PLANT SCIENCE TODAY
ISSN 2348-1900 (online)
Vol 11(1): 634–640
https://doi.org/10.14719/pst.2855

HORIZON
e-Publishing Group
HePG

RESEARCH ARTICLE

Evaluation of antibacterial and antifungal activities of *Pistacia atlantica* and *Pistacia khinjuk*

Hamid Dalvand[1], Seyed Mohammad Mahdi Hamdi[1]*, Fatemeh Nori Kotanaee[1] & Hassan Ahmadvand[2]

[1]Department of Biology, Central Tehran Branch, Islamic Azad University, Tehran, Iran
[2]Department of Biology, Research Center for Molecular Medicine, Institute of Mental Health and Addiction, Hamadan University of Medical Sciences, Hamadan, Iran

*Email: m.hamdi@iaucbt.ac.ir

OPEN ACCESS

ARTICLE HISTORY
Received: 09 August 2023
Accepted: 26 November 2023

Available online
Version 1.0 : 23 January 2024
Version 2.0 : 25 January 2024

Check for updates

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc
See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

CITE THIS ARTICLE

Dalvand H, Hamdi S M M, Kotanaee F N, Ahmadvand H. Evaluation of antibacterial and antifungal activities of *Pistacia atlantica* and *Pistacia khinjuk*. Plant Science Today. 2024; 11 (1): 634–640. https://doi.org/10.14719/pst.2855

Abstract

Medicinal plants are renowned for their various therapeutic properties, including antibacterial and antifungal activities. This study aimed to investigate the antibacterial and antifungal activities of *Pistacia atlantica* and *Pistacia khinjuk*. Hydroalcoholic extracts of *P. atlantica* and *P. khinjuk* were prepared to assess their antibacterial and antifungal activities. Standard strains of *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Aspergillus flavus* were utilized for the evaluation of antibacterial and antifungal activities. The inhibitory effects of the extracts on the growth of bacterial and fungal strains were evaluated using minimum inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) through a 96-well microplate analysis following CLSI guidelines. Our findings revealed that the MICs and MBCs of *P. atlantica* and *P. khinjuk* for bacterial strains ranged from 0 to 64 mg/mL. Additionally, the MIC and MFC values for fungal strains ranged from 16 to 64 mg/mL. The results indicated that *Pseudomonas aeruginosa* and *Klebsiella pneumonia* were the most sensitive bacterial strains to *P. atlantica*. Furthermore, *Aspergillus flavus* was identified as the most sensitive fungal strain to *P. atlantica*. In conclusion, these findings suggest that *P. atlantica* and *P. khinjuk* possess antibacterial and antifungal effects. The paper argues that these plant extracts could be used as a supplementary treatment alongside conventional antibacterial and antifungal drugs.

Keywords

Antibacterial effect; antifungal activity; medicinal plants; *Pistacia atlantica*; *Pistacia khinjuk*

Introduction

Infectious diseases rank among the world's most prevalent health issues, imposing a substantial financial burden on society (1). Treatment of infectious diseases with existing drugs often encounters challenges such as drug resistance, prompting the need to discover new antibiotic compounds (2). With the escalating resistance of bacteria and fungi to antimicrobial agents and the high side effects associated with synthetic antimicrobial chemicals, researchers are increasingly exploring herbal extracts and natural antibacterial agents for the treatment of infectious diseases (3). Throughout history, people and traditional healers have utilized medicinal plants for disease treatment, with many ailments successfully addressed by herbs (4). Abun-

dant evidence indicates that 70-80% of people worldwide rely on medicinal plants for primary healthcare (5). Medicinal plants offer a unique and renewable resource for discovering new therapeutically active biomolecules, thanks to the structural and biological diversity of their compounds (6). It is estimated that compounds isolated from medicinal plants contribute to 25% of commonly used drugs (7). Numerous studies have demonstrated that medicinal plants possess diverse biological properties, including antibacterial, anti-inflammatory, and antipyretic effects (8, 9). The antimicrobial properties of medicinal plants have proven effective against a wide range of microorganisms (10). Several studies argue that the presence of phytochemical constituents, such as polyphenolic compounds, is responsible for the various healing properties of medicinal plants (11, 12).

Over the years, extensive research has been conducted on the therapeutic significance of plant species in the genus *Pistacia* (13). It is now widely acknowledged that one of the most well-known medicinal plants of the *Anacardiaceae* family is *Pistacia atlantica* (*P. atlantica*). Traditionally, *P. atlantica* has been used for various purposes, including therapeutic effects on the stomach, intestine, brain, heart, lung, and kidneys (14). Numerous biological properties have been attributed to *P. atlantica*, encompassing antioxidative, anti-microbial, anti-inflammatory, anti-cancer, anti-diabetic, and wound-healing properties (13). Different parts of *P. atlantica* have been found to contain a diverse range of beneficial phytoconstituents, such as phenolic compounds, flavonoids, and tannins (13, 14). *Pistacia khinjuk* (*P. khinjuk*) is also a significant member of the genus *Pistacia*. In folk medicine, *P. khinjuk* has proven effective in treating issues such as cardiovascular disease, dental pain, dyspepsia, and cancer (15). There is substantial evidence regarding the wound healing, antibacterial (16), antioxidant (17), and antihyperlipidemic (18) effects of *P. khinjuk*. Detailed phytochemical analysis of *P. khinjuk* has revealed the presence of tannins, phenolics, and glycosides (19). To the best of our knowledge, previous studies have explored the anti-microbial and antifungal effects of the leaves of *P. atlantica* and *P. khinjuk*. However, few studies have focused on the anti-microbial and antifungal activities of the fruits of these plants. Furthermore, this study aimed to evaluate the antibacterial and antifungal activities of the fruits of *P. atlantica* and *P. khinjuk* for the first time on the pathogens studied in this research.

