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Original Article

Evaluation of Antimicrobial Properties of Bam Date Kernel Extract and Investigation of the Structure of Extract

Ali Monajjemi[1], Maryam Tabibi[2*], Fateme Kheiri[1], Alireza Rasouli[2], Amir Arsalan Asgari[3], Gholam Ali Jafari[4]

[1]Medical Student, School of Medicine, Qom University of Medical Sciences
[2]Cellular and Molecular Research Center, Qom University of Medical Sciences, Qom, Iran
[3]Researcher, Qom University of Medical Sciences, Qom, Iran
[4]Lab of Microbiology, School of Medicine, Qom University of Medical Sciences

Abstract

Background & Aims: The prevalence of hospital infections, especially of bacterial origin, is increasing and uncontrollable in many countries. Controlling them, because of their damage to the health and economy, is essential. Therefore, numerous efforts have been made to find new antibiotics as suitable alternatives to current ones. This study aimed to investigate the antibacterial activity of date kernel extract against several hospital pathogens.

Materials and Methods: Acetone extract of Mozafati date kernel from Bam city was prepared by immersion method and its antibacterial effects on hospital pathogens such as *Escherichia coli*, *Staphylococcus aureus*, *Salmonella enterica*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* were investigated by the minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and well diffusion method. Then, the structure of the obtained extract was determined by high-performance liquid chromatography (HPLC).

Results: The MIC was observed at 400 mg/mL of extract for *S. aureus* bacteria. In addition, the MBC of date kernel extract was 500 mg/mL for the tested bacteria, except for *A. baumannii*, where a decreasing trend was detected. The antibacterial activity was determined by the well diffusion method against all bacteria, and the greatest activity was observed against *S. aureus* with a growth inhibition zone diameter of 31 mm. The HPLC analysis showed the presence of 7 different structures, of which rutin was the most abundant.

Conclusion: This study indicates the high antibacterial effect of acetone extract of date kernel on the tested bacteria; however, further studies should be conducted on this plant as a new and powerful antibacterial agent.

Keywords: Anti-infective agents, Plant extracts, Pathogens, *Phoenix dactylifera* L, Date extract, Bacterial infections

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1. Introduction

The increasing prevalence of antibiotic-resistant hospital infections is one of the problems that patients and physicians encounter. The number of effective and available antibiotics for the treatment of these infections is continuously decreasing [1]. Nosocomial infections have always been among the major health and treatment problems and recently they have become more important, posing a serious challenge to the health systems of countries. The increased number of hospitals, the emergence of new infections, increasing microbial resistance, and the need for various medical services have made the occurrence of hospital infections inevitable. Therefore, the control of hospital infections is now considered a global priority [2]. Therefore, many efforts have been made to find new compounds as suitable alternatives to existing antibiotics [3]. Plants produce different types of bioactive substances that introduce them as a rich source of medicinal substances [4].

Due to the serious side effects of consumed antibiotics and the resistance that pathogenic bacteria have acquired against them, there is a growing scientific consensus that the inappropriate use of antibiotics to treat infectious diseases causes the development of bacterial antibiotic resistance. As a consequence, the use of natural antimicrobial agents is now considered important because it helps reduce the disadvantages of traditional medicine [5]. In medical science, much attention has been paid to extracts and compounds of plant origin with biological properties [6]. The use of medicinal plants has been growing in the past few years due to their fewer side effects compared to chemical drugs. Plant extracts are among the sources of antibacterial compounds against pathogenic bacteria [7,8].

Date palm (*Phoenix dactylifera* L.) is a monocotyledonous and tropical plant that is a member of the palm family [9]. Dates contain minerals such as iron, potassium, zinc, and vitamins such as A, B, and C [10,11]. Carbohydrates, amino acids, and fatty acids are also abundantly found in them [10]. This fruit contains large amounts of antioxidant, antimutagenic, anthocyanin, phenolic compounds, and free acids [7]. Dates contain sucrose, glucose, polyphenol compounds, water, proteins, salts, fat, mineral salts (such as iron, potassium, manganese, and zinc), vitamins (A,

*Corresponding Author: Maryam Tabibi, Email: ph.d.tabibi@gmail.com

B, C), and various enzymes (such as polyphenol oxidase, invertase, etc) [10,11]. Since ancient times, both date fruits and kernels have been used in various traditional and folk medicinal systems where the date palm is growing [12,13].

Based on current knowledge, it has been considered that phenolic compounds in date extracts are mainly responsible for the antimicrobial activities reported in the literature. This is believed to be caused by the ability of these chemicals to bind to the bacterial cell wall, which also explains their greater effectiveness against Gram-positive bacteria [14,15]. In addition, phenolic compounds produce hydrogen peroxide, which minimizes microbial growth [16]. Rutin, catechins, and sinapic acid are common flavonoids in food sources that have various properties, including anti-bacterial activity [17-19].

