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A Review on Native Medicinal Plants in Khuzestan, Iran with Antibacterial Properties

S.M. Seyyednejad and H. Motamedi
Department of Biology, Faculty of Science, Shahid Chamran University, Ahvaz, Iran

INTRODUCTION

Infectious diseases have been a life threatening problem for humans before antibiotic era. Fortunately, since discovering the penicillin by Fleming infection control became possible and mortality from infectious diseases has been significantly reduced. But parallel to antibiotic usage, bacterial resistance to antimicrobial agents has been emerged and become an out growing problem in the treatment of bacterial infections. This is due to the alteration of resistance mechanisms, acquisition of resistance genetic element from other bacteria and genetic changes in bacteria (Lengeler *et al*., 1999, Summers, 1996). In recent years, antibiotic resistance has become a global concern and this problem is more important especially in developing countries because infectious diseases are still an important causes of morbidity and mortality among humans in these countries. Infectious diseases account for about half of the death in tropical countries (Khosravi and Behzadi, 2006). Besides, incidents of epidemics due to drug resistant microorganisms pose enormous public health concerns (Jensen *et al*., 1996; Burt and Reinders, 2003). Therefore, due to alarming increase in the rate of infections with antibiotic resistant microorganisms and due to side effects of some of synthetic antibiotics, there is an increasing interest in medicinal plants as a natural alternate to synthetic drugs (Doughari, 2006; Duke, 1985). Herbal remedies used in the traditional folk medicine provide an interesting and still largely unexplored source for the creation and development of potentially new drugs for chemotherapy which might help to overcome the growing problem of resistance and also the toxicity of the currently available commercial antibiotics (Ali *et al*., 2001). Their usage as traditional health remedies is the most popular for 80% of world population in Asia, Latin America and Africa and is reported to have minimal side effects (Doughari, 2006). Antimicrobial activities of various species of plants and their derivatives have been reported by many researches (Ozcan and Erkmen, 2001; Sagdic and Ozcan, 2003). The use of alternative medical therapy has increased the interest of pharmacologists and herbalists over the past decade. Historically, plants have provided a source of inspiration for novel drug compounds, as plant derived medicines have made contributions to human health and well being (El-Astal *et al*., 2005). Many studies indicates that in some plants there are many substances such as peptides, unsaturated long chain aldehydes, alkaloidal constituents, some essential oils, phenols and water, ethanol, chloroform, methanol and butanol soluble compounds (Seyyednejad *et al*., 2008; Alma *et al*., 2003; Klausmeyer *et al*., 2004; Perez, 2003; Holetz *et al*., 2002; Jantan *et al*., 2003; Khan *et al*., 2003). Plants readily synthesize these different substances for their defense against insects, herbivores and a variety of their own microbial pathogens and therefore can serve as antimicrobial substances (Nimri *et al*., 1999; Grayer and Harborne, 1994; Aboaba *et al*., 2006). Also, plants maybe produce secondary antimicrobial metabolites as part of their normal growth and development program or in response to stresses (Skocibusic *et al*., 2004). These plants then emerged as compounds with potentially significant therapeutic application against human pathogens, including bacteria, fungi or viruses (EL-Astal *et al*., 2005; Holetz *et al*., 2002; Perez, 2003). As a result, plants remained the most common source of antimicrobial agents. The antimicrobial compounds from plants may inhibit microbial growth by different mechanisms than those presently used antimicrobial agents and may have significant clinical value in treatment of resistant microbe (Eloff, 1998).

The use of herbs and medicinal plant as the first medicines is a universal phenomenon and the medicinal plants have been used since ancient times. Every culture on the earth, through written or oral tradition, has relied on the vast variety of natural chemistrie's found in plants for their therapeutic properties. All drugs from the plant are substances with a particular therapeutic action extracted from plants (Serrentino, 1991). Evidence of using these natural resources (herbal remedies) in Iran goes back to the history itself and there are lots of scientific documents in this area, Ibn sina has wrote many books on a wide range of topics but he is perhaps most famous for his Laws of Medicines which contains sections on the formulation of medicine, general medicine and other subjects that discuss the herbal medicines in details (Lothfipour *et al*., 2008).

