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Catechin, as an Emerging Front-line Defense Flavonoid against Stress-Related Disorders: An Updated Review

Vaishnavi M, Raksha B, Durga M*, Brindha Banu B and Deepikaa R
Department of Biochemistry and Bioinformatics, Dr. MGR Janaki College of Arts and Science for Women, Adyar, Chennai - 600028, Tamil Nadu, India.

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***Corresponding Author Email:** durgam2k7@gmail.com

Abstract

Tea catechin is a class of flavonoids present in *Camellia sinensis* (green tea) and various other food sources synthesized by the Flavonoid pathway. It is known to have a wider range of biological activities, such as anti-inflammatory, anti-hyper lipidemic, anti-thrombogenic, anti-hypertensive, anti-ulcer, anti-oxidant, anti-proliferative and anticancer effects. Due to this wide range of properties, it has been used as an emerging front-line defence flavonoid against stress-related disorders. It is an effective flavonoid in the prevention and treatment of several stress-related diseases ranging from Obesity to Cancer, Diabetes to Neurodegenerative diseases, Urinary Tract Infections to Ulcers and Premenstrual Syndrome to Genetic disorders, Hypertension to Coronary Heart Disease and Brain aging. Thus, they have been used as a drug delivery system for the treatment of several stress-related diseases. It has been used as a nano encapsulated product, thereby increasing the medicinal values of green tea catechin. It is usually encapsulated with biopolymers to enhance its bioavailability, therapeutic efficiency and hydrophilicity. Catechin is being encapsulated by several methods such as Sonication and Ionic gelation etc. Antibiotics like Polyphenon 60 and Ciprofloxacin are derived from catechin and are used as intravaginal delivery treatment for curing Urinary Tract Infections. This review summarizes the properties of catechin that aid in the prevention of stress-related diseases and a brief view about polymeric nanoparticles.

Keywords
Anti-inflammatory, Anti-oxidant, Catechin, Stress

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INTRODUCTION:

A class of secondary metabolites [1] derived from plants is flavonoids [2]. They are composed of polyphenols [2]. Polyphenols are built up with repeated units of phenol groups [3], which may or may not include other functional groups [4]. They are biologically active plant extracts that are extremely soluble in water [5]. It has low absorption due to its inability to cross membranes made up of lipids [5]. According to reports, drinking green tea has various health advantages. After a boost in the catechin contents in green tea extract or by the use of purified catechin compounds, its use has even been lifted to a therapeutic level for the treatment of disorders, including cancer [6]. It has pro-oxidative as well as chemotherapeutic properties [7]. Tea catechin is usually extracted from a plant named *Camellia sinensis* [7]. It is mainly present in chocolates and tea,

the 2nd most consumed beverage worldwide [7]. Green tea polyphenols are not oxidized or fermented during its production [7]. Globally, it makes up about 20% of tea production [7]. The propensity to lipid oxidation is high in catechins [8]. It increases the duration of lipid oxidation, thus enhancing the shelf-life of lipids [8]. Catechin contributes to the colour, taste, aroma and flavour [8]. It affects us by interacting with the cells based on the concentration in the cell and its type [9,10]. Catechin possesses a benzopyran ring structure as depicted in Figure 1 [11]. It is a condensed tannin (poly flavonoids) with a ring and flavan-3-ol basic structure [12].

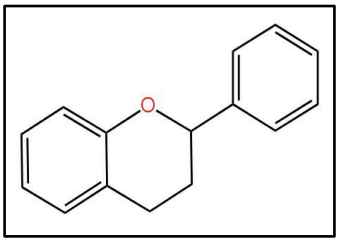

Figure 1. The Structure of Flavonoids

It constitutes about 75-80% water [12]. They are primarily used in pharmaceutical preparations, ointments, and cosmetics to extend the shelf life of the product and as a nutritional supplement to enhance human wellness [13]. They originated from Western China, Tibet, and Northern India [14].
A and B are benzene rings and C is a dihydropyran heterocycle with a hydroxyl group on carbon 3 (third carbon) [15] (Figure 2).

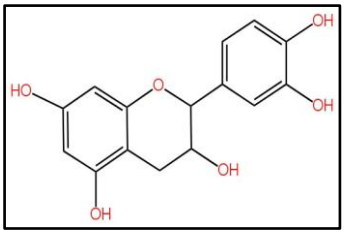

Figure 2. The Structure of Catechin

DIETARY SOURCES OF CATECHIN:
The distribution of Catechin and Epigallocatechin-3-gallate, a class of flavonoids that have a well-built experimental proof (by physical, *in vivo,* and *in vitro* methods) for its antioxidant, anti-tumour, anti-ulcer, antihyperlipidemic properties is present in a variety of foodstuff [16]. Catechin is widely present in many dietary sources and also constitutes several benefits when added as a dietary supplement [16,17]. Some dietary sources of catechin are plants, fruits (such as apples, blueberries, gooseberries, strawberries, cocoa, grape seeds, and kiwi), green tea, nuts, red wine, beer, cacao, liquor, chocolate, herbs, fruits, vegetables, beverages, algae, and confectionary items[16,17,68]. This can be obtained from various forms of green tea, such as loose-leaf form, bagged leaf form and infusions [17]. These foodstuffs and the quantity of catechin that constitutes it have been depicted in the table below (Table 1).

