

**MULTIFARIOUS PHARMACOLOGICAL POTENTIALS OF GREEN
AND BLACK TEA EXTRACTED FROM *CAMELLIA SINENSIS*: FROM
KITCHEN TO CLINIC****Harsimran Singh*, Jagdeep Kaur and Nitish Kumar**Department of Pharmacology, Sri Sai College of Pharmacy, Badhani, Pathankot,
Punjab, India.

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Correspondence for*Author****Harsimran Singh**Department of
Pharmacology, Sri Sai
College of Pharmacy,
Badhani, Pathankot,
Punjab, India.**ABSTRACT**

Camellia sinensis, imperative and therapeutically active basil broadly used as a beverage. The leaves of *Camellia sinensis* has been used extensively to prepare different types of tea. The various varieties of tea extracted from *Camellia sinensis* are green tea, black tea, oolong tea and white tea. These varieties of tea are useful for the treatment of number of pathological conditions. Out of these varieties the green tea has great potential in the prevention and treatment of pathological

disorders such as neurodegenerative disorders, cancer, diabetes mellitus and oxidative stress. In addition, the black tea shows a fabulous effect on cardiac disorders such as angina pectoris, congestive heart failure and myocardial infarction. In this review, we have critically discussed the possible mechanisms involved in the treatment of various disorders by the use of green and black tea.

KEYWORDS: Tea, Anti-oxidant, Anti-inflammatory, Anti-cancer.**INTRODUCTION**

Herbal medicine is meant to be the oldest method which includes using parts of plant for treatment of diseases. Ayurveda is being practised in India from about 5000 years and in some other countries such as China, Russia, Egypt, Greek and Rome. Now its practice and use has been spread throughout the world; about 75-80% of world population are using herbal medicine for their primary health treatment, mainly developing countries are shifting towards herbal medicines.^[1] Herbal drugs are the best alternative for the prescription drugs, because

of their universal compatibility and less side effects.^[2] Herbs are used after they are processed but some are used as it is derived from natural source.

Out of all the herbs, *Camellia sinensis* is the most commonly used; as beverage and as therapeutic aid. Tea originates from China, since hundreds of years and has various health benefits. Chinese *Camellia sinensis* is now cultivated throughout the world in tropical and subtropical regions.^[3] It can reach 6 feet, but trimmed to required height, evergreen shrub has a strong taproot and is cultivated for their leaves only. Flowers are yellow-white in colour with diameter ranges from 2.5-4 cm in diameter, with 7-8 petals.^[3] Seeds of these plants are compressed to yield Tea oil which is used for medicinal and cosmetic purposes.^[3] The various types of teas are available in the market but are derived from a single species i.e. *Camellia sinensis*. The difference in various formulations of teas occurs due to change in the time of harvesting and method used for processing (withering) tea in manufacturing unit. The most popular teas that manufactured are White Tea, Oolong tea, Green Tea and Black Tea.^[4] White tea and Oolong Tea are very rarely used but use of green tea has been increased, whereas black tea is most common and is widely consumed by consumers.^[5]

Further, tea contains many bioactive compounds out of which majorly found compounds are polyphenols mainly catechins. Moreover, it also contains alkaloids such as caffeine, theophylline and theobromine, amino acids, carbohydrates, proteins, vitamins, chlorophyll, volatile compounds, fluoride and minerals trace elements such as chromium, manganese, selenium and zinc.^[6]

The common pharmacological action shown by various teas are anti-oxidant, anti-aging, anti-inflammatory, anti-microbial, anti-arthritis, anti-viral, anti-diabetic, anti-mutagenic and hypocholesterolemic activities.^[3,7] All these activities make it an important beverage and therapeutic aid in treatment and prevention of various disorders in human beings. Therefore, in this review, the diverse pharmacological activities of different types of tea along with the explored signalling mechanisms are discussed in detail.

