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Review Article

Tea flavonoids: A promising ally against Alzheimer's and Parkinson's diseases

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Abstract

Tea is one of the most popular beverages consumed worldwide, which has several bioactive compounds with potential health advantages. The primary bioactive compounds in tea are phenolic compounds with one or more aromatic rings bearing hydroxyl, and these are classified as secondary metabolites. This comprehensive review delves into the intricate relationship between tea polyphenols and their potential role in shielding the brain from neurodegenerative diseases, focusing specifically on Alzheimer's and Parkinson's. It kicks off by offering an overview of tea's cultural importance and diverse varieties. The exploration then delves into the complex biochemistry of tea, emphasizing the presence of flavonoids, such as epigallocatechin gallate (EGCG) in green tea and theaflavin and thearubigins in black tea, recognized for their powerful antioxidant and anti-inflammatory properties. Acknowledging the widespread occurrence and severe consequences associated with Alzheimer's and Parkinson's diseases, the article underscores a focus on shared pathophysiological processes inherent in these disorders, encompassing protein aggregation, oxidative stress, and neuroinflammation. The current symptomatic relief provided by medicines necessitates the search for alternative approaches. Promisingly, tea flavonoids emerge as candidates capable of addressing the underlying mechanisms of neurodegenerative diseases. These compounds may enhance the growth of nerve cells and improve connections between them, offering a potential avenue for developing therapies for neurodegenerative diseases. The article examines existing literature, providing insights into the potential therapeutic effects of tea polyphenols, aiding our understanding of how these substances might slow down Alzheimer's and Parkinson's by studying their intricate interactions in our bodies. In summary, this detailed review combines historical context, complex chemistry, and neurological effects, offering a holistic view of how tea polyphenols might protect the brain. The findings presented herein lay the foundation for future research and therapeutic strategies, showcasing the potential benefits of tea in combating neurodegenerative diseases worldwide. The authors aim to explore existing research on tea, examining its health benefits and its relationship with different lifestyle-related diseases.

Highlights

Tea has a multitude of bioactive chemicals, the majority of which have beneficial effects on health.

The presence of flavonoids, such as epigallocatechin gallate (EGCG) in green tea and theaflavin and thearubigins in black tea, is recognized for their powerful antioxidant and anti-inflammatory properties.

The polyphenols found in tea could offer protection to the brain against neurological disorders. The findings presented in this analysis indicate that tea might play a significant role in combating neurodegenerative diseases like Parkinson's and Alzheimer's disease on a global scale.

Keywords: Tea, Catechins, Flavonoids, Bioactive compounds, Neuroprotective diseases, Alzheimer's disease, Parkinsons disease.

Introduction

One of the most widely consumed drinks in the world, tea contains several bioactive chemicals that may have positive health effects. *Camellia sinensis*, the scientific name behind tea, refers to a single species, yet within its leaves lies a vibrant spectrum of possibilities. Two main varieties, *sinensis* and *assamica*, each contribute unique characteristics to the final cup (Li *et al*., 2004). *Sinensis*, hailing from China, yields smaller leaves and brews into delicate teas like green and white, known for their subtle floral and vegetal notes (Kumar *et al*., 2013). *Assamica*, thriving in India and Sri Lanka, boasts larger leaves and imparts bolder, more robust flavors to black and Assam teas (Banerjee *et al*., 1996) (Table 1).

Tea is classified not just by where it comes from but also by its unique traits. The main varieties of tea include

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Table 1: Tea plant varieties and their origins

S. No.	*Type of tea*	*Place of origin*	*References*
1.	*Sinensis*	China	(Kumar *et al*., 2013)
2.	*Assamica*	India, Sri Lanka	(Banerjee *et al*., 1996)

green tea, black tea, white tea, and oolong tea (Table 2).

Green tea

Crafted from fully grown tea leaves, this type is neither fermented nor oxidized (Verma *et al*., 2013). The primary goal during its production is to maintain the natural polyphenols found in the leaves, ensuring that they are readily available in the brewed tea for health advantages (Soni *et al*., 2015).

Black tea

Also derived from mature tea leaves, this variety undergoes fermentation and complete oxidation (Verma *et al*., 2013). The process involves crushing the leaves to encourage enzymatic oxidation, resulting in the creation of theaflavins and thearubigins through fermentation (Soni *et al*., 2015).

White tea

This type is made from tea buds or young leaves, which are non-fermented and undergo minimal oxidation (15–80%) (Verma *et al*., 2013). It is produced from tender leaves and buds that are steamed to prevent polyphenol oxidation before being dried (Soni *et al*., 2015).

Oolong tea

Made from mature tea leaves, this variety is partially fermented and semi-oxidized (15–80%) (Verma *et al*., 2013). Often regarded as a bridge between black and green tea, oolong tea embodies the qualities of both (Soni *et al*., 2015).

Tea is rich in phytochemicals that offer a variety of health benefits. Phytochemicals are bioactive plant components that can be nutritious or non-nutritional and are also found in fruits, vegetables, cereals, coffee, and other plant foods (Kumar *et al*., 2023). Secondary metabolites, especially phenolic molecules having one or more aromatic rings holding hydroxyl, are the main bioactive components of tea. In recent years, there has been an enhancement in the application of tea as an antioxidant and for other health benefits. A huge number of studies and research are going on and producing detailed data on the cultivation, production, and utilization of tea every year. The beneficial role of tea and its usefulness in many lifestyle diseases. The authors would like to review the literature providing information about the details of tea and their application as a nutraceutical and helping to control many lifestyle diseases.

