volatile terpenoids are essential class of compounds for the quality of tea since their important contributions to flavour and fragrance. In semi- fermented and fermented teas, mono-terpenoids such as linalool (9, Fig. 3) and linalool oxides (10, Fig. 3) are present in concentrations of up to 50% of the volatiles components with their signature sweet floral, citrus like and fruity smell (Yang *et al.* 2013). Geraniol (11, Fig. 3) is a different variety of monoterpenoid which shows rose- like floral aroma.

Two volatiles namely benzylalcohol (12, Fig. 3) and phenylethanol (13, Fig. 3), are present at high concentrations in tea. They are major contributors to the fruity, floral smells of flowers, fruits, and plants. Additionally, coumarin (14, Fig. 3) is the important volatile derivative present in tea which has very sweet-herbaceous cherry flower like odour and can be found in Japanese and Chinese green teas.

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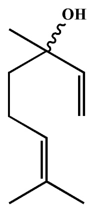
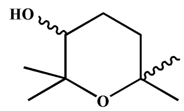
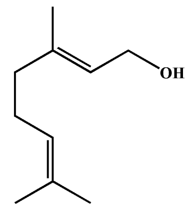
In general, volatile aroma compounds differ primarily on the manufacturing process, even from the same categories but of different origins. Some important tea volatiles, with their characteristic odour and precursors are summarized in Table 1.



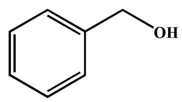
Linalool
9



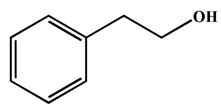
Linalool oxide (Pyranoid)
10



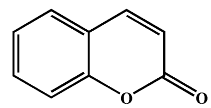
Geraniol
11



Benzyl alcohol
12



2-phenylethanol
13



Coumarin
14

Figure 3. Terpenoid, phenylpropanoid and benzenoid aroma compounds in tea

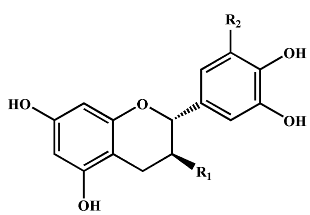
Table 1. List of volatile compounds and their characteristic aroma.

Volatile compounds	Aroma	Volatile compounds	Aroma
β-ionone	Woody, violet like	Linalool	Floral, citrus-like
β-damascenone	Honey-like, fruity	Linalool oxide	Sweet floral, citrus, fruity
Dihydroactinidiolide	Fruity	Geraniol	Floral, rose-like
Theaspirone	Flowery	2-phenylethanol	Flowery, rose-like, honey-
Hexanol	Green, grassy	Benzylalcohol	Sweet, fruity
Hexanal	Green, grassy	Coumarin	Sweet-herbaceous cherry

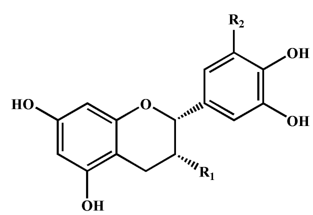
1.2 Taste constituents of tea: The characteristic taste of tea is the fabrication of an ingenious blending of different gustatory perception. The compounds, which contribute to distinctive tea taste, are a variety of polyphenols, amino acids and caffeine (Yamanishi, 1995). Polyphenols are the effective class of compounds present in different concentration, which primarily determines the variation of taste among green, black and oolong tea. Moreover, the bitterness and briskness of caffine and 'umami' or meaty taste of various kinds of amino acids contributes to the characteristic taste of variety of teas.

1.2.1 Polyphenols in tea: The numbers of polyphenolic compounds present in the tea plants presumably strengthen the defence mechanism against insects, birds, and animals, which would consume the plant as food (Harbowy and Balentine, 1997).The discharge of salivary proline-rich proteins, which attach with polyphenols effectively has alleviated this resistance mechanism, switching it to 'astringency' which is perceived as a puckering, shrinking, rough, and drying sensation in the mouth (Yamanishi, 1995).The total content of polyphenols in tea flushes are 25-35% on a dry weight basis. Flavanols and flavonols are the main classes of components among the flavonoids, found in teas which are present in 30% of the dry weight of fresh leaf and principally responsible for the astringency and partial bitterness of the tea beverage.

