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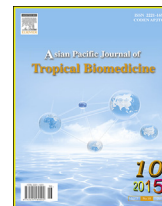
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Identification of medicinal plants effective in infectious diseases in Urmia, northwest of Iran

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ABSTRACT

Objective: To identify the medicinal plants effective in infectious diseases.**Methods:** Initially, we obtained a list of herbalists and traditional healers from Food and Drug Deputy. Direct observations and interviews as well as collection of herbarium specimens of indigenous medicinal plants effective in infectious diseases of urinary tract, reproductive, digestive, respiratory and skin systems were performed. This study was conducted through questionnaires and interviews; the questionnaires were distributed among traditional healers and simultaneous interviews were also run. The plants were herbariumized, herbarium specimens were authenticated, and their species were determined by using reliable flora and other sources. Finally, the data were input into Excel 2010 and analyses were performed.**Results:** Out of the studied plants, 35 native medicinal plants belonging to 17 families were effective in the treatment of various diseases and infections. In this study, the Lamiaceae family had the highest frequency of plants for the treatment of infections. Traditional healers of Urmia in 24% of cases used the leaves of medicinal herb to treat patients. In 68% of cases, they prescribed medicinal herbs in the boiled forms. Most medicinal herbs showed therapeutic effect on the digestive system.**Conclusions:** Traditional medicinal sources, valuable knowledge of traditional healers in Urmia, the scientific investigation of the effects of the herbs offered in this study and their effects in traditional medicine may provide a good source for new drugs in modern medicine.

1. Introduction

One of the most important challenges in human health is infectious diseases due to their high incidence and outbreak rate [1].

One of the most common human infections is urinary tract infection (UTI) which requires urgent and continuous treatment [2]. UTI is an infection involving the kidneys, ureters, bladder or urethra. These are the structures through which urine passes before being discarded from the body. If the disease develops with no effective treatment, its complications progress and may result in kidney failure. The most common pathogens causing UTIs are *Escherichia coli* (*E. coli*) and other Enterobacteriaceae bacteria such as *Klebsiella* [3]. About 250 million people are estimated to suffer from UTIs annually. In addition, 20%–50% of adult women are projected to have had at least one symptomatic UTI [4].

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The significant reasons for UTIs may include the possibility of septicemia, congenital anomalies of the urinary tract such as posterior urethral valve, ureteropelvic junction obstruction, ureterocele, and other obstructive uropathies as predisposing factors for frequent infection, damage of kidney tissue or vesicoureteral reflux which can cause kidney-induced hypertension, growth failure, and renal failure.

Bacterial vaginosis is the most common vaginitis in women of reproductive age. Bacterial vaginosis is caused by a complex alteration in vaginal flora in which hydrogen peroxide-producing lactobacilli decrease and anaerobic pathogens overgrow. Although one half of bacterial vaginosis patients are asymptomatic, the symptoms include a gray, thin, fishy-smelling vaginal discharge and itching. Diagnosis is confirmed by testing vaginal secretions. Bacterial vaginosis appears to increase the risk of pelvic inflammatory diseases, postabortion and postpartum endometritis, post-hysterectomy vaginal cuff infection, chorioamnionitis, premature rupture of membranes, preterm labor, and preterm birth [5].

The incidence of invasive fungal infections has been increased during the past three decades. One of these infections is vulvovaginal candidiasis infection. This disease is considered as the second most common vaginal infection involving approximately 75% of women in lifetime. Moreover, in 50% of patients, the infection occurs at age of 25 years. The most common symptom is vaginal itching that may be severe. Other symptoms include burning urination, white and thick vaginal discharge with typically no bad smell, painful intercourse, and redness around the vagina [6].

In recent years, yeasts and particularly candidate species have emerged as one of the most common pathogens isolated from human infections [7].

Diarrheal diseases, after respiratory infections, are the second leading cause of mortality worldwide. Diarrhea is one of the most common diseases in children, especially in developing countries with poor sanitation and/or poor personal hygiene standards. Globally, there are nearly 500 million pediatric cases of diarrheal disease under the age of 5 years every year, of whom two million die. Gastroenteritis or infectious diarrhea is a medical condition from inflammation of both stomach and small intestine. It causes some combination of diarrhea, vomiting, dehydration, abdominal pain, and cramping. Gastroenteritis has been referred to as gastro, stomach bug, and stomach virus. Globally, most cases in children are caused by rotavirus, whereas in adults norovirus and campylobacter are more common. Less common causes include other bacteria and parasites. Generally, the Enterobacteriaceae family, rotavirus and *Giardia lamblia* are the main bacteria, virus, and parasite, respectively that can cause diarrhea. Transmission may occur via consumption of improperly prepared food or contaminated water or due to close contact with the infected [8].

