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EGCG: A POTENTIAL PHARMACOLOGICAL COMPOUND

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ABSTRACT

The emergence of new ailments such as obesity, diabetes, cancer, heart disease, and neurological disorders has left society with a significant health issue. Investments in materials that improve public health are therefore crucial. In this case, a flavonoid called epigallocatechin gallate (EGCG) is present in a variety of plants, including tea. Numerous researches back up the idea that EGCG helps prevent obesity, diabetes, heart disease, cancer, and other ailments. Consuming tea catechins over an extended period of time may help prevent obesity, type II diabetes, and heart disease caused by high-fat diets. It is necessary to do more research that complies with worldwide requirements in order to track the pharmacological and therapeutic properties of green tea as well as to clarify how it works. However, the primary disadvantage of using EGCG in preventive and treatment is its low intestine absorption and volatility. The encapsulation of EGCG into nanocarriers results in an increase in its therapeutic benefits and stability. There will be a thorough analysis of all the research that are now accessible on EGCG encapsulation using nanocarriers.

KEYWORDS: (–)-Epigallocatechin-3-gallate, EGCG, Green Tea, inflammation, oxidative stress, apoptosis, cancer, neurological, cardiovascular.

INTRODUCTION

Tea is an herbal infusion prepared by steeping the dried leaves, buds, or twigs of the Camellia sinensis tea shrub in hot water for a few minutes. The resulting liquid is then consumed. Drinking tea regularly has long been linked to health advantages; it is the second most popular beverage in the world, after water, and far more popular than coffee, beer, wine, and soft drinks with carbonation. Currently, millions of people worldwide drink 3 billion cups of tea each day. The six main types of tea have different chemical compositions and production processes: green tea, black tea, oolong tea, white tea, pu'erh tea, and red tea.[1]

Epidemiological investigations indicate decreased occurrences of some malignancies and cardiovascular problems in Asian nations, where tea consumption is a four millennium-old cultural custom. The Western lifestyle is linked to several malignancies and cardiovascular disorders, particularly when it comes to the impact of nutrition on the quality of life.

Green tea's polyphenolic flavonoids, or catechins, are mostly responsible for its health benefits. These include epicatechin (EC), epicatechin-3-gallate (ECG), and the main flavonoid (-)-epigalloca-techin-3-gallate (EGCG). Up to 40% of the weight when dry of green tea is made up of these polyphenols, and recent studies have concentrated on pure EGCG. Over the past 10 years, a lot of study has been conducted on green tea, particularly on the isolated catechin EGCG. Nevertheless, the majority of these studies depend on in vitro and animal tests.[2]

Fig. 1: Health Benefits of Green Tea.[4]

The fundamental evidence supporting for green tea's suggested chemo-preventive and cardiovascular benefits is being provided by this growing body of research. Green tea polyphenols are well-known antioxidants, and it has been suggested that these phytochemicals affect the biochemical and physiological processes that cause and promote the development of cardiovascular and cancerous disorders.[3] Due to its appealing flavour and taste, green tea was favoured as a beverage for quite some time. However, the public press and researchers have lately speculated that green tea may offer health benefits. Anti-inflammatory, anti-oxidative, anti-mutagenic, and anti-carcinogenic benefits have been linked to its ingestion.

Chemical composition of green tea

Numerous variables, such as environment, season, horticultural techniques, plant type, and age, affect the composition of tea leaves. Green tea's chemical makeup is comparable to the chemical makeup of the leaf. The aforementioned chemical structure is complex that includes proteins (15—20% dry weight) that have enzymes make up a significant portion; amino acids (1—4% dry weight) with the value asteanine or 5-N-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, lysine; carbohydrates (5—7% dry weight) such as cellulose, pectins, glucose, fructose, sucrose; lipids to be linoleic and a-linolenic acids; sterols asstigmasterol; vitamins (B, C, E); xanthine bases such as caffeine and theophylline; pigments as chlorophylland carotenoids; volatile compounds with the value as aldehydes, alcohols, esters, lactones, hydrocarbons, etc.; minerals andtrace elements (5% dry mass) with the value as Ca, Mg, Cr, Mn,Fe, Cu, Zn, Mo, Se, Na, P, Co, Sr, Ni, K, F, and Al.[4,5]