EXTRACTION OF DIFFERENT TYPES OF TEA

The different varieties of teas are mass-produced from one single species i.e. *Camellia sinensis*. The different varieties of tea are formulated with the help of several processing methods.^[8] The procedure of processing of different tea includes:-

1. Harvesting: Harvesting of leaves and buds are done according to the type of tea to be manufactured in their respective season. For e.g. – for oolong tea, a leaf and bud are plucked.^[9]

2. Withering: The leaves picked up and spread out under the sun for withering. This is done to soften the cell walls of the leaves (due to accumulation of moisture on the surface for evaporation) and followed by beginning of natural enzymatic fermentation and sets it up for next step of processing i.e. oxidation^[9].

3. Oxidation: Oxidation is done before curling and twisting of leaves. During this process the leaves turn to darker green or red color due to break down of cell structure of the leaves. This step causes development of grassy, fruity and flowery taste of leaves.^[10]

4. Kill green (Fixing): This step of processing is used to prepare oolong tea and involves steaming of leaves followed by hand pressing in a hot pan and baking techniques to remove green color from leaves.^[8]

5. Rolling: In the next step, to intensify the tea flavor, the leaves are passed through hot or cold roller to slightly break down the shape of leaves.^[10]

6. Drying: The rolling is followed by drying, which is generally used to stop fermentation, prevention of mold growth, removal of grassy taste and maintains the necessary moisture content develops the tea's aroma. The drying can be done by methods of hot air, pan heating and sun drying.^[11]

7. In the last step of processing sorting can be done according to different grades followed by packaging.^[9] The complete processing of various teas are mentioned in the table 1

Processing of different Types of Teas				
Type of Tea	White Tea	Green Tea	Oolong Tea	Black Tea
Part Used	Unopened leaf and buds covered with white fine hairs	Two leaves & a bud	A leaf & a bud	Two Leaves & bud
Time period of harvesting	February-April	March- August	November-March	July-October
Withering	Very little	No	55-60% withered	Trough Withering
Oxidation / Fermentation	Unfermented	Unfermented	8-85%	Fully Fermented
Rolling	No-rolling	Yes	Hand Rolling	Yes
Drying	Air, solar & mechanical	Steam or dryer	Low Drying	Yes

Table no. 1- Detailed processing of tea

PHARMACOLOGICAL ACTIONS OF VARIOUS FORMULATIONS OF TEA

The various types of tea are employed in treating number of pathological disorders. Tea has a great potential in the treatment and prevention of number of diseased conditions such as Aging, Cancer, Cardiovascular disease, inflammation, oxidative stress, neuron degenerative disorders.^[7] Recently, it has been observed in no. of studies that, oxidative stress is found to be main causative agent for development of number of pathological conditions. It causes cellular swelling, change in cellular functioning and cell death neuronal cell death and responsible for disease such as Alzheimer, Parkinson disease, Huntington's diseases etc.^[12] The various activities of different preparation of tea along with the detailed pathological mechanisms are discussed as

1. Green Tea and Neurodegenerative disorders

Neuron degeneration is state characterised by progressive dysfunction, degeneration and death of specific population of neurons which are often synaptically interconnected.^[13] Neuron degeneration occurs due to various Patho physiological changes. Green tea mainly active constituent catechins has shown to prevent neuron degeneration either by prevention of

death of dopaminergic neurons in substantia nigra or by maintaining the required dopamine levels.^[14] Following are some factors involved in neuron degeneration and mechanism of action of tea to prevent neuron degeneration

a) The Protein Kinase C (PKC) is protein involved in signalling pathways such as cell survival and cell apoptosis.^[15] It involves in the conversion of amyloid precursor protein (APP) into amyloidogenic soluble APP (sAPP) which further causes inhibition of formation of β -amyloid and prevents the β -amyloid induced neuronal cell death.^[12] Moreover, PKC also causes inhibition of 6-hydroxydopamine and prevents neuronal cell death.^[16] The green tea, mainly catechins at the dose of 2mg/kg/day activates PKC and shows its neuro protective effect by preventing dopaminergic neuron cell death in substantia nigra in mice.^[12]