Materials and Methods

Chemicals and Reagents

All of the required chemicals, including ethanol, Muller Hinton broth, Muller Hinton agar, and potato dextrose agar (PDA), were purchased from Merck (Germany) Company.

Collection of Plant Materials

In May 2020, fruits of *P. atlantica* and *P. khinjuk* were collected from the Khargūshān Mountains at the end of the Khorramabad-Andimeshk freeway and the Bisim Mountains in Khorramabad County, Lorestan Province, Iran. Subsequently, the plant samples were identified by botanists from the Lorestan Agriculture and Natural Resources Research Center in Khorramabad, Iran.

Preparation of Extract

Fresh fruits of the plants were collected and air-dried under shaded conditions for ten days at room temperature to prepare hydroalcoholic extracts of *P. atlantica* and *P. khinjuk*. After drying, the fruits were pulverized, and hydroalcoholic extracts were obtained using the maceration method. The resulting powder was dissolved in a hydroalcoholic mixture (50% distilled water and 50% ethanol) in a ratio of 1:3 (w/v) at 70°C. Hydroalcoholic solutions, combining alcohol and water, are known for their enhanced efficacy in extracting medicinal substances from herbs. The suspension was maintained at 30 °C for 72 hours and later filtered through filter paper. The solvent was then removed using a rotary evaporator (IKA-RV10, Germany) (20).

Bacterial Strains

The bacterial strains, including *Bacillus cereus* (ATCC: 14579), *Pseudomonas aeruginosa* (ATCC: 27853), *Escherichia coli*, *Staphylococcus aureus* (ATCC: 12600), and *Klebsiella pneumonia* (ATCC: 700603), were received from the National Cell Bank of Iran (NCBI, Pasteur Institute, Tehran).

Fungal Strains

The standard strain of *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Aspergillus flavus* were received from the National Cell Bank of Iran (NCBI, Pasteur Institute, Tehran).

Determination of Antibacterial Activity

To assess antibacterial properties, we determined the Minimal Inhibitory Concentration (MIC) and Minimal Bactericidal Concentration (MBC) using the microbial broth dilution method with 96-well plates, following the Clinical and Laboratory Standards Institute (CLSI) guidelines. The stocks of *P. atlantica* and *P. khinjuk* extracts were prepared in Muller Hinton broth. Initially, 50 mL of sterile Muller Hinton broth was added to each well. Serial dilutions were then created by adding 100 mL of the stock, resulting in concentrations ranging from 50 mg/mL to 0.097 mg/mL. Each well's extract concentration was half that of the previous well. Subsequently, 50 mL of a 24-hour microbial culture (equivalent to 1.5 × 105 CFU/mL) was introduced to each well. After shaking, the plates were incubated at 37°C for 24 hours. Post-incubation, the wells were examined for turbidity, indicating bacterial growth. The MIC was identified as wells without turbidity. For MBC determination, 5 mL from clear wells was plated on Muller Hinton Agar medium and observed for microbial growth after 24 hours. The MBC was considered the well with the lowest extract concentration where no bacterial growth occurred on the corresponding plate. The control contained diluted extract plus medium, while the negative control included microbial suspension plus medium. Tetrazolium salt was added to each well, and the MIC was determined by the color change to red-pink. Each test was conducted in triplicate (21).

Determination of Antifungal Activity

To assess the antifungal activity of *P. atlantica* and *P. khinjuk* extracts, the broth microdilution method was employed to determine the Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC) in accordance with CLSI guidelines. In the initial step, a 96-well microplate was prepared, with each well receiving 100 µL of Potato Dextrose Agar (PDA) medium. To observe the antifungal effects of extracts, two-fold serial dilutions ranging from 50 mg/ml to 0.097 mg/ml were meticulously prepared in the microplates. Afterward, the concentrations of *P. atlantica* and *P. khinjuk* extracts were added to separate rows in the 96-well plate. Additional rows were assigned for control (PDA medium + fungi suspension), negative control (PDA medium + extracts), and blank (distilled water). A fungus suspension (1.5 × 105 CFU/mL) was prepared in 100 µL of PDA medium and added to the wells, excluding those designated for the blank and negative control. Subsequently, the microplates were incubated at 35 °C for 48 to 72 hours. All experiments were conducted in triplicate. Following the incubation period, careful scrutiny of the microplates was performed to identify turbidity due to fungal growth. The last dilution of extracts without turbidity in each well was determined as the MIC.For MFC determination, 20 µL from the pre-MIC wells was cultured in PDA medium and incubated at 35°C for 24 hours (22).

Statistical Analysis

All values were presented as the mean ± standard deviation (SD). Data analysis was conducted using SPSS version 22.0 and Microsoft Office Excel 2019. Each assay was repeated three times for the samples, and the results were averaged. ANOVA and t-test methods were employed to compare the means of two groups. All P values < 0.05 were considered statistically significant.

