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A REVIEW OF THE ROLE OF GREEN TEA IN ANTIPHOTOAGING, STRSS RESISTANCE, NEUROPROTECTION, AUTOPHAGY

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ABSTRACT

Tea is one of the most widely consumed beverages world wide, and is available in various forms. Green tea is obtained from the plant camellia sinensis belonging to family the aceae. Green tea is richer in antioxidants compared to other form of tea. It was used to detoxify the body. Tea is composed of polyphenols, caffeine, minerals, and trace amounts of vitamins, amino acids and carbohydrates. Green tea have many therapeutic properties such as antimicrobial to curing various infection. The phytochemicals present in green tea are known to stimulate the central nervous system and overall health in humans. Skin aging is a complex process mediated by intrinsic factors such as senenscenes, along with extrinsic damage induce by external factors such as chronic exposure to ultraviolet (UV) irradiation. Its ROS savenging activity makes it a potent stress mediator, as it can also regulate the stress induced by metal ions.

KEYWORDS: Green tea; Photoaging; Neuroprotective; Autophagy; Polyphenols.

INTRODUCTION

Tea is one of the most widely consumed beverage worldwide, and is the second-most consumed drink after water.[1] Tea is known to stimulate the central nervous system and cardiac function in humans.[2] Commercialy tea is mostly available in three varieties viz. Black (red tea),green and oolong (yellow tea) tea which differ in their physical and chemical characteristics arise from their different manufacturing process.[3,4,5,6] Green tea mainly consists of catechins, whereas black tea mainly contains tannins.[2] Black tea consumption is highest in western countries which accounts for around 78% of worldwide consumption. The green tea is mostly consumed in Japan and china and accounts for 20% whereas oolong tea is

consumed 2% only. Black tea is widely consumed in India and India is one of the largest tea producers in the world and it occupies about 70% of domestic consumption of the total tea production in the country.[3,4,5,6]

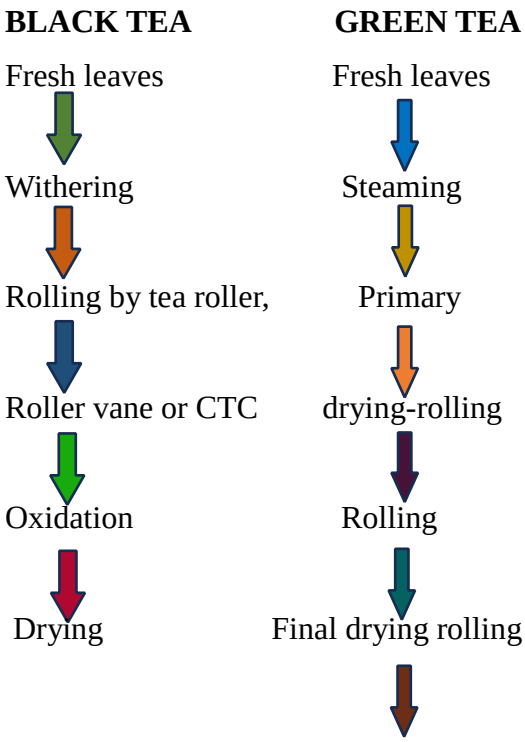
It is a popular beverage crop having medicinal, anti-oxidative and anti-microbial properties. The tea plant has been cultivated in asia for thousands of years. Traditionally, it was prescribed for a number of ailments while also being consumed for its refreshing qualities and the prevention of future health problems. The increase in popularity is in the part due to increasing awareness of green tea's many health benefits. Tea as an aromatic beverage commonly prepared by pouring hot or boiling water over cured leaves of the tea plant camellia sinensis.[7]

According to the european food safety authority (EFSA), 126mg of catechins are present per 100ml of green tea. However, according to the food and drug administration (FDA), 71mg of epigallocatechins gallate will be present per 100ml of green tea. In the case of black tea, 200mg of flavonoids are present per 100 mL.[8] Tea contents a variety of bioactive compounds such as polyphenols, vitamins, amino acids etc. having medicinal properties which can be used as food additives in preparation of neutraceuticals.[2,3,4,5]

Aging can be defined as the progressive loss of the cells, tissues, and organs of an individual across the lifespan.[9,10]

- **PREPARATION**

It is prepared by exposing the freshly collected leaves to the air until most of the moisture is removed. Then they are roasted and stirred continuously until leaves become moist and flaccid. Then they are past to rolling table rolled to into balls and subjected to a pressure which removes the moisture. Then the leaves are shaken out on the copper pans in roasted again till the leaves assume dull green colour. Then the leaves are winnowed, screened and graded into various varieties.[11,12]



- **Composition**

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Compound	Green Tea*	Black tea*	Infusion*
Protein	15	15	trace
Amino acids	4	4	3.5
Fiber	26	26	0
Others carbohydrates	7	7	4
Lipids	7	7	trace
Pigments	2	2	trace
Minerals	5	5	4.5
Phenolic compounds‡	30	5	4.5
Oxidized phenolic compounds§	0	25	4.5

