Received: 9 August 2019 | Revised: 9 January 2020 | Accepted: 30 January 2020

DOI: 10.1111/1541-4337.12549

COMPREHENSIVE REVIEWS IN FOOD SCIENCE AND FOOD SAFETY

Comprehensive REVIEWS in Food Science and Food Safety WILEY

Antivirulence properties and related mechanisms of spice essential oils: A comprehensive review

Dan Zhang[1] | **Ren-You Gan**[1,2] | **Jia-Rong Zhang**[1] | **Arakkaveettil Kabeer Farha**[1] | **Hua-Bin Li**[3] | **Fan Zhu**[4] | **Xiao-Hong Wang**[5] | **Harold Corke**[1]

[1]Department of Food Science & Technology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, China

[2]Research Center for Plants and Human Health, Institute of Urban Agriculture, Chinese Academy of Agricultural Sciences, Chengdu, China

[3]Guangdong Provincial Key Laboratory of Food, Nutrition and Health, Department of Nutrition, School of Public Health, Sun Yat-Sen University, Guangzhou, China

[4]School of Chemical Sciences, University of Auckland, Auckland, New Zealand

[5]College of Food Science and Technology, Huazhong Agricultural University, Wuhan, Hubei, China

Correspondence

Ren-You Gan, Research Center for Plants and Human Health, Institute of Urban Agriculture, Chinese Academy of Agricultural Sciences, Chengdu, China.
Email: ganrenyou@caas.cn

Harold Corke, Department of Food Science & Technology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai 200240, China.
Email: hcorke@sjtu.edu.cn

Funding information

the National Key R&D Program of China, Grant/Award Number: 2017YFC1600100; the Shanghai Basic and Key Program, Grant/Award Number: 18JC1410800; the Agri-X Interdisciplinary Fund of Shanghai Jiao Tong University, Grant/Award Number: Agri-X2017004; the Shanghai Agricultural Science and Technology Key Program, Grant/Award Number: 18391900600; the Shanghai Pujiang Talent Plan, Grant/Award Number: 18PJ1404600

Abstract

In recent decades, reduced antimicrobial effectiveness, increased bacterial infection, and newly emerged microbial resistance have become global public issues, leading to an urgent need to find effective strategies to counteract these problems. Strategies targeting bacterial virulence factors rather than bacterial survival have attracted increasing interest, since the modulation of virulence factors may prevent the development of drug resistance in bacteria. Spices are promising natural sources of antivirulence compounds owing to their wide availability, diverse antivirulence phytochemical constituents, and generally favorable safety profiles. Essential oils are the predominant and most important antivirulence components of spices. This review addresses the recent efforts of using spice essential oils to inhibit main bacterial virulence traits, including the quorum sensing system, biofilm formation, motility, and toxin production, with an intensive discussion of related mechanisms. We hope that this review can provide a better understanding of the antivirulence properties of spice essential oils, which have the potential to be used as antibiotic alternatives by targeting bacterial virulence.

KEYWORDS

biofilm, mechanisms, motility, quorum sensing, spice essential oils, toxin

1 | INTRODUCTION

Antibiotics are one of the greatest discoveries of the 20th century. They have long been used to prevent and treat infectious diseases, and are applied as growth promoters in animal feeds (Allen, Levine, Looft, Bandrick, & Casey, 2013; Seal, Lillehoj, Donovan, & Gay, 2013). However, the emergence of drug-resistant bacteria, which is predicted to cause more deaths than cancer by the year 2050, makes it more difficult to treat microbial infections and ensure food safety, posing great threats to public health (Kraker, Stewardson, & Harbarth, 2016). In recent decades, more attention has been paid to "antivirulence drugs," which are considered to be potential alternatives or adjuvants to antibiotics (Dickey, Cheung, & Otto, 2017). Virulence is described as the ability of a pathogen to infect and cause disease in a host, and bacterial virulence factors, such as toxins, enzymes, as well as the factors involved in biofilm formation, can facilitate the infection of host organisms by bacteria. The expression of virulence genes is mainly regulated by quorum sensing (QS) (Sharma et al., 2017; Vestergaard & Ingmer, 2019). The antivirulence strategy aims at neutralizing or suppressing the production of virulence factors that are essential for bacterial pathogenicity rather than for their survival, thus imposing much less pressure for bacteria to develop drug resistance (Lee, Lee, Kim, Cho, & Lee, 2014). Additionally, the antivirulence strategy avoids long-term and unwanted side effects of traditional antibiotics, such as killing commensal bacteria in the gut that play important roles in human health, promoting immune system development, and resisting colonization by pathogenic bacteria. Due to the lack of virulence factors, especially bacterial toxins, gut commensal bacteria are not generally vulnerable to antivirulence drugs (Dickey et al., 2017).

Plants are important natural resources for the development of antivirulence drugs, and over 80% of people in the world use plant-derived drugs to treat various health problems (Stanojevic et al., 2017). Additionally, potentially carcinogenic and acute toxicological properties of synthetic antimicrobials have prompted increasing attention to natural products (Kumara, Sayeed, & Rani, 2016). Essential oils, also called volatile oils, are aromatic oily liquids obtained from the flowers, leaves, stems, roots, or fruits of plants by steam distillation, extrusion, cold-soaking, or solvent extraction, and may contain the most pharmacologically active and effective components in such plants (Solorzano-Santos & Miranda-Novales, 2012). Spice essential oils have been widely used as flavoring agents and antimicrobial agents due to their multiple terpenoid and phenolic constituents, and their antibacterial, antifungal, and antiviral abilities have been well studied and reviewed (Liu et al., 2017; Tajkarimi, Ibrahim, & Cliver, 2010). In recent years, the antivirulence properties of spice essential oils and their major compounds (Figure 1) have been increasingly investigated. To provide a better understanding of the antivirulence properties of spice essential oils, this review is written mainly based on Web of Science Core Collection Publications from 2010 to 2019. We first summarize the major spice essential oils and their components, and then review the research progress on the use of spice essential oils to suppress bacterial virulence factors, including toxins, QS, bacterial biofilms, and motility. Intensive discussion on related mechanisms of action is integrated into the review. We hope that this review can stimulate further research and utilization of the antivirulence properties of spice essential oils, by highlighting the role of spices as a promising natural reservoir of antibiotic alternatives.

2 | SPICE ESSENTIAL OILS AND THEIR MAJOR COMPONENTS

Most commercial spices belong to the families *Apiaceae*, *Lamiaceae*, *Myrtaceae*, *Rutaceae*, *Rosaceae*, and *Zingiberaceae*. The most well-known species are from the genera *Thymus*, *Origanum*, and *Ocimum*, and all of these belong to the family *Lamiaceae*. These spices are most commonly used for processing into essential oils, wherein the variable chemical constituents can be mainly divided into several groups, that is, terpenes and their oxygenated derivatives (terpenoids), phenylpropanoids, aldehydes, ketones, alcohols, esters, phenols, ethers, and other small molecules. Usually, two or three of these constituents account for a relatively high proportion (20% to 70%), while many other constituents may exist in trace amounts (Mirzahosseini, Noori, Amanzadeh, Javid, & Howyzeh, 2017). Due to their specific fragrance, antioxidant, and antibacterial properties, spices have long been recognized as food flavorings, preservatives, cosmetic additives, and air fresheners (Abdel-Hameed, Salman, Fadl, Elkhateeb, & Hassan, 2018; Toker, Gölükcü, & Tokgöz, 2017). Moreover, some are classified as generally recognized as safe (GRAS) by the U.S. Food and Drug Administration (FDA), such as cinnamon, oregano, clove, and ginger oils (Campana & Baffone, 2018; Cui, Li, Li, Vittayapadung, & Lin, 2016). Although spice essential oils are generally safe when used in moderate amounts, some of these highly concentrated oils may irritate skin and mucous membranes, induce epilepsy, or show toxic effects in excessive dosages, especially in children who are particularly susceptible (Halicioglu, Astarcioglu, Yaprak, & Aydinlioglu, 2011; Vigan, 2010). The pharmacological benefits of spice essential oils gain more and more attention, such as their antiinfective, anticancer, antipyretic, and carminative effects (Hosseini, Nadjafi, Asareh, & Rezadoost, 2018; Koch et al., 2017). These characteristics of essential oils are strongly related to the bioactive phytochemical composition, and this composition is an important parameter for evaluating the quality of essential oils and potential application prospects. Therefore, we summarize the main chemical composition of major

