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BREWING INSIGHTS: A COMPREHENSIVE REVIEW ON THE COMPOSITION, HEALTH IMPLICATIONS, AND CULTURAL SIGNIFICANCE OF BRICK TEA

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Abstract
Tea, a globally cherished beverage, is under extensive research for its complex composition and diverse effects. This paper focuses on Brick Dark Tea (BDT), a distinctive fermented type known for its fungal aroma, exploring production techniques and bioconversion processes. Types like Heizhuan, Fuzhuan, Qingzhuan, Kangzhuang, and Pu-erh Brick Tea are detailed, showcasing microbial fermentation's pivotal role. The review covers BDT's bioactive compounds, such as alkaloids, proteins, phenols, polysaccharides, and pigments, contributing to potential health benefits. Recent strides in understanding BDT's anti-obesity, anti-diabetic, cardioprotective, hepatoprotective, neuroprotective, and anti-cancer activities are discussed, supported by studies. BDT's multifaceted health-promoting properties open avenues for therapeutic applications. In conclusion, as BDT gains global interest, further research is suggested, including microbial enzymatic reactions, specific starter strains, additional bioactive compounds, and clinical trials. This comprehensive review unveils BDT's nuanced world, underscoring its significance in diets and potential as functional foods or nutraceuticals.

1. Introduction

Tea, a globally cherished beverage, has captivated the attention of researchers who delve into its intricate chemical composition and diverse biological effects. The age-old tradition of tea classification divides it into six main types—green tea, white tea, yellow tea, oolong tea, black tea, and dark tea. All these variations stem from the *Camellia sinensis* plant, predominantly its major varieties, *C. sinensis var. sinensis* and *C. sinensis var. assamica*. The fermentation degree further refines this classification into non-fermented (green tea), partially-fermented (white tea, yellow tea, oolong tea), fermented (black tea), and post-fermented (dark tea) [1].

Dark tea, a distinctive variety subject to microbial fermentation, stands out prominently with primary production hubs in China and Japan. Within the realm of dark tea, unique subtypes like Brick Dark Tea (BDT), Bowl tea, and Tuo tea emerge, each characterized by its distinctive shape. BDT, particularly renowned for its characteristic fungal aroma, has not only captured sensory appreciation but has also become a focal point for potential health benefits. These include anti-obesity, antibacterial, antihyperlipidemia, antihyperglycemia, antioxidation, and anti-mutagenic properties. The Brick Dark Tea was the item of currency exchange in the medial China, was in prominence in the 17th century and its trade was conducted via Tea Hourse Raod [2]

Recent strides in the understanding of BDT processing technology and its biological components underscore the significant progress in this field. With the burgeoning popularity of this unique tea variant, the objective of this paper is to offer a comprehensive review of recent advances. The focus lies on the evolution in BDT production techniques and the bioconversion processes of its major chemical constituents. A meticulous detailing of the chemical components of BDT is presented, providing valuable insights into the intricate world of this captivating tea variant. As appreciation for dark tea continues to grow, this review serves as a gateway to understanding the nuances that make it a distinct and cherished segment within the vast tapestry of tea culture.

2. Types of BDT

BDT, or Brick Dark Tea, also known as border-sale tea, is a distinctive compressed tea made primarily in China and Japan from older, coarse leaves and branches of *C. sinensis var. sinensis* or *C. sinensis var. assamica* [3]. Modern BDT production involves a crucial solid-state fermentation stage, contributing to its unique qualities such as a mellow taste, stable flavor, and special fungal aroma in the tea infusion. Highly esteemed along the ancient Tea-Horse road, BDT is a staple in Northwest Chinese life and popular in Central Asia and Russian regions [3].