Results

Antibacterial Activity

The antibacterial effects of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* were illustrated in Fig. 1 and 2. The results of the antibacterial tests showed that the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* had antibacterial effects. Based on the data in Fig. 1, the MIC values of the hydro-alcoholic extract of *P. atlantica* were obtained as 64, 16, 64, 64, and 0 mg/ml for *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*, respectively. Furthermore, the MIC values of the hydro-alcoholic extract of *P. khinjuk* were found to be 64, 64, 64, 64, and 0 mg/mL for *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*, respectively (Fig. 1). Additionally, the MIC values of the hydro-alcoholic extract of *P. atlantica* were significantly lower than the MIC values of the hydro-alcoholic extracts of *P. khinjuk* for *Pseudomonas aeruginosa* ($p < 0.0001$). However, there was no significant change in the MIC values of the hydro-alcoholic extract of *P. atlantica* and *P. khinjuk* for *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*.

Looking at Fig. 2, it is apparent that the MBC values of the hydro-alcoholic extract of *P. atlantica* were obtained as 64, 16, 64, 64, and 0 mg/ml for *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*, respectively. In addition, the MBC values of the hydro-alcoholic extract of *P. khinjuk* were found to be 64, 64, 64, 64, and 0 mg/ml for *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*, respectively (Fig. 2). Furthermore, the MBC values of the hydro-alcoholic extract of *P. atlantica* were significantly lower than the MBC values of the hydro-alcoholic extract of *P. khinjuk* for *Pseudomonas aeruginosa* ($p < 0.0001$). However, there was no significant change in the MBC values of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella pneumonia*.

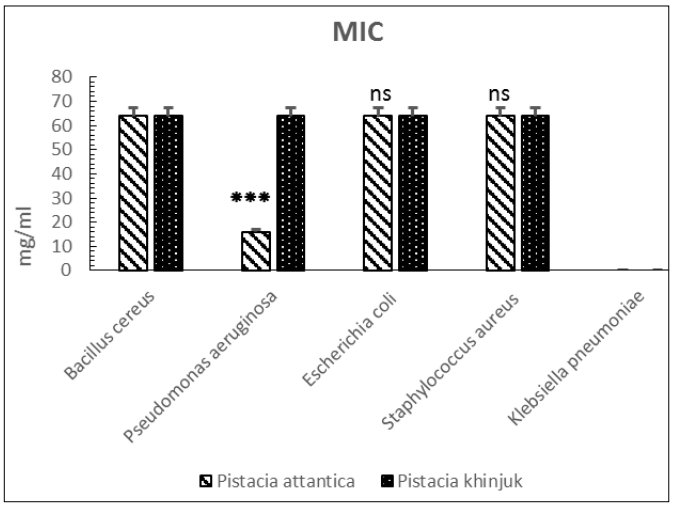

Fig. 1. Determined MICs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for selected bacterial strains. ***Significant change at $p < 0.0001$. **ns**: Non-significant change.

Antifungal Activity

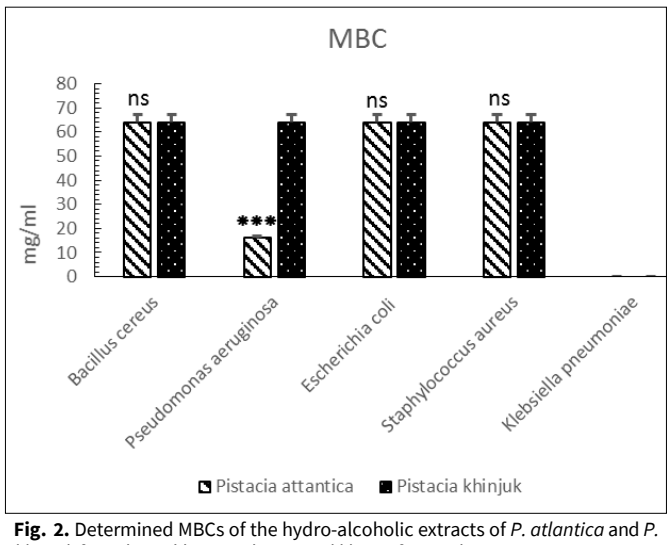

Fig. 2. Determined MBCs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for selected bacterial strains. ***Significant change at $p < 0.0001$. **ns**: Non-significant change.

The results, as seen in Fig. 3, indicate that the hydro-alcoholic extract of *P. atlantica* exhibited potent antifungal activity against *Aggregatibacter actinomycetemcomitans* (MIC value = 32 mg/ml) and *Porphyromonas gingivalis* (MIC value = 64 mg/ml). Moreover, our results revealed an antifungal effect of the hydro-alcoholic extract of *P. khinjuk* against *Aggregatibacter actinomycetemcomitans* (MIC value = 64 mg/ml) and *Porphyromonas gingivalis* (MIC value = 64 mg/ml) (Fig. 3). The results showed a significant difference in the MIC value of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aggregatibacter actinomycetemcomitans* ($p < 0.0001$). However, a non-significant difference was observed in the MIC value of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Porphyromonas gingivalis*.

We found that the MFC value of the hydro-alcoholic extract of *P. atlantica* was obtained at 64 mg/ml for *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. Furthermore, the MFC value of the hydro-alcoholic extract of *P. khinjuk* was found to be 64 mg/ml for *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* (Fig. 4). We also found that there was no significant difference between the MFC values of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*.