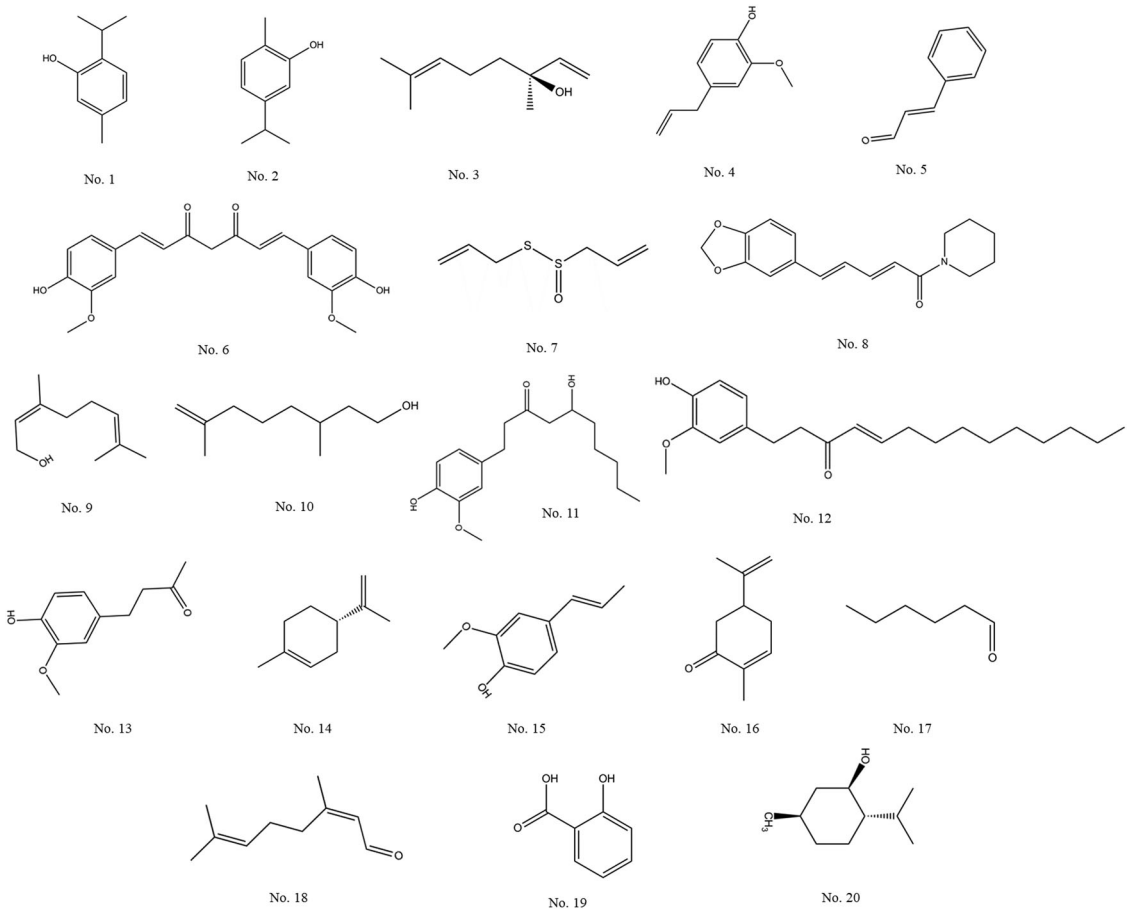

FIGURE 1 The chemical structures of spice essential oil constituents with antivirulence activities mentioned in the context: No. 1, Thymol; No. 2, Carvacrol; No. 3, Linalool; No. 4, Eugenol; No. 5, Cinnamaldehyde; No. 6, Curcumin; No. 7, Allicin; No. 8, Piperine; No. 9, Geraniol; No. 10, Citronellol; No. 11, 6-Gingerol; No. 12, 6-Shogaol; No. 13, Zingerone; No. 14, Limonene; No. 15, Isoeugenol; No. 16, Carvone; No. 17, Hexanal; No. 18, Citral; No. 19, Salicylic acid; No. 20, Menthol

spice essential oils in Table 1. The oil content and main bioactive compounds are influenced by various factors, including geographical origin, varieties, harvesting stages, climatic conditions, and distillation techniques. In addition, the essential oils of spices such as thyme, oregano, coriander, cloves, cinnamon, turmeric, garlic, and black pepper are characterized by high concentrations of thymol, carvacrol, linalool, eugenol, cinnamaldehyde, curcumin, allicin, and piperine, respectively. Among them, terpenoids such as thymol, carvacrol, linalool, geraniol, and phenylpropenes, such as eugenol, cinnamaldehyde, and curcumin, are effective antibacterial agents (Gottardi, Bukvicki, Prasad, & Tyagi, 2016; Sandeep et al., 2017). However, terpenes such as *p*-cymene and *α*-pinene have less antibacterial effectiveness, mainly due to the presence of reactive functional groups, such as hydroxyl groups and double bonds, which can improve their water solubility and hydrogen binding capability (Alves, Duarte, Sousa, & Domingues, 2016).

3 | BACTERIAL TOXINS

3.1 | Inhibition of bacterial toxins by spice essential oils

Many bacteria-mediated illnesses are caused by the ingestion of preproduced toxins rather than the effect of living bacteria themselves (Werber et al., 2013). Therefore, toxins are critical for controlling and treating widespread bacterial diseases (Rasko & Sperandio, 2010). Recently, increasing reports have highlighted the possibility of spice essential oils in inhibiting the production of bacterial toxins in several toxin-producing bacteria (Table 2) at sub-minimum inhibitory concentrations (MICs), such as *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus (Sc.)*, *Vibrio cholerae*, *Campylobacter jejuni*, and *Pseudomonas aeruginosa.* The most studied compounds in spice essential oils are allicin, carvacrol, thymol, cinnamaldehyde, eugenol, and menthol.

TABLE 1 Spices and their major essential oil compounds

Family	Latin name	English name	Part used	Growing location	Extraction method	Major active ingredients	References
Apiaceae	*Coriandrum sativum* L.	Coriander	Whole plant	Guangzhou	Steam distillation	Linalool (37.12%), geranyl acetate (35.72%), menthol (5.07%)	(Wang et al., 2018)
	Foeniculum vulgare Mill.	Fennel	Seeds	Iran	Hydrodistillation	*Trans*-anethole (85.1% to 90.4%), fenchone (2.1% to 4.2%), estragole (1.2% to 3.3%)	(Salami et al., 2016)
				Poland		*Trans*-anethole (87.2%), fenchone (4.1%), estragole (1.9%)	
				Albania		*Trans*-anethole (86.1%), fenchone (3.1%), estragole (2.0%)	
				Spain		*Trans*-anethole (86.4%), fenchone (3.8%), estragole (1.3%)	
				England		*Trans*-anethole (88.7%), fenchone (4.5%), estragole (1.4%)	
	Petroselinum crispum Mill.	Parsley	Fresh green parts	Madinah, Saudi Arabia	Hydrodistillation	Myristicin (20.7%), β-phellandrene (17.45%), myrcene (11.42%)	(Farouk, Ali, Al-Khalifa, Mohsen, & Fikry, 2018)
			Fresh green parts	Gizain, Egypt		Myristicin (26.4%), β-phellanderene (11.6%), α-phellandrene (10.5%)	
	Therachyspermum ammi L. (23 ecotypes)	Ajowan	Seeds	Tehran, Iran	Hydrodistillation	Thymol (34% to 55%), γ-terpinene (18% to 40%), *p*-cymene (17% to 29%)	(Mirzahosseini et al., 2017)
	Trachyspermum ammi L.	Ajowan	Aerial parts (inflorescence stage)	Ahvaz, Iran	Hydrodistillation	γ-Terpinene (45.87% to 74.75%), thymol (10.13% to 30.77%), *p*-cymene (9.54% to % to 19.51%),	(Howyzeh, Noori, & Shariati, 2018)
Lamiaceae	*Lavandula stoechas* L.	Lavender	Leaves and flowering tops	Ain Safra region of Djebel Maouna		α-Thujone (25.5%), 1-camphor (20.1%), 1-bornyl acetate (5.5%)	(Djebir et al., 2019)
	Mentha longifolia L.	Mint	Fresh leaves	Taif governorate, KSA	Hydrodistillation	Pulegone (61.66%), 1,8-cineol (17.15%), piperitenone oxide (3.88%)	(Abdel-Hameed et al., 2018)
					Microwave assisted hydrodistillation	Pulegone (54.88%), 1,8-cineol (17.56%), piperitenone oxide (9.77%)	

(Continues)

TABLE 1 (Continued)

Family	Latin name	English name	Part used	Growing location	Extraction method	Major active ingredients	References
					Solvent free microwave extraction	Pulegone (38.93%), 1,8-cineol (19.85%), piperitenone oxide (17.75%)	
	Ocimum basilicum L.	Basil	Aerial parts	Northwestern Republic of Srpska	Hydrodistillation	Linalool (31.6 %), methyl chavicol (23.8 %), β-elemene (6.9%)	(Stanojevic et al., 2017)
	Origanum majorana L.	Marjoram	Aerial parts	Yemen	Static headspace	*Trans*-sabinene hydrate (16.0%), sabinene (14.1%), *cis*-sabinene hydrate (11.8%)	(Al-Fatimi, 2018)
	Origanum majorana L.	Marjoram	Aerial parts		Hydrodistillation	Carvacrol (83.5%), γ-terpinene (6.5%), *o*-cymene (2.8%)	(Bagci, Kan, Dogu, & Celik, 2017)
						Carvacrol (69.5%), *o*-cymene (8.1%), γ-terpinene (6.8%)	
	Origanum minutiflorum O. Schwarz Et.	Oregano	Aerial parts, flowering stage	Isparta province, west Mediterranean region of Turkey	Hydrodistillation (10 to 120 min)	Carvacrol (62.60% to 86.40%), *p*-cymene (4.29% to 8.07%), γ-terpinene (1.72% to 5.12%),	(Toker et al., 2017)
	Origanum vulgare L. spp.	Oregano	*O. vulgare* L. ssp. *virens*	Southern Italy	*n*-Hexane hydrodistillation	Carvacrol (63.8%), γ-terpinene (7.4%), *p*-cymene (6.7%)	(De Falco, Roscigno, Landolfi, Scandolera, & Senatore, 2014)
			O. vulgare L. ssp. *viridulum*)			Linalool (19.5%), *p*-cymene (11.2%)	
			O. vulgare L. ssp. *viridulum*)			Thymol (49.1%), carvacrol (15.7%), γ-terpinene (10.8%)	
	Origanum vulgare subsp. *viride*	Oregano		Khorasan Razavi, Iran	Ohmic assisted hydrodistillation	Thymol (29.2% to 32%), 4-terpineol (10.1% to 12.1%), α-terpinene (8.0% to 10.0%)	(Hashemi et al., 2017)
					Hydrodistillation	Thymol (28.1%), 4-terpineol (10.2%), α-terpinene (7.5%)	
	Plectranthus amboinicus	Patchouli	Leaves and stems	Northeast Brazil	Hydrodistillation	Carvacrol (88.17%), caryophyllene oxide (5.85%), 1,8-cineol (2.01%)	(Vasconcelos et al., 2017)
	Salvia officinalis	Sage	Leaves	North of Tunisia	Hydrodistillation	Camphor (33.61%), 1,8-cineole (22.22%), α-thujone (21.43%)	(El Euch, Hassine, Cazaux, Bouzouita, & Bouajila, 2019)

