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Quorum-quenching activity of some Iranian medicinal plants

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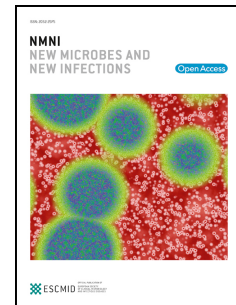
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Title page

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Quorum-quenching activity of some Iranian medicinal plants

Abstract:

Background: Today, 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 the Iranian medicinal plants with anti-QS sensing properties.

Methods: 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, it was identified 47 papers were published during 2010-2020. Finally, we categorized and summarized 19 papers that particularly presented the anti-QS activity of Iranian medicinal plants.

Results: Based on our results, different studies have been completed on QQ effects of medicinal plants. We identified 106 plant species with different properties in medicine, which have been evaluated for anti-QS activities in Iran. These QQ effects of herbal extracts were identified through different *in-vitro* examination on biosensor and clinically bacterial strains. Only 35 medicinal plants have shown these effects at sub-minimum inhibitory concentrations.

Conclusion: Our review summarized the Iranian medicinal plants with anti-QS sensing properties. Some of these herbal extracts showed anti-QS activity against biosensors, standard and clinically bacterial strains. This result is very important because the QS systems can be considered as a new target for the progress of new remedial strategies and it is a good opportunity to develop QQ studies to effectively fight with bacterial infections in the future.

Keywords: Medicinal plants, Quorum Quenching, Anti-quorum sensing, Iran.

1. Introduction

Since, controlling the vital functions in different bacterial communication such as biofilms formation or expression of virulence factor genes, are rely on quorum-sensing signaling system (QS), it's attractive to determine or design new powerful agents to interfering with these signaling system to develop antibacterial drugs and new antimicrobial therapy to control bacterial infections [1]. This novel inhibition in bacterial pathogens is popularly known as quorum quenching (QQ) and the agents with this action name quorum quenchers. This process known as 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 combating with bacterial pathogens especially through inhibiting the QS system of them is a natural plants or traditional herbal medicine. In summary, QS system in gram-negative or gram-positive bacterial populations included produce and diffuse signal molecules such as acyl-homoserine lactones around the bacterial cells, identification of these signal through specific receptors at the high concentration during the population growth, and increasing the transcription of target gene under QS system control. So, the medicine plant compounds introduce as an active quorum quencher because they disrupt to these pathways through interfering with signal molecule synthesis, inactivation of signals by destroying them, interfering with signal receptors in bacterial cells, and blockage of target gene under QS controls (Fig1) [3,4]. This new approach is also appropriate to combating bacterial infections with high resistance to chemical antibiotics and it may help to design new drug's base on herbal medicines. More than 4500 species of plants have

been grown from all over the world which they are used for medicinal purposes. Today's several research in different countries showed 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 such as phenolics, quinones, flavanones, and alkaloids [1-4]. Traditionally medicine plants and their extracts have been the main source in medicines and in different countries they are used in pharmaceutical industries, to increase the safety of food systems, veterinary medicine, and treatment of different illnesses to health promotion of human society. Because many people in different countries still rely on traditional herbal medicines for the treatment of many infectious diseases, changing the focus from the antibacterial studies to evaluation of anti-QS activity of medicinal plants can be expose new quorum quencher agents to control of many bacterial infections [3,5,6]. Because the traditional medicine plants with antibacterial properties have played an important role in therapeutic purposes and treating bacterial infections in the Middle East region countries especially in Iran, we decided to perform this brief review to provide a current overview of the traditionally and endemic medicine plants with anti-QS properties in Iran. Since 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 quorum quenching activity of different traditionally medicine plant species with antibacterial properties. In this review, we summarized this information about herbal extracts which acts as a quorum quencher in Iran.

2.Methods

2.1. 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, it was identified 47 papers were published between 2010-2021 (Fig 2).

2.2. Inclusion and exclusion criteria

In this review, we selected published literature about Iranian medicine plants with anti-quorum sensing properties according to 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. So, we collected studies that are related to the anti-QS system activity of herbal extracts, for example, anti-biofilm activity. But articles that only provided other effects of Iranian medicine plants such as antioxidant, anticancer, anti-inflammation, and some others were excluded. Also, Other studies on QQ effects of other agents such as a different form of vitamins, metal complexes (e.g. copper, iron, curcumin, zinc), many microorganisms (quorum quencher isolated from bacterial strains), and herbal medicine in other countries, and duplicate documents were excluded.

