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GREEN TEA: A HEPATOPROTECTIVE HERB

Gurfateh Singh, Deepika Bhatia, S.L. Hari kumar

[1]Department of Pharmacology, University School of Pharmaceutical Sciences, Rayat -Bahra University, Mohali, Punjab, India

Abstract:
Camellia sinensis is commonly known as Green Tea which is most consummated beverage in the world. The diversify properties of the C. sinensis encourage us to new research in few recent years. There are lots of finding in the process of the tea and there are so many positive aspects also found in it. Present review is an attempt to summarize the various pharmacological effects like anti hepatoprotective and antioxidant activity, a powerful protective tool for future era. This article is enlighting the possible beneficial effects of green tea on the drug/chemicals induced hepatotoxicity.

Keywords: *Green tea, Hepatoprotection, EGCG*

Corresponding Author:
Dr. Gurfateh Singh
Asst. Professor,
Department of Pharmacology,
University School of Pharmaceutical Sciences,
Rayat-Bahra University, Mohali, Punjab, India
Tel: +919216781466
E-mail address: dr_sugga@yahoo.co.in

QR code

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INTRODUCTION:

Green tea (GT) is one of the most consumed drinks in the world [1]. The Camellia sinensis is a biological name of GT and belonging to family Theaceae. *C.sinensisis* is cultivated in India mainly in Assam. It is an evergreen shrub or tree and can grow to heights of 30 feet, but is usually pruned to 2-5 feet for cultivation. The leaves are dark green, alternate and oval, with serrated edges, and the blossoms are white, fragrant, and appear in clusters or singly. Depending on the manufacturing process, teas are classified into three major types: 'non-fermented' GT (produced by drying and steaming the fresh leaves to inactivate the polyphenol oxidase and thus, non-oxidation occurs); 'semi-fermented' oolong tea (produced when the fresh leaves are subjected to a partial fermentation stage before drying); and 'fermented' black and red (*Pu-Erh*) teas which undergo a post-harvest fermentation stage before drying and steaming, although the fermentation of black tea is due to an oxidation catalyzed by polyphenol oxidase, and that of *Pu-Erh* tea is attained by using microorganisms [2]. Approximately 76–78% of the tea produced and consumed in India is black tea, 20–22% is a GT and less than 2% is Oolong tea [3].

GT has many beneficial effects clinically, moreover it is a 'non-fermented' tea, contains more catechins, than black tea or Oolong tea. Catechins have shown a strong antioxidants effect [4]. The dosage of GT beverage varies, depending on the clinical situation and desired therapeutic effect. The phenolic content of GT infusion is between 50-100 mg polyphenols per cup, depending on species, harvesting variables, and brewing methods. Cancer preventative effects are usually associated with higher range of the dosages. The recently possible effect of GT has been noted the anti cancer [5], Cardiprotective [6], Anti-inflammatory [7], Anti-arthritic [8], Anti-bacterial [9], Anti angiogenic [10], anti-viral [11], Neuroprotective [12] and cholesterol-lowering effects [13]. GT contains catechin derivatives including gallic acid (GA), epigallocatechin (EGC), epicatechin (EC), epigallocatechin 3-gallate (EGCG) and epicatechin 3-gallate (ECG) however EGCG is a major active ingredient [14]. However EGCG is a major constituent and is also the component with the highest anti-oxidant properties by the decreased ROS generation [15], expression of PPARϒ, Interleukins formation, TNF alpha and ATP generation [7]. It has been observed that EGCG up regulate the JAK/STAT [16], MAPK and PI_3K/AKT pathways [17, 18] leading to hepatoprotection.

The United States Department of Agriculture (USDA) has recently published a database for the flavonoid content of selected foods. The four major catechins are (-)-Epigallocatechin-3-Gallate (EGCG), that represents approximately 59% of the total of Catechins; (-)-Epigallocatechin (EGC) (19%, approximately); (-)-Epicatechin-3-Gallate (ECG) (13.6% approximately) and (-)-Epicatechin (EC) (6.4%, approximately) chemical structure (FIG.1) GT also contains gallic acid (GA) and other phenolic acids such as chlorogenic acid, caffeic acid, and flavonols i.e. kaempferol, myricetin and quercetin. The main chemical components of unfermented tea are polyphenols of which the main ones are catechins, mainly (-)-Epigallocatechin Gallate (EGCG, 5–12%) and (-)-Epicatechin Gallate (ECG, 1–5%). GT is also a good source of methyl xanthines, primarily in the form of caffeine (2–5%), with smaller quantities of theobromine and theophylline. Epigallocatechin Gallate is the most abundant of the tea catechins and thought to be responsible for the majority of the biological activity of GT extracts.

