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What about the Antibacterial Activity of Fresh Ginger Juice (*Zingiber officinale*)?

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The aim of this study was to determine the antibacterial activity of the juice obtained by squeezing fresh ginger roots (*Zingiber officinale*) against the standard strains *Staphylococcus aureus* (ATCC® 25923) and *Escherichia coli* (ATCC® 25922), as well as *Acinetobacter baumannii* and *Klebsiella pneumoniae* isolated from patients hospitalized in intensive care units.
Methods: For this purpose, the antibacterial effect of the fresh ginger juice was tested against antibiotics such as ampicillin, cefazolin, cefuroxime, meropenem, colistin, ofloxacin, sulfamethoxazole/trimethoprim, tetracycline, and gentamicin. The antibacterial effects against the tested bacteria were determined by the disc diffusion method using 5 µL, 10 µL, 15 µL and 20 µL amounts of ginger juice impregnated on sterile discs.
Results: As a result of the study, it was detected that the antibacterial effect increased in parallel with the increasing amounts of fresh ginger juice in all tested bacteria.
Conclusion: Consequently, fresh *Zingiber officinale* can provide protection to a certain extent against bacterial pathogens due to its antibacterial action.

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Keywords: Antibacterial activity; fresh Zingiber officinale; ginger; bacteria.

1. INTRODUCTION

Plants have been used as a remedy for different infections since ancient times. The World Health Organization has cataloged more than 20,000 plant species with medicinal properties that provide treatment for diseases [1]. Inspired by the historical and public uses of medicinal plants, bioactivity and phytochemical analysis are carried out today. Some herbal medicines are in higher demand than their synthetic counterparts in Europe [2]. It is reported that plants show antimicrobial activity with some aldehydes, organic acids and phenolic compounds in their contents [3]. However, in many studies, it was reported that bacterial pathogens impair the efficacy of antibiotics by natural, acquired, genetic, phenotypic or biological mechanisms, such as enzymatic hydrolysis, group transfer, ribosome protection and biofilm formation [4,5,6,7,8]. Due to the resistance to antibiotics used in the treatment of humans and animals in recent years, thousands of plants are used for therapeutic purposes all over the world and an increasing trend towards herbal medicines has been observed in the last 30-40 years [9,10].

Ginger has more than 45 genera and 800 species in the *Zingiberaceae* family. It has been reported that ginger is consumed worldwide as a spice and flavoring agent and has many medicinal properties [11,12,13]. Carbohydrates, lipids, terpenes, and phenolic compounds are the major constituents in ginger rhizomes. Zingiberene, β-bisabolene, α-farnesene, β sesquiphellandrene, and α- curcumene are the terpene components of ginger. Phenolic compounds comprise gingerol, paradols, and shogaol [12,13]. Ginger is a medicinal herb used in tropical and subtropical countries to treat many ailments, such as diarrhea, cough, and gastrointestinal disorders. It is a well-known and widely used spice and condiment, especially in Asia. Ginger is used fresh or cooked in Asia, India and various Arab countries, as well as in juice or dried and powder form [14,15,16]. It is reported that ginger root is being demanded in North America for its bioactive components important for health, as well as being used as a food additive [17]. The swollen rhizome/stem of ginger has been associated with antimicrobial, anti-inflammatory, and anti-carcinogenic properties, and also antifungal due to gingerol, main active compound in fresh ginger [12,15,18,19]. It has been reported to have an antibacterial effect in vitro studies by different researchers [19,20].

