Overview

Tea is a Health Promoting Beverage in Lowering the Risk of Premature Killing Chronic Diseases

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ABSTRACT

Green and black tea are widely used beverages, second only to water. Tea is an extract of the leaf of the plant *Camellia sinensis*. The major health benefit of tea is that the leaf contains several polyphenols such as epigallocatechin gallate, and in addition an enzyme, polyphenol oxidase. If upon harvest the leaves are heated, these enzymes are deactivated, and thus, after drying and grinding, the result is green tea. If the leaves are ground and incubated in air at about 40 degree C the polyphenol oxidase converts the original polyphenol to a number of other products such as theaflavin and thearubigins. Upon drying, these are the polyphenols typical of black tea. In most instances, the polyphenols from green tea and black tea have similar properties in health promotion. Coronary heart disease stems from the oxidation by reactive oxygen species of LDL-cholesterol. The tea polyphenols inhibit this reaction. There are data in humans that tea drinkers have a lower risk of heart disease. In animal models, similar findings were made. In the field of cancer causation, we distinguish between genotoxic carcinogens effecting DNA and genes, and other steps associated with the development of cancer, in part also involving reactive oxygen species. Tea and tea polyphenols induce enzymes such as glucuronosyl transferase that detoxify carcinogens. Thus, tea drinkers have a lower risk of cancer and the mechanisms of these reactions have been explored in animal models and through *in vitro* approaches. Of importance also is that tea decreases the growth of neoplastic cells, but not of normal cells. Tea also enhances apoptosis, a phenomenon of elimination of cancer cells. Tea drinkers also have a healthier intestinal flora, through the inhibition of bacteria that have adverse effects and promotion of the growth of beneficial bacteria. Through the elimination of reactive oxygen species, associated with premature aging, tea drinkers display good health to an old age.

Keywords: green tea; black tea; polyphenols; reactive oxygen species; heterocyclic amines; coronary heart disease; cancer; aging inhibition; health promotion; disease prevention.

Main Causes of Chronic Diseases

Mainly based on cancer research we have learned to distinguish between agents that modify the DNA and generate a mutation. Such materials or synthetic chemicals are called mutagenic and genotoxic. On the other hand, there are chemicals or situations that enhance the development and growth of lesions initiated through a genotoxic modification of cells. We have learned to distinguish between these two classes of chemicals based on the permanence of their effect and the doses and continuity of exposure needed for their action.

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Reactive oxygen species

Living cells require oxygen to generate energy and to develop fully. However, under some circumstances cells generate reactive oxygen species (ROS) in the form of reactive entities such as hydrogen peroxide and especially hazardous oxygen radicals.

Heterocyclic aromatic amines

This class of chemicals was discovered about 25 years ago when Dr. Sugimura, at the National Cancer Center Research Institute in Tokyo, wondered about the mechanisms of the browning reaction when cooking, that is frying or broiling of meat and fish. His laboratory showed that the surface of brown meat contained powerful mutagens. At that time, it was thought that mutagens were likely cancer causing agents that subsequently were shown to be genotoxic. In part with our collaboration, such cooking-derived

mutagens were shown to belong to a new class of carcinogens, the heterocyclic aromatic amines. When they were ingested, this class of chemicals also generated ROS, and damaged cells not only through reaction with DNA, but also through a cellular toxic reaction, to which the cells responded by attempts to repair, leading to cell regeneration and duplication. Thus, a cell with an altered DNA subjected to forced growth would regenerate numerous abnormal cells with an abnormal DNA, typical of an early cancer cell.

Salt

Salt does not damage DNA and is not genotoxic. However, importantly, it severely impinges on the stability of cells and during attempts at repair, cells exposed to high levels of salt undergo rapid cell duplication. The concentration of salt is usually highest at the point of ingestion namely the stomach. Therefore, there is severe damage to the stomach with possible alteration, especially in the tissue also generating ROS and carrying a bacterium discovered in 1984, *Helicobacter pylori*. Eventually, stomach cancer and possibly ulcers stem from excessive salt intake. Through tradition in Japan and parts of China people use as much as 30 grams of salt per day. The Japanese have instituted a plan to progressively lower salt intake and currently, the amount consumed is about 12 grams. However, only about 3 grams are needed to meet physiological sodium needs.

Tea as a health promoting beverage

Tea is a frequently used drink by people Worldwide. It is an extract of the leaves of the plant *Camellia sinensis*. Upon harvest, the best teas are obtained by plucking the top two leaves and the bud of the tea bush. The leaves contain the polyphenol, epigallocatechin gallate and an enzyme polyphenol oxidase. When the leaves are withered (dried) and steamed, the polyphenol oxidase is inactivated, and result is green tea. When the leaves are processed (crushed) and incubated for about 60 minutes, the polyphenols oxidase converts the polyphenol to other polyphenols, such as theaflavin and thearubigin, typical of black tea. A lesser time of incubation, such as about 25-35 minutes yields an intermediate product, oolong tea that is popular in southern China and in Taiwan.

We have described the history of tea and use worldwide, including the original discovery of tea in China some 4,000 years ago, in the form of green tea, and later of black tea in Northern India. Currently, green tea is used mainly in China, in Japan and in North Africa.