2.3. Data extraction and analyses

We extracted and categorized all of the information about medicinal plants that evaluated for QQ activity in Iran included scientific name, part of plant species used for anti-QS examination, type of extraction and products (ethanol extract, methanol extract, essential oil, etc.), 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 which authors recommended. Statistical analyses were completed, using EXCEL 2019 to numerical calculations.

3. 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 medicine plants were commonly used for different treatment purposes in Iran. Only 35 species of these medicinal plants have shown QQ effects at sub-minimum inhibitory concentrations. These effects are acceptable because at this concentration, microbial population is stable and bacterial species are alive, and they carry out signal exchange under QS systems. Also, these studies were 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* PAO1 wild type or PAO1 (MH873), and *Aeromonas veronii* bv. Sobria strain BC88) or different bacterial species that isolated from clinical specimens such as *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi* and *Salmonella typhimurium*. These anti-QS sensing effects have been studied phenotypically (e.g. repress violacein production in *C. violaceum*, prevented biofilm formation by *P. aeruginosa* or *S. aureus*, reduced pyocyanin, protease, and elastase production in *P. aeruginosa*) and molecularly such as down-regulated of QS genes (*sdiA* & *luxS* in *S. Typhimurium*, *LuxS* & *pfs* in *S. pneumoniae*, or *las I* & *las R* in *P. aeruginosa* through different methods. For example real-time PCR method for gene expression assay, microtiter plate assay for anti-biofilm activity, different bacteriological or innovation methods (e.g. use of soft top

agar contained Luria Britanie (LB) agar and semisolid 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., Iran. They extracted these herbal medicines with polar and nonpolar solvents (e.g. acetone, methanol, ethanol, *n*-hexane) or preparing essential oils with different methods (include; Soxhlet, maceration, digestion, and superficial extraction). Some of the studies, reported the QQ activity of some herbal extracts at high concentration and researchers used different solvent to maximum extract of polar and dipolar compounds from these medicinal plants instead of using alcoholic or watery extracts which just extracted some of the bioactive compounds. It may due to this fact that medicinal plants consist of many different compounds. A few studies used different chromatography methods such as thin-layer and gas chromatography to identify bioactive compounds of herbal medicine. In different studies, some of the plant extracts with antibacterial properties showed QQ effects. Hence, researchers have a different comment for new application of these herbal extracts with anti-QS properties. For example treatment of chronic infections caused by bacterial pathogens through permitting the human immune system to eradicate this pathogens, designing the new anti-biofilms agent base on herbal medicine compounds, use of this plant compounds as an alternatives to antibiotics for control and treatment of multidrug-resistant bacterial strains, and developing herbal drugs such as mouthwash against dental bacterial infection. All of this information is provided in table1.

4. Discussion

Today, an effective treatment system and developing new antibacterial drugs to control bacterial infections is very important, because the appearance of new resistance genes in many pathogenic

bacteria and the spread of antibiotic resistance has been increased. Hence, interfering with bacterial communication systems and inhibition of signal exchange in microbial populations through quorum quenching activity of medicine plants can be recommended as a new treatment in microbiology. Following this inhibition, the ability of bacterial species to control and express of virulence genes to invasive actions critically decreases. Some of the studies documented the side effects for herbal products that caused by toxic constituents (e.g., allergens, pollen, spores, toxins or carcinogens compounds) and they produce negative effects such as allergic reactions, rashes, asthma, headaches, nausea, vomiting, irritability, increased blood pressure, heart rhythm disorders and diarrhea. Furthermore, nephrotoxicity from aristolochic acid and other components of herbal medicine that cause adverse renal effects or the hepatotoxicity of pyrrolizidine-alkaloid-containing medicine plants. Most serious side effects originate from overuse or misuse of such herbal medicines [29,30]. Although these studies introduced the side effects for medicinal plants, but numerous trainings reported that traditional herbal medicine can be 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 in conclusion they will lose their resistance to the human immune system. They are growing in different parts of the world and the use of these herbal medicines may be help to decrease in production or consumption of chemical drugs and the human body will be protected from the side effects of chemical drugs. Based on different climates a wide variety of medicinal plants were grown in the Middle East countries, including Iran. Iran is an ancient country with 7500-8000 plant species that have been used as medicinal plants in medicine and treatment of microbial infections. Many of these medicinal plants were grow endemic in various natural places, including mountainous areas. Some of these species are not specific to Iran and thy are grow in some other countries [29,31].