In a study conducted by Sivasothy et al [21[with a microdilution technique, it was determined to be moderately active against Gram-positive bacteria such as *Bacillus licheniformis* (*B. licheniformis*), *Bacillus spizizenii* (*B. spizizenii*), and *Staphylococcus aureus* (*S. aureus*), and Gram-negative bacteria such as *Escherichia coli* (*E. coli*), *Klebsiella pneumonia* (*K. pneumonia*), and *Pseudomonas stutzeri* (*P. stutzeri*). In a study conducted to determine the antimicrobial potential of the extracts of spices such as ginger, turmeric and garlic prepared with different solvents and to determine the synergistic effect of these spices when used together with antibiotics, it was determined that all extracts most affected *E. coli* among the six bacteria [22]. It has been reported that ginger and other crude extracts have synergistic effects with antibiotics against bacterial pathogens, and this synergistic effect can be used to design a good therapeutic approach to combat bacterial pathogens [22]. Islam et al. [23] reported that ginger extract shows strong antimicrobial activity against all tested bacterial pathogens in their study on 24 isolates containing 6 different food pathogens, using soybean oil extract of dried ginger powder with agar diffusion method. Researchers also reported that ginger and soybean oil extracts at boiling temperature have potential antimicrobial activity and it would be appropriate to use soybean and ginger together to increase their synergistic activities in foods [23]. It is known that the unconscious and excessive use of antibiotics around the world has led to the evolution of drug resistance mechanisms among pathogens [24,25]. The effects of the four components of ginger, [6]-dehydrogingerdione, [10]-gingerol, [6]-shogaol and [6]-gingerol, on extensively drug-resistant *Acinetobacter baumannii* (XDRAB) were investigated and it was reported that all these components shows antibacterial effects against XDRAB [26]. In a study in which the antibacterial activity of the essential oil produced by the hydrodistillation method of black ginger (*Kaempferia parviflora*) was determined by the disc diffusion method, it was determined that the essential oil of black ginger had an antibacterial effect against *S. aureus*, but not against *K. pneumoniae* [27]. In a study conducted by Aghazadeh et al. [28], the minimum inhibitory concentrations of ginger extract for *P. aeruginosa*, *E. coli*, *S. aureus*, *K. pneumoniae*,

Bacillus cereus (*B. cereus*), *Acinetobacter baumannii* (*A. baumannii*), *Candida albicans* (*C. albicans*) and *Candida krusei* (*C. krusei*) were determined as 40, 40, 20, 20, 20, 20, 10 and 5 mg/mL, respectively. Researchers also found that ginger extract successfully inhibited biofilm formation by *A. baumannii*, *B. cereus*, *C. krusei* and *C. albicans* [28]. Karuppiah and Rajaram [29] examined the antibacterial potential of ethanolic extracts of garlic cloves and ginger rhizomes against clinical five Gram-negative and two Gram-positive pathogenic bacteria with multidrug resistance, and all isolates were found to be susceptible to crude extracts of both plant extracts.

This study was carried out to determine the antibacterial activity of fresh ginger juice against highly multi-drug resistant *A. baumannii* and *K. pneumoniae* isolated from the intensive care unit of Bursa Uludag University Hospital, Turkey and standard bacterial strains *S. aureus* (ATCC®25923) and *E. coli* (ATCC®25922) from Bursa Uludag University Faculty of Medicine Microbiology Laboratory, Turkey culture collection**.**

2. MATERIALS AND METHODS

2.1 Samples Collection

One Kg fresh ginger root samples imported from China were purchased from a local greengrocery store and immediately transported to the laboratory for analysis.

2.2 Preparation of Fresh Ginger Juice

The fresh ginger root samples were rinsed first in running tap water followed by ultra-purified water. Then it was peeled with a knife wiped with 70% alcohol and cut into small slices. The slices were squeezed with a food grade juicer wiped with 70% alcohol. The resulting fresh ginger was filtered with Whatman No.1 filter paper and transferred to sterile jars. It was stored at +4°C for experiments.

2.3 Bacterial Strains

For determining the antimicrobial activity of fresh ginger juice following four bacterial species were used; *S. aureus* (ATCC®25923) and *E. coli* (ATCC®25922), which are quality control strains with known susceptibility, recommended by the Clinical and Laboratory Standards Institute (CLSI), and *A. baumannii* and *K. pneumoniae* isolated from intensive care patients.

2.4 Antibacterial Activity and Sensitivity Comparison of Fresh Ginger Juice

The antimicrobial assay of fresh ginger juice was performed by disc diffusion method according to CLSI [30]. All the experiments were performed under sterile conditions. Filter paper discs (6 mm in diameter) were sterilized in a dry heat sterilizer and kept in the refrigerator for further use. After removing the bacterial strains from the freezer (-20°C) and thawing, they were inoculated onto Columbia agar (supplemented with 0.5% sheep blood, BD 254005) plates and grown overnight at 37°C separately before performing an antimicrobial assay. These bacterial strains were then harvested using a loop and placed into a test tube containing sterile physiological saline separately and prepared to a turbidity of 0.5 McFarland (1.5 x 10^8CFU/mL) for use as bacterial inoculum. Each bacterial inoculum was streaked onto 3 Mueller Hinton (MH) agar (BD 254030) plates using a sterile cotton swab. The plates were left at ambient temperature for 15 minutes. Afterwards, five sterile filter paper discs were placed aseptically on a dried MH agar plate, and fresh ginger juice (5 µl, 10µl, 15µl, 20 µl), and %0.9 NaCl (10µl) as control on each disc were added separately. The other MH agar plates were placed with ampicillin (10 µg) (AM), cefazolin (30 µg) (CZ), cefuroxime (30µg) (CXM), meropenem (10 µg) (MEM), ofloxacin (5 µg) (OFX), sulfamethoxazole/ trimethoprim (23.75/1.25 µg) (SXT), tetracycline (30 µg) (TE), and gentamicin (10 µg) (GM). For *A. baumannii* and *K. pneumoniae* strains, colistin (10 µg) (CL) disc was placed instead of meropenem. The plates were incubated at 37°C for 24h. and the diameter of the inhibition zones was measured with a ruler. Each test was performed in triplicate and the results were provided as mean values in milimeters.

