

Quorum-quenching activity of some Iranian medicinal plants

F. Moradi and N. Hadi

Department of Bacteriology & Virology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Anti-quorum sensing (QS) or quorum quenching (QQ) is known as a new anti-bacterial strategy to combat bacterial infection. One of the best candidates for this strategy is a natural plant or traditional herbal medicine. This review aimed to summarize and introduce Iranian medicinal plants with anti-QS properties. Biomedical databases (PubMed, Scopus, Google Scholar and Web of sciences) were investigated to retrieve all related manuscripts published in English and Persian. Out of 65 documents, 47 papers were published during 2010–2020. We categorized and summarized 19 papers that particularly presented the anti-QS activity of Iranian medicinal plants. Based on our results, different studies have been completed on the QQ effects of medicinal plants. We identified 106 plant species with different properties in medicine that have been evaluated for anti-QS activities in Iran. The QQ effects of herbal extracts were identified through different *in vitro* examinations on biosensor and clinical bacterial strains. Only 35 medicinal plants have shown these effects at sub-MICs. Our review summarizes Iranian medicinal plants with anti-QS properties. Some of these herbal extracts showed anti-QS activity against biosensors, standard and clinical bacterial strains. This result is very important because QS systems can be considered as a new target for the development of new remedial strategies and it is a good opportunity to perform QQ studies to effectively combat bacterial infections in the future.

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Keywords: Anti-quorum sensing, bacterial signaling, in-vitro assays, Iran, medicinal plants, new remedial, quorum quenching

Original Submission: 27 January 2021; **Revised Submission:** 14 April 2021; **Accepted:** 19 April 2021

Article published online: 23 April 2021

Corresponding author: Farhad Moradi, Department of Bacteriology & Virology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

E-mail: f.moradi1993@gmail.com

Introduction

Controlling vital functions for different types of bacterial communication, such as biofilm formation or expression of virulence factor genes, relies on the quorum-sensing (QS) signalling system. It would be attractive to determine or design new powerful agents to interfere with these signalling systems to develop antibacterial drugs and new antimicrobial therapies to control bacterial infections [1]. This novel inhibition in bacterial pathogens is popularly known as quorum quenching (QQ) and the agents with this action are named quorum quenchers. This process is a hot topic in microbiology because

the quorum quenchers are not related to expansion of bacterial resistance and they inhibit the vital activity of bacterial cells in a unique population. Quorum quencher compounds have been isolated from various natural sources, such as many eukaryotes, different microorganisms, fruits, vegetables, and natural plants [1,2]. One of the best candidates to combat bacterial pathogens, especially through inhibiting the QS system, is traditional herbal medicine or natural plants. The QS systems in Gram-negative or Gram-positive bacterial populations produce and diffuse signal molecules such as acyl-homoserine lactones around the bacterial cells; identification of these signals through specific receptors occurs at high concentrations during population growth, and increases the transcription of target gene under QS system control. So, the medicinal plant compounds act as an active quorum quencher because they disrupt these pathways by interfering with signal molecule synthesis, inactivating signals by destroying them, interfering with signal receptors in bacterial cells, and blocking target genes under QS controls (Fig. 1) [3,4]. This new