Various types of BDT products are categorized based on origin and processing methods:

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a. **Heizhuan Brick Tea and Huazhuan Brick Tea:** Produced mainly in Anhua, Hunan, from crude dark tea. Huazhuan brick tea has surface patterns, distinguishing it from Heizhuan.
b. **Fuzhuan Brick Tea (FBT):** Manufactured by Yiyang Tea Manufactory in Hunan and Xianyang Jingwei Fu Tea Manufactory in Shanxi, FBT is pressed using crude dark tea from Hunan or sun-dried leaves in the south of Shanxi. Unique "golden flora" appears after the fungal fermentation process.
c. **Qingzhuan Brick Tea:** Produced by Zhaoliqiao Tea Manufactory in Hubei, it is also known as "Chuanzi tea" due to the Chinese character "川" on its surface. Pressed with high-quality Hubei old tea.
d. **Kangzhuang Brick Tea:** Mainly produced in Yingjing, Ya'an, and other counties in Sichuan province, Kangzhuang brick tea features round corners.
e. **Pu-erh Brick Tea:** Produced in Dali, Yunnan province, using sun-dried leaves of the broad-leaf tea species (*C. sinensis var. assamica*).

3. Manufacture of BDT

Tea production significantly shapes its unique characteristics [4]. The fresh leaves for Brick Dark Tea (BDT) are harvested from *C. sinensis* var. *sinensis* and *C. sinensis* var. *assamica*. Although manufacturing processes vary among BDT varieties, they generally involve two main phases: processing of fresh tea leaves and processing of raw dark tea.

3.1. Processing of Fresh Tea Leaves:

In Hunan, dark tea typically utilizes leaves from *C. sinensis var. sinensis* with one bud and three or four leaves, while Hubei and Sichuan have less stringent standards, requiring only absence of deadwood or diseased leaves.After plucking, fresh leaves are spread indoors to control respiratory heat. The subsequent process includes steaming, rolling, microbial fermentation, and drying, resulting in the production of raw dark tea.Steaming involves heating around 10 kg of fresh leaves at 300 °C until the colour changes from fresh green to dark green. This process makes the leaves supple, and the peduncle becomes less prone to breakage. During this stage, the activity of endogenous enzymes like Polyphenoloxidase (PPO) and Peroxidase (POD) declines due to high temperature.Microbial fermentation is a crucial step, requiring stacked rolled leaves in a room with a temperature above 25 °C for 24–40 hours and a relative humidity of about 85%. This conditions complex oxidation, condensation, and degradation of chemical components in tea.Drying is the final step, ensuring moisture content of 12% in Hunan dark tea, 13% in Hubei old tea, and 14% in both Sichuan and Shanxi dark tea [3,5].

3.2. Processing of Raw Dark Tea:

The processing of raw dark tea involves softening with steam, piling, brick-pressing, and drying. Particularly, Fuzhuan Brick Tea (FBT) has a unique pre-drying step: fungal fermentation. In this stage, various fungi, including *Eurotium* spp., Saccharomyces spp., and *Aspergillus* spp., are cultivated in raw brick tea.Upon completion of fungal fermentation, FBT is covered by "golden flora"—specifically *Eurotium* spp. inside. Xu et al. (2011) [6] associate dominant genera—*Eurotium, Debaryomyces, and Aspergillus*—as beneficial fungi linked to the fermentation of FBT.

3.3. Microbial fermentation

Microbial fermentation is pivotal in shaping the distinctive features of dark tea. Essential microorganisms, including *Aspergillus, Bacillus, Candida, Cyberlindnera, Debaryomyces, Eurotium, Klebsiella, Lactobacillus, Lactococcus, Lichtheimia, Penicillium, Rasamsonia, Uwebraunia*, play a crucial role in forming dark tea's primary quality components [7-11] Fungal species identified during pile fermentation are believed to be responsible for converting volatile compounds, contributing to the unique flavour of dark tea [11-13]