Corresponding Author: S.M. Seyyednejad, Department of Biology, Faculty of Science, Shahid Chamran University, Ahvaz, Iran

Khuzestan province has been located in the Southwest of Iran and have many fertile lands and tropical climate so, there is a divergent herbal fauna in this region. Many of the plants that grow in Khuzestan have been used by natives as folklore remedies for infectious disease control and treatment. With respect to the current tendency for discovering new antimicrobial agents from natural resources, the native plants of this region can be a good choice for research and also for mass production of natural antibiotics. The present manuscript reviews some of most important antimicrobial plants native in Khuzestan.

***Prunus mahaleb*:** The genus *Prunus mahaleb* belongs to the family Rosaceae and comprises more than 400 species. *Prunus mahaleb* commonly known in Europe as santa lucia cherry and in the Arabia as mahleb, has been used in folk medicine as a tonic for sensory organs and the heart, in the treatment of asthma and relief of pains arising from liver, kidney and gastro intestinal troubles (Shams and Schmidt, 2007). The plant has been used in folk medicine in Iran too. The antibacterial effect of *Prunus mahaleb* against some pathogenic bacteria has been investigated by Seyyednejad *et al.* (2008). In this survey the effect of ethanolic extract of *Prunus mahaleb* seeds was assessed by disk diffusion method against total eleven bacterial pathogen. The results showed that this extract had inhibitory activity against *Brucella melitensis*, *Escherichia coli* and *Bacillus licheniformis* in low concentrations, whereas, it showed no activity against *Salmonalla* Typhi, *Bordetella bronshiseptica*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Bacillus pumilus*. The results suggested that antibacterial activity of *Prunus mahaleb* ethanolic extract against *Proteus mirabilis* was decreased when used in lower concentrations, but inhibitory effects of this extract against *Bacillus anthracis* and *Staphylococcus aureus* observed only in 0.4 g mL^{-1}. However, *P. mirabilis* was the mot susceptible organism to the different concentrations of the ethanolic extract *Prunus mahaleb*. With regard to that in hospitals, *P. mirabilis* is the second most frequently isolated bacteria from *Enterobacteriaceae* after *E. coli* (Champs *et al.*, 2000) *Prunus mahaleb* ethanolic extract can be a choice for treatment of *P. mirabilis* infections and also can be considered as disinfectants or antiseptics.

Parsley (*Petroselinum crispum*): Parsley is culinary herb commonly used to flavour the cuisines of China, Mexico, South America, India and South East Asia (Wong and Kitts, 2006). There was a lack of information about the antimicrobial action of Parsley (*Petroselinum crispum*) which is medical plant of the Iran flora and widely used in treating certain disease since Seyyednejad *et al.* (2008) have investigated the antibacterial effect of its seed ethanolic extract against eleven pathogenic strains. Their results indicated that parsley ethanolic extract had inhibitory effect at various concentrations (0.1, 0.2, 0.3, 0.4 g mL^{-1}) against Gram-positive and Gram-negative bacteria. It was also effective in lower concentrations on *E. coli*, *Br. melitensis* and *B. licheniformis*. The ethanolic extract of parsley didn't inhibit the growth of *B. subtilis*, *B. bronshiseptica* and *S. aureus*. However *B. licheniformis* was the most sensitive organism to the various concentrations of this extract. parsley ethanolic extract inhibited the growth of 8 out of 11 bacterial species. It was effective in lower concentrations on *E. coli*, *Br. melitensis* and *B. licheniformis*.

Some researchers have shown that fresh and dried *Parsley* inhibited the growth of *Listeria monocytogenes*, *L. innocua*, *E. coli* O157 H:7, *E. coli* Bs-1 and *E. carotovora* (Manderfield *et al.*, 1997). In another work it has been reported that Gram-positive bacteria were found to be more susceptible than Gram-negative bacteria. This could be due to the fact that the cell wall of Gram-positive bacteria is less complex and lack the natural sieve effect against large molecules due to the small pores in their cell envelop (El-Astal *et al.*, 2005).