(Continues)

TABLE 1 (Continued)

Family	Latin name	English name	Part used	Growing location	Extraction method	Major active ingredients	References
	Rosmarinus officinalis L.	Rosemary	Leaves and flowering tops	Wilaya of Tebessa in Ouenza region	Hydrodistillation	1,8-Cineole (26.9%), 1-camphor (19.0%), α-pinene (12.1%)	(Djebir et al., 2019)
	Thymus capitatus L.	Thyme	Leaves and flowering tops	Ouled Chiha region of Hammam Ouled Ali		Carvacrol (78.8%), *p*-cymene (6.62%), γ-terpinene (3.96%)	
	Thymus sipyleus subsp. *sipyleus* var. *davisianus*	Thyme	Aerial parts, full flowering stage	Usak province of Turkey	Hydrodistillation	Thymol (38.31%), carvacrol (37.95%), γ-terpinene (7.28%)	(Ceylan & Ugur, 2015)
	Thymus serpyllum L.	Thyme		Greek pharmacy in Thessaloniki	Hydrodistillation	Thymol (56.02%), carvacrol (14.00%), *p*-cymene (6.2%)	(Nikolic et al., 2014)
	Thymus algreriensis Boiss.		Flowering stage (in May)	Zentan, Libya		Thymol (38.5%), *p*-cymene (8.9%), terpinene (7.1%,),	
	Thymus vulgaris L.		Flowering stage (in July)	Serbia		Thymol (49.1%), *p*-cymene (20.0%)	
Lauraceae	*Cinnamomum zeylanicum*	Cinnamon			Hydrodistillation	Cinnamaldehyde (86.59%), benzaldehyde (4.2%), cineole (1.7%)	(Budri et al., 2015)
Liliaceae	*Allium sativum* L.	Garlic	Garlic cloves	Giza, Egypt	Hydrodistillation	Allicin (28.4%), dimethyl tetrasulfide (15.3%), di-2-propenyl-trisulfide (10.4%)	(Mossa, Afia, Mohafrash, & Abou-Awad, 2018)
	Allium sativum	Garlic	Bulbs	LasPedroñeras, Spain	Clevenger-type laboratory distillation	Allitridin (33.4%), allicin (20.8%), allyl methyl trisulfide (19.2%)	(Satyal, Craft, Dosoky, & Setzer, 2017)
					Industrial hydrodistillation	Allitridin (31.2%), diallyl disulfide (25.9%), allyl methyl trisulfide (14.5%)	
	Allium vineale (4 species)	Wild garlic	Whole plant	Huntsville, Alabama	Hydrodistillation followed by dichloromethane extraction	Allyl methyl trisulfide (7.9% to 13.2%), allyl (E)-1-propenyl disulfide (7.9% to 12.5%), dimethyl trisulfide (4.3% to 17.4%)	
Myrtaceae	*Pimenta officinalis*	Pimento berry			Hydrodistillation	Eugenol (71.10%), methyleugenol (13.67%)	(Kim et al., 2016)

(Continues)

TABLE 1 (Continued)

Family	Latin name	English name	Part used	Growing location	Extraction method	Major active ingredients	References
	Syzygium aromaticum	Clove			Hydrodistillation	Eugenol (77.08%), β-Caryophyllene (9.1%)	(Kim et al., 2016)
	Syzygium aromaticum	Clove		Johannesburg, South Africa	Hydrodistillation	Eugenol (88.3%), β-caryophyllene (8.1%), α-humulene (2.0%)	(Leonard, Virijevic, Regnier, & Combrinck, 2010)
	Syzygium aromaticum	Clove			Hydrodistillation	Eugenol (90.2%), eugenol acetate (6.5%), β-caryophyllene (1.3%)	(Budri et al., 2015)
Oleaceae	*Pimenta racemosa*	Bay			Hydrodistillation	Myrcene (7.93%), chavicol (16.48%), eugenol (61.99%)	(Kim et al., 2016)
Piperaceae	*Piper nigrum* L.	Black pepper	Seeds	Gia Lai Province	Hydrodistillation	3-Carene (29.21%), limonene (20.94%), β-caryophyllene (15.05%)	(Tran et al., 2019)
Poaceae	*Cymbopogon flexuosus*	Lemongrass		Northampton, UK	Hydrodistillation	Geranial (47%), neral (33%)	(Adukwu, Allen, & Phillips, 2012)
	Cymbopogon citratus D.C. Stapf.	Lemongrass	Fresh leaves	Minas Gerais, Brazil	Hydrodistillation	Geranial (42.91%), neral (30.90%)	(de Oliveira et al., 2010)
	Cymbopogon nardus L. Rendle	Citronella				Citronellal (34.60%), geraniol (23.17%), citronellol (12.09%)	
Rutaceae	*Citrus limon* L. Burm.	Lemon	Peels	Sichuan Province		Limonene (48%), β-terpinene (17%), 4-carene (8.5%)	(Sun et al., 2018)
	Citrus paradisi	Grapefruit		Northampton, UK	Hydrodistillation	Limonene (93.5%), myrcene (2.32%)	(Adukwu et al., 2012)
	Citrus aurantifolia	Lime				Limonene (47.3%), β-pinene (22.7%), γ-terpinene (7.5%)	
	Citrus bergamia	Bergamot				Limonene (38.5%), linalyl acetate (27.9%), β-pinene (7.2%),	
Verbenaceae	*Lippia rehmannii*		Aerial parts (in March)	Pretoria, South Africa	Hydrodistillation	Geranial (42.3%), neral (26.8%) caryophyllene oxide (3.7%)	(Leonard et al., 2010)
Zingiberacae	*Alpinia galanga* Willd.	Greater galangal	Rhizomes	South India	Hydrodistillation	1,8-Cineole (47.5% to 67.3%), β-farnesene (7.0% to 14.6%), β-sesquiphellandrene (2.4% to 10.8%)	(Raina & Abraham, 2017)

TABLE 2 Inhibitory effects of spice essential oils and their major compounds on bacterial toxins

Spice essential oils	Bacteria	MIC	Concentrations used	Inhibitory effects on toxins	References
Anethole and 4-allylanisole from sweet fennel seeds	*V. cholerae* CO533		10 μg/mL (no growth inhibition)	Inhibit 50% of cholera toxin production	(Chatterjee et al., 2016)
			50, 100 μg/mL (no growth inhibition)	Inhibit 92% to 93% of cholera toxin production	
Allicin	MSSA and MRSA	32 to 64 μg/mL	2 to 16 μg/mL	Inhibit α-toxin production in a dose-dependent manner	(Leng et al., 2011)
	Sc. pyogenes		0.2 μM	Inhibit the hemolytic activity of SLO completely	(Arzanlou & Bohlooli, 2010)
	Sc. pneumoniae	3.15 μM/mL	0.61 μM/mL	Inhibit the hemolytic activity of PLY in bacterial cell lysate completely	(Arzanlou et al., 2011)
			1.84 μM/mL	Inhibit the hemolytic activity of PLY inside intact bacterial cell completely	
Carvacrol	*S. aureus*		0.3 μL/mL (sub-MIC)	Inhibit enterotoxin production completely	(Souza, Oliveira, Stamford, Conceicao, & Neto, 2013)
Cinnamaldehyde	*Ca. jejuni* S-8		0.01% (sub-MIC)	Inhibit the expression of toxin related genes *cdtA*, *cdtB*, *cdtC*	(Upadhyay et al., 2017)
Cinnamon	*E. coli* O157:H7	0.025%	0.75 MIC	Inhibit Stx2 production to a nondetectable level	(Sheng et al., 2016)
	EHEC		0.01% (v/v)	Inhibit >threefold of Shiga-like toxin gene (*Stx2*) expression	(Y.G. Kim, Lee, Kim, Baek, & Lee, 2015)
Eugenol	26 strains of *S. aureus*	128 to 512 μg/mL	16 to 64 μg/mL	Inhibit SEA, SEB, TSST, and α-hemolysin production significantly	(Qiu et al., 2010a)
Mentha piperita L.	28 clinic strains of *S. aureus*	64 to 256 μg/mL	8 to 64 μg/mL	Inhibit α-toxin, TSST-1, SEA, and SEB production in a dose-dependent manner	(Li et al., 2011)
Menthol	*S. aureus* ACTT 29213, MRSA strain 2985, 3701	>2 mg/mL	6 to 84 μg/mL	Inhibit SEA, SEB, TSST-1, and α-hemolysin production significantly	(Qiu et al., 2011a)
Origanum vulgare L.	*S. aureus*		0.3 and 0.15 μL/mL (sub-MICs)	Inhibit enterotoxin production completely	(de Souza, de Barros, de Oliveira, & da Conceicao, 2010)

(Continues)

TABLE 2 (Continued)

Spice essential oils	Bacteria	MIC	Concentrations used	Inhibitory effects on toxins	References
Perilla frutescens L. Britton	*S. aureus* ATCC 29213, MRSA strain 2985, MRSA strain 3701	0.4 μL/mL	0.0625 MIC to 0.5 MIC	Inhibit α-toxin, TSST-1, SEA, and SEB production in a dose-dependent manner	(Qiu et al., 2011b)
Thymol	*S. aureus*		0.15 μL/mL (sub-MIC)	Inhibit enterotoxin production completely	(Souza et al., 2013)
	S. aureus ATCC 29213 and MRSA strain 2985	128 μg/mL	0. 0625 MIC to 0.5 MIC	Inhibit α-hemolysin, SEA, and SEB production in a dose-dependent manner	(Qiu et al., 2011a)

Abbreviations: *Ca*., *Campylobacter*; *E*., *Escherichia*; EHEC, Enterohemorrhagic *E. coli*; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MIC, minimum inhibitory concentration; PLY, pneumolysin; *S*., *Staphylococcus*; *Sc*., *Streptococcus*; SEA, *Staphylococcus aureus* enterotoxin A; SEB, *Staphylococcus aureus* enterotoxin B; SLO, Streptolysin O; TSST-1, toxic shock syndrome toxin 1; *V*., *Vibrio*.