b) Chelation of iron ions: Iron is necessary for the neuro-embryogenesis and participates in various physiological functions in the body such as heme production, reduction of reactive oxygen species through SOD (anti-oxidant enzyme), myelination, electron transport etc.^[17] The accumulations of iron in brain causes generation of hydroxyl ion on reaction with endogenous hydrogen peroxide, leading to cell death^[18], results in the development of Alzheimer disease, Parkinson disease and other neurological disorders.^[17] Catechins present in green tea are good chelating agents and had shown to chelate iron ions and prevents accumulation of iron ions in brain as they can cross blood brain barrier. Hence, prevents the death of dopaminergic neurons in substantia nigra.^[11] Recent study by Sharma M. et al, 2014, confirms the potential of green tea to preserve the striatal levels of dopamine and reduces the risk of occurrence of neuronal disease.^[19] Overall, catechins have great potential to treat neurological disorders. The diagrammatic presentation of possible mechanism of catechins as neuroprotective agent has been depicted in figure 1.

2. Black Tea and Cardio-protection

Distorted functioning of blood vessels and heart are termed as cardiovascular disorders such as myocardial infarction, hypertension, atherosclerosis etc.^[20] Black tea has been shown to prevent lipid peroxidation by increasing the activity of superoxide dismutase, glutathione peroxidase and catalase enzymes^[21], which results in reduction in LDL levels, inhibition of human vascular smooth muscle proliferation, reduction of aortic cholesterol and atheromatous areas^[12] and hence useful in prevention of atherosclerosis and hence reduces the risk of heart failure.^[19]

Catechins have been shown to reduce absorption of cholesterol in the intestine by reducing the solubility of cholesterol in mixed micelle (intestine).^[22] This causes lowering of cholesterol and lipid levels in blood. Thus reduces a risk of occurrence of cardiac disorders such as angina, congestive heart failure (CHF), Myocardial infarction etc.^[23] The data concerning the beneficial effects of various types of teas in cardiovascular disorders lack. Hence, it is recommended to explore the unexplored potential of various tea in in-vitro and in-vivo.

3. Green Tea and Anti-cancer action

Cancer is the uncontrolled growth of abnormal cells in the body. Cell's division and death occurs normally only when it is controlled by various factors. But when these factors fails to control the division and death of cell, the normal gets converted into malignant cell and leads to progression of cancer in the body.^[24] Green Tea has great potential in the prevention of cancer and some of its effects are mentioned below

a) Induction of apoptosis of malignant cells: It has been seen that tumour cell proliferation occurs due to over expression of growth factors and factor receptors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF).^[25] Some other factors are also involved in cell growth and differentiation such as NK- κ B and AP-1. These both regulate genes that are involved in cell survival, differentiation, Inflammation and growth.^[14] Tea catechins have shown to inhibit tumour cell proliferation through the inhibition of growth factor, growth factor receptor^[25] and scavenging of reactive oxygen species (ROS) causes inhibition of transcription factors NK- κ B & AP-1, which leads to inhibition of cell growth and induction of apoptosis of tumour cell and produces its cancer protective effects.^[12]

b) Angiogenesis is linked with the wound healing, cancer and various ischemic and inflammatory diseases.^[20] Various factor are involved in inducing angiogenesis are vascular endothelial growth factor (VEGF), matrix metalloproteinase (MMP) and cell signalling.^[26-28]

i) VEGF is involved in inducing angiogenesis. Tumour cells are deficient in oxygen and nutrient due to reduced supply of blood to these cells. Due to activation of angiogenesis process, results development of new blood vessels and causes increased supply of oxygen and nutrients to tumour cells and increases growth of tumour cells.^[26]

ii) MMP structurally belongs to zinc-dependent endopeptidases and have capacity to degrade all the components of extracellular matrix (ECM). It has been found that MMP are significantly involved in the tissue morphogenesis, growth, tissue repair and angiogenesis. As MMP are involved in ECM degradation, alterations in this process can cause development of tumour cells.^[27]

iii) Cell signalling is important for a cell to receive information from other cells. This information is analysed by the cell and regulate various process such as cell differentiation, apoptosis, protein synthesis, cell growth, cell architecture and polarity. Normal cells get converted into malignant cells if there is alteration in cell signalling machinery.^[28]

