Chapter 22
Functional Mechanisms of Green Tea Polyphenols and Their Molecular Targets in Prevention of Multiple Cancers

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ABSTRACT

Cancer is portrayed as a group of disease characterized by alteration in the normal regulation of cell growth by the successive acquisition of genetic, somatic, and epigenetic alteration. Synthetic drugs are single targets while natural products are multi-targeted to prevent cancer. NF-κB is persistently active in a number of disease states, including cancer, and therefore has a critical role in cancer development and progression. It also provides a mechanistic link between inflammation and cancer and is a major controlling factor resistant to apoptosis in both pre-neoplastic and malignant cells. Importantly, NF-kB and the signaling pathways that mediate its activation have become attractive targets for the development of new chemopreventive and chemotherapeutic approaches. Natural antioxidants have been shown to possess chemopreventive and chemotherapeutic potential via targeting NF-κB signaling, among which tea polyphenols have been studied extensively. In this chapter, the authors summarize the regulation of NF-κB pathway by green tea polyphenols in different cancer types.

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INTRODUCTION

Cancer is a very complex disease involving gradual accumulation of germ line, somatic and epigenetic mutation that cause the alternation in homeostasis that controls normal cellular proliferations and potential to spread or invade other parts of the body (Hanahan & Weinberg, 2011). After cardiovascular, cancer is one of the major ailment effecting humankind and still remains as one of the leading causes of mortality worldwide, for instance, more than 10 million new patients are diagnosed with cancer every year and over 6 million deaths documented and roughly 12% deaths worldwide (Nagai & Kim, 2017). Near about 15 million new cancer cases are estimated to be diagnosed by the year 2020which is alarming that cancer cases will increase over 20 million by 2025(Siegel, Miller, & Jemal, 2020). The progression of cancer is a multistep and multifactorial process that may be caused by external factors like environmental pollutants, tobacco, infectious organisms and aflatoxin contaminated food product or internal factors such as genetic mutations (inherited/acquired), hormonal imbalance and immune conditions can act together/singular to cause the incipience of cancer (Hanahan & Weinberg, 2011). As cancer is linked with high morbidity and mortality worldwide, therefore it is an urgent need to develop the ways to manage this dreadful disease, however, the existing treatment modalities includes chemotherapy, surgery, radiotherapy, hormonal therapy, targeted therapy, gene therapy and stem cell therapy (Arruebo et al., 2011). Natural products, mainly derived from plant sources have great interest to cure the ailment and according to WHO report more than 60% population worldwide rely on plant product as a medicinal source (Veeresham, 2012) In addition to this, according to the National Center for Complementary and Alternative Medicine (USA), 38% of adults in the United States opted for complementary and alternative medicine over conventional drugs. Synthetic drugs are single targets while natural products are multi-targeted to control cancer (Chamberlin et al., 2019). By and large, existing synthetic drug has major side effects over the natural product derive especially from plants. Among natural compounds, green tea and its polyphenolic derivative display a meaningful role in different cancer prevention and cure which was extensively studied worldwide against in vitro and in vivo model (H. Wang et al., 2012). Green tea leaves have different components and each component display a diverse role that can be beneficial to the mankind worldwide (Prasanth, Sivamaruthi, Chaiyasut, & Tencomnao, 2019). One of the green tea polyphenols flavonols is catechins which are found in greater amount and demonstrated the diverse pharmacological properties (Khan & Mukhtar, 2019). However, (-)-epigallocatechin-3-gallate (EGCG) near about 59% of the total catechins from the leaves of the green tea, 19% (-)-epigallocatechin (EGC), 13.6% (-)-epicatechin-3-gallate (ECG) and 6.4% (-)-epicatechin (EC) (V. Nair, Bandyopadhyay, & Kundu, 2013). The chemical structural and functional difference between these catechins are of hydroxyl group present on the B-ring as well as the presence /absence of a moiety of galloyl (Botten, Fugallo, Fraternali, & Molteni, 2015). It was observed that among of all catechins, EGCG is the most studied and demonstrated the vital role in cancer-preventive and therapeutic. A large number of studies were evaluated to demonstrate the effects of EGCG on different in vitro molecular targets and in vivo molecular targets as potential cancer chemoprevention as well as therapy (Singh, Shankar, & Srivastava, 2011). We observed that majorities of these studies showed that EGCG regulated large array of anticancer molecular targets and specially targets NF-kB associated signaling pathway (L.-X. Wang et al., 2019). Despite the tremendous study on EGCG, its applicability and validation to human model has met with limited success for many reasons like the inefficient systemic delivery and bioavailability (Siddiqui, Adhami, Ahmad, & Mukhtar, 2010). To overcome these limitations, researcher adopted various approaches, including nanoparticles-based delivery, surface modification, addition of additional adjuvant and combination therapy to enhance the