For example, *Aspergillus niger* enhances the content of β-ionone, geraniol, linalool oxides, and 9,12-octadecadienoic acid, while *Eurotiumcristatum* increases the levels of α-terpineol, β-ionone, cis-jasmone, nonanal, and 2-pentylfuran [12]. Changes in bioactive contents during pile fermentation are attributed to various microorganisms. *Aspergillus tubingensis*, for instance, is employed for producing high theabrownins content through a novel submerged fermentation strategy for Pu-erh tea [14]. *Aspergillus sydowii,* isolated from the aerobic fermentation of Pu-erh tea, exhibits high caffeine-degrading capacity, converting caffeine into theophylline [15]. *Aspergillus tamarii* and *Aspergillus ustus* degrade theophylline, with their main degraded metabolites being xanthine and 3-methylxanthine.

Favourable transformations take place due to microorganisms like Aspergillus [16], which produce various extracellular enzymes responsible for degrading and metabolizing macromolecules, leading to the bioconversion of chemical contents in dark tea. Core microorganisms drive a range of reactions such as condensation, oxidation, glycosylation, and methylation, contributing to the generation of distinct flavors and beneficial compounds in dark tea.

4. Bioactive compound in BDT

4.1. Alkaloids

Teas serve as vital sources of purine alkaloids, with caffeine typically being the most prevalent alkaloid. A study by Lv, Zhang, Shi, and Lin (2017) [17] reported no significant differences in caffeine content among Pu-erh tea (30.92 ± 2.71

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mg/g), Fu brick tea (27.51 ± 2.13 mg/g), and Liubao tea (25.80 ± 2.65 mg/g). Caffeine content was noted to remain stable across different manufacturing processes and all six types of tea produced from the same batch of tea leaves [18,19]
Contrarily, recent findings by Zhou et al. (2019) [15] suggest that caffeine content in Pu-erh tea can be influenced by natural microbiota. *Aspergillus sydowii* was identified as having the potential to convert caffeine (28.8 mg/g) into theophylline (24.6 mg/g) significantly through the aerobic fermentation of Pu-erh tea.

4.2. Proteins

Free amino acids are recognized for their crucial role in shaping the aroma and taste of tea. The pile fermentation process exerts a significant impact on amino acid profiles, leading to a notable decrease in total free amino acid content. However, the individual changes in free amino acids vary during fermentation, with some decreasing, while others remain consistent or even slightly increase [14]. In Pu-erh tea, major amino acids such as alanine, arginine, aspartic acid, glutamic acid, theanine, and tyrosine were identified [20]. Pingwu Fu brick tea, on the other hand, exhibited elevated levels of amino acids including alanine, asparagine, aspartic acid, γ-aminobutyric acid (GABA), theanine, and threonine (Li et al.).

4.3. Phenols

In contrast to the abundant polyphenol content found in green, white, and yellow teas, recent data reveals that total polyphenols in dark teas constitute only about 10%. This information stems from a study analyzing 44 dark tea samples, encompassing Pu-erh tea, Fu brick tea, and Liubao tea [17]. Although dark teas contain catechins, prevalent in green teas, their overall content is notably lower after undergoing oxidation during fermentation. This oxidation process results in elevated pigment levels in dark teas, accompanied by the formation of new catechin derivatives like 2R,3R-6-methoxycarbonylgallocatechin-3-O-gallate (EGCGD) and 2S,3R-6-methoxycarbonylgallocatechin (MCGE). Additionally, the fermentation process significantly increases the content of another crucial tea polyphenol, gallic acid [19].

Dark teas also exhibit the presence of flavonoids such as kaempferol, myricetin, and quercetin, with reports of acylated flavonol glycosides as novel compounds in dark teas [21,22]. Recent attention has been directed towards non-extractable polyphenols, which cannot be extracted from residues using water or organic solvents. Dark teas, among various tea types, were found to contain non-extractable polyphenols in a recent study, although their content and antioxidant effects were lower compared to extractable polyphenols.