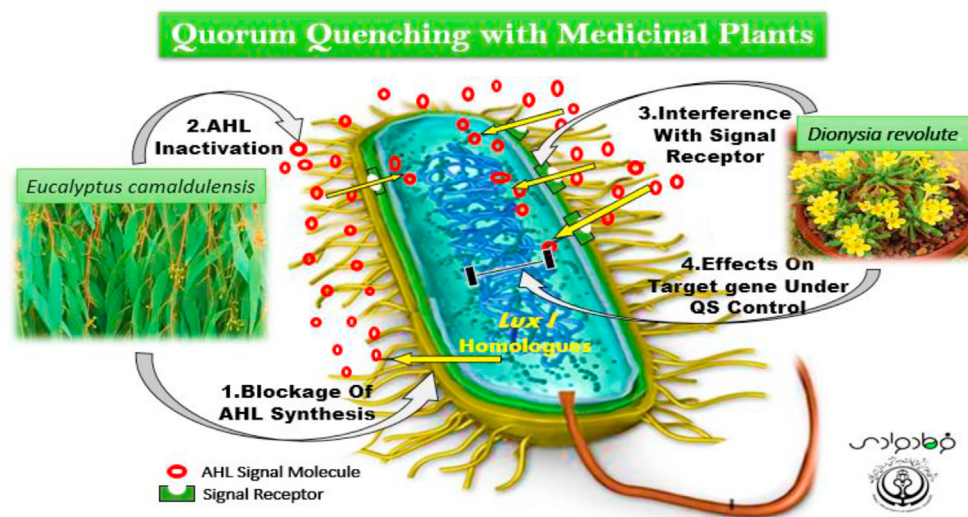


FIG. 1. Schematic of quorum-quenching strategies in a bacterial cell through traditional herbal medicines.

approach is also appropriate to combat bacterial infections with high resistance to chemical antibiotics and it may help to design new drug, based on herbal medicines. More than 4500 species of plants have been grown from all over the world that are used for medicinal purposes. Research in various countries shows the QQ activity of the extracts of many traditional medicinal plants with numerous secondary metabolites (e.g. essential oils, alkaloids, saponins, flavonoids, tannins) and antimicrobial compounds (e.g. phenolics, quinones, flavanones and alkaloids) [1–4]. Traditionally, medicinal plants and their extracts have been the main source of medicines and in some countries they are used in pharmaceutical industries, to increase the safety of food systems, in veterinary medicine and in the treatment of different illnesses to promote the health of human society. Many people in different countries still rely on traditional herbal medicines for the treatment of many infectious diseases, so changing the focus from antibacterial studies to evaluation of the anti-QS activity of medicinal plants could expose new QQ agents to control many bacterial infections [3,5,6]. Because traditional medicinal plants with antibacterial properties have played an important role in therapeutic purposes and treating bacterial infections in the Middle East, especially in Iran, we decided to perform this brief review to provide a current overview of the traditional and endemic medicinal plants with anti-QS properties in Iran. As the medicinal plant extracts with anti-QS activities could be considered as a novel anti-pathogenic drug, several studies have been completed in Iran to identify the QQ activity of different traditional medicine plant species with antibacterial properties. In this review, we summarize this information about herbal extracts that act as a quorum quenchers in Iran.

Materials and methods

Search strategy

Biomedical databases (PubMed, Scopus, Google Scholar and Web of sciences) were searched to retrieve all related manuscripts published in English and Persian from January 2010 to January 2021. We used the terms 'Quorum sensing AND medicine plant AND Iran', 'anti-quorum sensing AND traditionally herbal medicine AND Iran', 'Quorum Quenching AND medicine plant AND Iran', 'medicine plant OR herbal medicine AND quorum sensing AND Iran', 'anti-quorum sensing OR Quorum Quenching AND plant products AND Iran'. Also, references cited within these articles were implemented to find additional relevant articles. Out of 65 papers, 47 papers were identified that were published between 2010 and 2021 (Fig 2).

Inclusion and exclusion criteria

We selected published literature about Iranian medicinal plants with anti-QS properties in the years between 2010 and 2020. Medicinal plants with QQ effects that have grown endemic or non-endemic in a different region of Iran were selected. We considered all of the herbal extracts with phenotypic or molecular QQ effects on the QS system of different bacterial biosensor strains, or bacterial pathogens isolated from clinical specimens in Iran. For this reason, we collected studies that were related to the anti-QS system activity of herbal extracts, for example, anti-biofilm activity. Articles that only provided other effects of Iranian medicine plants such as antioxidant, anticancer, anti-inflammation and some others were excluded. Also, studies on QQ effects of other agents, such as a different