Considering the increasing need to find new antibacterial compounds and to investigate the applications of these compounds, the purpose of this research was to prove the antibacterial activity of the extract of Mazafati date kernel from Bam city on several hospital bacteria whose antibacterial effect has not been proven until now.

2. Materials and Methods

2.1. Sample collection

Packaged Mazafati dates from Bam city were prepared and after separating the kernels from the fruit, the date kernels were completely washed with tap water for 5 minutes to remove possible surface contamination. Then, 200 g of date kernels was crushed into a powder and mixed with 200 mL of acetone. Then, it was placed in a shaker at 130 rpm for 48 hours at room temperature. After 48 hours, the homogenized mixture was filtered twice with Whatman No. 1 filter paper. Next, the solvent was separated from the extract by a rotary evaporator, and with the help of a vacuum pump (vacuum distillation), the remaining acetone was removed from the solution. Afterwards, the date kernel extract was dried in an oven. Then, the date kernel extract was hydrated in a nutrient broth, passed through a 0.22 µm filter, and stored at -80°C for further tests. The final concentration of date kernel extract was 1000 mg/mL [20].

2.2. Bacterial pathogens

In this research, hospital pathogens (*Staphylococcus aureus* ATCC 12600, *Escherichia coli* ATCC 10536, *Pseudomonas aeruginosa* ATCC 27853, *Acinetobacter baumannii* ATCC BAA-747, and *Salmonella enterica* CCM 3807) were used to investigate the antibacterial effect of date kernel extract. The pathogens were purchased from the Scientific and Industrial Research Organization of Iran.

2.3. Antibacterial Effect

First, a suspension of the tested strains with turbidity equal to 0.5 McFarland standard was prepared and uniformly inoculated on Mueller-Hinton agar (MHA) culture medium. Then, using a sterile Pasteur pipette, wells with a diameter of 6 to 8 mm were created in MHA culture medium at regular intervals. Date fruit extract at concentrations of 500 and 1000 mg/mL was poured into the well. Then, the plates were incubated for 24 hours at a temperature of 37 °C and the activity of date kernel extract on the tested bacteria was determined by measuring the diameter of the inhibition zone [21].

2.4. Minimum inhibitory concentration (MIC)

The broth microdilution method was used to measure the MIC. According to the references, serial dilutions were prepared in a 96-well microplate with a volume of 200 µL for each well, so that the first well contained the highest concentration and the last well contained the lowest concentration of date kernel extract. Next, from the 24-hour culture of the tested bacteria, a bacterial suspension of 0.5 McFarland standard was prepared and 20 µL of the final inoculation suspension was added to each well. One well was considered a positive control (containing 10 µL of microbial suspension in the well without date kernel extract) and one well was a negative control (containing 200 µL of medium without bacterial inoculation and date seed extract). Then, the microplates were incubated at 37°C for 24 hours. After the incubation, bacterial growth was evaluated in terms of turbidity. The MIC value was defined as the lowest concentration of date kernel extract at which no macroscopic growth was detectable. The results were recorded by ELISA readers (Hiperion MRP 4+, Germany) [22].

2.5. Minimum bacterial concentration (MBC)

First, 10 µL of the content of the wells in which the inhibitory concentration of bacterial growth was observed was poured on the plates containing MHA, and the plates were incubated for 24 hours at 37 °C. Then, the plates were examined after 24 hours. The amount of MBC was determined based on the minimum concentration of the antimicrobial substance that prevents the growth of bacteria on the plate [22].

2.6. Analysis of extract structure by HPLC

The structure of the extract was investigated using a high-performance liquid chromatography (HPLC) device (Agilent HPLC 1260 Infinity II). The device had a four-chamber pump, a sampler, and an automatic detector. The column type was Zorbax Eclipse, the size of the column was 150×4.6 mm, and the injection volume was 20 µL. Electrospray ionization settings included: temperature of 30 °C, electrospray ionization of 4500 volts, curtain gas with 8 psi pressure, and CEM detector (2300 V). A 1% solution of formic acid in methanol was prepared with volume ratios of 10:90, 25:75, 60:40, and 70:30. The mobile phase flow rate was 1 mL/min. The phenolic compounds in the extract were identified by comparing the inhibition

time of the compounds with the standard compound and their amount was expressed as a percentage [23].

2.7. Statistical analysis

All experimental procedures were performed with three repetitions. Microsoft Excel was used for statistical and graphical analysis of the data. The data were analyzed by one-way analysis of variance and expressed as mean and standard deviation.

