White Tea (Camellia Sinensis (L.)): Antioxidant Properties And Beneficial Health Effects


Abstract

Tea is one of the most widely consumed beverages in the world, next to water. It can be categorized into three major types, depending on the level of fermentation, i.e., green and white (unfermented), oolong (partially fermented) and black (fermented) tea. Each type of tea has a distinct composition, dependent on how the leaves are processed, as well as maturation, geographical location and agricultural practices. White tea (WT), the least processed tea, is one of the less studied and is ascribed to have the highest content of phenolic compounds. Tea polyphenols, especially catechin derivatives, are potent antioxidant agents, with positive effects on human health. Antioxidant components have aroused great interest because of their ability to scavenge free radicals, thereby inhibiting oxidative stress. During the past years, oxidative damage induced by reactive species has been linked to the development of several human diseases such as cardiovascular diseases, diabetes mellitus, neurodegenerative disorders and certain types of cancer. Therefore, tea antioxidants may be of great value in preventing the onset and/or the progression of oxidative stress mediated diseases, when endogenous defences are insufficient against reactive species. The possible beneficial health effects of WT are being investigated and have received considerable attention in recent years. In this review, we aim to explore the new findings concerning WT effects on health.

Keywords: White tea; Camellia sinensis; Polyphenols; Catechins; Antioxidants; Free radicals.

Introduction

Tea is one of the most widely consumed beverages in the world, next to water [1,2] with a per capita consumption of ~120 mL/day [3]. This popularity is probably related withits sensorial properties, relatively low retail price, stimulating effects and potential health benefits [4,5]. Despite tea is largely drunk for pleasure, its medicinal effects have been widely investigated, having a long, rich history with its first references nearly 5,000 years ago [6]. Tea is prepared as an infusion with the leaves of Camellia sinensis (L.), a plant cultivated in over 30 countries across the world that belongs to the Theaceae family [7]. There are two main varieties of tea plants: C. sinensis var. sinensis, a small-leaved, bushlike plant indigenous from China, which grows in several countries of Southeast Asia experiencing a cold climate, and C. sinensis var. assamica, a large-leaved tree discovered in the Assam region of India which grows in several countries with a semitropical climate [8]. There are different types of tea depending on botanical varieties, geographical origin and processing [8]. Concerning to the level of “fermentation”, it can be categorized into three major types: not fermented (green and white tea), partially fermented (oolong tea) and completely fermented (black tea). Although this process is often assumed, incorrectly, to be fermentation, the most correct term should be oxidation (frequently followed by polymerization), which means exposure to air[9] and is a reaction catalyzed by the enzyme polyphenol oxidase [3]. To produce green tea (GT), the leaves are rolled and steamed to minimize oxidation and inactivate polyphenol oxidase prior to drying (Figure 1) [3]. In black tea production, after the leaves are rolled, which disrupts cellular compartmentation and brings phenolic compounds into contact with polyphenol oxidases, they undergo oxidation for 90–120 min [10]. Oolong tea is produced with a shorter “fermentation” period than black tea and has a taste and color somewhere between green and black teas [11]. White tea (WT) is prepared from very young tea leaves or buds covered with tiny, silvery hairs, which are harvested only once a year in the early spring [10]. The buds may be shielded from sunlight during growth to reduce the formation of chlorophyll, giving the young leaves a white appearance [12]. In WT production, plant materials are steamed and dried immediately after picking to prevent oxidation, giving it a light and delicate taste [10]. According to Almajano et al., it is one of the less studied teas but its flavor is more accepted in Europe than that of GT [13].

Although health benefits have been attributed to tea consumption since the beginning of its history, scientific investigations of this beverage and its constituents have been underway for less than three decades. Tea contains several bioactive compounds that are believed to have a wide range of physiological proper-
ties, including being stimulants [14] and antidepressants [15], anti-inflammatory [16-18], antioxidant [19-22], antiatherosclerotic [23], antihypertensive [24], anti-infectious diseases [25], antimutagenic [26,27], anticarcinogenic and anticancer promoting [28-30] antimicrobial [31,32], hypolipidemic [33,34], hypocholesterolemic [35], neuroprotective [36], and antidiabetic agents [37,38], as well as improving immune responses[39,40] in several studies. Despite many of these physiological mechanisms are associated with the chemical properties of polyphenols and their healthy antioxidant effects, they are still controversial [13,41]. In spite of numerous data about the phenolic constituents, antioxidant activity and ameliorating effects of green and black tea on human health, little is known in this sense about WT, which is the rarest and the least characterized. The possible beneficial health effects of WT are being investigated and have received a great deal of attention in recent years. The purpose of this review is to bring together the most recent scientific information about the properties of WT and their physiological effects.

