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Colibacillosis Phytotherapy: An Overview on the most important world medicinal plants effective on *Escherichia coli*

Majid Aminzare[1],Zahra Abbasi[1],Elham Amiri[1], Mohammad Hashemi[2],Mojtaba Raeisi[3],Neda Mousavi[4],Hassan Hassanzadazar[1*]

[1] *Department of Food Safety and Hygiene, School of Public Health, Zanjan University of Medical Sciences, Zanjan, Iran*
[2] *Department of Nutrition, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[3] *Department of Nutrition, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran*
[4] *Department of Nutrition, Faculty of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran*

Abstract

Escherichia coli is a Gram-negative, non-sporulating facultative anaerobe found in water and soil and is a normal flora in gastrointestinal tract of human, warm-blooded animals and reptiles. E. coli strains are categorized into six pathotypes caused different syndromes and shows high rate of resistance to different antibiotics. The aim of this study was to identify the most important native medicinal plants of world, effective on E. coli.All required information was obtained by searching keywords such as E.coli, medicinal plant extracts or essential oils in published articles in authentic scientific databases such as Science Direct, Wiley-blackwell, Springer, Google scholar, Scientific Information Database (SID) and Magiran. According to the literature review, our results showed 44 different native medicinal plants were effective against E.coli and used to colibacillosis treatment traditionally in all over the world. The results of this review indicated that some of the most important plants that have anti-E.coli effect include Rosmarinus officinalis (rosemary), Syzygium aromaticum (clove), Thymus vulgaris (Thyme), Zataria multiflora (Avishane shirazi), Salvia officinalis (Sage), Cymbopogon martini (Palmarosa), Aloysia triphylla (Lemon beebrush), Origanum vulgare (Oregano), Satureja cuneifolia (wild savory), Pluchea indica (Indian camphorweed), Eucalyptus tereticornis (Forest Red Gum), Aloe vera (Aloe) and Foeniculum vulgare (Fennel). An overview on phytochemical analysis has shown that bioactive compounds of medicinal plants with their antioxidant and antimicrobial properties are good alternative for synthetic drugs in food and drug industry and in other word to treatment microbial diseases in medicine.

Keywords: Medicinal plants, *Escherichia coli*, Antimicrobial, Colibacillosis

INTRODUCTION

Escherichia coli, is a Gram-negative, non-sporulating facultative anaerobe, which consists of more than 500 species of bacteria and 10^{10}–10^{11} cells per gram of large-intestinal content in warm-blooded animals and reptiles. As *E. coli* can transit in water and sediment, it is often used as an indicator of fecal pollution of water [1-4]. The most successful combinations of virulence factors have persisted to become specific Pathotypes of *E. coli* that are responsible for causing disease in healthy individuals. *E. coli* strains are categorized into six pathotypes: enteropathogenic *E. coli* (EPEC), enterohaemorrhagic *E. coli* (EHEC), enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAEC), enteroinvasive *E. coli* (EIEC) and diffusely adherent *E. coli* (DAEC) [5]. The most common syndromes can be caused from one of these pathotypes include gastrointestinal diseases, urinary tract infections (UTIs) and sepsis/meningitis. Molecular mechanism of *E. coli* pathogenicity consists of adherence to specific receptors on the intestinal epithelial cells, colonization of mucosal site, evasion of host defenses, multiplication and damage to host cells. [6-8].

Antibiotics are the main drugs in the treatment of these bacterial infections, but due to increasing antibiotic resistance and side effects of these medications, auxiliary method is particularly important [9]. Natural additives like plant essential oil and extracts have reached a great interest, due to their pharmacological activities, low toxicity and economic viability [10]. Plant essential oils are secondary metabolites that are generally recognized as safe (GRAS) as flavoring agents for consumption by animals and human. They have been shown to be promising alternatives to chemical sanitizers against foodborne bacteria [11]. Hence, the aim of this study was presenting an overview on the most important world medicinal plants affecting on *E.coli*.

MATERIAL AND METHODS

All required information was obtained by searching various keywords including, *Escherichia coli*, medicinal plant, extracts or essential oils of published articles in authentic scientific databases such as Science Direct, Wiley-Blackwell, Springer, Google scholar, Scopus, PubMed and Scientific Information Database (SID).