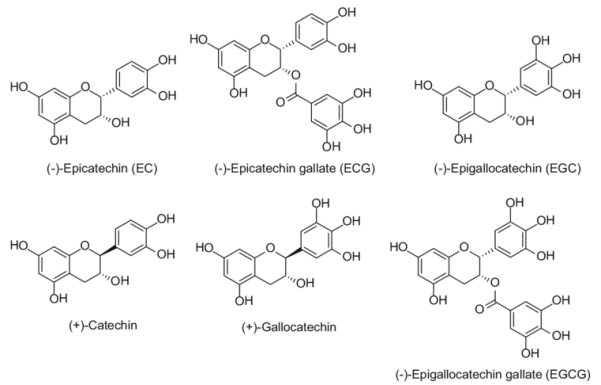

Fig. 2: Chemical composition of green tea.[6]

(–)-Epigallocatechin-3-gallate (EGCG)

The predominant constituent of green tea catechins is unquestionably EGCG, or the ester of epigallocatechin and gallic acid. After undergoing animal testing, cell-based research, and clinical investigations, it is believed to account for 50–80% of the total catechins in green tea and confers a number of health benefits. Anti-oxidant, pro-oxidant, anti-neurodegenerative, anti-microbial, anti-diabetic and anti-cancer properties are only a few of these health benefits.

Recent findings indicate that EGCG may have a function in chemotherapy and chemoprevention of several types of cancer by obstructing the onset, growth, and spread of cancer. Even though polyphenol stability, solubility, and bioavailability are frequently criticised, it has been shown that EGCG may penetrate the nucleus and bind to DNA and RNA, perhaps contributing to gene regulation.[7] Furthermore, it has been documented that EGCG binds a broad range of proteins, including the proteasome, kinases, apoptotic proteins, and the Epidermal Growth Factor receptor, demonstrating its capacity to obstruct several signalling pathways. Therefore, in order to fully comprehend the possible mechanism of action of EGCG in various experimental setups in addition to in clinical investigations, it is imperative to identify the molecular targets of EGCG and the biomarkers that indicate EGCG interactions.[8]

PHARMACOLOGICAL POTENTIAL

1. Impacts on metal ion absorption

Although their impacts on other ions are insufficiently understood, tea catechins have the potential to impact iron absorption, especially in populations susceptible to of iron deficiency. Long-term use of green tea appears to have little effect on copper absorption, although it enhances manganese absorption and lowers zinc absorption. Nevertheless, consumption of catechins has no effect on these ions' plasma concentration. Although flavonoids react with a range of metal ions, green tea catechins may have an impact on ion absorption and metabolism.[9]

2. Effect on Obesity

A medical condition known as obesity is defined by an excessive build-up of fat in the body, which can negatively impact general health and increase the risk of developing conditions like diabetes and arteriosclerosis. Dietary changes and other lifestyle reeducation are the mainstays of therapy for obesity. Nonetheless, there are situations when using medications and supplements is necessary to aid in the weight loss process. As mentioned earlier, EGCG directly disrupts the digestion of fats by inhibiting phospholipase A2 and interfering with the gut's lipid/cholesterol emulsion.[10] The ability of EGCG to inhibit lipids can play a significant role in weight reduction and weight management strategies. Furthermore, EGCG has the ability to improve lipid metabolism, which increases calorie burn and therefore results in fat reduction. By inhibiting α-amylase, EGCG can also obstruct the digestion of starch. In addition, the administration of EGCG during a weight reduction programme is highly beneficial due to its significant correlation with improved circulation, scavenging of free radicals, and improvement of mood.

Consuming green tea and green tea extracts may increase postprandial thermogenesis and fat oxidation, which may

help reduce body weight, particularly body fat, according to recent findings from human studies. Six overweight males received 300 mg of EGCG daily for two days as part of a randomised, double-blind in placebo-controlled, cross-over pilot trial. The consumption of energy and oxidation of substrates variations while fasting and after meals were evaluated. While there was no significant difference in resting energy expenditure between the EGCG and placebo treatments, there was a significant difference in respiratory quotient values between the EGCG and placebo throughout the initial postprandial monitoring period.[11] According to these results, EGCG by itself may be able to boost fat oxidation in males, which might support green tea's anti-obesity properties. To determine the ideal dosage, additional research with a bigger number of participants and a wider range of ages and body mass indices is necessary.