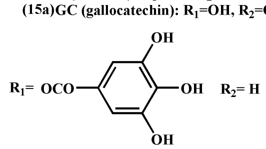
(a) Catechins: Abundant flavanols in tea: Catechins are members of a class of flavanols and represent the major polyphenolic constituent of green tea. The catechin fragment has two chiral centres which results in four diastereoisomers with two of the isomers are in *trans*-configuration and the other two are in *cis*-configuration. The *trans*-isomers are referred to as the catechin (15, 15a, 15b, 15c, Fig. 4) whereas the *cis*-isomers are known as epicatechin (16, 16a, 16b, 16c, Fig. 4). A large proportion of the catechins in tea exist as gallic acid (17, Fig. 4) esters and gallation takes place predominantly at the 3-position. The four most common catechins present in tea leaves are epicatechin (EC) (16, Fig. 4), epigallocatechin (EGC) (16a, Fig. 4), epicatechin gallate (ECG) (16b, Fig. 4) and epigallocatechin gallate (EGCG) (16c, Fig. 4). Catechin (C) (15, Fig. 4) and gallocatechin (GC) (15a, Fig. 4) are also present in smaller quantities whereas catechin gallate (CG) (15b, Fig. 4) and gallocatechin gallate (GCG) (15c, Fig. 4) are produced in tea plants as a result of racemisation (Nakagawa, 1970). Catechins have been found to greatly contribute to the astringent and bitter taste of tea (Yamanishi, 1995). Gallated catechins have bitterness and astringency stronger than those of simple tea catechins. Additionally, the concentrations of C (15, Fig. 4), EC (16, Fig. 4) and EGC (16a, Fig. 4) are correlated positively with very persistent aftertaste of sweetness (Obanda *et al.*, 2001). Nakagawa *et. al* further studied that the higher percentage level of catechins and gallocatechins in tea leaves produced optimal bitterness and astringency level which augment the excellence and acceptance of tea flushes among consumers (Nakagawa, 1975).



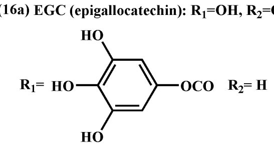
(15) C (catechin): R_1=OH, R_2=H
(15a) GC (gallocatechin): R_1=OH, R_2=OH



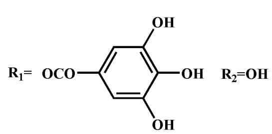
(16) EC (epicatechin): R_1=OH, R_2=H
(16a) EGC (epigallocatechin): R_1=OH, R_2=OH



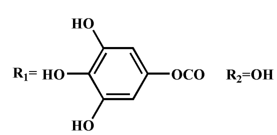
(15b) CG (catechin gallate)



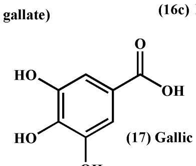
(16b) ECG (epicatechin gallate)



(15c) GCG (gallocatechin gallate)



(16c) EGCG (epigallocatechin gallate)



(17) Gallic acid

Figure 4. Chemical structures of major catechins in tea

(b) Flavonols in tea: Flavonols such as quercetin, kaempferol, myricitin (18, 19, 20 respectively in Fig. 5) and their mono-, di- and tri- glycosides make up 2 to 3% of the water-soluble extract solids of tea (Yamanishi, 1995). Flavonol glycosides, except catechins, have been reported to be the significant contributor to the astringency of both back and oolong tea infusions. The flavonol glycosides are found to have a smooth, mouth-puckering and velvety mouth-coating sensation at extremely low threshold concentrations spanning from 0.001 to 19.8 μmol/L.