Most synthetic drugs are produced by imitating the herbal medicines, but they are produced artificially in pharmaceutical laboratories. At least one third of all used products have plant origin. The use of plants as natural, safe, accessible and inexpensive materials, compared to synthetic antibiotics, has been growing for the treatment of bacterial infections. Also, herbal medicines have more popularity to the people compared with chemical ones [9].

Medicinal plants have been shown as a good source for development of new drugs [10–15]. They have demonstrated promising effects in a wide variety of diseases such as cancer

[16,17], diabetes [18,19], atherosclerosis and cardiovascular diseases [20–23], learning and cognitive complications [24–26], and wounds [27–29]. Furthermore, medicinal herbs are also effective in prevention and treatment of the toxicity induced by other drugs or toxins [30–37]. Medicinal plants are a rich source of bioactive substances, antioxidants, flavonoids, and phenolic substances and have multiple health effects [12,38–55].

With pristine nature and unique flora, Urmia is one of the most significant regions in Iran with widespread and rich source of medicinal plants frequently used for treatment of various infectious diseases. In this study, we seek to identify medicinal plants that are used for treatment of various infections.

2. Materials and methods

This study was conducted via questionnaires and interviews from November, 2013 to February, 2014 in Urmia, Iran. Initially, we obtained a list of traditional healers of Urmia from Food and Drug Deputy. Direct observation and interviews as well as collection of herbarium specimens of indigenous medicinal plants effective in the treatment of infectious diseases of urinary tract, reproductive, digestive, respiratory, and skin systems were performed. The questionnaires were distributed among traditional healers and simultaneous interviews were also run.

After collection of traditional and therapeutic data about the plants mentioned in each questionnaire, different plant specimens were collected, dried and herbariumized. Herbarium specimens were identified and their species were determined by using reliable sources and flora such as Ghahreman, flora of Iranica, flora of Turkey [56], and flora of Iraq [57]. Finally, the data obtained from the questionnaires were input into Excel 2010 and the frequency of family, used plant parts, traditional usage form, and frequency of the treated diseases were analyzed.

3. Results

After finalizing and analyzing the collected data from questionnaires and interviews, comprehensive information such as scientific name, local name, the used parts and different ways of application, and anti-infective therapeutic effects in various body systems was derived.

Overall, 35 medicinal plants were identified for the effective antibacterial and anti-infectious properties in urinary tract, reproductive, digestive, respiratory, and skin systems (Table 1).

The analysis results of 35 traditionally medicinal plants with anti-infectious and antimicrobial property used in the present study showed 17 plant families in Urmia carried antimicrobial and anti-infectious effects. Based on the data of the studied medicinal plants, Lamiaceae family demonstrated the most frequency out of other plant families (Figure 1).

Data analyses showed that traditional healers of Urmia in 24% of cases already knew that the leaves of medicinal herb had therapeutic effects. In 68% of cases, they prescribed medicinal herbs in the boiled form. The results also revealed that most of medicinal herbs showed therapeutic effect on the digestive system.

Details about used parts, the ways of usage, and the percentage of medicinal plants effective in different body systems were illustrated in Figures 2–4.

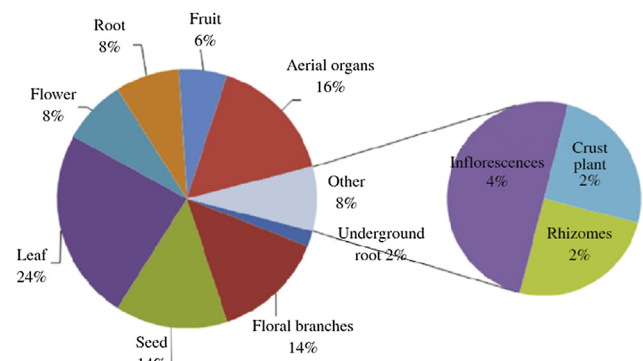
Table 1

Medicinal plants effective against infectious diseases of various body systems and their traditional therapeutic effects.

