In vitro antimicrobial activity of *Cinnamomum verum, Allium sativum,* and *Zingiber officinale* extracts on metallo-β-lactamase-producing *Pseudomonas aeruginosa*: A potential therapeutic approach

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Summary

Metallo-β-lactamase (MBL)-producing *Pseudomonas aeruginosa* is a leading cause of nosocomial infections, especially in burn patients worldwide. The antimicrobial properties of *Cinnamomum verum, Allium sativum*, and *Zingiber officinale* known as cinnamon, garlic, and ginger, respectively have not yet been reported on *P. aeruginosa* producing metallo-β-lactamase. The present study aimed to detect MBL genes and evaluate the inhibitory effect of cinnamon, garlic and ginger extracts on MBL-producing *P. aeruginosa*.

Antibiotic resistance pattern of MBL-producing *P. aeruginosa* isolates was evaluated by Kirby-Bauer disk diffusion method. MBL-producing isolates were phenotypically tested by combined disk test (CDT). The prevalence of bla_{VIM} and bla_{IMP} genes encoding metallo-β-lactamase was detected by PCR. Minimum inhibitory concentration (MIC) of the acetonic, methanolic, and chloroformic extracts of cinnamon, garlic, and ginger on MBL-producing isolates was evaluated by the broth microdilution method.

Eighty-one out of 95 (85.2%) imipenem-resistant *P. aeruginosa* isolates were MBL-producing. Thirteen out of 81 (16.0%) and 18 out of 81 (22.2%) MBL-producing *P. aeruginosa* were positive for bla_{IMP} and bla_{VIM} genes, respectively. The inhibitory concentrations of the acetonic, methanolic, and chloroformic extracts of cinnamon, garlic, and ginger ranged from ≥1.50 mg/ml to ≥12.50 mg/ml.

We find that the methanolic extract of cinnamon and garlic as well as the acetonic extract of ginger has significant antibacterial activity against the MBL-producing *P. aeruginosa*. These medicinal plants can be considered as a source of forgotten antimicrobial agents to avoid treatment failure and mortality.

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Burns, Cinnamon, Garlic, Ginger, Pseudomonas aeruginosa

Introduction

Burn wound infection is one of the most damaging forms of trauma and serious public health problems in many countries.[1,2,3] In 2013, the Centers for Disease Control and Prevention (CDC) reported that *Enterobacteriaceae, Pseudomonas aeruginosa*, and *Acinetobacter spp.* are the most common pathogens associated with burn wound infections.[4] Approximately 8% of all healthcare-associated infections reported to CDC's National Healthcare Safety Network are caused by *P. aeruginosa*.[4,5] However, some strains of *P. aeruginosa* have been found to be resistant to nearly all or all antibiotics including aminoglycosides, cephalosporins, fluoroquinolones, and carbapenems.[4,6] The resistance in *P. aeruginosa* is mainly related to the production of β-lactamases, such as extended-spectrum beta-lactamase (ESBL), metallo-beta-lactamase (MBL), and OXA-type β-lactamase known as enzymes of Ambler classes A, B, and D, respectively.[7] Several MBLs encoded by mobile DNA have emerged in serious pathogens, including *P. aeruginosa, A. baumannii,* and *Enterobacteriaceae* since the 1990s.[8] The *bla*IMP, VIM, SPM, GIM, SIM, KHM, AIM, and NDM are the most well-known MBLs in *P. aeruginosa*.[9] MBLs have extended hydrolyzing activity against all β-lactam antibiotics

including carbapenems except for monobactams.[10,11] Furthermore, MBL-producing *P. aeruginosa* can cause infections with higher rates of mortality, morbidity, and health care costs.[12] Nowadays, rapid growing antibiotic resistance, as well as unpleasant side effects of the synthetic drugs has led to focus on natural alternatives and therapeutic aspects of herbal extracts.[13] In this regards, the use of herbal remedies has also been widely embraced in many countries due to the availability, inexpensive, effectiveness, and minimal side effects.[14,15] The antimicrobial activity of commonly used spices namely, cinnamon (*Cinnamomum verum*), garlic (*Allium sativum*), and ginger (*Zingiber officinale*) has been demonstrated against antibiotic-resistant bacterial pathogens.[15,16] Nevertheless, the antimicrobial properties of cinnamon, garlic, and ginger have not yet been reported on MBL-producing *P. aeruginosa*.