Numerous studies showed the medical application of Iranian medicinal plants. For examples more than 20 species of *Scutellaria* (skullcaps) used as an anti-arteriosclerosis, anti-allergy, antimicrobial and antiviral drug or 13 species of the *Stachys* (Lamiaceae) are endemic and they used as antitoxic, anti-anoxia, and antiseptic effects. Also, other herbal medicines such as *Achillea kellalensis* Bioss (for treatment of wounds and skin infection), *Tanacetum polycephalum* Schultz or *Artemisia kermanensis* (as an anti-Candida agents), and *Zataria multiflora* ((Latiatae family) that use for pain-relieving) were used in Iranian medicine treatments [23-25]. Since, QS and interfering with these communication systems in bacterial species has been introduced as a hot topic in microbiology, many researchers in Iran have been attracted to investigation in this field and have studied the anti-QS effects of various Iranian medicinal plants. These medicine plants with active compounds were used as antioxidative, antimicrobial, and antifungal agents to developing new antimicrobial drugs, for the treatment of various diseases, and inhibition of pathogenic bacteria with antibiotic resistance [26-28]. In this review, we tried to summarize and introduce Iranian medicinal plants with anti-QS sensing properties. These medicine plant has been used for treatment of infectious disease in Iran. Some of these herbal extracts showed anti-QS activity against biosensors, standard and clinically bacterial strains. This result is very important because the QS systems can be considered as a new target for the development of new remedial strategies and it is a good opportunity to developing QQ studies to effectively fighting with bacterial infections in the future. In several types of research on the QQ activity of medicinal plants, researchers have expressed different useful comments and suggestions for future QQ studies. For instance, improving the QQ studies to recognizing all of 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 in different researches, it's essential to identify these bioactive agents to expanding and developing the anti-QS researches. Also, many anti-QS examinations were completed on biosensor strains or standard species and it's better to develop this research's on different bacterial species isolated from clinical specimens or polymicrobial biofilms. Furthermore, defining minimal QS inhibitory concentration (MQSIC) and MQSIC/MIC ratio for different herbal extracts are useful to discuss the respective efficacy of these plant species. In conclusion, empirical methods in the QS study completed with different examinations by discovering new quorum quenchers use of them as a novel treatment agent in medical microbiology, especially for traditionally herbal extracts in all of the world.

Author contributions

Conceptualization, Methodology, Data Curation, and Writing Review & Editing: FM, NH

Conflict of interest

None

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Ethical statement

None, our study was a review.

Data availability

Data will be made available upon request.

