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Novel Perspectives on Quorum Quenching Properties, Antibacterial, Antioxidant and Phytochemical Capabilities of Different Spices - A Systematic Review

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Abstract: ***Quorum quenching (QQ), which is inhibition mechanism of quorum sensing (QS), reduces the pathogenicity of bacteria without introducing resistance. QQ may be accomplished by enzymatic destruction of the autoinducer chemical or by blocking the formation of autoinducers in a way that imitates them. A novel approach to combating bacterial infections may involve QQ system with their fundamental mechanisms is necessary. A spice plant produces large number of terpenes, terpenoids, flavanoids, tannins and possess sophisticated mechanism to combat pathogens. Thus, a diverse array of substances occurring naturally, chiefly spice plant extracts, were assessed for their capacity to regulate QS in Gram - negative (G - neg.) bacteria. This systematic literature review looks to focus on the most significant spice plant derived capabilities QQ characteristics, antibacterial, antioxidant and phytochemical of different spices.120 articles were searched with the keywords "Quorum quenching system, spices, phytochemicals, plant derived, QS, antibacterial, antioxidant" which were screened and filtered for the SLR in the methodology. Later on only 30 articles were selected based on keywords. The phytochemicals from the spice plants and their molecules identify their targets and QQ mechanism used to inhibit effectively bacterial growth. The QQ action of aqueous extracts of Syzygium aromaticum on the Serratia sps and aqueous extracts of the dietary stimulant Cinnamomum verum versus the three bacterial pathogens have been documented. This review is intended to provide additional information on increasingly interested in the development of alternative or complementary QQ therapeutics that are based on aromatic and medicinal plants.***

Keywords: Quorum quenching, Antibacterial, Antioxidant, Spices, Phytochemicals

1. Introduction

Quorum quenching (QQ) is a promising technique that is relatively new and is being utilised to mitigate the negative impacts of microbes in a variety of fields. A highly effective method for treating numerous detrimental maladies and other related issues is the application of quorum - quenching in various sectors for the benefit of humans, plants, and other organisms. QQ has been referred to as the mechanism that inhibits the QS process. QS is the procedure via which microorganisms influence the behaviour of their bacterial community by transmitting and receiving chemical signals, which are also referred to as "autoinducers". The quorum - sensing process is disrupted as a result of the interruption of quorum - sensing autoinducers (Ramsundar et al., 2023). Indian spices were employed as medicine for centuries owing to their advantageous effects on infectious illnesses (Aparna et al., 2014). Recent research has demonstrated that a limited number of spices possess the ability to modulate the bacterial QQ system, thus decreasing virulence (de Barros et al., 2024). The bacterial QQ system is typically targeted by plant compounds in a variety of ways, counting the prevention of signal molecule synthesization, signal molecule's degradation, and targeting of the signal receptor (Mutungwa et al., 2015).

Since ancient times, a variety of spices, counting turmeric, and clove, and black pepper, along with garlic, have been employed to avert gastrointestinal, and pulmonary, along with urinary tract infections. The ethnobotanical reports of spice plants are the initial step in the evaluation of QQ action. In conventional medical practice, these substances are acknowledged for their utilisation in bacterial infections' management and prevention. These spices are consumed by humans and can prevent the colonisation and infiltration of pathogenic bacteria (Chaudhuri, 2017). Additionally, they generate a diverse array of secondary metabolites, counting phenolics, and quinones, and flavonoids, and alkaloids, and terpenoids, along with polyacetylenes (Roy et al., 2024). Phytochemicals gotten from said spice dietary sources are recognised to possess antimicrobial characteristics versus a variety of significant bacterial pathogens, like Escherichia, and Helicobacter, and Streptococcus, along with Salmonella species (Issac et al., 2024). The compounds hinder the bacterial communication system, thereby attenuating the expression of genes accountable for pathogenesis. AHLs are the autoinducer molecules that have been thoroughly investigated in Gram - neg. bacteria (Deryabin et al., 2019). Various gram negative phytopathogenic bacteria utilise AHL in the bacterial communication system in QQ mechanism to drop the production of virulence factors by phytopathogenic bacteria (Kar et al., 2024).