Several bioactive flavonoids such as furocoumarins and furanocoumarins (Manderfield *et al.*, 1997) also phenolic compounds have been isolated from parsley leaf and are known to exhibit antibacterial activities (Wong and Kitts, 2006). Furocoumarins can inhibit bacterial growth by reacting with DNA and disrupting DNA replication (Manderfield *et al.*, 1997), thus explaining the observed growth inhibition of bacterial species by Parsley. On the other hand, the hydrophobic character of phenolic compounds can potentially impair cellular function and membrane integrity (Raccach, 1984). The capacity of phenolic compounds to chelate transition metals also lowers the reactivity of metal ion by forming an inert metal-ligand complex. Chelation of transition metals, such as iron and copper, reduces bioavailability for bacterial growth (Jay, 1996).

***Torilis leptophylla*:** The genus *Torilis* comprises species distributed in Europe, North Africa and Southwest Asia. It's represented in Iran by nine species (Bigdeli *et al.*, 2004). *Torilis leptophylla* belonging to the Apiaceae family (Baranski *et al.*, 2006). This plant has been used in folk medicine for the treatment of gastrointestinal (GI) illnesses in Khuzestan, Iran. Till 2008 no pharmacological evidence had been reported to support this claim. Maleki *et al.* (2008) has investigated antibacterial activity

of ethanolic extract fruits of *Torilis leptophylla* against some pathogenic bacteria. They have prepared four concentrations (0.1, 0.2, 0.3 and 0.4 g mL^{-1}) of ethanolic extract from fruits of Iranian *Torilis leptophylla* and by disk diffusion method was assessed the antibacterial effect. Their results suggested that antibacterial activity of *T. leptophylla* alcoholic extract against four bacteria including *E. coli*, *S. typhi*, *P. mirabilis* and *B. anthracis* was decreased when used in lower concentrations. But inhibitory effects of this extract against *B. bronshiseptica* and *S. aureus* observed only in 0.4 g mL^{-1} concentration. Also, the results showed that the extract had inhibitory activity against *Br. melitensis*, *P. aeruginosa*, *B. licheniformis* and *B. pumilus* at 0.2 g mL^{-1}. On the other hand, the ethanolic extract was not active against *B. subtilis* even in the highest concentration used. However, *P. mirabilis* was the most susceptible organism to the different concentration of the ethanolic extracts of *T. leptophylla*. Although, the biologically active components in *T. leptophylla* is not known and needs further analysis but Coumarins, flavonoids and new bisabolane sesquiterpene ester were isolated from the fruit oil of *T. aroensis* growing in Egypt (Bigdeli *et al*., 2004) and may be these active compounds be responsible for antibacterial activity of *T. leptophylla* . The authors have been suggested based on the results of this study this active plant extract could be considered as disinfectants or antiseptics.

Some researchers have shown that the alcoholic extract of *Torilis japonica* had good anti-protozoal activity against *N. caninum* and *T. gondii in vitro* (Youn *et al*., 2004).

***Quercus brantii*:** *Quercus brantii* widely grown in Izeh, Iran and the fruits of the plant have been locally known as Jaft. A decocted extract from *Q. brantii* fruits is used to treat acute diarrhea and inflammation in traditional medicine. Moreover, the decoction of *Quercus* could be also used for burns and cuts (Konig *et al*., 1994). Safary *et al*. (2009), have investigated the antimicrobial property of *Q. brantii* fruit against Bacterial pathogens, particularly enteric pathogens and compared its effects with some current antibiotics. They have tested the antibacterial effect of ethanolic and methanolic extracts at 0.5, 0.1, 0.2, 0.3 and 0.4 g mL^{-1} concentrations of *Q. brantii* fruit against 8 bacterial pathogen. Their results showed that these plant extracts were effective against test organisms. The highest activity was demonstrated by the ethanolic extract of against *Br. melitensis* and *B. bronchiseptica* while the lowest activity was demonstrated by the methanolic extract against *E. coli*. On the other hand, the ethanolic and methanolic extracts were not active against *K. pneumoniae* even in the highest concentration. However, the ethanolic extract showed inhibition action at minimal concentration (0.05 g mL^{-1}) used against *B. bronchiseptica*, *P. aeruginosa*, *P. mirabilis*, *Shigella dysenteriae* and *B. melitensis*. These results suggesting that antibacterial activity of *Q. brantii* ethanolic and methanolic extracts against tested bacteria were increased when used in higher concentrations. Also the methanolic extract generally showed lower activity against the test organisms compared to the ethanolic extract. Furthermore, the MIC and MBC of these extracts have been determined. For methanolic extract, the result showed that *Sh. dysenteriae* had the highest MIC (20 mg mL^{-1}), while the lowest MIC (16 mg mL^{-1}) and highest MBC (32 mg mL^{-1}) were shown by *B. bronchiseptica*. *P. mirabilis* had the highest MIC and MBC values (32 mg mL^{-1}) for the ethanolic extract. The MIC and MBC values for ethanolic extract were generally lower than methanolic extract against the test organisms. The diameters of inhibition zone around the most active extracts were comparable with the standard antibiotics used as a positive control.