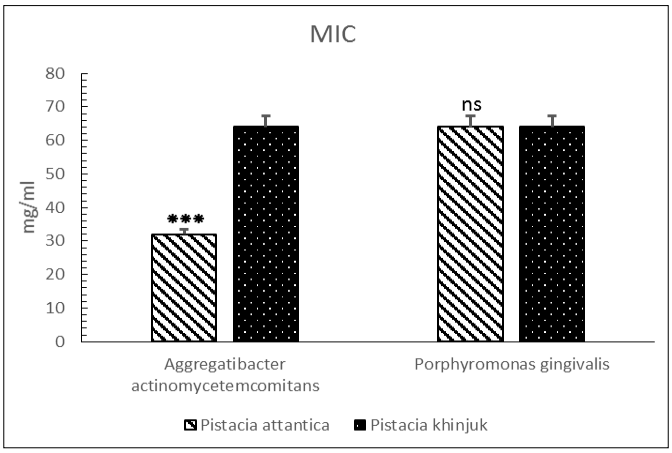

Fig. 3. Determined MICs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. ***Significant change at $p < 0.0001$. **ns**: Non-significant change.

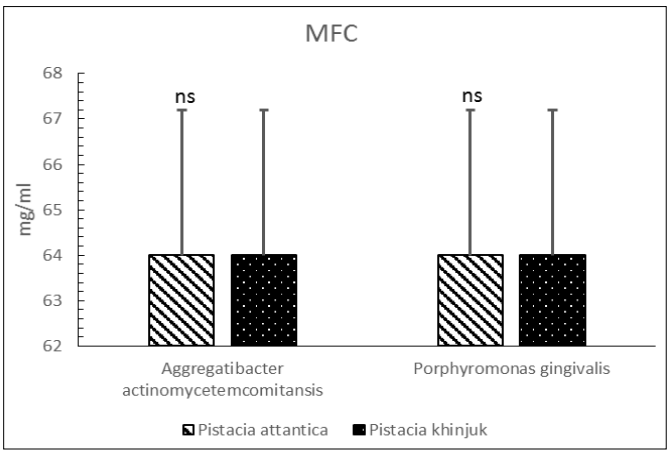

Fig. 4. Determined MFCs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. **ns**: Non-significant change.

As shown in Fig. 5, our finding determined the MIC values of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* as 16 and 32 mg/ml for *Aspergillus flavus*, respectively. Furthermore, our results indicated that the MIC value of the hydro-alcoholic extract of *P. atlantica* was significantly lower than the MIC value of the hydro-alcoholic extract of *P. khinjuk*.

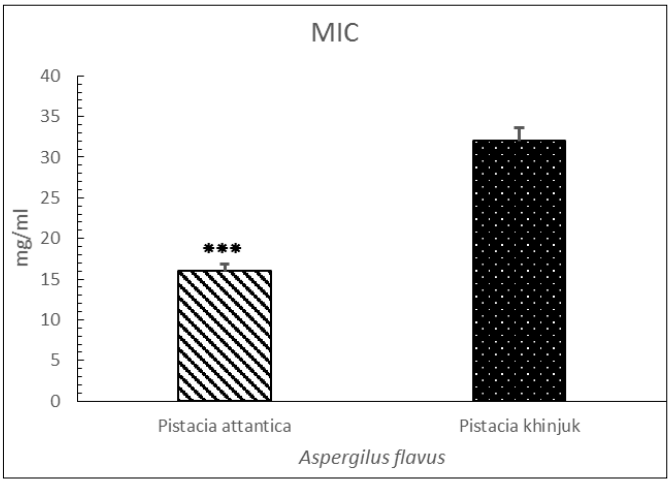

Fig. 5. Determined MICs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aspergillus flavus*. ***Significant change at $p < 0.0001$. **ns**: Non-significant change.

It is evident from the data in Fig. 6 that the MFC value of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* was 32 mg/ml for *Aspergillus flavus*. Furthermore, it has been observed that there was no significant difference between the MFC values of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aspergillus flavus*.

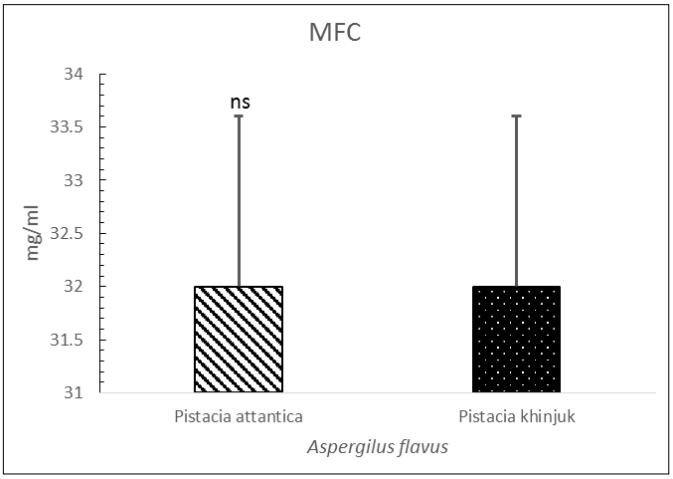

Fig. 6. Determined MFCs of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* for *Aspergillus flavus*. **ns**: Non-significant change.

