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Review Article

Anti E. *coli* Activity of Herbal Medicines: a Systematic Literature Review

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Abstract

Escherichia coli is the gram negative bacilli of Entrobacteriaceae family that commonly found in intestinal infections and many infections outside the intestine, like urinary tract infections (UTI), cholecystitis, wound infections, meningitis, septicemia, pulmonary infections, and many more. Plants are rich sources of bioactive compounds, hence they can be effective in a wide variety of diseases. The pandemic spread of multidrug-resistant (MDR) bacteria (i.e., extended-spectrum b-lactamase-producing Enterobacteriaceae (ESBLPE). Carbapenemase-producing Enterobacteriaceae (CPE),) threaten healthcare Worldwide. The present review is a report of the most effective medicinal plants against E. *coli*. In this research, the required online database searches were conducted using the key words such as bacteria, *E. coli* and medicinal plants. Databases of Web of Science, PubMed, Scopus, Google Scholar, and ScienceDirect were explored to find and explore related articles. Since the incidence of *E. coli* is high, the aim of this study is to identify and report anti *E. coli* medicinal plants in Iran. The obtained results showed that there were 51 medicinal herbs that could be considered as the main medicinal plants capable of affecting *E. coli*.

Keywords: *E. coli*, plant extracts, herbal plants, antibacterial activity

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Introduction

Escherichia coli is the gram negative bacilli of Enterobacteriaceae family that commonly found in intestinal infections and many infections outside the intestine, like urinary tract infections (UTI), cholecystitis, wound infections, meningitis, septicemia, pulmonary infections and many more (1-3). Also, *E. coli* is one of the most frequent cause of bloodstream infections (BSIs) involving Gram-negative bacteria (4-9). Bloodstream infections (BSIs) pose a serious problem in clinical settings and high treatment costs (10-12).

In the last two decades, a striking increase in the number of infections caused by antibiotic resistant strains of *E. coli*, has had an important impact on the outcomes of BSIs (13). Multidrug-resistant (MDR) *E. coli* strains, and particularly extended-spectrum β-lactamases (ESBL) producing organisms, not only are endemic in many health care settings but also have

become major causes of community acquired infections (14-16). These organisms are resistant to most of the antimicrobial agents recommended for the treatment of infections caused by *E coli*, hence these strains make antimicrobial therapy ineffective against these infections (17-20).

Previous studies have indicated that the failure to provide prompt and effective antimicrobial therapy for BSIs caused by ESBL-producing *E. coli* leads to increased mortality and longer hospital stays. Other studies have reported the same findings (13, 21, 22).

Indeed, *E. coli* is now the most common cause of BSI in children's specialty hospitals. However, the annual number of cases of *E. coli* BSI increased from 20.3 to 25.3 from 2010 to 2016. The improvement of urinary catheters and management of urinary tract infections (UTI) are the key interventions capable of preventing *E. coli* BSI (23).

ESBLs confer resistance to penicillins and cephalosporins, and have the greatest contributions to resistance to fluoroquinolones, aminoglycosides, and trimethoprim-sulfamethoxazole (24). Therefore, ESBL producing strains are most of the times truly multidrug resistant strains. Both antibiotic resistance and inappropriate empirical therapy are independently associated with increased rates of mortality among individuals with *E. coli* bacteremia (13, 25, 26). MDR pathogens raise a major therapeutic hindrance for clinicians worldwide (27).

Therefore, the introduction of new antibacterial compounds with improved activity is necessary (28). Antimicrobial properties of herbs have been documented in ancient literature. Nevertheless, few of them have ever been investigated for their antimicrobial properties. Herbal medication is an alternative therapy for different diseases. Native herbal based medicines are easily available and inexpensive. The effectiveness of some native herbal intervention against *E. coli* has been confirmed in Africa, England and China (29-31).

The significance of traditional medicine has been confirmed for thousands of years. In some Asian and African countries, more than 80% of people use this type of medicine for primary health care. Herbal and botanical based medicines can be thought of as a lucrative business with the capacity to generate billions of dollars in revenue. Currently, more than 100 countries have regulations for herbal medicines (32).

Plants produce a high diversity of secondary metabolites that protect them against many biological threats such as microbial pathogens (33). Moreover, among 3000 types of essential oils, about 300 of them are commercially important and used by flavor and fragrance industries (34). Natural products have been beneficial as good sources of novel drug molecules, and have attracted high consideration in the pharmaceutical industry as well as in human health problems (35).