The objective of the review is to discuss the mechanism of QQ characteristics of spice plant along with antibacterial and antioxidant actions.

2. Methodology

The following databases were utilized in the course of this literature review: Medline, and Embase, and ISI Web of Knowledge, and the Cochrane Library, and Scopus, and BioMed Central, along with Science Direct. Additionally, a secondary search was undertaken, encompassing an

examination of pertinent literature and supplementary sources of data that remained exclusive during the initial search. In conducting this literature review, the years 2014 to 2024 were incorporated into the analysis, with the following keywords considered: QQ, spices, medicine plant, anti - QS or QQ. The inclusion criteria are based on studies searched with the QQ system's action of plant extracts, like their antibacterial, antioxidant, and phytochemical characteristics. Research articles that examined the role of QQ and were written in English were considered for inclusion. Articles that exclusively addressed the anticancer, anti - inflammatory, and other medicinal plant characteristics were excluded. In addition, the bibliographies of the chosen articles were manually reviewed to spot any entries that were overlooked by the computerised search. Letters, case reports, and abstracts were excluded.

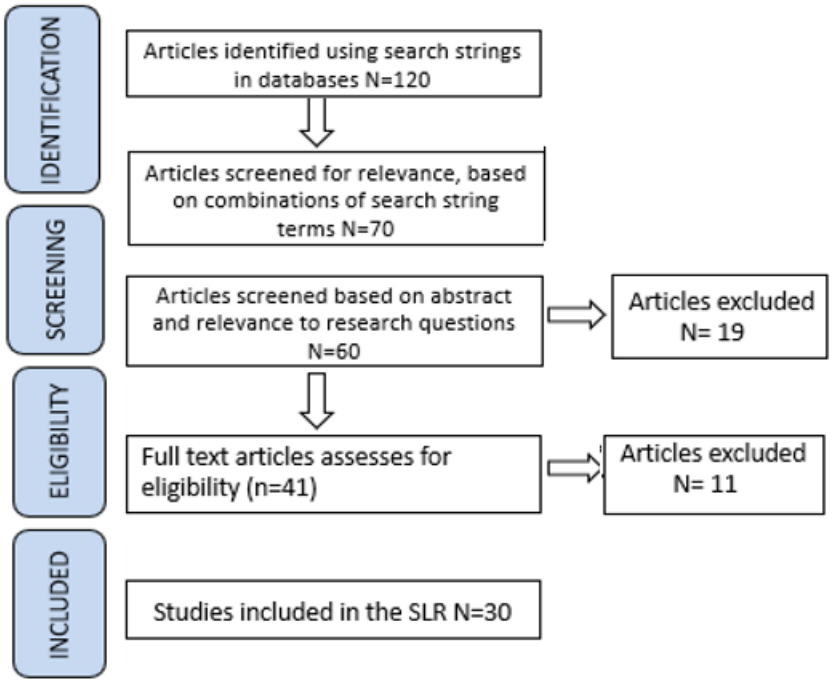

Figure 1: The process of selecting articles for inclusion in the SLR via literature search, as illustrated in the PRISMA flow diagram

The references that met the inclusion criteria were imported using Endnote, and they were subsequently filtered to eliminate duplication, resulting in an overall of 120 unique articles. The gathered references were subsequently saved to an Excel document for further analysis and filtering, which included the authors, the year of publication, heading, and abstract. A total of 60 papers were exported to Excel. The abstracts of each article were analysed in Excel, with a particular emphasis on the ones that were directly relevant to the research objectives. At first, 41 articles were identified; however, a few of those had been grey literature, publications, or book portions, and were subsequently excluded. The final shortlist consisted of 30 articles. The flow diagram (Figure 1) illustrated the literature research procedure for article evaluation included for review.