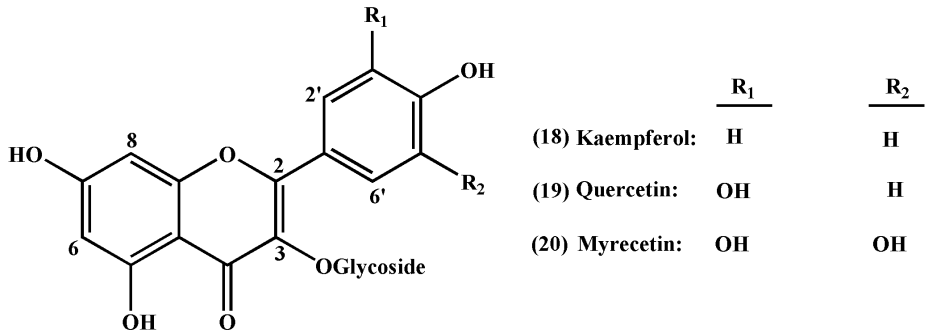
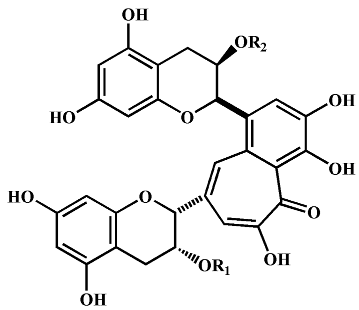


Figure 5. Structures of major tea flavonols

(c) Theaflavins: Theaflavins are a distinct class of flavonoid biopolymers, produced during fermentation process in both black and oolong teas and are one of the main classes of taste active compounds contributing to the gustatory sensation. The basic framework of theaflavins is benzotropolone, which is a fused bicyclic ring of benzene and tropolone structure.

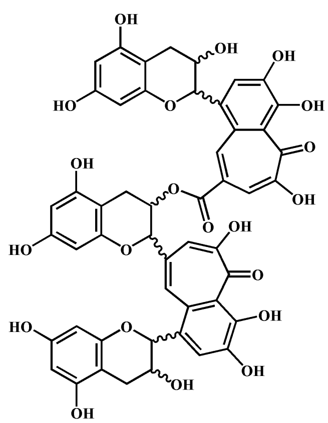
A numbers of theaflavins are theoretically possible to synthesize upon dimerization of epicatechins and epigallocatechins. However, the major theaflavins found in tea plants are theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3, 3'-digallate (21, 21a, 21b and 21c respectively in Fig. 6). The relative proportions of the theaflavins in black tea are theaflavin (21), 18%, theaflavin-3-gallate (21a) 18%, theaflavin-3'-gallate (21b) 20% and theaflavin-3, 3'-digallate (21c) 40% whereas in oolong tea, theaflavin is the richest component representing 77.8–85.8% among the whole theaflavin contents (Pan-Pan *et al.*, 2018). As a taste-active constituent of tea, aqueous solutions of various theaflavin components isolated from black tea brew were reported to induce a mouth-drying, rough astringent and brisk sensation at a threshold levels between 13 and 26 μmol/L (Scharbert *et al.*, 2004). Theaflavin-3, 3'- digallate (21c) is the most astringent component which is 6.4 times more astringent than theaflavin (21) and theaflavin monogallates are 2.2 times more astringent compare to theaflavin.



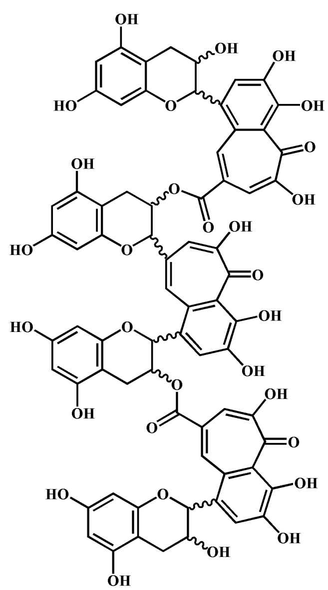
	R_1	R_2
(21) Theaflavin	H	H
(21a) Theaflavin-3-gallate	Gallate	H
(21b) Theaflavin-3'-gallate	H	Gallate
(21c) Theaflavin-3, 3'-digallate	Gallate	Gallate