4.4. Polysaccharides

Dark teas boast a substantial content of polysaccharides. According to reports, Fu brick tea polysaccharides are characterized as typical acidic heteropolysaccharides, primarily composed of Man, Rha, GalA, Glc, Gal, and Ara, with small amounts of Rib and GIcA [7]. In a recent study, a purified fraction from crude Fu brick tea polysaccharides, denoted as FBTPS-3, exhibited a molecular weight of 741 kDa, featuring Man, Rha, GalA, Gal, and Ara in a molar ratio of 8.7:15.5:42.2:19.7:13.9, respectively [23]. Additionally, two fractions, TPS-1 and TPS-2, were isolated from crude Qing brick tea polysaccharides in a study by Yang et al. (2017) [24].

4.5. Pigments

Dark teas boast a wealth of pigments, including theabrownins, thearubigins, and theaflavins, formed through the oxidation of tea catechins during piling fermentation. Theabrownin, the most abundant and bioactive pigment in dark teas, reaches its highest concentration in Pu-erh tea, surpassing 13% (equivalent to 13 mg theabrownins per 100 mg Pu-erh tea). Liubao tea follows with around 10%, while Fu brick tea contains approximately 7% [17]. The levels of thearubigins and theaflavins in dark teas are approximately 1% and 0.1–0.2%, respectively [17]. Innovative submerged fermentation techniques involving *Aspergillus niger* or *Aspergillus tubingensis* have been developed to enhance the theabrownin content in dark tea products [25,]. Submerged fermentation by *Aspergillus tubingensis* has demonstrated nearly a fourfold increase in theabrownin content compared to the traditional piling fermentation of Pu-erh tea [14].

4.6. Others

The aroma is a critical aspect of dark tea flavor quality, distinguished by its unique volatile composition attributed to diverse fungal species during microbial fermentation. Numerous studies have explored the major volatile compounds in various dark teas, including Pu-erh tea, Fu brick tea, and Liubao tea, revealing components such as acids, alcohols, aldehydes, alkanes, alkenes, arenes, esters, ketones, and methoxy-phenolic compounds. Hexadecanoic acid, constituting 15–20% of total volatile oils, is a prevalent compound in different dark teas. Terpenoids like α-terpineol, α-ionone, β-ionone, linalool, and linalool oxides are also significant [17,26]. Fu brick tea has found application in enhancing the flavor and fermentation efficiency of food products, such as glutinous rice [13].
In summary, dark teas contain a variety of bioactive compounds,encompassing alkaloids, catechin-related compounds, flavonols, free amino acids, pigments, polysaccharides, volatile terpenoids, and other constituents. These compounds contribute to the diverse biological functions of dark teas, potentially benefiting human health, a topic explored in the following section. While saponins, significant in green teas for their health-promoting effects, are seldom reported in dark

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teas. The intriguing question arises whether dark tea contains saponins or if they undergo degradation by microbes during the fermentation process.

5. Health Benefits of BDT

Recent *in vivo* and human studies provide compelling evidence for the diverse biological functions and health benefits associated with dark tea. The regular intake of 2 g or 3 g of dark tea has been linked to reductions in blood glucose levels and improvements in lipid profiles in human subjects. The dosages employed in animal studies vary, ranging from 5 mg/kg/day to 3 g/kg/day in mice, equivalent to approximately 30 mg to 20 g of dark tea consumption per day for a person weighing 60 kg.

Furthermore, certain dark teas exhibit superior biological functions compared to other tea types. Ripened Pu-erh tea, in particular, displayed more potent effects on hyperglycemia and hyperlipidemia in streptozocin-induced diabetic rats compared to raw Pu-erh tea [27]. The heightened biological functions of dark tea are attributed to the emergence and augmentation of bioactive components such as theabrownins, polysaccharides, eurocristatine, and gallic acid. Additionally, specific microorganisms found in dark tea, such as *Eurotium cristatum*, are believed to play a pivotal role in enhancing these health benefits. The subsequent sections delve into a comprehensive summary and discussion of the primary biological functions and health advantages associated with dark teas, with a focus on potential molecular mechanisms.