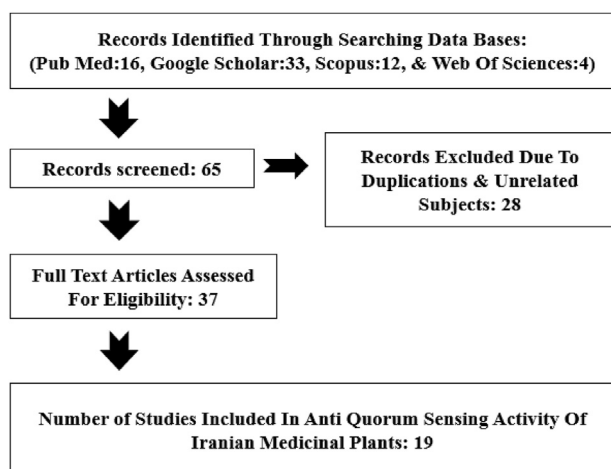


FIG. 2. Flow chart of study.

form of vitamins, metal complexes (e.g. copper, iron, curcumin, zinc), many microorganisms (quorum quenchers isolated from bacterial strains) and herbal medicine in other countries, as well as duplicate documents were excluded.

Data extraction and analyses

We extracted and categorized all of the information about medicinal plants evaluated for QQ activity in Iran including scientific name, part of plant used for anti-QS examination, type of extraction and products used (ethanol extract, methanol extract, essential oil), bacterial strains for QQ assays (bacterial biosensor strain or isolated from clinical specimens), plant species with positive anti-QS actions or other effects related to QQ such as antibiofilm activity, type of QQ effect on different strain (phenotypic or molecular), the purpose of studies and application of herbal extracts that authors recommended. Statistical analyses were completed, using Microsoft EXCEL 2019 for numerical calculations.

Results

Based on our results, different studies have been performed on the QQ effects of medicinal plants in Iran. We identified 106 plant species with different effects in medicine, which have been evaluated for anti-QS properties. These medicinal plants were commonly used for different treatment purposes in Iran. Only 35 species of these medicinal plants have shown QQ effects at sub-MICs. These effects are acceptable because at this concentration, the microbial population is stable, bacterial species are alive, and they carry out signal exchange using QS systems. These studies evaluated the QQ activity of herbal extracts on

biosensor strains (e.g. *Chromobacterium violaceum* wild type or CV026, *Pectobacterium carotovorum*, *Agrobacterium tumefaciens* NTL/PZLR4, *Pseudomonas aeruginosa* PAOI wild type or PAOI (MH873), and *Aeromonas veronii* Sobria strain BC88) or different bacterial species isolated from clinical specimens such as *Streptococcus pneumoniae*, *P. aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi* and *Salmonella Typhimurium*. These anti-QS effects have been studied phenotypically (e.g. repress violacein production in *C. violaceum*, prevent biofilm formation by *P. aeruginosa* or *Staphylococcus aureus*, reduce pyocyanin, protease and elastase production in *P. aeruginosa*) and molecularly such as down-regulation of QS genes (*sdiA* and *luxS* in *Salmonella Typhimurium*, *LuxS* and *pfs* in *Streptococcus pneumoniae*, or *lasI* and *lasR* in *P. aeruginosa* through different methods. For example, real-time PCR method for gene expression assay, microtitre plate assay for anti-biofilm activity, different bacteriological or innovative methods (e.g. use of soft top agar contained Luria–Bertani (LB) agar and semi-solid LB with biosensor strains, melted LB agar with biosensor strains, molten semi-solid LB agar and signal molecules, and LB soft agar with herbal extracts) for in vitro QQ assay of herbal extracts. Plant materials were obtained from natural areas in different regions of Iran or purchased from reputable companies, for instance Bonyan Salamat Kasra Co. (Tehran, Iran). Herbal medicines were extracted using polar and non-polar solvents (e.g. acetone, methanol, ethanol, n-hexane) or preparing essential oils by different methods (including Soxhlet, maceration, digestion and superficial extraction). Some of the studies reported the QQ activity of some herbal extracts at high concentrations and researchers used different solvents to maximally extract polar and dipolar compounds from these medicinal plants instead of using alcohol or water extraction, which just extracts some of the bioactive compounds. It may for this reason that medicinal plants consist of many different compounds. A few studies used different chromatography methods, such as thin-layer and gas chromatography, to identify the bioactive compounds of herbal medicines. In some studies, some of the plant extracts with antibacterial properties showed QQ effects. Researchers have new applications for these herbal extracts with anti-QS properties. For example, treatment of chronic infections caused by bacterial pathogens by permitting the human immune system to eradicate the pathogens, designing the new anti-biofilm agents based on herbal medicine compounds, using these plant compounds as alternatives to antibiotics for control and treatment of infections caused by multidrug-resistant bacterial strains, and developing herbal drugs such as mouthwashes against dental bacterial infection. All of this information is provided in Table I.