In this study, we introduced the antibiotic resistance patterns of *P. aeruginosa*, prevalence assay of bla_{VIM} and bla_{IMP} MBL genes, and inhibitory effect of acetonic, methanolic, and chloroformic extracts of cinnamon, garlic, and ginger on MBL-producing *P. aeruginosa* isolated from burn patients hospitalized in Shahid Motahari Burns Hospital, Tehran, Iran.

Materials and methods

Bacterial isolation and identification

In this cross-sectional study, a total of 100 non-duplicated *P. aeruginosa* isolates were collected from burn wounds of patients hospitalized in Shahid Motahari Burn Hospital in Tehran, Iran, over a 14-month period ranging from July 2015 to September 2016. The bacterial isolates were identified by standard microbiological methods and common biochemical laboratory tests, including oxidase, catalase, oxidation-fermentation (OF), arginine dehydrolase, lysine, ornithine decarboxylase, TSI, H_2S production, indole formation, motility, growth on Simmons citrate agar, growth at 42°C, methyl red, and Voges-Proskauer. The identified strains were stored in glycerol broth cultures at −70°C.[17]

Antimicrobial susceptibility testing

Antimicrobial susceptibility of clinical isolates of *P. aeruginosa* was determined by Kirby-Bauer disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. Antibiotic paper discs were prepared from MAST group (Mastdiscs®, Mast Group Ltd., UK) as follows: ciprofloxacin (CIP 5 µg/ml), imipenem (IMP 10 µg/ml), meropenem (MEM 10 µg/ml), doripenem (DOR 10 µg/ml), gentamicin (GEN 10 µg/ml), piperacillin (PIP 100 µg/ml), piperacillin/tazobactam (TZP 100/10 µg/ml), amikacin (AMK 30 µg/ml), ceftazidime (CAZ 30 µg/ml), cefepime (FEP 30 µg/ml), aztreonam (ATM 40 µg/ml), ticarcillin (TIC 75 µg/ml), colistin (CST 10 µg/ml). *Pseudomonas aeruginosa* ATCC® 27853 was used as a positive control strain.[18]

Minimum inhibitory concentration (MIC)

Broth microdilution method was used to determine the minimum inhibitory concentrations (MICs) of *P. aeruginosa* clinical isolates according to the breakpoint interpretation of CLSI. MIC testing to the following antibiotics was tested: ceftazidime, ciprofloxacin, meropenem, and imipenem.[18] All antibiotics were purchased from Sigma-Aldrich (Sigma Aldrich, St. Louis, Missouri, United States). *Escherichia coli* ATCC® 25922 was used as a positive control strain.

Phenotypic detection of MBL-producing P. aeruginosa

Combination disk diffusion test (CDDT) was carried out to identify the MBL-producing *P. aeruginosa* using imipenem with 0.5 M EDTA and meropenem with 0.5 M EDTA. The culture plate was incubated at 37°C for 24 hours. The diameter of inhibition zone of imipenem and meropenem alone was compared to the imipenem-EDTA and meropenem-EDTA. MBL-producing *P. aeruginosa* PA53 (Accession: KM359726) was used as the control strain.[7,18]

DNA extraction and PCR detection

Bacterial DNA was extracted by PrimePrep Genomic DNA Isolation Kit (GeNet Bio, Daejeon, Korea; Cat. No. K-3000) according to the manufacturer's procedures. The bla_{IMP} and bla_{VIM} genes were detected by conventional PCR method. PCR amplification of the genes was done by specific primers as follows: IMP-F (5′-GAAGGCGTTTATGTTCATAC-3′) and IMP-R (5′-GTAAGTTTCAAGAGTGATGC-3′), VIM-F (5′-GATGGTGTTTGGTCGCATA-3′) and VIM-R (5′-CGAATGCGCAGCACCAG-3′). PCR was carried out in a final volume of 25 µl mixture containing 12.5 µl of 2.0x *Taq* Master Mix RED with 2.0 mM $MgCl_2$ (Cat. No. AMP 190301, Ampliqon, Denmark), 1 µL (10 pmol/µL) of each forward and reverse primer, 8.5 µL of sterile distilled water and 2 µL of prepared DNA (100 ng/µl). The PCR was performed in Mastercycler AG 22331-Hamburg (Eppendorf, Germany) under thermal cycling conditions: initial denaturation at 94°C for 3 min, followed by 35 cycles of denaturation at 94°C for 45 s, annealing at 47°C for IMP and 54°C for VIM for 45 s, extension at 72°C for 45 s, and final extension at 72°C for 3 min. PCR products were separated in a 1% agarose gel at 95 V for 50 min and visualized under UV light following the ethidium bromide staining. *P. aeruginosa* PA53 (ACCESSION: KM359726) and *P. aeruginosa* Psa1 (ACCESSION: KT313641) were used as the control strains for bla_{IMP}