5.1. Antioxidant Activity

Various studies have highlighted the robust antioxidant properties of dark teas, with variations observed among different types. An analysis of 44 dark tea samples, processed through diverse methods, employed assays like DPPH, ABTS, FRAP, and CAA (HepG2 cells). Notably, a positive correlation between EGCG levels and antioxidant activities tested by ABTS and FRAP assays was observed, while total flavonoids and theabrownins correlated positively with antioxidant activities using the CAA assay [17].

In addition to flavonoids and theabrownins, polysaccharides, phenolics, and Teadenol A from dark teas have demonstrated in vitro or in vivo antioxidant activities. Interestingly, the antioxidant activities of teas can differ between in vitro and in vivo assessments. While green tea generally exhibits strong in vitro antioxidant activities compared to other types, several dark teas, including Black Fu brick tea, Pu-erh tea, and Qing brick tea, surpass green teas in in vivo antioxidant activities [28]. This discrepancy may arise from differences in the bioavailability of various bioactive components.

Exploring the antioxidant mechanisms of dark tea in cellular and animal models revealed protective effects. For instance, Fu brick tea polysaccharides safeguarded PC12 cells from H2O2-induced oxidative injury and mitigated high-fat diet-induced oxidative damage in mice by reducing malondialdehyde (MDA) content and enhancing superoxide dismutase (SOD) levels [29]. Pu-erh tea extract demonstrated a dose-dependent reduction in alcohol-induced MDA elevation [30], and Qing brick tea exhibited antioxidative effects in monosodium glutamate-induced obese mice [31].

Moreover, dark teas have found applications beyond beverages, enhancing antioxidant activities in food products and packaging materials. Fu brick tea supplementation improved the antioxidant activity of set-type yogurt, and the addition of Pu-erh tea extracts enhanced the antioxidant activities of biodegradable films applied to salmon nigiri [32, 33]. Overall, dark teas and their bioactive compounds, such as flavonoids, theabrownins, phenolics, and polysaccharides, exhibit potent antioxidant activities by enhancing antioxidant enzyme activities and modulating the Nrf2 pathway. These antioxidants hold promise as functional ingredients or packaging materials in diverse food products.

5.2. Anti- obesity activity

The escalating global prevalence of obesity has prompted substantial research on dark tea's potential role in mitigating weight gain and fat accumulation, supported by findings from both animal models and clinical trials. Pu-erh tea extract treatments have shown efficacy in reducing lipid droplet size and fat accumulation in Caenorhabditis elegans, with potential gene-regulating effect [34]. Fu brick tea has exhibited similar fat-reducing properties in *C. elegans* through regulation of DAF-16/FOXO and insulin/IGF-1 signaling pathways [35]. Furthermore, dark tea extracts or components have demonstrated preventive effects on body weight gain and fat accumulation in high-fat diet-induced obese rodents, as well as anti-obesity properties associated with *Eurotium cristatum* from Fu brick tea [36-38].

The mechanisms underlying the reduction in fat accumulation involve the promotion of fatty acid oxidation, lipolysis, and suppression of fatty acid synthesis and lipogenesis. Pu-erh tea treatment altered body composition, free fatty acid composition, and lipid metabolism in mice fed a high-fat diet, enhancing lipid oxidation and promoting the browning of white adipose tissue [39, 40]. Additionally, Pu-erh tea extract altered the expression of genes related to free fatty acid uptake and β-oxidation, contributing to its anti-obesity effects [36]. Clinical trials involving Pu-erh tea extract supplementation have reported significant weight loss, reduced fat mass, and improved lipid profiles [41].