TABLE 1. Anti-quorum sensing studies of traditional medicinal plants in Iran

First authors, publication year [reference]	Plant species evaluated (part tested)	Products	Strains tested	Plant species with anti-quorum-sensing properties	Quorum-quenching effects	Other effects and authors comments
Mahmoudi E et al., 2014 [16]	<i>Pelargonium hortorum</i> , <i>Triticum aestivum</i> , <i>Lycopersicon esculentum</i> , <i>Hordeum vulgare</i> , <i>Cucumis sativus</i> , <i>Oryza sativa</i> , <i>Mentha</i> spp., <i>Allium sativum</i> , <i>Zea mays</i> , <i>Onobrychis sativa</i> , <i>Coriandrum sativum</i> , <i>Capsicum annuum</i> , <i>Allium porrum</i> , <i>Foeniculum vulgare</i> , <i>Beta vulgaris</i> , <i>Olea europaea</i> , <i>Sage Salvia officinalis</i> , <i>Petroselinum crispum</i> , <i>Phaseolus vulgaris</i> , <i>Lentis sativa</i> , <i>Cicer arietinum</i> , <i>Pisum sativum</i> , <i>Ocimum basilicum</i> , <i>Vicia radiata</i> , <i>Raphanus sativus</i> , <i>Phaseolus vulgaris</i> , <i>Allium ampeloprasum</i> , <i>Anethum graveolens</i> , <i>Althea officinalis</i> , <i>Abelmoschus esculentus</i> , <i>Foeniculum vulgare</i> , <i>Solanum melongena</i> , <i>Medicago sativa</i> , <i>Capsicum annuum</i> , <i>Amaranthus blitum</i> , <i>Zataria multiflora</i> , <i>Artemisia dracunculul</i> , <i>Apium graveolens</i> , <i>Trifolium repens</i> , <i>Satureja hortensis</i> , <i>Cucumis melo</i> , <i>Thymus</i> sp., <i>Solanum tuberosum</i>	Methanolic extract of 44 medicine plant species	<i>Chromobacterium violaceum</i> CV026, <i>Pectobacterium carotovorum</i> subsp. <i>Carotovorum</i>	<i>Althea officinalis</i> , <i>Artemisia dracunculul</i> , <i>Raphanus sativus</i>	Repress violacein production in CV026, inhibit QS-regulated virulence in <i>Pectobacterium</i> on potato tubers, contains AHL-mimicking molecules that can activate QS function in <i>Trifolium repens</i>	Plants have quorum sensing-mimicking signals that could potentially be used for disrupting quorum sensing
Makhfian M et al., 2015 [5]	<i>Artemisia dracunculul</i> , <i>Coriandrum sativum</i> , <i>Trigonella foenum</i> , <i>Satureja hortensis</i> , <i>Tagetes minuta</i> , <i>Ocimum basilicum</i> , <i>Descourainia sophi</i> , <i>Spinacia oleracea</i> , <i>Cicer arietinum</i> , <i>Medicago sativa</i> , <i>Cardaria draba</i> , <i>Equisetum arvense</i> , <i>Anethum graveolens</i> , <i>Sophora secundiflora</i> , <i>Trifolium</i> spp., <i>Hordeum morinum</i> , <i>Solanum tuberosum</i> , <i>Cyclamen hederifolium</i> , <i>Lactuca sativa</i> , <i>Phleum</i> spp., <i>Zea mays</i> , <i>Centaurea cyanus</i> , <i>Allium ampeloprasum</i> , <i>Triticum</i> spp., <i>Daucus carota</i> , <i>Allium sativum</i> , <i>Capsicum frutescens</i> , <i>Apium graveolens</i> , <i>Abelmoschus esculentus</i> , <i>Phaseolus vulgaris</i> , <i>Mentha piperata</i>	Ethanol extracts of 31 medicine plant species	<i>C. violaceum</i> CV026, <i>P. carotovorum</i> subsp. <i>carotovorum</i> strain 116B	<i>Trigonella foenum</i> , <i>Cardaria draba</i> , <i>Equisetum arvense</i> , <i>Anethum graveolens</i> , <i>Phleum</i> spp., <i>Allium ampeloprasum</i> , <i>Capsicum frutescens</i>	Inhibition of violacein pigmentation in <i>C. violaceum</i> CV026 and reduction in tissue maceration in test plants	These plants can mimic quorum-sensing signals (especially Eugenol as major component in <i>Anethum graveolens</i>)