Table 1. The Distribution of Catechin and Epigallocatechin-3-gallate in a variety of foodstuffs [17].

S.No	FOODSTUFF	CONTENT
1	Green tea	4.62 mg/100 ml
2	Green tea (loose leaf form)	56.5-205.0 mg/g dry tea
3	Green tea (bagged leave form)	54.3-153.0 mg/g dry tea
4	Green tea (infusions)	117 to 442 mg/l
5	Raw cranberries	0.97 mg/100 g edible portion
6	Nuts, pecans	2.30 mg/100 g edible portion
7	Tea, black, brewed, prepared with tap water	9.36mg/100 g edible portion
8	Tea, fruit(dry)	415.0 mg/100 g edible portion
9	Brewed green tea	64.0 mg/100 g edible portion

10	Tea, green, large leaf, Quingmao, dry leaves	7380 mg/100 g edible portion
11	Tea, white, dry leaves	4245 mg/100 g edible portion
12	Japanese green tea	18.1-23.1 mg/g
13	Long-jing tea	32.9-35.5 mg/g
14	Jasmine tea	29.8-31.0 mg/g

CATECHIN BIOSYNTHESIS:

Catechin is an important flavonoid synthesized by the flavonoid pathway, briefly known as the FL pathway [18]. According to the study in the year 2014 on the differential regulation of Catechin biosynthesis in dark-treated green tea, the gene expression of catechin enhances in response to darkness and Leucoanthocyanidin-4-reductase (LAR), the enzyme that catalyse the reaction involving the conversion of Leucoanthocyanidin to Catechin would get elevated in the dark [18].

Phenylalanine, an aromatic amino acid, which acts as the primary source of catechin biosynthesis [18]. This leads to the production of cinnamic acid and 4-coumaric acid by the action of C4H(Cinnamate 4-hydroxylase) and 4CL (4-Coumarate Coenzyme A ligase).

The FL pathway starts with the production of Chalcone, as a product in the chemical reaction of 4-Coumaroyl CoA and the primary enzyme CHS (Chalcone synthase) [18]. Chalcone isomerization is catalyzed by CHI (Chalcone isomerase) forming flavanones [19]. This metabolic reaction occurs at an optimum hydrogen ion concentration (i.e.,pH=5.0-7.0) [19]. Enzyme F3H (Flavanone 3-hydroxylase) catalyzes the production of Dihydroflavonol from flavanones. F3'H (Flavonoid 3'-hydroxylase) catalyzes the formation of Dihydroquercitin and Dihydromyricetin from Dihydroflavonol. DFR (Dihydroflavonol 4-reductase) catalyzes the reduction of Flavanones to Dihydroquercitin, Dihydromyricetin and Dihydroxyflavonol [20]. These three compounds are further catalyzed by the enzyme Dihydroflavonol 4-reductase (DFR) to form Leucoanthocyanidin [20,21]. The reaction is then catalyzed by the enzyme LAR (leucoanthocyanidin-4-reductase) to form Catechin as depicted in Figure 3.

According to the research done in the year 2021 on the Co-regulation of Biosynthesis of catechin in regard with change in temperature by gene expression of catechin present in *Camellia sinensis* green tea and shoot growth, the amount of total catechin shooted up by 87.7% as the temperature increased from 15°C -30 °C [22].

