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ANTIBACTERIAL ACTIVITY OF SELECTED PLANTS SPECIES EXTRACT CITED IN THE HOLY QURAN AGAINST CLINICAL ISOLATES

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ABSTRACT

Background Medicinal plants have been regarded as new resources for generating substitutes to antibiotics against the antibiotic-resistant bacteria. Holy Quran is the reference which has described the significance of using plants for curing different diseases in various verses. The goal of this investigation was to evaluate 15 plant extracts cited in Holy Quran against the antibacterial activity and the other bacterial species isolated from humans. Methods: The activities of 15 plants' extract as well as some antibiotics against Escherichia coli, Staphylococcus aureus (MRSA), Klebsiella pneumonia, and Shigella sonnei were assessed through in vitro experiments. The activity against 4 isolates of each bacterium was identified by well diffusion method. For identifying the minimal inhibitory concentrations (MICs) of the plant extracts, Microdilution susceptibility assay was applied. Results: Among the evaluated plants, methanolic extract showed anti-bacterial activity and water extract indicated no activity. The minimum inhibitory concentration (MIC) values of these crude methanolic extracts against tested bacterial strains were indicated to range between 0.05 to 12.5 µl/ml. It was found that all the examined extracts prevented the activity against the bacterial strains ($p < 0.05$). Conclusion:15 plant extracts cited in Quran were found that could act as the bactericidal agents against Gram-negative and Gram-positive bacteria, and the potential candidate species to develop the novel veterinary drugs with low cost and few side effects. More research studies are required to investigate the novel antibacterial bioactive molecules.

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Introduction

In ancient times, fruits were regarded to be endowed with magic or divine properties. Fresh and dry fruits have been regarded as good medicine as they contained substantial of the essential nutrients and they have been excellent sources of minerals, vitamins and enzymes which are easily digestible, and they can clean the blood and the digestive tracts [1]. Over the last decade, there has been a shift in the focus of cancer research toward how the body's immune defense system can be used to support the effectiveness of living cells' anticancer therapies [2]. The infections have still been considered as the major causes of morbidity and mortality in cancer patients [3]. In most cases, not only the cancer can change the immune system, but also the cancer treatment. The treatments can cause short or long-term damages. The infection in cancer patients has been defined as a balance between the safety of host defense and the density of the exposure to pathogenic microorganisms in the host's environment. Damage to the host defense would increase the risk of infection in cancer patients. These defense means included the humeral immunity such as the immunoglobulins, cell-mediated immunity monocytes/ macrophages and those related to the hosts' integument as a skin and mucous membranes. Host defense safety may be compromised by several factors involving the patients' pre-morbid health and performance status, factors related to the cancer, and the anti-cancer treatments [4]. Moreover, thousands of plants species have been found against many bacterial strains. The extracts from medicinal plants and pure compounds have been active against Gram-positive and negative bacteria [5]. Recently, plant materials or their extracts as substitute and supportive medicine have been used increasingly, and several antimicrobial agents have been discovered and identified. Medicinal plants contain phytochemicals like flavonoids, tannins, terpenoids, and glycosides that impose

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antibacterial activities against Gram-positive and Gram-negative bacteria [6]. Plants produce an enormous array of phytochemicals arising from various biosynthetic pathways. More than 200,000 defined structures of phytochemicals have been recognized, and about 20,000 phytochemicals have been identified from edible plant sources such as fruits, vegetables and grains. The phytochemicals are used in pharmaceuticals, pesticides, flavors, perfume, coloring, bio-pesticides and food additives. These plant bioactive compounds are not significant in usual physiological functions, but the significance of special plant bioactive has been well identified for health improving activities such as immunomodulation, prevention of cancer and cardiovascular diseases, anti-aging and anti-diabetics [7]. The Holy Quran is a reference explaining the importance of plants used for different ailments in various Surahs. The importance of different medicinal plants and medicinal culture of Islam have been found, therefore, all of these were used to increase the awareness on the fruit plant species enlisted in Holy Quran and Hadith to increase health of human societies around the world [1]. Many edible and non-edible plants such as ginger, pomegranate, grape and banana, which have been cited in the Holy Quran, have been used as remedies for various ailments such as cough, intestinal bleeding and diarrhea. Therefore, plants mentioned in the Holy Qur'an have been attracted by the botanists, biochemists and pharmacognosists (Natural drug specialists) for research purposes [8]. In the Holy Quran, about nineteen medicinal plants have been identified. These plants include camphor, date palm, fig, ginger, grape, garlic, lentil, olive, onion, pomegranate, sweet basil, athel tamarix, tooth-brush tree, mustard, cucumber, arak, summer squash, acacia and cedrus. Thus, this study has discussed two main fields; which were (1) the antibacterial activity of some plants that have been cited in the Holy Quran, (2) the determination of the lowest concentration of these plants which inhibit visible growth of bacteria.

Materials and Methods

Source of microorganisms

Pathogenic bacteria used in this study as test organisms were obtained from king abdulaziz Hospital, Jeddah, Saudi Arabia.