White tea chemical composition

The chemical composition of tea leaves has been thoroughly studied. The main constituents of tea include proteins, polysaccharides, polyphenols, minerals and trace elements, amino and organic acids, lignins, and methylxanthines (caffeine, theophylline, and theobromine) [42-43]. Apart from the energizing effect due to methylxanthines such as caffeine, phenolic compounds have received immense attention among tea phytochemicals, in particular flavonoids class [44]. Flavonoids are phenolic derivatives synthesized in substantial amounts (0.5 to 1.5%) that are widely distributed among plants [45] and have unique biological properties that may be responsible for many of the health benefits attributed to tea [46]. Over 4000 different flavonoids have been described, and they are categorized into flavonols, flavones, catechins, flavanonols, anthocyanidins and isoflavonoids [47]. The major phenolic compounds present in tea leaves are catechins (also known as flavan-3-ols) and their derivatives, which constitute up to 30% of their dry weight. The main catechins present in WT are: (-)-epicatechin (EC), (-)-epicatechin 3-gallate (EGC), (-)-epigallocatechin (EGC), collectively known as flavon monomers, (-)-epicatechin 3-gallate (ECG), and (-)-epi-gallocatechin 3-gallate (EGCG) (Figure 2), which are flavanol gallates [8,41]. EC has an ortho-dihydroxyl group in the B-ring at carbons 3’ and 4’ and a hydroxyl group at carbon 3 on the C-ring (Figure 2). Differently of EC, EGC has a trihydroxyl group at carbons 3’, 4’, and 5’ on the B-ring, while ECG has a gallate moiety esterified at carbon 3 of the C-ring and EGCG has both a trihydroxyl group at carbons 3’, 4’, and 5’ on the B-ring and a gallate moiety esterified at carbon 3 on the C-ring (Figure 2) [48]. EGCG is the most abundant catechin in tea leaves, representing 50–80% of the total catechins, and is thought to contribute to the beneficial effects ascribed to tea [49,50]. The oxidation by polyphenol oxidase during processing leads to the formation of catechins and gallic acid complexes such as theaflavins, theaflavonic acids, thearubigins and proanthocyanidin polymers [51,52]. Theaflavins, which have higher molecular weights, are poorly chemically characterized. Theaflavins are characterized by the benzotropolone ring structure and bright red-orange color, and contribute to the unique taste of black tea [50]. A typical tea beverage, prepared in a proportion of 1 g of dried leaves to 100 ml water in a 3-min brew, usually contains 250–350 mg tea solids, comprised of 30–42% catechins and 3–6% caffeine [53]. Tea also contains small amounts of flavonol (kaempferol, quercetin and myricitin) in the form of glycosides [52]. Other bioactive compounds found in tea are gallic, p-coumaric and caffeic acids [42]. Tea also contains many amino acids, but L-theanine (γ-glutamylethylamide), specific to the tea plant, is the most abundant, accounting for 50% of the total amino acids [54]. It is a free amino acid and is thought to be a flavourous constituent of tea leaves. It constitutes between 1 and 2% of the dry weight of tea [55]. Chlorophylls, carotenoids, lipids, and volatile compounds are not major constituents in a tea brew but they play an important role in the development of the aroma [54].