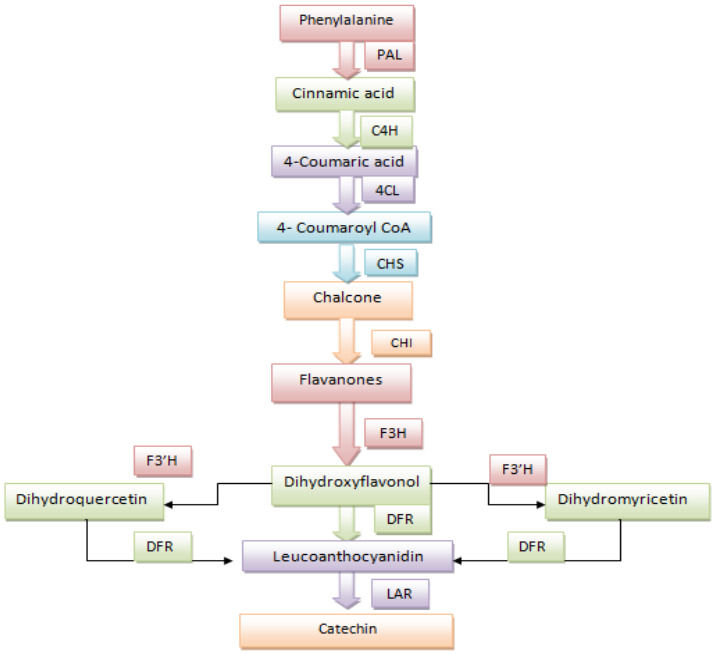

Figure 3. Catechin biosynthesis

CATECHIN ACTS AS A THERAPEUTIC DRUG:

Many common diseases and disorders can be cured and prevented by the action of green tea catechin and also aids in Weight loss[23], Anti-aging[24], HIV[24], Food poisoning[24], Boosting Immunity[25], Liver Disease[26,27], Cardiovascular Disease[28], Cancer[29,30], Arthritis[31,32], Diabetes[33], Alzheimer's[34], Parkinson's[35], Cold and flu[36], Asthma[37], Stress[38], Reduce Blood Cholesterol level[39], Anti-inflammatory[40], Genital warts[41]

SYMPTOMS AND DISEASES CAUSED DUE TO STRESS:

Stress causes structural and functional changes in the hippocampus of the brain [42]. Stress acts as an etiology of many health and mental disorders [43]. Thus, the change in the hippocampus leads to 'steroid psychosis'[43], an extreme effect of high levels of glucocorticoids[44]. Structural changes in the brain's hippocampus may result in atrophy and even neurogenesis disorders [45]. Stress also causes gastrointestinal diseases, such as IBD (Inflammatory Bowel Disease). This is mainly caused due to adverse effects on the immune system, which affects the intestine [46].

PROPERTIES OF CATECHIN THAT AID IN THE PREVENTION OF STRESS-RELATED DISEASES:

- Anti-inflammatory [47,48,16],
- Anti-thrombogenic [16],
- Antioxidative [16],
- Antihypertensive [16],
- Antiproliferative [16],
- Cell death regulation [16],
- Regulation of degradation of ECM (Extracellular matrix) [16],
- Multi-drug resistance in cancer [16],
- Anti-carcinogenic [16],
- Stabilizing effect on cell membrane [49],
- Anti-hyperlipidemic [16], and
- Anti-ulcer [50]

are some major properties that aid catechin to act as an emerging front-line defence against stress-related disorders. Thus, this acts as an anti-stressor in several ways as illustrated in Figure 4.