and *bla*$_{VIM}$ genes, respectively.[19,20] All PCR products were sequenced by ABI 3730XL DNA Analyzer (Bioneer, Korea). The nucleotide sequences were analyzed by Chromas 2.6.5 software and BLAST algorithm of NCBI web server.

Plant material and extract preparation

The three commonly used plant spices of different families were purchased from local market of Tehran, Iran. The plant spices were re-identified and verified by Herbal Medicine Center of Agricultural Research Education and Extension Organization (AREEO), Tehran, Iran. ARREO is an umbrella organization under the ministry of Jihad-e Agriculture which is responsible for Research, Education, and Extension issues of agricultural sector in Iran.

The fresh plant spices were first washed by tap water, then 3 times by sterile distilled water and dried in laminar air flow cabinet for 7 days at 25°C. The dried materials were crushed with mortar and pestle and powdered by a grinder. Ten g of each cinnamon, garlic, and ginger powder was separately soaked in 100 ml acetone (99%, v/v), methanol (96%, v/v), and chloroform (99.4%, v/v) (Merck, Germany) for a period of 72 hours at room temperature (25°C) in the dark. The extracts were filtered through Whatman filter paper No.1 (Sigma-Aldrich, USA) and then sterilized through the Filter PTFE Membrane 0.45 µm Pk5 (Thomas Scientific, USA). Filtered extracts were evaporated in a rotary evaporator under vacuum and reduced pressure. All dried extracts were stored at 4°C.[15]

MIC and MBC values of herbal extracts

MIC of the herbal extracts was evaluated by the broth microdilution method in 96-well microplates according to the CLSI guidelines.[21] Two hundred mg of each extract powder of cinnamon, garlic, and ginger were separately dissolved in 2 ml DMSO 2% (Merck, Germany) to obtain a final concentration of 100 mg/ml. Different dilutions in the range of 50 mg/ml to 0.19 mg/ml were prepared from the stock solution. One hundred µl of cation-adjusted Mueller-Hinton broth was added in the each well of 96-well microplate. Then, 100 µl of extract was added in all wells of one column (column 3). Serial dilution of extracts was prepared in all wells of each column (from column 3 to column 12) using a multi-channel sampler. Bacterial suspension was adjusted by using a 0.5 McFarland standard (~1×10^8 colony forming units (CFU) ml^{-1}) and diluted 1:10 to obtain a concentration of 10^7 CFU mL^{-1}. Ten µl of diluted bacterial suspension was added in all wells except the column of negative control. Column 1 was selected as a negative control containing Mueller-Hinton broth and extract solution. Column 2 was selected as a positive control containing Mueller-Hinton broth and standard suspension of *P. aeruginosa* ATCC® 27853. The plates were incubated at 37°C for 24 hours. The lowest concentration (highest dilution) of the extract preventing appearance of turbidity was reported as MIC. The MBC of extracts were determined by sub-culturing 10 µL from the wells with concentrations above the MIC on Mueller Hinton Agar (MHA). The lowest concentration of the extract killing bacteria was considered as MBC.

Statistical analysis

All deduced data were analyzed using MINITAB statistical software release 13 (Minitab, Inc., State College, Pennsylvania, USA). A P value <0.05 was considered statistically significant.

Results

Sample collection

A total of 100 *P. aeruginosa* isolates were obtained from burn wounds of patients admitted to the burn care unit of Shahid Motahari Hospital, Tehran, Iran. Seventy-four out of 100 (74%) and 26 out of 100 (26%) isolates of *P. aeruginosa* belonged to male and female patients, respectively. Distribution of isolates based on age group of patients were 6%, 32%, 52%, and 10% for 10, 10-30, 30-60, and up to 60 years old, respectively.