- **Health Benefits**

Studies using animal models show that green tea catechins provide some protection against degenerative disease[13] The secret green tea lies in the fact that it is rich in catechines, polyphenols, particularly EGCG. The EGCG is the powerful antioxidant: besides inhibiting the growth of cancer cells, it kill cancer cells without harming healthy tissue.[14] Green tea, its extract, and its isolated constituents were also found to be effective in preventing oxidative stress.[15] and neurological problems.[16] Green tea consumption has been linked to the prevention of many types of cancer, including lung, colon, esophagus, mouth, stomach, small intestine, kidney, pancrease and mammary gland.[17] A recent study appearing in the journal

of allergy and clinical immunology stated that EGCG found in green tea can help to boost one's immune system, therefore helping to prevent HIV. The EGCG prevents the binding of HIV to human T-cells, the first step in HIV infection.[18]

- **Reactive Oxygen Species, Oxidative Stress and Antioxidants**

In aerobic conditions, the transfer of electrons occurs between atoms, wherein oxygen is the ultimate electron acceptor which produces ATP.[19] However, the transfer of uncoupled electrons results in the generation of free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS).[20] ROS are produced regularly inside the body, specifically in the mitochondria, during respiration and other immune-related functions.[21,22] They can act as a mobile signaling messenger inside the host. The overall cellular health is dependant on the level of ROS inside the host.[23]

Green tea is a popular neutraceutical as an antioxidants. Antioxidants are compounds that protect cells against the damaging effects of reactive oxygen species, such as singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals, and peroxynitrite. An imbalance between antioxidants and reactive oxygen species results in oxidative stress, leading to cellular damage.[24] Intake of green tea extracts also increases the activity of superoxide dismutase in serum and the expression of catalase in the aorta; these enzymes are implicated in cellular protection against reactive oxygen species.[25,26]

Any shift in the equilibrium, which may happen due to a reduction of antioxidants inside the system or due to an increase in ROS as a result of immune-related processes, will lead to oxidative stress.[27,28] Prolonged stress and aging may play a major role in reducing the efficiency of endogenous antioxidants against oxidative stress.[29] ROS promote peroxidation of the lipids in the cell membraces, along with altering the structure and function of different enzymes and promoting carbohydrate oxidation.[30]

The consumption of antioxidant-rich (like polyphenolics and flavonoids)fruits and vegetables.[31] is known to reduce the impact of different age-related diseases, including coronary heart disease and cancer.[32,33] Ascorbic acid (vitamin c) is considered to be one of the most powerful, water-soluble, natural antioxidants, with very little toxins associated with it and which is present in many dietary foods or plants.[34] Ascorbic acid is abundantly found in citrus fruits, kiwi, cherries, melons, and tomatoes, as well as leafy vegetables like broccoli,

cauliflower, and cabbage. Tocopherols (vitamin E) are the most widely used antioxidants, and are mainly present in nuts, seeds, and vegetable oils.[35]

Flavonoids are the most common antioxidant components found in plant sources. Flavonoids are the major antioxidants in the diet, and are known to protect against cardiovascular diseases by reducing the level of oxidation of low-density lipoproteins. Apigenin, chrysin, luteolin, datiscetin, quercetin, myricetin, morin, and kaempferol are some of the most commonly found flavonoids.[35] Green tea extract, specifically, can also have significant effects against ROS and RNS.[36]

- **Photoaging**

Skin is the largest organ of the human body, and creates an effective external barrier against the detrimental effects of environmental and xenobiotic agents, such as smoking, contaminants in the air and water, excessive oils and fats, drugs, and heavy metals, which induce extrinsic aging.[37] Skin aging is a complex process mediated by the intrinsic process of senescence, and extrinsic damage induced by external factors like chronic exposure to UV irradiation – a process known as photoaging.[38,39] UV can cause skin damage either directly, through absorption of energy by biomolecules, or indirectly, by increased production of ROS.[40] The depletion of the ozone layer allows easier penetration of UV radiation into the earth, which subsequently increases the level of skin cancer among people. Sunscreens are widely used to protect skin from UV. It can be used to scatter, reflect, or absorb radiation. However, compounds like titanium dioxide and zinc oxide in commercial sunscreen creams may create an opaque layer over the skin, which can damage the proper functioning and nourishment of the skin cells.[41] Natural products with antioxidants activity, which could enhance the endogenous capacity of the skin and help neutralize ROS.[40] Should be considered as an effective alternative for these chemical agents.