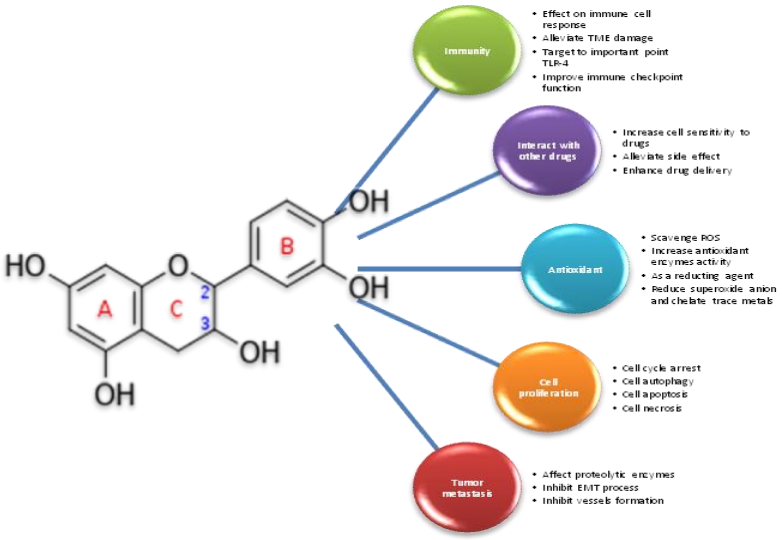

Figure 4: Anticarcinogenic effect of catechin

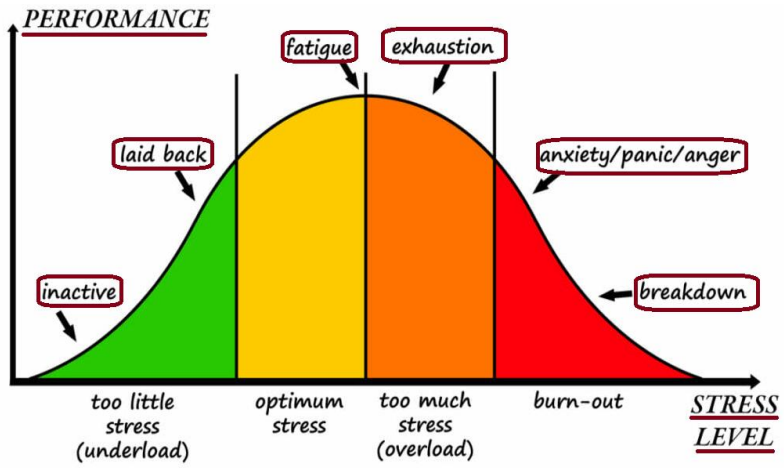

Figure 5: Graph depicting the effects of eustress and distress on health and performance

TEA CATECHIN, AN ANTI-STRESSOR:

As stress acts as an etiology of many health and mental disorders [43]. An external or internal stimulus that results in biological responses (stress responses) is called stress [43]. Stress causes many diseases ranging from homeostasis imbalance to

death and neurodegenerative diseases to cancer [47]. Catechin, a flavonoid that is usually present in green tea, has enormous therapeutic benefits against the diseases catalysed and triggered by stress [13,51]. Thus, green tea catechin acts as an anti-stressor [16]. The negative consequences of stress can be overcome by consuming green tea catechin in our diet [51]. Stress-illness relationships are complicated and are based on some factors namely, style of coping, social support and personality [51]. Eustress usually do not affect the person as a distress would affect them by causing confusion, clouded thoughts and overreaction as depicted in figure 5[51]. Stress may be short term or long term or chronic stress [51]. Chronic stress may lead to illnesses which are caused due to the elevation of catecholamine and suppressor T helper cells, thereby inhibiting the action of the immune system [51]. It may even cause building up of plaque in the atrial walls [51]. (±)-Catechin helps plants during their periods of stress [52]. It is considered a 'chemical weapon' extracted from a plant source [52].

CATECHIN IN THE CURE OF ALZHEIMER'S DISEASE:

Epicatechin gallate is being utilized in the 'in Silico' docking, which acts as a crucial part in the care and cure of Parkinson's disease and Alzheimer's disease [47]. Alzheimer's disease is a common neurodegenerative disease worldwide [48]. It is an etiology of dementia in about 60 to 80% of the cases [48]. Catechin has anti-inflammatory properties [48]. It significantly improves memory and learning and reduces acetylcholinesterase (AChE) activity [48]. These catechin are permeable through BBB (Blood Brain Barrier) [48]. Green tea catechin plays a major role in Alzheimer's disease treatment [48]. Figure 6 is pictorial representation of neuronal damage leading to neuronal death by the secretion of inflammatory elements. These inflammatory elements are secreted due to neuronal injury.

Figure 6. Neuronal damage causes Neuronal death. Neuronal damage or injury leads to the secretion of pro-inflammatory elements, which triggers neuronal death.

THERAPEUTIC BENEFITS OF CATECHIN IN INFLAMMATORY BOWEL DISEASE (IBD):

Inflammatory Bowel Disease (IBD) may be caused due to stress leading to a negative effect on the intestinal microflora, its dysmotility, and the immune system gets strongly affected along with neuroendocrinological damage [46]. Stress has been proven to induce IBD recurrence [46]. Catechin inhibits extreme oxidative stress by exhibiting anti-oxidant effects [53]. It also promotes the activation of substances that are anti-oxidative [53].

GPO (glutathione peroxidases) and GSH (Glutathione) [53]. These suppress oxidative damage to the colon [53]. It regulates the infiltration and inflammation of neutrophils, colonic epithelium, T lymphocytes, and macrophages [53]. It activates and deactivates the pathways of cell signalling [53]. This also checks the worsening of intestinal lesions by regulating gap junctions in the cell [53]. This enhances the flora balance in the intestine [53]. Thus, this benefits the intestine in many ways thereby relieving inflammatory bowel disease [53]. IBD has many health manifestations such as haematochezia, weight loss, wasting, and even cancer may ultimately develop [53]. Catechin exhibits an appreciable level of anti-inflammatory effects [53]. This helps in the treatment and prevention of cancer and inflammatory diseases like Inflammatory Bowel Disease [54], Ulcerative colitis (UC), and Crohn's disease (CD) [55]. Green tea catechin is one of the best curative polyphenols that greatly benefit IBD, as it focuses on pharmaceutical aspects and cellular mechanisms [56].