Green tea, mainly catechins has been shown to prevent cancer by its anti-angiogenic through the inhibition of expression of vascular endothelial factor receptor.^[29] Further, gelatin zymography of human brain tumour (glioblastoma and pituitary tumours) confirmed that green tea polyphenols has strongest power of inhibition of metalloproteinase.^[30] Squamous carcinoma cells treated with green tea extracts, lead to alteration in cell signalling and decreased the protein release from 107 to 21 and mentioned that alteration occurred through EGFR and Notch Pathways of cell signalling.^[28]

4. Green Tea and Anti-diabetic action

Diabetes Mellitus is a group of metabolic disorder which is identified as high blood glucose levels can either because of inadequate release of insulin or increase resistance of body cells towards insulin. Patients suffering experience polyuria, polydipsia and polyphagia.^[31] Tea has found to be effective in both type-1 and type-2 diabetes mellitus, the green tea has been shown to be beneficial in type-2 diabetes mellitus.^[32] Further, the catechins, major constituent of green tea increased the insulin sensitivity in SD Rats and also enhanced the basal and insulin stimulated glucose uptake leading lowering of fasting plasma levels of glucose ^[32] In addition, increased lipid peroxidation causes increased formation of superoxide radicle within the cell, results in inhibition SOD enzyme (anti-oxidant). Lipid peroxidation at its maximum levels causes over production of cholesterol and related products such as triglycerides, VLDL, LDL etc., and causes tissue and organ damage, resulting increased complications of diabetes mellitus.^[33] Hence, inhibition of lipid peroxidation by green tea catechins causes decrease in levels of cholesterol and other related products in plasma and improves lipid profile.^[12] Moreover, scavenging of reactive oxygen species (ROS) by tea catechins reduces oxidative stress induced β -cell destruction.^[7] In another study, the immune cells produces

cytokine that infiltrates pancreatic islets is the main cause β -cells destruction in insulin-dependent diabetes mellitus.^[34] The inducible nitric oxide synthase (iNOS) causes generation of nitric oxide (NO) within the cell and produces cytokines induced pancreatic β -cell damage^[35], demonstrated that green tea catechins reduced the levels of nitric oxide by inhibiting iNOS gene expression and lead to reduction in level of cytokines. Thus, green tea catechins prevents the diabetes mellitus progression. The possible mechanism of green tea as anti-diabetic agent has been depicted in figure 3.

5. Green Tea and Anti-Aging action

Aging is natural phenomenon, followed by progressive alteration in the body's homeostatic adaptive responses and following are causes of aging and beneficial effect of tea in preventing them.

As the age increases, 8-oxo-deoxyguanosine (8-oxo-DG) starts accumulating in multiple mitochondria genomes (mitochondrial DNA) and leads to mitochondrial dysfunction.^[36] The mechanism is not so clear that how the green tea causes reduction in the levels of 8-oxo-deoxyguanosine and shows its action in the prevention of oxidative damage to DNA.^[37] In addition, reactive oxygen species (ROS) are found to protective agents as they help in tissue repair and adaptation by enhancing tissue signalling. But increased release of ROS produces toxic effects in the body such as lipid per oxidation, tumour cell proliferation, aging etc.^[38] Thus, regular consumption of green tea (catechins) has been shown to maintain the balance between ROS and anti-oxidants in the body^[39], increases the activity of anti-oxidant enzymes such as SOD^[11] from various organs (kidney and brain) of the body. These all collectively reduce oxidative stress in the body, preserves the serum lipid^[12] and protein from oxidative damage and prevents the memory loss through prevention of the iron accumulation related cell death.^[11]

6. Green Tea and Anti-inflammatory action

Inflammation is a protective mechanism against any type of harmful stimuli to vascular tissues in order to prevent the damage to other tissues.^[20] There is number of pathological mechanisms by which the green tea has shown anti-inflammatory action. The ROS causes progression of inflammation in the body. The dysfunction of endothelial and tissue damage is caused by increased release of ROS by polymorphonuclear neutrophils at the site of inflammation.^[40] Green tea causes neutralisation of ROS and causes reversal of cellular changes induced by ROS.^[41]

The MMP enzyme are present in almost all the tissues of the body and is involved in regulation of barrier function, inflammatory cytokines and chemokine activity in an inflammation.^[27] Thus, green tea polyphenols have shown to inhibit MMP which produces anti-angiogenic and anti-inflammatory effects in the body.^[30] In addition, green tea causes reduction in inflammation by stimulating ROS scavenging enzymes, results in scavenging of ROS causing inhibition of NF- κ B mediated gene expression and causes induction of apoptosis of tumour cells and reduction of inflammation.^[14] Hence, the green tea has a potential to act as anti-inflammatory agent and the possible mechanisms has been described in figure 5.