Discussion

Several reports have shown the antibacterial and antifungal activities of *P. atlantica* and *P. khinjuk*. The present study was designed to determine the antibacterial and antifungal effects of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk* against selected bacterial and fungal strains. The current study found that the hydro-alcoholic extract of *P. atlantica* possesses antibacterial property. Our findings revealed that selected bacterial strains, including *Bacillus cereus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus*, displayed sensitivity

to the extract of *P. atlantica*. Similar finding was reported by Rigane and colleagues (2016). They observed a similar antibacterial effect on Gram-positive and Gram-negative bacteria post-treatment with ethanolic and aqueous extracts of *P. atlantica* (23). Comparison of our findings with those of other studies confirms the antibacterial effect of *P. atlantica* (24, 25). This result may be attributed to the high content of phytochemical constituents responsible for the antibacterial effect of *P. atlantica*. It has been established that chemical compounds, such as α-pinene and D-limonene, are present in abundance in *P. atlantica* (26). There is ample evidence regarding the antibacterial role of these compounds (27). The results of our study indicated an antibacterial effect of the hydro-alcoholic extract of P. khinjuk. Our findings in the present study are consistent with those of Azadpour and colleagues (2015), who reported the antibacterial effect of the methanolic extract of P. khinjuk against both Gram-positive and Gram-negative bacteria (28). Our experiments align with the results of a previous study conducted by Taghizadeh *et al*. They documented the inhibitory effect of P. khinjuk essential oil on bacterial strains. (15). There are several possible explanations for this result. For example, *P. khinjuk* is a rich source of phytoconstituents such as α-pinene, β- pinene and D-limonene which have a wide range of biological capacities, including antibacterial effects (27, 29). In our study, the antifungal analysis demonstrated the inhibitory effect of the hydro-alcoholic extract of *P. atlantica* on the growth of fungal strains. A considerable amount of literature has been published on the antifungal effects of *P. atlantica*. For instance, Falahati and colleagues showed that the methanolic extract of *P. atlantica* was effective against *Candida strains* (30). Many organisms live in and on our body; they are usually harmless or even useful, but some of them may cause disease under certain conditions (31-35). For the treatment of infectious diseases, medicinal plants and natural substances can be a suitable choice (36-38) because they are rich in secondary medicinal compounds such as phenols, flavonoids, anthocyanins, tannins, and plant antioxidants (39-42). The results of this study are consistent with the findings of our study. Our findings broadly support the work of other studies in this area. In a similar study conducted by Shialy *et al*., the ethanolic extract of *P. atlantica* possessed antifungal effects against fungal strains, including *Aspergillus flavus*, with a MIC value ranging from 6.25 to 25 mg/ml (43). The findings of this study are consistent with the results of our research. *P. atlantica* is recognized as a medicinal plant with a variety of pharmacological effects (20). Indeed, numerous types of biologically active compounds have been identified in *P. atlantica*, which are attributed to its therapeutic effects, including antifungal ones (44). In another part of our study, we identified the antifungal effect of *P. khinjuk* against fungal strains, including *Aspergillus flavus*. This result aligns with previous findings in the literature. For example, our results support the findings of Tahvilian *et al*., who reported the antifungal activity of the essential oil of *P. khinjuk* against *Candida albicans*. They demonstrated a potent antifungal effect of *P. khinjuk* on *Candida albicans* (45). *P. khinjuk* is a medicinal herb with several therapeutic effects, including antifungal properties (28). It has been observed that there is a relationship between the presence of phytochemical constituents in *P. khinjuk* and the biological properties of this plant (15). Indeed, the results of the current study revealed that bacterial strains, especially *Pseudomonas aeruginosa*, were more sensitive to *P. atlantica* than *P. khinjuk* due to the lower MIC value. In addition, fungal strains, including *Aspergillus flavus* and *Aggregatibacter actinomycetemcomitans*, showed a lower MIC value to *P. atlantica* compared to *P. khinjuk* and were subsequently more sensitive to *P. atlantica* than *P. khinjuk*. Bioactive components of *P. atlantica* including α-pinene and β-pinene, may be attributed to this antimicrobial effect (16). These findings suggest the therapeutic potential of *P. atlantica* and *P. khinjuk* in the pharmaceutical industry. Traditional herbalists use plants to treat diseases caused by microbial contamination (46-49). The problem of antibiotic resistance has made it necessary to try to identify effective antibacterial compounds against pathogenic bacteria resistant to existing antibacterial compounds (50-52).

Conclusion

The present study aimed to investigate the antibacterial and antifungal activities of *P. atlantica* and *P. khinjuk*. The findings clearly indicate the antibacterial and antifungal effects of the hydro-alcoholic extracts of *P. atlantica* and *P. khinjuk*. Taken together, these results suggest that *P. atlantica* and *P. khinjuk* could be considered as alternative antifungal agents to inhibit the growth of bacterial and fungal strains. A future study exploring the other biological properties of these plants would be very interesting.

Acknowledgements

The authors acknowledge the support of in Department of Biology, Islamic Azad University, Tehran-98734, Iran successful completion of this study.

Authors contributions

All authors contributed equally in the preparation well as revision of the manuscript and approved the final version.

Compliance with ethical standards

Conflict of interest: No conflict of interest was stated by the author(s).

Ethical issues: None.