Sepahi E et al., 2015 [17]	<i>Ferula (Ferula asafetida)</i> , <i>Dorema (Dorema aucheri)</i>	Essential oils	<i>Pseudomonas aeruginosa</i> PA01, <i>C. violaceum</i> CV026	<i>Ferula asafetida</i> , <i>Dorema aucheri</i>	Reduced the violacein in <i>C. violaceum</i> , Pyocyanin, pyoverdine, elastase and biofilm production and decrease QS-dependent genes in <i>P. aeruginosa</i> . But <i>Dorema</i> oil could not show anti-biofilm effects	These plants as novel QS and virulence inhibitors.
Korkorian N et al., 2017 [18]	<i>Rumex alveolatus</i> (leaves and roots)	Aqueous and methanol extracts	<i>P. aeruginosa</i> , <i>Staphylococcus aureus</i>	<i>Rumex alveolatus</i>	Prevented biofilm formation by <i>P. aeruginosa</i> and <i>S. aureus</i> , reduced pyocyanin production in <i>P. aeruginosa</i> . Main phenolic compound was 1,2-benzene dicarboxylic acid	Aqueous extracts of <i>R. alveolatus</i> had not antibacterial and anti-QS activity.
Kordbacheh H et al., 2017 [19]	<i>Pistacia atlantica</i> (leaf)	Methanolic extract	<i>P. aeruginosa</i> PAOI	<i>Pistacia atlantica</i>	Inhibition of biofilm and pyocyanin and LasR protein with active compounds (myricetin, 3-O-rutinoid, kaempferol-3-O-rutinoid)	Treatment of infections caused by <i>P. aeruginosa</i>
Mohabi S et al., 2017 [1]	<i>Quercus infectori</i> (galls)	Methanol extract	Five strains of <i>P. aeruginosa</i> (ATCC 27853, PAOI wild, PAOI (MH873), MS.PS.S0/35, and PDO 300 (mucA2e, a hyper alginate producer)), <i>C. violaceum</i> CV026	<i>Quercus infectori</i>	Decreasing the biofilm formation, level of protease LasA, LasB, swarming and twitching motility & <i>lasR</i> gene expression in <i>P. aeruginosa</i> strains. Inhibited the QS in <i>C. violaceum</i> CV026	Antibacterial effects & best candidate for alternative treatment of pseudomonad infections in future.
Karbasizade V et al., 2017 [20]	<i>Quercus infectoria</i> , <i>Zataria multiflora</i> , <i>Trachyspermum copticum</i>	Acetone extract of <i>Q. infectoria</i> and methanol extracts of <i>Z. multiflora</i> and <i>T. copticum</i>	<i>P. aeruginosa</i> strain (PTCC 1430)	<i>Quercus infectoria</i> , <i>Zataria multiflora</i> , <i>Trachyspermum copticum</i>	Inhibition of pyocyanin, protease, elastase production and biofilm formation	These herbs can be used as antipathogenic drugs
Sharifi A et al., 2018 [21]	<i>Thymus daenensis</i> , <i>Satureja hortensis</i> , <i>Origanum vulgare</i>	Essential oils	<i>S. pneumoniae</i>	<i>Thymus daenensis</i> , <i>Satureja hortensis</i> , <i>Origanum vulgare</i>	Anti-biofilm activity, down-regulated <i>LuxS</i> and <i>pfs</i> (QS genes) by	Introduced as new anti-biofilm and QS inhibitor agents