7. Green Tea and Anti-oxidant action

Oxidative stress is a phenomenon in which there is disturbance in equilibrium/balance between free radical reactive oxygen species and antioxidant defence mechanism of the body which may lead to cellular damage.^[42] Oxidative stress leads to the production of peroxides and free radicals that can damage all the components of a cell, including proteins, lipids and DNA. ROS can lead to variation in the cellular function of the cell and may lead to death of the cell.^[42] Reactive oxygen species can be beneficial too as they are the important signalling mediators, stimulate immune system as a way to attack and kill pathogens; a short-term oxidative stress may also be important in prevention of aging.

Antioxidant activity of tea is studied a lot as increased oxidative stress leads to production of different pathological disorders such as atherosclerosis, hypertension, alzheimer, parkinson disease and eye disorder.^[44] Supplementation of green tea causes reduction of Nitric oxide plasma concentration by inhibiting the expression of nNOS^[35], inhibition of lipid peroxidation.^[12] Increased activity of Superoxide dismutase (SOD) and catalase enzymes, results in neutralisation of ROS and maintains the balance between oxidants and anti-oxidant substances in the body. Hence, enhances the anti-oxidant strength of body.^[12,39]

8. Green Tea and Anti-obesity action

The Green Tea extracts at doses 400 & 800 mg/Kg has reduced absorption of fatty acids and metabolism reduce the expression of the IL-6 and TNF- α gene in high fat fed rats in 6 weeks.^[44] Green Tea catechins have shown reduction in proliferation and differentiation of adipocytes; levels of triglycerides, free fatty acids, cholesterol, glucose and leptin. These all effects of catechins causes' reduction in body weight and body fat in human subjects. Cell

culture system and animal models of obesity confirmed catechins also increase beta-oxidation and thermogenesis.^[46] These all effects may be useful in the treatment of obese patients.

