Journal of Traditional and Complementary Medicine 5 (2015) 15–20

HOSTED BY

ELSEVIER

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Review article

Effects of green tea on *Escherichia coli* as a uropathogen

Afsaneh Noormandi, Fatemeh Dabaghzadeh*

Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

ARTICLE INFO

Article history:
Received 3 June 2014
Accepted 1 July 2014
Available online 16 December 2014

Keywords:
anti-infective agents
Camellia sinensis
catechin
Escherichia coli
urinary tract infection

ABSTRACT

Escherichia coli is the most common cause of urinary tract infections. The development of antibiotic resistance in *E. coli* is an important problem. Finding alternative antimicrobial agents from plant extracts has received growing interest. *Camellia sinensis* is a safe, nontoxic, cheap beverage that has been reported to have antimicrobial effects against various pathogenic bacteria including *E. coli*. Polyphenolic components of green tea (綠茶 lǜ chá) have antibacterial activity. Catechins also have synergistic effect with antibiotics such as chloramphenicol, amoxicillin, sulfamethoxazole, azithromycin, levofloxacin, gentamycin, methicillin, naldixic acid, and, especially ciprofloxacin. In this review, all experimental studies that evaluated the effect of green tea on *E. coli* were collected. Data from *in vitro* studies on the antimicrobial effects of green tea are promising, but human data are currently lacking. *In vivo* studies on antibacterial effects of green tea and evaluating the efficacy of its catechins in the treatment of urinary tract infection are needed.

1. Introduction

Urinary tract infections (UTIs) are the most common type of nosocomial infection in females and males, and have resulted in billions of dollars in medical care costs.[1,2] The most important cause of 80–90% of all UTIs is *Escherichia coli.*[3] Nonpathogenic strains of *E. coli* are important facultative aerobes in the normal intestinal flora of human and animals. However, pathogenic strains of these bacteria are the most common cause of urinary tract infections.[4] Uropathogenic *E. coli* infects the urinary tract by producing special surface proteins (adhesins), which make them to attach to and attack the epithelial cells that line the urinary bladder.[5] If pathogenic *E. coli* is in the bladder (uncomplicated UTI), and is not eliminated, it may travel up the ureters to the kidneys and cause complicated UTIs which can be accompanied by renal damage and renal failure.[3,4,6] The development of antibiotic resistance in bacteria is a growing problem worldwide. A number of *E. coli* isolates have been collected from urine specimens of patients with UTI that are resistant to antimicrobial agents commonly used to treat UTIs (β-lactams, trimethoprim–sulfamethoxazole, fluroquinolones, nitroforantoin, etc.).[1,7,8] Therefore, treatment options are replaced with a second or third choice of antibiotics, which are much more expensive.[9] These challenges have been receiving growing interest to find alternative antimicrobial agents from plant extracts that need to be developed and used to control multidrug-resistant bacteria.[3,10,11] *Camellia sinensis* is one of the most popular beverages in the world, and has been reported to have antimicrobial effects against various pathogenic bacteria.[6,10,12–24] Tea can be cultivated in many regions from sea level to high mountains. It is generally safe, nontoxic, cheap, and available and is a popular drink, traditionally in Asian countries.[3,4] These properties make it a very good alternative antimicrobial agent. For green tea (綠茶 lǜ chá) production, freshly harvested tea leaves of *C. sinensis* must be processed with the least amount of oxidation, while oolong and black tea are made from fermented leaves of the same plant. Studies on the antibacterial activity have shown that green tea inhibits the growth of *E. coli* by its polyphenolic components (also known as catechins). The most important catechins in green tea are (−)-epicatechin (EC), (−)-epigallocatechin-3-gallate (EGCg), (−)-epigallocatechin (EGC), (−)-epicatechin-3-gallate (ECG). EGC and EGCg have been shown to have the greatest antimicrobial effects, but only EGC has been shown to be excreted in urine.[25] EGC and EGCg have the highest amounts in green tea and are excreted in bile.[3,4,6,14,26,27]

There are different mechanisms for antimicrobial effects of green tea such as:

* Corresponding author. Faculty of Pharmacy, Kerman University of Medical Sciences, Haft-Bagh High-Way, 76169-13555. P.O. Box: 76175-493, Kerman, Iran.
E-mail address: fatemeh_dabaghzadeh@yahoo.com (F. Dabaghzadeh).

Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

http://dx.doi.org/10.1016/j.jtcme.2014.10.005
2225-4110/

1. Polyphenols are anti-inflammatory agents that inhibit clinical symptoms of UTIs.[7,26]
2. Catechins induce production of cytokines such as IL-12 and IL-10.[7]
3. Green tea polyphenols decrease tumor necrosis factor-α gene expression, which is important in pathogenesis of *E. coli* infection.[7]
4. Catechins, by blocking the connection of conjugated R plasmid in *E. coli*, have bactericidal and antitoxin effects.[7]
5. Catechin-copper (II) complexes damage the cytoplasmic membrane of *E. coli*.[28–30]
6. EGC can bind to the ATP site of the DNA gyrase β subunit of bacteria and inhibit the activity of the gyrase enzyme.[7,28]
7. The bactericidal action of catechin is due to its hydrogen peroxide generation.[29]
8. The highest antimicrobial activity of tea is due to presence of catechins and polyphenols which damage the bacterial cell membrane.[30]
9. Catechins interfere with the expression of β-lactamases in staphylococci and inhibit the extracellular release of verotoxin from enterohemorrhagic *E. coli* (EHEC) 0157.[27,31]

Several research studies have focused on the effects of green tea on microorganisms. In the present review, the antimicrobial effect of green tea on *E. coli* (the major pathogen of UTI) is discussed in experimental studies.