RESULT AND DISCUSSION

Effective medicinal plants against *E.coli* are listed in Table 1. The results of this review indicated that some of the most important plants that have anti-*E.coli* effect include *Rosmarinus officinalis* (rosemary), *Syzygium aromaticum (*clove), ***Thymus vulgaris*** (Thyme), ***Zataria multiflora*** (Avishane shirazi)*,* ***Salvia officinalis*** (Sage), *Cymbopogon martini* (palmarosa), *Aloysia triphylla* (lemon beebrush), *Origanum vulgare* (Oregano), Satureja cuneifolia (wild savory), *Pluchea indica* (Indian camphorweed), Eucalyptus tereticornis (Forest Red Gum), *Aloe vera*(aloe) and *Foeniculum vulgare* (Fennel).

Table1. List of effective world medicinal plants against *Escherichia coli* used to treatment of Colibacillosis

Scientific name	Plant Family	Common name	PersianName	Discussion
Rosmarinus officinalis	Lamiaceae	Rosemary	Rozmari	An experimental study indicated that the most effective essential oil on *E. coli O157:H7* caused a 21±1 mm inhibition and had a 0.6 ml/100ml MIC and 0.7 ml/100ml MBC [12]. In another study, MIC and MBC were achieved 3000mg/ml and 3200mg/ml, respectively [13]. Results of an Iranian study showed that the effect of rosemary essential oil on *E.coli* formed a growth inhibition diameter of 23.2±0.4 mm. MIC and MBC were 1250 and 2500 ppm respectively [14].
Syzygium aromaticum	Myrtaceae	Clove	Mikhak	Growth inhibition diameter of *S. aromaticum* essential oil was 54±2 mm and MIC and MBC were obtained 0.25 and 0.3 ml/100ml, respectively [12]. Clove essential oil in a test bactericidal activity against food-borne bacteria were analyzed using the fusion drive. The diameter of inhibition for *Escherichia coli* bacteria was 0.36mm, and MIC was 1250μg / ml [15].
Thymus vulgaris	Lamiaceae	Thyme	Avishan baghi	The essential oils of *Thymus vulgaris* showed strong antibacterial activity with the widest inhibition zone and MIC was 2.5μl/ml [16]. An experimental study demonstrated that MIC of essential oil was 0.45–1.25 μg/mL for *E. coli* [17].
Zataria multiflora	Lamiaceae	Avishan-e Shirazi, Satar	Avishan Shirazi	A study showed that 0.1 mg/ml of *Z. multiflora* essential oil caused a 35.0±1.9 mm inhibition zone and had a 0.315 mg/ml MIC [18]. In another study, *Z. multiflora* essential oil showed MIC and MBC of 0.25 μg/ml [19].
Salvia officinalis	Lamiaceae	Sage	Maryam Goli	MIC and MCC of *S. officinalis* essential oil on *E. coli* were 5.0 – 10.0 and >10.0, respectively [20]. In an Iranian study, MIC and MBC of *S. officinalis* ethanol extracts were 26.56 and 53.125 mg/mL**,** respectively [21].