DIAGRAMS

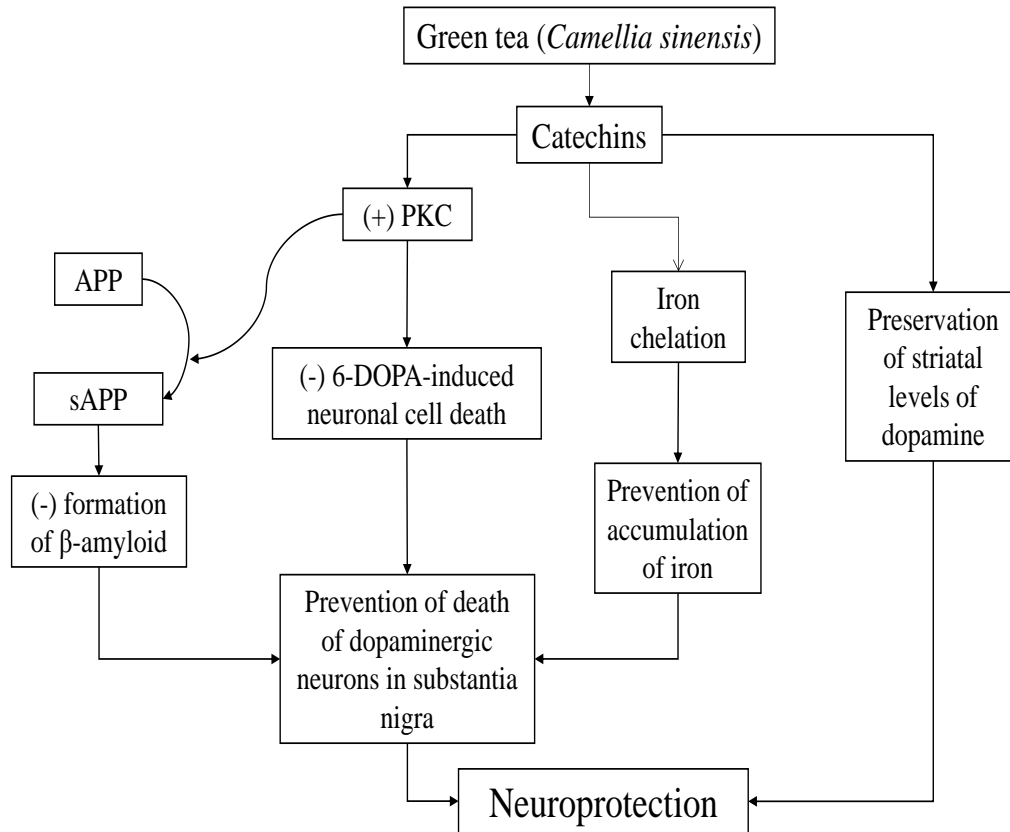


Fig. 1:- Mechanism of Green tea in treating Neurodegenerative disorders.

(+) indicates Activation; (-) indicates Inhibition; APP indicates amyloid precursor protein; sAPP indicates soluble amyloid precursor protein; PKC indicates Protein kinase C; 6-hDOPA indicates 6-hydroxydopamine

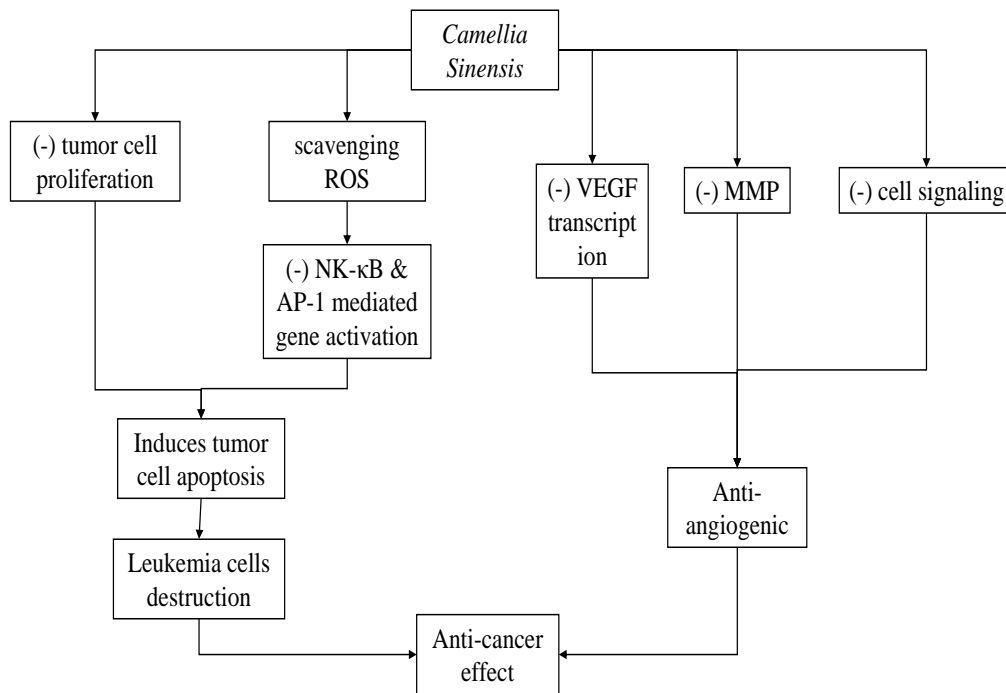


Fig.2 Mechanism of Green tea treating cancer

(+) indicates Activation; (-) indicates Inhibition; ROS indicates Reactive Oxygen Species; VEGF indicates Vascular Endothelial Growth Factor; MMP indicates Matrix Metalloproteinase