Figure 6. Structures of major tea theaflavins

(d) Thearubigins: Thearubigins consist of ~10-20% of dehydrated weight of black tea and due to its hot water solubility; they comprise of ~30-60% of the solids in black tea infusion. Roberts *et. al.*, who has coined the terms theaflavin and thearubigin, considered that the thearubigins are one of the most important constituents controlling the flavor and quality of black tea and consequent studies revealed that thearubigins are primarily responsible for ashy and slightly astringent taste and rich fullness of the tea brew (Roberts and Smith, 1961). Nakagawa and Torii found that the ratio of theaflavins to thearubigins of 1:10 to 1:12 by weight had a high positive correlation with their evaluation of the taste of tea brews (Nakagawa and Torii, 1964). A few examples of identified thearubigins in tea extracts are theadibenzotropolones A, B, and C (22, Fig. 7) and theatribenzotropolone A, B (23, Fig. 7) etc (Drynan *et al.*, 2010).



Theadibenzotropolones A/ B/ C
(22)

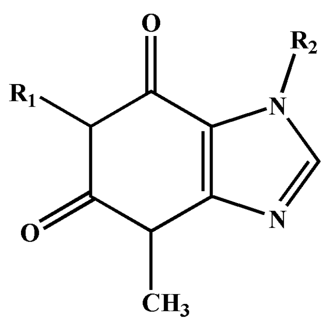


Theatribenzotropolones A/ B/ C
(23)

Figure 7. Structures of thearubigins present in tea

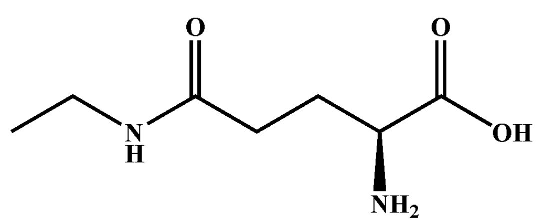
1.2.2 Caffines in tea: Xanthine compounds such as caffeine (1,3,5-trimethylxanthine), theobromine (3,7-dimethylxanthine) and theophylline (1,3-dimethyl- 7H-purine-2,6-dione) (24, 25 and 26 respectively in Fig. 8) are classified as alkaloids in tea extract among which caffeine is the key xanthine component due to its mild stimulating property and cognitive-enhancing effect. Pure caffeine (24) tastes bitter and the detection threshold is ~3.0 parts per million (ppm) in water. Theobromine (25) and theophylline (26) are also known to be bitter-tasting components in tea extract. In the tea brew, part of the caffeine naturally forms complex with flavonoid biopolymers (theaflavins, thearubigins, etc.) which reduce the astringency of the flavonoid biopolymers as well as the bitterness of the caffeine and improves the quality of tea (Nakagawa and Torii, 1964). In addition, high level of caffeine in tea, leads to the 'creaming down' in the liquors which is an indication of high quality of the tea brew.

1.2.3 Amino acids in tea: Amino acids are the major component in tea extract that contribute rich umami flavour or brothy and sweet taste. The amino acids present in tea have been identified as aspartic acid, threonine, glutamic acid, glycine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, arginine, glutamine, asparagine, tryptophan and theanine (Bhatia and Deb, 1965). Among the amino acids present in tea leaves, theanine or N-ethyl glutamine (27, Fig. 9) is the most abundant component and accounts for 50% of the total amino acids and 1% of the dry weight of tea. In green tea, theanine contributes to the 'brothy' taste, whereas for oolong tea the bitterness and astringency is moderated by increasing its sweetness (Chen *et al.*, 2019). Nishimura and Kato also reported that glycine and alanine have considerably strong sweetness and monosodium glutamate in tea has a characteristic umami taste (Nishimura and Kato, 1988). Additionally, Kaneko *et al.* also revealed that theanine is the key components responsible for umami taste of tea (Kaneko *et al.*, 2006).