3. Results

3.1. Antimicrobial effect of date kernel extract

The MIC of date kernel extract for *Escherichia coli*, *Salmonella enterica*, and *Pseudomonas aeruginosa* was 500 mg/mL and for *Staphylococcus aureus*, it was 400 mg/mL. However, a decreasing trend was observed for *Acinetobacter baumannii*.

MBC test results were negative for the tested concentrations. The antimicrobial effects of the extract were investigated at concentrations of 500 and 1000 mg/mL.

MIC and MBC data and a comparison of the antimicrobial effect of the examined concentrations are shown in Table 1.

3.2. Structural investigation of date kernel extract by HPLC

Based on the results, 7 effective compounds including gallic acid, catechin, chlorogenic acid, rutin, vanillin, quercetin, and sinapic acid were identified in date kernel extract. The findings showed that rutin was the most effective composition of date kernel extract, followed by catechin, sinapic acid, chlorogenic acid, vanillin, gallic acid, and quercetin, respectively. The effective compounds in date kernel extract are listed in Table 2. The chemical composition of date kernel extract is given in Figure 1.

Table 1. Antimicrobial activity of date kernel extract on bacteria

Bacterial Strains	MIC (mg/mL)	MBC (mm)	
		500 (mg/mL)	1000 (mg/mL)
Escherichia coli	500	20	30
Salmonella enterica	400	13	22
Pseudomonas aeruginosa	500	11	17
Staphylococcus aureus	500	21	31
Acinetobacter baumannii	N/A	10	15

N/A, Not-available.

4. Discussion

The antimicrobial activity of date kernel extract was determined by the well diffusion method, the MIC, and the MBC. The results of this study showed that the acetone extract of date kernel had antimicrobial capacity against *S. aureus*, *A.* baumannii, *S. enterica*, *E. coli*, and *P. aeruginosa*. Moreover, the HPLC analysis showed the presence of gallic acid, catechin, chlorogenic acid, rutin, vanillin, quercetin, and sinapic acid in the date kernel extract. In previous studies, the presence of various compounds including gallic acid [24], chlorogenic acid [25], and rutin [26] and their antimicrobial effects have been proven. The antimicrobial effect of date kernel extract in the present study can be attributed to the presence of these compounds in the extract and it can be stated that the date kernel has various valuable antimicrobial compounds.

In the study conducted by Shariati et al, the antimicrobial activity of date fruit and kernel extracts was investigated against *S. aureus* strains and it was found that none of the acetone and ethanol extracts of date fruit had an antimicrobial effect on the above-mentioned bacteria [3]. In the study by Shariati et al, date fruit extract had no antimicrobial effect, but date kernel extract, like the extract used in the present study, showed the antimicrobial effect against the investigated pathogens, including *S. aureus*.

Celik et al evaluated the antimicrobial activity of date kernels (*Fructus dactylus*). They found that aqueous and methanol extracts of date kernels had high phenolic and flavonoid compounds, and this extract had high antibacterial activity against 11 bacteria. The MIC was in the range of 12.50 to 250 mg/mL [27]. In both studies, date kernel extract showed a strong antimicrobial effect, and the common results prove the value of examining and determining the content of date kernels in future research.

Aljazy et al investigated the effect of date kernel extract on several hospital pathogens including *A. baumannii*, *Bacillus subtilis*, *E. coli*, *Klebsiella pneumoniae*, *P. aeruginosa*, *Proteus mirabilis*, *S. aureus*, and *Streptococcus pyogenes* and showed that the ethanolic extract was the most effective extract compared to other extracts in preventing the growth of pathogens [28]. In the present

Table 2. Chromatogram characteristics of date kernel extract with HPLC

Compound	mg/L	Retention time (min)	Width (min)	Area (mA.s)	Height (mA)	Area (%)
Gallic acid	1.49	3.23	0.8	239.13	31.26	20.32
Catechin	24.1	7.3	0.20	115.22	9.75	11.10
Chlorogenic acid	5.18	10.9	0.21	109.88	7.11	9.77
Rutin	31.67	13.1	0.19	95.39	8.84	7.53
Vanillin	5.3	14.4	0.16	327.39	27.65	28.30
Quercetin	1.03	15.1	0.15	62.56	6.23	6.66
Sinapic acid	19.44	16.9	0.22	95.38	6.19	7.8