3.2 | Mechanisms of inhibition of bacterial toxins by spice essential oils

Major toxins in *S. aureus* include α-toxin (α-hemolysin), enterotoxin (SEA and SEB), and toxic shock syndrome toxin 1 (TSST-1), and they play key roles in the pathogenesis of infection (Grumann, Nubel, & Broker, 2014). The production levels of these exotoxins are coordinately regulated by complex networks, including the SarA protein family and many two-component regulatory systems, such as AgrAC, SrrAB, and SaeRAS (Leng et al., 2011; Oscarsson, Kanth, Tegmark-Wisell, & Arvidson, 2006). Some studies find that essential oils can block global regulators or the transcription of genes involved in toxin production of *S. aureus*. For instance, 1/2 MIC of thymol can reduce the transcriptional levels of *hla*, *sea*, and *seb* genes by 10.2, 8.6, and 5.2 fold, respectively (Qiu et al., 2010b). Similarly, 16 μg/mL of allicin can reduce the transcription of *hla* by 7.4-fold, accompanied by reduced α-hemolysin production (Leng et al., 2011). Thymol and allicin at sub-MICs also decrease the transcription of *agrA* locus, which positively regulates the production of α-hemolysin, SEB, and TSST-1 (Qiu et al., 2011b).

Shiga toxin-producing *E. coli* (enterohaemorrhagic *E. coli*) can produce Shiga toxins (Stx1 and Stx2) that are destructive to blood vessels, causing bloody diarrhea and severe hemolytic uremic syndrome (HUS) (Etcheverria & Padola, 2013). Shiga toxins are encoded by the *stx* gene on the prophage, and remain silent due to the presence of the cI repressor. Once the lytic cycle of prophage is induced, the cI protein begins self-cleavage, activating the transcription and translation of *stx* gene to produce Shiga toxins (Iversen, L'Abee-Lund, Aspholm, Arnesen, & Lindback, 2015). Several studies report that spice essential oils can inhibit Shiga toxin-coding gene and block the phage lytic cycle. Application of 1/2 and 3/4 MIC of the essential oil from *Zataria multiflora* Boiss. reduces the production of Stx2, verified by the upregulated expression of *Stx2A* gene (Khatibi et al., 2018). In addition, oregano essential oil and its main active ingredient, carvacrol, also significantly downregulate the *stx* gene at a very low sub-MIC concentration (0.005%), and the *luxS* gene is also significantly downregulated (Mith, Clinquart, Zhiri, Daube, & Delcenserie, 2015). Moreover, sub-MIC of cinnamon reduces the Shiga toxin of *E. coli* O157:H7 to an undetectable level, which may be due to the decreased amounts of Stx2-converting phage by blocking phage lytic cycle (Sheng, Rasco, & Zhu, 2016).

Streptolysin O (SLO) and pneumolysin (PLY) are ubiquitous virulence factors found in almost all serotypes of *Sc. pyogenes* and clinical isolates of *Sc. pneumoniae*, respectively. SLO and PLY belong to the family of pore-forming toxins, which are also known as the thiol-activated toxins, or the recently mentioned cholesterol-dependent cytolysins (CDCs) (Chiarot et al., 2013). These toxins are highly active only in their reduced state, and sulfhydryl-group (-SH) blocking agents are capable of inhibiting their activities. Allicin, a main compound of essential oil from garlic, completely inhibits the hemolytic activity of PLY at a concentration of 0.61 μM/mL, and it is speculated that allicin has a high affinity to the SH group of cysteine residues via forming a disulfide bond between them, hindering the binding of the toxins to the cells and formation of transmembrane pores (Arzanlou, Bohlooli, Jannati, & Mirzanejad-Asl, 2011). Another similar study also shows that 0.2 μM/mL of allicin significantly inhibits the hemolytic activity of SLO (Arzanlou & Bohlooli, 2010).

The mechanisms of spice essential oils on inhibiting the production of toxins in toxin-producing bacteria mentioned above are shown in Figure 2. Overall, spice essential oils and their compounds can inhibit bacterial toxins mainly by

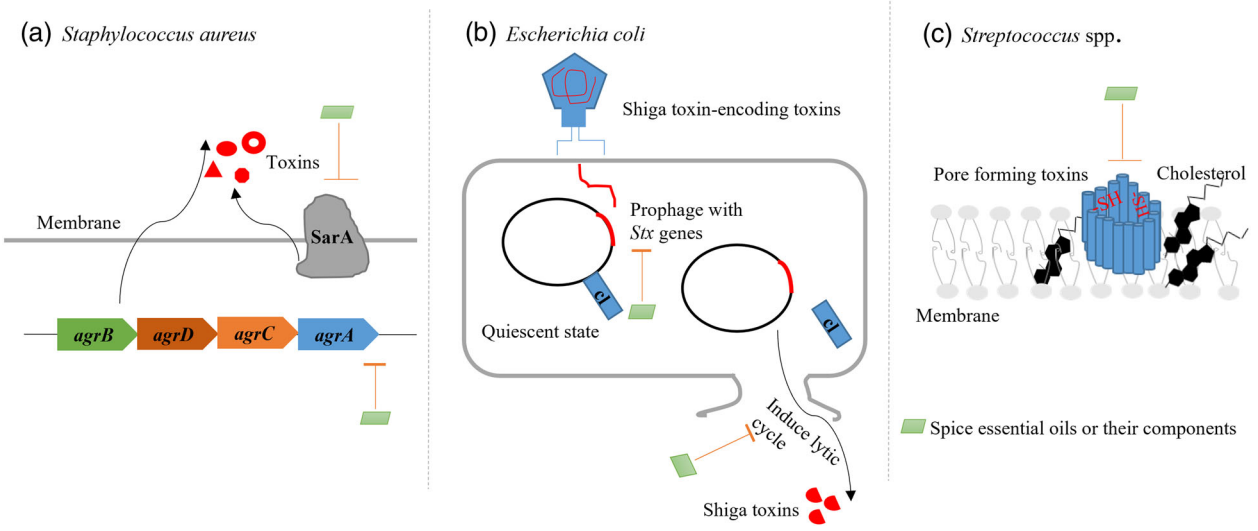

FIGURE 2 The schematic diagrams of the mechanisms of toxin inhibition by spice essential oils in *Staphylococcus aureus* (a), *Escherichia coli* (b), and *Streptococcus* spp. (c)

disrupting the process of toxin production and its upstream regulatory systems. Further studies are required to discover more spice essential oil compounds with potent inhibitory effects on bacterial toxins, and clarify the related molecular mechanisms.

3.3 | QS and its inhibitors

It is well known that there exists information exchange among bacteria, and many bacteria can synthesize and release signal molecules called auto-inducers (AIs), the concentration of which increases with the bacterial density. Once the signal accumulates to a certain threshold, it can activate the expression of related genes to adapt to environmental changes, resulting in bioluminescence production, biofilm formation, sporulation, competence, and the secretion of other virulence factors (Grandclement, Tannieres, Morera, Dessaux, & Faure, 2016; Schuster, Sexton, Diggle, & Greenberg, 2013). Such a regulatory system of bacterial biological behavior that depends on the population density of bacteria is defined as QS (Gokalsin, Aksoydan, Erman, & Sesal, 2017). QS has been shown to play an important role in the pathogenesis of pathogenic bacteria, and a number of virulence factors are under its control (Harjai, Kumar, & Singh, 2010). Thus, it is a reasonable and innovative strategy to target QS to attenuate infections or other bacterial-induced diseases (S. Kumar, Kolodkin-Gal, & Engelberg-Kulka, 2013; Reen, Gutierrez-Barranquero, Parages, & O'Gara, 2018). Unlike traditional bacteriostatic or bactericidal agents, QS inhibitors (QSIs) usually act at concentrations below the MIC, avoiding influencing bacterial growth and selective pressure for the development of drug resistance (Defoirdt, 2018). The first described QSI, halogenated furanones, and other synthetic substances are limited in real application due to their inherent toxicity and instability (Abdullah, Asghar, Butt, Shahid, & Huang, 2017). Therefore, it is necessary to seek natural QSI, which overall may be safer compared to synthetic ones.