ISSN-2394-5125 VOL 07, ISSUE 01, 2020

Beyond lipid metabolism, dark tea's impact extends to obesity-related inflammation. In vitro studies demonstrated that Pu-erh tea extract and *Eurotium cristatum* from Fu brick tea exhibited anti-inflammatory effects by modulating specific signaling pathways [42, 43]. In vivo studies supported these findings, with dark tea extracts ameliorating inflammation in various tissues, such as the liver and visceral adipose tissue [37, 44, 45].

Furthermore, the intricate interplay between dark tea consumption and gut microbiota has emerged as a key factor in its anti-obesity effects. Fu brick tea, for instance, altered gut microbiota composition, promoting beneficial bacteria and suppressing harmful ones [46]. Ripened Pu-erh tea displayed probiotic effects on specific beneficial gut microbiota, further contributing to reduced body weight gain and fat accumulation in obese mice [27, 37]. Notably, depletion of gut microbiota abolished the anti-obesity effects observed with Fu brick tea, highlighting the crucial role of the gut microbiota in these processes [46].

In summary, the anti-obesity properties of dark tea are multifaceted, encompassing regulation of lipid metabolism, mitigation of obesity-related inflammation, and modulation of gut microbiota composition. These insights pave the way for potential therapeutic applications and further exploration of dark tea's mechanisms in combating obesity-related health issues.

5.3. Anti diabetic activity

Recent research, spanning *in vitro*, *in vivo*, and human studies, underscores the anti-diabetic potential of dark teas. In vitro studies highlighted the inhibitory effects of dark teas on α-glucosidase, with Qing brick tea extracts, particularly rich in EGCG and ECG, demonstrating potent inhibitory activity [47]. Fu brick tea acylglycosides flavones also exhibited strong α-glucosidase inhibition, contributing to the array of bioactive compounds with anti-diabetic properties [48]. Flavanols from Pu-erh tea extract showcased inhibitory actions against α-glucosidase, sucrase, and maltase [49]. Additionally, dark tea proteins and peptides exhibited *in vitro* inhibitory activities against α-amylase, α-glucosidase, and dipeptidyl peptidase, while dark tea water extracts enhanced glucose uptake in HepG2 cells [50-52].

In vivo studies delved into the anti-diabetic effects of dark tea, revealing its ability to alleviate insulin resistance in obese animals and lower fasting blood glucose in streptozocin-induced diabetic models. Qing brick tea extract, for instance, enhanced insulin signaling by stimulating AKT signaling and up-regulating GLUT4 protein levels in the skeletal muscles of obese mice [31]. Fu brick tea water extract attenuated insulin resistance in high-fat diet-induced obese rats by influencing insulin signaling pathways [53]. Pu-erh tea extract exhibited systemic insulin resistance benefits by elevating GLUT4 expression in visceral adipose tissue and improving glucose tolerance [45]. Furthermore, compared to raw Pu-erh tea extract, ripened Pu-erh tea extract displayed a stronger inhibitory effect on fasting blood glucose and postprandial blood glucose in streptozocin-induced diabetic rats, possibly attributed to newly formed or increased bioactive components during fermentation [27].In human studies, individuals consuming beverages with Pu-erh tea extract experienced significantly lower postprandial blood glucose levels [54].
In summary, dark tea extracts or components manifest significant anti-diabetic activities by lowering blood glucose levels and alleviating insulin resistance, highlighting their potential as functional ingredients for diabetes-related applications.

5.4. Cardioprotective activity

Cardiovascular disease stands as a pervasive and life-threatening ailment worldwide. In vitro investigations point to dark tea flavanols, acylglycoside flavones, and their metabolites as pivotal contributors to the observed hypolipidemic effects. Pu-erh tea water extract, containing certain flavanols, exhibited lipase inhibitory activities [49]. Notably, Fu brick tea acylglycoside flavones and their metabolites displayed robust inhibition of 3-hydroxy-3-methyl-glutaryl (HMG)-CoA reductase, a key enzyme in cholesterol synthesis by hepatocytes [48].