Each type of tea has a distinct composition. The relative catechins content of tea is dependent on how the leaves are processed prior to drying, as well as geographical location and growing conditions [3]. The flavonoid concentration also depends upon the type of tea (e.g., blended, decaffeinated, instant) and preparation (e.g., amount used, brew time, temperature)[3]. Highest concentrations of flavonoids are found in brewed hot tea (541-692 μg/mL) [56].
Figure 2. Chemical structures of the main white tea catechins. The figure illustrates two phenolic rings (A- and B-rings), the dihydropyran heterocycle (C-ring), with a hydroxyl group on carbon 3 and the gallate group. EC: (-)-epicatechin; EGC: (-)-epigallocatechin; ECG: (-)-epicatechin 3-gallate and EGCG: (-)-epigallocatechin 3-gallate.

less in instant preparations (90-100 µg/mL) and lower amounts in iced and ready-to-drink tea [57]. According to the formation process it was reported that WT contains relatively high concentrations of catechins and low concentrations of theaflavins and thearubigins (Figure 1). Otherwise, the flavonol content in tea is less affected by processing, being present in comparable amounts in all teas [52]. Some reports showed that the concentrations of total polyphenols, total catechins, caffeine, gallic acid, theobromine, EGC, ECG and EGCG are significantly higher in the WT compared to GT [58,59]. Thus, the possible increased antioxidant activity of WT could be related to higher concentrations of several of the major constituents [59]. However, there are studies reporting that GT is a richer source of polyphenols than WT [10]. So, due to the contradictory studies reported in this field, it seems that the phenolic content is not an ideal criterion of differentiation between GT and WT.

Antioxidant potential of white tea and associated health benefits

In recent years, antioxidant components have aroused great interest because of their ability to scavenge free radicals, thereby inhibiting oxidation [60,61]. Most living organisms possess efficient enzymatic and non enzymatic defense systems against excess production of reactive oxygen and nitrogen species (RONS). However, different external factors (smoke, diet, alcohol, some drugs) and aging decrease the capability of such endogenous antioxidant defences, resulting in disturbances of the redox equilibrium that is established in healthy conditions [46,62]. Chronic exposure to RONS can damage DNA, membrane lipids, lipoproteins, and functional and structural proteins [63,64]. As during the past years, RONS-induced oxidative damage has been linked to the development of several human diseases such as cardiovascular diseases, diabetes mellitus, chronic inflammation, neurodegenerative disorders and certain types of cancer [65,66], its reduction is seen as beneficial to public health. Therefore, antioxidants that scavenge RONS may be of great value in preventing the onset and/or the progression of oxidative diseases [62]. Tea polyphenols, especially catechin derivatives, are considered to be potent antioxidant agents, with a particularly important role in protecting against these deleterious diseases [13]. So, teas could be taken as a good complement to antioxidants intake in the human diet [67].

The knowledge of pharmacokinetics, absorption, distribution, metabolism, and excretion of tea components is essential to determine its potential bioactivities and overall significance in disease prevention [6]. Despite the proven antioxidant capacity of tea polyphenols, many clinical studies and animal models have shown that these compounds, especially the polymers, esters, and glycosides, are abundant, but are not always absorbed by oral administration. The functional effect of the compound depends not only on the amount ingested, but on its bioavailability [77]. Several clinical trials have demonstrated that a single dose of tea improves plasma antioxidant capacity of healthy adults within 30 to 60 minutes after ingestion [78-80]. In a recent study Koutelidakis et al. reported that supplementation of WT extract for a five consecutive days not only increases the antioxidant capacity of plasma but also in different organs in mice, such as heart and lungs [81]. Despite catechins, especially EGCG, theaflavins and flavonol glycosides are also thought to be responsible for antioxidative properties of tea. The antioxidant effectiveness depends on the tea variety and the content of EGCG is very important [58]. Several epidemiological studies, experimentation with animals,
and in vitro studies lead to the conclusion that WT has potentially protective effects for a wide variety of health conditions that are subsequently summarized (Table 1). However, the evidence is not always clear cut.

### Cardioprotective effects

The onset of cardiovascular disease (CVD) depends on numerous factors that can be modulated by components in the diet [50]. Oxidative stress (OS) in cardiac and vascular myocytes has been linked with cardiovascular tissue injury [82]. RONS-induced OS is linked to the onset of various CVD such as atherosclerosis, ischemic heart disease, hypertension, cardiomyopathies, cardiac hypertrophy and congestive heart failure [83]. For instance, the oxidation of low density and very low density lipoproteins (LDL and VLDL) brings about the progressive obstruction of arteries or atherosclerosis, and can lead to coronary heart disease infarction [84]. Natural antioxidants, such as polyphenolic compounds of dietary origin, may inhibit lipid oxidation and attenuate the progression of atherosclerosis and thrombosis [85,86]. An epidemiologic study indicated that European populations with higher plasma concentrations of natural antioxidants, L-ascorbic acid and L-theanine [95], reduce blood pressure in animals and in man and thus lower the risk for the development of cardiovascular diseases. Until now, there are still not evidences concerning the cardioprotective effects of WT. Although, since WT is richer in catechins and other polyphenols than other teas and those components are ascribed to have important cardioprotective roles, it is expected that WT will be beneficial against CVD. Further studies are needed to confirm WT potential against CVD.