3. Effect on the enzymes that break down drugs

Green tea consumption over an extended period of time raises UDP-glucuronosyl transferase activity in rats. Once absorbed, catechins are broken down by enzymes that break down drugs in different organs.[12] Therefore, it is hypothesised that the enhanced glucuronidation caused by UDP-glucuronosyl transferase stimulation aids in the conversion of chemical carcinogens into easily excreted inert compounds, thereby contributing to green tea's anti-carcinogenic properties.[13] We looked explored how the metabolism of green tea catechins and 2-amino-3-methylimidazol (4,5-f)quinoline (IQ) interacted. The pre-carcinogen known as IQ was first found in a fried beef extract. Rats mostly undergo IQ biotransformation via cytochrome P450 in the first phase, which is then conjugated to a glucuronide and a sulphate. Green tea alters the metabolism of IQ in rats by promoting the synthesis of IQ glucuronides, which are subsequently eliminated through the urine.[14]

Furthermore, green tea catechins may prevent malignancies brought on by polycyclic aromatic hydrocarbons by inhibiting their cytochrome P450 metabolism; however, the specific type of green tea will determine how it affects these enzymes. In normal rats, over time tea made from green tea drinking raises cytochrome P450 1A1 and 1A2 activities but not 2B1 or 2E1 activities.[15] Conclusions on the protective properties of green tea against carcinogens that solely include this metabolic pathway's modification are challenging to come at, nevertheless.

4. Effect on Infectious Disease

Immunisation is the primary method of fighting viruses nowadays. Regretfully, there isn't a single effective vaccination for many viral illnesses, HIV infection constituting the most significant.[16] Strong HIV inhibition that is dose-dependently induced by EGCG in cell cultures has been demonstrated by Nance et al. Furthermore, Li et al. have demonstrated that EGCG inhibits reverse transcriptase and functions in concert with azidothymidine, another inhibitor of reverse transcriptase. According to certain research, EGCG can bind to CD4 cells and stop the virus from attaching itself to the cell and infecting the host.[17]

Additional viruses including hepatitis C, enterovirus 71, adenovirus, herpes simplex virus, and influenza virus can also be inhibited by EGCG. The MAP-kinases pathway and NF-kB are two molecular targets that appear to be dysregulated as a result of the viral infection. EGCG may therefore trigger a necessary immune response that aids in the battle against the viral infection.[18] In terms of antibacterial and antifungal properties, EGCG appears to be less successful in treating bacterial and fungal infections. The majority of pertinent researches in the literature indicate that EGCG and antibiotics may have some synergistic benefits when fighting multidrug-resistant types of bacteria like Staphylococcus aureus and *Stenotrophomonas maltophilia*. It was additionally observed that EGCG has antifungal effect against human-pathogenic yeasts like *Candida albicans*. But the exact mechanisms of action remain unknown.

5. Effect on oxidative stress and antioxidant indicators

Green tea is a well-liked antioxidant nutraceutical. Antioxidants are substances that shield cells from reactive oxygen species (ROS) including superoxide, singlet oxygen, peroxyl and hydroxyl radicals, and peroxynitrite. Oxidative stress is caused by a disparity among reactive oxygen species and antioxidants, which damages cells. Together with antioxidant vitamins (such vitamins C and E) and enzymes (like superoxide dismutase and catalase), catechins are thought to contribute to the overall antioxidant defence system, which helps prevent certain illnesses.[19]

Green tea catechins have been shown in vivo studies to raise total plasma antioxidant activity. Consuming green tea extracts also raises the expression of catalase in the aorta and enhances the activity of superoxide dismutase in blood, two enzymes linked to cellular defence against reactive oxygen species. A drop in the plasma concentration of nitric oxide combines this activity with its immediate effect on oxygen species.[20,21] The oxidative stress marker malondialdehyde also drops following consumption of green tea. These findings imply that catechins may function as an antioxidant directly or indirectly through increased activity or expression. Given that catechins have antioxidant properties in in vitro conditions, stop other antioxidants, such vitamin E, from oxidising.[22] Nevertheless, the plasma status of vitamins E and C remains unchanged in vivo when green tea catechins are consumed. However, one study found that catechins raise the amount of vitamin E in the low-density lipoprotein, which may help to shield the protein against peroxidation.[23]

The ability to tolerate of tableted green tea and its impact on the antioxidant status indicators were evaluated by Pilipenko et al. The study comprised twenty-five patients

with various gastrointestinal diseases, who were then split into control and treatment groups.[24] The treatment group had improved relationships among quality-of-life indexes particularly in scales of physical discomfort and functioning in society, and exhibited a favourable response to tableted green tea.[25]