3.4 | The QS system in Gram-positive bacteria

The QS system with autoinducer peptides (AIPs) as a signaling molecule is present in a variety of Gram-positive bacteria. One well-studied bacterium is *S. aureus*, and most of its virulence factors are regulated by the paradigmatic Agr system. In this system, pro-AIPs are first produced by AgrD, and then transported and processed into mature AIP by AgrB. Subsequently, mature AIP binds to membrane-bound histidine kinase AgrC, and the formed complex phosphorylates and passes phosphate to a cognate cytoplasmic response regulator AgrA. Finally, the phosphorylated AgrA binds to P2 and P3 promoters and regulates the transcription of a series of downstream virulence genes (Le & Otto, 2015). Moreover, another QS cascade system, which is exemplified in *Bacillus cereus*, regulates its virulence factors by AIP-binding transcription factors. In this system, pro-AIP is secreted by PapR and transferred to the extracellular environment, and then processed into mature AIP by the neutral protease B (NprB). PapR-AIP can be imported back into the cell by the oligopeptide permease (Opp) system, and binds to the transcription factor PlcR, altering its DNA-binding domain and promoting oligomerization, and finally regulates the transcription of target genes (Banerjee & Ray, 2017). The QS systems in these two typical Gram-positive bacteria are illustrated in Figure 3.

3.5 | The QS system in Gram-negative bacteria

N-acyl homoserine lactones (AHLs)-mediated LuxI/LuxR-type QS system is the main QS system in many

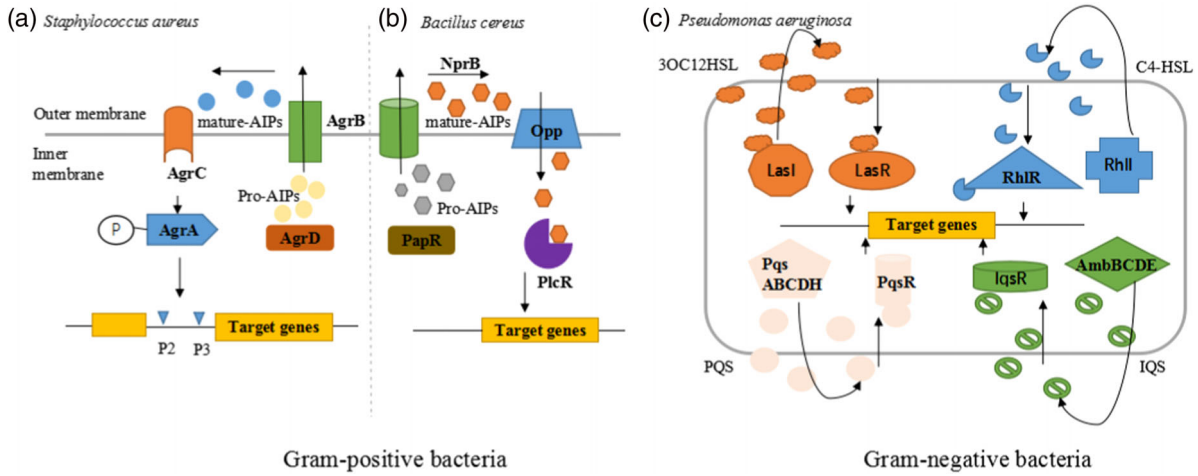

FIGURE 3 The schematic diagrams of QS systems in Gram-positive bacteria represented by *Staphylococcus aureus* (a) and *Bacillus cereus* (b), as well as in Gram-negative bacteria represented by *Pseudomonas aeruginosa* (c)

Gram-negative bacterial species (Rutherford & Bassler, 2012). In this system, LuxI homolog catalyzes AHL formation by forming an amide bond between an acyl side chain of an acyl-carrier-protein (acyl ACP) and homoserine of S-adenosylmethionine (Al), and then AHLs bind to LuxR homolog, forming binary complexes to activate the transcription of downstream genes (Chang et al., 2014). Some examples are the CviI/CviR in *Chromobacterium violaceum* and CqsA/CqsS in *V. cholerae* (Al-Shabib, Husain, Ahmad, & Baig, 2017; Martin-Rodriguez et al., 2015). At present, the QS system (Figure 3) is more deeply understood in *P. aeruginosa*, which harbors four types of QS systems, including two LuxI/LuxR-type (LasI/LasR and RhlI/RhlR) systems, a pseudomonas quinolone signal (PQS) system, and an integrating quorum sensing signal (IQS) system, all of which influence almost 10% of gene expression in *P. aeruginosa*, constituting a hierarchical regulatory network (Shrikant & Chandrajit, 2018). These four types of systems synthesize N-3-oxododecanyol-L-homoserine lactone (3OC12HSL), N-butanoyl-L-homoserine lactone (C4-HSL), 2-heptyl-3-hydroxy-4-quinolone (PQS), and IQS as respective signal molecules to form complexes with corresponding receptors, and then activate genes encoding virulence factors such as elastase, proteases, rhamnolipids, hemolysins, toxins, pyocyanin, and alginate, which usually damage tissues and organs and interfere with the defense mechanisms of the human immune system, triggering different types of infection (Guo et al., 2014; Kitao et al., 2018). Moreover, swarming motility and biofilm formation are also under the control of QS system in *P. aeruginosa* (Rutherford & Bassler, 2012).

3.6 | The QS system in both Gram-positive and Gram-negative bacteria

The LuxS/AI-2 QS system is considered as a way for communication among interspecies, and a highly homologous *luxS* gene is widely distributed in both Gram-positive and negative bacteria, catalyzing the production of AI-2 molecules with similar chemical structures (Galloway, Hodgkinson, Bowden, Welch, & Spring, 2011). The function of LuxS/AI-2 QS system varies in different bacteria. LuxS/AI-2 QS system was first identified in *V. harveyi* and was found to have the ability to regulate bioluminescence in this bacterium. AI-2-based QS system in *Vibrio* spp. also played important roles in regulating biofilm formation, stress tolerance (starvation and antibiotic treatment), and virulence production, such as pigments and proteases (Brackma et al., 2008). Other biological processes in diverse bacteria, such as biofilm formation in *E. coli*, *Sc. suis*, and *Sc. pneumoniae*, pathogenicity, and tolerance toward oxidative stress and heat shock in *Haemophilus parasuis*, antibiotic susceptibility in *Sc. Anginosus*, as well as acid resistance and transcription of many virulence genes in *Sc. Agalactiae*, are also reported to be controlled by AI-2-based QS, making QS inhibition an interesting antibacterial strategy (Ma et al., 2017; Wang et al., 2015; Yadav et al., 2018; Zhang et al., 2019; Zhao, Xue, Shang, Sun, & Sun, 2010). Here, we take *V. harveyi* as a typical example to explain this AI-2-based QS system (Martin-Rodriguez et al., 2015). If only basal amounts of diffusible signal molecules are produced, the QS cascade is initiated by the membrane-associated receptors LuxPQ, which is in its active autophosphorylated state, and can transfer phosphate to LuxO via the phosphotransfer protein LuxU. The phosphorylated LuxO can then activate the production of quorum-regulatory sRNAs (Qrr sRNAs), which can work together with the chaperone protein Hfq, resulting in the destabilization of mRNA that encodes the response regulator LuxR. However, at high autoinducer concentrations, AI-2 molecules bind to the receptors LuxPQ and convert them from kinases into phosphatases, causing dephosphorylation of LuxO and thereby inhibiting the formation of Qrr sRNAs. The altered gene expression pattern keeps the

LuxR mRNA stable and then results in the production of LuxR.

3.7 | Interference with QS system by spice essential oils

Recent studies have reported that essential oils derived from natural spices are ideal QSIs due to their wide availability and environmental friendliness. The effects of spice essential oils on the inhibition of QS are usually evaluated by the production of a purple pigment violacein in *C. violaceum* and virulence factors in *P. aeruginosa,* such as pyocyanin, elastase, rhamnolipids, EPS production, and biofilm formation, as well as the bioluminescence production of *Vibrio* spp. (Alvarez et al., 2014; Husain et al., 2015). The inhibitory effects of spice essential oils and their major components on the QS system are summarized in Table 3. Generally, spice essential oils inhibit QS at sub-MICs and attenuate a variety of QS indicators in a concentration-dependent manner. Importantly, essential oils at sub-MICs have no influence on the bacterial growth, suggesting that the reduction of QS indicators by essential oils is not likely due to decreased bacterial density. Overall, the diversity in the anti-QS potential of spice essential oils can be related to their different chemical structures, and the compounds such as cinnamaldehyde, eugenol, citronellol, and carvacrol seem more effective for QS inhibition.

3.8 | Mechanisms of QS inhibition by spice essential oils

Two mechanisms, which are shown in Figure 4, have been proposed to explain the anti-QS activity of spice essential oils, including inhibition of the synthesis of QS signaling molecules and the inactivation of cognate receptors, which, in turn, inactivate the expression of virulence genes necessary for cooperative behaviors.

The generation and accumulation of signal molecules is the premise of activating the QS system, so suppressing the production of signals can be relatively effective. *Thymus vulgare* essential oil and its major bioactive compounds like carvacrol and thymol can inhibit the production of AHLs in *P. fluorescens* KM121 by 78% to 90% at sub-MIC, measured by an indicator strain of *C. violaceum* CVO26 and verified by LC-MS (Myszka et al., 2016). From the molecular level, sub-MICs of carvacrol reduce the expression of AHL synthase-encoding gene *cviI* in *C. violaceum* in a dose-dependent way (Burt, Ojo-Fakunle, Woertman, & Veldhuizen, 2014). In other research, molecular docking assay is used to reveal that carvacrol forms π–π interaction with Phe123 and Phe102 residues in ExpI (LuxI homologue), resulting in reduced accumulation of AHLs in *Pectobacterium* species (Joshi et al., 2016). Curcumin at 1 μg/mL inhibits the formation of signaling molecules in *P. aeruginosa* PAO1, causing a 25% decrease of 3OC12HSL and more than 2% decrease of C4-HSL (Rudrappa & Bais, 2008). Besides, cinnamaldehyde significantly reduces the production of AHLs in *P. aeruginosa*, and the decrease might be caused by hydrophobic interaction and hydrogen bonding between cinnamaldehyde and LasI (Chang et al., 2014). In *Sc. pyogenes,* cinnamaldehyde binds efficiently with a homologous protein of LuxS, resulting in the reduction of AI-2 production (Shafreen, Selvaraj, Singh, & Pandian, 2014).