The present investigation was carried out to study the in vitro antimicrobial activity of medicinal plants used by Iranian people in order to display that the therapeutic properties of some plants used in traditional medicine coincide with laboratory detection.

Materials and Methods

A search of related literature published from 2000 to 2017 was undertaken on Web of Science, PubMed, Scopus, Google Scholar, and ScienceDirect using the key words *E. coli*, Plant extracts, herbal plants, herbal medicines and antibacterial activity. Articles written in English and related to the subject were recorded in this study. Additional citations were identified by reviewing reference lists of relevant articles. We excluded studies which had not control group and also those with minimal importance on the topics and methodological weakness.

Results and Discussion

Dianthus caryophyllus, Cinnamomum zeylanicum, Stachys inflata Benth, Heracleum lasiopetalumBoiss, Saturja bachtiaricaBunge, Thymus daenensisCelak, Ziziphora teniurL, Echiophora platylobaL, Dracocephalam multicaule Montbr and Auch, Kelussia odoretascima Mozff, Mentha longifolia Hudson, Achillea kellalensis Boiss, Stachys lavandulifoliaVahl, Euphorbia helioscopa L, Euphorbia microsciadia Boiss, Eryngium billardieri F, Nerium oleander L, Centaurea cyanus L, Lactuca serriola L, Berberis integrrima Bunge, Peganum harmala , Datura stramonium L, Verbascum speciosum Schrad, Apium graveolensL,

Table 1: In vitro activity of medicinal plants affecting *E. coli*.

Scientific Name	Family Name	Part Used	Result	Ref.
Dianthus caryophyllus	Caryophyllaceae	Whole Plant	Inhibition zone diameter of methanol extracts of this plant was 12 mm by agar well-diffusion bioassay	(36)
Cinnamomum zeylanicum	Lauraceae	Stem Bark	Inhibition zone diameter of methanol extracts of this plant was 14 mm by agar well-diffusion bioassay	(36)
Stachys inflata Benth	Lamiaceae	Aerial parts	Inhibition zone diameter of methanol extract of this plant was 11 mm and diameter inhibition zone of a-Terminal and Linalool were 32 and 27mm respectively and the MIC of methanol extract was 500 mg/ml and MIC of a-Terpineol and Linalool were 500 and 125 mg/ml respectively. Inhibition zone diameter of rifampin and gentamicin were 11 and 20 mm and MIC of these antibiotics were 500 that were used as positive controls	(37)
Heracleum lasiopetalum Boiss	Apiaceae	Fruit	Antibacterial activity of ethanol extract and essential oil were 18 and 17 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 70.66 and 67.38 respectively (10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were 156.25 and 39 respectively (µg/ml)	(38)
Saturja bachtiarica Bunge	Lamiaceae	Leaves	Antibacterial activity of ethanol extract and essential oil were 22 and 23 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 77.58 and 76.30respectively (10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were 156.25 and 39 respectively (µg/ml)	(38)
Thymus daenensis Celak	Lamiaceae	Flowers	Antibacterial activity of ethanol extract and essential oil were 16 and 18 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 67.02 and 74.55 respectively	(38)

			(10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were 156.25 and 39 respectively (µg/ml)	
Ziziphora teniurL.	Lamiaceae	Leaves	Antibacterial activity of ethanol extract was 18 mm by agar diffusion assay (100 µg/disc) and effect of extract on growth bacteria strains were 57.48 (10 mg/ml) by serial dilution assay. MIC of ethanol extract was 625 (µg/ml)	(38)
Echiophora platylobaL.	Apiaceae	Stem	Antibacterial activity of ethanol extract was 12 mm by agar diffusion assay (100 µg/disc) and effect of extract on growth bacteria strains were 44.43 (10 mg/ml) by serial dilution assay. MIC of ethanol extract was >1000 (µg/ml)	(38)
Dracocephalam multicaule.	Lamiaceae	Seed	Antibacterial activity of ethanol extract was 22 mm by agar diffusion assay (100 µg/disc) and effect of extract on growth bacteria strains were 70.59 (10 mg/ml) by serial dilution assay. MIC of ethanol extract was 625 (µg/ml)	(38)
Kelussia odoretascima Mozff	Apiaceae	Leaves	Antibacterial activity of ethanol extract and essential oil were 10 and 16 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 44.43 and 65.64 respectively (10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were >1000 and 39 respectively (µg/ml)	(38)
Mentha longifolia Hudson	Lamiaceae	Flowers	Antibacterial activity of ethanol extract and essential oil were 14 and 17 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 61.94 and 66.81respectively (10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were >1000 and 156.25respectively (µg/ml)	(38)
Achillea kellalensis Boiss	Asteraceae	Flowers	Antibacterial activity of ethanol extract and essential oil were 21 and 18 mm respectively by agar diffusion assay (100 µg/disc) and effect of extract and essential oil on growth bacteria strains were 73.38 and 68.71 respectively (10 mg/ml) by serial dilution assay. MIC of ethanol extract and essential oil were 39 and 39 respectively (µg/ml)	(38)