### Antidiabetic potential

Diabetes mellitus (DM) is an increasingly common, potentially devastating, expensive, treatable but incurable lifelong disease [96]. According to a widely accepted estimation, the number of diabetic patients will reach 366 million by the year 2030 [97]. It is a metabolic disorder of multiple aetiologies, characterized by chronic hyperglycemia and trouble some disruptions in carbohydrate, fat, and protein metabolisms emanating from deficiencies or disruptions in insulin secretion [98], defects in reactive oxygen species scavenging enzymes [99], and high oxidative stress impairing pancreatic beta cells [100,101]. Type 1 DM results from an absolute deficiency of insulin due to an autoimmune destruction of the pancreatic beta cells while type 2 DM is characterized by impaired insulin secretion and increased insulin resistance [102]. The levels of glycemia and insulinenia must be controlled in order to avoid later complications of DM, such as atherosclerosis, hypertension, hypertriglyceridemia, hypercholesterolemia, myocardial infarction, ischemic attacks, impotence, retinopathy and nephropathy [103]. The pharmacological treatment of DM includes oral hypoglycaemic and insulin. Although these drugs are effective in reducing glycaemia, they may cause undesirable side effects (such as weight gain, hypoglycaemia, edema, gastroin-

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Testinal disturbances and insulin resistance) that can discourage patient compliance [104]. In recent years, interest has increased in using natural products for pharmacological purposes, as a form of complementary or replacement therapy. Published reports show that numerous extracts obtained from plants are effective in reducing glycermia, causing fewer side effects and with lower cost than the usual antidiabetic agents [105-108]. There is some evidence that tea is a hypoglycemic agent [109]. In vitro rat studies suggest that EGCC and other catechins and theaflavins help prevent hyperglycaemia by enhancing insulin activity and possibly by preventing damage to β-cells [37]. Although the exact mechanisms by which tea polyphenols ameliorate diabetes are not clear at the moment, all the studies suggest that polyphenols don’t increase insulin secretion, but decrease insulin resistance and improve insulin sensitivity [110].

Various studies have reported that DM is associated with increased formation of RONS and decreased antioxidative potential [111]. Increased OS has been proposed to be one of the major causes of the hyperglycemia-induced trigger of diabetic complications [65]. Due to these events, the cellular balance between radical formation and protection against them is disturbed. In both insulin dependent and non-insulin-dependent diabetes there is increased OS [112]. It was previously shown that EGCC ameliorates cytokine-induced β-cell damage in vitro [113] and prevents the decrease of islet mass induced by treatment with multiple low doses of streptozotocin (STZ) in vivo [114]. However, in a latter study STZ was co-injected with EGCC, which possesses strong antioxidative activity [115], and it was unclear whether the protective effects observed in this study were due to direct inactivation of the co-injected STZ. Another study with EGCC reported that supplementation with it reduces serum glucose, total cholesterol and triglyceride and LDL-cholesterol in STZ-induced diabetic rats[116]. This effect however can be different from the effect of the tea extract, with all of its bioactive components. In contrast to studies indicating an antioxidative capacity of EGCC, investigations in the insulinoma cell line HIT-T15 showed that EGCC treatment was associated with increased production of RONS and reduced cell viability [117]. Thus, the antioxidative effects of EGCC are not entirely clarified. The in vivo relevance of potentially antioxidative WT catechins remains to be demonstrated. Recently, WT was reported to have strong lipolytic and anti-adipogenic activity in vitro[118]. Hence, WTEA may demonstrate antioxidative effect by reducing OS and hyperlipidemia followed by insulin resistance [110]. Since diabetes mellitus is increasing worldwide as is associated with several complications, there is a large interest in finding an effective therapy and WT seems to be a good alternative. Furthermore, in-depth investigation is needed to fully understand the mechanisms of action of WT against this disease.