References

1. Smith KM, Machalaba CC, Seifman R, Feferholtz Y, Karesh WB. Infectious disease and economics: The case for considering multi-sectoral impacts. One Health. 2019;7:100080. https://doi.org/10.1016/j.onehlt.2018.100080
2. Zheng W, Sun W, Simeonov A. Drug repurposing screens and synergistic drug-combinations for infectious diseases. British

Journal of Pharmacology. 2018;175(2):181-91.https://doi.org/10.1111/bph.13895. Epub 2017 Jul 9

3. Ayaz M, Ullah F, Sadiq A, Ullah F, Ovais M, Ahmed J *et al*. Synergistic interactions of phytochemicals with antimicrobial agents: Potential strategy to counteract drug resistance. Chemico-Biological Interactions. 2019;308:294-303. https://doi.org/10.1016/j.cbi.2019.05.050
4. Asadbeigi M, Mohammadi T, Rafieian-Kopaei M, Saki K, Bahmani M, Delfan M. Traditional effects of medicinal plants in the treatment of respiratory diseases and disorders: An ethnobotanical study in the Urmia. Asian Pacific Journal of Tropical Medicine. 2014;7:S364-S368. https://doi.org/10.1016/S1995-7645(14)60259-5
5. Qari SH, Alrefaei AF, Ashoor AB, Soliman MH. Genotoxicity and carcinogenicity of medicinal herbs and their nanoparticles. Nutraceuticals. 2021;1(1):31-41. https://doi.org/10.3390/nutraceuticals1010005
6. Altaf MM, Khan MSA, Ahmad I. Diversity of bioactive compounds and their therapeutic potential. New Look to Phytomedicine. Elsevier. 2019;15-34. https://doi.org/10.1016/B978-0-12-814619-4.00002-1
7. Ahn K. The worldwide trend of using botanical drugs and strategies for developing global drugs. BMB Reports. 2017;50(3):111. https://doi.org/10.5483/bmbrep.2017.50.3.221
8. Qamar M, Akhtar S, Ismail T, Wahid M, Abbas MW, Mubarak MS *et al*. Phytochemical profile, biological properties and food applications of the medicinal plant *Syzygium cumini*. Foods. 2022;11(3):378. https://doi.org/10.3390/foods11030378
9. Narain N, Shanmugam S, de Souza Araújo AA. Antioxidant, antimicrobial, analgesic, anti- inflammatory and antipyretic effects of bioactive compounds from *Passiflora* species. Medicinal Plants: From Farm to Pharmacy. 2019:243-74. https://doi.org/10.1007/978-3-030-31269-5_11
10. Vaou N, Stavropoulou E, Voidarou C, Tsigalou C, Bezirtzoglou E. Towards advances in medicinal plant antimicrobial activity: A review study on challenges and future perspectives. Microorganisms. 2021;9(10):2041. https://doi.org/10.3390/microorganisms9102041
11. Hassan MA, Xu T, Tian Y, Zhong Y, Ali FAZ, Yang X *et al*. Health benefits and phenolic compounds of *Moringa oleifera* leaves: A comprehensive review. Phytomedicine. 2021;93:153771. https://doi.org/10.1016/j.phymed.2021.153771
12. LIczbiński P, Bukowska B. Tea and coffee polyphenols and their biological properties based on the latest *in vitro* investigations. Industrial Crops and Products. 2022;175:114265. https://doi.org/10.1016/j.indcrop.2021.114265
13. Ahmed ZB, Yousfi M, Viaene J, Dejaegher B, Demeyer K, Vander Heyden Y. Four *Pistacia atlantica* subspecies (atlantica, cabulica, kurdica and mutica): A review of their botany, ethnobotany, phytochemistry and pharmacology. Journal of Ethnopharmacology. 2021;265:113329. https://doi.org/10.1016/j.jep.2020.113329
14. Mahjoub F, Rezayat KA, Yousefi M, Mohebbi M, Salari R. Pistacia atlantica Desf. A review of its traditional uses, phytochemicals and pharmacology. Journal of Medicine and Life. 2018;11(3):180. https://doi.org/10.25122/jml-2017-0055
15. Taghizadeh SF, Davarynejad G, Asili J, Riahi-Zanjani B, Nemati SH, Karimi G. Chemical composition, antibacterial, antioxidant and cytotoxic evaluation of the essential oil from pistachio (*Pistacia khinjuk*) hull. Microbial Pathogenesis. 2018;124:76-81. https://doi.org/10.1016/j.micpath.2018.08.039. Epub 2018 Aug 20
