Green tea as an effective antimicrobial for urinary tract infections caused by Escherichia coli

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Background: Urinary tract infections (UTIs) are a very common type of infection worldwide, and result in billions of dollars in medical care costs. Escherichia coli is the infective agent for 80–90% of all UTIs. Green tea, derived from leaves of the Camellia sinensis plant has been shown to have various potential health benefits (e.g., cardiovascular disease and cancer). The major beneficial components of green tea have been characterized, and are now known to be polyphenolic catechins. The main catechins in green tea are (−)-epicatechin-3-gallate, (−)-epigallocatechin (EGC), (−)-epicatechin, and (−)-epigallocatechin-3-gallate (EGCG). EGC and EGCG have been shown to have the greatest antimicrobial effects, but only EGCG has been shown to be excreted in urine. Isolates of E. coli from UTIs collected between 2007 and 2008 were characterized for antimicrobial resistance to standard drugs. Then 80 of these isolates, representing a wide spectrum of antimicrobial susceptibility patterns, were selected for testing using an extract of green tea.

Results: The concentrations of green tea extract tested were 0, 2.5, 3.0, 3.5, and 4.0 mg/ml. All of the strains tested, except one, had minimum inhibitory concentrations (MICs) of ≤3.0 mg/ml (99%), with 94% of the isolates having an MIC of ≤3.0 mg/ml. The isolates having an MIC of ≤3.0 mg/ml and 40% of the isolates having an MIC of ≤2.5 mg/ml. Two control strains varied in susceptibility, one having an MIC of ≤2.5 mg/ml and the other having an MIC of ≤3.5 mg/ml.

Conclusion: Since EGCG has been shown to have antimicrobial effects on E. coli, and EGCG has been shown to be excreted in the urine in a high enough concentration to potentially have potential antimicrobial effects on UTIs caused by E. coli.

Keywords: green tea, antimicrobial, urinary tract infections, Escherichia coli, antimicrobial resistance

INTRODUCTION

Urinary tract infections (UTIs) are the second most common type of infection found in any organ system, and the most common type of nosocomial infection (Carson and Naber, 2004). These UTIs are responsible for over eight million doctors visits per year in the U.S. (National Institute of Diabetes and Digestive and Kidney Diseases, 2005), and result in medical costs of over six billion dollars worldwide per year (Anderson et al., 2004; Kau et al., 2005). Most UTIs (80–90%) are the result of infections with Escherichia coli (Karlowsky et al., 2002). Non-pathogenic strains of E. coli are an important part of the normal flora in the human intestinal tract.

The strains of E. coli that infect the urinary tract are categorized as uropathogenic E. coli (UPEC; Kaper et al., 2004). The UPEC are able to produce special surface proteins (adhesins) that allow them to attach to and invade the epithelial cells that line the urinary bladder (Anderson et al., 2004; Schaeffer et al., 2004; Kau et al., 2005; Marrs et al., 2005). If the infection is not eradicated while it is in the bladder (uncomplicated UTI), some strains of UPEC may then travel up the ureters to the kidneys and cause even more severe infections (complicated UTIs), which can lead to renal damage and possibly renal failure (Kaper et al., 2004; Pichon et al., 2009). There are 14 serogroups of UPEC that are most commonly found in UTIs, and 79% of UTIs have been shown to be caused by serogroups 04, 06, 014, 022, 075, and 083 (Stenutz et al., 2006; Li et al., 2010). The most common serogroups involved in causing UTIs worldwide are 02, 04, 06, and 075 (George and Manges, 2010). In the U.S., 49% of UTIs in women have been found to be caused by serogroups 06, 04, and 075, in descending frequency of occurrence (Vosti, 2007).

The antimicrobial agents that have traditionally been used to treat UTIs (β-lactams, fluoroquinolones, trimethoprim–sulfamethoxazole, nitrofurantoin, etc.) are becoming less effective (Warren et al., 1999; Wagenlehner and Naber, 2005). In recent years, the number of antimicrobial resistant strains of E. coli isolated from UTIs has been increasing, including resistance to antimicrobial agents normally used to treat UTIs (Sahn et al., 2001; Kahlmeter, 2003; Muratsu and Matsumoto, 2004; Landgren et al., 2005; Zhan et al., 2006). Even though scientists are constantly working to develop new and improved antimicrobial agents, the overall success of treating UTIs has been limited.
antimicrobials, almost as soon as a new drug is released, the bacteria show resistance to it. These isolates are also showing resistance to drug combinations such as amoxicillin/clavulanic acid, piperacillin/tazobactam, and trimethoprim/sulfamethoxazole (Dias et al., 2009; Gündoğdu et al., 2011; JadHAV et al., 2011; Molina-López et al., 2011; Oliveira et al., 2011).

Green tea is derived from non-fermented leaves of the *Camellia sinensis* plant. Oolong and black tea are made from fermented leaves of the same plant. Green tea has been a favored drink, traditionally, in Asian countries. Because of studies that have shown the potential health benefits of green tea, it is now gaining worldwide popularity as a drink that is important in preventative medicine. Studies using green tea have shown it to have potential benefits, most notably in: cardiovascular disease, cancer, diabetes, obesity, oral health, bone health, and cognitive function (McKay and Blumberg, 2002; Cabrera et al., 2006; Chacko et al., 2010; Mak, 2012). In addition, green tea has been shown to have antimicrobial effects (Yam et al., 1997, 2003; Friedman, 2007; Song and Seong, 2007).