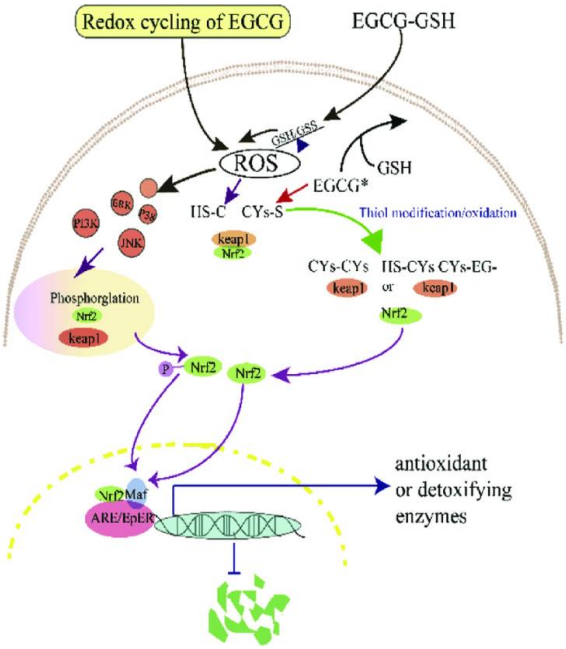

Fig. 3: EGCG action impact on oxidative stress and antioxidant indicators.

6. Effect on Neurodegenerative Conditions

Though many ideas have been put out, the origins of neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD) are still unclear. Clinical characteristics of both disorders include the buildup of iron in certain brain regions and oxidative damage to neurons. An additional relevant factor is the build-up of misfolded proteins in deposits, with the value the β-amyloid peptide in AD, which prevents neurons from surviving and causes early death.[26] The potential therapeutic function of antioxidants in neurodegenerative disorders has garnered significant attention. The EGCG agent's anti-inflammatory, antioxidant, and iron-chelating qualities are all linked to its neuroprotective qualities. Moreover, EGCG can pass across the blood-brain barrier (BBB).[27]

This hydrophilic compound's mode of entry across the BBB is yet unclear. According to published research, EGCG is more effective as vitamin C as well as vitamin E in scavenging free radicals, and its capacity to chelate iron helps to considerably alleviate the symptoms of several neurodegenerative illnesses.[28] As previously noted, EGCG functions as a cellular modulator by interaction with many routes. This catechin enhances neuronal health by promoting cell survival responses and inhibiting cell death signals in neuronal cells.[29] Cell signalling alterations also stimulate the nonamyloid α-secretase pathway, which reduces the amount of Aβ-amyloid peptides produced. Numerous investigations verify that EGCG possesses neuroprotective qualities in humans, encouraging an improvement in cognitive function following oral treatment. These investigations also support the notion that EGCG causes a generalised rise in brain activity and relaxation.[30]

7. Effect against Cancer

The last stage of cellular growth lesions, which include dysplasia, neoplasia, metaplasia, and hyperplasia, is cancer. Every ailment listed below is a stage in the development of cancer, which ends in the malignant neoplasia commonly referred to as cancer. The majority of contemporary cancer treatments are now exceedingly costly, hazardous, and ineffective in curing the illness.[31] Thus, it is essential to look into natural substances like EGCG that are extracted from the leaves of green tea for both the treatment and avoidance of cancer as well as other illnesses. Previous research indicates that EGCG is a potential chemical for the treatment and prevention of cancer. The ability of EGCG to scavenge free radicals and prevent the damage that free radicals cause to cell structures is thought to be responsible for some of its anticancer effects.[32]

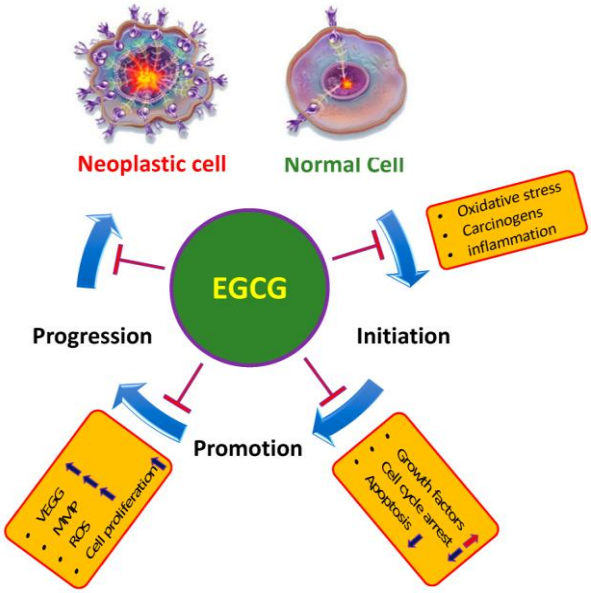

Fig. 4: EGCG action against Cancer.

In addition to functioning as an antioxidant, EGCG may bind to and control the activity of a number of signalling molecules linked to cell death, survival, and mitosis, which can moderate the cellular reactions seen in cancer. It has been shown in earlier research that EGCG can block the start, advancement, and advancement of all carcinogenesis-related processes. Certain proteins linked to misregulated molecular processes in malignant cells can be bound by EGCG.[33] Tumour regression is really caused by EGCG's induction of the repression of two crucial transcription factors: the tumour suppressor p53 and nuclear factor kappa-light-chain activator of activated B-cells (NF-kB). To meet the cells' needs for

nutrients and oxygen, more capillaries are required, which will aid in the tumor's development.