Anticarcinogenic and antimutagenic activities

Cancer is generally considered as uncontrolled cell division that results in the aggregation of cells to form tumours. It is one of the major causes of death in the modern world and has shown to be a largely preventable disease, highly susceptible to modulation by dietary factors [119]. There are many factors which are involved in the pathogenesis of cancers, e.g. genetic mutations, smoking, heavy metal ingestion, and other pollution and indeed lack of proper diet [120]. OS induces a cellular redox imbalance, which has been found to be present in various cancer cells and may be related to oncogenic stimulation. Permanent modification of genetic material resulting from OS represents the first step in-volvedin mutagenesis, carcinogenesis, and ageing. DNA mutation is a critical step in carcinogenesis and elevated levels of oxidative DNA lesions have been noted in various tumours, strongly implying such damage in the etiology of cancer [65]. Polyphenols present in tea may play an important role in the prevention of cancer by decreasing DNA damage in the cell and reducing the activation of cancer that leads to malignancy [121]. Many studies have indicated that tea and its constituents, mainly EGCC, are antimutagenic and anti-inflammatory by intercepting carcinogenic agents and by reducing oxidant species before they can damage DNA [122,126]. Catechins also protect cell membranes against oxidation, keep RONS in confined zones and probably block cell membrane receptors required for cancer cell growth. The initiation of carcinogenesis can be overcome by the repression of some catalytic activities and of other specific enzymes involved in cancer initiation. This is complemented by the enhancement of detoxifying enzymes by EGCC[123,127].

In different cell lines and animal models, it has been shown that tea polyphenols inhibit angiogenesis, metastasis and cell proliferation, and induces cell cycle arrest and apoptosis through regulation of multiple signaling pathways [3,121]. For instance, Cao and Cao reported that EGCC inhibits angiogenesis [128]. Later, Sharangi showed that EGCC reduces angiogenesis in part by decreasing vascular endothelial growth factor (VEGF) production and receptor phosphorylation [121]. Importantly, the putative chemopreventive effect of tea also varies by the specific type of cancer [3]. So far, there are few studies concerning the anticarcinogenic potential of WT but recently it has been shown that WT has chemopreventive and antineoplastic effects in lung cancer cells [129] and can protect human skin from solar-stimulated ultraviolet light [130].

Neuroprotective activity

In the central nervous system (CNS), OS caused by increased production of RONS represents an important mechanism for neuronal dysfunction and cell loss in different neurodegenerative disorders [36]. The brain is particularly vulnerable to oxidative damage because of its high oxygen utilisation, its high content of oxidizable polyunsaturated fatty acids (PUFA), and the presence of redox-active metals (such as Cu, Fe) [65]. OS is one of the most important factors that contribute to aging processes and neurodegenerative disorders such as Alzheimer’s disease, Parkinson’s disease (PD) or Huntington’s disease [131-134]. Although neuronal cells may respond to such stress using enzymatic and non-enzymatic detoxification mechanisms, there are certain populations of neurons that are particularly vulnerable to OS [132]. Food antioxidants may enhance the antioxidative capacity of the organism to prevent from neurodegenerative diseases associated with RONS and other oxidative damage inducing agents [7]. This neuroprotective effect has been ascribed to tea’s high polyphenolic content, mainly of catechins and other flavanols[13,50,135-137]. Given that catechins exhibit higher antioxidant activity than theaflavins, it has been hypothesized that higher protection might be expected from teas that have undergone the minimal processing [59,138], such as WT and GT. WT, which has received little attention for its health benefits, has similar or even higher antioxidant activity than certain GT[59,139-141].

Isolated constituents from tea have previously been demonstrated to exert protective effects in neuronal cells. For instance, EGCG was shown to have neuroprotective activity in a mice model of PD [142], and an epidemiologic study indicated that the risk of PD was reduced if tea consumption was ≥ 2 cups/day [143]. In
addition, L-theanine is ascribed to be a neuroprotective and cognitive enhancing agent [144,145]. It is thought to cross the blood-brain barrier to exert its effects directly on the brain within 30 minutes [146]. Recently, L-theanine has been linked to the feelings of relaxation reported by those who drink tea. Experimental studies have also shown that L-theanine appears to negate some of the effects of caffeine [147]. It is believed to lower cortisol levels, thus reducing psychological and physiological stress [148]. In this sense, results suggest that protection may be due to a synergistic effect among various compounds of tea. Recently, using a model of striatal immortalized cell lines, Almajano et al. have evaluated the neuroprotective effect of WT extracts against H₂O₂-induced toxicity [36]. They have demonstrated that WT is able to completely protect striatal cells from OS and suggested that WT consumption may have beneficial effects on neuronal cells contributing to reduce OS associated with age-related brain disorders.