Tea and heart disease prevention

Epidemiological studies in Europe revealed that black tea drinkers had a lower incidence of heart disease. The underlying reason rests on the fact the tea polyphenols act as effective antioxidants inhibit the oxidation of LDL- cholesterol caused by reactive oxygen species, and lead to atherogenesis. In has been shown that the mechanism can be reproduced using a copper catalyzed oxidation of LDL cholesterol, inhibited by tea polyphenols. A number of investigations confirmed a lower risk of heart disease as a function of tea intake. A meta analysis of stroke and coronary heart disease “cardiovascular disease” evaluated the results of many studies and found that heart disease decreased 11% by intake of 3 cups (about 700 ml) of tea per day. In Japan, it was noted that the relative risk of cardiovascular disease and cancers were significantly lower with 10 cups of tea per day. One explanation is that tea also beneficially affects platelet aggregation, a possible cause of heart attacks that are prevented by tea.

Tea and cancer prevention

Mutations of the cellular DNA are a key step leading to cancer. Mutational events can be used as markers for environmental genotoxic products that might be possible cancer risks. This approach is effective in research on products that might have antimutagenic and thus, likely anticarcinogenic effects.

This method has been applied to study the effect of tea polyphenols from black tea and from green tea. It was found that both types of polyphenols decreased in a dose-related fashion the mutagenicity of different types of carcinogens. In parallel, tea inhibited the formation of cancer of the colon and the mammary gland in rats. Other investigators have found that cancer of the esophagus is decreased in animal models by tea, just as a lower risk is noted in parts of China of cancer of the esophagus in people who drink tea. There are more cigarette smokers in Japan than in the USA but the incidence of lung cancer in Japan is lower than in the USA, possibly, because there are more tea drinkers in Japan, accounting for this protection. In parallel, mice and rats, exposed to the tobacco specific nitrosamines displayed a lower incidence of lung tumors when the animals were drinking tea. My colleague, Chung has found that this inhibition by tea was due to lower oxidation of DNA, through the tobacco

carcinogen associated formation of reactive oxygen species, yielding as marker 8-OH-dG.

We described above the formation of powerful mutagens during the cooking, frying or broiling of meat, as heterocyclic aromatic amines. Epidemiological findings that regular consumers of well done cooked meat have a higher risk of cancer of the colon and breast. These are the target organs in rats, where cancer of the prostate and of the pancreas is also seen. The reason meats generate these kinds of compounds was discovered by a Swedish colleague, Jägerstad, namely meats contain creatinine, that forms the 2-aminomethylimidazo part of the heterocyclic amines. Jägerstad developed an in vitro approach to model cooking, namely to heat glucose, creatinine and an amino acid, such as glycine, or phenylalanine. We have found that addition of black tea or green tea polyphenols to this in vitro system prevents the formation of heterocyclic amines. Also, based on that experiment, we have shown that addition of green tea or black tea polyphenols during the frying of ground meat prevents the formation of mutagenic heterocyclic amines, that seems to be a practical way to cook hamburgers without loss of taste.

Tea induces detoxification enzymes

My colleague, Sohn discovered that the administration of 2% solutions of black tea or green tea to rats for 6 weeks modifies the metabolic enzymes in the liver, namely such rats display higher levels of cytochrome P450 1A1, 1A2 and 2B1, but of no other cytochromes. In addition, the phase II enzyme UDP-glucuronosyl transferase that detoxifies many environmental chemicals was significantly increased. Heterocyclic amines, described above are subject to the biochemical activation through N-hydroxylation, and these N-hydroxy compounds are converted to the N-hydroxy glucuronides. Since green and black tea increased the available UDP-glucuronosyl transferase, it was observed that tea drinking animals form the detoxified metabolites of heterocyclic amines. Earlier, we found that decaffeinated tea was less effective than regular tea in carrying out these reactions. Thus, caffeine may have a role, most likely together with the tea polyphenols.

Growth control and apoptosis by tea

Several investigators reported that tea and tea polyphenols decrease the rate of growth of tumor cells through mechanisms involving alterations in gene expression. Tea even inhibited the formation of spontaneous lung tumors in A/J mice, that we reported in 1966 to have a stable incidence. Thus, the growth control effect of the polyphenols is remarkable. In addition, tea polyphenols increase the rate of apoptosis (cell death) of tumor cells and lead to their elimination. Inhibition of angiogenesis may play a role (cell to cell communication). This mechanism may hold even during tumor development. A clinical trial with a polyphenol from green tea is under way through the Division of Cancer Prevention at the National Cancer Institute, USA.

Intestinal microflora is improved in tea drinkers

Tea polyphenols affect on viruses and on bacteria. Enterobacterioaceae in the intestinal tract have mostly unpleasant properties since they generate smelly chemicals of the type of skatole and related indoles. The tea polyphenols suppress the growth of these bacteria but have no adverse effects on beneficial bacteria such as lactobacilli. Therefore, regular tea drinkers have a healthier intestinal bacterial flora. Tea polyphenols have antiviral actions, as described in detail in the monograph of Hara.

Effect of tea polyphenols on reactive oxygen species and aging

Tea and tea polyphenols suppress the reactive oxygen species formed during metabolism of cell systems. It was noted above that the oxidation of LDL-cholesterol and of DNA may stem from the reactive oxygen. Premature aging is also result of cellular reactive oxygen species. It can be concluded that regular intake of 5 or more cups of tea per day facilitates healthy aging, which has

been demonstrated on cellular systems, in animal models, and also, through studies of humans where regular tea intake is part of a health promoting lifestyle, as in Japan and in India. In that part of the world, one does find populations at advanced ages in good health.

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