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MINIREVIEW

Antimicrobial Properties of Tea (*Camellia sinensis* L.)

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The beverage known as tea is an infusion of variously processed leaves of one of the varieties of an evergreen shrub, *Camellia sinensis* L. Tea is the most widely drunk beverage in the world (39). Green tea, popular in the Far East, differs from the black tea familiar in the West in that an oxidation step (called "fermentation") occurs in the processing of the latter compound but not the former compound. Although it has little nutritional value per se, tea is refreshing, mildly stimulating, and produces a feeling of well-being. The latter two properties have been assumed to be due to caffeine, about 50 mg of which is present in a cup of tea; caffeine is known to have "stimulant and anti-soporific actions, that elevate mood, decrease fatigue and increase capacity for work" (32). However, other components of a cup of tea, notably, the polyphenols, may also contribute to the effects of tea, in view of their known pharmacological properties (40) (see below).

The complex of oxidized polyphenols in tea is often called "tannin" (20). It should be stressed, however, that unlike some compounds from other plants also given this generic name, tea tannins are not harmful. Contrary to widespread belief, tea does not contain tannic acid (39, 47).

BIOLOGICAL EFFECTS OF TEA

Nonmicrobiological effects. Tea has been shown to have a wide range of beneficial physiological and pharmacological effects. Among these are slowing the catabolism of catecholamines, strengthening capillaries ("vitamin P effect"), exerting an anti-inflammatory effect by enhancing the effectiveness of ascorbic acid (23, 40), acting as an antioxidant, inhibiting angiotensin-converting enzyme, having a hypocholesterolemic action, and inhibiting the growth of implanted malignant cells (13).

Microbiological effects. In one of the earliest reports (3), an army surgeon recommended the use of tea in soldiers' water bottles as a prophylactic against typhoid. Until recently, good evidence for a useful antimicrobial activity of tea was missing. Although there had been several reports (some anecdotal) of the antibacterial effects of tea in vitro and in vivo, mainly against intestinal pathogens (7, 33, 34, 37), these were somewhat superficial and fragmentary.

Within the past few years, this situation has changed. A series of well-conducted, systematic studies, mainly from Japan, now suggests that tea extracts show several useful antimicrobial effects. Toda et al. (42) found that extracts of tea inhibited and killed *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Salmonella typhimurium*, *Salmonella enteritidis*, *Shigella flexneri*, *Shigella dysenteriae*, and *Vibrio* spp., including *Vibrio cholerae*. Toda et al. (41) later reported that tea at concentrations identical to those found in the beverage (a "cup" of tea contains ca. 3 mg of solids per ml) inhibited methicillin-resistant *S. aureus*. A similar finding was made with respect to *Bordetella pertussis* (16). Other workers (19, 30, 36) showed that aqueous extracts of green tea inhibited cariogenic streptococci, including *Streptococcus mutans*; activity against other harmful mouth flora has been reported in the patent literature (45). Tea extracts have been found to be active against *Clostridium* spp. and phytopathogens such as *Erwinia* spp. and *Pseudomonas* spp. (1, 2, 10–12).

There is some disagreement over precisely which bacterial species are inhibited by tea. For example, Hara and Ishigami (11) found that *S. typhimurium* and *Campylobacter jejuni* were resistant, while others (34, 42) reported that the former species was susceptible, and Toda et al. (44) found that the latter species was also susceptible. Presumably, these differences are due to strain variations, the sources and the infusion strengths of the various teas used, and the definition of "susceptible." Clarification is needed here.

Trichophyton mentagrophytes and *Trichophyton rubrum*, but neither *Candida albicans* nor *Cryptococcus neoformans*, were inhibited by tea (28). There was activity against *Mycoplasma pneumoniae* and *Mycoplasma orale* but not against *Mycoplasma salivarium* (6).

Tea extracts prevented rotavirus and enterovirus from infecting monkey kidney cells in tissue culture (24); this was ascribed to interference with viral adsorption rather than a direct antiviral effect. Preventive and curative effects of tea on influenza virus have been claimed in a patent (38).