- **Antiphotoaging**

In a recent study**,** tea polyphenols were fed to mice which had undergone a UV mediated photoaging process. A significant increase in hydroxyproline content was observed in vitro, and catalase activity increased along with decreased protein carbonyl content.[42] An aqueous extract of green tea was found to improve the skin of mice affected by photoaging. It was found to increase the level of collagen and elastin fibers and reduced the expression of collagende grading MMP-3 enzymes, thereby showing potential antiwrinkle effects.[43]

Topical treatment with EGCG on mouse skin results in prevention of UVB-induced immunosuppression and oxidative stress. The protective effects of green tea treatment on human skin either topically or consumed orally against UV light-induced inflammatory or carcinogenic responses are not well understood. Based on documented extensive effects of green tea on mouse skin models and very little in human skin, many pharmaceutical and cosmetics companies are supplementing their skin care products with green tea extracts.[44] In a recent study, human volunteers were made to consume green tea polyphenols in the form of capsules for a limited period, and it was observed that green tea catechins conjugate their metabolites in plasma, blister fluid, and skin biopsy samples.[45] In another study, 18 individuals aged between 21 years and 71 years were asked to apply green tea extract and a placebo topically, before exposure to UV radiation. The biopsy analysis and level of erythema suggested that the green tea pretreatment showed a significant reduction in the number of cells with sunburn.[46]

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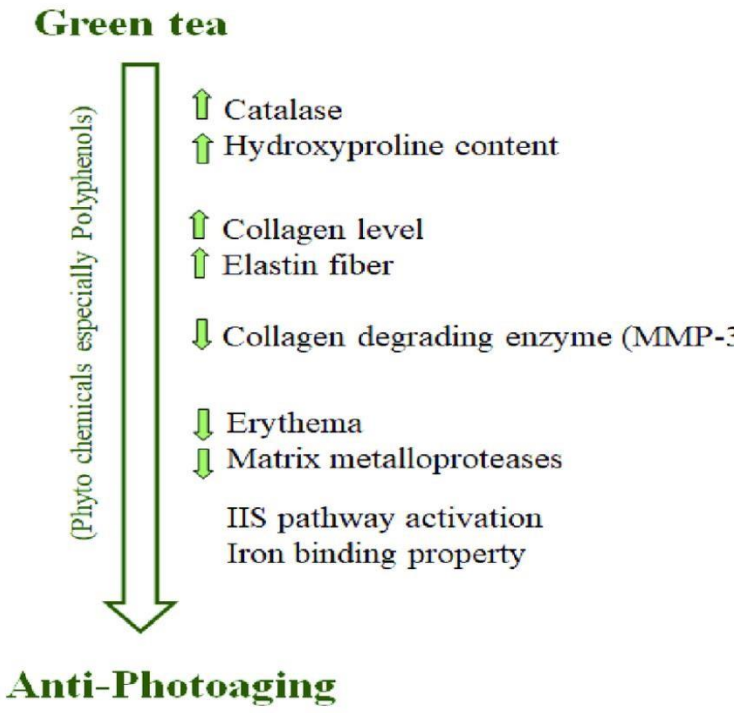

Twenty Chinese women volunteers in analyzing the effect of varying concentrations of green tea extract (2-5%) in protecting skin from UV induced photoaging through topical application. Along with the levels of erythema, the thickness of stratum corneum and epidermis, as well as the level of matrix metalloproteases, were measured by using

microscopic and immunohistochemical analysis. On day 1, a 3% topical application showed less erythema, whereas 5% showed damage along with the vehicle control and control with no topical application, which also showed post inflammatory hyperpigmentation. The sample using a 3% topical application showed mild pigmentation, whereas the other samples (2 and 4%) showed moderate pigmentation. Between 2 and 3% of topical applications showed a controlled level of thickening of the stratum corneum and epidermis when compared to other samples. A significant reduction of matrix metalloproteases was observed in applications ranging from 2 to 4%. Overall, this study suggests that an optimum concentration of green tea extract (3%) can protect the skin from UV radiation-induced damage.[47]

- **Neuro protective properties of green tea**

Human brains consume approximately 20% of the oxygen inhaled, but its antioxidant activity is less than that of other organs.[48,49] Tea polyphenols were found to directly scavenge ROS and RNS, inhibit the activity of nitric oxide synthase, xanthine oxidase, cyclooxygenases, and lipoxygenases, along with nuclear factor-κB and activator protein-1, and induce antioxidant enzymes such as glutathione S-transferases and superoxide dismutases to bind and chelate excess metals such as iron (Fe2+) and copper, in vitro.[50] EGCG was found to suppress the neurotoxicity induced by Aβ, as it could activate the glycogen synthase kinase-3β (GSK-3β), along with inhibiting c-Abl/FE65—the cytoplasmic nonreceptor tyrosine kinase which is involved in the development of the nervous system and nuclear translocation.[51] In another study, EGCG was observed to suppress the expression of TNFα, IL-1β, IL-6, and inducible nitric oxide synthase (iNOS), restoring the levels of intracellular antioxidants against free radical-induced pro-inflammatory effects in microglia, nuclear erythroid-2 related factor 2 (Nrf2), and heme oxygenase-1 (HO-1)(52).EGCG, besides its numerous putative bioactive benefits including anti-oxidative, ROS-scavenging, iron-chelating and anti-apoptotic properties, is frequently featured in PD biological therapy.[53] The two main advantages making it an attractive compound for PD therapy are its complete permeability in crossing the blood-brain barrier and its activation of the adenosine monophosphate-activated protein kinase (AMPK) pathway(54). This molecular mechanism for EGCG-mediated neuroprotective effects is via the increase of cytosolic Ca^{2+} levels, thereby influencing the activity of Ca^{2+-} /calmodulindependant protein kinase (CaMKKβ), an upstream kinase of AMPK.[55]