Scientific name	Family	Persian name	Used parts	Way of usage	Therapeutic effect
<i>Agrimonia eupatoria</i> L.	Rosaceae	Ghasef	Inflorescences	Boiled and brewed	Swelling and infection of stomach
<i>Alhagi camelorum</i> Fisch	Fabaceae	Kharshotor	Aerial part	Boiled and brewed	Intestinal infection, bladder infection
<i>Althea hirsuta</i> L.	Malvaceae	Khatmi	Root	Boiled and brewed, fumigation	Pulmonary infections
<i>Bryonia dioica</i> L.	Cucurbitaceae	Fashra	Root and fruit powder	Boiled	Kidney infection, intestinal infection
<i>Capsella bursa-pastoris</i> (L.) Medik.	Brassicaceae	Kise keshish	Leaf	Boiled	UTI
<i>Cardaria draba</i> (L.) Desv.	Brassicaceae	Azmak	Leaf, seed	Boiled and brewed, fumigation	Respiratory infection
<i>Datura stramonium</i> L.	Solanaceae	Tatoure	Seed	Boiled and poultice	Wound disinfection
<i>Dipsacus laciniatus</i> L.	Dipsacaceae	Khaje bashi	Root, leaf, seed	Boiled and poultice	Anti-infection of urinary tract and genital system
<i>Equisetum arvense</i> L.	Equisetaceae	Dome asb	Aerial part	Boiled	Kidney infection, antipyretic
<i>Galium humifusum</i> Bieb.	Rubiaceae	Shir panir	Aerial part	Boiled	Infectious diarrhea
<i>Glycyrrhiza glabra</i> L.	Fabaceae	Shirin bayan	Root, aerial part	Boiled	Stomach infection
<i>IXillirion tataricum</i> (Pall.) Roem et Schult	Ameyllidaceae	Khiarak	Gland, flowering shoot	Poultice	Washing skin abscesses, disinfection of infected wounds
<i>Lamium album</i> L.	Lamiaceae	Gazane sefid	Flowering shoot	Boiled and washed with boiled form	Kidney infection, UTI, vaginitis
<i>Lamium purpureum</i> L.	Lamiaceae	Gazane ghermez	Flowering shoot	Boiled	Vaginitis
<i>Mentha spicata</i>		Pouneh kouhi	Aerial part	Boiled	Infectious diarrhea
<i>Malva neglecta</i> Wallr.	Malvaceae	Panirak	Seed, leaf, flowering shoot	Boiled and poultice	Infection
<i>Mentha longifolia</i> L.	Lamiaceae	Pouneh	Aerial part	Boiled and brewed, fumigation	Pulmonary infections
		Hendavaneye kouhi	Fruit	Boiled	Intestinal inflammation
<i>Cuminum cyminum</i> L.	Apiaceae	Zire sabz	Seed	Boiled	Intestinal inflammation
<i>Phragmites australis</i> (Cav.) Trin	Poaceae	Ney	Rhizome	Boiled	Gastroenteritis
<i>Plantago major</i> L.	Plantaginaceae	Barhang	Seed, leaf, root	Boiled	Pulmonary infections, stomach ulcers and infections
<i>Salix alba</i> L.	Salicaceae	Bid sefid	Bark, leaf	Boiled	Antipyretic
<i>Salvia verticillata</i> L.	Lamiaceae	Maryamgoli banafsh	Leaf, flowering shoot	Boiled	Antipyretic, antimicrobial
<i>Sanguisorba minor</i> Scop.	Rosaceae	Tout robahi	Fruit	Boiled and raw	Disinfectant of skin wounds
<i>Scrophularia kurdica</i> subsp. <i>glabra</i>	Scrophulariaceae	Gole meymouni	Aerial part	Boiled	Antimicrobial and antiseptic
<i>Lactuca serriola</i> L.	Asteraceae	Kahouye khiardar	Leaf	Boiled	Antipyretic
<i>Sisymbrium officinale</i> L.	Brassicaceae	Khakeshir tebi	Seed	Boiled	Antipyretic
<i>Tanacetum parthenium</i> (L.) Schultz.	Asteraceae	Baboune kabir	Leaf, flower	Boiled	Sinusitis, gastritis
<i>Teucrium orientale</i> L.	Lamiaceae	Maryam nokhodi	Aerial part	Boiled	Antipyretic
<i>Teucrium polium</i> L.	Lamiaceae	Maryam nokhodi	Flowering shoot	Boiled	Antimicrobial
<i>Thymus kotschyanus</i> Boiss.	Lamiaceae	Avishan	Flowering shoot	Brewed, fumigation	Infectious diarrhea
<i>Verbascum agrimonifolium</i>	Scrophulariaceae	Gole mahour	Leaf, flower	Boiled	Bacterial infection of the wound
<i>Verbascum macrocarpum</i> Boiss.	Scrophulariaceae	Gole mahour	Leaf, flower	Boiled	Fungal infection of nail
<i>Verbascum speciosum</i> Schord.	Scrophulariaceae	Gole mahour	Leaf, flower	Poultice, boiled and concentrated	Bacterial infection of the wound
<i>Ziziphora tenuior</i> L.	Lamiaceae	Kakouti	Inflorescences	Boiled	Gastritis