Antimicrobial susceptibility profile

Out of the 100 *P. aeruginosa* isolates, 94 (94%) were resistant to ciprofloxacin, 95 (95%) to gentamicin, 95 (95%) to imipenem, 95 (95%) to meropenem, 94 (94%) to doripenem, 82 (82%) to piperacillin/tazobactam, 91 (91%) to amikacin, 75 (75%) to ceftazidime, 98 (98%) to ticarcillin, 93 (93%) to cefepime, 90 (90%) to piperacillin, 90 (90%) to aztreonam and 0 (0%) to colistin (Figure 1).

The MIC of clinical isolates for imipenem, meropenem, ceftazidime, and ciprofloxacin confirmed that 95 out of 100 (95%) isolates were resistant to imipenem and meropenem, 75 out of 100 (75%) to ceftazidime, and 97 out of 100 (97%) to ciprofloxacin.

Phenotypic detection of MBL-positive strains

MBL screening by CDTT showed that 81 out of 95 (85.2%) imipenem non-susceptible *P. aeruginosa* strains were MBL producers. The inhibition zone resulted from imipenem-EDTA combined disk on Mueller-Hinton agar indicated diameter of ≥7 mm in comparison with the imipenem.

Prevalence of bla$_{IMP}$ and bla$_{VIM}$

Thirteen out of 81 (16.0%) and 18 out of 81 (22.2%)

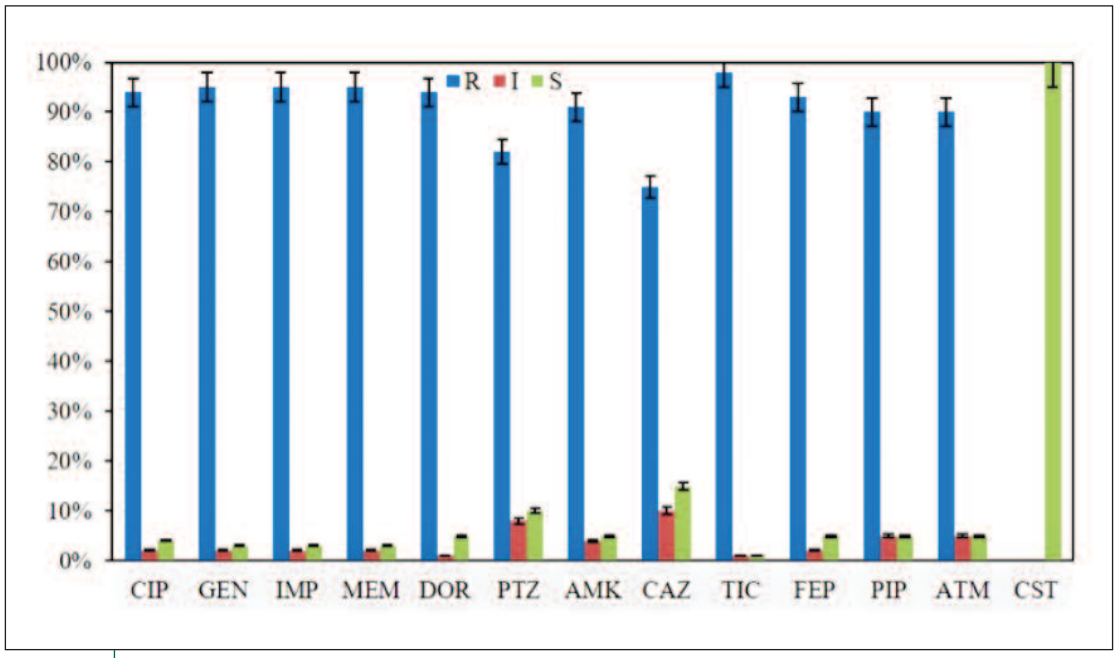

Figure 1 In vitro antibiotic susceptibility of clinical isolates of P. aeruginosa (CIP: ciprofloxacin, GEN: gentamicin, IMP: imipenem, MEM: meropenem, DOR: doripenem, PTZ: piperacillin/tazobactam, AMK: amikacin, CAZ: ceftazidime, TIC: ticarcillin, FEP, cefepime, PIP: piperacillin, ATM: aztreonam, and CST: colistin)

MBL-producing *P. aeruginosa* were positive for bla_{IMP} and bla_{VIM} genes, respectively. PCR amplification of bla_{IMP} and bla_{VIM} genes showed expected amplicon sizes of 587 bp and 390 bp, respectively (Figures 2, 3).