- **Autophagy properties of green tea**

Autophagy is an internal process that aids in the lysosomal degradation and removal of old and unwanted cellular molecules, including proteins, ribosomes, lipid droplets, and other organelles, thereby maintaining cellular homeostasis and survival under metabolic stress.[56,57]

Autophagy plays a critical role in modulating the overall health benefits of green tea. For instance, tea polyphenols were reported to activate autophagy through the mTOR pathway, thereby delaying apoptosis upon endoplasmic reticulum stress in HEK293T cells.[58] Green tea activated autophagy in HL-60 xenografts by increasing the activity of PI3 kinase and Beclin-.[59] In primary neuronal cells by inducing sirtuins.[60]

Cancer cells use autophagy to protect themselves from harsh conditions and increase their survival during chemotherapy and ionizing radiation.[61] In a recent study, EGCG was combined with a low strength pulsed electric field (PEF) and a low energy ultrasound (US) as a novel method for cancer treatment. After 72h of treatment, it was observed that this combination could achieve 20% alteration in the viability of human pancreatic cancer when compared to the control. Additionally, it could increase the level of intracellular ROS and inhibited Akt phosphorylation. Altogether, this combinatorial treatment induced autophagy as it switched from cytoprotective to cytotoxic, thereby causing cancer cell death with apoptosis.[62]

EGCG was also observed to increase the specificity and sensitivity of radiation in targeting cancer cells through autophagy, and the Nrf2 mechanism in colorectal cancer cells.[63] Doxorubicin, the chemotherapeutic drug for treating osteosarcoma cancer cells, was observed to have synergistic effects when combined with EGCG, thereby aiding in improving the clinical efficacy of antitumor drugs and promoting their further development.[64] Prevention and treatment of hepatocellular carcinoma in HepG2 cells were initiated by EGCG by regulating α-fetal protein secretion, thereby modulating autophagy.[65]

- **Stress resistance properties of green tea**

Green tea is a popular neutraceutical as an antioxidant. Antioxidants are compounds that protect cells against the damaging effects of reactive oxygen species, such as singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals, and peroxynitrite. An imbalance between antioxidants and reactive oxygen species results in oxidative stress, leading to cellular damage.[66]

ROS is essential for normal cellular metabolism and signaling. However, an alteration in the level of ROS can lead to oxidative stress, which damages cells and thereby the whole organism. Exposure to antioxidants during oxidative stress aids in the protection of the host by radical scavenging activity, or by other indirect antioxidant mechanisms.[67] An abundance of antioxidants allows green tea to impart stress resistance under these different physiological conditions. One of the important functions of green tea polyphenols is their vascular protective effect by anti-oxidative, anti-hypertensive, anti-inflammatory, anti-proliferative, antithrombogenic, and lipid-lowering activity. They can scavenge free radicals, chelate redox active transition metal ions and inhibit redox active transcription factors, alter enzymes involved in lipid biosynthesis, and reduce intestinal lipid absorption. They can prevent vascular inflammation, thereby preventing atherosclerotic lesions, inhibiting proliferation of vascular smooth muscle cells, and suppressing platelet adhesion.[68] These properties help green tea to reduce the stress level in the body, and thereby provide protection against cardiovascular ailments. Theanine, an ingredient in green tea, has been observed to promote resistance against paraquat,thereby promoting longevity in C. elegans.[69]

Green tea extract, when analyzed for its effect on Caco2 cells, was found to decrease the level of ROS. Additionally, after using a pretreatment of green tea extract for 20 h before exposure to oxidative stress, cell viability was increased and the production of free radicals was reduced when compared to controls.[70] Intestinally, consumption of green tea in chronic smokers was associated with a significant reduction of smoking-induced micronuclei in the white blood cells.[71]

- **CONCLUSION**

Laboratory studies showed the health effects of green tea. As the human clinical evidences is still limited, future research needs to define the actual magnitude of health benefits, establishes the safe range of tea consumption associated with these benefits, and elucidates the mechanism of action. Green tea is consumed throughout the world in various forms. The years of safe consumption of this beverages, supported by numerous studies showing health benefits, warrant a general recommendation to consume it regularly. Definitive conclusion concerning the protective effect of green tea have to come from well-designed observational epidermiological studies and intervention trials. The development of biomarkers for green tea consumption, as well as molecular markers for its biological effects, will facilitate future research in this area. Excessive use of green tea can impart negative results, as these

polyphenols inside the system will make them unstable, leading to autoxidative reactions and resulting in ROS production and the increase of other DNA damaging factors.