Angiogenesis is the procedure by which new blood vessels develop. The tumour releases signalling molecules into the surrounding tissues, particularly vascular endothelial growth factor (VEGF), to encourage the creation of new capillaries. The activity of NF-kB and hypoxia-inducible factor 1α (HIF-1α) factors, which are regulated by EGCG, directly affects VEGF. These explanations explain why EGCG can inhibit tumour angiogenesis and stop tumour development. Furthermore, there is compelling evidence that EGCG can reduce tumour migration and metastases development.[34] According to earlier research, EGCG facilitates a decrease in tumour cell migration and metastasis development when tumour size is reduced, resulting in a more dependable and effective treatment.

While it is doubtful that EGCG would be used alone in chemotherapy because it is not effective in curing the cancer entirely, using EGCG as a cytostatic medication adjuvant might be fascinating. Several in vitro, in vivo, and preclinical investigations have documented this synergism; it may be helpful in lowering the dosage of required cytostatic medications, hence lowering adverse effects. Furthermore, EGCG's anti-inflammatory and antioxidant qualities help guard against the negative effects of chemotherapy.[35] Lastly, the health advantages of EGCG would help improve the patients' general state of health.

8. Effect on Cardiovascular Diseases

Cardiovascular problems are quite common, especially in industrialised nations where sedentary lifestyles, poor diets, and environmental causes are prevalent. Coronary disorders such as ischemia and arteriosclerosis can be brought on by a diet high in sugar, saturated fat, and cholesterol. According to recent research, EGCG can improve capillary circulation by dilation of the capillaries, reduction of inflammation, and disruption of the digestion and absorption of lipids. However, in the lipid digestion process, EGCG directly disrupts the lipid emulsion mechanism.[36] The following is accomplished by directly interfering with the creation of micelles and by blocking phospholipase A2, an enzyme that is crucial to the digestion of lipids. The combination of the two mechanisms has the potential to reduce the quantity of plasmatic lipids and cholesterol by restricting lipid absorption.

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9. Effect on Carbohydrate Metabolism

Type II diabetes is a multifactorial illness characterised by insufficient insulin production by pancreatic β cells and resistance of peripheral organs' glucose and fat metabolism to the biological function of insulin. There exist several animal models of diabetes: streptozotocin or alloxan injection, which kills pancreatic β cells; genetically obese Zucker rats; as well as therapy with diets high in sucrose, which causes obesity and increased resistance to insulin. GTPs (500 mg/kg) were given to normal rats in a research by Sabu et al.[38], and within 60 minutes, the animals' glucose tolerance dramatically increased. At a dosage of 100 mg/kg, GTPs were additionally shown to dramatically lower blood glucose levels in rats with alloxan diabetes.

The raised blood glucose level caused by alloxan treatment was reduced by 29% and 44%, correspondingly, when the extract was continued to be administered daily for 15 days at a dose of 50 or 100 mg/kg. GTPs were shown to considerably lower increased hepatic and renal enzymes caused by alloxan.[39] Alloxan increased the amount of serum lipid peroxidation, but 100 mg/kg of GTPs markedly decreased it. Following GTP therapy, hepatic glycogen levels that had been reduced due to alloxan administration significantly increased. GTP-treated group demonstrated improved glutathione and superoxide dismutase levels, indicating higher antioxidant capability. Catalase, glutathione peroxidase, and lipid peroxidation, however, remained unaltered.[40] These findings suggest that giving rats GTPs partially restored changes in the glucose-utilizing system and oxidation state that were exacerbated by alloxan.

Moreover, in a test for oral glucose tolerance conducted on normal rats, catechins decreased plasma triglyceride levels. Intake of green tea extract decreased these levels in rats given a diet high in sugar as well as Zucker rats. Green tea and its flavonoid may have antidiabetic properties, according to a number of researches conducted on both humans and animals. It has also been demonstrated that green tea flavonoids contain insulin-like and insulin-enhancing properties.