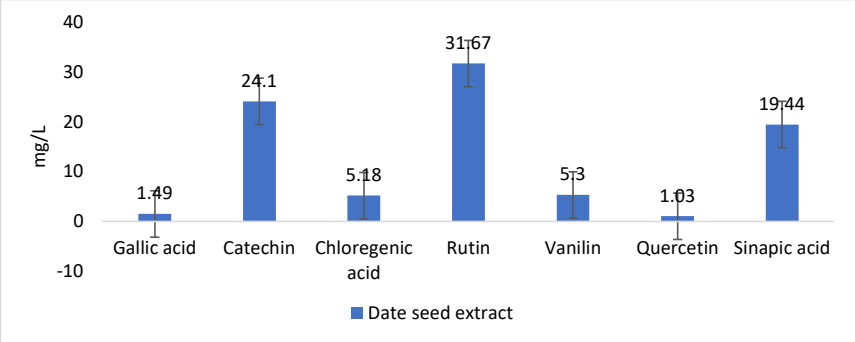

Figure 1. Comparison of the amount of date extract compounds

study, the acetone extract of date kernel was used, and the comparison of the results of Aljazy et al (28) with ours shows that both types of extracts have strong antimicrobial properties.

In a study, Al-Shwyeh investigated the antimicrobial properties of date (*P. dactylifera* L) and showed that due to the presence of phenolic compounds, antioxidants, benzoic acid, cinnamic acid, and flavonoids, date fruit had strong biological activities against several gram-positive and gram-negative bacterial pathogens and it showed the best activity against *E. coli* bacteria [29]. In both studies, the antimicrobial properties of date fruit and kernel extracts were shown, and it can be said that dates have different bioactive compounds with strong antimicrobial effects. However, in the study by Shariati et al (3), date kernel extract had no antibacterial effect.

Alrajhi et al investigated the antibacterial activity of date palm extract (*P. dactylifera*) in a study. The study aimed to evaluate the active compounds of date seeds in terms of their antimicrobial activity. The extraction of date seed powder was performed using high-polarity solvents such as hexane and ethyl acetate by cold extraction method. The isolates were later tested for antibacterial activity against Gram-positive and Gram-negative bacteria including *P. aeruginosa*, *E. coli*, *K. pneumoniae*, *Proteus vulgaris*, *P. mirabilis*, methicillin-resistant *S. aureus* (MRSA), and *Enterococcus faecalis* using the agar well diffusion method. The potential antibacterial activity of the ethyl acetate extract was observed against a large number of gram-positive pathogens [30]. In the study by Alrajhi et al, the obtained date extract showed antimicrobial activity against a wide range of hospital pathogens like the present study, and the findings of both studies confirm the antimicrobial properties of date extract.

Boudghane et al investigated the antimicrobial properties of different extracts of Algerian date seeds. Based on the results of this research, the methanolic extract had the highest percentage of phenolic and tannin compounds and this extract showed the highest antimicrobial activity [31]. Bhaskaracharya et al in a systematic review of the antibacterial activity of polyphenol extract of date kernel (*P. dactylifera* L) showed that similar to other fruit processing industry by-products, date kernels, waste from date processing industry, are rich in extractable polyphenols. The rich polyphenolic content suggests that date kernel extracts can be a cost-effective source of antimicrobial agents; however, their antibacterial activity is not well understood [32]. In the present study and studies conducted by Boudghane et al and Bhaskaracharya et al, date kernel extract, which has different metabolites, showed antimicrobial properties against the investigated pathogens, indicating the importance of using the basic compounds of this plant in dealing with hospital pathogens.

5. Conclusion

Today, due to the increase in bacterial resistance in various types of pathogens, there is a need for research to find new compounds with antibacterial properties. According to the results of the experiments conducted in this research, it can be claimed that the extract of Mazafati date kernel from Bam city has an antibacterial effect on the tested pathogens, including *E. coli*, *S. aureus*, *A. baumannii*, *S. enterica*, and *P. aerogenes*. Therefore, by conducting more research on the date kernel extract and comparing it with the antimicrobial properties of other plant extracts, some compounds can be found to combat antibiotic resistance of pathogens.

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Authors' Contribution

Conceptualization: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Data curation: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Formal analysis: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Funding acquisition: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Investigation: Maryam Tabibi, Alireza Rasouli, and Ali Monajjemi.
Methodology: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi, Gholam Ali Jafari, Amir Arsalan Asgari, Fateme Kheiri.
Project administration: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Resources: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.

Software: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi
Supervision: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Validation: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi, Gholam Ali Jafari, Amir Arsalan Asgari, Fateme Kheiri.
Visualization: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Writing–original draft: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.
Writing–review & editing: Maryam Tabibi, Alireza Rasouli, Ali Monajjemi.

Competing Interests

The authors declared no conflict of interests regarding the publication of the current article.

Ethical Approval

This study was approved by the ethics committee of Qom University of Medical Sciences (Research Code: 3336).

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