Killing of pathogenic protozoa by tea extracts has been reported in the Russian-language literature (quoted in reference 5), but it is difficult to assess the significance of this.

At a subcellular level, these observations have been extended by the demonstration that extracts of black and green tea inhibited the hemolytic activities of staphylococcal alpha-toxin and the thermostable direct hemolysin of *Vibrio parahaemolyticus* against rabbit erythrocytes (27). A potentially valuable anticariogenic effect is suggested by the inhibition of the synthesis of insoluble glucans by *S. mutans* (13).

CHEMICAL COMPOSITION OF TEA

For an insight into the difficulties in determining the nature of the constituent(s) of tea that may be responsible for the various biological activities described above, a brief description of the chemistry of tea is essential (20, 39, 40).

The chemical composition of tea is complex and not completely understood. The detailed investigations which have been made were done mainly to understand how tea gets its characteristic flavor and appearance; the results can be applied to the search for the antimicrobial and pharmacologically active principles.

Black tea has many more components than green tea, partly

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because of the oxidation processes that occur during "fermentation." Further reactions take place when the dried finished tea leaves are extracted into water, increasing the complexity of the chemical mix in a cup of tea. In addition, further chemical changes occur when a cup of tea is left to stand.

Most interest has been shown in the polyphenolic compounds based on the isoflavan structure; these make up some 30% of the dry weight of flush (the growing point of the plant, consisting of the buds and immature leaves that are picked for processing) and black tea leaf. The simplest compounds in this class are the catechins (see below); the larger molecules include theaflavins and thearubigins, which are oxidation and polymerization products of simple isoflavanoids. Theaflavins, found predominantly in black tea, contain a unique seven-membered aromatic ring (tropolone). They combine with caffeine (3 to 4% of both flush and black tea) to form a substance known as "cream," thereby modulating the bitterness and astringency of the individual compounds and giving tea its flavor. About 5% of the dry weight of black tea (10% in the case of green tea) and its aqueous extracts is made up of catechins, which are simple, well-characterized isoflavanoids. These mainly consist of four compounds, (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), and (−)-epigallocatechin gallate (EGCG), that may be present at concentrations of up to 1 mg/ml in a cup of tea (36). EGCG is not found in other plants and is the major catechin in flush (20).

Leaf tea also contains small amounts of flavonols, such as quercitin, kaempferol, and myricetin (20).

Plant polyphenols are generically known as "tannins" (14). These are perceived in general as toxic compounds (37), perhaps because of their ability to precipitate proteins. This property, called "astringency" in a chemical sense, was taken advantage of clinically in former times, when tannic acid ointment was used to treat superficial burns. It is very important to note, however, that tea tannins are chemically different from other plant tannins and in no way conform to descriptions of tannic acid (37, 47). The latter consist mainly of the glycoside penta-*O*-(*m*-digalloyl)-β-D-glucose, a compound with a molecular weight of almost 1,500. On the other hand, the most abundant tea polyphenols are the simple isoflavanoids, the largest of which is EGCG (molecular weight, 458). The properties of isoflavanoids differ markedly from those of the much larger glycosidic tannins. Tannic acid is described (22) as "harmful if swallowed, inhaled or absorbed through the skin; irritant to eyes, skin, mucous membranes and upper respiratory tract." It has been shown to be carcinogenic following subcutaneous administration to rats and mice, and cases of liver damage were reported after its clinical use on burns and in barium enemas (4). In contrast, the lack of toxicity of EGCG and other tea polyphenols is amply demonstrated by the safe consumption of some 2.5 billion cups per day (100 ml per person per day [20]).

BIOLOGICAL ACTIVITIES OF TEA COMPONENTS

Nonmicrobiological activities. Many of the physiological activities reported for tea extracts have been found to be due to the polyphenol moiety (40). Some of the more interesting of these include activation of leukocytes in various ways (35), antioxidant (48) and antimutagenic (15) activities, lowering of plasma cholesterol levels (17), and protection from the effects of radiation (46).

