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Review Article

A Tale of Green and Pink (Effects of Green Tea in Oral Cancer): A Review

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Abstract

Tea is one of the most ancient and popular beverages consumed around the world. It is made from the leaf of the plant *Camellia sinensis*. It is divided into three types based on the fermentation process: Green tea (non-fermented), Oolong tea (semi-fermented), and Black tea (fermented). Consumption of tea, especially green tea, has been associated with many health benefits including cancer prevention. Some epidemiological observations have revealed that there was an inverse correlation between increased green tea intake and relative risk for cancers. The primary goal of chemoprevention here is to reverse, suppress, or inhibit the progression of premalignant lesions to cancer. Using green tea extracts (GTE)/polyphenols in chemoprevention of oral premalignant lesions along with the use of GTE as a chemo preventive agent in various other cancers as well. It is proved by research for more than a decade that green tea polyphenols influence a number of pathways that are relevant to tumor growth proliferation and metastasis. The need of the hour for chemoprevention using green tea is development and validation of biomarkers that can be evaluated by clinical trials in a clinical setting. "The problem with a lot of chemotherapy drugs is that they really just target rapidly dividing cells, so cancer divides rapidly, but so do cells in your hair follicles and intestines", "But you don't see these sorts of side effects with green tea consumption".

Keywords: Green Tea Extracts [GTE]; Polyphenols; Pre-Malignant Lesions; and Chemoprevention

Introduction

First and foremost, everybody might be thinking what could be this Green and Pink; here green is representing green tea and pink representing the burgundy pink ribbon for oral cancer awareness. The use of tea leaves probably first originated in the southwest 'area of China more than 3,000 years ago [1] and was likely initially used by people just for chewing and eating, in just the same way that coffee was first used by people eating the beans directly in Ethiopia. Over time, the use of leaves and buds from the tea tree gradually expanded as people began to use in cooking and when added to boiling water to flavor the water they drunk [2].

Green Tea is an infusion of the leaves of the *Camellia sinensis* plant. First discovered in China, tea is grown in over 30 countries and is the most widely consumed beverage in the world [3], aside from water. Recently, tea has attracted attention for its health benefits, particularly with respect to its potential for preventing and treating cancer and cardiovascular diseases [4]. Increasing scientific and consumer interest in the health benefits of tea has led to the inclusion of tea extracts in oral nutritional supplements, and topical preparations, whose potential for decreasing the risk of skin cancer is under investigation [5,6]. While tea contains a number of bioactive chemicals, it is particularly rich in flavonoids, including catechins, and their derivatives. These polyphenolic compounds, the most abundant of which is epigallocatechin gallate (EGCG), are thought to contribute to the beneficial effects ascribed to tea. Although abundant evidence suggests that catechins and their derivatives are effective antioxidants *in vitro*, the evaluation of their efficacy as antioxidants *in vivo* is more complex [7]. In the following review, we have assessed the available evidence that tea consumption confers significant health benefits to humans, as well as the evidence that tea catechins and polyphenols mediate the proposed health benefits of tea consumption by functioning as effective antioxidants *in vivo* [8].

Health Benefits of Green Tea [9,10]

- Reduced fat absorption
- Increased energy expenditure
- Weight loss
- Reduced number of cavities
- Reduced LDL oxidation
- Reduced heart disease risk
- Increases insulin sensitivity
- Inhibition of cancer development

Why is Green Tea Beneficial?

The benefits are attributed to polyphenols called catechins, which make up 30% of the dry weight of green tea leaves. Green tea has the highest content of polyphenols compared to black or oolong tea.

Green tea promotes detox, and it's vital for cancer patients, it regulates blood sugar because glucose spikes cause cancer and feed cancer, it fights against inflammation because it helps cancer to start, grow and spread.

The major catechins, a group of polyphenols, in green tea include: [11,12].

1. Epigallocatechin-3-Gallate (EGCG) [3-7%]
2. Epigallocatechin (EGC) [3-6%]
3. Epicatechin (EC) [1-3%] and
4. Epicatechin Gallate (ECG) [3-6%]

EGCG is the most abundant and best studied [13]

Active ingredients in green tea

Epigallocatechin-3-gallate or EGCG, one of THREE catechins in green tea and the most abundant. One cup of green tea contains approximately 117 - 442 milligrams/liter of EGCG. Other components found in green tea include caffeine, theanine, theaflavins, theobromine, theophylline, and phenolic acids such as Gallic acid [14]. In the scientific world, green tea is probably best known, and most studied for its effects on cancer prevention.

Although epidemiological studies have not shown a clear link between cancer prevention and green tea, animal studies have been very convincing. They have demonstrated the preventative effects of green tea and EGCG against liver, stomach, breast, prostate, lung, and skin cancers at any stage (initiation, promotion, or progression) Studies have clearly demonstrated the preventative effects of green tea and EGCG against many types of cancers at any stage (initiation, promotion, or progression). The National Cancer Institute (NCI) has funded extensive research with green tea as a potential cancer chemoprotective agent [15].