Collection of Plant Materials

A total of 15 plant materials (8 fruits, 5 vegetables and 2 types of grains) were chosen from those cited in the holy Quran. These food items were purchased from local markets in Makkah, Jeddah and Taif, Saudi Arabia, during summer 2017.

Preparation of Plant Extracts

Water Extraction

Five gram of each ground plants was weighed, and 50 ml of distilled water was added, and then the mixtures were shaken. Then, the mixtures were heated and brought to boil three times. After that, the mixtures were left until cooled and filtered through a filter paper (no. 1). The centrifugation and filtration processes were repeated three times and stored in falcon tube (50ml) at -20^{0}C until analyzed within two weeks.

Methanol Extraction

Five gram of each ground plants was weighed and 50 ml of methanol was added and left the whole night in dark place. Then, the mixtures were filtered through a filter paper (no. 1) into a small beaker (50ml), and the methanol was evaporated in a freeze-dryer. After that, 2 ml of Dimethyl sulfoxide was added to the mixtures to dissolve all the samples and scratch if necessary. Then, the samples were kept in Eppendorf tube (2ml) at -4^{0}C until analyzed within two weeks.

Determination of Antibacterial Activity

Bacteria were taken and shaken in the sterile distilled water corresponding to 10^8 CFU/ml. Nutrient Agar medium was used for growing bacteria. About 500 ml of the sterilized medium was poured into each sterile Petri-dish (7 cm diameter) and allowed to solidify. 0.1ml of the prepared bacterial suspension was spread evenly onto the agar surface using sterilized cotton swab, and left aside for 2 hours. Wells (7mm) were cut into the plates using sterile cork borer and 50µl of plant extracts was placed into each wells. All the prepared plates were incubated at 37°C for 24 hours. The diameter of the resulting inhibition zone (mm) around the wells was measured, and the mean value of three readings was calculated and taken as a criterion for the antimicrobial activity.

Determination of Minimum Inhibitory Concentration (MIC)

MIC was determined as the lowest concentration of extracts that inhibited visible growth (turbidity) of the test organisms after 24h [9]. The minimal inhibitory concentration was determined using Broth microdilution method. The tested bacterial samples were used to evaluate the inhibitory activity of plant extracts. Seeded broth corresponding to 10^8 CFU/ml with some drops of phenol red indicator was added into 12 wells in a microtiter plate (50µl/well), then 50µl of the selected plant extracts was added to the well number 1, and the mixture was mixed. For serial dilution, about 50µl of the well number 1 was transferred to the well number 2 and then, diluting the mixture was kept on. The last well number 12 served as the growth control. Then, the microtiter plate was incubated at 37°C for 24 hours in the shaking incubator. MIC was determined by changing the broth color from yellow to pink. The experiment was carried out in triplicates.

Statistical analysis

Each test was performed in triplicate, and all data analysis was expressed as a mean ± standard deviation. The significant differences between means were analyzed statistically using tow-way analysis of variance (ANOVA) according to Dunnett new multiple-range test through SPSS 17.0 (SPSS Inc., Chicago, USA) software package in Microsoft Windows 8.0 operating system. The differences were considered significant when $p < 0.05$.

Results

Antibacterial Activity of the Plants:

The antibacterial activity was detected using agar well diffusion assay. The plates were incubated 37°C for 24h then, the inhibition zones were measured by using millimeters. All the experimental data were determined in triplicate. Table (1) shows the zones of inhibition for water extracts obtained for different tested bacteria. From the results illustrated in the table, the antibacterial actions of the water extract were stronger on *Klebsilla pneumonia* comparing to the others. The highest inhibition zone for *Klebsilla pneumonia* was 3 mm for red grape, followed by 1.8 mm for ginger, and 1.5 mm for pomegranate, fig, gourd and onion; and the lowest inhibition zone was 0.7 mm for black olive. For *Shigella sonni* only ginger (1.5 mm), garlic (1.2 mm) and wheat (0.9 mm) had antibacterial activities. For *Escherichia coli,* the antibacterial activity was recorded for garlic (1.5 mm), white grape, red grape and gourd (0.9 mm) and ginger (0.8 mm), no activity was recorded for MRSA.
Table (1) shows the antibacterial activity of the methanolic extract. The maximum inhibitory effect was recorded for *Klebsilla pneumonia* for onion (3 mm) followed by date for *Escherichia coli (*2.9 mm) and the minimum inhibitory effect was recorded for date (0.8 mm) for MRSA. All the extracts were found to significantly inhibit the antibacterial activity.

Table 1: The Antibacterial Activities (diameter of inhibition zone (IZD mm)) of methanol and water extract of 15 tested plants against pathogenic bacteria.