Gomes et al. reported that black tea has an antihyperglycemic effect. It was discovered that EGCG increases blood sugar regulation by blocking the sodium-dependent glucose transporter SGLT1 from absorbing

intestinal glucose. Dietary catechins from green tea have the potential to ameliorate the anomaly of increased susceptibility to platelet aggregation and thrombosis observed in streptozotocin-diabetic mice.[41]

Aiming to assess the relationship between different sociodemographic, bio-clinical, dietary, and additional lifestyle choices and the incidence of prevalent risk factors for coronary artery disease (i.e., hypertension, dyslipidemia, diabetes, and obesity) among older people who reside on the islands of the Mediterranean who have no history of chronic illness, the Mediterranean Islands (MEDIS) epidemiological investigation is an a cross-section nutritional and medical questionnaire. In the context of the MEDIS study, the authors aimed to assess whether or not green tea consumption has no connection with fasting blood sugar levels and the incidence of type II diabetes mellitus given that data associated tea usage alongside clinical features has not been collected in elderly individuals.[42]

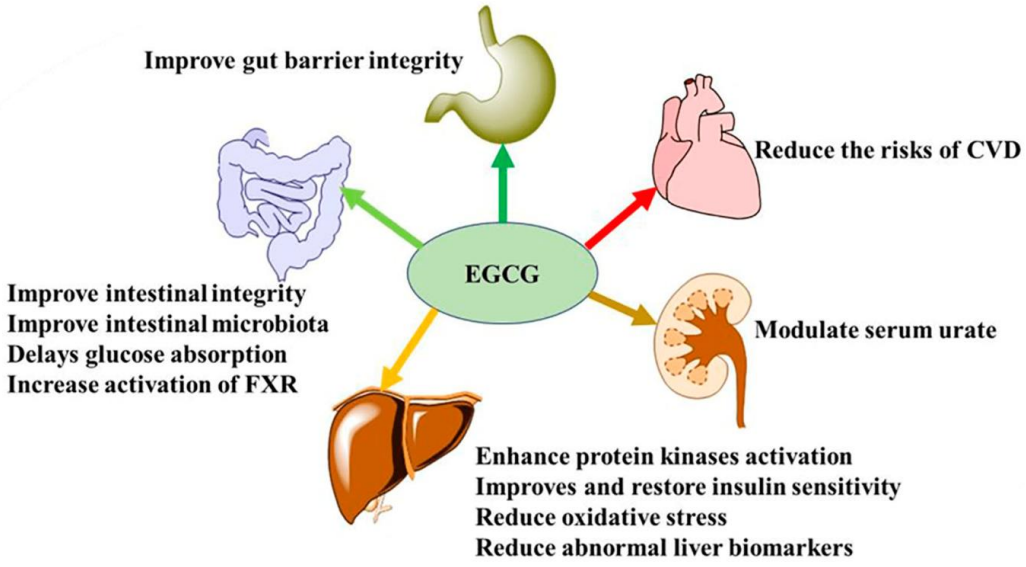

Fig. 5: EGCG Effect on Carbohydrate Metabolism.

ADVERSE EFFECTS OF EGCG

While the consumption of green tea has many positive health effects, the effects of green tea and its ingredients may be advantageous at specific amounts, while greater dosages may have some unidentified negative consequences. Furthermore, not everyone will experience green tea catechins' benefits in the same way. Higher consumption of green tea can cause acute cytotoxicity in liver cells, a key organ involved in metabolism.[43] This is because green tea extract contains EGCG, which is cytotoxic. According to further research, consuming more green tea may lead to oxidative DNA damage in the liver and pancreas of hamsters. Yun et al. expounded on how EGCG functions in vivo in pancreatic β cells as a pro-oxidant as opposed to an antioxidant. Consequently, a high green tea diet may make it more difficult for diabetic animals to regulate their blood sugar levels.[44]

In normal rats, green tea extract produced goitre (enlarged thyroid) at an elevated dose (5% of food for 13 weeks). The thyroid hormones' plasma concentrations were altered by this intensive therapy. It seems improbable, though, that consuming even an extremely large dietary quantity of tea made from green tea could have these negative consequences on people.

Three key variables contribute to the harmful consequences of excessive tea drinking (either green or black): (1) the tea's caffeine content; (2) the amount of aluminium; and (3) the tea polyphenols' impact on iron bioavailability. Patients with significant circulatory issues or cardiac ailments shouldn't drink green tea.[45] Caffeine can elevate heart rhythm, therefore women who are pregnant or nursing should limit their daily intake to one or two cups. Because caffeine has diuretic properties, it's also vital to monitor the use of tea made from green tea along with certain medications concurrently. Investigations have shown that tea plants may collect large amounts of aluminium. This is a crucial factor for people with renal failure since excessive consumption of aluminum-containing foods can lead to neurological disorders due to the metal's accumulation in the circulatory system. Similarly, green tea catechins could be attracted to iron, and drinking green tea infusions might significantly reduce the amount of iron that is available in a person's diet.[46]