CATECHIN IN THE PREVENTION OF DOWN SYNDROME, A GENETIC DISORDER:

Down syndrome is one of the most common diseases that affects newborn babies [58]. It is a chromosomal abnormality causing trisomy 21[58]. Down syndrome may be associated with clinical complications such as Alzheimer's disease, leukemia, hypertension, gastrointestinal problems, congenital heart disease, cancer [60]. DYRK1A, a dosage-sensitive gene

encoding a protein kinase involved in brain defects and metabolic disease is affected by catechin, thereby acting as a therapeutic drug for down syndrome [61]. Down syndrome can be recognized by the following physical features namely, Muscular hypotonia[59], small chin[59], slanted eye[59], flat nasal bridge[59], single crease in the palm[59], protruding tongue[59]. The positive effects of catechin on the phenotypic and molecular aspects of Down syndrome is depicted in Figure 7.

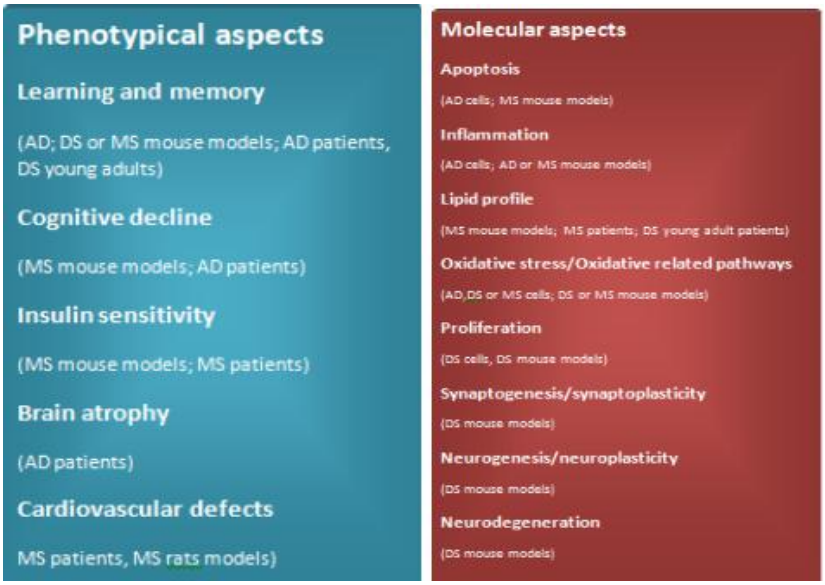

Figure 7. Major positive effects of catechin on several aspects of Down syndrome (DS) and its main comorbidities, Alzheimer's disease (AD) and Metabolic Syndrome (MS)[3].

CATECHIN IN THE ACTION AGAINST MUSCLE DYSTROPHY:

Epicatechin, ECG (Epicatechin gallate), and EGCG (Epigallocatechin-3-gallate) play a major role as a potential medication in curing muscular dystrophy or muscle atrophy, or muscle wasting [62]. Mitochondrial function in skeletal muscle is improved by epicatechin [62]. Skeletal muscle is considered the organ that plays a major role in physical performance [62], glucose metabolism [63], free FA metabolism [63], and metabolizing protein [63]. Muscle atrophy is also known as muscle wasting or muscle dystrophy as this causes a reduction in the cross-sectional area, muscle mass, and its function [64]. Sarcopenia and cachexia are the main causes of muscle atrophy [65]. Sarcopenia is a type of atrophy of muscle that is triggered due to aging, whereas Cachexia is triggered due to chronic diseases [65]. These have close relation with inflammatory disorders [66, 67].

THE ACTION OF CATECHIN IN MENTAL ILLNESSES LIKE SCHIZOPHRENIA:

Polyphenols like catechin consumed through diet are filled with the potential to act as medicaments in mental illnesses such as schizophrenia [69]. Green tea catechin improves memory and learning [70]. It plays a significant role in antidepressant-like effects in mental disorders [71]. The apoptotic hypothesis of schizophrenia and oxidative stress are related [72]. Apoptosis, also known as "programmed cell death," is a mechanism of cell death that functions in healthy neurodevelopment and is becoming more widely understood for its function in a variety of neuropathological conditions [72]. In the central nervous system (CNS), apoptosis activation can result in the quick and complete death of neurons and glial cells [72]. Proapoptotic triggers may occasionally result in localised, sublethal apoptosis that results in synaptic and neuritic loss without resulting in cell death [72]. Reduced neuropil (especially synaptic elements) and limited, frequently layer-specific reductions of neurons suggest progressive loss of cortical grey matter during the initial psychotic episode when anti-oxidant activity is low [72].