Scientific name		Common name	Pathogenic isolates							
			MRSA (Gram positive)		Shigella sonnei (Gram negative)		Escherichia coli. (Gram negative)		Klebsiella pneumonia (Gram negative)	
			Water Extract	Methanol Extract	Water Extract	Methanol Extract	Water Extract	Methanol Extract	Water Extract	Methanol Extract
1	Allium cepa	Onion	NI	1.5±0.0	NI	1.4±0.1	NI	1.03±0.05	1.5±0.7	3±0.0
2	Vitis vinifera	Red grape	NI	0.9±0.16	NI	NI	0.9±0.0	2±0.7	3±3.49	0.9±0.15
3		White grape	NI	0.9±0.19	NI	NI	0.9±0.05	2.3±0.2	1±0.1	1.02±0.15
4	Phoenix dactylifera	Date	NI	0.8±0.15	NI	NI	NI	2.9±0.5	NI	2.7±0.3
5	Cucumis sativus	Cucumber	NI	1±0.0	NI	1±0.17	NI	2.1±0.2	NI	2.6±0.11
6	Musa cavendish	Banana	NI	0.9±0.13	NI	1.02±0.01	NI	NI	1.1±0.4	2.6±0.4
7	Ficus sycomorus	Fig	NI	1.1±0.05	NI	1.1±0.04	NI	2.5±0.4	1.5±0.05	2.5±2.5
8	Cucurbita pepo	Gourd	NI	NI	NI	1±0.02	0.9±0.1	0.8±0.1	1.5±0.11	2.5±0.5
9	Zingiber officinale	Ginger	NI	1.4±0.01	1.5±0.25	1.4±0.05	0.8±0.3	NI	1.8±0.4	1±0.05
10	Punica granatum	Pomegranate	NI	1.3±0.11	NI	1.2±0.15	NI	1.5±0.05	1.5±0.0	1.1±0.0
11	Allium sativum	Garlic	NI	NI	1.2±0.1	1±0.0	1.5±0.05	NI	1.4±0.5	1.5±0.7
12	Lens culinaris	Lentil	NI	0.9±0.05	NI	0.8±1.5	NI	NI	0.9±0.05	1.6±0.05
13	Olea europaea	Green olive	NI	1.2±0.14	NI	1.2±0.3	NI	NI	1±0.11	1.01±0.01
14	Triticum durum	Wheat	NI	0.8±0.11	0.9±0.4	0.8±0.17	NI	1.1±0.15	0.9±0.32	1.2±0.4
15	Olea europaea	Black olive	NI	NI	NI	NI	NI	0.9±0.2	0.7±0.05	1±0.02
Antibiotic Agent 1 (Imipenem IMI)			_____	_____	3.3±5.4	3.3±5.4	3.9±0.05	3.9±0.05	3.4±0.1	3.4±0.1
Antibiotic Agent 2 (Vancomycin VAN)			1.6±0.0	1.6±0.0	_____	_____	_____	_____	_____	_____

NI: no inhibition

Determination of the minimum inhibitory concentration (MIC)

MICs for methanolic and water extracts were determined for all the tested bacteria using broth microdilution method.
The MICs of the plants' extracts were carried out using pathogenic bacteria that were sensitive to the previous extracts. The results have been presented in Table (2). The growth of the bacteria was measured after 24h, and the MICs of the plants' extracts for the tested bacteria were calculated and compared. The MICs of the tested plants ranged from 0.05 to 25 µg/ml.

Table 2: MIC expressed in µg/ml of methanol and water extract of 15 plants against some pathogenic bacteria

Scientific name		Common name	Pathogenic isolates							
			MRSA (Gram positive)		Shigella sonnei (Gram negative)		Escherichia coli. (Gram negative)		Klebsiella pneumonia (Gram negative)	
			Water Extract	Methanol Extract	Water Extract	Methanol Extract	Water Extract	Methanol Extract	Water Extract	Methanol Extract
1	Allium cepa	Onion	_____	0.78	____	0.78	____	0.05	12.5	0.39
2	Vitis vinifera	Red grape	____	1.56	____	____	25	1.56	12.5	0.39
3		White grape	____	6.25	____	____	25	0.78	12.5	0.78
4	Phoenix dactylifera	Date	____	1.56	____	____	____	0.78	____	1.56
5	Cucumis sativus	Cucumber	____	0.78	____	0.78	____	1.56	____	1.56

6	Musa cavendish	Banana	____	6.25	____	0.78	____	____	25	1.56
7	Ficus sycomorus	Fig	____	3.12	____	1.56	____	1.56	25	0.78
8	Cucurbita pepo	Gourd	____	____	____	1.56	25	1.56	25	0.78
9	Zingiber officinale	Ginger	____	0.78	12.5	3.12	25	____	25	1.56
10	Punica granatum	Pomegranate	____	1.56	____	0.78	____	1.56	25	1.56
11	Allium sativum	Garlic	____	____	6.25	6.25	12.5	____	25	1.56
12	Lens culinaris	Lentil	____	12.5	____	12.5	____	____	25	6.25
13	Olea europaea	Green olive	____	1.56	____	0.78	____	____	12.5	0.78
14	Triticum durum	Wheat	____	12.5	25	12.5	____	12.5	25	1.56
15	Olea europaea	Black olive	____	____	____	____	____	6.25	25	6.25