Table 2: Classification of tea based on characteristics

S. No.	*Type of tea*	*Characteristics*	*References*
1.	Green tea	Fully grown tea leaves Neither fermented nor oxidized	(Verma *et al*., 2013) (Soni *et al*., 2015)
2.	Black tea	Mature tea leaves Completely fermented and oxidized.	(Verma *et al*., 2013) (Soni *et al*., 2015)
3.	White tea	Tea buds or young leaves Non-fermented and minimal oxidation	(Verma *et al*., 2013) (Soni *et al*., 2015)
4.	Oolong tea	Mature tea leaves Partially fermented and semi-oxidized	(Verma *et al*., 2013) (Soni *et al*., 2015)

Tea, a globally cherished beverage, is celebrated for its diverse flavors and is consumed in various forms across different regions. Recognized as a comforting drink throughout the day, it holds a universal appeal enjoyed from sunrise to sunset. In the global tapestry of cultural indulgences, tea stands as a venerable thread, weaving together centuries of tradition, discovery, and, perhaps, untapped health potential. But beneath its comforting surface lies a fascinating history, a diverse array of types, and a burgeoning potential as a source of health-beneficial compounds such as neuroprotective compounds against Alzheimer's and Parkinson's disease. This introduction delves into the heart of tea, unveiling its essence and setting the stage for a deeper exploration of its flavonoids and their potential role in neurodegenerative diseases.

Beyond varietals, the anatomy of the tea plant itself plays a crucial role in shaping the final beverage. The young leaves and buds at the apex, rich in phenolic compounds and essential oils, are prized for their superior quality (Lu *et al*., 2002). These delicate structures harbor the building blocks of tea's flavor complexity and potential health benefits. The intricate flavors of tea, originating in the delicate leaves and buds, find their roots in a deep connection with history. Legend traces its origins back to 2737 BC in China, where Emperor Shen Nung is said to have discovered the beverage by chance (Adshead *et al*., 2000). From its initial use as a medicinal tonic, tea blossomed into a cornerstone of art, literature, and religious ceremonies. The Tang Dynasty (618-907 AD) witnessed a flourishing tea culture, complete with dedicated rituals and specialized equipment (Adshead *et al*., 2000). As its fame spread beyond China, tea embarked on a global voyage. Buddhist monks carried it to Japan in the 8th century, where it became deeply ingrained in Zen practices and refined into intricate ceremonies (Hōgetsu, K *et al*., 2002). Portuguese and Dutch merchants introduced it to Europe in the 16^{th} century, igniting a passionate love affair with the beverage across the continent (Brown 2007). In India, the arrival of British tea plantations in the 19^{th} century irrevocably altered the landscape and social fabric of the region (Keay *et al*., 2011).

India, indeed, boasts a unique relationship with tea. From Darjeeling's delicate high-mountain varieties to the robust flavors of Assam, tea has become interwoven with the nation's identity. Today, India stands as the world's second-largest tea producer and consumer, with chai, a spiced milk tea, serving as a ubiquitous symbol of daily life and shared social experiences (Sharma *et al*., 2020). But beyond its cultural significance, tea also holds significant potential for promoting health and well-being. This potential lies in the diverse array of bioactive compounds it contains, including flavonoids, a class of polyphenols with potent antioxidant and anti-inflammatory properties (Pan *et al*., 2018). Tea flavonoids, like a vibrant orchestra, comprise various players, each with unique strengths. Epigallocatechin gallate (EGCG), the star of green tea, boasts potent antioxidant and anti-inflammatory properties, protecting neurons from oxidative stress [Pan *et al*., 2018]. Black tea, meanwhile, offers theaflavin and thearubigins, which wield anti-inflammatory and cognitive-enhancing weapons (Pan *et al*., 2018; Scholey *et al*., 2012). These flavonoids do not work alone but operate collaboratively, orchestrating a range of effects by impacting enzymes, combating detrimental substances, and engaging with gut bacteria (Li *et al*., 2013). Together with other bioactive compounds, these flavonoids could offer numerous health advantages, including potential assistance for the prevention of neurodegenerative illnesses like Parkinson's and Alzheimer's.

Millions of people worldwide are impacted by two of the most prevalent neurological conditions, Alzheimer's disease (AD) and Parkinson's disease (PD) (Hebert *et al*., 2015). Both are characterized by progressive decline in cognitive and motor function, with devastating consequences for individuals and their families. While distinct in their primary symptoms, both diseases share underlying pathophysiological processes, including protein aggregation, oxidative stress, and neuroinflammation (Vila *et al*., 2019).

Alzheimer's disease is primarily characterized by memory loss and cognitive decline, driven by the accumulation of amyloid-beta plaques and tau tangles in the brain (Selkoe *et al*., 2002). PD, on the other hand, manifests as a movement disorder with tremors, rigidity, and bradykinesia, resulting from the progressive loss of dopamine-producing neurons in the substantia nigra and the accumulation of alpha-synuclein Lewy bodies (Poewe *et al*., 2020). Despite their differences, both AD and PD exhibit chronic neuroinflammation, suggesting a potential shared therapeutic target (Ransohoff *et al*., 2015). Due to the complex and poorly understood nature of these diseases, effective treatments remain elusive. Currently, available pharmacotherapies provide symptomatic relief but fail to halt disease progression (Tariot *et al*., 2016). This has fostered significant interest in exploring alternative therapeutic approaches, with natural products like tea flavonoids emerging as promising candidates due to their anti-inflammatory, antioxidant, and neuroprotective properties (Pan *et al*., 2018).

Therefore, exploring the potential of tea flavonoids in modulating the shared and specific pathophysiological pathways of AD and PD holds significant promise for developing novel therapeutic strategies against these debilitating neurodegenerative diseases. This review article delves deeper into the current understanding of AD and PD, the role of tea flavonoids in neuroprotection, and their potential application in managing these devastating conditions.

Tea phytochemicals

Behind the sensory pleasure of sipping a warm cup of tea lies a treasure trove of bioactive compounds known as phytochemicals. These natural compounds, derived from plants, contribute to the diverse flavors, aromas, and colors of tea, making it a fascinating subject of scientific inquiry. The important phytochemicals found in tea include polyphenols. The most abundant and well-studied group of phytochemicals in tea are polyphenols, encompassing flavonoids and non-flavonoids. Catechins, a subset of flavonoids, such as epicatechin, epicatechin gallate, epigallocatechin, and epigallocatechin gallate, are predominant in tea (Smith *et al*., 2010).