16. Tohidi M, Khayami M, Nejati V, Meftahizade H. Evaluation of antibacterial activity and wound healing of *Pistacia atlantica* and *Pistacia khinjuk*. Journal of Medicinal Plants Research. 2011;5(17):4310-14.
17. Mohammadi B, Maboud HE, Seyedi SM. Nutritional value and antioxidant properties of hull and kernel in *Pistacia atlantica* and *Pistacia khinjuk* fruits. Journal of Food Science and Technology. 2019;56:3571-78. https://doi.org/10.1007/s13197-019-03881-9. Epub 2019 Jul 10
18. Kamal F, Shahzad M, Ahmad T, Ahmed Z, Tareen RB, Naz R *et al*. Antihyperlipidemic effect of *Pistacia khinjuk*. Biomedicine andamp. Pharmacotherapy. 2017;96:695-99. https://doi.org/10.1016/j.biopha.2017.10.061. Epub 2017 Nov 6
19. Ezatpour B, Saedi Dezaki E, Mahmoudvand H, Azadpour M, Ezzatkhah F. *In vitro* and *in vivo* antileishmanial effects of *Pistacia khinjuk* against *Leishmania tropica* and *Leishmania major*. Evidence-Based Complementary and Alternative Medicine. 2015;2015. https://doi.org/10.1155/2015/149707
20. Bagheri S, Khorramabadi RM, Assadollahi V, Khosravi P, Cheraghi Venol A, Veiskerami S *et al*. The effects of pomegranate peel extract on the gene expressions of antioxidant enzymes in a rat model of alloxan-induced diabetes. Archives of Physiology and Biochemistry. 2021;1-9. https://doi.org/10.1080/13813455.2021.1877308
21. Rashidipour M, Ashrafi B, Nikbakht MR, Veiskarami S, Taherikalani M, Soroush S. Encapsulation of *Satureja khuzistanica* jamzad essential oil in chitosan nanoparticles with enhanced antibacterial and anticancer activities. Preparative Biochemistry andamp. Biotechnology. 2021;51(10):971-78. https://doi.org/10.1080/10826068.2021.1881907
22. Sadeghi N, Sadeghi H, Mohan DN, Sepahvand A, Alizadeh A, Garavand S. Chemical composition, anti-fungal and cytotoxic effects of *Ferula macrecolea* essential oil against *Candida albicans* resistant and sensitive strains. Journal of Herbmed Pharmacology. 2023;12(2):228-32. https://doi.org/10.34172/jhp.2023.24
23. Rigane G, Ghazghazi H, Aouadhi C, Ben Salem R, Nasr Z. Phenolic content, antioxidant capacity and antimicrobial activity of leaf extracts from *Pistacia atlantica*. Natural Product Research. 2017;31(6):696-99. https://doi.org/10.1080/14786419.2016.1212035. Epub 2016 Aug 3. 10
24. Hamelian M, Hemmati S, Varmira K, Veisi H. Green synthesis, antibacterial, antioxidant and cytotoxic effect of gold nanoparticles using *Pistacia atlantica* extract. Journal of the Taiwan Institute of Chemical Engineers. 2018;93:21-30. https://doi.org/10.1016/j.jtice.2018.07.018
25. Hamelian M, Zangeneh MM, Shahmohammadi A, Varmira K, Veisi H. *Pistacia atlantica* leaf extract mediated synthesis of silver nanoparticles and their antioxidant, cytotoxicity and antibacterial effects under *in vitro* condition. Applied Organometallic Chemistry. 2020;34(1):e5278.
26. Bagheri S, Sarabi MM, Khosravi P, Khorramabadi RM, Veiskarami S, Ahmadvand H *et al.* Effects of *Pistacia atlantica* on oxidative stress markers and antioxidant enzymes expression in diabetic rats. Journal of the American College of Nutrition. 2019;38(3):267-74. https://doi.org/10.1080/07315724.2018.1482577
27. Wang CY, Chen YW, Hou CY. Antioxidant and antibacterial activity of seven predominant terpenoids. International Journal of Food Properties. 2019;22(1):230-38. https://doi.org/10.1080/10942912.2019.1582541
28. Azadpour M, Rezaei M, Taati M, Ghasemi Dehnoo M, Ezatpour B. Antioxidant, antibacterial and wound-healing properties of methanolic extract of *Pistacia khinjuk*. Comparative Clinical Pathology. 2015;24:379-85. https://doi.org/10.1007/s00580-014-1908-8
29. Salehi B, Upadhyay S, Erdogan Orhan I, Kumar Jugran A, LD Jayaweera S, A. Dias D *et al.* Therapeutic potential of α-and β-