MIC and MBC of extracts

The acetonic, methanolic, and chloroformic extracts of cinnamon, garlic, and ginger exhibited appreciable antibacterial efficacy against 81 MBL-producing *P. aeruginosa* strains. MICs and MBCs (mg/ml) results of cinnamon, garlic, and ginger extracts against 81 MBL-producing *P. aeruginosa* strains were shown in Tables 1-3, respectively. MIC and MBS values are given by a mean of three replicates ± standard error regarding $P<0.05$. MIC of cinnamon ranged from 1.50 mg/ml to 12.50 mg/ml in both acetonic and methanolic extracts and from 3.12 mg/ml to 12.50 mg/ml in the chloroformic extract. Also, MIC of garlic and ginger ranged from 1.50 mg/ml to 12.50 mg/ml in all extracts. MICs of extracts corresponded to MBCs in all bacterial strains. The antibacterial activity of acetonic, methanolic, and chloroformic extracts of garlic and ginger was at ≥3.12 mg/ml. MBL-producing *P. aeruginosa* strains were more susceptible to the methanolic extract of cinnamon and garlic than the acetonic and chloroformic extracts, however acetonic extract of ginger showed higher antibacterial activity than the methanolic and chloroformic extracts ($P<0.05$).

Discussion

MBL-producing *Pseudomonas aeruginosa* is a serious concern in clinical settings.[22] Increasing antibiotic resistance among MBL-producing *P. aeruginosa* strains makes it a life-threatening complication in burned patients.[7] We found a high rate of antibiotic resistance to the β-lactam, carbapenem, fluoroquinolone, aminoglycoside, cephem, monobactam, penicillin, and β-lactam/β-lactamase inhibitor combination groups. The most effective antibiotic was colistin (lipopeptides group) to which no resistance was seen in the study. The previous retrospective studies conducted in different geographical regions, especially in Iran has been revealed similar results of antibiotic resistance against MBL-producing *P. aeruginosa*.[23–27] It has been shown that current mechanism of resistance in MBL-producing *P. aeruginosa* is commonly associated with the production of Ambler classes A, B, and D enzymes with hydrolyzing activity of β-lactam antibiotics, specifically carbapenems.[7,28] Furthermore, the mechanisms of carbapenem resistance in Gram-negative bacilli are related to the resistance of other classes of antibiotics, including penicillins, cephalosporins, and monobactams causing parallel resistance mechanisms.[20]

In the current study, we report a high frequency of 85.2% for MBL-positive *P. aeruginosa* which is in correspondence with the study carried by Fallah *et al*.[1] In

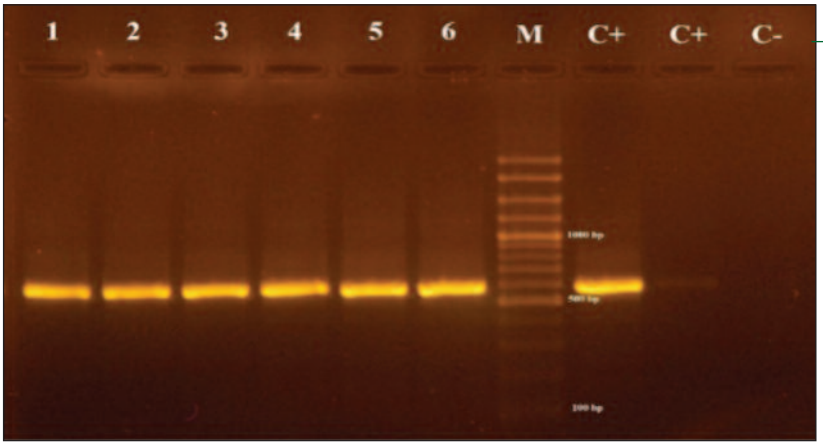

Figure 2

PCR amplification of *bla*$_{IMP}$ in MBL-producing *P. aeruginosa*. Lane 1-6: PCR products of *bla*$_{IMP}$ (587 bp) in clinical strains of MBL-producing *P. aeruginosa*, M: 100 bp Plus DNA Ladder (SinaClon, Iran. Cat. No. PR901644), C+: Positive control, C-: Negative control