	R_1	R_2
(24) Caffeine	CH_3	CH_3
(25) Theobromine	H	CH_3
(26) Theophylline	CH_3	H

Figure 8. Structures of caffine, theobromine and theophylline



Theanine
(27)

Figure 9. Structure of theanine

In general, taste of a cup of tea primarily depends on the proportion of three broad classes of non-volatile compounds namely polyphenols, caffine and amino acids. Some important non-volatile taste constituents and their gustatory sensation as summarized as follows in Table 2.

Table 2. List of non- volatile compounds and their taste.

Compuounds	Taste	Compounds	Taste
Catechins	Astringent	Caffine + Theaflavins	Less bitter
Flavonols	Velvety	Amino acids	Umami,
Theaflavins	Brisky	Glycine and alanine	Sweet
Thearubigins	Ashy	Arginine	Bitter
Xanthine (caffeine, theobromine	Bitter	Theanine	Brothy

1.3 Colour components of tea: In evaluating the quality of tea, the colour of tea infusion is one of the important aspects along with aroma and taste that influence consumers in making a decision which product to purchase. Tea infusion is characterized by various kinds of pigments. It is well known that the intrinsic pigments like chlorophyll, carotene and xanthophylls that are present in the tea leaves remain intact by the methods of preparing tea infusions. Chlorophylls are a group of green pigments that can be found in photosynthesizing tissues and its amount regulates the colour of non-fermented tea infusions (Hörtensteiner and Kräutler, 2011). Tea carotenoids are another group of pigments found in tea leaves and are mainly composed of carotenes which are orange and xanthophylls which are yellow. It is also believed that the yellow colour of green tea infusion is largely dependent on the flavonol pigments such as kaempferol, quercetine, myricitrin etc. (18, 19, 20 in Fig. 5) as mono-, di- and triglycosides and manifest a clear yellowish hue when dissolved in hot water (Chaturvedula and Prakash, 2011). Black tea quality is known to be strongly influenced by the concentration of theaflavins, which are a group of yellow-orange pigments and constitute around 0.5 to 2% of dry weight of black tea. The striking bright colour of the tea infusion is due to the presence of theaflavins and emerges as a key quality parameter of black tea (Li *et al.*, 2013). Thearubigins, the brown-orange compounds, are another class of key components comprising of about 6 to 18% of dry weight in fermented tea. The thearubigin group of pigments also contributes around 35% of the total colour and plays a significant role in the brown appearance of made tea. In addition, infusion colour of oolong tea varies from green to greenish yellow to golden yellow, depending on the extent of fermentation (Kunbo *et al.*, 2010). Critical insight of oolong tea reveals that theaflavins and chlorophylls show significant correlation with the tea infusion colour.

In general, a variety of polyphenolic compounds (Flavanol, theaflavin, thearubigin) as well as two major groups of pigments: chlorophylls and carotenoids are primarily responsible for the colour of tea infusions. Some important colour constituents and their respective colour are enlisted in Table 3.

Table 3. List of colour constituents and their colour.

Constituents	Colour	Constituents	Colour
Chlorophyll	Green	Flavanol	Yellow
Carotene	Orange	Flavones	Yellow

Xanthophyll	Yellow	Theaflavin	Bright yellow-orange
Catechins	Colourless	Thearubigin	Dark orangish-brown

2. Bioactivity and health benefits of tea: Since ancient times, tea has always been considered as a traditional medicine in China which has capability to prevent various diseases. In recent times, tea infusions are popularly categorized as antioxidants, which have led to their evaluation in numerous diseases allied with reactive oxygen species (ROS), such as cancer, cardiovascular and neuro-degenerative irregularities (Khan and Mukhtar, 2013). Recent studies also revealed that EGCG and theaflavins have shown a significant interaction with the receptors present on SARS-CoV-2 and support the use of tea polyphenols as potential candidates in prophylaxis and treatment of COVID-19 (Park *et al.*, 2021, Jang *et al.*, 2020). Various other health related benefits attributed to tea include anti-diabetic, anti-obesogenic activities etc.