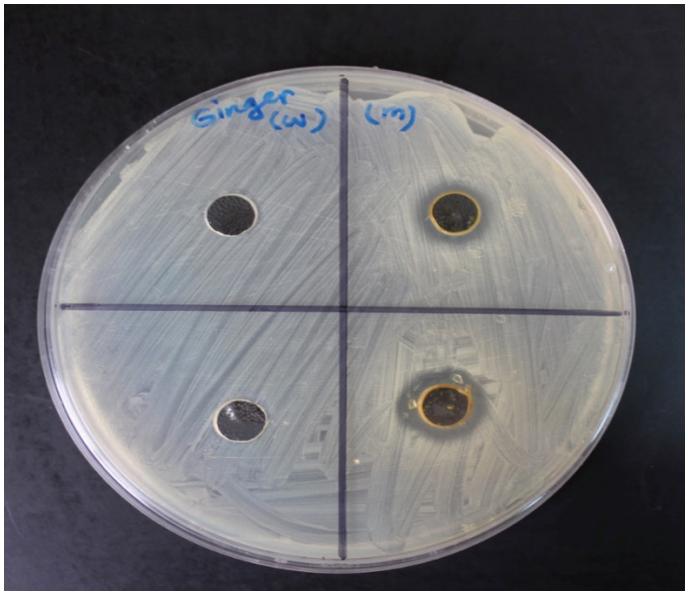

Figure 1: The antibacterial activity of plant extract against MRSA (1) Water extract, (2) Methanol extract

Discussion

The oldest health care known to humanity has been controlling infectious diseases using medicinal plants. Medicinal vegetables are still playing a pivotal role in the health care system, regardless of the large advents occurring in the field of modern medicine. Meanwhile, the bioactive compounds have been examined for medicinal plants which may vary in various agents [10]. Phytochemicals are safe and low cost source of many compounds which are beneficial for human health such as anti-inflammatory, antimicrobial, antihypertensive, and antidiabetic effects and also, they are effective in a large number of microorganisms. Medicinal plants may have the ability as many types of antibiotics in treating bacterial resistance [11]. The emergence of the antibiotic resistance has encouraged researchers to use medicinal plants, not only to determine the claims of the effectiveness and safety, but also to discover the substitute candidates for drug development. In the same regard, this study indicated that the methanol and water extracts of some plants that have been cited in the Holy Quran were against the antibacterial activity.

The preventive influence of fruits and vegetables may be due to their natural antioxidant, vitamins, carotenoids and polyphenols [12].

Fruits and vegetables contain polyphenol which enhances the antioxidant status, and reduces the oxidative DNA damages, and stimulates the immune cell functions because of their natural antioxidants which can scavenge free radicals, which are responsible for the oxidative damage of lipids, proteins, and nucleic acids [13]. The selected plants, cited in the Holy Quran, were (fig, pomegranate, onion, garlic, red grape, white grape, lentil, wheat, black olive, green olive, banana, gourd, cucumber, date and ginger). Most of the previous plants have been well known to be used to treat some diseases.

The natural antioxidants' rich and healthy compounds which can be found in the fruits, flowers and many plants can scavenge the free radicals. The factors influencing the active constituents and efficacy of the plants used included the location of plants, the time of collection, the climate, the soil, and the propagation method [14]. In the current research, some plants which were traditionally used, were collected and studied to examine the availability of their use as the antibacterial agents. The antibacterial activity was measured by the inhibition zone diameter and agar well diffusion method. The present technique was used to measure the antibiotic activity [15]. In addition, the minimum inhibitory concentration (MICs) has been determined

by the microdilution method on the selected plants' extracts. The definition of minimum inhibitory concentration (MIC) was the lowest concentration of the extracts for inhibiting the visible growth of each microorganism on the agar plate. The MIC has been the most basic parameter in pharmacokinetics and pharmacodynamics. Excellent antibacterial activity (inhibition zone diameters, IZD) against all the tested bacteria was recorded for methanolic extract, and no activity was recorded for the water extract except against *Klebsiella pneumonia*. In this study, the antimicrobial activity was evaluated, and it was compared with the standard antibiotics Imipenem IMI and Vancomycin VAN which showed that the IZD values were between 3.9 to 1.6 mm

The results from 15 plants showed that the MIC value of the methanolic extract and the water extract indicated the antibacterial activity which ranged from 0.05 µg/mL to 12µg/m and 6.25 to 25 µg/mL; respectively.

