Inhibition of Carcinogenesis by Tea: Bioavailability of Tea Polyphenols and Mechanisms of Actions (44368)

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The inhibitory activity of tea and tea polyphenols has been demonstrated in many studies with animal models in different laboratories, but such activity has been observed only in some of the epidemiological studies. A key question is whether tea consumption lowers cancer risk in humans. To answer this question, we need to know the effective components of tea and the mode of their inhibitory actions against tumorigenesis. It is important to know the levels of the putative active components in the target tissues and whether such levels are capable of inhibiting cancer formation and growth. In this report, we plan to review the inhibitory activities of tea and tea polyphenols against the development of lung tumors in animals and the growth of human cancer cells in culture, discuss the possible active components involved and mechanisms of action, and describe the tissue levels and pharmacokinetics of tea polyphenols in animal models and humans.

Inhibition of Lung Tumorigenesis in Animal Models

The tobacco carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) effectively induces adenomas and adenocarcinomas in the lungs of A/J mice. In typical experiments, decaffeinated green or black tea (DGT or DBT) was given to mice in the drinking fluid as 0.3% or 0.6% solution of tea solids. The tea solids were dehydrated water extracts of tea leaves. Tea was administered to mice during the NNK treatment period (for 3 weeks beginning 2 weeks before a single dose of NNK, 103 mg/kg, i.p.) or after the NNK treatment period (beginning 1 week after the NNK treatment until the termination of the experiment 15 weeks later). The tea treatment markedly inhibited tumorigenesis, especially tumor multiplicity (1). In these experiments, the inhibitory activities of decaffeinated green and black tea were comparable, although green tea might be slightly more effective in some experiments. Administration of DGT for a shorter period of time during (or after) the carcinogen treatment period also inhibited tumorigenesis, although it was less effective than the above described protocol (2). In this model, theaflavins (a mixture of theaflavin, theaflavin monogallates, and theaflavin digallate isolated from black tea), when administrated in the drinking fluid starting 1 day after the NNK treatment, also significantly inhibited tumorigenesis analyzed at Week 16 (3). When the mice were given black tea 16 weeks after the NNK injection, at which time almost all of the mice developed adenomas, the progression of these tumors to adenocarcinomas was significantly inhibited. These included cancer incidence, cancer multiplicity, and the volume of the adenocarcinoma analyzed at 52 weeks (4). In the above study, inhibition of cell proliferation (based on BrdU incorporation) by black tea was observed in the adenomas but not in adenocarcinomas (4). The antiproliferative effects of tea and polyphenols were also demonstrated in short-term experiments (4). A dose of NNK induced hyperproliferation of the lung bronchiolar epithelial cells, which peaked at Day 5. When green tea polyphenols, black tea polyphenols, epigallocatechin (EGC), or theaflavins were administered in the drinking fluid starting 1 day after the NNK treatment until Day 5, the cell hyperproliferation was significantly inhibited.

Brewed black tea and green tea infusions (similar to those consumed by humans and brewed in a Bunn tea brewing machine), when given to A/J mice as the sole source of drinking fluid, also inhibited spontaneous lung tumorigenesis (5). In this experiment, rhabdomyosarcomas were also found in the mice, and the tumor incidence and size were inhibited by black and green tea. These experiments indicate that tea has broad inhibitory effect against both spontaneous and chemically induced tumorigenesis, and can inhibit lung carcinogenesis when administered during the initiation, promotion, or progression stages of carcinogenesis. Similar activities have also been demonstrated in a skin carcinogene-

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Future Directions

Tea is one of the few agents that can inhibit carcinogenesis at the initiation, promotion, and progression stages. It is a challenge for us to determine the relevant mechanisms involved and whether this activity can be used for human cancer prevention. In this context, only activities displayed by tea constituents at concentrations that are achievable in human tissues are important. Therefore, information on the bioavailability and tissue levels of EGCG, EGC, theaflavins, and other tea constituents should be a vital part of future mechanistic studies. The bioavailability and bioactivities of thearubigens should be studied thoroughly. These parameters could determine the differences between green and black tea. The effects of different doses of tea on tissue levels of tea polyphenols are rather intriguing. Further studies are needed to determine the best dosage and route to deliver certain tea constituents to particular organs. Large doses of pure compounds in capsules may not be the best way to deliver the active components effectively to many tissues. Knowledge gained on the tissue levels and biological activities of tea polyphenols as well as on reliable biomarkers for tea consumption would be useful in the planning of future epidemiological studies and human cancer prevention trials.

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