3. Result and Discussion

Natural products are viable for providing QQ compounds possessing the potential to hinder QS. The presence of these compounds in spice plants is highly intriguing due to the fact that, in the majority of cases, spices are readily available and non - toxic to humans (Pellegrini and Ponce, 2020). Despite the extensive research conducted on the antimicrobial abilities of aromatic plants, there is a scarcity of reports on the use of spices dietary phytochemicals as potential QQ modulators (Bouyahy a et al., 2017). P. aeruginosa's LasR receptor protein has been selected as the target site for direct molecular docking analysis and the ligand binding domain. The active compound was subsequently selected and analysed for its QQ ability in dropping the production of QS - reliant factors in specific Gram - neg. bacterial pathogens, as per the docking score (Mangal et al., 2022). The mechanism of the quorum quenchers by phytochemical compounds present in the spices for QQ, antibacterial and antioxidant actions, are discussed below:

3.1 Phytochemical capabilities of different spices

Numerous research organisations are currently conducting clinical trials of crude spice plant extracts to evaluate phytochemicals as QQ agents. Burt et al., (2014) investigated that the QQ action of dietary phytochemicals, which are plants' secondary metabolites, versus C. violaceum and P. aeruginosa. Plant extracts governed virulence factors' production inside P. aeruginosa via QQ (Chan et al., 2015). Mohan et al., (2019) published that multiple aromatic plant extracts derived from the Indian subcontinent exhibited QQ action versus P. aeruginosa. Abdullah et al., (2017) conducted a quorum quencher screening of compounds of green cardamom essential oil (E. oil). Many of these compounds, counting terpenes, and phenylpropanoids, and flavonoids, along with tannins, exhibit direct effects on receptor proteins (Snoussi et al., 2022).

The most thorough the extraction of chemical compounds from the spices via differing degrees of polarity is

accomplished by dehydrating the chosen plant material and processing it using water, and ethanol, or even ethyl acetate. The preliminary screening procedure, which entails the utilisation of agar diffusion or as micro - broth dilution assays, is used to ascertain the direct antibacterial characteristics of the extracts obtained. Diluted concentrations (conc. s) (dilutions) that are below the min. inhibitory conc. (sub- MIC) have exclusively employed in future studies (Lafta and Sadeq, 2024).

The biological action of plant extracts versus bacterial species which utilise AHL - mediated QQ mechanisms for functional differentiation is determined during the second stage of the screening phase. The methods that were used in the preliminary stage should be implemented: the diffusion of plant extract via agar, followed by the measurement of the region of pigment suppression, the production that is contingent upon QQ action can be observed by the development of a colourless and opaque, however apparent halo inside the well, caused by pigmentation loss), and the microbial dilution procedure, which quantifies the pigment by determining the optical density utilising a spectrophotometer (Naga and Shaaban, 2023).

The aforementioned compounds could represent the most enticing "ideal quorum quenchers, " as described in the cited source (de Barros et al., 2024). Terpenes (counting carvacrol with l - carvone), and phenylpropanoids (counting cinnamaldehyde with eugenol), as well flavonoids (counting quercetin) are categorised as: (i) Durable compounds that are not easily broken down by the body's metabolism, making it easier for them to be transported to the intended location; (ii) Small molecules entering bacterial cells by interacting with specific proteins; (iii) Phytochemicals with a high level of specificity that interact right with QQ activators (Deryabin et al., 2019). Polymerised tannins (ellagitannins) are not wholly satisfactory in this context owing to comparatively high molecular (mol.) weight along with their capacity to be hydrolysed right into low - mol. monomers which likely possess QQ action also (Snoussi et al., 2022).