Alkaloids

Caffeine, an alkaloid, is a characteristic component of tea, influencing its stimulant properties. The amount of caffeine varies among different tea types, with green tea generally containing lower levels than black tea (Heckman MA *et al*., 2010).

Amino acids

Theanine, an amino acid unique to tea, is renowned for its relaxing and mood-enhancing effects. Green tea is rich in theanine, contributing to its distinctive flavor profile (Juneja LR *et al*., 1999).

The phytochemical makeup of various tea types is notably unique (Figure 1). Green tea, renowned for its

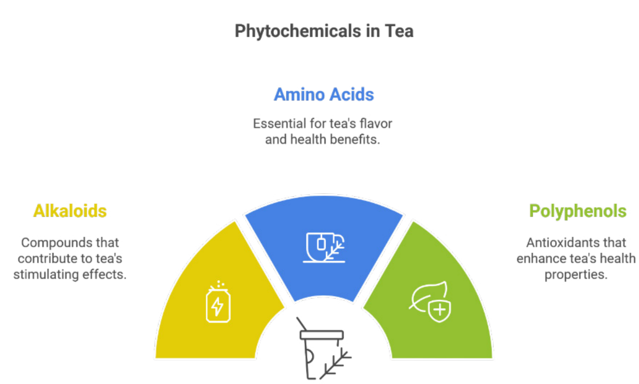

Figure 1: Major phyto-chemicals found in tea

minimal oxidation during processing, is rich in catechins, particularly epigallocatechin gallate (EGCG), which offers impressive antioxidant and anti-inflammatory properties (McKay DL *et al*., 2002). In contrast, the oxidation that occurs in black tea production converts catechins into theaflavins and thearubigins. These compounds not only give black tea its distinctive color and flavor but also present potential cardiovascular benefits and anticancer effects (Tipoe GL *et al*., 2007). Oolong tea, which falls between green and black teas in terms of oxidation, features a harmonious blend of catechins, theaflavins, and thearubigins. This varied phytochemical composition may play a role in the unique health benefits linked to oolong tea consumption (Yang CS *et al*., 2011).

Phytochemicals such as flavonoids, terpenoids, phenolic compounds, and alkaloids are crucial in safeguarding the brain against neurodegenerative diseases (Figure 2). Flavonoids, particularly catechins like EGCG, are praised for their potent antioxidant properties, which help reduce oxidative stress—a key factor in neurodegeneration (Zhang *et al*., 2020). Furthermore, these compounds possess anti-inflammatory effects that can mitigate neuroinflammation by inhibiting pro-inflammatory cytokines and affecting signaling pathways vital for neuronal health (Rana *et al*., 2022). Terpenoids present in tea have been associated with enhanced cognitive function and protection of neurons from apoptosis by promoting the production of neurotrophic factors (Ali *et al*., 2021). Additionally, phenolic compounds contribute to these protective mechanisms by neutralizing free radicals and binding metal ions, thereby preventing oxidative damage to nerve cells (Nobahar *et al*., 2021). Alkaloids, including caffeine, also play a role in neuroprotection by boosting neurotransmitter activity.

Tea polyphenols are linked to numerous significant health benefits, including:

Antioxidant activity

The polyphenolic compounds in tea, particularly catechins, exhibit strong antioxidant effects, scavenging free radicals and mitigating oxidative stress (Chu KO *et al*., 2011).

Anti-inflammatory effects

The bioactive components in tea have been linked to anti-inflammatory responses, potentially mitigating chronic inflammation associated with various diseases (Zhao CN *et al*., 2019)

Cardiometabolic benefits

Research suggests that tea consumption may contribute to cardiovascular health by positively impacting lipid metabolism blood pressure regulation, and reducing the risk of atherosclerosis (Arab L *et al*., 2009).

Antioxidants in tea

Tea is high in antioxidant potential and capable of slowing down, preventing, or eliminating oxidative damage to a target molecule (Halliwell B *et al*., 2007). In simpler terms, an antioxidant is described as "any substance that, when found in lower concentrations compared to an oxidizable substrate, slows down or hinders the oxidation process of that substrate" (Rosenblat M *et al*., 2006). Antioxidants encompass phytochemicals, vitamins, and nutrients that shield our cells from harm caused by free radicals. They possess the ability to stabilize or deactivate free radicals, preventing them from damaging cells (Chib *et al*., 2020). Tea is renowned for its rich content of antioxidants, essential compounds that help protect our cells from damage caused by free radicals (Figure 3). The subclasses of antioxidants found in tea include catechins, theoflavins, thearubigins, flavonoids, and L-theanine. Catechins, prominent in green tea, are potent antioxidants known for their ability to combat oxidative stress and potentially reduce the risk of chronic diseases (Cabrera *et al*., 2006). Theoflavins, a subgroup derived from catechins during fermentation, contribute to the antioxidant profile of black tea (Henning *et al*., 2003). Thearubigins, responsible for the dark color and robust flavor of black tea, also possess antioxidant properties (Friedman *et al*., 2007). Additionally, L-theanine, an amino acid unique to tea, has been associated with antioxidant and neuroprotective properties (Kakuda *et al*., 2000). The combined action