CATECHIN, A POTENTIAL NUTRITIONAL SUPPLEMENT AGAINST ANGIOGENESIS:

The process of new capillaries developed from preexisting blood vessels is called angiogenesis [73]. catechin changes the miRNA expression profile [73]. This profile is associated with the process of angiogenesis in various types of cancers [73]. The effect of catechin on (EC) endothelial cells and (VSMCs) vascular smooth muscle cells against angiogenesis have been studied recently and proven

to be effective in destroying inflammatory modulators like tumour necrosis [74].

Green tea catechin is one of the most targeted nutritional supplements that effectively works as an anti-angiogenic drug [73]. Epigallocatechin-3-gallate (ECGC) efficiently stops angiogenesis and its development [75]. When this is consumed along with vitamin E as a dietary supplement, it benefits us by preventing various forms of cancer [76]. Angiogenesis is a major factor that promotes tumour growth [76]. This is inhibited by suppressing IL-8 (a chemoattractant) production [76].

CANCER SIGNALING PATHWAYS ARE AFFECTED BY TEA CATECHIN:

Cancer is prevented by consuming green tea catechin as it modulates cancer signalling [77]. The direct actions of catechin are because of its redox action and activity of physical binding [77]. Catechin are antioxidants and prooxidants, thereby generating ROS [78]. A decrease in the level of ROS promotes tumor progression [79,80]. Tea catechin gets auto oxidized to generate ROS in the cell and cause cell death [77]. This is then initiated inside the mitochondria, inducing tumour cell apoptosis [77]. This plays a major role in the death of tumour cells/cancer cells [77]. Thus, tea catechin is a very good therapy for the prevention and treatment of cancer [77]. The major signalling pathways RTKs are Ras/ERK and PI3K/AKT pathways. Even a small quantity of about 0.6 µM of ECGC (Epigallocatechin gallate) has a significant capacity to block HGF-induced phosphorylation of HGFR and AKT completely. HGFR and HGF play key roles in epithelial-mesenchymal transition [57]. Epithelial-mesenchymal transition is associated with the invasion of the tumour [58].

CIPROFLOXACIN NANOEMULSION IN THE CURE OF UTI:

A recently accepted study on a delivery system based on nano emulsion, in which the delivery system constitutes green tea catechin has proved that it cures Urinary Tract Infections [81]. Polyphenon 60 and Ciprofloxacin are the catechin present in green tea that is used for intravaginal delivery, which has a significant role in the treatment of urinary tract infections [81]. Ciprofloxacin belongs to a broad-spectrum fluoroquinolone class antibiotic, which is significantly used as a therapeutic drug in the cure of Urinary Tract Infection caused by *Escherichia coli (E. Coli)*[59]. The ultrasonication technique is a technique that facilitates the preparation of nano emulsion [81].

CATECHIN AND CANCER:

Catechin has been proven to have antioxidant properties that aid them in acting as a free radical scavenger [82] and chemotherapeutic effects against cancer [83]. The anticarcinogenic property of green tea was reported in the 1980s [84]. Its antioxidant property facilitates the prevention of lipid peroxidation [85]. It acts as a reactive oxygen scavenger [85]. Green tea catechin inhibits cancer by suppressing proliferation and cancer cell metastasis, antioxidation, free radical scavenging, and body immunity enhancement and by being involved in controlling the signalling pathways of cancer, thereby acting as one of the best therapeutic drugs for cancer [84]. The intake of catechin through diet is an effective way to act against some common cancers such as pancreatic cancer [86], breast cancer [87,88], prostate cancer [89], and leukaemia [90].

ANTI-HYPERTENSIVE GREEN TEA CATECHIN:

Hypertension can be defined as systolic blood pressure ≥130/ diastolic blood pressure ≥80[91]. Green tea catechin is rich in antihypertensive properties and anticoagulant properties [83]. Catechin reduces elevated blood pressure, more effectively than usually used therapeutic drugs [91]. The naturally occurring flavonoids have been proven to act against hypertension [91] by acting on the metabolism of Arachidonic acid [92]. Arachidonic acid metabolism plays a significant role in the regulation of vascular tone and in reducing high blood pressure [92]. It has been the most studied and abundant flavonoid in the last two decades [92,93,94,95,96,97].

CATECHIN IN THE REDUCTION OF THE CLINICAL MANIFESTATIONS OF CORONARY HEART DISEASE:

Catechin is a flavonoid that aids in almost every health issue, the cardioprotective factor also gets added to its good effects [98]. It acts as a key mediator by altering the mechanisms of blood flow and blood pressure [99]. An increase in FMD (Flow-mediated vasodilation) has been proven to be effective in acting against peripheral artery diseases [100]. Figure 8 depicts the clinical manifestations of coronary heart disease is reduced by catechin's action on the following mechanisms:

- Lowering the blood pressure.
- Enhancing the flow-mediated vasodilation.
- Reducing atherosclerosis.