- **REFERENCE**

1. Graham, H.N. Green tea composition, consumption, and polyphenol chemistry. Prev. Med., 1992; 21: 334–350. [CrossRef]
2. Wierzejska, R. Tea and health—A review of the current state of knowledge. Przegl. Epidemiol, 2014; 68: 595–599.
3. Stagg GV, Millin DJ. The nutritional and therapeutic value of tea: A Review. Journal of Science of Food and Agriculture, 1975; 26: 1439-1459. DOI:10.1002/jsfa.2740261002
4. Xing L, Zhang H, Qi R, Tsao R, Mine Y. Recent Advances in the Understanding of the Health Benefits and Molecular Mechanisms Associated with Green Tea Polyphenols. Journal of Agricultural and Food Chemistry, 2019; 67(4): 1029-1043. doi:10.1021/acs.jafc.8b06146.
5. Harbowy ME, Balestine DA, Davies PA, Cai Y. Tea Chemistry. Critical Reviews in Plant Sciences, 1997; 16(5): 415-480. DOI: 10.1080/07352689709701956
6. Senanayake SN. Green tea extract: Chemistry, antioxidant properties and food applications−A review. Journal of Functional Foods, 2013; 5(4): 1529−1541. DOI: 10.1016/j.jff.2013.08.011
7. Kaur HP, Kaur S. Antibacterial activity and phytochemical profile of green tea, black tea and Divya peya herbal tea. Inter J Pure App Biosci., 2015; 3: 117-123.
8. Rietveld, A.; Wiseman, S. Antioxidant effects of tea: Evidence from human clinical trials. J. Nutr., 2003; 133: 3285–3292. [CrossRef] [PubMed]
9. Childs, B.G.; Durik, M.; Baker, D.J.; van Deursen, J.M. Cellular senescence in aging and age-related disease: From mechanisms to therapy. Nat Med., 2015; 21: 1424–1435. [CrossRef] [PubMed]
10. Santilli, V.; Bernetti, A.; Mangone, M.; Paoloni, M. Clinical definition of sarcopenia. Clin. Cases Miner. Bone Metab. 2014, 11, 177–180. [CrossRef] [PubMed]
11. Vanessa C, Gary W. A Review of the Health Effects of Green Tea Catechins in In Vivo Animal Models. J Nutr., 2004; 134: 3431S–3440S. [PubMed] [Google Scholar].
12. Katiyar SK, Elmets CA. Green tea polyphenolic antioxidants and skin photo protection (review). Int J Oncol., 2001; 18: 1307–13.
13. Babu PV, Sabitha KE, Shyamaladevi CS. Therapeutic effect of green tea extract on oxidative stress in aorta and heart of streptozotocin diabetic rats. Chem Biol Interact, 2006; 162: 114–120. doi: 10.1016/j.cbi.2006.04.009. [PubMed] [CrossRef] [Google Scholar].
14. Unno K, Takabayashi F, Yoshida H, Choba D, Fukutomi R, Kikunaga N, Kishido T, Oku N, Hoshino M. Daily consumption of green tea catechin delays memory regression in aged mice.

Biogerontology, 2007; 8(2): 89–95. doi: 10.1007/s10522-006-90368. [PubMed] [CrossRef] [Google Scholar].