The components in green tea that are responsible for these various effects are polyphenols (also known as catechins). The main catechins in green tea are (−)-epicatechin (EC), (−)-epigallocatechin (EGC), and (−)-epigallocatechin-3-gallate (EGCG), which have been shown to make up approximately 30–40% of the water-soluble solids in brewed green tea (Yang and Ho, 2009). Three of these catechins, EGC, EGC, and EGCG have been shown to have antimicrobial effects against a wide variety of microorganisms (Yam et al., 1997, 2004; Taguri et al., 2006; Chacko et al., 2010; Mak, 2012). In addition, green tea has been found to have antimicrobial effects (Yam et al., 1997; Taylor et al., 2005; Friedman, 2007; Song and Seong, 2007).

The two found in the highest amounts in green tea are EGC and EGCG. Both of these are excreted in bile, but EGC is also excreted in the urine, suggesting the possibility for green tea having antimicrobial activity in UTIs (Yang et al., 1999; Lee et al., 2002; Cabrera et al., 2006; Luo et al., 2006). Most of the studies on how these compounds accomplish the antibacterial activity have focused on EGCG. Because EGCG is not excreted in the urine (Yang et al., 1998), it is not the compound of interest for this study. One study has found that EGC is able to bind to the ATP binding site of the bacterial gyrase B subunit, thus inhibiting gyrase activity (Gradislav et al., 2007). The aim of the current study was to investigate the susceptibility of UPEC strains, representing a wide variety of antimicrobial susceptibility patterns, to green tea.

**MATERIALS AND METHODS**

**BACTERIA STRAINS**

The bacterial strains used in this study were part of a research collection of *E. coli* isolated from UTI cultures during the years of 2007–2008. There were 80 isolates selected from this collection that represented a wide spectrum of antimicrobial susceptibility patterns; in addition, two control strains that were isolated from UTI cultures during the years of 2007–2008. There were 80 isolates selected from this collection that represented a wide spectrum of antimicrobial susceptibility patterns; in addition, two control strains that were selected.

**MIC DETERMINATION**

The MICs and susceptibility results are as follows: 99% were susceptible to the green tea extract at a concentration of ≤ 4.0 mg/ml.
Table 2 | Minimum inhibitory concentrations for total green tea extract (GTE) and the EGC component.

| Component | Number of isolates tested (% out of 79) |
|-----------|----------------------------------------|
| 32 (40%)  | 32 (40%)  |
| 29 (37%)  | 29 (37%)  |
| 14 (18%)  | 14 (18%)  |
| 4 (5%)    | 4 (5%)    |

Total GTE (mg/ml) ≤ 3.5 ≤ 3.0 ≤ 3.5 ≤ 4.0
EGC (μg/ml) ≤ 450 ≤ 540 ≤ 830 ≤ 720

(one strain was not susceptible at even 4.0 mg/ml); 94% were susceptible at ≤ 3.5 mg/ml; 76% were susceptible at ≤ 3.0 mg/ml; 48%, were susceptible at ≤ 2.5 mg/ml; The control strains varied; one being susceptible at ≤ 2.5 mg/ml and the other susceptible at ≤ 3.5 mg/ml. Table 2 shows the MIC results for the 79 strains that were susceptible at ≤ 4.0 mg/ml.

**DISCUSSION**

The green tea extract was shown to have an inhibitory effect on the growth of *E. coli* strains isolated from UTIs. The MIC results can be adjusted to reflect the EGC content, using a value of 18% EGC as the content in total green tea polyphenols (Vuong et al., 2011). That makes the adjusted results as follows: 40% of strains tested were susceptible at a concentration of EGC at ≤ 0.45 mg/ml (450 μg/ml); 36% susceptible at ≤ 0.34 mg/ml (340 μg/ml); 18% susceptible at ≤ 0.63 mg/ml (630 μg/ml); and 5% susceptible at ≤ 0.72 mg/ml (720 μg/ml). Since all of the strains tested (99%) were susceptible at a concentration of ≤ 0.72 mg/ml, this suggests that EGC might be a good inhibitor of bacterial growth. Table 2 shows the MIC data for total green tea extract and for the EGC component.

The data was collected by in vitro experiments, but the effect can be described using information that is known about the metabolism of EGC from green tea. The amount of green tea polyphenols that would be present in the urine, including the amount of EGC, will vary according to the origin of the tea. It has been found, for instance, that Japanese tea (an average of 15 teas) contained approximately 20 mg of EGC per gram of dry tea (Vuong et al., 2011). An average cup of Japanese green tea is made with one tablespoon of dry tea (instructions from package of tea) which is equivalent to approximately 7.5 g of dry tea (a package of 60 g of dry tea makes eight cups). That equates to approximately 150 mg of EGC per cup of Japanese green tea.

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