A wealth of evidence supports the lipid-lowering impact of dark tea extracts or components in diverse models, including fish, rodents, and humans.Sichuan dark tea and Chinese Liupao dark tea polysaccharides demonstrated preventive effects against dyslipidemia in mice and rats, respectively [55, 56]. Pu-erh tea extracts, particularly theabrownins, were found to improve lipid profiles and cholesterol levels in hyperlipidemic individuals [41]. Additionally, Pu-erh tea demonstrated potential in alleviating hypertension by relaxing rat thoracic aorta through theabrownins and caffeine [57].

Research suggests that Pu-erh tea may combat atherosclerosis by inhibiting foam cell formation and alleviating plaque progression. Pu-erh tea extract treatment hindered nicotine-induced up-regulation of oxidized low-density lipoprotein receptors and α 9-nicotinic-acetylcholine-receptor (α 9-nAchR), key factors in the initial stages of atherosclerosis [58]. Clinical trials and *ex vivo* studies demonstrated Pu-erh tea's ability to inhibit α 9-nAchR expression in monocytes, countering foam cell formation even in heavy smokers [21]. Furthermore, Pu-erh tea's impact on atherosclerosis progression was associated with increased apoptotic macrophages and reduced inflammatory markers in atherosclerotic plaques [59]. In summary, dark teas, particularly Pu-erh tea, showcase promising cardiovascular benefits by influencing lipid metabolism, preventing dyslipidemia, and potentially mitigating atherosclerosis-related processes.

ISSN-2394-5125 VOL 07, ISSUE 01, 2020

5.5. Hepatoprotective Activity

Pre-treatment with Pu-erh tea extract exhibited a noteworthy anti-steatotic effect, alleviating oleic acid-induced steatosis in HepG2 cells, indicating its potential role in mitigating liver fat accumulation. This in vitro finding was corroborated by a study where mice given water containing Pu-erh tea extract demonstrated a significant reduction in high-fat diet-induced hepatic steatosis, showcasing a protective impact on liver health [42]. Additionally, Pu-erh tea extract, when administered, up-regulated genes associated with de novo lipogenesis and induced adipogenesis in visceral adipose tissue, demonstrating an inverse relationship with hepatic steatosis in mice on a high-fat diet [45]. Notably, the combined application of Pu-erh tea extract and Silibinin exhibited enhanced prevention of nonalcoholic steatohepatitis compared to the individual components in mice [60]. Furthermore, Jing-Wei Fu brick tea demonstrated potent hepatoprotective effects by reducing hepatic oxidative stress, inhibiting the formation of inflammatory cytokines, and modulating gut microbiota [445].

5.6. Neuroprotective activity

Dark teas demonstrate neuroprotective properties in both cellular and animal models. Pu-erh tea extract, for instance, has shown efficacy in preventing the onset of FET family protein-associated neurodegenerative diseases and slowing the progression of amyotrophic lateral sclerosis by promoting the degradation of FET family proteins [61]. Anhua dark tea yielded a novel catechin derivative, MCGE, which exhibited neuroprotective effects by mitigating N-methyl-D-aspartate-induced brain injury and apoptosis. This was achieved through the regulation of N-methyl-D-aspartate receptor subtype-2B expression, along with stimulation of the PI3K/Akt signaling and caspase-dependent pathways in SH-SY5Y cells [62]. Pu-erh tea has also demonstrated its neuroprotective potential by reducing excess glutamate-induced neural cell necrosis and alleviating LiCl-pilocarpine-induced epilepsy through the inhibition of metabotropic glutamate receptor 5 (mGluR5) expression and its synaptic scaffolding protein, Homer [63]. Furthermore, dark tea microbial metabolites were found to alleviate age-related neurodegenerative disorders in senescence-accelerated mouse prone 8 (SAMP8) mice, including improvements in body weight, reduced 4-HNE formation, decreased ubiquitinated protein aggregates, relief from cell hypoxia, and a reduction in neuronal apoptosis [Cai et al, 2018].