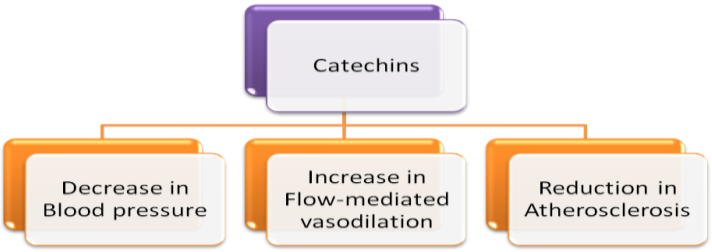

Figure 8. Mechanisms that are regulated by catechin

Catechin enhanced many conditions, which were associated with the malfunction of the vascular system, including inflammation and proliferation of myocytes, platelet aggregation, oxidation of lipoproteins, lipid profile alteration, and vascular reactivity [101]. It improves blood circulation and clears out cholesterol deposition [101].

DIABETES CAN BE CONTROLLED BY TEA CATECHIN:

Diabetes mellitus is one of the greatest health problems at the global level [102]. Around 6.4% of the adult population is suffering from this disease [102]. It has been manifested as a global epidemic [102]. Diabetes is of two types:

- An aberration in insulin secretion or synthesis as in Type I Diabetes mellitus [102]
- Pancreatic duct stenosis, insulin resistance, or insufficient insulin secretion as in Type II diabetes [102].

Diabetes is mainly caused due to increasing obesity and aging [102]. It brings other major health problems, such as hyper ketonemia [103]. This may be caused due to an acute lack of insulin [103]. This may also result in the onset of hypomagnesemia [104].

Tea catechin has the ability to improve the effects of insulin resistance [105]. Its ingestion in the form of beverages, like green tea, contributes a great chunk to the prevention of diabetes [106]. A minimum of 12 weeks of regular green tea catechin intake results in the elevation of insulin levels [106]. Insulin secretory ability can be recovered up to a very good standard by the regular consumption of catechin-rich beverages [106]. Tea catechin acts very well against obesity and hypercholesterolemia thereby, controlling diabetes [106]. It regulates glucose metabolism and body fat (lipid) metabolism [106]. Fasting glucose has been proven to be reduced significantly by the dietary supplementation of green tea catechin [107]. However, it does not show any difference or vast improvement in fasting insulin and HbA1c [107].

CATECHIN VS PREMENSTRUAL SYNDROME:

About 78% of women suffer from physical symptoms of Premenstrual syndrome [108]. PMS (Premenstrual syndrome) is one of the most common problems in women worldwide [109]. This involves psychological, physiological, and behavioural symptoms [109]. Green tea catechin has been used as a therapeutic drug in curing physical symptoms of PMS [109].

CATECHIN AND ENDOMETRIOSIS:

Along with various therapeutic effects of green tea catechin, it also acts against diseases that affect the female reproductive system such as PCOS (polycystic ovarian syndrome) or PCOD (polycystic ovarian disease), endometriosis, dysmenorrhea, etc [108]. The properties that mainly enhance the effect against endometriosis and other reproductive system disorders are:

- Anti-angiogenic
- Anti-fibrotic
- Anti-proliferative
- Pro Apoptotic mechanisms [108]

EFFECT OF CATECHIN AGAINST OBESITY AND HYPERCHOLESTEROLEMIA:

Obesity leads to many other health problems affecting the bone, joints, lungs and causes much more serious ailments such as diabetes, cancer and stroke [110]. Catechin, Epigallocatechin, and Epigallocatechin gallate play a significant role in acute weight loss and prevention of weight gain [110,111]. It has a remarkable role in body weight [111] and energy expenditure [112]. Oral consumption of catechin present in green tea can affect the serum level, LDL, HDL, and serum glucose [111,113,114]. These effects may get altered as green tea constitutes several phytochemicals, thus inhibiting the effects of catechin [115].

CATECHIN IN THE PREVENTION OF BRAIN AGING:

Catechin plays a major role in the prevention and cure of brain aging [116]. A pictorial representation of brain aging has been shown in Fig 8. The property of catechin to chelate redox-active transition metal ions, such as iron (Fe) or copper (Cu), depends on the carboxyl and hydroxyl groups that contribute to the antioxidant property of catechin [117,118].

BIOAVAILABILITY OF GREEN TEA CATECHIN:

Green tea has high amounts of catechin comprising eight or more polyphenolic compounds. They are loaded with EGCG (-) epigallocatechin gallate and

EGC (-) epigallocatechin [119]. Oral administration of green tea catechin has a limited therapeutic effect, due to poor stability in the gastrointestinal tract and limited permeability of the intestinal membrane [119]. No effectively specific receptors are present in epithelial cells of the small intestine [119]. The catechin absorption mechanism across the intestine's epithelial cells is mainly based on paracellular and transcellular diffusion [119]. Catechin bioavailability is influenced by processes like chemical degradation, membrane permeability, microbial metabolism, intestinal metabolism, hepatic metabolism, and even transporter mediators [119].