From the present results, the extract of onion, red grape and date showed a wide spectrum activity on different antibiotic resistant isolates. This might be due to the presence of polyphenols such as phenolic acids, flavonoids, anthocyanidins, tannins, and organosulfur compounds found in onion, which inhibited the bacterial growth. The antibacterial activities of onions have been checked against all the tested bacteria. Characteristic aromas and flavors of onions (*Allium cepa*) which have been important ingredients of foods and the organic sulfur containing compounds are the medicinal components of onion oil. Onion has high antibacterial activity against all the tested bacteria. In this research, the methanolic extract of onion inhibited the growth of *Klebsiella pneumonia* and *Escherichia coli* with MICs ranged from 0.39µg/ml and 0.05µg/ml; respectively. The result from the onion essential oils showed that the antibacterial activity could be mainly due to the organosulfur containing compounds, such as methyl 5- methylfuryl sulfide, methyl 3,4-dimethyl-2-thienyl disulfide and 1-propenyl propyl disulfide. Similar to the current result, Ye *et al.* 2013 indicated that the onion essential oil showed a moderate antibacterial activity against *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus* and also possessed an interesting antioxidant activity[16]. Other results indicated the onion extract as a natural antioxidant additive, and antimicrobial agent for functional foods with potential applications in the medical and food industries [17]. The *Allium* family has been widely used as exhibiting antioxidant and antibacterial effects containing the organosulphur compounds. The onion essential oil can be used in packaging in the food industry. The reactive oxygen species scavenger activity was observed in the onion essential oil compound. Reports indicated that the grapes (*Vitis vinifera*) have been a rich source of phenolic compounds, such as anthocyanins and flavonoids [18]. Also, it has been reported that phenolics compounds in grape extract is the most important active compound against the bacteria. Peng et al. 2008 showed that the extracts from grapevines had antimicrobial activities because of Gram- positive pathogens [19]. The results of this study indicated that red grapes showed high antibacterial activity than white grape; these results were similar to Yilmaz et al. 2015 who indicated that the red grape varieties generally had higher total phenolic contents and antioxidant activity values than white varieties and also, it was reported that phenolics have been the most important compounds in grape extracts acting against the bacteria [18]. Gibbons 2004 found that the phenolics compounds as anti-Staphylococcus were phenylpropanoids, flavonoids and stilbenoids. Stilbenes, a kind of phytoalexin, such as resverarol, pterostilbene were synthesized using grape leaves, and acted as defense in plant tissues [20]. In this research, the methanolic extract of grapes inhibited the growth of *Klebsiella pneumonia* and *Escherichia coli* with MICs ranged from 0.39µg/ml and 1.56µg/ml; respectively while it was 1.56µg/ml for MRSA, and there was no activity on *Shigella sonnei.* Grapes contained several compounds performing antibacterial activity including gallic acid, hydroxycinnamic acids, flavanols, flavonols, trans-resveratrol, and tannins [21]. Rhodes et al. 2006 studied the activity of grape juice and grape extracts, and also the results documented that the grape juice was inactive against B. cereus, Salmonella Menston, E. coli, and S. aureus [22]. Moreover, the grape seeds were rich in phenolic compounds such as catechins and epicatechins, and had numerous antiviral and antimutagenic properties. Jayaprakasha et al. 2003 reported that all the grape seed extracts were antibacterial against Bacillus spp., S. aureus, E. coli, and Pseudomonas aeruginosa [21].

In the present study, the methanolic extract of date had the antibacterial activity against all bacteria except for *Shigella sonnei*. The highest IZD antibacterial activity was against *Escherichia coli* with inhibition zone of 2.9 mm, and the lowest was against MRSA 0.8 mm. However, the water extract was not active for the all. The dates (*Phoenix dactylifera*) had high nutritional value which might cause it to be rich in fructose, glucose, and sucrose. In addition, dates have contained a variety of polyphenols, including phenolic acids, hydroxycinnamates, flavonoid glycosides, and proanthocyanidins [23]. From the obtained results, it seemed that the date fruit possessed a potential antioxidant activity which was attributed to phenolic compounds, flavonoids and procynadins and also vitamin C. Due to the presence of these components, the date fruit has been used in the treatment of various infectious diseases [24].

Polyphenols have had significant antibacterial activity through the precipitation of proteins and the inhibition of enzymes of microorganisms. [25]. Carotenoids and anthocyanins in dates' variety increased their value with increasing the ripening stages. Lutein compound has been the major carotenoids in dates' varieties followed by β-carotene [26].

Cucumbers (Cucumis sativus) from Cucurbitaceae family were rich in cucurbitacins due to their medicinal and toxic properties. In folk medicine, cucurbitacin-containing plants have been used for their antipyretic, analgesic, anti-inflammatory, antimicrobial and antitumor activities [27]. In this study, the highest antibacterial activity, caused by cucumber extract was against *Klebsiella pneumonia* with inhibition zone of 2.6 mm, and the lowest was against MRSA 1 mm. However, the water extract was not active for all. Sotiroudis *et al.* 2010, showed the same results on extracts of the pulp and the peel of cucumber which were studied against six Gram negative and Gram positive bacterial strains and three human-pathogen fungi. The results