Landolphia owerrience	Apocynaceae	Igbo		Inhibition zone diameter (IZD) of ethanol extract of *L. owerrience* against *E. coli* was 16 mm and had a 50 mg/ml MIC and 50 mg/ml MBC [22].
Quercus infectoria	Fagaceae	Aleppo oak	Balut	Results of a study showed that *Q. infectoria* aqueous extract on *E.coli* formed a growth inhibition diameter of 10.9 mm. MIC and MBC were 0.09 and 0.78 mg/ml respectively [23]. In an experimental study, ethanol extracts of *Q. infectoria* exhibited growth inhibition zone of 11.9±0.49mm [24].
Punica granatum	Punicaceae	Pomegranate	Anar	Results showed that aqueous and ethanol extracts of *P. granatum* were 11.7 and 10.9 respectively. Also MIC and MBC of ethanol extracts against *E.coli* were 0.39 and 3.12 mg/ml respectively [23]. A study indicated that 8 mg of P. *Granatum* extract on *E. coli O157:H7* formed a growth inhibition zone of 10.3mm. MIC and MBC were 83.3 and 125 mg/ml, respectively [25].
Pimpinella anisum	Apiaceae	Anise	Anison	An experimental study indicated that *P. anisum* essential oil caused a 4.37±0.31 mm inhibition zone on disk diffusion method and 8.30±0.40 mm on well diffusion method and had a 2500 μg/ml MIC [14]. Obtained results showed *P. anisum* essential oil had a MIC of 12.5μg/ml against *E.coli* [26].
Lippia adoensis	Verbenaceae	Koseret	_	Methanol extract *of L. adoensis* has shown quite anti-E.coli effect in a 10 g/ml dose in vitro. The inhibition zone diameter of methanol extract against *E.coli* was 14±0.8 [27].
Cymbopogon martinii	Poaceae	Palmarosa	Alaf Limu	Essential oil from *C. martinii* exhibited a broad inhibition spectrum, presenting strong activity (MIC between100 and 900 μg/mL) against different serotypes of *E.coli* [28].
Aloysia triphylla	Verbenaceae	Lemon beebrush	Beh Limu	A study showed that *A. triphylla* essential oil had a MIC of 500-1000 μg/mL against different serotypes of *Escherichia coli* [29].
Agastache foeniculum	Lamiaceae	Anise hyssop	Gol Mekziki	Results of a study by disk diffusion method showed that *A. foeniculum* essential oil caused a 9 ± 0.58 mm inhibition zone. MIC and MBC values were 500μg/mL and 1000 respectively [29].
Myrtus communis	Myrtaceae	Myrtle	Murd	Growth inhibition zone in disk diffusion method was 35 mm (in diameter). Also a 2% concentration of *myrtle* extract had bactericidal effect on the growth of *E. coli* O157:H7 for the fifth day while 0.5%, 1% and 1.5% concentrations of myrtle extract had bacteriostatic effect on the bacteria [30]. An experimental study indicated that leaf extract of *M. communis* had minimum inhibitory concentration (MIC) of 8mg/ml and minimum lethal concentration (MBC) against *E. coli* was determined as 40 mg/ml [31].