15. Koo MWL, Cho CH. Pharmacological effects of green tea on the gastrointestinal system. Eur J Pharmacol, 2004; 500: 177–185. doi: 10.1016/j.ejphar.2004.07.023. [PubMed] [CrossRef] [Google Scholar].
16. Nance CL, Shearer WT. Is green tea good for HIV-1 infection? J Allergy Clin Immunol, 2003; 112: 851–3.
17. Gulcin, I. Antioxidant activity of food constituents: An overview. Arch. Toxicol, 2012; 86: 345–391. [CrossRef] [PubMed].
18. Sohanaki, H.; Baluchnejadmojarad, T.; Nikbakht, F.; Roghani, M. Pelargonidin improves memory deficit in amyloid β25-35 rat model of Alzheimer's disease by inhibition of glial activation, cholinesterase, and oxidative stress. Biomed. Pharmacother, 2016; 83: 85–91. [CrossRef] [PubMed].
19. Gulcin, I. Antioxidant and antiradical activities of L-carnitine. Life Sci., 2006; 78: 803–811. [CrossRef] [PubMed].
20. de Barboza, G.D.; Guizzardi, S.; Moine, L.; de Talamoni, N.T. Oxidative stress, antioxidants and intestinal calcium absorption. World J. Gastroenterol, 2017; 23: 2841– 2853. [CrossRef] [PubMed]
21. Delaunay-Moisan, A.; Appenzeller-Herzog, C. The antioxidant machinery of the endoplasmic reticulum: Protection and signaling. Free Radic. Biol. Med., 2015; 83: 341– 351. [CrossRef] [PubMed]
22. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. Oxford: Clarendon Press; 1985. [Google Scholar]
23. Skrzydlewska E, Ostrowska J, Farbiszewski R, Michalak K. Protective effect of green tea against lipid peroxidation in the rat liver, blood serum and the brain. Phytomedicine, 2002; 9: 232–238. doi: 10.1078/0944-7113-00119. [PubMed] [CrossRef] [Google Scholar]
24. Negishi H, Xu JW, Ikeda K, Njelekela M, Nara Y, Yamori Y. Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. J Nutr., 2004; 134: 38–42. [PubMed] [Google Scholar]
25. Sies, H. Oxidative stress: Oxidants and antioxidants. Exp. Physiol., 1997; 82: 291–295. [CrossRef] [PubMed]
26. Somogyi, A.; Rosta, K.; Pusztai, P.; Tulassay, Z.; Nagy, G. Antioxidant measurements. Physiol. Meas, 2007; 28: R41–R55. [CrossRef] [PubMed]

27. De Barboza, G.D.; Guizzardi, S.; Moine, L.; de Talamoni, N.T. Oxidative stress, antioxidants and intestinal calcium absorption. World J. Gastroenterol, 2017; 23: 2841– 2853. [CrossRef] [PubMed]
28. Bosch, R.; Philips, N.; Suárez-Pérez, J.A.; Juarranz, A.; Devmurari, A.; Chalensouk Khaosaat, J.; González, S. Mechanisms of Photoaging and Cutaneous Photocarcinogenesis, and Photoprotective Strategies with Phytochemicals. Antioxidants, 2015; 4: 248–268. [CrossRef] [PubMed]
29. Bocco, A.; Cuvelier, M.E.; Richard, H.; Berset, C. Antioxidant activity and phenolic composition of citrus peel and seed extracts. J. Agric. Food. Chem. 1998; 46: 2123– 2129. [CrossRef
30. Eberhardt, M.V.; Lee, C.Y.; Liu, R.H. Antioxidant activity of fresh apples. Nature 2000; 405: 903–904. [CrossRef] [PubMed]
31. Ganesan, K.; Kumar, K.S.; Rao, P.V.S. Comparative assessment of antioxidant activity in three edible species of green seaweed, Enteromorpha from Okha, Northwest coast of India. Innov. Food Sci. Emerg., 2011; 12: 73–78. [CrossRef].
32. Weber, P.; Bendich, A.; Schalch, W. Vitamin C and human health-a review of recent data relevant to human requirements. Int. J. Vit. Nut. Res., 1996; 66: 19–30.
33. Gulcin, I. Antioxidant activity of food constituents: An overview. Arch. Toxicol., 2012; 86: 345–391. [CrossRef] [PubMed].
34. Ding, L.; Gao, X.; Hu, J.; Yu, S. (−)Epigallocatechin-3-gallate attenuates anesthesiainduced memory deficit in young mice via modulation of nitric oxide expression. Mol. Med. Rep., 2018; 18: 4813–4820. [CrossRef] [PubMed].
35. Petruk, G.; Del Giudice, R.; Rigano, M.M.; Monti, D.M. Antioxidants from Plants Protect against Skin Photoaging. Oxid. Med. Cell. Longev, 2018; 2018; 1454936. [CrossRef] [PubMed].
36. Lorencini, M.; Brohem, C.A.; Dieamant, G.C.; Zanchin, N.I.; Maibach, H.I. Active ingredients against human epidermal aging. Ageing Res. Rev., 2014; 15: 100–115. [CrossRef] [PubMed].
37. Roh, E.; Kim, J.E.; Kwon, J.Y.; Park, J.S.; Bode, A.M.; Dong, Z.; Lee, K.W. Molecular mechanisms of green tea polyphenols with protective effects against skin photoaging. Crit. Rev. Food Sci. Nutr., 2017; 57: 1631–1637. [CrossRef] [PubMed].
38. Dunaway, S.; Odin, R.; Zhou, L.; Ji, L.; Zhang, Y.; Kadekaro, A.L. Natural Antioxidants: Multiple Mechanisms to Protect Skin from Solar Radiation. Front. Pharmacol, 2018; 9: 392. [CrossRef] [PubMed].