TABLE I. Continued

First authors, publication year [reference]	Plant species evaluated (part tested)	Products	Strains tested	Plant species with anti-quorum-sensing properties	Quorum-quenching effects	Other effects and authors comments
Jamalifar H et al., 2019 [22]	Green coffee beans powder (<i>Coffea arabica</i> L.)	Dissolved in boiling distilled water	<i>P. aeruginosa</i> (ATCC 15449), <i>P. aeruginosa</i> strains were isolated from clinical samples	(<i>Coffea arabica</i> L.)	thymol, carvacrol, p-cymene, pulegone and 1,8-cineole Pathogenesis-related genes, <i>lasI</i> and <i>lasR</i> in <i>P. aeruginosa</i> are down-regulated through chlorogenic acid	Could be useful as an adjuvant & effective inhibition and eradication of <i>P. aeruginosa</i>
Pishgar E et al., 2019 [23]	<i>Rubus ulmifolius</i> (Raspberry blossom), <i>Artemisia dracunculus</i> (leaves), <i>Centaurea cyanu</i> (flower), <i>Descurainia sophia</i> (leaves and flower)	Ethanol extract	<i>Agrobacterium tumefaciens</i> NTL/PZLR4. <i>S. aureus</i> were isolated from patients with dental implant infection	<i>Rubus ulmifolius</i> ,	Showed the QQ effects on biosensor strain by producing the blue colony and without hydrolysis of X-gal, anti-biofilm effects by microtitre plate (MTP) assay	<i>Rubus ulmifolius</i> can be considered as a mouthwash against dental bacterial infection, other plant species just show Antibacterial effects
Arjmandi A et al., 2020 [24]	<i>Citrus limon</i> (L.) (lemon peel)	Essential oil	<i>P. aeruginosa</i> Biosensor strain	<i>Citrus limon</i> (L.)	Inhibition of biofilm with essential oil ligands geranyl acetate, α-terpineol and β-bisabolene	It can be considered as a source of anti-biofilm and antimicrobial formulation.
Sharchi R et al., 2020 [25]	<i>Satureja sahendica</i> (flower)	Hydroalcoholic extract	<i>Salmonella</i> Typhimurium isolated from avian	<i>Satureja sahendica</i>	Decrease the expression of QS-associated gene (<i>sdIA</i>)	Antibacterial effects and it can be used to control the expression of virulence genes in <i>S. Typhimurium</i> .
Moradi F et al., 2020 [2]	<i>Syzygium aromaticum</i> (Stem), <i>Dionysia revoluta</i> (whole plant), <i>Eucalyptus camaldulensis</i> (leaves)	n-hexane, methanol, 96% ethanol mixed solvent	<i>C. violaceum</i> CV026, <i>Aeromonas veronii</i> bv. Sobria strain BC88, <i>P. aeruginosa</i> isolated from a patient with cystic fibrosis	<i>Syzygium aromaticum</i> <i>Dionysia revoluta</i> <i>Eucalyptus camaldulensis</i>	Anti-QS activities by reducing the violacein formation and depletion of QS signals produced in <i>A. veronii</i> and <i>P. aeruginosa</i>	Antibacterial effects, and depleting the signalling system in bacterial clonality, thus permitting the immune system to eradicate the infection
Ghaderi L et al., 2020 [9]	<i>Lavandula angustifolia</i> , <i>Rosmarinus officinalis</i> , <i>Satureja khuzistanica</i>	Essential oil nanoemulsions, carvacrol and 1,8-cineol)	<i>P. aeruginosa</i> PAOI	<i>Satureja khuzistanica</i> , carvacrol and 1,8-cineol	Eradication of PAOI biofilm and decrease pyocyanin production	Nanoemulsions could improve the antibacterial and antibiofilm activity of essential oil