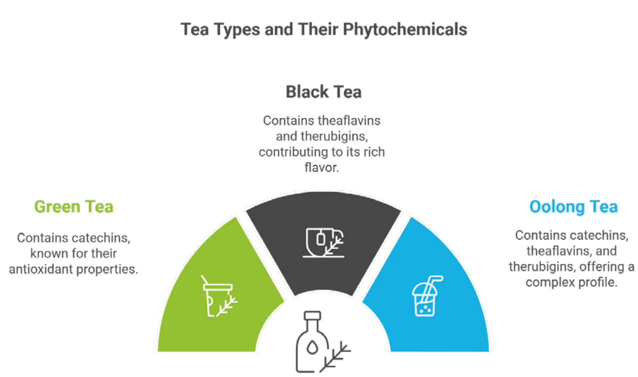

Figure 2: Phytochemicals in different types of teas

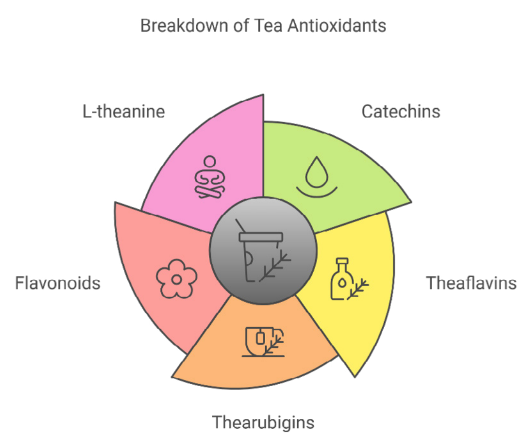

Figure 3: Subclass of antioxidants in tea

of these antioxidant subclasses in tea underscores its potential health benefits. This is also stabilized that regular consumption of tea has been linked to reduced oxidative stress, inflammation, and a lower risk of chronic diseases (Arab *et al*., 2003).

Tea phenolic compounds

Plants use the shikimic acid pathway to produce phenolic chemicals, which are integral secondary metabolites. Alternatively, phenylpropanoid metabolization occurs via the pentose phosphate pathway (Randhir *et al*., 2004). These compounds, characterized by benzene rings and one or more hydroxyl substituents, exhibit a wide spectrum from simple phenolic molecules to highly polymerized compounds (Velderrain-Rodríguez G.R *et al*., 2014). Among the major bioactive constituents in plant leaves are phenolic acids, terpenoids, flavonoids, alkaloids, tannins, and phytosterols (Figure 4) (Vastrad *et al*., 2014). The abundance of various phenolic compounds in tea leaves is well-known, and these compounds change in concentration and type with the age stage of the leaves (Tan *et al*., 2017). Tea, renowned for its numerous health benefits, possesses antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic effects with regular consumption, all attributed to its rich phenolic compound content (Vastrad *et al*., 2021). As a result, tea phenolics are acknowledged for hosting valuable phytochemicals and have become the focus of considerable attention (Yang *et al*., 2013).

Catechins, comprising epigallocatechin-3-gallate (EGCG), epigallocatechin, epicatechin-3-gallate, epicatechin, gallocatechins, and gallocatechin gallate, stand as the primary polyphenolic compounds in tea (Khan N *et al*., 2018). Beyond catechins, tea is abundant in various phenolic compounds, each contributing to its diverse health benefits: Theaflavins significantly contribute to the antioxidant properties and distinctive characteristics of black tea (McKay *et al*., 2002). Thearubigins, on the other hand, play a pivotal role in defining the sensory attributes of black tea (Balentine *et al*., 1997). Flavonols, including epicatechin and epicatechin gallate, are vital contributors to the antioxidant capacity of tea (Rietveld *et al*., 2003). These diverse phenolic compounds in tea collectively underscore its potential as a health-promoting beverage.

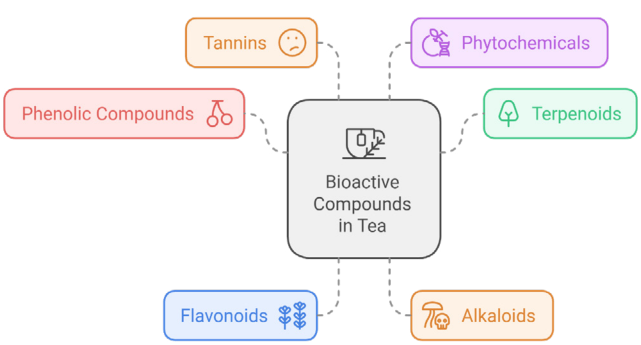

Figure 4: Bioactive compounds present in tea

Tea flavonoids

Tea is also a good source of flavonoids. Flavonoids, a prominent category of natural compounds, are characterized by a polyphenolic structure and serve as essential plant secondary metabolites. Abundant in fruits, vegetables, and beverages, they are particularly rich in tea (Panche *et al*., 2016). These phenolic compounds, known as flavonoids, stand out as the most abundant and diverse non-nutrient bioactive constituents in foods, with tea being a notable source (Dwyer JT *et al*., 2013). Flavonoids are regarded as dietary components with health-promoting qualities because of their high potential for antioxidants in both *in-vitro* and *in-vivo* systems (Cook NC *et al*., 1996). Widely distributed in the plant kingdom, flavonoids can be categorized into six classes based on the structure of the heterocyclic oxygen ring, including flavones, flavanones, isoflavones, flavonols, flavonols, and anthocyanins (H. Wang *et al*., 2000) (Table 3; Figure 5). The therapeutic significance of flavonoids found in tea is noteworthy, encompassing activities such as anticarcinogenic, antimicrobial, antiviral, anti-arteriosclerosis, antihypertensive, antidiabetic, anti-inflammatory, and antidiuretic properties (Bansode 2015). Green tea contains primary flavonoids called catechins, including epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), and epigallocatechingallate (EGCG) (Hodgson *et al*., 2010). However, during the production of black tea, catechins undergo oxidation, leading to condensed flavonoids like theaflavins and thearubigins (55). The health benefits of flavonoids extend to mitigating age-related neurodegenerative diseases, including dementia and Parkinson's disease (Nakajima A *et al*., 2014; Datla K.P *et al*., 2001; Gao X *et al*., 2012). Consumption of flavonoids through tea is associated with various health benefits, making them valuable natural compounds (Nakajima A *et al*.., 2014; Datla K.P *et al*., 2001; Gao X *et al*., 2012). Flavonoids are further divided into subclasses-viz., flavonols, flavanones, flavon 3-ol etc (Table 3).