39. Smijs, T.G.; Pavel, S. Titanium dioxide and zinc oxide nanoparticles in sunscreens: Focus on their safety and effectiveness. Nanotechnol. Sci. Appl., 2011; 4: 95–112. [CrossRef] [PubMed].
40. Zhang, L.; Zheng, Y.; Cheng, X.; Meng, M.; Luo, Y.; Li, B. The anti-photoaging effect of antioxidant collagen peptides from silver carp (Hypophthalmichthys molitrix) skin is preferable to tea polyphenols and casein peptides. Food Funct., 2017; 8: 1698–1707. [CrossRef] [PubMed]
41. Lee, K.O.; Kim, S.N.; Kim, Y.C. Anti-wrinkle Effects of Water Extracts of Teas in Hairless Mouse. Toxicol. Res., 2014; 30: 283–289. [CrossRef] [PubMed]
42. Lee MJ, Maliakal P, Chen L. Pharmacokinetics of tea catechins after ingestion of green tea and(-)-epigallocatechin-3-gallate by humans: formation of different metabolites and individual variability.Cancer Epidemiol Biomarkers Prevent, 2002; 11: 1025–32.
43. Clarke, K.A.; Dew, T.P.; Watson, R.E.; Farrar, M.D.; Osman, J.E.; Nicolaou, A.; Rhodes, L.E.; Williamson, G. Green tea catechins and their metabolites in human skin before and after exposure to ultraviolet radiation. J. Nutr. Biochem, 2016; 27: 203–210. [CrossRef] [PubMed]
44. Mnich, C.D.; Hoek, K.S.; Virkki, L.V.; Farkas, A.; Dudli, C.; Laine, E.; Urosevic, M.; Dummer, R. Green tea extract reduces induction of p53 and apoptosis in UVB-irradiated human skin independent of transcriptional controls. Exp. Dermatol, 2009; 18: 69–77. [CrossRef] [PubMed]
45. Li, Y.H.; Wu, Y.; Wei, H.C.; Xu, Y.Y.; Jia, L.L.; Chen, J.; Yang, X.S.; Dong, G.H.; Gao, X.H.; Chen, H.D. Protective effects of green tea extracts on photoaging and photommunosuppression. Skin Res. Technol, 2009; 15: 338–345. [CrossRef] [PubMed]
46. Váli, L.; Hahn, O.; Kupcsulik, P.; Drahos, A.; Sárváry, E.; Szentmihályi, K.; Pallai, Z.; Kurucz, T.; Sípos, P.; Blázovics, A. Oxidative stress with altered element content and decreased ATP level of erythrocytes in hepatocellular carcinoma and colorectal liver metastases. Eur. J. Gastroenterol. Hepatol, 2008; 20: 393–398. [CrossRef] [PubMed]
47. Uttara, B.; Singh, A.V.; Zamboni, P.; Mahajan, R.T. Oxidative stress and neurodegenerative diseases: A review of upstream and downstream antioxidant therapeutic options. Curr. Neuropharmacol, 2009; 7: 65–74. [CrossRef] [PubMed]
48. Caruana, M.; Vassallo, N. Tea Polyphenols in Parkinson's Disease. Adv. Exp. Med. Biol., 2015; 863: 117–137. [PubMed]
49. Lin, C.L.; Chen, T.F.; Chiu, M.J.; Way, T.D.; Lin, J.K. Epigallocatechin gallate (EGCG) suppresses beta-amyloid-induced neurotoxicity through inhibiting c-Abl/FE65 nuclear translocation and GSK3 beta activation. Neurobiol. Aging, 2009; 30: 81–92. [CrossRef] [PubMed]