2.1. Antioxidant and anti-oxidative stress activity of tea polyphenols: Reactive oxygen species (ROS) are the highly active free radicals, produced during cellular respiration and normal metabolism and are closely related to physiological and pathological processes in human body. When the balance between the accumulated ROS and the body's normal antioxidant content get disrupted, it creates oxidative stress which damage cells and tissues and causes various diseases (Mao *et al.*, 2017). Tea polyphenols (TP), most particularly flavonoids are a class of effective antioxidant that can prevent and treat these diseases by scavenging free radicals and controlling the action of different types of oxidase enzymes in the body. Mechanistically, the phenolic –OH groups weaken the binding ability of hydrogen ions owing to the conjugative stability of phenoxide moiety and consequently the active hydrogens scavange the free radicals and other ROS (Deka *et al.*, 2021). In a study by Shah *et al.*, antioxidant activity of green tea extract was shown to be more effective than black tea extract possibly due to the higher content in polyphenolic compositions found in green teas (Shah *et al.*, 2015). Hence, the antioxidant status by tea polyphenols could be strategic therapeutic targets in the prevention and treatment of various metabolic diseases.

2.2. Cancer versus Tea Consumption: Tea polyphenols, more particularly EGCG (16c, Fig. 4) are potent anti-carcinogenic and chemo-preventive agents which have a distinct preventive action on prostate, colorectal, and breast cancers. EGCG has shown to modulate several biological pathways and promote malignancy dependent DNA repair which eventually enhance cytotoxic T-cell activities and block cancer growth by inhibiting carcinogenic signal transduction pathways (Ahmed *et al.*, 2004).

Breast cancer is the most common oncogenesis for post-menopausal women throughout the globe. Tea polyphenols are shown to decrease MDA-DNA adduct(M_1dG) levels significantly in human-derived breast carcinoma cells and regulate the risk of breast cancer (Nair *et al.*, 2007). Tea polyphenols are also explored for their anti-proliferative effects in human colorectal cancer cells. A population-based potential cohort study reported that the consumption of 250 g/month or ≥5 cups/day of green tea had significantly lowered the risk of colorectal and gastric cancer among the non-smokers irrespective of gender (Yang *et al.*, 2011). For the prostate cancer, green tea polyphenols have been reported to decrease the serum levels of prostate-specific antigen (PSA), hepatocyte growth factor, and vascular endothelial growth factor in men. Black tea also showed noteworthy potential to regulate the risk of prostate cancer in advanced stage (Geybels *et al.*, 2013). In a sense, tea polyphenols have a definite contribution towards the development of a promising alternative therapeutic avenue for cancer treatment.

2.3. Anti-cardiovascular activity of tea: A number of studies have been reported on the anti-cardiovascular activity of tea consumption and its effectiveness to lower the risk of mortality among middle-aged and elderly adults (Pang *et al.*, 2015). According to the investigation done by Pang *et al.*, the risk of coronary heart diseases (CHD) was significantly decreased by the reduction of hyperlipidemia and total cholesterol content among patients, habituated to drink green tea regularly. The protective effect of green tea towards cardiovascular diseases originates from the increase in the activity of oxido-reductase system and reduces ROS levels. EGCG (16c, Fig. 4), the major tea catechin, effectively inhibits the action of angiotensin-converting enzyme. Green tea catechins further affect lipid metabolism by decreasing the absorption of triglycerides and cholesterol, increases the excretion of fat and prevent the formation of atherosclerotic plaque (Ahn *et al.* 2010). In a different aspect, activated platelets originating from sub-endothelial collagen and thrombin matrix, damage blood vessel and initiate thrombus formation to promote the thrombotic disease (Jin *et al.*, 2008). EGCG, present in tea extract, showed antithrombotic and antiplatelet activities due to its inhibitory action on arterial thrombus formation along with suppression of collagen and arachidonic acid-induced platelet aggregation. In a sense, the drug interactions between tea extracts and cardiovascular therapy have a definite therapeutic efficacy against cardiovascular diseases.