Figure 3

PCR amplification of *bla*$_{VIM}$ in MBL-producing *P. aeruginosa*. M: 100 bp plus DNA Ladder (SinaClon, Iran. Cat. No. PR901644), Lane 1-8: PCR products of *bla*$_{VIM}$ (390 bp) in clinical strains of MBL-producing *P. aeruginosa*, C+: Positive control

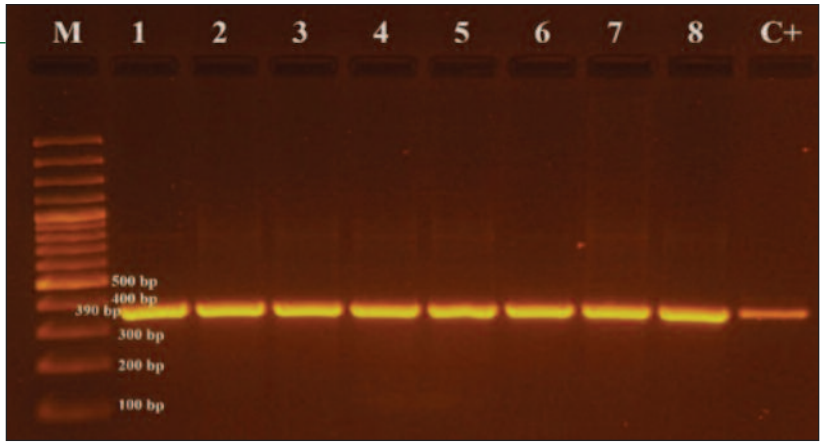

Table 1 MIC and MBC values of *Cinnamomum verum* extract

Conc. (mg/ml)	Acetonic extract		Methanolic extract		Chloroformic extract	
	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)
12.50	81 (100)	81 (100)	81 (100)	81 (100)	81 (100)	81 (100)
6.25	38 (46.91)	38 (46.91)	81 (100)	81 (100)	45 (55.55)	45 (55.55)
3.12	13 (16.04)	13 (16.04)	71 (87.65)	71 (87.65)	36 (44.44)	36 (44.44)
1.50	30 (37.03)	30 (37.03)	10 (12.34)	10 (12.34)	0	0
0.78	0	0	0	0	0	0
0.39	0	0	0	0	0	0
0.19	0	0	0	0	0	0
0.09	0	0	0	0	0	0

Table 2 MIC and MBC values of *Allium sativum* extract

Conc. (mg/ml)	Acetonic extract		Methanolic extract		Chloroformic extract	
	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)
12.50	18 (22.22)	18 (22.22)	13 (16.04)	13 (16.04)	10 (12.34)	10 (12.34)
6.25	46 (56.79)	46 (56.79)	26 (32.09)	26 (32.09)	40 (49.38)	40 (49.38)
3.12	17 (20.98)	17 (20.98)	42 (51.85)	42 (51.85)	31 (38.27)	31 (38.27)
1.50	0	0	0	0	0	0
0.78	0	0	0	0	0	0
0.39	0	0	0	0	0	0
0.19	0	0	0	0	0	0
0.09	0	0	0	0	0	0

Table 3 MIC and MBC values of *Zingiber officinale* extract

Conc. (mg/ml)	Acetonic extract		Methanolic extract		Chloroformic extract	
	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)	MIC No. (%)	MBC No. (%)
12.50	2 (2.46)	2 (2.46)	4 (4.93)	4 (4.93)	4 (4.93)	4 (4.93)
6.25	2 (2.46)	2 (2.46)	68 (83.95)	68 (83.95)	22 (27.16)	22 (27.16)
3.12	77 (95.06)	77 (95.06)	9 (11.11)	9 (11.11)	55 (67.90)	55 (67.90)
1.50	0	0	0	0	0	0
0.78	0	0	0	0	0	0
0.39	0	0	0	0	0	0
0.19	0	0	0	0	0	0
0.09	0	0	0	0	0	0

a similar study, Saffari *et al.*[26] indicated a higher frequency (96%) of MBLs than our study. IMP and VIM are the most common Ambler class B β-lactamases encoded by bla_{IMP} and bla_{VIM} genes, respectively, present in the MBL-producing *P. aeruginosa* strains.[25] In our report, the prevalence of bla_{IMP} and bla_{VIM} genes were 16.8% and 22.22%, respectively, which is in agreement with the study carried by Tarashi *et al.*[20] The IMP and VIM enzymes, first reported from Japan in 1980 and the Verona University Hospital of Italy in 1999, respectively, have since been reported worldwide especially Asian countries.[22,29] It has been observed that bla_{VIM} is more prevalent than the bla_{IMP} in Iranian's studies.[19] Nevertheless, increasing prevalence of either bla_{IMP} or bla_{VIM} genes mediated resistance in *P. aeruginosa* is an alarming threat in the clinical management.[29]