50. Wei, J.C.C.; Huang, H.C.; Chen, W.J.; Huang, C.N.; Peng, C.H.; Lin, C.L. Epigallocatechin gallate attenuates amyloid β-induced inflammation and neurotoxicity in EOC 13.31 microglia. Eur. J. Pharmacol, 2016; 770: 16–24.
51. Singh N.A., Mandal A.K., Khan Z.A. Potential neuroprotective properties of epigallocatechin-3-gallate (EGCG). Nutr J, 2016; 15(1): 60. [http://dx.doi.org/10.1186/s12937-016-0179-4]. [PMID: 27268025]. [PMC free article] [PubMed] [Google Scholar]
52. Hang L., Basil A.H., Lim K.L. Nutraceuticals in Parkinson's Disease. Neuromol. Med, 2016; 18(3): 306–321. [http://dx.doi.org/10.1007/s12017-016-8398-6]. [PMID: 27147525]. [PMC free article] [PubMed] [Google Scholar]
53. Kim J., Shin J., Ha J. Screening methods for AMP-activated protein kinase modulators: a patent review. Expert Opin. Ther. Pat, 2015; 25(3): 261–277. [http://dx.doi.org/10.1517/13543776. 2014.995626]. [PMID: 25535089]. [PubMed] [Google Scholar]
54. Wang, M.; Zhang, W.B.; Zhu, J.H.; Fu, G.S.; Zhou, B.Q. Breviscapine ameliorates hypertrophy of cardiomyocytes induced by high glucose in diabetic rats via the PKC signaling pathway. Acta Pharmacol. Sin., 2009; 30: 1081–1091. [CrossRef] [PubMed]
55. Calgarotto, A.K.; Maso, V.; Junior, G.C.F.; Nowill, A.E.; Filho, P.L.; Vassallo, J.; Saad, S.T.O. Antitumor activities of Quercetin and Green Tea in xenografts of human leukemia HL60 cells. Sci. Rep., 2018; 8: 3459. [CrossRef] [PubMed]
56. Ng C.H., Basil A.H., Hang L., Tan R., Goh K.L., O'Neill S., Zhang X., Yu F., Lim K.L. Genetic or pharmacological activation of the Drosophila PGC-1α ortholog spargel rescues the disease phenotypes of genetic models of Parkinson's disease. Neurobiol. Aging., 2017; 55: 33–37. [http://dx.doi.org/10.1016/j.neurobiolaging. 2017.03.017]. [PMID: 28407521]. [PubMed] [Google Scholar]
57. Whitworth A.J. Drosophila models of Parkinson's disease. Adv. Genet., 2011; 73: 1– 50. [http://dx.doi.org/10.1016/B978-0-12-380860-8.00001-X]. [PMID: 21310293]. [PubMed] [Google Scholar]
58. Choi J.Y., Park C.S., Kim D.J., Cho M.H., Jin B.K., Pie J.E., Chung W.G. Prevention of nitric oxide-mediated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinson's disease in mice by tea phenolic epigallocatechin 3gallate. Neurotoxicology, 2002; 23(3): 367–374. [http://dx.doi.org/10.1016/S0161-813X(02)00079-7]. [PMID: 12387363]. [PubMed] [Google Scholar]

59. Wang, Q.; He, W.Y.; Zeng, Y.Z.; Hossain, A.; Gou, X. Inhibiting autophagy overcomes docetaxel resistance in castration-resistant prostate cancer cells. Int. Urol. Nephrol, 2018; 50: 675–686. [CrossRef] [PubMed]
60. Hsieh, C.H.; Lu, C.H.; Kuo, Y.Y.; Chen, W.T.; Chao, C.Y. Studies on the non-invasive anticancer remedy of the triple combination of epigallocatechin gallate, pulsed electric field, and ultrasound. PLoS ONE, 2018; 13: e0201920. [CrossRef] [PubMed]
61. Enkhbat, T.; Nishi, M.; Yoshikawa, K.; Jun, H.; Tokunaga, T.; Takasu, C.; Kashihara, H.; Ishikawa, D.; Tominaga, M.; Shimada, M. Epigallocatechin-3-gallate Enhances
62. Radiation Sensitivity in Colorectal Cancer Cells Through Nrf2 Activation and Autophagy. Anticancer Res, 2018; 38: 6247–6252. [CrossRef] [PubMed]
63. Wang, W.; Chen, D.; Zhu, K. SOX2OT variant 7 contributes to the synergistic interaction between EGCG and Doxorubicin to kill osteosarcoma via autophagy and stemness inhibition. J. Exp. Clin. Cancer Res., 2018; 37: 37. [CrossRef] [PubMed]
64. Zhao, L.; Liu, S.; Xu, J.; Li, W.; Duan, G.; Wang, H.; Yang, H.; Yang, Z.; Zhou, R. A new molecular mechanism underlying the EGCG-mediated autophagic modulation of AFP in HepG2 cells. Cell Death Dis, 2017; 8: e3160. [CrossRef] [PubMed]
65. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. Oxford: Clarendon Press; 1985. [Google Scholar]
66. Yiannakopoulou, E.C. Targeting oxidative stress response by green tea polyphenols: Clinical implications. Free Radic. Res., 2013; 47: 667–671. [CrossRef] [PubMed]
67. Babu, P.V.; Liu, D. Green tea catechins and cardiovascular health: An update. Curr. Med. Chem., 2008; 15: 1840–1850. [CrossRef] [PubMed]
68. Zarse, K.; Jabin, S.; Ristow, M. L-Theanine extends lifespan of adult Caenorhabditis elegans. Eur. J. Nutr., 2012; 51: 765–768. [CrossRef] [PubMed]
69. Rodríguez-Ramiro, I.; Martín, M.A.; Ramos, S.; Bravo, L.; Goya, L. Comparative effects of dietary flavanols on antioxidant defences and their response to oxidantinduced stress on Caco2 cells. Eur. J. Nutr., 2011; 50: 313–322. [CrossRef] [PubMed]
70. Xue, K.X.; Wang, S.; Ma, G.J.; Zhou, P.; Wu, P.Q.; Zhang, R.F.; Xu, Z.; Chen, W.S.; Wang, Y.Q. Micronucleus formation in peripheral-blood lymphocytes from smokers and the influence of alcohol- and tea-drinking habits. Int. J. Cancer, 1992; 50: 702–705. [CrossRef] [PubMed]