EGCG AMALGAMATED IN NANO PARTICLES

In addition to their large surface area compared to volume ratio, which sets them apart from ordinary materials in terms of biological, physical, and chemical properties, nanoparticles are formations with a minimum of a single dimension in the realm of the nanoscale. Since of their adaptability, they are good drug carriers

since they can be altered in a number of ways, such as size and chemical makeup.[47] They may also be adjusted by adding different ligands to the outermost layer in order to give selectivity to particular cells and/or structures. Furthermore, certain medications' pharmacokinetics and stability can be altered by nanocarriers. This is especially true for EGCG, where the bioavailability of the aforementioned catechin may be significantly increased with the application of nanotechnology. Lipid nanoparticles, polymeric nanoparticles, liposomes, gold nanoparticles, inorganic nanocarriers, and protein/peptide-based nanocarriers are some of the nanosystems that are employed in the transport of EGCG. Lipid and polymeric nanocarriers are the most widely utilised among the aforementioned nanocarriers for the administration of EGCG.[48]

1. Lipid Nanoparticles

Since its introduction in the early 1990s, lipid nanoparticles have become one of the most popular nanosystems for delivering medications. The lipid matrix that makes up these nanocarriers has several benefits, such as substantial drug load, superior tolerability, controlled release characteristics, and physical stability. Lipid nanoparticles are currently employed to increase EGCG's oral bioavailability, maintain chemical release, and strengthen EGCG's stability in physiological settings. EGCG-loaded lipid nanocarriers have been used to treat a wide range of illnesses, such as atherosclerosis and neurodegenerative, skin, and ophthalmic conditions.[49]

Zhang et al. created chitosan-coated NLCs using two surfactants—soy lecithin and Kolliphor® HS15—and natural lipids—glyceryl tridecanoate and glyceryl tripalmitate—with the goal of halting and reversing the formation of atherosclerotic lesions by lowering the cholesterol level of macrophages.[50]

The NLC formulation reduces the release of inflammatory factors and boosts EGCG stability and cell absorption, which together result in a nine-fold reduction in cholesterol buildup in macrophage cells. The same scientists produced triglyceride-free formulations for EGCG encapsulating a few years ago. Alpha-tocopherol acetate was used in place of triglyceride, and the outcomes were identical. Nanovehicles facilitated the stability and concentration of EGCG inside the cytoplasm of macrophages and inhibited the formation of MCP-1, an inflammatory cytokine.[51] The potential contribution of EGCG-loaded nanocarriers to avoiding the development of atherosclerosis is highlighted by both findings.

Chen and colleagues have created lipid nanoparticles that can encapsulate different active chemicals, such as EGCG, for use in skin care applications. High homogeneity lipid nanoparticles were demonstrated in their ability to effectively encapsulate hydrophobic and hydrophilic substances alone and in combination.[52] However, photostability tests showed that following 168 hours of being exposed, nanocarriers were unable to shield EGCG from photodegradation caused by UVA radiation.

To increase the stability and anticancer benefits of EGCG, Radhakrishnan et al. created SLN as a delivery system. EGCG's stability under serum and physiological settings was successfully increased by SLNs, and the molecule was released continuously at pH 5.When compared to free EGCG, in vitro experiments employing the prostate cancer cells DU-145 and the breast cancer cells MDA-MB-231 showed a significant drop in cell viability and increased levels of apoptosis.[53]

2. Liposomes

Phospholipid vesicles, or liposomes, are made up of an aqueous medium and at minimum one lipid bilayer. As a result of having amphiphilic nature, which allows them to entrap hydrophobic, hydrophilic, and amphiphilic medicines in both hydrophilic and hydrophobic surroundings, liposomes are a diverse class of nanocarriers.[54]

Egg lecithin and cholesterol were used to create EGCG-loaded nanoliposomes, which Gharib and colleagues then tested for effectiveness against methicillin-resistant *Staphylococcus aureus* (MRSA). The findings demonstrated that, both in vitro and in vivo, EGCG encapsulated into cationic nanoliposomes improved its efficacy against MRSA burn wound infections. These findings demonstrated the effectiveness of EGCG as a drug against bacteria.[55]

Phosphodiethylcholine (PhC)/cholesterol liposomes were synthesised by Luo et al. with the intention of preventing carcinogenesis. With a cargo loss of about 20% in stomach circumstances and up to 40% in intestinal fluid, the generated liposome showed excellent stability. Furthermore, at greater concentrations, the formulation improved EGCG's inhibitory influence on tumour cell survival.[56]

Song et al. improved the oral consumption of EGCG by synthesising liposomes with cholesterol and nonionic surfactants. In addition, the scientists looked at how permeable Caco-2 cell monolayers were to EGCG-entrapped liposomes as opposed to free EGCG. The perceived permeability of EGCG might be markedly increased by the liposomes. The formulation showed reduced toxicity and greater stability in comparison with free medicines. These encouraging findings encourage further research into a liposome-based nanoformulation that increases the gastrointestinal permeability of EGCG to improve its absorption into the bloodstream.