Stachys lavandulifoliaVahl	Lamiaceae	Arial parts	Antibacterial activity of ethanol extract was 13 mm by agar diffusion assay (100 µg/disc) and effect of extract on growth bacteria strains were 41.53 (10 mg/ml) by serial dilution assay. MIC of ethanol extract was >1000 (µg/ml)	(38)
Euphorbia helioscopa L	Euphorbiaceae	Aerial Parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Euphorbia microsciadia Boiss	Euphorbiaceae	Aerial Parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Eryngium billardieri F.	Apiaceae	Aerial Parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Nerium oleander L.	Apocynaceae	Flowering Stem	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)

Centaurea cyanus L	Asteraceae	Total parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Lactuca serriola L.,	Asteraceae	Aerial parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Berberis integrrima Bunge	Berberidaceae	Leaf and Stem	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Peganum harmalaL	Zygophyllaceae	Aerial parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Datura stramonium L	Solanaceae	Aerial parts	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that	(39)

			indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	
Verbascum speciosum Schrad	Scrophulariaceae	Leaf	In each plate one positive control (gentamycin 0.8 mg/0.2 ml and one negative control (methanol 0.2 ml) were included. Zones of inhibition were measured and antimicrobial activities of the extracts were. expressed in comparison with gentamycin as a positive control that indicated good antimicrobial activity of this plant extract using the disc diffusion method significant	(39)
Apium graveolens	Apiaceae	Leaves	Inhibition zone diameter was 7-9 mm by agar well-diffusion bioassay (2 mg/well)	(40)
Trachyspermum ammi	Apiaceae	Seeds	Inhibition zone diameter was 7-9 mm by agar well-diffusion bioassay (2 mg/well)	(40)
Alhagi maurorumMedik. Syn.A camelorum; A. pseudalhagi	Leguminosae-Papilionoideae	Stem gum	Inhibition zone diameter was >15mm by agar well-diffusion bioassay (2 mg/well)	(40)
Trigonella foenum-graecum	Leguminosae-Papilionoideae	Seeds	Inhibition zone diameter was >15mm by agar well-diffusion bioassay (2 mg/well)	(40)
Lawsonia inermis	Lythraceae	Leaves	Inhibition zone diameter was >15mm by agar well-diffusion bioassay (2 mg/well)	(40)
Lilium candidum	Liliaceae	Roots	Inhibition zone diameter was 7-9 mm by agar well-diffusion bioassay (2 mg/well)	(40)
Ziziphus ziziphus	Rhamnaceae	Fruit	Inhibition zone diameter was 10-14 mm by agar well-diffusion bioassay (2 mg/well)	(40)
Cuminum cyminum	Umbelliferae	Seeds	Inhibition zone diameter was >15mm by agar well-diffusion bioassay (2 mg/well)	(40)
Rhus coriaria	Anacardiaceae	Fruit	Activity ethanolic extracts in disc and well diffusion assays were 17 and 24 mm respectively. Positive control discs contained 30µg of gentamycin. Zone of inhibition was 17 mm by disc diffusion. MICs of extracts was 0.20 %	(41)