In addition, many spice essential oil components have been reported to share similar chemical structures with signals and can compete for binding with corresponding LuxR-type receptors, resulting in the inactivation of QS signal receptors and inhibition of QS-dependent virulence factors (Miller et al., 2015). Spice essential oil constituents with diverse chemical structures have wide inhibitory spectra against the different lengths of AHLs produced by bacteria (Ahmad, Viljoen, & Chenia, 2015). Molecular docking analysis reveals that cinnamaldehyde can form hydrogen bonds with residues Lys58 and Pro57 in the LuxR-type protein model, interfering with the formation of AHL-LuxR complexes of *P. fluorescens* (Li et al., 2018). Another study shows that the putative conserved ligand-binding sites of LuxR homologs in *V. cholerae* are composed of polar amino acid side chains and hydrophobic residues, and the amphiphilic cinnamaldehyde may irreversibly conjugate with LuxR via its nucleophilic amino acid side chains and electrophilic acyl group, reacting as Michael-type addition reaction, thereby changing the LuxR conformation and consequently decreasing the binding of LuxR to its promoter DNA (Brackman et al., 2011). In addition, 6-gingerol, a pungent oil derived from fresh ginger, can bind with QS receptor LasR through hydrogen bonding with Trp60, Arg61, and Tyr93, as well as hydrophobic interactions with Leu40, Tyr47, Ala50, Ala70, Val76, and Ala127 in *P. aeruginosa* (J.S. Kim, Lee, Byun, & Park, 2015). 6-Shogaol and zingerone are another two phenolic compounds in ginger with strong QSI activity. Phenolic hydroxyl group of zingerone can form hydrogen bonds with the residue Ser129 in LasR from *P. aeruginosa*, and the π–π interaction between aromatic group and Tyr56 strengthens the overall binding ability (L. Kumar, Chhibber, Kumar, Kumar, & Harjai, 2015; N.V. Kumar, Murthy, Manjunatha, & Bettadaiah, 2014), indicating that other phenolic substances such as eugenol, carvacrol, and thymol sharing similar chemical structures can exert a similar anti-QS mechanism via binding with QS receptors. This above hypothesis is supported by the study of Jayalekshmi et al. (2016), who demonstrate that the aromatic hydroxyl and methoxy groups on eugenol can form hydrogen bonds with critical amino acids Arg61 and Tyr47 of LasR, inhibiting the activation of LasR and downstream genes. Besides, the length of the alkyl side chain and the hetero linkage introduced between the phenolic moiety and

TABLE 3 Anti-QS effects of spice essential oils and their major compounds

Spice essential oils	Bacteria	MIC	Concentration used	Effects on QS or QS-regulated phenotypes	References
Carvacrol	*C. violaceum* ATCC 12472	0.7 mM	0.7 mM (no cell viability inhibition)	Inhibit 50% of violacein production	(Tapia-Rodriguez et al., 2017)
	P. aeruginosa	7.9 mM	3.9 mM	Inhibit 60% of pyocyanin production, 57% of biofilm biomass	
	C. violaceum CV026	0.156 mg/mL	0.1 mg/mL	Inhibit 8.35% of violacein production	(Zhang et al., 2018)
			2.0 μL/mL (no growth inhibition)	Inhibit 80% of violacein production	(Myszka et al., 2016)
Carvone	*C. violaceum* CV026	0.625 mg/mL	0.1 mg/mL	Inhibit 8.23% of violacein production	(Zhang et al., 2018)
Cinnamaldehyde	*V. anguillarum* LMG 4411		250 μM (no growth inhibition)	Inhibit 25% to 74% of protease activity, 15% to 65% of violacein production	(Brackman et al., 2011)
	V. harveyi BB170		250 μM (no growth inhibition)	Inhibit 65% of QS-regulated bioluminescence (AI-2)	
	C. violaceum CV026	0.175 μL/mL	0.1 μL/mL	Inhibit 51.0% of violacein production	(Li et al., 2018)
	P. fluorescens	0.125 μL/mL	0.1 μL/mL	Inhibit 54.5% of biofilm formation, 58.5% of extracellular enzymes production, 40.76% of swimming motility, 58.42% of swarming motility	
	P. aeruginosa PAO1	11.31 mM	0.2 MIC	Inhibit 13-fold of the *lasI* level, sevenfold of the *lasR* level, 65% of protease production, 22% of elastase production, 32% of pyocyanin production	(Ahmed et al., 2019)
Cinnamic acid	*C. violaceum* CV026	0.625 mg/mL	0.1 mg/mL	Inhibit 10.13% of violacein production	(Zhang et al., 2018)
Citrus clementina	*C. violaceum* wild-type strain (CIP 103350T)	1.5 mg/mL	0.4 mg/mL	Inhibit 50% of violacein production	(Poli et al., 2018)
Citral	*C. violaceum* CV026	1.25 mg/mL	0.1 mg/mL	Inhibit 6.33% of violacein production	(Zhang et al., 2018)
Clove	*C. violaceum* strain CV026		0.0025% (v/v) (no growth inhibition)	Inhibit 80% of violacein production	(Eris & Ulusoy, 2013)
	C. violaceum VIR07			Inhibit 72% of violacein production	
	C. violaceum ATCC 12472			Inhibit 39% of violacein production	
Cuminum cyminum	*C. violaceum* CV026	60 μg/mL	50 μg/mL	Inhibit 72.8% of violacein production	(Venkadesaperumal, Rucha, Sundar, & Shetty, 2016)

(Continues)

TABLE 3 (Continued)

Spice essential oils	Bacteria	MIC	Concentration used	Effects on QS or QS-regulated phenotypes	References
Curcumin	*P. aeruginosa* PAO1	30 μg/mL	1 μg/mL	Inhibit twofold of elastase activity, 25% of 3OC12HSL production, >2% of C4-HSL production	(Rudrappa & Bais, 2008)
			1.5 to 3 μg/mL	Inhibit 60% to 80% of pyocyanin production	
	C. violaceum CV026	384 μg/mL	100 μg/mL	Inhibit 89% of violacein production	(Packiavathy, Priya, Pandian, & Ravi, 2014)
	P. aeruginosa PAO1	192 μg/mL	100 μg/mL	Inhibit 63% of alginate production, 58% of prodigiosin production Reduce the diameter of the rhamnolipid zone from 18 to 8 mm	
	V. harveyi	150 μg/mL	100 μg/mL	Inhibit 88% of bioluminescence, 69% of biofilm formation, 61% of EPS production, 45% of alginate production, 59% of β-galactosidase production	(Packiavathy, Sasikumar, Pandian, & Ravi, 2013)
	V. vulnificus	300 μg/mL		Inhibit 79% of biofilm formation, 62% of EPS production, 65% of alginate production, 55% of β-galactosidase production	
	V. parahaemolyticus	150 μg/mL		Inhibit 56% of biofilm formation, 71% of EPS production, 78% of alginate production, 36% of β-galactosidase	
Dorema aucheri Bioss	*P. aeruginosa* PAO1		25 μg/mL (no growth inhibition)	Inhibit pyoverdine and elastase production, and the transcription of *lasI*	(Sepahi, Tarighi, Ahmadi, & Bagheri, 2015)
Eugenol	*C. violaceum* CVO26 and PAO1	160 mg/mL	96 mg/mL	Inhibit 80% of violacein production	(Al-Shabib et al., 2017)
			21 to 84 mg/mL	Inhibit 47% to 82% of elastase production, 44% to 87% of total protease activity, 45% to 85% of pyocyanin production, 9.6% to 49.1% of EPS production	
	C. violaceum PAO1	100 to 800 μM	50 μM	Inhibit 56% of violacein production	(Zhou, Zheng, Tang, Yu, & Gong, 2013)
			200 to 400 μM	Inhibit 32% to 46% of elastase production	
Eugenyl acetate from clove bud	*C. violaceum* DMST 21761		75 μg/mL (no growth inhibition)	Inhibit 27.7-fold of violacein production	(Musthafa & Voravuthikunchai, 2015)

(Continues)

TABLE 3 (Continued)