Microbiological activities in vitro. The polyphenol fractions of tea have been closely examined for their antimicrobial properties. Several studies have shown that purified catechin fractions from green and black tea, and ECG and EGCG in particular, inhibit the growth of many bacterial species and possess anticariogenic properties (1, 7, 19, 31). Specifically, a commercially available preparation of tea polyphenols, Sunphenon, prevented the attachment of a cariogenic *S. mutans* strain to hydroxyapatite and also inhibited its glucosyltransferase activity (31). Hattori et al. (13) and Fukai et al. (10) reported that the activities of the theaflavins were similar to those of the simple catechins, thus casting doubt on the importance of the gallate moiety in the antimicrobial activity of black tea extracts. These compounds display activity at cup-of-tea concentrations, unlike caffeine (7).

ECG and EGCG, but not EC or EGC, have been reported to be powerful antagonists of human immunodeficiency virus reverse transcriptase, causing 50% inhibition at concentrations of 10 to 20 ng/ml (26).

Ikigai et al. (18) showed that EC was much less active than EGCG. *S. aureus* was more susceptible than *Escherichia coli*, consistent with a much greater binding of EGCG to staphylococci. The MICs of EGCG and EC were 73 and 573 μg/ml, respectively, for *S. aureus* and 183 and >1,140 μg/ml, respectively, for *E. coli*. The bactericidal effect of EGCG was attributed to membrane perturbation.

The flavonols quercitin, kaempferol, and myricetin showed activity against gram-positive bacteria and phytopathogenic fungi in a screening test (8). Quercitin had an MIC of 37 μg/ml for *S. aureus* and was inactive against *E. coli*.

Volatile flavor components make up a very small fraction of flush and tea leaf (10 to 20 ppm) but play an important part in providing taste. More than 300 such components have been reported in black tea leaf (39), and more than 100 such components have been reported in green tea (21). Kubo et al. (21) found some of these to be microbiologically active, but not at cup-of-tea concentrations. Combinations of the flavor compounds, especially indole with some of the sesquiterpenes, displayed marked bactericidal synergy (25).

The conclusion to be drawn from the work reviewed in this section is that the microbiological activity shown by tea extracts at cup-of-tea concentrations is probably due mainly to the catechin EGCG. The contributions of other molecules are limited by the fact that only small amounts are present.

Microbiological activities of tea in vivo. In microbiological terms, much of the postulated benefit to be derived from tea drinking is anecdotal (e.g., see reference 33). Toda et al. (43) found that a mixture of tea catechins protected rabbits from an experimental infection caused by *V. cholerae* and suggest that patients with cholera could benefit if tea extracts were added to oral rehydration solutions.

Work in animals (cited in reference 31) suggests that tea reduces the incidence of caries. There is a report in the Japanese-language literature that drinking green tea reduced the incidence of dental caries among schoolchildren (29, 30), but the validity of the conclusions is difficult to assess. It has been suggested (13) that this effect was due to an increased intake of fluoride, but this seems unlikely (36); rather, the polyphenol moiety of tea was thought to be responsible. Elvin-Lewis and Steelman (9) claimed to have noted statistically improved dental health in children who drank at least one cup of tea daily compared with the dental health of those whose intake was less than 3 cups per week. Unfortunately, these findings are reported in abstract form only and do not appear to have been followed up. There are suggestions from the patent literature that tea catechins may have some commercial usefulness in the general field of mouth hygiene (e.g., see reference 45).

CONCLUSIONS

It is clear from the above that "the cup that cheers but does not inebriate" contains a veritable witches' brew of biologically active ingredients. In view of the antistaphylococcal activity of tea, it seems that Mrs. Beeton's advice to bathe styes with cold tea was rational therapy, and now a scientific approach to identifying the molecule(s) responsible is being made. The use of tea is clearly still a long way from clinical application, but there are promising leads in the dental context. The concept of being able to exploit an antimicrobial agent which is a new chemical entity found in an abundantly available and renewable source is indeed a beguiling one.

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