**Antimicrobial properties**

Tea also exhibits some antimicrobial properties, which are attributed mainly to its polyphenols. The degree of this activity depends on the bacterial species and the polyphenol structure [149][150] Gram negative bacteria seem to be more resistant to polyphenols than Gram positive bacteria, due to differences in the external membrane [151]. The antimicrobial activity of non-fermented tea is higher than that of semi-fermented or fermented tea. Moreover, the highest antimicrobial activity occurs in samples with the highest total polyphenol concentration and antioxidant activity [152]. So, WT is expected to have higher antimicrobial activity than other teas. The main components responsible for the antimicrobial activity are EGCG and EGC, since these are also the ones with more antioxidant activity [153]. EGCG at 10–100 µM has showed to reduce Escherichia coli growth by approximately 50%[152].

The use of natural antioxidants as preservatives in food has great potential because consumers request additive-free, fresher and more natural-tasting food. However, it is necessary to maintain microbiological safety and minimize the number of food-borne microorganisms[152]. WT is considered to be one of the best sources of extracts that can act as microbiological inhibitors. The use of WT in combination with other antimicrobial additives or methods for stabilizing food products represents an alternative way of maintaining a high flavour quality without the use of conventional food preservatives.

Even if up to date findings demonstrate the protective effect of WT against the OS, characteristic in the pathology of several human diseases, more in-depth research is needed to clearly define the health benefits and clinical effects of this rare type of tea. Therefore, we expect to have contributed to the future expansion of the virus in host cells [156]. Therefore, WT can also be a very interesting alternative to fight microorganisms-induced diseases. Nevertheless, this field needs further investigation.

**Anti-obesity potential**

Although there are many proposed genetic and environmental factors that predispose individuals to weight gain, the fundamental cause of obesity is an imbalance between dietary intake and energy expenditure [157]. It is known to be a strong risk factor for lifestyle-related diseases [121]. Obesity has increased at an alarming rate in recent years and is now a worldwide health problem [158]. While conventional weight management programs show only limited success, particularly in the long-term, there is growing interest in alternative strategies for weight management. One natural ingredient in focus is tea. Some reports indicate that intake of tea catechins, together with regular exercise helps to reduce diet-induced obesity. This effect might be attributed to the activation of whole-body energy metabolism [121]. Bose et al. reported that treatment with 7.0 mmol/g dietary EGCG for 15 weeks reduced body weight gain (33–41%) in high-fat-fed male C57Bl/6j mice compared with high-fat-fed controls [159]. The mechanisms of action of tea in obesity are: stimulation of hepatic lipid metabolism [160]; inhibition of lipases [161]; stimulation of thermogenesis [161,163]; modulation of appetite [164]; and synergism with caffeine [165][166]. Simple tea drinking may have easier acceptance by the patients than prescription drugs, exercise and bariatric surgery. The main attractions of tea as an anti-obesity agent are that it is a more natural and safer alternative, there is no need for professional supervision and it is readily accessible and affordable [167]. Although laboratorial studies using animal models have largely demonstrated obesity preventive effects of GT, the effectiveness of WT has been less studied. Söhle et al. recently reported that WT extract effectively inhibits adipogenesis and stimulates lipolysis-activity [118]. Therefore, WT is an ideal natural source to modulate the adipocyte life cycle at different stages and to induce anti-obesity effects. However, the role of tea polyphenols and specifically of WT in the prevention of obesity has not been fully elucidated.

**Future Perspectives**

Even if up to date findings demonstrate the protective effect of WT against the OS, characteristic in the pathology of several human diseases, more in-depth research is needed to clearly define the health benefits and clinical effects of this rare type of tea. Therefore, we expect to have contributed to the future expansion of research on WT and to promote WT consumption since it has been shown to be a promising agent for prevention and treatment of several human diseases.

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