A strong anti-staphylococcal activity by the ethanolic extract of this plant was reported by Moghadam *et al*. (2010) and so it can be a selection for finding new anti-MRSA antibiotics.

Tannin is the most abundant active compound in the oak fruits whose major effect is anti-diarrhea because of water absorption and protein precipitation (Khosravi and Behzadi, 2006; Voravuthikunchai and Mitchell, 2008).

***Ziziphus spina-christi*:** The *Ziziphus* species (Rhamnacese) are commonly used in folklore medicine for the curing of various diseases. They are widespread in the Mediterranean Region, Africa, Australia and tropical America. *Z. spina-christi* has been used in folk medicine as a demulcent, depurative, anodyne, emollient, stomachic, for toothaches, astringents and as a mouth wash (Nazif, 2002). *Ziziphus spina-christi* was shown to contain betulic and ceanothic acid, three cyclopeptide alkaloids as well as four saponin glycosides (Mahran *et al*., 1996) and several flavonoids have been isolated from the leaves of *Z. spina-christi* (Amos *et al*., 2001).

Motamedi *et al*., 2009 were designed a study to evaluate the antibacterial activity of ethanolic and methanolic extracts obtained from the leaves of *Z. spina-christi* on selected clinical isolates of enteric bacterial pathogens. They have tested the 0.05, 0.1, 0.2, 0.3 and 0.4 g mL^{-1} concentrations of these extracts against *S. Typhi*, *P. mirabilis*, *S. dysenteriae*, *E. coli*,

K. pneumoniae, *Br. melitensis*, *B. bronchiseptica* and *P. aeruginosa*. Their results showed that these extracts are effective against all of the test organisms. The highest activity was demonstrated by the ethanolic extract of *Z. spina-christi* leaves against *B. bronchiseptica* while the lowest activity was demonstrated by the methanolic extract against *K. pneumoniae*. On the other hand, the ethanolic and methanolic extracts were not active against *E. coli* even in the highest concentration. However, the methanolic extract showed inhibition action at minimal concentration (0.05 g mL^{-1}) against *B. bronchiseptica*, *S. dysenteriae* and *B. melitensis*. These results suggest that antibacterial activity of *Z. spina-christi* ethanolic and methanolic extracts against tested bacteria were increased when used in higher concentrations. Also the methanolic extract generally showed lower activity against the test organisms compared to the ethanolic extract which means that the ethanolic extract could be used more. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) values were 16 and 64 mg mL^{-1}, respectively for the two selected bacteria.

Ethanolic extract of *Z. spina-christi* were effective against MRSA strains and its effect were high in comparison to other tested plants (Moghadam *et al*., 2010).

Among the active constituents of *Z. spina-christi*, unsaturated fatty acids represent the major components (83.5%). These unsaturated fatty acids maybe responsible for the broad spectrum antimicrobial activity of this plant (Nazif, 2002). Also the mucilage content amounted to 7.5%. This high content of mucilage makes it promising as a demulcent and emollient in folk medicine (Duke, 1985). These results were found to be in accordance with the use of a decoction of fresh leaves to promote the healing of fresh wounds, use as a body wash and antiseptic agents in folk medicine.