Spice essential oils	Bacteria	MIC	Concentration used	Effects on QS or QS-regulated phenotypes	References
Ferula asafoetida L.	*P. aeruginosa* PAO1		25 µg/mL (no growth inhibition)	Inhibit pyocyanin, pyoverdine, elastase production, biofilm formation, and the transcription of *lasI*	(Sepahi et al., 2015)
Foeniculum vulgare	*C. violaceum* PAO1	60 µg/mL	50 µg/mL	Inhibit 75.7% of violacein production	(Venkadesaperumal et al., 2016)
	C. violaceum wild-type strain (CIP 103350T)	0.8 mg/mL	0.2 mg/mL	Inhibit 50% of violacein production	(Poli et al., 2018)
6-Gingerol	*P. aeruginosa*		1 to 100 mM (no growth inhibition)	Inhibit 19% to 53% of biofilm formation, 21% to 43% of exoprotease production, 36% to 60% of pyocyanin production, 36% to 60% of rhamnolipid production	(Kim et al., 2015)
Geraniol	*C. violaceum* CV026	0.625 mg/mL	0.1 mg/mL	Inhibit 11.05% of violacein production	(Zhang et al., 2018)
Hexanal		0.156 mg/mL		Inhibit 12.65% of violacein production	
Lavandula angustifolia	*E. coli* (pSB1075)		0.01%, 0.025%, and 0.05% (no growth inhibition)	Inhibit light production expression	(Yap et al., 2014)
Lavandula stoechas	*C. violaceum* wild-type strain (CIP 103350T)	1.5 mg/mL	0.2 mg/mL	Inhibit 50% of violacein production	(Poli et al., 2018)
Linalool	*C. violaceum* ATCC 12472		20 µL over plate	Increase the diameter of violacein production inhibition from 1 nm to 53 mm	(Alves et al., 2016)
Mentha piperita	*C. violaceum* CVO26	0.6% (v/v)	0.1% (v/v)	Inhibit 83.3% of violacein production	(Husain et al., 2015)
	P. aeruginosa PAO1	6.4% (v/v)	3% (v/v)	Inhibit 80% of LasB elastase activity, 76% of protease activity, 78% of chitinase activity, 85.2% of pyocyanin production, 81.3% of swarming migration, 84% of biofilm formation	
Menthol	*C. violaceum* CVO26	800 µg/mL	400 µg/mL	Inhibit 85% of violacein production	

(Continues)

TABLE 3 (Continued)

Spice essential oils	Bacteria	MIC	Concentration used	Effects on QS or QS-regulated phenotypes	References
	P. aeruginosa PAO1	1,000 μg/mL	800 μg/mL	Inhibit 84.2% of total protease activity, 83.5% of pyocyanin production, 78.7% of elastase activity, 78% of swarming motility, 57.7% of EPS production, 54.6% of chitinase activity, 69.4% of biofilm formation	
Oregano	*C. violaceum* ATCC 12472		15.6 μg/mL (no cell viability inhibition)	Inhibit >50% of violacein production	(Alvarez et al., 2014)
Piper nigrum	*C. violaceum* CV026	110 μg/mL	50 μg/mL	Inhibit 49.3% of violacein production	(Venkadesaperumal et al., 2016)
Salicylic acid	*P. aeruginosa* PAO1	18.1 mM	0.2 MIC	Inhibit threefold of the *lasI* level, twofold of the *lasR* level	(Ahmed et al., 2019)
Syzygium aromaticum	*C. violaceum* CV12472 and CVO26	0.2% (v/v)	0.04% (v/v) 0.08% (v/v) 0.12% (v/v)	Inhibit 48.0% of violacein production Inhibit 58.0% of violacein production Inhibit 78.4% of violacein production	(Khan, Zahin, Hasan, Husain, & Ahmad, 2009)
	P. aeruginosa PAO1	3.2% (v/v)	0.2% (v/v) 0.4% (v/v) 0.8% (v/v) 1.6% (v/v)	Inhibit 40% of swarming motility Inhibit 56% of swarming motility Inhibit 68% of swarming motility Inhibit 78% of swarming motility	
Thymol	*C. violaceum* CV026	0.156 mg/mL	0.1 mg/mL	Inhibit 12.11% of violacein production	(Zhang et al., 2018)
			4.0 μL/mL (no growth inhibition)	Inhibit 78% of violacein production	(Myszka et al., 2016)
Thymus vulgare	*C. violaceum* CV026		20 μL/mL (no growth inhibition)	Inhibit 90% of violacein production	(Myszka et al., 2016)
Zingerone	*P. aeruginosa* PAO1		10 mg/mL (no growth inhibition)	Inhibit protease production to <100 U/L	(L. Kumar et al., 2015)

Abbreviations: *C.*, *Chromobacterium*; *E.*, *Escherichia*; EPS, extracellular polymeric substances; *P.*, *Pseudomonas*; *V.*, *Vibrio*.

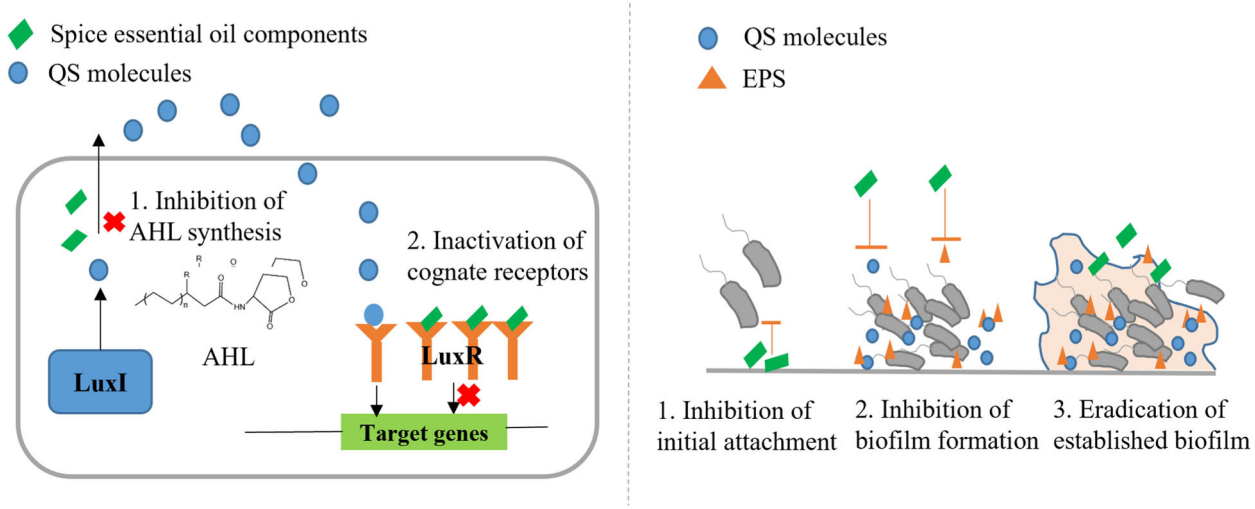

FIGURE 4 The schematic diagrams of the mechanisms of QS inhibition (left) and biofilm inhibition (right) effects by spice essential oils

long alkyl side chain may significantly affect the QSI activity of these phenolic compounds (Jaramillo-Colorado, Olivero-Verbel, Stashenko, Wagner-Dobler, & Kunze, 2012). For instance, zingerone with shorter side chains has much lower anti-QS ability than the other two compounds (6-gingerol and shogaol) with longer side chains (N.V. Kumar et al., 2014).

Overall, spice essential oils can mainly block the QS system by inhibiting the synthesis of QS signaling molecules and inactivating QS signal receptors. However, the analogs of signal molecule AIP are mainly obtained through chemical synthesis or microbial metabolites, and QSIs derived from spice essential oils are limited (Daly et al., 2015; Simonetti et al., 2016). Therefore, it is of great significance to discover novel hyperactive and safe QSIs from spice essential oils or other plant sources.

4 | BACTERIAL BIOFILM

Biofilms can be defined as organized aggregates of homogenous or heterogeneous microbial cells. Many bacteria have the ability to attach to various biotic and abiotic surfaces, on which they will proliferate, differentiate, and secrete a series of extracellular polymeric substances (EPSs) to form a physical barrier to protect the inner bacteria from external hostile conditions. EPS is a complex matrix that mainly contains exopolysaccharides, proteins, nucleic acids, metal ions, and water. Generally, biofilm formation can be divided into four consecutive stages, including attachment, microcolony formation, maturation, and dispersion, forming a dynamic and cyclical process (Gupta, Sarkar, Das, Bhattacharjee, & Tribedi, 2016). Biofilms formed in industrial and clinical environments can cause product contamination and food spoilage, and cause difficulties in clinical treatment. In developed countries, biofilm is closely associated with bacterial infections, which are the second leading cause of human death (Lewis, 2007). Moreover, secondary contamination can be caused by the release of bacteria, metabolites, and toxins during the process of biofilm rupture (Espina, Pagan, Lopez, & Garcia-Gonzalo, 2015).

Once the biofilm is established, eradication of the mature biofilm becomes difficult and requires mechanical forces and chemical disruption, since the cells undergo irreversible attachment and adhesion. The negatively charged EPSs adhering to the cell surface are conducive to the formation of stable microbial communities and three-dimensional structure of biofilm, protecting inner cells from environmental stress, such as the innate immune defenses, radiation, antibiotic treatment, and other damaging agents (de Oliveira, Brugnera, Cardos, Alves, & Piccoli, 2010; Jadhav, Shah, Bhave, & Palombo, 2013). In addition to the physical barrier, absorption or mutual reaction may also occur between antimicrobial agents and intercellular matrix components, thus neutralizing the activities of these agents. Most of these events occur at the outer part of biofilm, so the innermost bacteria cannot be reached and finally survive (Cabarkapa et al., 2015). Another factor contributing to the difficulty in preformed biofilm eradication is that most antimicrobial agents are more effective against actively growing cells. Due to the lack of nutrients and oxygen, the bacteria embedded in biofilm are metabolically inactive and nondividing persister cells, and their tolerance is about 10 to 100 times higher than planktonic bacteria (Cabarkapa et al., 2015; Miladi et al., 2017). Gene expression patterns between planktonic and sessile cells are different. Some genes involved in the upregulation of secondary metabolic pathways, including antibiotic resistance, have been found in the bacteria embedded within the biofilm (Jafri, Ansari, & Ahmad, 2019). Therefore, biofilm is one of the major targets for reducing bacterial resistance and infective ability. Accordingly, the inhibition

of biofilm formation and eradication of preformed biofilms are considered as effective strategies to treat biofilm-related infections. Spice essential oils show both biofilm inhibition and biofilm eradication abilities (Table 4).