Flavonols

Flavonols, a specific subtype of flavonoids characterized by a ketone group, play a vital role as fundamental building blocks for proanthocyanins and are abundant in a diverse range of fruits and vegetables. Tea, notably green

Table 3: Tea flavonoids and their sources

S. No.	*Flavonoid*	*Source*	*References*
1.	Flavonols	Fruits, vegetables, tea	(Lopez M *et al*., 2001)
2.	Flavanones	Citrus fruits, aromatic plants	(Panche *et al*., 2016)
3.	Flavon 3-ol	Apples, tea	(Shi *et al*., 2023)
4.	Anthocyanin	Fruits and vegetables	(He *et al*., 2010)
5.	Isoflavones	Legumes	(Li *et al*., 2019)

tea, is recognized as the primary source and exclusive dietary reservoir for flavonols, featuring notable members like catechin, epicatechin, and epigallocatechin (Lopez M *et al*., 2001). Previous research highlights the substantial flavonol content in tea, especially in green tea (Smith A *et al*., 2022). The antioxidant properties of tea flavonols have been emphasized in studies, showcasing their critical role in neutralizing free radicals and potentially reducing the risk of chronic diseases (Johnson C, *et al*., 2018). Moreover, flavonols have demonstrated links to cardiovascular health, influencing endothelial function and blood pressure regulation (White D *et al*., 2020). The process involves the fermentation process that leads to making black tea. In black tea, the oxidation process leads to the formation of distinctive flavanol compounds, such as theaflavins and thearubigins, contributing to the unique flavor and characteristics of black tea (Lee E, *et al*., 2017).

Flavanones

Flavanones, a significant class found in citrus fruits like oranges, lemons, and grapes (Panche *et al*., 2016), as well as in specific aromatic plants (Claudine Manach *et al*., 2004), are also recognized as 2-arylchroman-4-ones. The flavonoid route produces them and involve the use of chalcone-flavanone isomerase to help in the isomerization of 2′,4′,6′,4-tetrahydroxychalcone. These compounds are distributed among various plant families, including Compositae, Fabaceae, and Rutaceae (Dias *et al*., 2021; Pietta *et al*., 2003; Brahmachari *et al*., 2008). Like other flavonoids, flavanones exhibit potential health benefits, with studies suggesting anti-inflammatory and antioxidant properties. Tea is also rich in flavanones, imparting health benefits, including antioxidant properties to the consumers (Alexander *et al*., 2019)

Flavon 3-ol

Tea contains a good quantity of flavon 3-ol and the amount varies with varieties as well as the age of leaves and climatic conditions for tea cultivation (Shi *et al*., 2023). Flavan-3-ols, a subset of bioactives with noteworthy implications for health, stand out as promising candidates in the formulation of dietary recommendations (Gunter G.C *et al*., 2018). Synthesized along the flavonoid pathway, the biosynthesis of these compounds involves key enzymes such as dihydroflavonol 4-reductase and flavan-3-ol synthase (Ferreyra *et al*., 2012). Widely dispersed across plant families, including Rosaceae, Theaceae, and Rosaceae (Robinson MJ *et al*., 2017), flavan-3-ols contribute significantly to the intricate polyphenolic profile of various botanicals. As one of the most frequently consumed types of flavonoids, flavan-3-ols are present in a diverse array of foods (Otaki *et al*., 2009). Notably, in cultures where tea holds prominence, it serves as the primary source of total flavan-3-ol intake (Otaki *et al*., 2009). Aligned with the broader category of flavonoids, flavan-3-ols are acknowledged for their potential to promote health and well-being.

Anthocyanins

Tea is rich in anthocyanins, and it has been found that the anthocyanin content of green tea is considerably greater than that of black tea (Yousuf *et al*., 2016). Anthocyanin, classified as water-soluble pigments within the flavonoid category, is accountable for the vibrant red, purple, and blue hues observed in a variety of fruits, vegetables, and flowers (He *et al*., 2010). Distinguished by their characteristic 3-ring structure, known as the flavylium cation, anthocyanins undergo diverse structural modifications that impact both their color spectrum and antioxidant capabilities (Kong *et al*., 2003). These compounds are present in a range of plant sources, encompassing fruits, vegetables, flowers, and leaves, with variations in content and composition across different plant species (Wallace *et al*., 2011). Like other flavonoids, anthocyanins have been linked to potential health benefits, specifically in terms of antioxidant and anti-inflammatory properties. Such attributes may contribute to their positive impact on cardiovascular health (Cassidy *et al*., 2019). Beyond their role as antioxidants, anthocyanins have demonstrated potential anticancer effects and neuroprotective activities, underscoring their multifaceted contributions to promoting health (Zafra-Stone *et al*., 2007).

Isoflavones

Tea isoflavones are found to be effective in retarding many cell-related diseases, including cancer (Umeno *et al*., 2016). Derived from plants, isoflavones are natural compounds classified as "phytoestrogens" due to their structural resemblance to estrogen (Setchell KD *et al*., 1999). With a distinctive 3-phenylchromen-4-one core scaffold adorned with hydroxyl and methoxyl substituents, isoflavones are notably present in legumes, particularly soybeans, constituting a vital component of many diets (Li *et al*., 2019). Trace amounts of isoflavones are also found in select teas like rooibos and red clover (Kumar *et al*., 2020). In addition to their widespread presence in legumes, studies have suggested that isoflavones, akin to other flavonoids, offer notable health benefits (Messina *et al*., 2010). Particularly intriguing is their potential role in mitigating menopausal symptoms such as hot flashes, possibly attributed to their mild estrogenic activity (Davis *et al*., 2017). As documented in research, the paper "Health Benefits of Isoflavones: A Review" (Smith *et al*., Journal of Nutritional Science, 2019) underscores the significance of these plant-derived compounds in promoting well-being. Embracing isoflavone-rich sources in one's diet may thus contribute to a spectrum of health advantages (Figure 5).