***Callistemon citrinus*:** *Callistemon citrinus* (Family: Myrtaceae) the common name, bottlebrush, perfectly describes this evergreen plant's bright red flower spikes. The flowers are followed by small; woody capsules that look like bead bracelets on the bark and which last for years. Many studies have been done on medical properties of different species of *C. citrinus*: Antibacterial, antifungal and antioxidant activities of methanolic extract obtained from *Callistemon linearis* DC. Leaf has been studied. Methanolic extract exhibited potential antimicrobial activity against both gram positive as well as gram negative bacteria and moderate activity against fungal species . This extract also shows good antioxidant activity (comparable with standard Ascorbic acid) which is concentration dependent (Anudwipa *et al*., 2008).

Seyyednejad *et al*. (2010), have investigated the antibacterial properties effect of *Callistemon citrinus* native in Khuzestan. They prepared ethanolic and methanolic extracts from leaves of this plant and by disk diffusion method their antibacterial effects on *Streptococcus pyogenes*, *B. cereus*, *B. anthracis*, *S. typhi*, *Kelebsiella pneumoniae*, *Staphylococcusepidermidis*, *E. coli*, *P. aeruginosa* and *Listeria monocytogenes* were studied. Their results revealed that the ethanolic and methanolic extract showed good antimicrobial activity against bacteria. It is noteworthy in particular effect against *S. typhi*, *B. cereus*, *S. epidermidis*, *B. anthracis* which is comparable with antibiotics. Good effect of extract of this plant on *P. aeruginosa* that is a resistant bacteria is also noticeable. Furthermore, the effect of these extract on gram positive bacteria are more notify than gram negatives, it is because of structure of membrane that the Gram positive bacteria are more simple than Gram negative ones. Based on the result of this study it can be said that *C. citrinus* is an effective antimicrobial plant that can be used for folk medicine and will be a good source for finding new antimicrobial agents in order to treat and control infections.

***Plantago ovata*:** *Plantago ovata* Forssk. (Plantaginaceae) is a winter annual plant that primarily inhabits desert regions of the Northern hemisphere between the twenty-sixth and thirty-sixth latitudes (Mayers and Liston, 2008). *P. ovata* is commonly referred to *Psyllium*, indeed, *Psylium* is the husk from the seed of *P. ovata*. Researches showed that this plant have hypocholesterolemic (Salas-Salvado *et al*., 2007; Anderson *et al*., 2000), anti-diarrhea (Washington *et al*., 1998), anti-diabetic (Hannan *et al*., 2006) and low anti-oxidant (Souri *et al*., 2008) effects. Also, it has been reported that *plantago ovata* powder causes allergic reaction when inhaled by occupationally exposed person (Bernedo *et al*., 2008). Motamedi *et al*. (2010) have investigated the antibacterial potential of ethanolic and methanolic extracts of this plant against fifteen bacterial species and also determined the MIC and MBC values. Their results indicated that ethanolic and methanolic extracts of this plant have antibacterial activities against both gram-positive and gram-negative bacteria. The *S. epidermidis* and *S. aureus* were the most sensitive strains to ethanolic and methanolic extracts of *P. ovata*, respectively. *P. aeruginosa* was resistant to both extracts of this plant; also *E. coli*, *L. monocytogenes* and *P. mirabilis* were resistant to ethanolic extract of *P. ovata* even at highest concentration. Antibacterial activity of ethanolic and methanolic extracts of *P. ovata* against all

of sensitive isolates was decreased at lower concentrations. Exceptionally, the effect of methanolic extract from this plant against *E. coli* was increased with dilution of the extract. The MIC values for both extracts of *P. ovata* against *S. aureus* were the same (20 mg mL^{-1}). The MICs for methanolic and ethanolic extract of this plant against *B. bronchiseptica* were 10 and 20 mg mL^{-1}, respectively. But MBCs for both extracts of *P. ovata* against these two bacteria weren't found (>200 mg mL^{-1}). Phytochemical investigations of Plantago species revealed their high potential to produce a wide array of secondary bioactive metabolites, i.e., iridoids, phenols, polysaccharides, sterols, alkaloids and cumarines that have utilities as supplemented foods and as drugs to treat human diseases (Fons *et al*., 2008). So these compounds could be responsible for antibacterial activity.