Scientific name	Plant Family	Common name	PersianName	Discussion
Cuminum cyminum	Umbelliferae	Cumin	Zire Sabz	Spice extract of *C. cyminum* had significantly inhibitory effect on the growth of *Escherichia coli* bacteria in 17 mm diameter. All concentrations of cumin extract (0.5, 1, 1.5 and 2 %) had a bacteriostatic effect on *E. coli O157:H7* [30]. Result of an Iranian study revealed that 10µl of *C. cyminum* essential oil formed a growth inhibition zone of 18.3mm [32].
Origanum vulgare	Labiataea	Oregano	Marzanjush	An experimental study demonstrated that growth inhibition zone of *O. vulgare* on *E. coli O157:H7* was 30 mm (in diameter). 1, 1.5 and 2% concentrations of oregano extract had bactericidal effect on the growth of E. coli O157:H7 [30]. Both MIC and MBC of *O. vulgare* leaf essential oil for *E. coli* were confirmed as 500 ppm [33].
Satureja cuneifolia	Lamiaceae	Wild savory	Marzeh	Results of a study showed that *S. cuneifolia* essential oil on *E. coli* formed a growth inhibition diameter of 37.5 mm [34].
Jatropha curcas	Euphorbiaceae	Barbados nut	Jatropha	Inhibition growth zone of methanol extract of *J. curcas* at a concentration of 10 mg/ml is equivalent to 14 ± 0.2 mm. MIC and MBC of methanol extracts on *Escherichia coli* were 5 and 10 mg/ml respectively [35].
Pluchea indica	Asteraceae	Indian camphorweed	–	A study showed that methanol extract of *P. indica* was effective on *E.coli* growth with 31.25 mg/ml MIC and 62.50 mg/ml MBC [22].
Chrysanthemum indicum	Asteraceae	Guldaudi	Davoodi	Results of a study showed that *C. indicum* essential oil on *E.coli* formed a growth inhibition diameter of 26 mm [36].
Citrus bergamia	Rutaceae	Bergamot	Toranj	An experimental study indicated that the most effective essential oil on *E.coli O157* caused a 24 mm inhibition zone [37]. In another study, growth inhibition zone was 15.75mm. MIC and MBC were 2 and 4g/ml, respectively [38].
Diospyros discolor	*Ebenaceae*	Butterfruit	Sib Makhmali	Methanol extract of *D. discolor* leaves at a concentration of 1000µg/100µl showed maximum inhibitory activity against *E. coli* and caused 27 mm inhibition zone [39].
Juniperus foetidissima	Cupressaceae	Foetid juniper	Chataneh	Obtained results showed that *J. foetidissima* extract had 11 mm inhibition zone diameter. Also minimum inhibitory concentration was 25µg/mL[40]. In other study, MIC value of *J. foetidissima* leaves against *E. coli* was 3.125 mg/mL [41].
Eucalyptus tereticornis	Myrtaceae	Forest Red Gum	Eucalyptus	The findings showed that all concentrations of plant extract were effective against *E. coli* with different zones of inhibition. The maximum antimicrobial activity exhibited by the leaf extracts of *E. tereticornis* against *E. coli* was recorded to be 28.6 mm [42]. Result of a study showed that inhibition diameter of *E. tereticornis* essential oil was equal to 22mm [43].
Anisophyllea laurina R. Br.	Anisophylleaceae	Anisophylle	–	The crude extracts of pulp and seed exhibited antibacterial activity against bacterial strains. According to the results obtained from the disc diffusion assay given in ethanol extract of pulp showed inhibition zone diameter of 23.33 mm against *E.coli O157:H7* [44].
Anogeissus acuminate	Combretaceae	Button tree	-------------	A study showed that inhibition zone diameter was 22mm and had antimicrobial effects on *E.coli* with MIC and MBC 3.41 mg/ml and 4.27 mg/ml, respectively [45].
Azadirachta indica	Meliaceae	Neem	Cherish	Obtained results showed that *A. indica* extract caused 19 mm inhibition zone and MIC and MBC were 4.27 mg/ml and 9.63 mg/ml, respectively [45].
Bauhinia variegata L.	Fabaceae	Mountain ebony, Kanchan	Orkide	Inhibition zone diameter was 19mm for *E. coli*. MIC and MBC of *B. variegata* extract were obtained 4.27 mg/ml and 9.63 mg/ml, respectively [45].
Terminalia chebula Retz	Combretaceae	Chebulic myrobala, Harida	–	A study indicated that extract of *T. chebula* on *E. coli* formed a growth inhibition zone of 16 mm and had 9.63 mg/ml MIC and 21.67 mg/ml MBC, respectively [45].
Alcea pallida	Malvaceae	Mallow	Khatmi	The antimicrobial activities of *A. pallida* extract against *E.coli* were assessed about 10±2 mm [46]. In another study, *A. pallida* extracts showed inhibition zone diameter of 19 ± 0/57 against *E. coli* [47].
Ocimum basilicum	Lamiaceae	Basil	Reyhan	Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for *O. basilicum* essential oil was 10 mg/mL against *E. coli* [48]. Result of another study showed that growth inhibition zone of *O. basilicum* ethanol extract in a dilution of 100 and 200 mg/l were 5 and 9 mm, respectively [49].