2.4. Antidiabetic Effects: The consumption of tea is found to reduce body mass, regulate body fat as well as enhance the metabolism of glucose and lipid which is evident from various epidemiological investigations (Kawser *et al.*, 2016). Tea catechins, theaflavins, and caffeines are primarily responsible for the anti-diabetic effects of tea and can modulate the key signal pathways involved in the regulation of insulin, blood sugar and glucose metabolism. In case of type 1 diabetes mellitus (T1DM), green tea catechins are found to reduce ROS and inhibit the inflammatory actions within pancreatic-β-cells. For type 2 diabetes mellitus (T2DM), associated with relative lack of insulin secretion by islet-cells, green tea polyphenols enhance glucose-stimulated insulin secretion (Hameed *et al.*, 2015). Moreover, black tea theaflavins can control obesity and thereby inhibit the action of ROS to reduce the risk of T2DM. In a retrospective cohort study among U.S. middle-aged and older women, those who had taken more than or equal to 4 cups of black tea per day, experienced 30% lower risk of developing T2DM than those who did not consume tea (Song *et al.*, 2005). The results indicated that, tea consumption can be effective to control obesity and a potentially promising candidate for the prevention of diabetes.

2.5. Green tea against COVID-19: On the eve of 2020, the world was attacked by a novel virus called Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which lead to a pandemic of acute respiratory ailment, COVID-19, due to high transmission rate and pathogenicity of the virus. Recent studies suggest that EGCG and theaflavins (TFs) are potentially useful against COVID-19 virus (Park *et al.*, 2021; Jang *et al.*, 2020) 3-chymotrypsin-like (3CL)-protease cleaves the SARS-CoV-2 encoded polyproteins into individual functional proteins which facilitates the virus to show its pathogenicity. In early 2020, the three-dimentional structure of SARS-CoV-2-3CL protease was determined and peptidomimetic inhibitors showed inhibitory effects on 3CL protease enzyme activity as well as on SARS-CoV-2 replication (Du *et al.*, 2021). Notably, the SARS-CoV-2-3CL protease appeared to be more sensitive to EGCG and TFs and in silico molecular docking studies revealed that both the compounds are potential SARS-CoV-2-3CL protease inhibitor. It is also well-known that coronavirus contains RNA and the corresponding RNA-dependent RNA polymerase (RdRp) enzyme is also a key target of SARS-CoV-2 antiviral drugs (Wang *et al.*, 2020). In silico structural analysis has revealed that EGCG and TFs forms a stable complex with SARS-CoV-2 RdRp enzyme and potentially inhibit SARS-CoV-2 RdRp action as well as viral replication (Singh *et al.*, 2020). In another outlook, the SARS-CoV-2 spike glycoprotein binds with angiotensin converting enzyme-2 (ACE2) proteins of host cell to stimulate viral infection. Recent reports indicate that, EGCG and TFs bind with the SARS-CoV-2 spike proteins and block the interaction between the viral spike protein and ACE2 and thereby prohibit viral passage into host cells (Mhatre *et al.*, 2021). Fig. 10 shows possible mechanism of actions for tea polyphenols on different active sites. As the safety of green tea has long been verified, an adequate amount of green tea can be directly used without toxicity concerns.

An overall view related to the tea components that are responsible for various health related effects has been summarized in tabular form in Table 4.