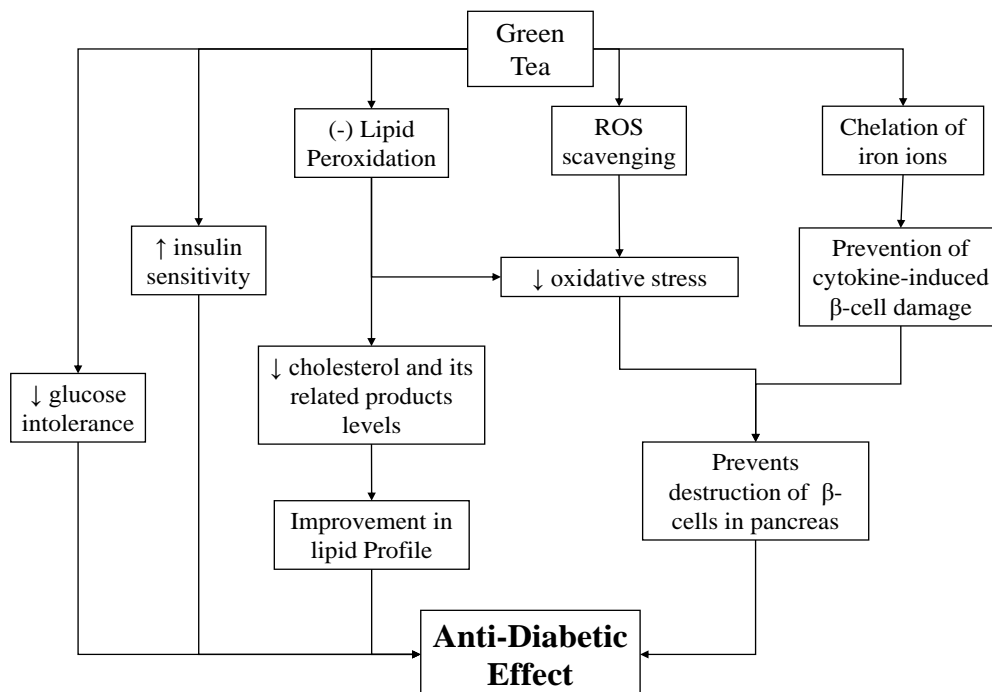


Fig. 3 Mechanism of Green tea in treating Diabetes Mellitus

↑ indicates Increase; ↓ indicates Decrease; (-) indicates Inhibition; ROS indicates reactive oxygen species