**Figure 1.** Frequency of plant families effective in infectious diseases of various body systems.

A: Ameyllidaceae; B: Apiaceae; C: Asteraceae; D: Brassicaceae; E: Cucurbitaceae; F: Dipsacaceae; G: Equisetaceae; H: Fabaceae; I: Lamiaceae; J: Malvaceae; K: Plantaginaceae; L: Poaceae; M: Rosaceae; N: Rubiaceae; O: Salicaceae; P: Scrophulariaceae; Q: Solanaceae.

**Figure 2.** Percentage of used parts of plants effective in infectious diseases of various body systems.

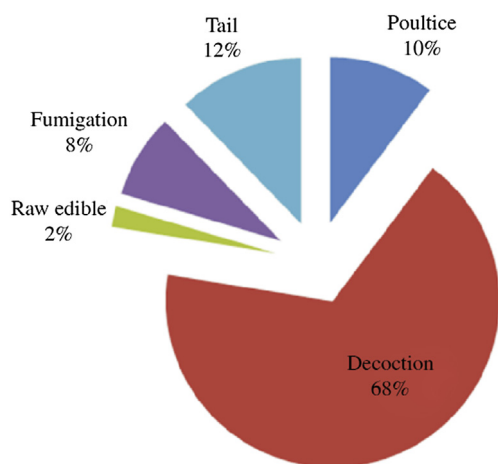


Figure 3. Frequency of used form of medicinal plants effective in infectious diseases of various body systems.

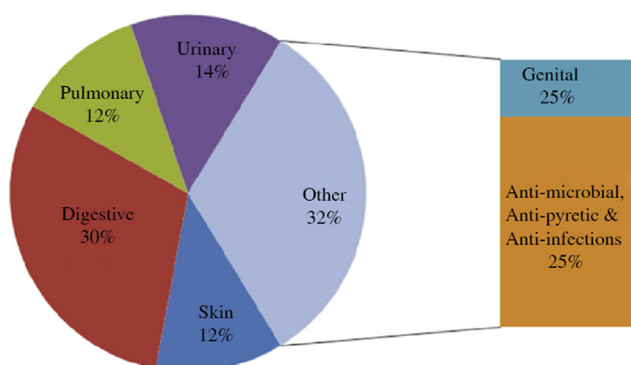


Figure 4. Percentage of plants effective in infections of urinary tract, reproductive, digestive, respiratory, and skin systems.

4. Discussion

Iran has a long history of application of traditional medicine and medicinal plants for treatment of various diseases [58]. The rich flora in Iran, Iranians' valuable knowledge of the use of medicinal plants, presence of prestigious academic centers in Isfahan, Shiraz, and Ray, existence of credible scientific sources such as Ibn Sina's *Ghanoon* book and also other famous scientists such as Rhazes that introduced medicine with herbs among Iranians, along with the Iranians' interest in medicinal plants, highlight the significance of further attention to this field [59]. Different regions of the country have different cultures and traditions in the use of medicinal plants. Hence, the ethnobotanical investigation of medicinal plants in Urmia and recognition of their therapeutic effects have led to a context for understanding the therapeutic effects of these plants and developing new ideas for producing new drugs.

In the present study, after finalizing and analyzing the collected data from questionnaires and interviews, a total of 35 medicinal plants belonging to 17 families were identified for effective antibacterial and anti-infectious properties.

In traditional medicine, sweat camel's thorn in boiled form has different properties or Manna of *Hedysarum* ("Toranjabin" in Persian) has a cold humor and is used for bile excretion and treatment of kidney and bladder stones. It is also known to have diuretic, anti-pertussis, and anti-age activities with no special side effect [60–62]. A study conducted on camel's thorn (*Alhagi maurorum*) reported the protective effect of its aqueous extract (not its sweat) on preventing gastric ulcer caused by stress and

alcohol in rats [63]. Mallow plant flowers contain anthocyanins and mucilage and all parts of the plant, especially the flowers, exhibit softening effect on the respiratory tract, which may be due to its high mucilage content [64].