3.2 Spice plant derived quorum quenching system

Quorum sensing, a communication mechanism in bacterial cells, is facilitated by signal molecules, counting AHLs (Mohan et al., 2019). S. aromaticum inhibited the violacein pigment on C. Violaceum in a conc. - reliant manner (Snoussi et al., 2018). Indian spices like *Cuminium cymium, and Murraya koenigii,* and *Curcuma longa,* and *Zingiber officinale,* and *Myristica fragrans (mace and nutmeg),* and *Trigonella foenum graceum, along with Elettaria cardamomum* right on AHL - mediated QS exposed the incidence of tannins, and flavonoids, and terpenoids, and cardiac glycosides, and carbohydrates, and alkaloids, along with phenolic compounds E. oil like caryophyllene, and caryophyllene oxide, and cinnamaldehyde, and α - , along with β - phellandrene alongside eugenol which act as quorum quenchers (Mutungwa et al., 2015).

3.3 Mechanism for quorum quenching characteristics of spice derived molecules

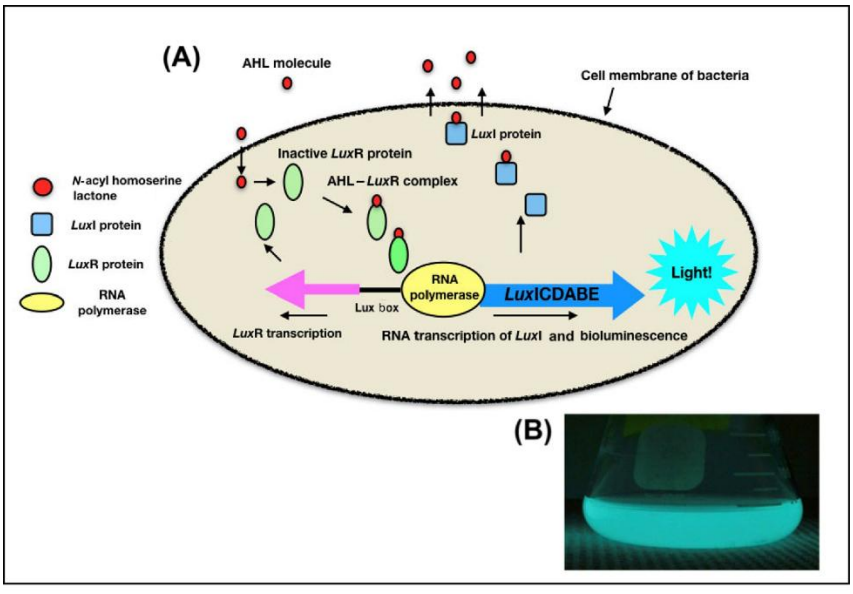

Figure 2: A general mechanism QQ signaling molecular network (Prescott and Decho, 2020)

The mechanism of QS inhibition or "quorum quenching" can be attained by the enzymatic breakdown of the autoinducer compound, the blockade of autoinducer fabrication, or by the inhibition of their reception and known as "inhibitors from the spice plant" (Snoussi et al., 2022).

QS, a kind of chemical communication, enables bacteria to detect and synchronise their activities via the use of AHLs as signalling molecules. In order for AHL - grounded communication to take place, bacteria must synthesise and perceive identical signals, which then trigger analogous gene activation in various species. Figure 2 depicts the mechanism of AHL based signaling mechanism with bacterial communication of a plant (Prescott and Decho, 2020). AHL - QS signalling is a dynamic and flexible mechanism with some constraints. AHLs have a high degree of conservation as signals, although their associated receptor

proteins (LuxR) display a noteworthy level of variability (Prescott and Decho, 2020).

The components of autoinducer synthases (LuxI homologues) are synthesising these signal molecules. The signalling molecules that were synthesised are secreted from the cell and bind to LuxR homologues in the cell walls of neighbouring bacteria. Specific genes' expression accountable for numerous phenotypes, like violacein pigment inside Chromobacterium violaceum (CviI/R), and virulence factor manufacture in P. aeruginosa (LasI/R), and flagellar motility inside Proteus mirabilis (RsbA) along with Serratia marcescens (SwrI/R), and bioluminescence inside Vibrio harveyi (LuxM/N), along with biofilms' development in said organisms (Kar et al., 2024).