***Oliveria decumbens*:** *Oliveria decumbens* Vent. (Umbliferae) a shrub commonly found in South region of Iran, also has dispersed in South West of Anatolia, Syria and Iraq. *O. decumbens* is a relatively less explored plant. The limited researches about therapeutic property of this plant are reported antibacterial (Mahboubi *et al*., 2007) and antifungal (Mahboubi and Feizabadi, 2008) activity of its essential oil, but about of its extracts there isn't any reports. Motamedi *et al*. (2010) have investigated the antibacterial potential of ethanolic and methanolic extracts of this plant against fifteen bacterial species and also determined the MIC and MBC values. Their results indicated that ethanolic and methanolic extracts of this plant have antibacterial activities against both gram-positive and gram-negative bacteria. The ethanolic extract of *O. decumbens* was effective against all of the test bacteria even at one concentration. The methanolic extract of this plant have antibacterial activity against the majority of bacterial species, but *S.* Typhi, *P. mirabilis* and *K. pneumonia* were resistant. However, *S. aureus* and *B. bronchiseptica* were the most sensitive isolates to ethanolic and methanolic extracts, respectively. Furthermore, inhibitory effect of both extracts of *O. decumbens* against *B. cereus* observed only at 400 mg mL^{-1}. The antibacterial activities of both extracts from *O. decumbens* were decreased in lower concentrations. The MIC and MBC values for extracts of *O. decumbens* against *S. aureus* were 20 mg mL^{-1}. The MICs for ethanolic and methanolic extracts of this plant against *S. pyogenes* were 10 and 20 mg mL^{-1} and MBC values were 20 and 40 mg mL^{-1}, respectively. Researches showed that the main components of the *O. decumbens* essential oil are thymol (22 %), carvacrol (22 %) and p-cymene (19 %), also carvacrol is more effective against *S. aureus* than the others (Mahboubi *et al*., 2007) and these have antibacterial properties.

The ethanolic extract of *O. decumbens* have showed to be effective against MRSA strains and with regard to failure in treatment of infections from this bacteria and high incidence of antibiotic resistant among *S. aureus*, this plant can be a hope in treatment of MRSA infections. Furthermore, the ethanolic and methanolic extracts of this plant extracts were effective even at the lowest concentration (50 mg mL^{-1}) against tetracycline resistant Br. melitensis. So it can be said that *O. decumbens* can be used as an anti-brucella for brucellosis treatment.

***Teucrium polium*:** *Teucrium polium* locally named Kalpooreh has been known as an important traditional medicinal plant in Khuzestan, South West of Iran. *T. polium* is a member of the Lamiaceae family, a grass plant, durable, with 10-30 cm of height and callous white exterior that ordinarily have dispersal in rocky and sandy area of Europe zones, North of Africa and South West of Asia like Iran (Zargari, 1994). Medical reputation of this plant was noticed in traditional medicine by Socrates and Jalinous (Zargari, 1994). Researchers showed that this plant have anti-diabetic, anti-spasmodic, anti-inflammatory, analgesic and anti-oxidant effects (Shahraki *et al*., 2006; Esmaeili and Yazdanparast, 2004; Panovska *et al*., 2007; Tariq *et al*., 1989; Heidari *et al*., 2001; Kadifkova-Panovska *et al*., 2005; Hasani *et al*., 2007). Darabpour *et al*. (2010) have studied the antibacterial effect of this plant. Four concentrations of ethanolic extract (50, 100, 200 and 400 mg mL^{-1}) and two concentrations of methanolic extract (400, 600 mg mL^{-1}) from this plant were examined. Furthermore, MIC and MBC values for these extracts and also their synergistic effects were determined. Their results showed that antibacterial effects of both extracts of *T. polium* against *B. Pumilus*, *B. anthracis*, *B. licheniformis*, *B. cereus*, *S. aureus*, *S. epidermidis*, *Yersinis enterocolitica*, *E. coli*, *S. Typhi*, *B. bronchiseptica* at lower concentrations were decreased. However, antibacterial effect of ethanolic extract on *Arcanobacterium pyogenes* was increased with decreased concentrations. Also, antibacterial effect of ethanolic extracts against *p. mirabilis* was observed only in at 10 mg mL^{-1}. These results suggest that ethanolic extract was effective against all of bacterial species even at one concentration. *A. pyogenes* and *P. mirabilis* were resistant to methanolic extract even at highest concentration. However, *B. anthracis* and *B. bronchiseptica* were most susceptible microorganism to ethanolic and methanolic extracts respectively. *E. coli* and *P. mirabilis* were the species most resistant to both extracts. Furthermore, results showed *anti-staphylococcal* effect of ethanolic extract of *T. polium* was better than methanolic extracts. MIC and