TECHNIQUES TO IMPROVE CATECHIN BIOAVAILABILITY:

Extracts of catechin alone may not provide sufficient biological activities and ensure a trusted level of therapeutic benefits [120]. Nano-structured systems may be used as drug delivery systems to enhance the action of flavonoids such as catechin [5]. For instance, Chitosan-tripolyphosphate can be used to encapsulate and enhance encapsulation efficiency [121]. Per acetylated epigallocatechin-3-gallate (AcEGCG) enhances growth-inhibitory activity in human colon and oesophageal cancer cells. It increases biopotency in invitro setup and in-vivo EGCG bioavailability. It boosts its activity in cancer prevention [122]. The anionic process of polymerization is applied to encapsulate hydrophilic drugs with good efficiency [123]. Some common hydrophilic drugs are ampicillin and doxorubicin [123].

POLYMERIC NANOPARTICLES:

Nanoparticles are the most assured area in the field of nanotechnology [124]. Nanoparticles are nano-encapsulated to enhance their functional activity by fabricating from natural as well as artificial/man-made macromolecules [124]. These are used in drug delivery as they can be targeted [125]. It is a reassuring formulation [126,127]. Its diameter ranges from 10 - 1000nm [125]. These act as vectors, controlling the release of drugs to the specific locations targeted [5]. These increase the solubility of its components, reducing the therapeutics' dose [5]. It also enhances the absorption of the active ingredients [5]. These are usually obtained from polymers, which may be natural, artificial, or even biodegradable [5].

Nanoscale systems, also called sub-micro-meter have a particle diameter of less than 1 micrometre[5]. During oral administration, active constituent degradation is promoted by the sharp acidic pH in the stomach [5]. Thus, losing the required effect after its consumption [5]. In the process of ophthalmic administration, the polymeric nanoparticles regulate active component delivery thereby enhancing ocular bioavailability and lowering the side effects [5]. About 50% of drugs acknowledged and certified in 1981-2006 were derived as the primary or secondary source of nature [5]. Low-caffeine green tea has been proven to reduce the response to stress in students [128]. The enzyme sAA, salivary-alpha-amylase is a stress marker, thus the reduction in the secretion of this enzyme indicates suppression of excess stress in our body [128].

Advantages of natural polymeric nanoparticles

- The ability to transport multiple active constituents using a single carrier [5].
- The capability to enhance the potential to prepare a release system with outstanding sustainability [5].

GREEN TEA CATECHIN ENCAPSULATED IN A BIOPOLYMER MATRIX:

Biodegradable CH-PLGA nanoparticles/nano capsules were used to supplement hydrophilicity, and bioavailability [129]. There are several ways of encapsulation of nanoparticles and producing desired products of encapsulated therapeutic drugs (Figure 9) and (Figure 10) [130]. Green tea catechin encapsulated with a biopolymer matrix plays a significant role in supplementing the therapeutic effects, efficiency, and eco-friendly nature [131]. Over 3000 formulations and supplements are offered online with magnificent health benefits [131].

Figure 9: Various Methods of encapsulation

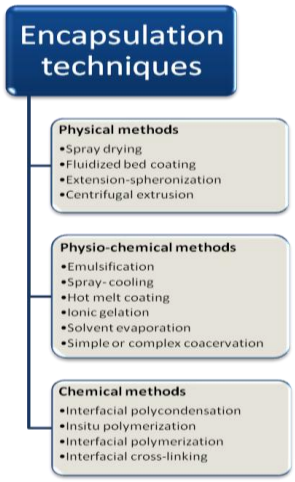

Figure 10: Physical, Physio-chemical, Chemical Methods of encapsulation

CONCLUSION:

Catechin is a biologically active secondary plant metabolite. Catechin and its derivatives plays an important role in the care and cure of psychological illnesses like Schizophrenia, Gastrointestinal disorders on the lines of Inflammatory Bowel Disease (IBD), Neurodegenerative ailments namely Parkinson's disease and Alzheimer's disease, Genetic disorders in particular, Down syndrome and Muscular atrophy. Angiogenesis supports cancer to a greater extent and catechins are well known for its anti-cancer properties and acts as a potential nutritional supplement. It is acting as an emerging flavonoid in treating stress-related disorders. Future implications demand the wide spectrum of therapeutic properties of catechin in enhancing human health.

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