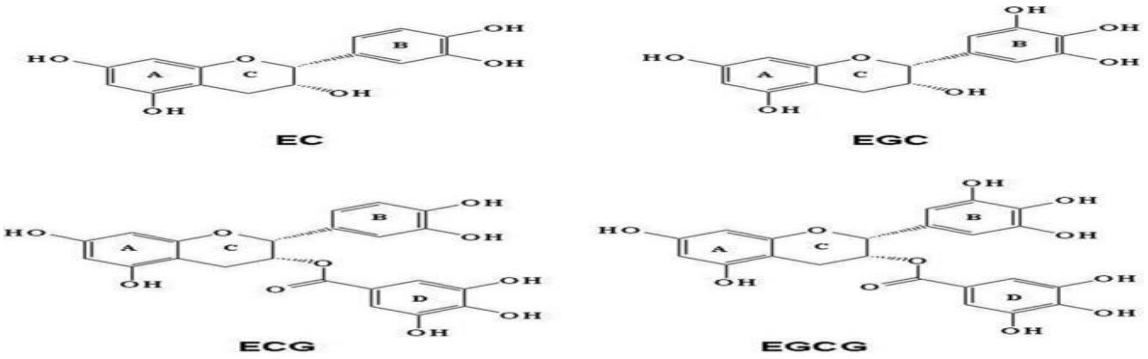

Fig 1: Chemical Structure of GT Ingredients

Hepatoprotective Effect of GT:

Anti oxidant Effect of GT

Oxidative stress is considered to play a prominent causative role in many diseases, including liver damage [19]. It is the state of imbalance between the level of antioxidant defense system and production of oxygen-derived species. Increased O_2 concentration and production of oxygen-derived species such as superoxide radical (O_2), hydroxyl radical (OH) and hydrogen peroxide (H_2O_2) cause oxidative stress [20]. It will lead to cellular damage and DNA damage due to consumption of hepatotoxicant agent. GT is a popular neutraceutical and as per previous studies GT catechins counteracted oxidative mitochondrial damage in the livers of rats [21]. EGCG scavenged hepatic mitochondrial free radicals effectively and the benefit would prevent liver mitochondrial damage and apoptosis [22]. Moreover the alcohol induced liver injury also attenuated with EGCG [23].

Anti- inflammatory Effect of GT

A high concentration of free radicals leads to activation of inflammation and cellular injury. The expression of iNOS and Cyclo-oxygenase-2 (COX-2) are the key modulators of inflammation [24, 25]. The consequence of high levels of iNOS and COX-2 caused the production of high concentrations of NO and eicosanoids through the initiation of the COX-Prostanoid pathway respectively [26, 27], which caused cellular inflammation and necrosis [26, 27]. EGCG a significantly reduced the release of tumor necrosis factor (TNF)-α activated by kuffer cells, interferon (IFN)-γ, interleukin (IL-4), and IL-6 in serum induced Nitrite Oxide Synthase as well as the COX-2, Moreover it reduced malondialdehyde (MDA) and restored the glutathione (GSH) content including superoxide dismutase (SOD) activity in liver [28] by modulating the activities of TGF/SMAD, PI3K/Akt pathways [29, 30, 31]

Effect of GT on Mitochondria

Mitochondria are to be primary targets in hepatotoxicity, with particular attention on the mitochondrial permeability transition [32]. The mitochondrial oxidative process plays a central role in the cellular energy metabolism by providing about 95% of cellular energy needs in the form of high energy phosphate bond i.e. adenosine Triphosphate (ATP) [33]. The active transport of sodium-potassium across the cell membrane is controlled by sodium-potassium adenosine triphosphates (Na^+ K^+ ATPase) enzyme, which is an integral plasma membrane protein responsible for a large part of the energy consumption constituting the cellular metabolic rate [34]. The hepatic necrosis are associated with damage to sub-cellular organelles including mitochondria. Interleukin-1 (IL-1) and Tumor Necrosis Factor- α (TNF-α) are extracellular mediators, produced by activating Kuffer cells known to have a central role in inflammatory responses. The cytokines induced the release of chemotactic mediators, increased the expression of adhesion molecules, activate neutrophils and endothelial cells [35]. EGCG administration also increased resting hepatic energy stores as determined by an increase in cellular Adenosine Triphosphate (ATP) novel cell-specific mechanism for the control of the translation of mRNAs required in mitochondrial function [36].

Effect of GT on Nitric Oxide Associated Injury

The nitric oxide activated by the increased levels of cytokines and endotoxins and different isoforms of NO synthase (NOS): indicible (iNOS), endothelian (eNOS) and neuronal (nNOS) in a variety of cells which leads to cellular injury [35, 37]. It is well known that nitric oxide plays a diverse range of physiological and pathophysiological actions in hepatic metabolism [38, 39]. GT Polyphenols reduce the severity of liver injury in association with lower concentrations of lipid peroxidation and pro inflammatory nitric oxide-generated mediators [40].

Adverse Effects of GT

Although GT has several beneficial effects on health, the effects of GT and its constituents may be beneficial up to a certain dose yet higher doses may cause some unknown adverse effects. GT extract induced a thyroid enlargement (goiter) in normal rats [41, 42].

CONCLUSION:

Human studies suggest that GT may contribute to decrease many types of risk to the human body due to its antioxidant properties. Increasing interest in its health benefits has led to the inclusion of GT in the group of beverages with functional properties. The development of biomarkers for GT consumption, as well as molecular markers for its biological effects, will facilitate future research in this area. As per present review it as concluded that GT is very much effective as a hepatoprotective agents, Thus, there is clearly need to improve and standardize the GT, and a better understanding of the mechanisms involved in hepatoprotection may help to define new therapeutic strategies.

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