Tea tannins

The bitter taste of tea after strong boiling may be due to the presence of tannins (Soares *et al*., 2020). Tannins,

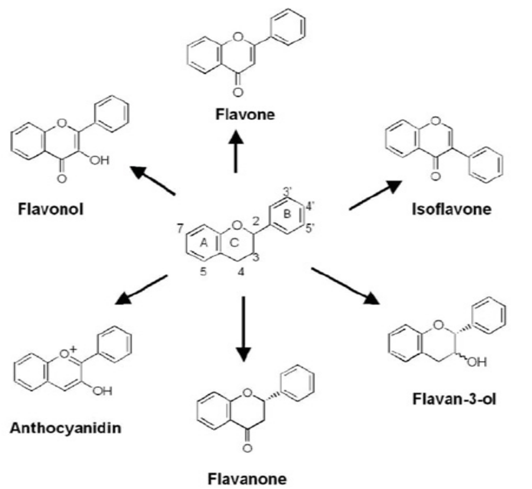

Figure 5: Chemical structures of different tea flavonoids

also known as tannic acid, possess a molecular formula typically expressed as C27H24O18 and are water-soluble astringent, bitter polyphenolic compounds with high molecular weight. They are naturally found in the vacuoles or surface wax of various parts of both edible and non-edible plants (Basher *et al*., 2021). Exhibiting amorphous masses with a yellowish to light brown hue, tannins display powdery, flaky, or spongy characteristics and stand as the most prevalent antioxidants in human diets. Common dietary sources of tannins include fruits, vegetables, and green tea (R. Masella *et al*., 2005) (X. Han *et al*., 2007). The tannins present in black tea, such as theaflavins, demonstrate robust antioxidant and anti-inflammatory properties, potentially reducing the risk of chronic diseases (Cao *et al*., 2015). Green tea, distinguished by its unique combination of tannins like EGCG and catechins, showcases synergistic antioxidant and anticancer properties (Saito M *et al*., 2005). These findings underscore the diverse health benefits associated with tannins, highlighting their potential role in promoting well-being and preventing chronic diseases.

Tea phenolic acids

Phenolic acids, categorized as tea polyphenols, constitute approximately 5% of the dry weight of fresh tea leaves. Noteworthy phenolic acids such as gallic acid (GA), chlorogenic acid (CGA), and caffeic acid (CA) contribute to a sour and astringent taste, intensifying with higher phenolic acid concentrations (Robichaud *et al*., 2010) (Kaneko *et al*., 2006). Derived from caffeic acid, chlorogenic acids (CGA) dominate the phenolic fraction in green coffee beans (Das *et al*., 2016). Tea boasts a notable abundance of gallic acid derivatives, and phenolic acids like gallic and caffeic acid serve as potent antioxidants in tea, actively scavenging free radicals and offering protection against oxidative stress (Yan Z *et al*., 2020). Additionally, these remarkable molecules showcase anti-inflammatory properties, potentially mitigating chronic inflammation associated with various diseases (Joubert *et al*., 2012). The presence of phenolic acids in tea not only contributes to its distinctive taste but also offers significant health benefits, acting as powerful antioxidants and demonstrating potential anti-inflammatory effects.

Tea lignans

Lignans, prevalent natural products widely distributed in the plant kingdom, share identical monomers with lignin, constituting phytoestrogens with either estrogenic or antiestrogenic activity, primarily composed of 2-phenylpropane units (Jean-Louis *et al*., 2017). Key dietary lignans such as matairesinol, secoisolariciresinol, pinoresinol, and lariciresinol are prominent in plant-based foods, notably in various vegetables, fruits, legumes, whole grain cereals, and oilseeds (Durazzo A *et al*., 2013; Durazzo A., Turfani V *et al*., 2013). Tea and coffee also contribute to smaller amounts of lignans in the diet. These bioactive compounds, lignans, showcase a spectrum of biological properties encompassing anti-inflammatory, antioxidant, and antitumor activities (Ionkova I *et al*., 2011). Some epidemiological studies have suggested a potential reduction in the risk of cardiovascular disease associated with lignan consumption. However, their effects on other chronic diseases, such as breast cancer, remain a subject of controversy (Peterson J *et al*., 2010). The intricate role of lignans in human health continues to be a topic of research and debate. Further studies are needed to elucidate the full range of their effects on various chronic conditions.

Tea quinones

Quinones, a diverse class of quinoid compounds, are extensively distributed in nature, with over 1,200 described members. Their common structural pattern involves an ortho or para-substituted dione conjugated to either an aromatic nucleus, known as benzoquinones, or a condensed polycyclic aromatic system (Ahmed S *et al*., 2007; Ahmed S *et al*., 2009). Tea, a well-known source of quinones, showcases their influence on its distinct characteristics. In black tea, the amber hues are attributed to quinones formed during leaf processing and their oxidation is further intensified by the addition of sugar (Chen *et al*., 2009). Conversely, green tea, while lacking prominent quinones, undergoes enzymatic conversions leading to the formation of theaflavins in black tea, contributing to its unique color and antioxidant properties (Yamamoto *et al*., 2001). Beyond their role in coloration, quinones in black tea have been associated with potential anti-inflammatory and neuroprotective effects. However, it is essential to note that further research is required to substantiate these specific health benefits in humans (Suzuki *et al*., 2012; Wang *et al*., 2003).