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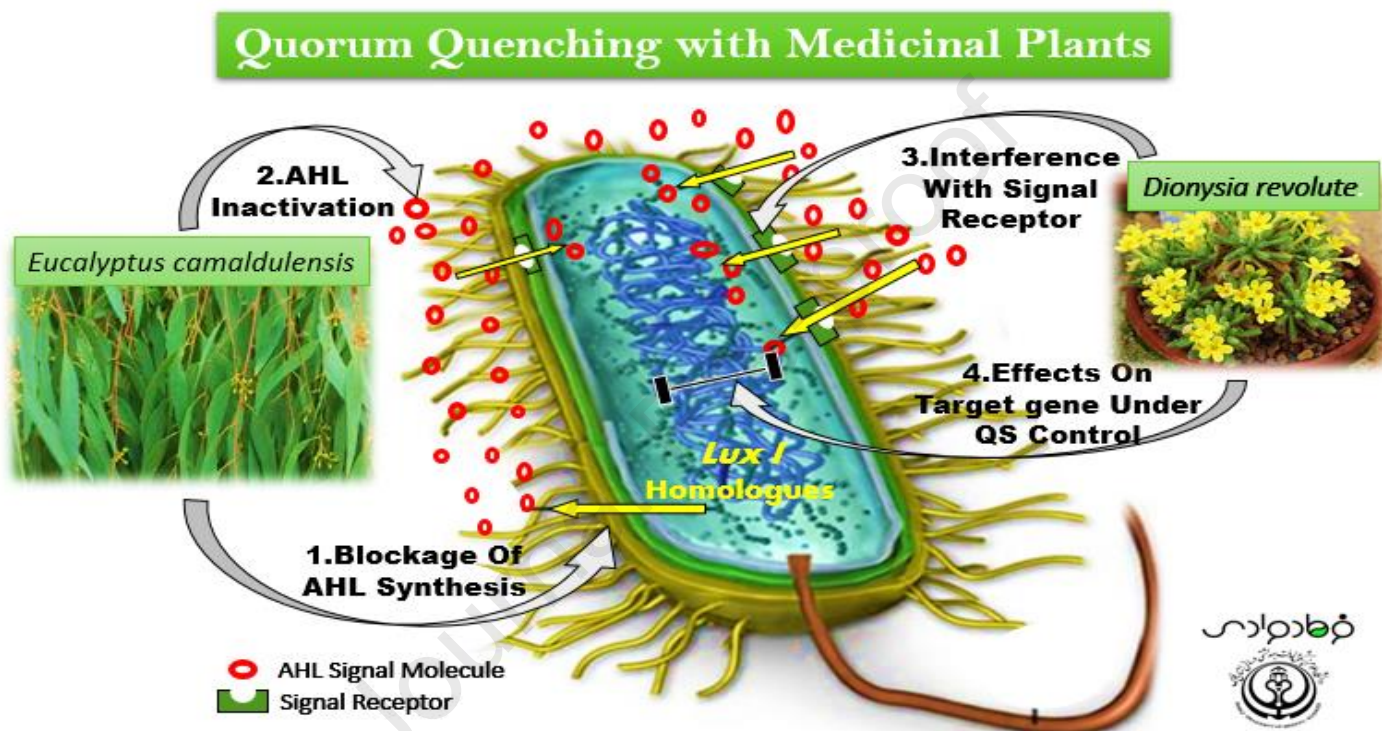


Fig.1. Schematic of quorum quenching strategies in bacterial cell through traditionally herbal medicines.