2. Method

A literature review was conducted using PubMed, Scopus, Medline, Cochrane central register of controlled trials, Cochrane database systematic reviews and Google scholar. Search Keywords used were 'green tea', 'catechin', '*E. coli*', 'UTI', 'EGC', 'synergistic', 'antimicrobial', and 'mechanism'. No time limit was considered when organizing this review. All English language studies that evaluated the effect of green tea on *E. coli* as a main surrogate endpoint were included.

3. Results

3.1. Experimental studies on the antimicrobial effects of green tea against E. coli

Antimicrobial effects of green tea on *E. coli* have been suggested in different experimental studies.[3,12,32,33] In this part, all the experimental studies that were found are reviewed. A summary of these studies is shown in Table 1.

Ikigai et al[34] reported the results of their research on EGCg and EC, two of the strongly antimicrobial catechins found in green tea. They used *E. coli* K-12 strain G6 and *Staphylococcus aureus* ATCC25932 as Gram-negative and Gram-positive bacteria, respectively. EC and EGCg were extracted from water-soluble extract of green tea. The minimal growth inhibitory concentration (MIC) was determined by the agar dilution method. The MIC of EGCg for *E. coli* and *S. aureus* were 573 μg/mL and 73 μg/mL respectively. The MIC of EC for *E. coli* and *S. aureus* were >1145 μg/mL and 183 μg/mL, respectively. Catechins had greater activity against Gram-positive than Gram-negative bacteria. Liposomes were used as a model of bacterial membranes. EC showed little absorption through liposome membranes at 0.6 mM. They used EGCg to examine the effects of catechin on bacterial membranes. EGCg inhibited cytoplasmic membrane function by inducing leakage of small molecules from the intraliposomal space. Therefore, catechins damaged bacterial membranes and impaired membrane function.[34]

Hoshino et al[28] studied the effect of catechins (EGC and EC)-copper (II) complexes on the cytoplasmic membrane of *E. coli*. *E. coli* were incubated with EGC in the presence of Cu^{2+} at 37°C and, after 60 minutes, the supernatant was separated by centrifuging and the copper concentration of the supernatant (using atomic absorption with a Shimadzu spectrophotometer, Kyoto, Japan AA-660) and also the amount of copper ions binding to *E. coli* cells were determined. They concluded that EGC and EC (100 μM each) and Cu^{2+} (1 μM) separately have no effect on the viability of *E. coli*, while the combination of Cu^{2+} (1 μM) with EGC (1 μM, 10 μM, and 100 μM) or EC (100 μM) killed *E. coli* cells. To determine ATP levels in *E. coli* cells, they incubated *E. coli* with EGC or EC in the presence of $Cu^{2+}$for 60 minutes at 37°C and ATP (using an ATP bioluminescence assay kit based on the method of Stanley) and cellular and unbinding potassium levels (using atomic absorption) were measured. To analyze DNA of *E. coli* cells, first they isolated DNA from *E. coli* cells and then incubated it with EGC or EC in the presence of Cu^{2+} for 60 minutes at 37°C. They found that the DNA double strands did not break in the killing process, while depletion in both the ATP and potassium pools of the had an important role in killing of *E. coli*. Therefore, bactericidal activity of catechins in the presence of Cu^{2+} is derived from damage to the cytoplasmic membrane of *E. coli*.[28]

Sugita-Konishi et al[27] investigated the effects of six catechin derivatives of green tea (catechin, EGC, EC, ECG, EGCg, and gallocatechin gallate) on the production and extracellular release of verotoxins (VTs) from EHEC. Different concentrations of mentioned catechins were added to culture medium of EHEC (10^7 cells/L) and incubate at 37°C for 24 hours. They used the reversed passive latex agglutination assay to determine the amounts of VT in the EHEC culture supernatant fluid. Among the six catechins examined, EGCg

Table 1
A summary of experimental studies on antimicrobial effect of green tea extract.

Reference	Pathogen	Result
Ikigai et al[34]	*Escherichia coli* [1] K-12 strain G6	Catechins acted on and damaged bacterial membranes.
Hoshino et al[28]	*E. coli* ATCC 11775	Bactericidal activity of catechins in the presence of Cu^{2+} is derived from damage to the cytoplasmic membrane of *E. coli*.
Sugita-Konishi et al[27]	Enterohemorrhagic *E. coli* O157:H7	Epigallocatechin gallate and gallocatechin gallate in green tea inhibited extracellular release of Vero toxin from *E. coli*.
Arakawa et al[29]	*E. coli* ATCC 25922	Hydrogen peroxide, which is generated by EGCg, appears to be involved in the bactericidal action of EGCg.
Shahidi et al[35]	Two strains of *E. coli* (PTCC No. 1330 and PTCC No. 1338)	Green tea has antibacterial effect against only one strain of *E. coli* (PTCC No. 1338) with 10 mm inhibition zone diameter.
Cho et al[30]	*E. coli* ATCC 25922	Tea polyphenols have a dose-dependent bactericidal effect on *E. coli* and a unique change in saturated and unsaturated fatty acids was seen in cell membrane of *E. coli* cultures treated with tea polyphenols.
Kumar et al[32]	*Staphylococcus*, *Streptococcus*, *Pseudomonas*, *E. coli*, *Proteus*, *Bacillus*	Aqueous extract showed little antimicrobial activity against six bacteria isolated; methanolic extract showed maximum antibacterial activity.
Reygaert et al[3]	*E. coli* isolated from UTI cultures during 2007–2008.	All of the strains tested, except one, had minimum inhibitory concentrations of ≤4.0 mg/mL (99%). Green tea had antimicrobial effect on *E. coli* causing UTI.

EGCg = epigallocatechin-3-gallate; UTI = urinary tract infection.