Molecular mechanisms in cancer prevention promoted by green tea as follows [16]

- Modulation of ROS - Reactive Oxygen Species
- Inhibition of NF-Kb - Nuclear Factor Kappa B pathway
- Regulation of MAPKs - Mitogen-activated protein kinases
- Epigenetic modulation

EGCG targeting the cancer cell mitochondria [17]

Epigallocatechin-3-gallate (EGCG) is an abundant polyphenol in green tea and considered to be a key component of green tea that contributes to its anticancer property. It has been shown that EGCG was able to rapidly cause apoptotic cell death in various malignant B-cell lines by triggering the mitochondria-related cell death events including loss of mitochondrial transmembrane potential; release of various mitochondrial apoptogenic proteins (cytochrome c, Smac/DIABLO, and AIF), activation of caspases, and ROS generation [18-20]. Apoptosis induced by EGCG could be reduced by antioxidant compounds, catalase, and SOD2, suggesting that ROS may play a key role in mediating the cell death process [21]. Similar results were found in pancreatic cancer, colon cancer, and melanoma cell lines as well as breast cancer xenograft animal models [22-24]. In addition, tumor cells lacking caspase-3 expression could escape apoptosis when treated by EGCG [25]. Interestingly, EGCG selectively killed melanoma cells without exerting a toxic effect to normal melanocytes [26]. High concentration of EGCG treatment caused a severe ROS increase in oral malignant cells but led to a ROS decrease in normal epithelial cells [27]. Further analysis of cellular antioxidants in both cells showed that normal cells had a higher level of catalase than cancer cells, which might explain why EGCG caused an increase of ROS only in cancer cells [27], combined with chemotherapy drugs like arsenic acid and erlotinib, EGCG showed a synergetic effect in killing cancer cells [21,28]. The precise mechanisms responsible for the preferential cytotoxic effect of EGCG against cancer cells remain to be investigated. Interestingly, a recent study showed that the vast majority of this compound (over 90%) is accumulated in the mitochondria after incubation of neurons with EGCG in culture and that such accumulation seemed to confer a protective effect on normal neurons under oxidative stress conditions [29]. In contrast, in vitro incubation of multiple brain tumor cells with EGCG resulted in significant growth inhibition [30]. It is possible that the differences between normal and cancer cells in their mitochondrial function might be responsible for such different responses, and that mitochondrial dysfunction in cancer cells might render them vulnerable to EGCG. Currently, it is unclear if EGCG could directly bind to a specific target molecule in the mitochondria. EGCG has entered clinical trials in cancer prevention and cancer treatment.

Effects of EGCG on chemoprevention and chemotherapy [31,32]

Cancer prevention is enacted through its antioxidant or pro-oxidant activities by decreasing cancer cell proliferation, hindering the angiogenesis and increases the process of apoptosis and cell cycle arrest.

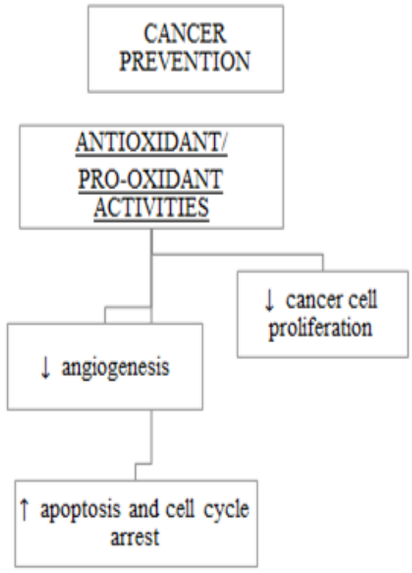

Table 1

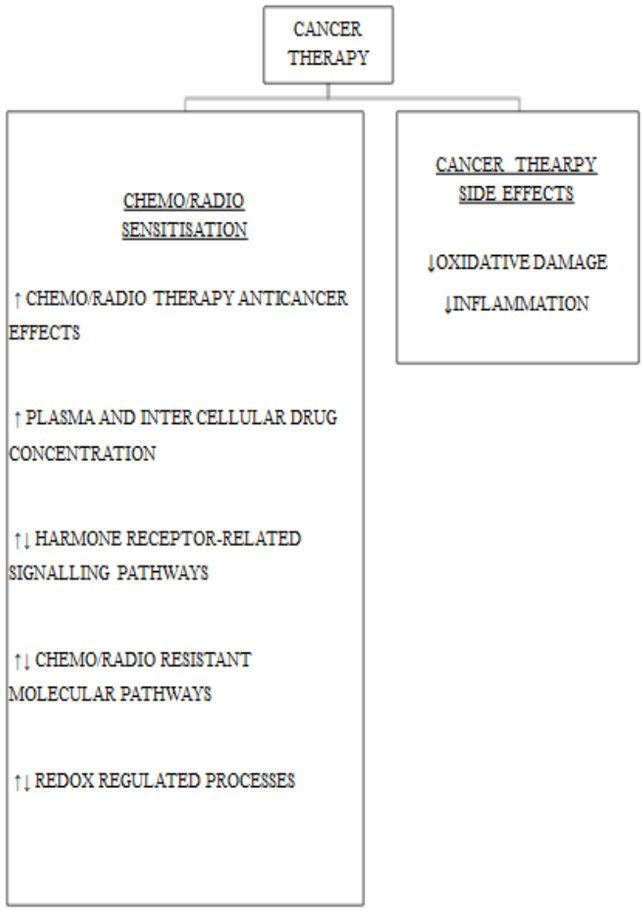

Table 2

The effects of EGCG over cancer therapy is off by two means, chemo/radio sensitization by increasing chemo/radiotherapy anticancer effects, increases plasma and intercellular drug concentration, balancing hormone receptor-related signaling pathways, chemo/radio-resistant molecular pathways and redox-regulated processes and decreasing cancer therapy side effects by decreasing inflammation and oxidative damage

Conclusion

Now a day's green tea become a status symbol, we should not think like that instead of cost of availability we should be more conscious about the beneficial aspects of the product, this review article only stresses about the beneficial effects of the green tea over oral cancer, there are so many health benefits from drinking green tea, so start drinking the green tea.

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