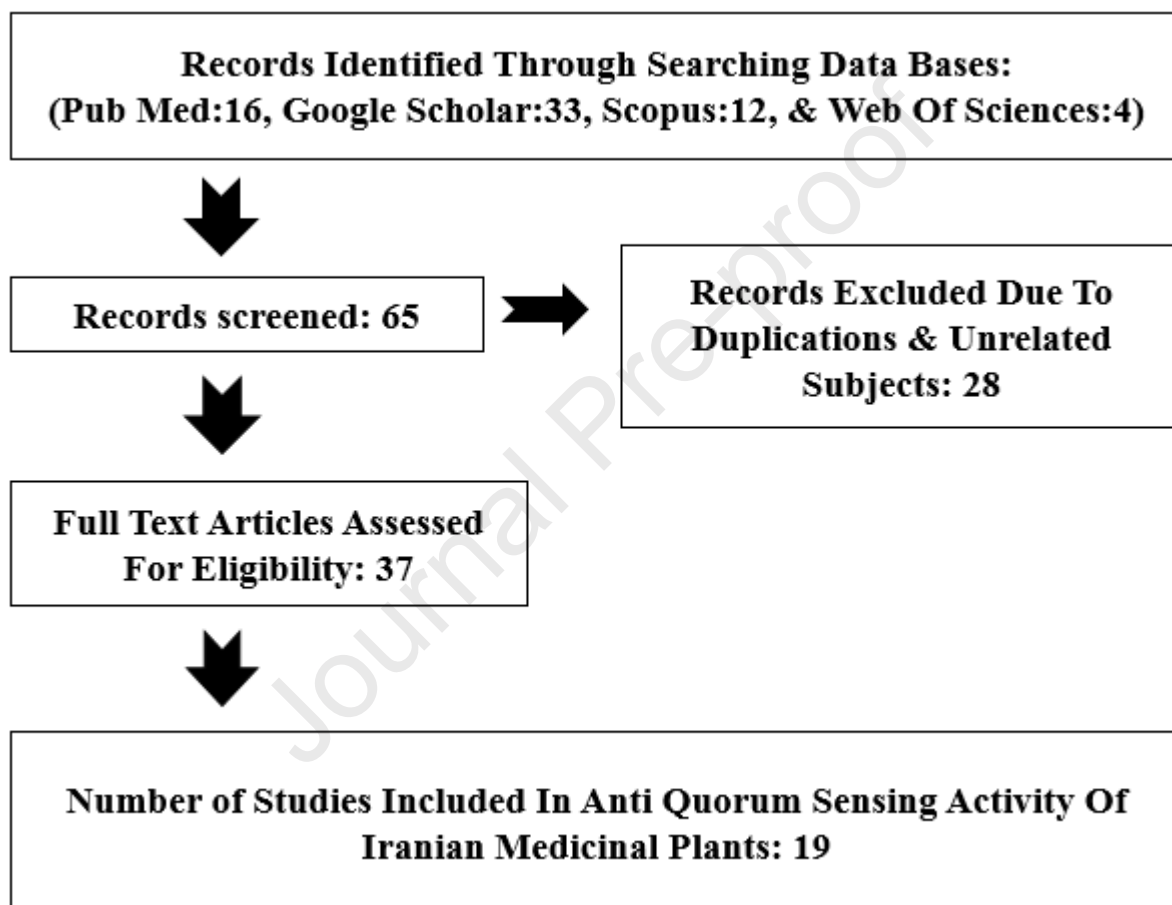


Fig.2. Flowchart of study

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table 1 Anti-quorum sensing studies of traditionally medicine plants in Iran

First Authors, publication year, References	Plant species were evaluated (part of tested)	Products	Strains tested	Plant species with anti- QS properties	QQ effects	Other effects & Authors comments
Mahmoudi E et al., 2014 /13	<i>Pelargonium hortorum</i> , <i>Triticum aestivum</i> , <i>Lycopersicum 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</i> <i>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 dracunculus</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>C. violaceum</i> CV026, <i>P. carotovorum</i> subsp. <i>Carotovorum</i> .	<i>Althea officinalis</i> , <i>Artemisia dracunculus</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>T. 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 dracunculus</i> , <i>Coriandrum sativum</i> <i>Trigonella foenum</i> , <i>Satureja hortensis</i> <i>Tagetes minuta</i> , <i>Ocimum basilicum</i> <i>Descurainia 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>)

First Authors, Publication year/ References	Plant species were tested (part of tested)	Products	Strains tested	Plant species with anti-QS properties	QQ effects	Other effects & Authors comments
Sepahi E, et al, 2015/15	<i>Ferula</i> (<i>Ferula asafoetida</i>), <i>Dorema</i> (<i>Dorema aucheri</i>)	Essential oils	<i>P. aeruginosa</i> PA01, <i>C. violaceum</i> CV026	<i>Ferula asafoetida</i> , <i>Dorema aucheri</i> .	Reduced the violacein in <i>C. violaceum</i> , Pyocyanin, pyoverdine, elastase and biofilm production & decrease QS- dependent genes in <i>P. aeruginosa</i> . But Dorema oil couldn't show anti-biofilm effects.	These plants as novel QS and virulence inhibitors.
Korkorian N, et al., 2017/ 8	<i>Rumex alveolatus</i> (leaves & roots)	Aqueous & Methanol extracts	<i>P. aeruginosa</i> , <i>S. aureus</i>	<i>Rumex alveolatus</i>	Prevented biofilm formation by <i>P.</i> <i>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 R. alveolatus had not antibacterial and anti-QS activity.
Kordbacheh H, et al., 2017 /7	<i>Pistacia atlantica</i> (leaf)	Methanolic extract	<i>P. aeruginosa</i> PAO1	<i>Pistacia atlantica</i>	Inhibition of biofilm and pyocyanin & LasR protein with active compounds (myricetin, 3-O-rutinoside, kaempferol- 3-O-rutinoside)	Treatment of infections caused by <i>P. aeruginosa</i>
Mohabi S, et al., 2017/ 1	<i>Quercus infectori</i> (galls)	Methanol extract	5 strains of <i>P. aeruginosa</i> (ATCC 27853, PAO1 wild, PAO1 (MH873), MS.PS.50/35, 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., 2017/18	<i>Quercus infectoria</i> , <i>Zataria multiflora</i> , <i>Trachyspermum</i> <i>copticum</i>	Acetone extract of <i>Q. infectoria</i> & Methanol extracts of <i>Z.</i> <i>multiflora</i> & <i>T. copticum</i>	<i>P. aeruginosa</i> strain (PTCC 1430)	<i>Quercus infectoria</i> , <i>Zataria multiflora</i> , <i>Trachyspermum</i> <i>copticum</i>	Inhibition of pyocyanin, protease, elastase production and biofilm formation	These herbs can be used as antipathogenic drugs
Sharifi A, et al, 2018 /19	<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, downregulated <i>LuxS</i> and <i>pfs</i> (QS genes) by Thymol, carvacrol, p-cymene, pulegone, and 1,8-cineole	Introduced as new anti- biofilm and QS inhibitor agents