In a more recent study, Ramadass et al. created a liposome that was coloaded with paclitaxel and EGCG to treat breast cancer.[57] In MDA-MB-231 cells, the generated nanoformulation may significantly enhance the

complementary effects of the two chemicals and stimulate the death of breast cancer cells.

3. Gold Nanoparticles

A layer containing functional molecules covering a gold core gives rise to gold nanoparticles, which may carry complex molecules, such as medications and target molecules, for transportation.

Gold EGCG complexes are highly stable in acidic pH environments, but unstable in alkaline environments. The intratumoral administration was suggested by Shukla et al. and Chen et al. as a way to get over this drawback. Radioactive gold nanocarriers coated with EGCG were synthesised by Shukla and colleagues for use in treating solid tumours, including prostate cancer. Because of its anticancer qualities and strong affinity and specificity for the Laminin 67R receptor, which has been excessively expressed in a number of malignancies, especially prostate cancer cells, EGCG functioned as both a chemo-adjuvant and a targeted molecule in this instance.[58]

Consequently, prostate cancer cells can be targeted and internalised by receptor-mediated endocytosis by encapsulating gold nanocarriers with EGCG. The outcomes showed great promise, and the formulation's high effectiveness in shrinking the mice's tumour size was attained. Chen et al., on the other hand, created nonradioactive gold nanocarriers coated in EGCG to prevent the growth and appearance of tumours. Using a mouse model of melanoma cancer, the scientists discovered a promising cytotoxic impact on both in vitro and in vivo. In comparison to cells treated with free EGCG, the nanocarriers exhibited enhanced anticancer activity in murine melanoma cells, boosting cytotoxic effects 4.91 fold greater.

Cardiovascular disorders were additionally treated using EGCG conjugated gold nanoparticles subsequently. Gold nanocarriers were created by Khoobchandani and associates as a substitute for drug-coated stents. Through endocytosis mediated by the Laminin 67R receptor, smooth muscle and endothelial cells internalised the nanocarriers, which remained stable in a variety of biological conditions. Furthermore, EGCG-Au nanocarriers preserved the survival and proliferative potential of endothelial cells while blocking the migratory process of smooth muscle cells. The efficacy of EGCG-coated gold nanocarriers in treating neointimal hyperplasia and restenosis was demonstrated by these findings, underscoring the potential applications of these nanovehicles in the management of cardiovascular disorders.

CONCLUSION

Consuming green tea has been shown in multiple epidemiological investigations to be helpful in preventing illnesses such as cancer as well as neurological, cardiovascular, respiratory, and metabolic issues. EGCG is one of the green tea polyphenols whose biological effects have not yet been fully understood. Owing to its numerous interactions with nuclear transcription factors, intracellular signalling pathways, and cell surface receptors, EGCG has a broad range of tissue-protective, anti-inflammatory, antioxidant, antifibrotic, and anti-remodeling characteristics that make it potentially helpful in the management of the illnesses listed above. However, more investigation is required to determine suitable dosage schedules and innovative EGCG delivery formulations in order to provide sufficient localised EGCG concentrations in the tissues. Due to its nontoxicity and lack of known adverse effects, EGCG is a well-liked natural component for use in research as well as in the management and prevention of a number of illnesses. Unfortunately, the limited bioavailability of this polyphenol molecule means that a high dosage is needed to achieve therapeutic amounts. The application of nanocarriers to increase the stability and bioavailability of EGCG has been used in several researches.

Numerous forms of nanocarriers have been developed, such as liposomes, polymeric nanoparticles, gold nanoparticles, lipid nanoparticles, and other forms made of proteins, peptides, and inorganic elements. Lipid and polymeric nanocarriers have been the subject of most research, presumably because of their advantageous qualities including biocompatibility. However, there is still uncertainty regarding the health risks of inorganic nanocarriers and gold. The outcomes show great promise, with the bioavailability and stability of EGCG being enhanced by the nanocarrier formulations. Furthermore, some research revealed that when the particles were coated with ligands like chitosan, which serves as mucoadhesive and opens the tight junctions of the gut, the nanoformulations may significantly improve the permeability in the barrier between the intestines.

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