5.7. Anti cancer activity

Dark tea and its bioactive compounds demonstrate substantial anti-cancer activity, primarily observed in vitro. EGCGD, a novel epigallocatechin gallate derivative from Anhua dark tea, enhances the chemosensitivity of gefitinib against HCC827-Gef cells by inhibiting PI3K/mTOR signalling and epithelial-mesenchymal transition. Another compound, Camellikaempferoside A, found in Fu brick tea, inhibits the proliferation of MCF-7 and MDA-MB-231 cells [65]. Pu-erh tea exhibits a dose-dependent anti-proliferative effect on SMMC-7721 cells [66]. The water extract of Pu-erh tea dose-dependently suppresses cell proliferation in MDA-MB-231 human breast cancer cells, inducing cell cycle arrest, S phase accumulation, and apoptosis [67]. Pu-erh tea extract alters protein levels, increasing P-p53, p21, and P-JNK while decreasing PCNA, CyclinD1, and Cyclin E [67]. Dark tea extract enhances MAPKAPK2 phosphorylation, a downstream substrate of p38, and reduces AKT phosphorylation in cancer cells (SW1116, SW1990, PANC-1) but not in normal pancreatic duct epithelial cells (HPDE) [68]. Notably, dark tea extract exhibits a higher inhibitory efficiency for cancer cell growth than in HPDE cells. Additionally, the combination of dark tea extract and SB203580, a p38 inhibitor, synergistically inhibits cancer cell growth through down-regulating inhibitor of differentiation protein 1 (ID1). In vivo studies in a mice xenograft tumor model further confirm the significant inhibitory effect of dark tea extract on tumorigenesis [68]. In summary, dark tea extracts or components display potent anti-cancer activities by inhibiting cell proliferation and inducing apoptosis.

6. Conclusions

For future applications of dark teas, several considerations should be taken into account. Firstly, although microbial fermentation leads to favourable changes, the specific microbial-related enzymatic or metabolic reactions remain incompletely understood, necessitating further research. Secondly, as dark teas are primarily produced through natural fermentation, the microbial diversity during this process can impact their qualities. Evaluating specific starter strains of single or mixed dominantly functional microorganisms may enhance the consistency and quality of dark teas. Thirdly, efforts are required to identify and isolate specific functional microorganisms capable of producing high levels of beneficial compounds through microbial conversion. Fourthly, although novel compounds have been discovered in dark teas, their bioactivities remain undetermined. Future research should focus on identifying more bioactive compounds, particularly in less-studied types of dark teas, and investigating their health benefits and underlying mechanisms. Lastly, due to limited human-based studies on the health benefits of dark tea, well-designed clinical trials are essential to evaluate its protective effects against various diseases in humans.

In conclusion, dark teas are gaining increased attention due to their unique qualities and diverse biological functions. The piling fermentation process introduces various microorganisms, including genera like *Aspergillus, Bacillus, Candida, Cyberlindnera, Debaryomyces, Eurotium, Klebsiella, Lactobacillus, Lactococcus, Lichtheimia, Penicillium, Rasamsonia, Uwebraunia*, which contribute to the quality of dark tea. Dark tea is rich in diverse bioactive compounds, including alkaloids, free amino acids, peptides, catechins, pigments, and polysaccharides, exhibiting multiple biological functions

such as antioxidant, anti-obesity, anti-diabetic, anti-cancer, cardiovascular protective, gastrointestinal protective, hepatoprotective, neuroprotective, and photoprotective activities. In essence, dark tea plays a crucial role in dietary practices for preventing and managing chronic diseases, and its bioactive compounds hold promise for the development of functional foods and nutraceuticals. Dominace of the BDT has now been slowly degrading still its importance in connections with health and cultural legacy remains always.

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