showed the interesting and promising antibacterial activities. The accumulation of Cucurbitacins in fruits was higher, and more antibacterial activity was suggested for this part compared to the roots and leaves [28]. The results showed that the MRSA, *Shigella sonnei* and *Klebsiella pneumonia* were susceptible to the methanolic extract of banana with the inhibition zone of 0.9–1.02–2.6 mm; respectively. The *Klebsiella pneumonia* was susceptible to the water extract with the inhibition zone of 1.1 mm. Banana *(Musa Cavendish),* a tropical fruit belonging to *Musaceae* family, is grown in many countries all over the world. All parts of banana plant such as flower, pulp, stem, and leaves have a medicinal application[29]. Naikwade *et al*. 2014 reported that banana leaves exhibited antibacterial properties against *Escherichia coli* and *Staphylococcus aureus* [29]. According to Mokbel and Hashinaga 2005 who found that the extractions of green banana peel using ethyl acetate and water-soluble were rich in antioxidant and were antimicrobial. The compounds ß-sitosterol, malic acid, 12-hydroxystrearic acid and succinic acid were isolated from green peel, and their antibacterial activity was increased, and the antioxidant activity was decreased. While, the water soluble extracts contained compounds consisting of glycoside and monosaccharide components which had low antimicrobial activities [30].

Amutha and Selvakumari 2014 stated that the phytochemical analysis of methanolic banana stem extract showed the presence of effective biological activities. The compounds (alkaloids, glycosides, flavonoids, tannins and phenols, and saponins) could potentially be anti- microorganisms [31]. Fig (Ficus sycomorus) contained numerous bioactive compounds such as arabinose, β-amyrins, β-carotines, glycosides, β-sitosterols and xanthotoxol [32].

Fig products have been widely used both as food and as medicine in the Middle East. The aqueous extract of dried fig contain alkaloids, flavonoids, coumarins, saponins, and terpenes. Phenolic compounds have the biological activities like astringent, antioxidant, anticancer, anti-inflammation, and antibacterial activities [33]. Figs are rich in minerals including potassium, calcium, iron, magnesium and zinc which build bones. They have been shown to shrink tumors. The juice fights parasites and bacteria. The studies illustrated that figs contain important antioxidants and anti hepatotoxicity in preventing oxidative disadvantage in the tissues by inhibiting the production of free radicals in rats [34]. In this study, IZD of figs was 2.5mm which was nearly similar to the inhibition of the antibiotic Imipenem IMI control, the antibacterial activity of fig methanolic extract showed strong activities against *Escherichia coli*, *Staphylococcus aureus* (MRSA), *Klebsiella pneumonia*, and *Shigella sonnei* (MIC from 0.78µg/ml to 25µg/ml). Several studies showed that some flavonoid compounds act against the activity of oral bacteria [35].

Gourd (*Cucurbita pepo*) belongs to the family of *Cucurbitaceae*. It has been traditionally consumed in several countries such as India, China and America as antdiabetic and antihyperlipidemic, antitumor, antihypertensive, anti-inflammatory, immunomodulatory and antibacterial agents, and the seeds have also been used as anthelmintic, diuretic and nervine tonics, in nervous debility and also used as abortifacient and insecticidal medicines [36]. Gourd gives scavenging capacities due to the presence of flavonoid and phenylpropanoid glycoside-compounds known as potential hydrogen donors and radical scavengers. Phytochemical analyses of gourd extracts have revealed the presence of tannins, flavonoids, saponins, cyanogenic glycosides and cardiac glycosides. These extracts were used as food additives and supplements, and for the treatment of the bacterial infections. Also, it contained antioxidant beta-carotene, which helped to improve the immune function and reduce the risk of diseases like heart diseases and cancers [37]. Gourd extract has antibacterial activity against *Klebsiella pneumonia and Escherichia coli* with the inhibition zone ranged from (0.8-2.5 mm), and *Shigella sonnei* was inhibited only by methanol extract with the inhibition zone of (1 mm). Al-Ghazal 2012 reported that alcoholic and aqueous cortex of gourd possessed antibacterial activity against multiresistant pathogenic bacteria that infected the human urinary tracts [38].

On the other hand, Chonoko & Rufai 2011 reported that the methanol extract was active against *Staphylococcus aureus*, but *Staphylococcus typhi* was inactivated at 500 >g/disc. Meanwhile, both ethanol and methanol extracts had increased activity against *Staphylococcus aureus*, but they were inactive against *Staphylococcus typhi* [39]. Moreover, Nair *et al*. 2011reported that gourd showed significant antimicrobial activity against *Escherichia coli* and *Bacillus subtilis*. As the number of hydroxyl groups on flavonid group has been connected to their relative toxicity to the bacteria which intensified the hydroxylation results increasing the toxicity, the flavonoids compounds acted against the bacteria effectively [40].