Hakimi Alni R et al., 2020 [26]	<i>Allium sativum</i> <i>Cuminum cyminum</i>	Essential oils	<i>Salmonella</i> Typhimurium isolates	<i>Allium sativum</i> <i>Cuminum cyminum</i>	Down-regulated of QS (<i>sdIA</i> and <i>luxS</i>) and cellulose synthesis (<i>csgD</i> and <i>adrA</i>) genes and reduced the <i>S. Typhimurium</i> biofilm.	Antibiofilm effects without cytotoxic effect on the eukaryotic Vero cells with terpineol, carene and pinene in <i>C. cyminum</i> and sulfur in <i>A. sativum</i>
Fekrirad Z et al., 2020 [27]	Eugenol (the major clove extract)	Prepared by adding dimethyl sulfoxide	<i>Serratia marcescens</i> ATCC 13880 and <i>S. marcescens</i> Sm2 (isolates from clinical sample)	Eugenol (4-allyl-2 methoxyphenol)	Decrease the biofilm formation, haemolysis, protease, swarming, motility pigment formation and expression of genes involved in motility (<i>flhD</i>), attachment (<i>fimC</i>), biofilm formation (<i>bsmB</i> , <i>bsmA</i>), and QS regulatory (<i>swrR</i>) in <i>S. marcescens</i>	Anti-QS and anti-biofilm effects against <i>S. marcescens</i> strains.
Tanhay Mangoudehi H et al., 2020 [28]	<i>Curcuma longa</i>	Curcumin, component	<i>Aeromonas hydrophila</i> strains isolated from fish	<i>Curcuma longa</i>	Attenuate QS regulating genes (<i>ahylR</i>) and several QS-associated phenotypes (biofilm, swarming, proteolytic, haemolytic activity)	It can be used as an anti-QS agent, to be used in aquaculture.
Hosseinzadeh S et al., 2020 [29]	Licochalcone A, epigallocatechin-3-gallate	Stock solution was made in dimethyl sulphoxide	<i>S. Typhimurium</i> RITCC1730, 23 clinical isolates of <i>S. typhimurium</i> from poultry flocks	Licochalcone A, epigallocatechin-3-gallate	Anti-QS activity with down-regulation of both <i>sdIA</i> and <i>luxS</i> genes in <i>S. typhimurium</i>	Use of these plant for anti-QS based prophylactic/therapeutic against salmonellosis
Mohammadi Pelarti S et al., 2021 [30]	<i>Artemisia dracunculus</i>	Essential oil	<i>Salmonella enterica</i> serovar Typhimurium, <i>Staphylococcus aureus</i>	<i>Artemisia dracunculus</i>	Anti-biofilm activity and down-regulation of <i>luxS</i> , <i>pfs</i> and <i>hld</i> genes by estragole as a main compound	Use of this plant compounds as alternatives to antibiotics.

Abbreviations: QQ, quorum-sensing; QS, quorum-quenching.

Discussion

Today, an effective treatment system and development of new antibacterial drugs to control bacterial infections are very important, because of the appearance of new resistance genes in many pathogenic bacteria and the spread of antibiotic resistance are increasing. Interfering with the bacterial communication systems and inhibition of signal exchange in microbial populations through QQ activity of medicinal plants can be recommended as a new treatment in microbiology. Following this inhibition, the ability of bacterial species to control and express virulence genes for invasive actions decreases.