Tea stilbenes

Natural stilbenes, a group of polyphenols distinguished by the presence of a 1,2-diphenylethylene nucleus, encompass over 400 known compounds (T. Shen *et al*., 2009; V. *et al*., 2012). Among these, resveratrol (3,5,4′-trihydroxy-trans-stilbene) stands out as a well-known polyphenol phytoalexin, primarily located in the skin of grapes (Reinisalo M *et al*., 2015). Stilbene compounds are widespread in various plant species, including grape wine (*Vitis vinifera*), peanut (*Arachis hypogaea*), sorghum (*Sorghum bicolor*), and numerous tree species (Parage C *et al*., 2012). While commonly associated with grapes and berries, trace amounts of resveratrol and its glucoside have been identified in Japanese Itadori tea, presenting a potential alternative source for this stilbene (Tsuda *et al*., 2005). Noteworthy stilbenes include pterostibene, piceatannol, and pinosylvin (Sirerol JA *et al*., 2015). The presence of trace amounts of resveratrol and its glucoside in Japanese Itadori tea suggests potential anti-inflammatory properties; however, further research is imperative to validate their specific health benefits in this context (Tsuda *et al*., 2005).

Tea carotenoids

Carotenoids, vibrant yellow pigments abundantly present in fresh leaves, undergo degradation during tea manufacture, giving rise to the formation of terpenoid flavor compounds in black tea. This class of lipophilic pigments, found in plants, can be categorized into two major subclasses: carotenes and xanthophylls, each characterized by distinct biosynthetic pathways and accumulation patterns across various horticultural crops (Yuan *et al*., 2015). Crucial to the formation of tea aroma during processing, certain carotenoids serve as decisive factors influencing tea quality (Ho C.-T *et al*., 2015). Tea cultivars exhibit differentiation in their carotenoid profiles, with β-carotene and lutein identified as the major carotenoids in tea plants, collectively constituting more than half of the total carotenoid content (Jiang Shi *et al*., 2023). Carotenoid-rich teas enjoy preference among consumers due to their enhanced visual appeal, flavor, and perceived health benefits (Baker & Günther, 2004). Research suggests that diets rich in carotenoids may be linked to reduced risks of cardiovascular diseases, diabetes, and certain cancers (Stahl W *et al*., 2005).

Antioxidant properties

Tea stands as a remarkable source of bioactive compounds, particularly polyphenols, with flavonols such as catechins, (+)-catechin, (−)-epicatechin (EC), (−)-epicatechin-3-gallate (ECG), (−)-epigallocatechin (EGC), and (−)-epigallocatechin-3-gallate (EGCG) playing a pivotal role in various biological functions, notably antioxidant activities (Carloni P *et al*. 2013; Henning SM *et al*., 2003). Among the array of plant phenols, tea catechins emerge as the most potent antioxidants (Henning SM *et al*., 2003).

The antioxidant activity of tea exhibits variation, with research suggesting a descending order as follows: green tea > oolong > black tea (Khokhar S *et al*., 2002). However, conflicting findings are present in the literature, with some authors proposing higher antioxidant activity in black tea than green tea, while others report no significant differences (El-Moneim A *et al*., 2011). Moreover, the method of tea preparation plays a crucial role in influencing its antioxidant properties. Factors such as brewing time and temperature significantly impact the antioxidant capabilities of tea. It is evident from various studies that tea, through its diverse polyphenolic components, does possess antioxidant properties, contributing to its overall health benefits.

Neuroprotective potential

Tea, a globally popular beverage consumed in over 160 countries, is renowned for its rich composition of polyphenols, theanine, caffeine, and other natural bioactive components, contributing significantly to its taste and flavor (Kuroda K *et al*., 2005). Over the past decade, numerous studies have highlighted the neuroprotective functions of tea, with bioactive components such as tea polyphenols, theanine, caffeine, and theaflavins demonstrating neuroprotective effects (Molino S *et al*., 2016). Among these, tea polyphenols emerge as potent bioactive compounds with neuroprotection and neuromodulation capabilities, largely attributed to their robust antioxidant properties. Research conducted in both *in-vivo* and *in-vitro* settings, particularly in Parkinson's disease (PD) or Alzheimer's disease (AD), has substantiated the neuroprotective effects of tea polyphenols through their antioxidative properties (Chen SQ *et al*., 2018). Additionally, the volatile compounds produced by tea during Maillard reactions have shown potential in decreasing brainwave distribution, relieving stress, and inducing sedative effects, although the underlying mechanisms remain unclear (Zhou L.X *et al*., 2016).

Consistent findings from numerous cohort studies further reinforce the association between tea consumption and a reduced risk of cognitive impairment (Kandinov B *et al*., 2009). A specific study involving 278 PD patients revealed that consuming more than 3 cups of tea per day was linked to a remarkable delay in the onset of PD by 7.7 years (Kandinov B *et al*., 2009). In summary, tea's neuroprotective effects, particularly in diseases like AD and PD, underscore its potential as a beneficial beverage for brain health.

Alzheimer's disease

Alzheimer's disease (AD) represents a predominant neurodegenerative condition, accounting for approximately two-thirds of all dementia cases and