Ginger (Zingiber officinale) has been used as antimicrobial might be due to its essential oils, such as camphene, linalool, α-pinene, and borneol. In general, ginger activity has been higher against the Gram-positive bacteria. The extracts from ginger rhizome contained many components inhibiting the growth of Gram-negative and Gram-positive bacteria, and also, respiratory tract pathogens and influenza [41]. In this investigation, ginger showed antibacterial activity against all tested bacteria with IZD ranged from 0.8-1.8 mm. The antibacterial action of ginger might be caused by the weakness of cultivar of enzymes systems which caused the production of energy or synthesis of the structural components in the microbial cells. These results agreed with Park et al. (2008) who found that 10-gingerol and 12-gingerol were extracted from the ginger rhizome which proved potent antibacterial activities in vitro as anti anaerobic bacteria related to the periodontitis of the human oralcavity [42]. Moreover, Sharifi-Rad et al. 2017 showed the ginger efficacy against more bacteria. Furthermore, 6-gingerol and 12-gingerol indicated antibacterial activity against periodontal bacteria [43].

In recent years, Pomegranate (Punica granatum L.; Punicaceae) has been used to treat different ailments such as cuts, sore throats, tapeworms, dysentery, and gum diseases. It also possessed antibacterial, antioxidant, anti-atherosclerotic, anti-inflammatory and anti-allergic properties [44]. This activity has been caused by antioxidant polyphenols, including ellagitannins (hydrolyzable tannins) and anthocyanins (condensed tannins). Punicalagins are the major ellagitannins in the

fruits and can be hydrolyzed to ellagic acid and smaller polyphenols. In this study, pomegranate indicated moderate antibacterial activity against all tested bacteria. The methanolic extract of pomegranate inhibited the growth of *Shigellasonnei* with MIC0.78µg/ml. Several compounds were responsible for the antibacterial action; Tannins have been considered to inhibit microorganisms [45]. Mathabe et al. 2006 showed that the methanol, ethanol, acetone, and water extracts obtained from pomegranate were active, and the inhibition of the microorganisms may be caused by the phenols that may also render substrates unavailable to microorganisms or overlap with the bacterial protein secretions. [46]. It has been indicated that the phenolic compounds of pomegranate have a lot of prophylactic and therapeutic utilities against several pathological infections as well as non-infectious disorders. Pomegranate extracts are one among the many herbs that are available, and have been reported to have huge medical value. In ayurvedic medicine, the pomegranate has been seen as "a pharmacy unto itself "and has been used as a "blood tonic," to heal many health problems. The polyphenols which are extracted from the pomegranate have many good properties such as antibacterial, antioxidant, anti-inflammatory, antiproliferative, and DNA repair activities and thus can be used as a good alternative for systemic drugs [47]. Abdollahzadeh *et al*. 2011, reported that antibacterial effect of pomegranate is because of the presence of hydrolysable tannins and polyphenols such as punicalagin and gallic acid. These specific components act on bacterial cell membrane and increase the bacterial cell wall breakage, prevent adhesion of bacteria to the tooth surface, precipitate the protein, and inhibit several bacterial enzymes [48]. In a study done by Bhadbhade *et al*. 2011, the growth of anaerobic periodontal pathogens such as *Aggregatibacter actinomycete mcomitans*, *Prevotella intermedia*, and *Porphyromonas gingivalis* has been shown to be inhibited by pomegranate mouthwash. The study also demonstrated that pomegranate extract as a mouthwash resulted in more reduction of gingival and bleeding scores when compared to chlorhexidine mouthwash [49]. Recent studies have indicated that the extracts have been obtained from pomegranate aril and peel inhibition microorganisms activity, as the inhibitory effect on the bacterial growth of two important human pathogens, including Staphylococcus aureus and Escherichia coli, often involved in food borne illnesses [50]. Additionally, the experimental data have potently affirmed the antibacterial activity of pomegranate extracts against oral pathogen like *Streptococcus mutans*. Although, not much has been found out about the influence of pomegranate extracts on the other pathogens causing tooth decay like *Rothia dentocariosa*, which has been the first bacterium isolated from carious dentin [51]. In dentistry, the use of pomegranate has been more frequently reported in the control of forming biofilm microorganisms. Vasconcelos *et al*. 2006 evaluated the antimicrobial activity of pomegranate extracts and determined the minimum inhibitory concentration at the concentrations of 5% and 10% against the strains of *Candida albicans*, *Streptococcus mutans, and Streptococcus mitis*[52].

Allium sativum (garlic) is an important spice with medicinal properties common to most cuisines all over the world. This spice has been individually considered as general remedies for many diseases. [53] named antimicrobial, anticancer, antioxidant, antidiabetic, antiemetic, antihypertensive, hypoglycemic, hypolipidemic, and immunomodulatory as several biological activities of these spices. Phytochemical studies of this spice have shown that they are rich in alkaloids, tannins, carotenoids, saponins, phenols, and flavonoids and they have been reported to exhibit high antioxidant activities. In the present study, methanolic and water extract of garlic had no activity on MRSA. However, garlic extract has antibacterial activity against *Klebsiella pneumonia* and *Shigella sonnei* with the inhibition zone ranged from (1-1.5 mm), and *Escherichia coli* was inhibited only by water extract with the inhibition zone of (1.5 mm). Garlic showed the highest antibacterial activity in water extracts which might refer to its water-soluble organosulfur compounds that were found in allicin. Allicin is the inhibitor of the bacterial Acetyl-CoA-forming system, consisting of acetate kinase and phosphortransacetylase as well, it was found to be specific to the enzymes of the fatty acid synthesis sequence. There are different physiological processes in microorganisms, which were affected by allicin as lipid biosynthesis and RNA synthesis [54]. The most important antimicrobial impact of allicin has been because of its chemical reaction with enzymes as alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, which can influence the essential metabolism of cysteine proteinase activity. *Streptococcus mutans*, a Gram-positive, which is a facultative anaerobic microorganism causes dental caries which is an irreversible chronic disease [55]. For years, prohibiting and controlling dental caries have been considered a big problem. The garlic extract prevent Gram-positive and Gram-negative bacteria. The cut or crushed garlic cloves activate the enzyme alliinase which changes alliin to allicin which is responsible for antibacterial activity.