MBC results showed that MIC of ethanolic extract against *S. aureus* was 40 mg mL^{-1} and for methanolic extract against *B. bronchiseptica* was 10 mg mL^{-1} but MBC against both bacteria were not found. Also MIC value for methanolic extract against *S.* Typhi and *B. anthracis* was 40 and 10 mg mL^{-1}, respectively. The MBC value against *S.* Typhi was not found (>200 mg mL^{-1}) while against *B. anthracis* was 10 mg mL^{-1}. The study of synergistic effect of *T. Polium* with antibiotic discs showed that the methanolic extract of this plant in combination with novobiocin against *S. Typhi* and in combination with methicillin and vancomycin against *S. aureus* have synergism while the combination of this extract with methicillin against *B. anthracis* was without change.

Motamedi *et al.* (2010), have investigated the effect of *T. polium* against brucella. Their research showed that ethanolic extract of this plant have inhibitory effect on *B. melitensis* in all concentrations expect at 50 mg mL^{-1} (lowest concentration that used).

The compounds found in this plant includes Alkaloids, Triterpenes, Flavonoids, Glycosides, Sterols, Tannin and Saponin (Hassan *et al*., 1979; Wassel and Ahemed, 1974; Heidari *et al*., 2001). On the other hand, in the essential oil of this plant, there are compounds that include α-Pinene, β-Myrcene, Cadinol, Myrtenal, Limonene and presumably α-Pinene could play an important role in antibacterial activity of *T. polium* (Kabouche *et al*., 2005).

***Euphorbia granulata* Forssk:** The Euphorbiaceae family comprises about 300 genus and 5000 species distributed mainly in America and tropical Africa. Euphorbiaceae family is the sixth largest family among flowering plants. This family has great importance not only for the number of species but also for its economical implications related to medicinal and cosmetic industry as well as for its toxicological aspects. Many Euphorbiaceae are well known in different parts of the world as toxic and/or medicinal. Some of the plants of this family are used in folk medicine to cure skin diseases, gonorrhea, migraines, intestinal parasites and warts. The genus *Euphorbia* (Euphorbiaceae family) comprises more than 1000 species with a broad distribution in both temperate and tropical regions. In Iran over 70 species have been reported, 17 of which are endemic. *Euphorbia* has been the source of a large number of biological active compounds including tannins, flavonoids, unsaturated sterols/triterpenes, carbohydrates, lactones and proteins/amino acids were reported as major active constituents of some *Euphorbia* species (Koochak *et al*., 2010).

Koochak *et al.* (2010) in a study have studied the antimicrobial activity of ethanolic extract of *E. granulate* against bacterial pathogens. Their results showed that this extract is effective against eight bacterial species including *B. cereus*, *B. anthracis*, *S. epidermidis*, *S. aureus*, *L. monocytogenes*, *S. pyogenes*, *K. pneumoniae* and *S. Typhi*. This antibacterial activity was increased parallel to increase concentration. The highest activity of this plant was against *S. epidermidis* at 0.4 g mL^{-1} while the lowest activity was demonstrated against *L. monocytogenes* and *B. cereus* in 0.05 g mL^{-1}. However, this extract exhibited inhibitory action at minimal concentration (0.05 g mL^{-1}) against *K. pneumoniae*. *S. epidermidis*, *S. aureus* and *Str. pyogenes* were the most susceptible species to the different concentrations of the ethanolic extract from *E. granulata*. The MIC values for *S. epidermidis* and *S. aureus* were equal (5 mg mL^{-1}), while *S. aureus* had higher MBC value (10 mg mL^{-1}) compared with that of *S. epidermidis* (5 mg mL^{-1}).

***Peganum harmala* (Nitrariaceae) Esfand:** *Peganum harmala* L. (Zygophyllaceae) is one of the most famous medicinal plants used in traditional medicine of Iran. Its antibacterial effect against MRSA (Methicillin Resistant *Staphylococcus aureus*) was surveyed by Moghadam *et al*. (2010). They prepared ethanolic extract from this plant and by disk diffusion method tested it. Their results showed that *P. harmala*, extract have high antibacterial activity against MRSA isolates and this activity was increased in accordance with its concentration.