3. RESULTS

In this study, the antimicrobial activity of the extract of freshly squeezed ginger was tested on *S. aureus* (ATCC®25923) and *E. coli* (ATCC®25922), as well as *A. baumannii* and *K. pneumoniae* isolated from patients and known to have multidrug resistance. It was determined that the fresh ginger juice was the most effective against *E. coli* among the tested bacteria. However, the antimicrobial effect was not observed at low concentrations against *S.*

aureus, *A. baumannii* and *K. pneumoniae* agents. At the highest concentration, 20 µL, the inhibition zone diameter was detected least in *A. baumannii* (Fig. 1).

Eight antibiotics belonging to different classes were used in this study and the susceptibility profiles of each bacterial strain to these antibiotics were determined. *S. aureus* and *E. coli* were susceptible to five of the tested antibiotics, and resistant to the other three antibiotics (ofloxacin, sulfamethoxazole/ trimethoprim and tetracycline). However, *A.baumannii* and *K. pneumoniae* showed resistance to 6 antibiotics tested, while *A. baumannii* was sensitive to gentamicin and colistin, and *K. pneumoniae* was sensitive to colistin and ofloxacin (Fig. 2).

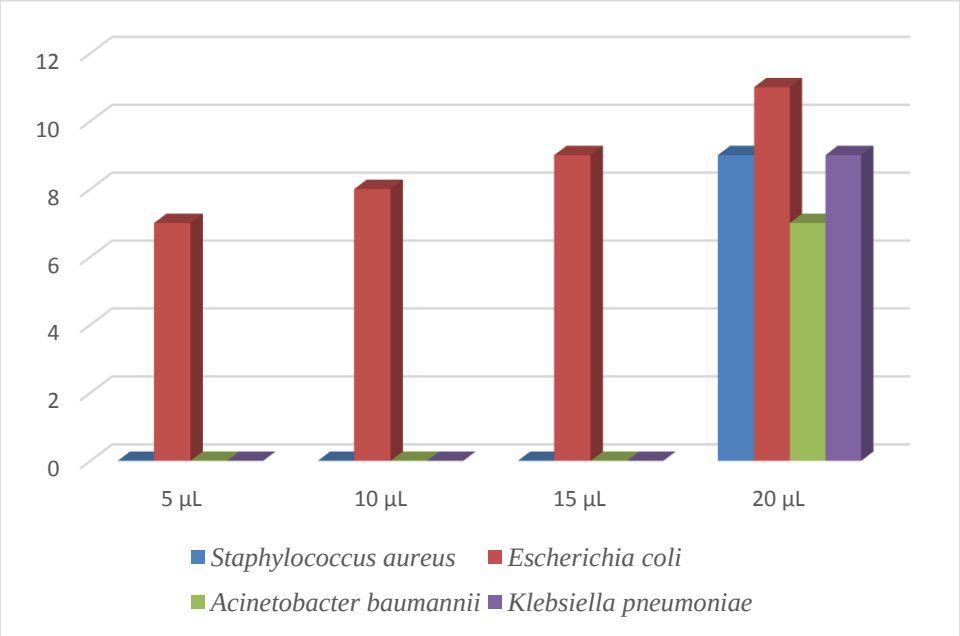

Fig. 1. The inhibition zone diameters formed by fresh ginger juice for bacterial strains (mm)