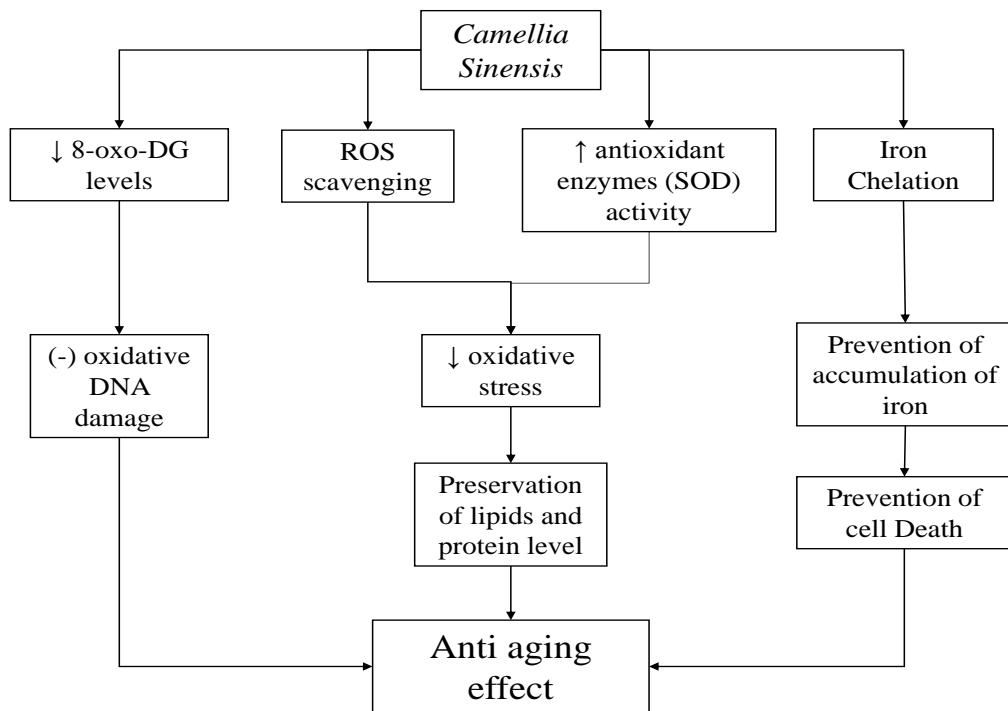


Fig. 4 Mechanism of Green tea in treating Aging

8-oxo-DG indicates 8-oxo-deoxyguanosine; ↑ indicates Increase; ↓ indicates Decrease; (-) indicates Inhibition

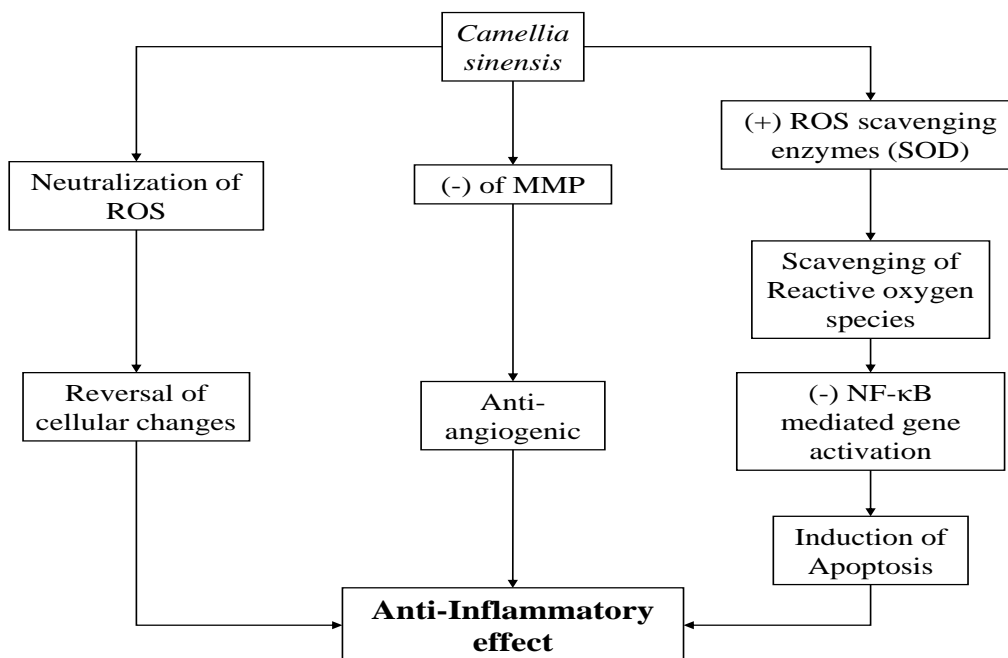


Fig. 5 Mechanism of Green Tea in treating Inflammation

(+) indicates Activation; (-) indicates Inhibition; MMP indicates Matrix Metalloproteinase; SOD indicates Superoxide dismutase

CONCLUSION

In this review, we have discussed the detailed therapeutic effects of green and black tea extracted from leaves of *Camellia Sinensis*. The various phytochemical analysis has been revealed that *Camellia Sinensis* contains many bioactive compounds out of which polyphenols primarily catechins are responsible for diverse pharmacological actions of green and black tea in various pathological conditions. The present review revealed that catechin major constituent of green and black tea has great potential to treat neurodegenerative disorders, cardiac disorders, cancer, diabetes mellitus, oxidative stress and aging. Further, the anti-oxidant and anti-inflammatory effect of black tea, green tea, oolong tea and white tea and their comparative effects are elucidated in our laboratory. We hope for a paradigm shift towards more focused research on other varieties of tea such as oolong tea, black tea and white tea in near future, which opens a new vista of understanding molecular mechanism of action involved in the treatment of various chronic disorders.

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CONFLICT OF INTEREST

The Author(s) declare(s) that he has no conflicts of interest to disclose.

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