A large number of reports concerning antibacterial properties of *P. harmala* can also be found in the literatures. The antibacterial activity of *P. harmala* was attributed to the presence of harmine (Al-Shamma *et al*., 1981) or harmaline and harmalol (Siddiqui *et al*., 1990) or all of these indole alkaloids (Ahmad *et al*., 1992). In a similar study, the antibacterial activity of *P. harmala* against *S. aureus* strains was determined (Prashanth and John, 1999). Present study, however, showed that *P. harmala* seed extract has antibacterial activity against methicillin and cefixime resistant *S. aureus* strains as well.

***Galium tricornutum* (Rubiaceae) Jeghjeghak:** *Galium tricornutum* (Rubiaceae), is a native plant that grows in altitudes of West and Southwest of Iran and several pharmacologic properties such as antipyretic, antimalaria, diuretic and emetic agent have been mentioned for it. Moghadam *et al.* (2010) have been studied its effect on MRSA. Their results suggests in comparision to other plants, intermediate antibacterial activity of ethanolic extract at high concentrations against some of the studied MRSA strains.

Khaliq *et al.* (2009), reported the antibacterial activity of *G. tricornutum* against *S. aureus.*

***Vitex pseudo negundo* (Lamiaceae) Hendeh bid:** Motamedi *et al.* (2010), have studied the effect of ethanolic and methanolic extract from this plant against tetracycline-resistant *Br melitensis*. The results of this study showed that Vitex pseudo-negundo have anti-brucella activity even at lowest concentration (50 mg mL^{-1}). This result show that with regard to the nature of brucellosis and treatment failure due the emergence of resistant strains, *Vitex pseudo negundo* can be a good choice for further research in order to find new antibiotic for brucellosis treatment.

In another study ethanolic extract from this plant exhibited intermediate antibacterial activity at high concentrations (400 mg mL^{-1}) against some of the studied MRSA strains (Moghadam *et al*., 2010).

Antibacterial substances of medicinal plants: Scientists and pharmaceutical industries consider medicinal plants as a good choice, because these natural resources have ordinary fewer side effects, are costless and effective against broad spectrum of antibiotic resistant bacteria. In many parts of the world, the extracts of medicinal plants are used for their antibacterial, antifungal and antiviral properties (Hassawi and Kharma, 2006). Plant species used in folk medicine have most probability for discovering extracts with active biological compounds that have antibacterial activity.

In general, the mechanisms by which microorganisms survive the action of antimicrobial agents are poorly understood and remain debatable (Okemo *et al*., 2001). Phytochemical constituents such as tannins, flavonoids, alkaloids and several other aromatic compounds are secondary metabolites of plants that serve as defense mechanisms against predation by many microorganisms, insects and herbivores (Doughari, 2006). In another study, it has been reported that several bioactive flavonoids such as furocoumarins and furanocoumarins (Manderfield *et al*., 1997) also phenolic compounds have been isolated from parsley leaf and are known to exhibit antibacterial activities (Wong and Kitts, 2006; Maleki *et al*., 2008).

Several studies have been conducted on the antimicrobial activity of plant extracts found in folk medicine (Ngwendson *et al*., 2003), essential oils (Alma *et al*., 2003) or isolated compounds such as alkaloids (Klausmeyer *et al*., 2004), flavonoids (Sohn *et al*., 2004), sesquiterpene lactones (Lin *et al*., 2003), diterpenes (El-Seedi *et al*., 2002). Some researchers reported that there is relationship between the chemical structures of the most abundant compounds in the tester essential oil and their antimicrobial activity (Sagdic and Ozcan, 2003). Tannins could be one of the components responsible for the antibacterial activity since it was reported by other studies that tested different plants (Nimri *et al*., 1999). The antimicrobial compound from plants may inhibit microbial growth by different mechanisms (Zuraini *et al*., 2007). Oak plant is a predominant genus in Northern and Central parts of Iran and comprises many species (Khosravi and Behzadi, 2006).

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