Emerging multi-drug resistant strains has led to di-

rect studies toward promising sources of herbs and spices with potential antibacterial activities.[15] Generally, the medicinal herbs are considered due to the production of secondary metabolites such as alkaloid, flavonoids, tannins and phenolic compounds as valuable sources of microbicides and pharmaceutical drugs.[16]

Cinnamon, garlic, and ginger are the most important medicinal plants which have been previously used in traditional medicine owing to the broad pharmaceutical applications, especially antimicrobial properties.[15,16] Cinnamaldehyde is a bioactive compound present in cinnamon which might be responsible for its antimicrobial properties. Phytochemical screening of the cinnamon plant's bark indicated that the presence of saponin, alkaloid, flavonoid and phenol alone or in combination together may be responsible for antimicrobial properties.[16] The antibacterial activity of garlic is mainly due to the presence of a sulfur compound namely diallyl thiosulphinate (allicin).[30] It has been said that the antimicrobial potency of garlic as a result of its ability to inhibit toxin production and expression of enzymes involved in pathogenesis. Other antimicrobial mechanisms are probably due to the inhibition of β-lactamase expression, aminoglycoside-modifying enzymes, and altered ribosomal binding.[31] Ginger also shows antimicrobial activity possessing the biological components such as gingerol, paradol, shogaol, and zingerone.[32] In addition, the main component of ginger attributing antibacterial activity is sesquiterpenoid belonging to a class of terpenes.[15]

Since most studies deal with the general pathogens, little information is accessible on remedying drug-resistant pathogens and MBL-positive bacteria.[33] Also antibacterial effect of cinnamon, garlic, and ginger extracts against MBL-producing *P. aeruginosa* has not been investigated yet. Our study affirms that the cinnamon, garlic, and ginger extracts have antibacterial effect on MBL-producing *P. aeruginosa* isolates. In a similar study, the inhibitory effect of garlic evaluated by Gull *et al.* was as follow: 0.1 mg/ml, 0.5 mg/ml, and 0.9 mg/ml for aqueous, ethanolic, and methanolic extracts, respectively, and 0.6 mg/ml, 0.4 mg/ml, and 0.5 mg/ml for aqueous, ethanolic, and methanolic extracts of ginger, respectively.[15] According to the Gull's study, different extracts of spices demonstrated variable degree of sensitivity against *P. aeruginosa* isolates[15] which are in agreement with our study. Notably, the solubility of plant bioactive compounds like flavonoids and volatile oil in different organic solvents (aqueous, alcoholic, ketogenic, and etc.) is a probable cause of their antibacterial activity.[15,16] So, water, ethanol, and methanol are considered for extract preparation by reason of the improved solubility as described by de Boer *et al.*[34]

In conclusion, the prevalence of MBL-producing *P. aeruginosa* in burned patients admitted to our burn center is alarming. Screening of the strains is necessary to manage infections caused by them. Accordingly, the clinical significance of the strains made us research alternative antimicrobial agents as a promising therapeutic approach. In this regard, we find that the methanolic extract of cinnamon and garlic as well as the acetonic extract of ginger has significant antibacterial activity against the MBL-producing *P. aeruginosa*. These medicinal plants can be considered as a source of forgotten antimicrobial agents to avoid treatment failure and mortality. Further studies are needed to evaluate other aspects of antimicrobial therapy.

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Competing interests

The authors declare that they have no competing interests.

Περίληψη

In vitro αντιμικροβιακή δραστικότητα των εκχυλισμάτων *Cinnamomum verum, Allium sativum* και *Zingiber officinale* σε *Pseudomonas aeruginosa* που παράγει μεταλλο-β-λακταμάση: Ενδεχόμενη θεραπευτική προσέγγιση

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Λέξεις κλειδιά
Έγκαυμα, κανέλα, σκόρδο, Τζίντζερ, Pseudomonas aeruginosa

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