Scientific name	Plant Family	Common name	PersianName	Discussion
Matricaria chamomilla	Asteraceae	Mayweed	Baboneh	Ethanol extract of *M. chamomilla* showed maximum inhibitory zone of 1.43cm against *E.coli* at 20 µg/ml concentration. In correlation with ethanol extracts, methanol extracts of *Matricaria chamomilla* showed maximum inhibitory zone of 1.2cm against *E.coli* at 12µg/ml [50]. In another study of *M. chamomilla* methanol extract, maximum inhibitory zone was 1.2cm against *E.coli* bacteria [51].
Aloe vera	Liliaceac	Aloe	Sabre zard	Growth inhibition zone of *Aloe vera* extract after 48 hours was recorded 15.42mm [52]. Another study showed that MIC and MBC of *Aloe vera* extract against *Escherichia coli* were 8mg/l, respectively [53].
Mentha piperita	Lamiaceae	Mentha	Naana	Essential oil from *M. piperita* showed MIC about 62.50 µg/ml [54]. Result of a study showed that growth inhibition diameter of *M. piperita* essential oil was 13.67mm [55].
Peumus boldus	Monimiaceae	Boldo wood tree	------------	According to the data, *E. coli* was sensitive to *P. boldus* essential oil and MIC was 31.25 µg/ml [54].
Malva sylvestris	Malvaceae	Mallow	Panirak	According to MIC and MBC values reported, the oils showed an interesting antimicrobial activity against *E. coli*. (MIC = 12.5µg/ml, MBC = 25µg/ml) [54]. The results of the study revealed that *M. sylvestris* leaf extract had inhibition zone diameter of 640mm [56].
Artemisia dracunculus	Asteraceae	Tarragon	Tarkhon	An experimental study indicated that the most effective essential oil on *E. coli O157:H7* caused a 8 mm inhibition zone and range of MIC and MBC were between 2 to 32mg/ml [57]. In another study, *Artemisia dracunculus* essential oil had antimicrobial effects on *Escherichia coli* in the MBC and MIC of 5000 and 2500µg /mL, respectively [58].
Morus nigra	Morus	Berry	Tameshk	Obtained results showed that leaf extracts of *M. nigra* showed the highest antimicrobial activity. MIC and MBC of berry leaf extracts for *Escherichia coli* were 187/ 375 and 63/ 125µg/ml, respectively [59].
Camellia sinensis	Theaceae	Green Tea	Chaye sabz	MIC of *C. sinensis* extract was 12.5 mg/ml against *E. coli* but the MBC was found to be 50 mg/ml which is 4 times higher than their MIC and produced an inhibition zone of 9 mm against *E. coli* [60]. In an Iranian study, MIC of green tea was recorded 5 mg/ml [61].
Zingiber officinale	Zingiberaceae	Ginger	Zanjabil	Result of analysis showed that ginger had the zone of inhibition about 24 mm [62]. In a survey conducted on the antimicrobial activity of ginger extract, MIC value was determined 40 mg/ml for *E. coli* [63].
Cratoxylum formosum	Hypericaceae	mempat tree	-------------	*C. formosum* extract had a strong antimicrobial activity against food-borne pathogens like *E.coli* and minimum inhibitory concentration (MIC) against *E.coli* was 3.0 mg/ml [64].
Citrus. limon	Rutaceae	Lemon	Limu	Lemon essential oil have strong inhibitory effect against *Escherichia coli* which had a MIC of 25.0 µg/ml [65]. In another evaluation of inhibitory effect of lemon against *E. coli*, MIC of 400µg /mL was expressed [66].
Cinnamon Zeylanicum	Lauraceae	Cinnamon	Darchin	Results showed that *C. zeylanicum* essential oil formed a growth inhibition diameter of 0.415 ± 0.05 cm and MIC value ranged from 0.14–0.43 mg/mL [67]. MIC of *C. Zeylanicum* essential oil on *E. coli* was expressed 50 ± 2.5mg/ml [68].
Foeniculumvulgare	Apiaceae	Fennel	Razyaneh	The results from the disc diffusion method showed MIC of fennel extract was 62.5 ± 3.1–500 ± 8.9 µg/ml and fennel seed extracts showed more inhibitory impact than leaf extracts [69]. In another study , E. coli affect inhibition zone diameter for oil F. Vulgare 11.2 ± 0.8mm And the amount was determined mic 125ug/ml [70].