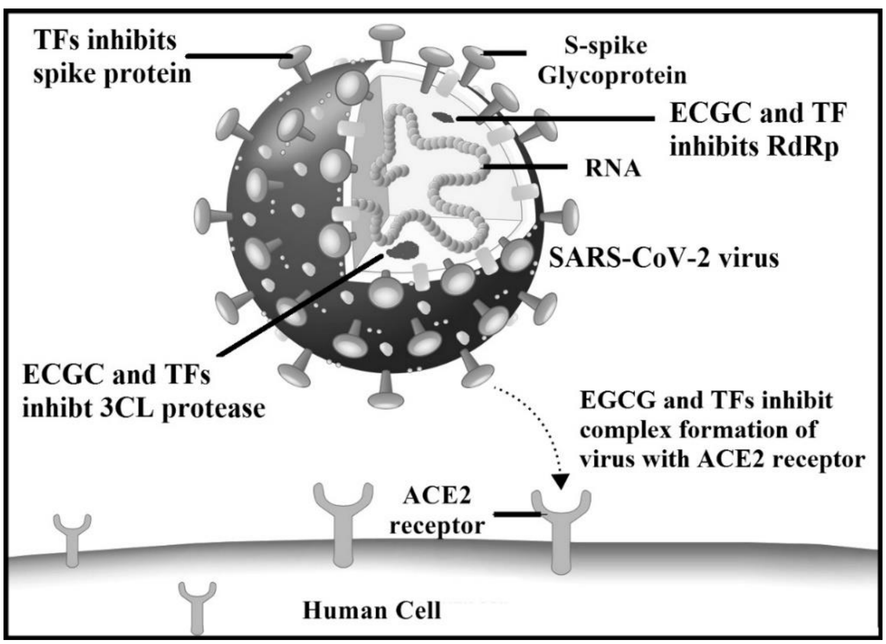


Figure 10. Role of tea polyphenols on different active sites of COVID-19 virus

Table 4. List of health related effects and responsible tea constituents.

Health related effects	Responsible tea constituents
Anti-oxidant	Flavonoids
Anti-cancer	
Chemo prevention	
Anti-cardiovascular	ECGC

Anti-thrombotic	
Anti-platelet	
Anti-SARS-CoV-2 (Against COVID-19)	ECGC, Theaflavins
ACE inhibitor	Catechins
Anti-diabetic	Catechins, theaflavins
Anti-obesity	Catechins, theaflavins

2.6. Safety concerns of tea consumption: Although it is well known that tea consumption have preventive and curative effects for most people, drinking excess tea may results in unexpected side effects like anxiety, poor sleep, restlessness, headache etc. Unfortunately, various adverse effects associated with the intake of variety of tea preparations have been found in literature. In April 2003, Exolise (Arkopharma, Carros, France), a green tea extract preparation containing higher EGCG levels and promoted as a weight loss supplement, have been withdrawn from the market due to liver damage of 13 cases as a result of its consumption (Sarma *et al.*, 2008). Again, Mazzanti *et al.* have reported few cases of hepatotoxicity, associated with consumption of high doses of green tea-containing dietary supplements indicating a relevant association between green tea and liver damage (Mazzanti *et al.*, 2009). In another study by Lambert *et al.*, 1500 mg/kg EGCG was fed to mice orally at a time and the toxicity in liver was found to be increased which decreased their survival rate by 85% (Lambert *et al.* 2010). This indicates that EGCG rich dosages was toxic to liver, which may be associated with the pro-oxidation activity of EGCG. These results conclude that the capability of catechins, particularly ECGC or its metabolites to induce oxidative stress in the liver may results in the associated hepatotoxicity in various cases.

CONCLUSIONS

The current review is an effort to investigate about the chemical components present in the tea extracts which are responsible for the characteristic aroma, taste and colour of the tea. The study enlightens about the fact that many volatile components originating from carotenoid, lipid, terpenoid and benzenoid precursors determine the aroma of tea infusions. Moreover, a number of non-volatile polyphenols, amino acids and caffine are responsible for the astringent, bitter and umami taste of various kinds of tea. Regarding the appearance, a variety of polyphenolic compounds along with major group of pigments (i.e. chlorophylls and carotenoids) are summarized as key colour contributors of tea infusions. In a different aspect, the review delineates about the potential applications of tea components towards various healths related benefits. As main constituents, tea polyphenols are documented for their antioxidant, anticancer, antihypertensive, antidiabetic and anti-obese activities. Most interestingly, the potential efficacy of tea constituents against COVID-19 has been discussed. However, unfortunately, various adverse effects are associated with the excess consumption of variety of tea preparations.

In spite of there being lots of research work on chemical elucidation and potential therapeutic applications of tea extracts, large scale well controlled human clinical trials are necessary to establish the health promoting effects of tea consumption. As a whole, the insight of tea not only as a natural beverage from plant but as a healthy element of the human diet and as a rich resource of new chemical compounds will advance tea research in new directions.

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