Some of the studies documented the adverse effects of herbal products caused by toxic constituents (e.g. allergens, pollen, spores, toxins or carcinogenic compounds), which can produce negative effects such as allergic reactions, rashes, asthma, headaches, nausea, vomiting, irritability, increased blood pressure, heart rhythm disorders and diarrhoea. Nephrotoxicity from aristolochic acid and other components of herbal medicine can cause adverse renal effects and pyrrolizidine-alkaloid-containing medicine plants can be hepatotoxic. Most serious adverse effects originate from overuse or misuse of such herbal medicines [7,8].

Although these studies described adverse effects for medicinal plants, they also reported that traditional herbal medicine can act as a powerful quorum quencher by inhibiting the QS pathways in bacterial cells. Unlike other chemical and synthetic antibiotics, bacterial species do not show resistance to these natural compounds and they will lose their resistance to the human immune system. Resistance is increasing in different parts of the world and the use of these herbal medicines may help to decrease the production and consumption of chemical drugs, resulting in the human body being protected from the adverse effects of chemical drugs.

Based on the different climates present, a wide variety of medicinal plants are grown in Middle Eastern countries, including Iran. Iran is an ancient country with 7500–8000 plant species that have been used as medicinal plants in medicine and the treatment of microbial infections. Many of these medicinal plants are endemic in various natural places, including mountainous areas. Some species are not specific to Iran and they also grow in other countries [7,9].

Numerous studies have show the medical application of Iranian medicinal plants. For example, more than 20 species of *Scutellaria* (skullcaps) are used as an anti-arteriosclerosis, anti-allergy, antimicrobial and antiviral drug and 13 species of *Stachys* (Lamiaceae) are endemic and are used for their antitoxic, anti-anoxic and antiseptic effects. Other herbal medicines such

as *Achillea kellalensis* Bioss (for treatment of wounds and skin infections), *Tanacetum polycephalum* Schultz or *Artemisia kermanensis* (as anti-*Candida* agents) and *Zataria multiflora* ((Latiatae family; used for pain-relief) are used in Iranian medicines [10–12].

Since QS and interfering with these communication systems in bacterial species were introduced as a hot topic in microbiology, many researchers in Iran have been attracted to investigate this field and have studied the anti-QS effects of various Iranian medicinal plants. These medicinal plants with active compounds were used as antioxidant, antimicrobial and antifungal agents to develop new antimicrobial drugs, for the treatment of various diseases, and for the inhibition of pathogenic bacteria with antibiotic resistance [13–15]. In this review, we have tried to summarize and introduce Iranian medicinal plants with anti-QS properties. These medicinal plants have been used for treatment of infectious disease in Iran. Some of these herbal extracts showed anti-QS activity against biosensors, standard and clinical bacterial strains. This result is very important because the QS systems can be considered a new target for the development of new remedial strategies and it is a good opportunity to develop QQ studies to effectively fight bacterial infections in the future.

In several types of research on the QQ activity of medicinal plants, researchers have made different suggestions for future QQ studies; for example, improving QQ studies to recognize all medicinal plants with anti-QS properties and evaluation of these studies in both in vitro and in vivo conditions. Additionally, because the effective compounds of some medicinal plants with QQ activity have not been identified, it is essential to identify these bioactive agents to expand and develop the anti-QS research. Many anti-QS examinations were completed on biosensor strains or standard species and it is better to develop this research on different bacterial species isolated from clinical specimens or polymicrobial biofilms. Furthermore, defining minimal QS inhibitory concentration (MQSIC) and the MQSIC: MIC ratio for different herbal extracts would be useful when discussing the respective efficacy of these plant species.

In conclusion, empirical methods in QS studies to discover new quorum quenchers and their use as a novel treatment agent in medical microbiology should be developed, especially for traditional herbal extracts worldwide.

Author contributions

Both authors were responsible for conceptualization, methodology, data curation, writing, reviewing and editing.

Conflict of interest

The authors declare that there are no conflicts of interest.

Data availability

We thanks Department of Bacteriology and Virology, School of Medicine, Shiraz University of Medical Sciences (SUMS) for scientific assistance in carrying out this study.

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