Zataria multi XoraBoiss	Labiatae	Aerial parts	Activity ethanolic extracts in disc and well diffusion assays were 10 and 22 mm respectively. Positive control discs contained 30µg of gentamycin. Zone of inhibition was 17 mm by disc diffusion test. MICs of extracts was 0.40 %	(41)
Funmaria vaillantii	Fumariaceae	Flowers & stems	Zone of inhibition (mm) in agar diffusion test was 11 and MIC (µg/ml) was 125. Tetracycline and gentamicin were used as positive control that zones of inhibition were 16 and 20 mm by agar diffusion test.	(42)
Falcaria vulgaris	Apiaceae	Leaves	Zone of inhibition (mm) in agar diffusion test was 11 and MIC (µg/ml) was 250. Tetracycline and gentamicin were used as positive control that zones of inhibition were 16 and 20 mm by agar diffusion test.	(42)
Prim-ula auriculata	Primulaceae	Leaves	Zone of inhibition (mm) in agar diffusion test was 10.5 and MIC (µg/ml) was 500	(42)
Zataria multiflora Boiss	Labiatae	Aerial parts	Antibacterial activity of ethanol extract was 16 by MIC (mg/ml)	(43)
Quercus brantii		Fruit	Inhibition zone diameter (mm) was 12 and inhibition zone diameter produced by gentamycin was 20	(44)
Artemisia siberi	Asteraceae	Aerial parts	Diameter of inhibitory zone diameter was (mm) 12	(45)
Peganum harmala.	Zygophyllaceae	Seed extract	Diameter of inhibitory zone diameter was (mm) 22 and MIC of seed was 0.625 mg/ml	(46)
Thymus daenensis	Lamiaceae	Aerial parts	15 mg/ml concentration of *T. daenensis* inhibited *E.coli* producing ESBL.	(47)
Carum copticum	Apiaceae	Aerial parts	MIC values of *C. copticum* against *E. coli* O157:H7 was 0.05 ± 0.002 %(v/v)	(48)
Zataria multiflora Boiss	Lamiaceae	Aerial part	Activity essential oils in disc and well diffusion assays were 19.8 and 19.3 mm respectively. Ciprofloxacin was used as positive control that zones of inhibition were 23.8. Minimum inhibitory concentrations (MICs) extracts was 2.1 (mg/mL)	(49)

Alhagi mamurorum Medik	Mimosoideae	Stem Gum	Inhibition zone diameter was 17 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Apium graveolens	Apiaceae	Leaves	Inhibition zone diameter was 9 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Trachyspermum ammi	Apiaceae	Seeds	Inhibition zone diameter was 17 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Trigonella foenum graecum	papilionoideae	Seeds	Inhibition zone diameter was 18 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Lilium candidum	Liliaceae	Roots	Inhibition zone diameter was 9 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Lawsonia inermis	Lythraceae	Leaves	Inhibition zone diameter was 17 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Ziziphus ziziphus	Rhamnaceae	Fruit	Inhibition zone diameter was 10 mm by agar well-diffusion method (20 mg ml^{-1})	(50)
Cuminum cyminum	Umbeliferae	Seeds	Inhibition zone diameter was 17 mm by agar well-diffusion method (20 mg ml^{-1})	(50)

Trachyspermum ammi, Alhagi maurorumMedik. Syn.A, camelorum; A. pseudalhagi, Trigonella foenum-graecum L, Lawsonia inermisL, Lilium candidumL, Ziziphus ziziphus, Cuminum cyminum, Rhus coriaria L, Zataria multiXoraBoiss, Funmaria vaillantii, Falcaria vulgaris, Prim-ula auriculata, Zataria multiflora Boiss, Quercus brantii, Artemisia siberi, Peganum harmala L, Thymus daenensis, Carum copticum, Zataria multiflora Boiss, Alhagi mamurorum Medik, Apium graveolens, Trachyspermum ammi, Trigonella foenum graecum, Lilium candidum, Lawsonia inermis, Ziziphus ziziphus, and Cuminum cyminum are the main medicinal plants that can affect E. coli. Additional information about native medicinal plants against E. coli was shown in table 1. According to the obtained results, Saturja bachtiarica Bunge, Dracocephalam multicaule, Achillea kellalensis Boiss, Rhus coriaria, Zataria multi XoraBoiss and Peganum harmala are the most important medicinal plants with anti- E. coli effect. A lot of studies have revealed that herbal medicines are good sources of molecules with antioxidant activity and antimicrobial trait which are able to keep the body on cellular oxidation and pathogens. Therefore, classification of various herbal medicines for their antioxidant and antimicrobial potentials is significant. Herbal compounds that are safe and combat pathogens are useful candidates for producing new antimicrobial medicines. Lots of them have been used for long times and by many cultures.

Conclusion

Despite the significance of the information obtained so far concerning the subject, the precise mechanisms peculiar to plant extracts that help them kill *E. coli* are still unknown and require more investigations to be revealed. These medicinal plants might be used for producing new drugs, though, their toxicology assessments are needed for more safe usage of these plants.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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