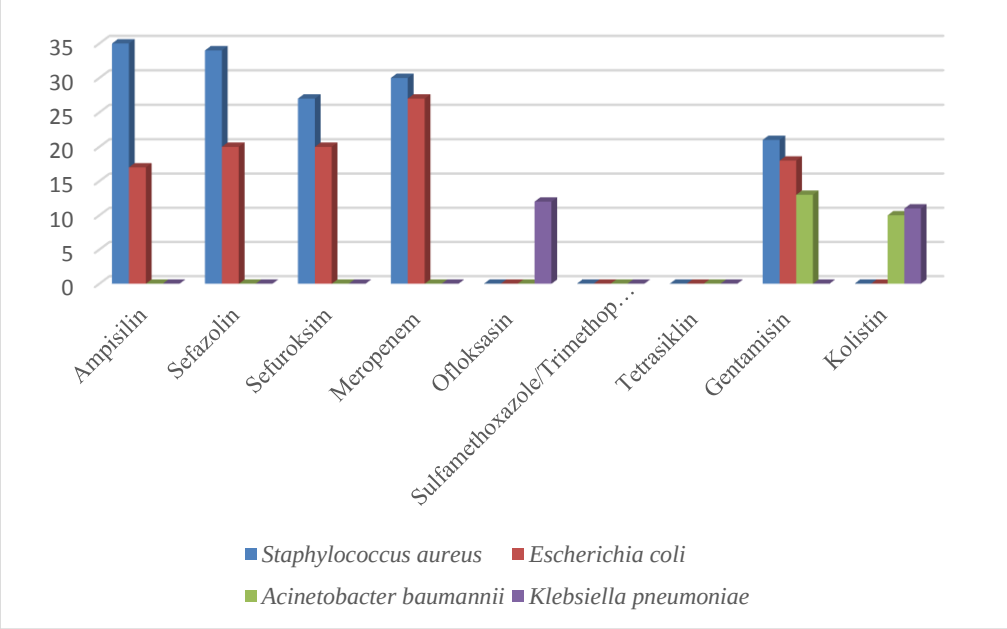

Fig. 2. The inhibition zone diameters formed by antibiotics for bacterial strains (mm)

4. DISCUSSION AND CONCLUSION

Medicinal herbs and spices have been traditionally used for thousands of years by many cultures as natural antimicrobial agents to control common health complications. However, regarding the increasing health problems in the world, in recent years, many studies have been carried out on the development of natural antimicrobials to control microbial diseases. In particular, the discovery of natural plant products-based antimicrobial drugs has gained great importance as newly discovered drugs are likely to be effective against multidrug-resistant bacteria [10,15]. It has been reported in many studies that low-cost medicinal plants have antibacterial effects due to the different phytotherapeutic substances contained in them [31,32]. Different researchers even emphasized that determining the antimicrobial effects of medicinal plants would be a solution to complementary therapy [33,34]. In addition, it is reported that plant extracts are more effective against multidrug resistant strains where antibiotic therapy has limited effect [35]. Moreover, it has also been reported that plant extracts have a synergistic effect with antibiotics. This synergistic effect is considered as a new approach that could help in solving the problem of bacterial resistance [36]. In our study, in parallel with the increasing amounts of fresh ginger plant juice (5µL-20 µL) had an antibacterial effect on the tested bacteria. In the literature review, it has been seen that ginger extracts (methanolic, ethanolic, and aqueous) are used more and there are very few studies where the juice of fresh ginger is used directly. In a study conducted by Akrayi and Tawfeeq (2019) [37], the researches investigated antibacterial effect of the juice of two plants, *Lepidium sativum* and *Allium porrum* on *K. pneumoniae, Proteus* spp*., P. aeruginosa, S. aureus, and S. mutans*, the juices of both plants was declared to show no antibacterial activity against bacteria tested in that study while ethanolic extracts and aquas extracts of both plants exhibited antibacterial effect on the tested bacteria [37]. In our previous study we investigated antibacterial effect of dried ginger ethanol extracts on the same bacteria studied in the current study [38]. The most antimicrobial effect was observed on *S. aureus* with the inreased amount of the extract, the lowest antimicrobial effect was observed on *E. coli*, and no antimicrobial effect was determined against *Acinetobacter baumannii* and *Klebsiella pneumoniae* [38]. We wondered about the antibacterial effect of fresh ginger juice on the same bacteria. In the present study, it was investigated and detected that the antibacterial effect increased in parallel with the increasing amounts of fresh ginger juice in all tested bacteria although in our previous study, no inhbition zone was detected against *Acinetobacter baumannii* and *Klebsiella pneumoniae* when dried ginger ethanol extracts applied [38]. When antibacterial effect of dry ethanol extract of ginger in the our previous study and fresh ginger juice in the current study was compared on *S. aureus* and *E.coli*, the antibacterial effect of extract and juice on *S. aureus* and *E. coli* was determined as vice versa. Since, we found that ginger juice formed more inhibition zones in *E. coli* than in *S. aureus*, which was consistent with the findings of Sibanda and Okoh [36] but not for the results of Guceyu et al. [38]. Similiar to our study, Ogori et al (2019) found that blend of ginger, pineapple and turmeric juice mix has an antibacterial effect to decrease bacterial cell counts [39]. In a study testing the antimicrobial activity of fresh and dried ginger extracts and oil on *S. aureus* and *E coli*, it was reported that 100% and 50% concentrations of squeezed ginger juice forms an inhibition zone of 15.00 ± 3.50 and 13.00 ± 2.66 in *E. coli* and 15,00 ± 1,40 ve 12,00 ± 2,83 in *S. aureus*, respectively [40]. The zone diameters of the antibacterial effect of the aqueous extract of ginger against *S. aureus*, *K. pneumoniae*, and *E. coli* agents were reported to be 12.3±0.27, 11±0, and 13±0.47, respectively, in another study [41]. The inhibitory effect on the same agents was observed only in *E. coli* in the range of 5 µL-15 µL in our study. In another study, 20 mg/ml ginger extract was reported to have antimicrobial activity against *E. coli* [42], as in our study. However, it was also reported that aqueous ginger extract have no effect on *E.* coli [19]. In our study, it was determined that squeezing ginger juice was effective only on *E. coli* at low concentrations, while inhibition was achieved on other microorganisms at higher concentrations. In a study on the antibacterial activity of bitter cola and ginger in Cameroon, it was determined that ginger has antibacterial activity on *S. aureus* [43], as in our study.