The therapeutic effects of *Mentha longifolia* L. have been demonstrated in improving digestive disorders, vomiting, anorexia, ulcerative colitis, and liver disorders. In addition, the antimicrobial and antioxidant properties of several species of this plant have been reported [65,66].

Preuss *et al.* investigated the inhibitory and cytotoxic effects of oregano and some other essential oils with monolaurin on *Staphylococcus aureus* (*S. aureus*), *Bacillus anthracis*, *E. coli*, *Klebsiella pneumoniae* and *Helicobacter pylori*. Oregano essential oil showed inhibitory activity against all studied microorganisms except for *Bacillus anthracis* [67]. The antibacterial effect of pulegone as the main component of oregano essential oil has been demonstrated [68]. Gulluce *et al.* reported that the antimicrobial effect of oregano essential oil was greater than that of its extract [66].

Since the antimicrobial active component of *Mentha* is pulegone, the extraction of this secondary compound can help to introduce stronger anti-infection and antimicrobial drugs.

In another study, the cumin oil was demonstrated to be effective against four types of bacteria including *S. aureus*, *Bacillus cereus*, *E. coli* and *Listeria monocytogenes* [69]. The antimicrobial effects of the cumin oil have been demonstrated on the growth of *Vibrio parahaemolyticus* [70].

The chemical composition of *Plantago major* includes mucilage, organic acids, polysaccharides, flavonoids, carotenoids, saponins, sorbitols, minerals, vitamins, tannins, resins, gum, *etc.* Plantain has been tested by the Commission E of Germany and its use was suggested for treatment of cough and respiratory infections and skin inflammation, as well.

There are numerous references on the antimicrobial effects of medicinal plants native to Iran including the antibacterial effect of *Scrophularia* against *S. aureus* and *Pseudomonas aeruginosa* [71]. Also, decocted and brewed forms of *Scrophularia striata* and *Scrophularia deserti*, in Western Iran, are traditionally used for treatment of deep, superficial, and internal infections [72]. Phenolic, flavonol, and flavonoid compounds have already been determined in the ethanol extract of *Scrophularia striata* [73].

The extract of *Teucrium polium* consists of diterpenoids, 5-7-glycoside, thymols, carvacrols, and volatile essences [74,75]. The results obtained in a study showed that *Teucrium chamaedrys* exhibited antibacterial activity against *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *E. coli*, and *Bacillus cereus* as well as antifungal activity against *Candida albicans* and *Aspergillus niger* [64].

A species of thyme, *Zataria multiflora* Boiss, is used as a flavoring agent in many foods in Iran with antioxidant, antibacterial and disinfecting effects [76]. The main components of Iranian thyme (*Zataria multiflora* Boiss) essential oil are carvacrols, linalools, and parasmine [77]. *Thymus vulgaris* has antibacterial effect due to the presence of phenolic compounds [78]. The higher levels of phenols in essence, will achieve the more antimicrobial properties. The phenolic compounds consist of carvacrols, eugenols, and thymols [78,79].

The main component of essential oil of a number of plants belonging to Lamiaceae such as *Ziziphora tenuior* is pulegone [80–82]. Pulegone has already shown antimicrobial activity against different strains of *Salmonella* and strong antimicrobial effect against *Candida albicans* and *Salmonella typhimurium* [82,83].

The action mechanisms of essential oils are related to their chemical compositions and antimicrobial activity, but the mechanisms are not similar in all cases. However, the effect of herbal extracts on cell wall structure has been confirmed in most cases [84]. Toxic effects of plant extracts or essential oils on membrane structure and function have been generally used to explain the antimicrobial action of essential oils and their phenolic and monoterpenoid compounds [85]. Because of the anti-lipophilic properties of essential oils, their monoterpenes will preferentially partition from an aqueous phase into membrane structures. This process results in membrane expansion, increased membrane fluidity and permeability, disturbance of membrane-embedded proteins, inhibition of respiration, and alteration of ion transport processes [85,86]. The antibacterial actions of medicinal plants have also been attributed to their phenolic compounds [85]. Therefore, other medicinal plants containing phenolic compounds could possess antibacterial activity which deserves investigation. Furthermore, infections are associated with oxidative stress and there are a lot of herbal medicines with antioxidant activity [32,87–110].

Therefore, the use of these plants, beyond contributing to reduction of infectious diseases, may have additional benefits for reduction of oxidative stress.

Conflict of interest statement

We declare that we have no conflict of interest.

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