AHL biosensors that lack the LuxI - type synthase but contain a functional LuxR - type protein. The most frequently employed biosensor happens to be C. violaceum 026 (NCTC 13278). The transposon insertion inside the cviI (luxI - type) gene of this double mini - Tn5 mutant is responsible for the production of a violet pigment, which is violacein, in retort to C6- AHL autoinducer conc. s (Abdullah et al., 2017). Other AHL biosensors happen to be recombinant bacteria containing plasmids having a LuxR - type protein - encoding gene along with a QQ - controlled promoter connected to the "reporter" genes, like lux - or even gfp - operons. Also, the promoter action inside said strains is reliant on the existence of exogenous AHL. The quorum quenchers that exist in the environment are quantified by the bioluminescence level and violacein production (Burt et al., 2014). Conversely, these bioassays facilitate the assessment of the QQ enzyme action of plant extracts right at controlled AHL conc. s which induce bioluminescence development and violacein biosynthesis. C. violaceum ATCC 31532 is a bacterium which is frequently used to evaluate QQ action and produces AHL. This strain is an initial strain of C. violaceum 026 and synthesises C6 - AHL (Deryabin et al., 2019).

The spice plants have been identified as having QQ characteristics, as the phytochemicals produced are effectively regulated bacterial phenomenon like biofilm formation and exopolysaccharide production. An assortment of peppers, as well as chamomile, and water lily, have been proven to possess QQ action versus the luxI reporter strain. According to prior research, LuxR - based QQ in P. aeruginosa can be inhibited by secondary metabolites counting disulphides along with trisulphides gotten from garlic (Ivanova et al., 2013). Elastase and protease's expression, alongside the formation of biofilm inside P. aeruginosa, can be reduced by the extraction of rosmarinic acid from sweet basil (Shankar et al., 2018).

Cinnamaldehyde hindered bioluminescence in two distinct Vibrio harveyi reporter strains that possess the ability to respond to AHL along with AI - 2, according to research conducted by Ghannay et al. (2022). Through the regulation of Lux R action, this inhibition was achieved. Cinnamaldehyde has been reported to be a potent 3 oxo C6 HSL (OHHL) QS system inhibitor inside a reporter strain, like E. coli, and inhibit QS inside Vibrio harveyi by inhibiting the QS signalling molecule 3 - hydroxy C4 HSL right at sub inhibitory conc. s by the same group (Ghannay et al., 2022).

3.4 Antibacterial action of different spices

An extensive investigation has been conducted into QQ phytochemicals as an innovative group of antimicrobial agents in traditional Indian spices like Syzygium aromaticum, and Trigonella foenum - graecum, and Cariandrum sativum, and Capsicum annuum, and Brassica juncea, and Pipper nigrum, and Papaver somniferum along with Nigella sativa (Mutungwa et al., 2015). These substances disrupt the signalling pathways of microorganisms (Moradi and Hadi, 2021). A diverse array of substances occurring naturally, chiefly plant extracts, have been assessed for their capacity to regulate QS in Gram - neg. bacteria (Das and Mehta, 2018).

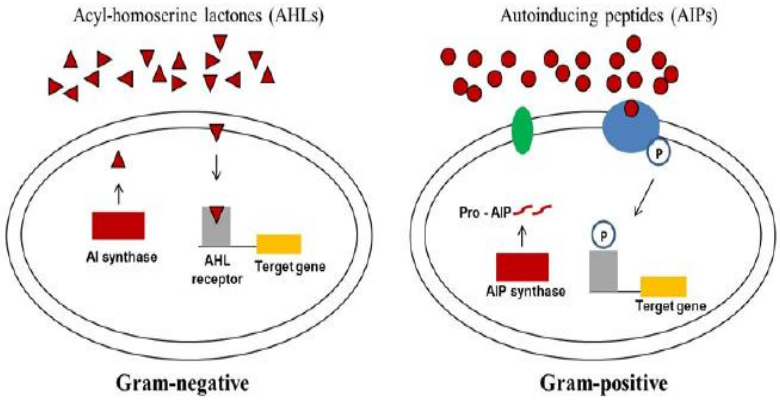

Figure 3: Bacterial quorum sensing systems (Ivanova et al., 2013)