Many researchers have attributed the antibacterial activity of ginger to the fact that the active components in ginger (zingiberen, α-farnesen, 6-gingerol and α-curcumene) increase the permeability of bacterial cell membranes and affect the release of intracellular components [44,45,46]. The integrity of the bacterial cell membrane is very important for bacterial growth.

When cell membrane integrity is evaluated, nucleic acids are indispensable macromolecules in bacteria [47,48,49,50,51]. This causes the bacteria to lose their basic structural functions and eventually, at certain concentrations, to bacterial cell death. In addition, it can disrupt the metabolism of bacteria by affecting the hydrophobic compounds in the structure of ginger, the lipophilic part of the bacterial membrane, and the isolated mitochondria and enzyme activity [47,48]. In our study, the inhibition zone diameters formed around the 20 µL applied discs suggested that the integrity of the cell membranes of the bacteria was destroyed, and this might have led to the leakage of nucleic acids from the bacterial cells and to failure in the transport of genetic information, and ultimately bacterial death in this way.

Biofilm is a consortium of bacterial cells embedded in a slimy extracellular matrix composed of extracellular polymeric substances. Biofilm formation is a major threat to society as it increases the severity of infection and causes resistance to antimicrobial agents [52]. The mechanism of biofilm formation varies among bacterial species and is strictly strain-specific and also highly dependent on environmental conditions [53]. Nikolić et al. [54] reported that ginger essential oils shows the highest percentage of biofilm inhibition against *S. aureus* (94%), followed by *K. pneumoniae* (91%), *E. coli* (89%), and *E. faecalis* (83%).

In their study, Njobdi et al. (2018) [40] found that the zone diameter (15.00±1.40) formed by *E. coli* against gentamicin was similar to our results. However, in our study, the largest inhibition zone diameter was detected in *S. aureus* against gentamicin while no zone of inhibition diameter was observed in *S. aureus*'un to gentamicin by the same authors [40]. However, In astudy conducted by Islam et al [23], the diameter of the zone of inhibition varied ranging from (8.0±1.73 mm) to (11.67±1.53mm) for ginger extract as compared to (12.33±7.09 mm) to (19.33±3.51 mm) for gentamicin. When *E.coli*, one of the microorganisms studied in this study, was examined, it was determined that gentamicin produces a larger inhibitory zone diameter than ginger, which is consistent with our findings. In a previous study by the same researchers, it was discovered that ginger has a small inhibitory zone diameter against *S. aureus*. In our investigation, only higher doses of ginger were found to be effective against *S. aureus*, which is consistent with the prior study [23]. Ekwenye and Elegalam [19], in their study, did not show any antibacterial effect of the liquid extract of ginger, although tetracycline created an inhibition zone diameter of 9.00 mm on *E.coli*. On the contrary, in our study, no antibacterial effect of the same antibiotic was observed on *E. coli*, while an antibacterial effect of fresh ginger was found on *E. coli* [55].

In conclusion, we envision that ginger has an extraordinary potential to produce biologically active materials that could be valuable in the treatment of many microbial diseases and this should be fully explored with the right approach. However, we believe that more studies should be needed to isolate active ingredients and determine their toxicities, side effects, and pharmacokinetic properties, and to evaluate their synergistic effects with antimicrobials.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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