pinene: A miracle gift of nature. Biomolecules. 2019;9(11):738. https://doi.org/10.3390/biom9110738

30. Falahati M, Sepahvand A, Mahmoudvand H, Baharvand P, Jabbarnia S, Ghojoghi A *et al*. Evaluation of the antifungal activities of various extracts from *Pistacia atlantica* Desf. Current Medical Mycology. 2015;1(3):25. https://doi.org/10.18869/acadpub.cmm.1.3.25
31. Darvishi M, Forootan M, Nazer MR, Karimi E, Noori M. Nosocomial infections, challenges and threats: A review article. Iranian Journal of Medical Microbiology. 2020 Mar 10;14(2):162- 81. https://doi.org/10.30699/ijmm.14.2.162
32. Seyed-Alagheband SA, Sharifian M, Adeli OA, Sohooli M, Shekouhi R. Primary synovial sarcoma of thyroid gland: A case report and review of literature. International Journal of Surgery Case Reports. 2021 Aug 1;85:106245. https://doi.org/10.1016/j.ijscr.2021.106245
33. Ranjbar J, Koosha M, Chi H, Ghasemi A, Zare F, Abdollahifar MA, Darvishi M, Li T. Novel chitosan/gelatin/oxidized cellulose sponges as absorbable hemostatic agents. Cellulose. 2021 Apr;28:3663-75.
34. Seyed-Alagheband SA, Shahmoradi MK, Adeli OA, Shamsi T, Sohooli M, Shekouhi R. Follicular dendritic cell sarcoma of the thyroid gland in a patient with preexisting hashimoto's thyroiditis: A rare case report with a literature review. Case Reports in Oncology. 2022 Jan 6;14(3):1698-705.
35. Darvishi M, Ziari K, Mohebbi H, Alizadeh K. Association between iron deficiency anemia and *Helicobacter pylori* infection among children under six years in Iran. Acta Medica Iranica. 2015;220-24.
36. Mobaraei M, Babaei S, Naseri M, Moosavi-Nasab M. Physical, mechanical and antibacterial properties of the gelatin film obtained from the by-product of Talang queenfish, Scomberoides commersonnianus. Aquatic Animals Nutrition. 2022;8(3):29-42. https://doi.org/10.22124/janb.2023.24038.1186
37. Ebrahimi Y, Abdalkareem Jasim S, Mohammed BA, A Salman N, Jabbar AM, M Hameed N, Goudarzi MA, Parsaei P. Determination of antioxidant properties of *Mentha longifolia*, *Pistacia khinjuk* and *Eucalyptus globulus*. Caspian Journal of Environmental Sciences. 2022;(11):1-6. https://doi.org/10.22124/cjes.2022.6065
38. Gholami A, Karami E, Ebrahimpoorghalehjoghi S, Hajjarzadeh M, Javadi K, Bakhtiari M *et al*. The therapeutic effects of *Ganoderma lucidum* on cancer and immune system such as anti -tumor, anti-metastatic, antioxidant, anti-angiogenic, anti-inflammatory and immuno-modulating. Plant Biotechnology Persa. 2023;5(2): URL: http://pbp.medilam.ac.ir/article-1-201-en.html
39. Shahsavari S, Kumar Mandal S, Kumar D. Determination of antioxidant capacity of methanolic extract of *Allium ampeloprasum* subsp *iranicum*. Journal of Biochemicals and Phytomedicine. 2023;2(1):3-6. https://doi.org/10.34172/jbp.2023.2
40. Sulieman AM, Al-Anaizy ES, Al-Anaizy NA, Abdulhakeem MA, Snoussi M. Assessment of antimicrobial and antioxidant activity of methanolic extract from *Arnebia decumbens* aerial parts growing wild in Aja mountain. Advancements in Life Sciences. 2023 Apr 14;10(1):84-92.
41. Habibi Z, Imanpour Namin J, Remazanpour Z. Evaluation of antimicrobial properties of diethyl ether and methanol extracts of *Scenedesmus dimorphus* against bacterial *Micrococcus lutesus* and *Aeromonas hydrophila*. Aquatic Animals Nutrition. 2017;3 (1):35-45. https://doi.org/10.22124/janb.2017.3154
42. Changaee F, Goudarzi MA, Ghobadi R, Parsaei P. Antioxidant effects of methanolic extracts of *Anthemis Susiana* Nabelek, *Alyssum campestre* and *Gundelia tournefortii*. Caspian Journal of Environmental Sciences. 2023;1-6. https://doi.org/10.22124/cjes.2023.6714
43. Shialy Z, Zarrin M, Nejad BS, Naanaie SY. *In vitro* antifungal properties of *Pistacia atlantica* and olive extracts on different fungal species. Current Medical Mycology. 2015;1(4):40. https://doi.org/10.18869/acadpub.cmm.1.4.40
44. Yu H, Lin ZX, Xiang WL, Huang M, Tang J, Lu Y *et al*. Antifungal activity and mechanism of D-limonene against foodborne opportunistic pathogen *Candida tropicalis*. Lwt. 2022;159:113144. https://doi.org/10.1016/j.lwt.2022.113144
45. Tahvilian R, Moradi R, Zhale H, Zangeneh MM, Zangeneh A, Yazdani H *et al*. Ethnomedicinal plants: Study on antifungal activity of essential oil of *Pistacia khinjuk* (combined with the dominance γ-Terpinene) against *Candida albicans*. International Journal of Pharmaceutical and Clinical Research. 2016;8 (10):1369-73.
46. Manouchehri N. Most important medicinal plants with antihalitosis property: An overview. Journal of Biochemicals and Phytomedicine. 2023 Mar 1;2(1):1-2. https://doi.org/10.34172/jbp.2023.1
47. Oboodiat M, Bakhtiari R, Shakib P, Manoocheri N, Khakpour A. The most important native Iranian medicinal plants affecting the bacteria that cause tooth decay; A systematic review . Indian Journal of Forensic Medicine andamp; Toxicology. 2021;15 (3):3421-25.
48. Abbasi N, Ghaneialvar H, Moradi R, Zangeneh MM, Zangeneh A. Formulation and characterization of a novel cutaneous wound healing ointment by silver nanoparticles containing *Citrus lemon* leaf: A chemobiological study. Arabian Journal of Chemistry. 2021 Jul 1;14(7):103246.
49. Karimi E, Abbasi S, Abbasi N. Thymol polymeric nanoparticle synthesis and its effects on the toxicity of high glucose on OEC cells: Involvement of growth factors and integrin-linked kinase. Drug Design, Development and Therapy. 2019 Jul 25:2513-32.
50. Kazempour M, Shahangian SS, Sariri R. *Dracocephalum kotschyi*: Inhibition of critical enzyme relevant to type-2 diabetes, essential oil composition, bactericidal and anti-oxidant activity. Caspian Journal of Environmental Sciences. 2023;1-15. https://doi.org/10.22124/cjes.2023.6256
51. Manouchehri N. A review of the most widely used medicinal plants in the treatment of dental and oral disorders and diseases. Journal of Biochemicals and Phytomedicine. 2022;1(1):3-7. https://doi.org/10.34172/jbp.2022.2
52. Seddiq SH. Efficiency of aqueous and alcoholic extract of *Costus speciosus* roots on Iraqi pneumonic isolated bacteria. Caspian Journal of Environmental Sciences. 2023;1-9. https://doi.org/10.22124/cjes.2023.6706