AHLs (red triangles) are secreted by Gram - neg. bacteria (left) at threshold conc. s (Figure 3). These AHLs penetrate the cells, facilitate cognate AHL receptor activation, and also induce QS - regulated genes' expression. Mature AIPs (red circles) are produced by Gram - positive bacteria (right) and subsequently interact with the transmembrane histidine kinase receptor, which activates the target gene expression right via the trascriptional regulator's autophosphorylation (Ivanova et al., 2013).

Antibacterial action versus multidrug - resistant bacteria is demonstrated by the E. oils of Cinnamomum verum

(cinnamon), and Origanum majorana (marjoram), and Thymus vulgaris (thyme), along with Eugenia caryophyllata (clove) (Alibi et al., 2020). Examining the antibacterial characteristics of green cardamom E. oil with a particular emphasis on the inhibition of QS in C. violaceum (Abdullah et al., 2017). Two biomonitor isolates, C. violaceum CV026 and P. aeruginosa PAO1, were employed in the investigation to characterise Chinese aromatic plants that are frequently employed as quorum quenchers in South East Asia (Wei et al., 2017). The QS - regulated phenotypes of P. aeruginosa, like the expression of lecA:: lux (max. inhibition by hexane extract), and swarming (max. inhibitor by methanol extract), and pyocyanin (max. inhibition by hexane extract), were inhibited by the anti - QS characteristics of clove extract (Syzygium aromaticum), as demonstrated by Aparna et al., (2014).

3.4 Antioxidant action

Antioxidant and QQ modulatory effects are demonstrated by certain E. oils. In a similar manner the E. oil of spices secretes secondary metabolites as quorum quencher compounds (Zhang et al., 2020). Spice plant E. oils include antioxidant - rich phenolic chemicals and terpenes, which may scavenge free radicals (Beddiar et al., 2021). Additionally, it was demonstrated that the antioxidant action of these E. oils is attributed to certain compounds, counting cinnamaldehyde, cuminaldehyde, eugenol, thymol, menthol, eucalyptol, and carvacrol (Nascimento et al., 2020). Beddiar et al., (2021) suggested that the phenolic compounds found in C. nepeta (Mint oregano) extracts may possess antioxidant characteristics, operate as free radical scavengers, provide hydrogen, or perform as oxygen singlet extinguishers and also metal ion chelating agents. C. nepeta extracts have demonstrated positive antioxidant action, which has been verified by prior research.

4. Research Gap

Exploring the use of QQ in spice - related food to prevent bacterial spoilage and pathogenicity is an emerging field. The effectiveness of different QS inhibitors or QQ compounds, especially those derived from spices, which is only limited to a group of plant species is a significant research gap. These gaps represent opportunities for further investigation that could lead to new strategies for combating bacterial resistance and improving food safety. The use of spices as a source of QQ agents is chiefly interesting due to their accessibility and potential for integration into food processing and preservation.

5. Conclusion and Future Prospects

According to the literature that has been reviewed, spices have the potential to safeguard individuals from acute and chronic diseases as a result of their high QQ, antibacterial and antioxidant action, in addition to enhancing the flavour, aroma, and colour of food and beverages. The phytochemicals present in different spices like flavanoids, tannins, terpenes, curcumin, cuminaldehyde, cinamaldehyde, disulphides have the capabilities to QQ, antibacterial and antioxidant. Spices - acquired molecule mechanism of action on QQ in bacteria caused an effective AHL reliant QQ system's development. QQ of different spices regulates a variety of bacterial actions, counting biofilm formation, antibiotic resistance, bioluminescence, and bacterial virulences.

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