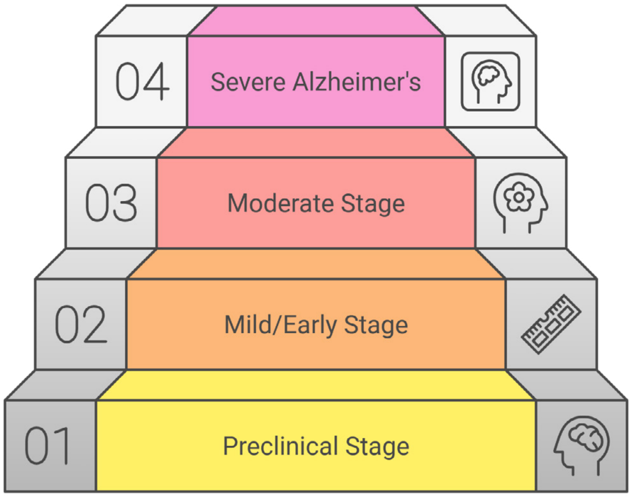

Figure 6: Different stages of Alzheimer's disease

affecting about 20% of individuals aged over 80 years (Cipriani G *et al.*, 2010) (Figure 6). Named by Emil Kraepelin in his 8th edition psychiatry handbook, AD is characterized by progressive deficits in memory, cognitive impairment, and behavioral changes leading to dementia (Cipriani G *et al.*, 2010). Presently, there is no cure for Alzheimer's disease, with available treatments focusing on symptom improvement (Yiannopoulou K.G *et al.*, 2020) (Livingston G *et al.*, 2020). Neuropathological changes in AD encompass positive lesions marked by neurofibrillary tangles, amyloid plaques, and other deposits, as well as negative lesions resulting from neural, neuropil, and synaptic loss (De-Paula V.J *et al.*, 2012).

The clinical stages of Alzheimer's disease include a pre-clinical stage with mild memory loss and early brain changes, devoid of functional impairment or clinical signs (De-Paula V.J *et al.*, 2012; Dubois B *et al.*, 2016). The mild or early stage involves difficulties in daily life, loss of concentration, memory issues, disorientation, mood changes, and depression emergence (Kumar A *et al.*, 2020; Wattmo C *et al.*, 2016). In the moderate stage, the disease extends to cerebral cortex areas, causing heightened memory loss, difficulty recognizing family and friends, loss of impulse control, and challenges in reading, writing, and speaking (Kumar A *et al.*, 2020). Severe Alzheimer's affects the entire cortex, leading to significant plaque and tangle accumulation, progressive decline, and eventual death due to complications (De-Paula V.J *et al.*, 2012).

AD is considered multifactorial, with risk factors including age, genetics, cardiovascular health, lifestyle, head injuries, and sleep disturbances (Barnes *et al.*, 2011; Corder *et al.*, 2021). Substantial epidemiological evidence links tea consumption to a reduced risk of AD and other neurodegenerative conditions, and a study used tea preparation to evaluate action-based memory in individuals with AD dementia (Rusted J *et al.*, 2002). Regular tea consumption is frequently associated with a reduced risk of mild cognitive impairment, cognitive decline, and related conditions in the elderly (Rusted J *et al.*, 2002).

Parkinsons disease

Parkinson's disease (PD) is a progressively neurodegenerative condition primarily linked to a dopamine deficiency in the brain. Dr. James Parkinson coined the term "shaking palsy" in 1817 during its initial description. The manifestation of PD symptoms typically occurs after a substantial loss of dopaminergic neurons, around 70 to 80% (El-Agnaf, O *et al.*, 2006).

The spectrum of PD symptoms encompasses motor impairments like tremors, bradykinesia, rigidity, and postural instability (Jankovic *et al.*, 2008). Alongside these, non-motor symptoms such as cognitive decline, mood disorders, and autonomic dysfunction often accompany motor symptoms, adding to the disease's complexity (Chaudhuri *et al.*, 2009).

Parkinson's disease progresses through stages marked by specific symptoms and functional impairments. In the early stages, individuals may experience mild motor symptoms, often on one side of the body (134). As the disease advances, symptoms intensify, affecting both sides and increasing the risk of falls due to postural instability (Goetz *et al.*, 2008).

Current treatments focus on symptom alleviation and enhancing the patient's quality of life. The gold standard pharmacological intervention involves levodopa, a dopamine precursor, along with dopamine agonists and monoamine oxidase-B inhibitors (Connolly *et al.*, 2014). Surgical intervention, particularly deep brain stimulation (DBS), has proven effective in providing relief, especially in advanced cases (Weaver *et al.*, 2009).

Exploring potential preventive measures, several studies suggest a correlation between tea consumption and a reduced risk of developing Parkinson's disease. Polyphenolic compounds in tea, including catechins and theaflavins, exhibit antioxidant and neuroprotective properties, potentially mitigating the neurodegenerative processes associated with PD (Tan *et al.*, 2017; Chuang *et al.*, 2018). Research indicates that these effects may involve the modulation of cellular signaling pathways and the inhibition of oxidative stress implicated in PD pathogenesis (Chuang *et al.*, 2018; Weinreb *et al.*, 2004). Notably, epigallocatechin gallate (EGCG), a major catechin in tea, has garnered interest for its potential anti-inflammatory and anti-aggregation effects on alpha-synuclein, a protein linked to PD pathology (Levites *et al.*, 2001).

Conclusion

One of the most widely consumed drinks in the world, tea contains several bioactive chemicals that may have positive health effects. Secondary metabolites, or phenolic molecules having one or more aromatic rings holding hydroxyl, are the main bioactive components of tea. The use of tea as an antioxidant and for other health benefits has increased in recent years. Every year, a great deal of research and studies are conducted and provide comprehensive information on the production, use, and cultivation of tea. The health benefits of tea and how helpful it is for numerous lifestyle diseases. The authors wish to examine the research on tea and its nutritional benefits in neuroprotective diseases.

Tea is super popular worldwide, not just because it is culturally important but also because it might be good for your health. It is filled with special chemicals, especially phenolic molecules, which make it a drink with lots of different benefits. People are using tea more and more because it has things that can protect you from harm and keep you healthy. We are learning more about what is in tea every year as researchers study how it's made, used, and grown. But in this review, we are looking specifically at how tea might help with diseases that affect the brain. We are checking out the research on tea and its health benefits, focusing on how it could keep our brains safe and sound. As we dig into how the chemicals in tea work to protect our brains, it is not just something for scientists to talk about. This exploration is exciting because it can help us figure out how to use tea to prevent and treat brain problems. The teamwork between the special chemicals in tea and the ways they protect our brains, as discussed in this review, shows that tea could be a good thing for keeping our brains healthy.

Conflict of Interest

There is no conflict of interest.

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