Table1 continue

First Authors, publication year, References	Plant species were evaluated (part of tested)	Products	Strains tested	Plant species with anti-QS properties	QQ effects	Other effects & Authors comments
Jamalifar H, et al 2019/14	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.)	Pathogenesis-related genes, las I & las R in <i>P.</i> <i>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/ 21	<i>Rubus ulmifolius</i> (Raspberry blossom) <i>Artemisia dracunculus</i> (Leaves) <i>Centaurea cyana</i> (Flower) <i>Descurainia sophia</i> (Leaves and flower)	Ethanol extract	<i>A. 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 hydrolyze of X-gal, anti-biofilm effects by microtiter 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/ 20	<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 & antimicrobial formulation.
Sharchi R, et al., 2020/11	<i>Satureja sahendica</i> (flower)	Hydroalcoholic extract	<i>Salmonella</i> Typhimurium Isolated from avian	<i>Satureja</i> <i>sahendica</i>	Decrease the expression of QS-associated gene (<i>sdiA</i>)	Antibacterial effects & 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>A. veronii</i> bv. Sobria strain BC88, <i>P. aeruginosa</i> isolated from a patient with cystic fibrosis	<i>Syzygium</i> <i>aromaticum</i> <i>Dionysia</i> <i>revoluta</i> <i>Eucalyptus</i> <i>camaldulensis</i>	anti-QS activities by reducing the violacein formation & depletion of QS signals produced in <i>A.</i> <i>veronii</i> & <i>P. aeruginosa</i>	Antibacterial effects, & depleting the signaling system in bacterial clonality, thus permitting the immune system to eradicate the infection
Ghaderi L, et al., 2020/29	<i>Lavandula angustifolia</i> , <i>Rosmarinus officinalis</i> , <i>Satureja khuzistanica</i>	Essential oil nanoemulsions, carvacrol & 1,8-cineol)	<i>P.aeruginosa</i> PAO1	<i>Satureja</i> <i>khuzistanica</i> , carvacrol & 1,8- cineol	Eradication of PAO1 biofilm and decrease pyocyanin production	Nanoemulsions could improve the antibacterial and antibiofilm activity of essential oil

Table 1 continue

First Authors, publication year, References	Plant species were evaluated (part of tested)	Products Fruit extract Essential	Strains tested	Plant species with anti-QS properties	QQ effects	Other effects & Authors comments
Hakimi Alni R, et al., 2020 / 10	<i>Allium sativum</i> <i>Cuminum cyminum</i>	Essential oils	Salmonella 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. & reduced the <i>S. typhimurium</i> biofilm.	Antibiofilm effects without cytotoxic effect on the eukaryotic Vero cells with terpineol, carene & pinene in <i>C.</i> <i>cyminum</i> & sulfur in <i>A.</i> <i>sativum</i>
Fekrirad Z, et al., 2020 / 9	Eugenol (the major clove extract)	prepared by adding dimethyl sulfoxide	<i>S. marcescens</i> ATCC 13880 and <i>S. marcescens</i> Sm2 (isolates from clinical sample)	Eugenol (4-allyl-2 methoxyphenol)	Decrease the Biofilm formation, hemolysin, 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/ 16	<i>Curcuma longa</i>	curcumin, component	<i>Aeromonas hydrophila</i> strains isolated from fish	<i>Curcuma longa</i>	Attenuate QS regulating genes(<i>ahyI/R</i>) & several QS associated phenotypes (biofilm, swarming, proteolytic, hemolytic activity)	It can be used as an anti- QS agent, to be used in aquaculture.
Hosseinzadeh S, et al., 2020 / 12	Licochalcone A, epigallocatechin-3-gallate	Stock solution was made in dimethyl sulfoxide	<i>S. Typhimurium</i> <i>RITCC1730</i> , 23 clinical isolates of <i>S.</i> <i>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/ 17	<i>Artemisia dracunculus</i>	Essential oil	<i>Salmonella enterica</i> serovar <i>Typhimurium</i> , <i>Staphylococcus aureus</i>	<i>Artemisia dracunculus</i>	Anti-biofilm activity & 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.

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