In a study by Jehan Bakht 2011, the aqueous and methanolic extracts of garlic exhibited *Staphylococcus aureus* and *Pseudomonas aeruginosa* at a concentration of 2 mg/disk [56]. While in a study by Gull *et al*. 2012, the aqueous and methanolic extracts of garlic exhibited antibacterial activity against both *Staphylococcus aureus* and *Pseudomonas aeruginosa* at an MIC of 0.5-1 mg/ml[57]. In addition, in a study by Abubakar, 2009, aqueous and ethanolic extracts of garlic exhibited antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, with MICs of 50 mg/mL for *Staphylococcus aureus* and 125 mg/mL for *Pseudomonas aeruginosa*. In addition, the aqueous extract had a stronger antibacterial activity [58].

According to the results of this study, lentil showed antibacterial activity against *Klebsiella pneumonia, Shigella sonnei* and MRSA tested bacteria except for *Escherichia coli*with inhibition zone from 1.6 mm 0.8 mm and 0.9mm; respectively. Similarly, Nair *et al*. 2013 showed that lentil lectin is an effective bacteriostatic agent, which helps in decreasing the growth of bacteria. Lentils *(Lens culinaris)* are a source of polyphenolic compounds with health- promoting properties. Lentils contain the highest of total phenolic content than the other legumes. Lentils polyphenolic-rich have health benefits as complementary and alternative medicines [59]. A bioactive peptide called "defending", which has been isolated from germinate lentil seeds

contains phenolic acids compounds acting as the inhibitor of microbial growth. The therapeutic utilities of *O. europaea* have been indicated in traditional medicine. Olive *(Olea europaea*) fruits contain appreciable amounts of phenolic compounds.
Olive fruits are rich in phenolic acids, phenol alcohols, flavonoids and secoiridoids. The latter group being characteristic of the oleaceae family [60]. The results of this study showed that green olives were more effective against bacteria than black olives. Green olives showed antibacterial activity against *Klebsiella pneumonia, Shigella sonnei* and MRSA tested bacteria except for *Escherichia coli* with the inhibition zone from 1.01 mm 1.2 mm and 1.2mm; respectively. Benincasa *et al.* 2014 showed that a metabolite from oleuropein was effective against *staphylo-cocci*, and could therefore be a potential source of natural antimicrobials for the treatment of skin infections [61].
In addition, Liu *et al.* 2017showed that the crude olive leaf extract was effective in inhibiting the growth of the three food borne pathogens including *Listeria monocytogenes*, *Escherichia coli*, and *Salmonella Enteritidis*., providing support that olive leaf extract could potentially be used alone or in conjunction with the other antimicrobials for the purpose of pathogen control in food products [62]. Wheat (*Triticum durum)* is one of the most important crops representing the staple food for about 40% of the world's population. In this study, wheat showed antibacterial activity against all tested bacteria except water extract; the maximum zone of inhibition for wheat was shown on *Klebsiella pneumonia* followed by *Escherichia coli* with the inhibition zone of 1.2 mm and 1.1 mm; respectively. Talas,T (2004) showed that the antimicrobial activity of germinated seeds of wheat was more effective than the dry seeds of wheat [63]. Additionally, Benincasa et al. 2014 confirmed that the whole grains of non-hulled and hulled wheat contained relevant amounts of phytochemicals [60].
Previous studies provided the results for methanol as the best solvent for the extraction of the antimicrobial substances from medicinal plants as compared to water and ethanol. Therefore, the methanol extracts of all of the examined plants had a significant antibacterial activities compared with the activity of the water extracts. The water fruit extracts of most of plants lacked antibacterial activity which might be either due to the polarity of the antibacterial compounds that make them more readily extracted by the organic solvents, or active compounds may be present in insufficient amount in the crude extract to show the activity with the employed dose level. Finely, there could be other constituents present in the extract exerting antagonistic effects of the bioactive compounds [63].

Conclusion

The reports of many studies about 15 plants mentioned in the Holy Quran and their extracts have provided a long-established use of these plants as a therapy for the comfort and cure for many problems, and also some other serious diseases. In this study, it was found that these plants contain rich compounds which can be used as antioxidant, antimicrobial and some other therapeutic purposes.

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