Antibiotic resistance among Gram negative bacteria has been called one of the world's most pressing public health problems [71]. Medicinal plants can be an alternative method for their safety, relatively low cost and effectiveness against multi-drug resistant pathogens [72]. Essential oils are complex volatile compounds, synthesized naturally in different parts of plants during the process of secondary metabolism. The presence of different types of aldehydes, phenolics, terpenes, and other antimicrobial compounds means that the essential oils are effective against a diverse range of pathogens [73-74].

Punica granatum (pomegranate) is one of the oldest fruit with antioxidant and antimicrobial activities. Pomegranate peel is an important source of compounds such as ellagic acid and its derivatives, ellagitannins such as punicalin and punicalagin [75]. Strong antimicrobial activity of *Foeniculum vulgare* (fennel) and *Bauhinia purpurea* (Orchid tree) can be partly reflects higher content of phenol and flavonoid [69, 76-77]. phytochemical studies on *Lippia* *adoensis* (koseret), *Citrus limon* (lemon) extracts, *Azadirachta indica*(neem) essential oil, and *Jatropha curcas* (Barbados nut) stem bark extracts showed the presence of saponins, steroids, glycosides, alkaloids and flavonoids [35,78-80]. *Rosemary officinalis* (rosemary) essential oil has demonstrated antimicrobial activity and controls blood lipid and antilipid peroxidation among many other activities. Hydrophobic diterpenes carnosol and carnosic acid and the hydrosoluble compound rosmarinic acid are the main ingredients of *R. officinalis* [81]. *Pimpinella anisum* (anise) analysis revealed that it can cause gastric protection, muscle relaxant and affect digestive system. The most important compounds of *P. anisum* essential oil are trans-anethole, estragole, γ-hymachalen, panisaldehyde and methyl chavicol [82]. Major component of *Cinnamomum zeylanicum* (cinnamon) leaf oil is eugenol. Cinnamaldehyde and camphor have been reported to be the active ingredients of volatile oils from stem bark and root bark, respectively. The main compound in fruits, flowers, and fruit stalks is trans-cinnamyl acetate [83] .The antimicrobial activities of *Salvia officinalis* (sage) can be related to the presence of high amounts of thujone, 1,8-cineole and camphor, three monoterpenes with well documented antibacterial and antifungic potential [19,84]. Phytochemical analysis of *Diospyros discolor* (Butterfruit) show that this plant contains alkaloids, tannins, phytosterols, diterpenes and phenols [38]. *Berry* fruits are recognized as plants rich of different phenolic compounds and have antioxidant, anti-cancer, antiinflationary and antimicrobial activities [59,85]. Eucalyptol, ethanone and α-pinene are some of the effective compounds of *Eucalyptus tereticornis* (eucalyptus) that have antimicrobial properties [86-87]. The significant antibacterial activities of *Cymbopogon martinii* (palmarosa) oil and its usefulness for treating diarrhoea caused by *E.coli* is due to presence of three major identified compounds: *trans*-geraniol, geranyl acetate and in a lower concentration *trans*-caryophyllene [28,88]. The galls of *Qurercus infectoria* (Aleppo oak) have also been documented to possess antibacterial, antifungal, larvicidal, antiviral and antiinflammatory activities. The main constituents found in the galls of *Q. infectoria* are tannin, free gallic acid and ellagic acid (89). High antimicrobial activity of *Camellia sinensis* (green tea) is due to presence of catechins and polyphones [90]. The leaves of *Aloysia triphylla* plant comprise limonene, tagetone, linalool, Z-Citral and E-Citral compounds [91]. Methylchavicol is active ingredient of *Artemisia dracunculus* (tarragon) that has antibacterial activi [58]. Chemical composition of the *Myrtus communis* essential oils contains E-2-hexenal, Z-3-hexenol, hexanol, tricyclene, α-thujene, α-pinene, sabinene, β-pinene and myrcene [92]. *Cuminum cyminum* as a plant of Umbelliferae has traditional medical usage. Some of its main compounds are coumarin, anthraquinone, glycoside, protein, resin and steroid [93]. The main constituents of *Agastache foeniculum (*Anise hyssop) essential oil were methyl chavicol, limonene, spathulenol and caryophyllene oxide [29]. *Chrysanthemum indicum* used in traditional drug formula for the treatment of some infectious diseases include pneumonia, colitis, stomatitis, cancer, fever and hypertensive symptom. Active compounds in *C. indicum* are glycosides, adenine, and flavonoids [94]. caryophyllene oxide, α-terpineol and geraniol are the main compounds of *Zingiber officinale* (Ginger) that are known to have antibacterial activity [95]. *Citrus bergamia* (bergamot) is a rich source of limonene, linalool, linalyl acetate, γ-terpinene, and β-pinene with antimicrobial effects against many bacteria such as *Escherichia coli* O157 [96].

Carvacrol and thymol are the two major phenolic components of *Thymus vulgaris* (thyme), *Origanum vulgare* (Oregano) , *Syzygium aromaticum*(clove), *Satureja cuneifolia* (Savory), *Mentha piperita* (Mentha) and Zataria multiflora(Za'atar)essential oils in different amounts and they have been found to possess antibacterial activity against E. coli in vitro experiments [12,16,34,97-99].

Inhibitory effect of essential oils on bacterial growth is related to different modes of action. Phenolic components, which are also present in the essential oils, show antimicrobial activity. These components make phospholipid bilayer membrane sensitive, and then cause an increase in membrane permeability, where compounds may disrupt membrane, lose cellular integrity and eventual lead to cell death [12]. This study showed that different plant species used in traditional medicine are promising resources for antimicrobial treatments of colibacillosis [100].

CONCLUSION

An overview on phytochemical analysis has shown that bioactive compounds of medicinal plants with their antioxidant and antimicrobial properties are good alternative for synthetic drugs in food and drug industry and in other word to treatment microbial diseases in medicine.

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