4.1 | Inhibition of biofilm formation by spice essential oils

Spice essential oils have been reported to interfere with biofilm formation of different bacteria at sub-MICs under *in vitro* conditions, without evidently affecting the growth and metabolic activities of bacteria. For instance, essential oils from oregano, clove, thyme, turmeric, garlic, lemon, and their major bioactive compounds, such as carvacrol, eugenol, thymol, curcumin, allicin, and limonene, show high biofilm inhibition activities (Kim et al., 2016). However, few *in vivo* studies are conducted to investigate their antibiofilm activities. Eugenol is found to exhibit a notable activity against the colonization (decrease 88%) of *S. aureus* in the middle ear of rats (Yadav, Chae, Im, Chung, & Song, 2015).

Although the mechanisms of biofilm formation are complicated, several factors still can be targeted for inhibiting biofilm formation. The prevention of bacterial initial adhesion and the subsequent irreversible maturation process have been well documented as the major strategies for biofilm inhibition (Silva, Zimmer, Macedo, & Trentin, 2016). The schematic diagram is shown in Figure 4. Targeting the initial adhesion step can be the most promising way to inhibit biofilm formation, as planktonic bacteria seem more sensitive than biofilm-associated cells, leading to easier inhibition by the application of certain spice essential oils (Hayat, Sabri, & McHugh, 2018). Bacterial attachment mainly involves the interaction between adhesive substances and receptors on the host surface. Adhesive substances are fimbria and fimbrial adhesin like surface-associated proteins, which are the main targets of spice essential oils involved in inhibiting the initial attachment. For instance, a remarkable downregulation of sortaseA encoding gene *srtA* is observed after the treatment of lemon essential oil at sub-MIC. SortaseA is responsible for sorting and anchoring surface protein P1 to the cell surface of *S. mutans* (Sun et al., 2018). Additionally, 400 μg/mL of limonene downregulates *mga* by over 80%, a surface associated-M protein-encoding gene that plays an important role in *Sc. pyogenes* adhesion (Subramenium, Vijayakumar, & Pandian, 2015). Clove oil and eugenol inhibit more than 75% of biofilm formation in *E. coli* O157:H7, accompanied by the downregulated expression of type I fimbriae genes (*fimCDH*) and curli genes (*csgABDFG*), which are important for bacterial attachment (Kim et al., 2016). In addition, 50 μg/mL of allicin reduces the expression of *fimH* type I fimbriae gene of uropathogenic *E. coli (UPEC)* CFT073 and J96 by 64% and 77%, respectively, possibly due to the hydrogen bonds formed between allicin and two amino acids (Phe1 and Asn135) in FimH (Yang et al., 2016). It is worth mentioning that attachment efficiency can be influenced by the characteristics of host surfaces, such as physicochemical interaction forces like hydrophobicity and electrostatic interactions (Gutierrez-Pacheco et al., 2018; Hayat et al., 2018). A simple isoeugenol coating inhibits the biofilm formation of *S. aureus*, *L. monocytogenes*, and *P. fluorescens* through changing the hydrophobic properties of the surface (Nielsen et al., 2018). Similarly, *Sc. pyogenes* fails to form biofilm on a limonene-coated glass, stainless steel, or titanium piece (Subramenium et al., 2015).

The formation of biofilm is really a complex process involving a variety of environmental factors, such as QS, extracellular polysaccharide, proteases, and other global regulators (Lee, Kim, Ryu, & Lee, 2016). With respect to *Staphylococci*, the most extensively reported genes involved in biofilm formation are intercellular adhesion genes *icaD*/*icaA*, coexpression of which provokes the synthesis of viscous polysaccharide intercellular adhesion or poly-N-acetylglucosamine (PIA/PNAG) (Budri et al., 2015). Some *S. aureus* is ica-independent, in which the biofilm-associated protein (Bap) is important for bacterial accumulation (Yadav et al., 2015). In addition, the biofilm of *Staphylococcus* is under the control of several genetic loci, namely, *sarA* (staphylococcal accessory regulator), *luxS*, and *agr* QS systems (Azmi, Qrei, & Abdeen, 2019). Several spice essential oils and their components have been revealed to show inhibitory effects on the production of EPS or the in-depth regulatory genes. For instance, the EPS production in *P. aeruginosa* PAO1 is reduced by 97.89% in the presence of *Murraya koenigii* oil, accompanied by 39.59% of biofilm inhibition (Bai & Vittal, 2014). Essential oil compounds, such as carvone, hexanal, citral, geraniol, salicylic acid, thymol, eugenol, and cinnamaldehyde, reduce EPS production in *P. fluorescens* and *Erwinia carotovora* to different degrees, in parallel to the reduction of biofilm formation (Zhang et al., 2018). Moreover, eugenol reduces the expression of *icaD* and *sarA* by 6.1- and 8.8-fold, respectively, in methicillin-resistant *S. aureus* (Dhanawade, Kalorey, Srinivasan, Barbuddhe, & Kurkure, 2010; Yadav et al., 2015). A further molecular docking analysis suggests the formation of hydrogen bonds and hydrophobic interaction between eugenol and key residues (L153, K154) in SarA protein (Al-Shabib et al., 2017).

4.2 | Eradication of established biofilm by spice essential oils

Biofilm eradication can be generally achieved in the presence of spice essential oils at concentrations higher than MIC values (Snoussi et al., 2015). Spice essential oils exhibit better antibiofilm performance than their individual

TABLE 4 Antibiofilm effects of spice essential oils and their major compounds

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
Achillea millefolium	*L. monocytogenes*	3.13% (v/v)	0.5 MIC	Inhibit 77.7% of biofilm biomass, 63.7% of metabolic activity	(Jadhav et al., 2013)
	L. innocua			Inhibit 79.4% of biofilm biomass, 65.3% of metabolic activity	
Allicin	*Pr. mirabilis* ATCC 12453	64 μg/mL	16 and 32 μg/mL	Inhibit 28.9% to 33.8% of biofilm development	(Ranjbar-Omid et al., 2015)
	Two clinical isolates of Pr. mirabilis	64 to 128 μg/mL		Inhibit 16% to 35.1% of biofilm development	
Bay, clove and pimento berry	EHEC	>0.1% (v/v)	0.005% (v/v)	Inhibit >75% of biofilm formation, >80% of biomass and mean thickness	(Kim et al., 2016)
Black pepper and myrrh oils	*S. aureus*		0.01% (little effect on growth)	Inhibit >75 % of biofilm formation	(Lee et al., 2014)
Carvacrol	*Sa. enteritidis*	0.156 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	(Cabarkapa et al., 2019)
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
	S. aureus SC-01, *L. monocytogenes*, and *E. coli* MG1655	200 μL/L	500 to 2,000 μL/L	Inhibit 99.99% of the initial biofilm mass	(Espina, Berdejo, Alfonso, García-Gonzalo, & Pagán, 2017)
	12 strains of oxacillin- and vancomycin-resistant *S. aureus*	0.25 mg/mL	0.062 to 0.25 mg/mL	Inhibit biofilm formation in a dose-dependent manner Inhibit the biofilm formation completely	(Vasconcelos et al., 2017)
	MRSA	200 μL/L	10 μL/L	Inhibit 40% of biofilm formation	(Espina et al., 2015)
	S. aureus, *S. epidermidi*, *P. aeruginosa*	0.125 to 0.5 μL/mL	0.125 MIC	Inhibit <12.7% of biofilm formation	(Ceylan & Ugur, 2015)
			0.25 MIC	Inhibit 32.3% of biofilm formation	
			0.5 MIC	Inhibit 16.3% to 50.7% of biofilm formation	
			MIC	Inhibit 41.2% to 72.9% of biofilm formation	
Cinnamaldehyde	*P. aeruginosa*	11.8 mM	1.5 mM	Inhibit 28.2% of biofilm formation	(Topa et al., 2018)
			3 mM	Inhibit 37.9% of biofilm formation	
			5.9 mM	Inhibit 79.7% of biofilm formation	
			11.8 mM	Inhibit 97.1% of biofilm formation	

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
	S. aureus	0.199 mg/mL (MIC90%)	0.106 mg/mL	Inhibit 45.3% of biofilm formation on polystyrene surface, 44.9% of biofilm formation on stainless steel surface	(Budri et al., 2015)
Cinnamomum zeylanicum	*S. aureus*	0.243 mg/mL (MIC90%)	0.106 mg/mL	Inhibit 74.7% of biofilm formation on polystyrene surface, 69.6% of biofilm formation on stainless steel surface	(Budri et al., 2015)
Citral	*S. aureus* SC-01, *L. monoytogenes*, and *E. coli* MG1655	200 to 500 µL/L	2,000 µL/L	Inhibit 99.99% of the initial biofilm mass	(Espina et al., 2017)
	MRSA	500 µL/L	20 µL/L	Reduce 55% of biofilm formation	(Espina et al., 2015)
	P. fluorenscens	5 mg/mL	0.1 mg/mL	Inhibit 38.39% of EPS production	(Zhang et al., 2018)
Curcumin	*E. coli*	192 to 384 µg/mL	100 µg/ml	Inhibit 52% of biofilm formation	(Packiavathy et al., 2014)
	P. aeruginosa PAO1			Inhibit 89% of biofilm formation	
	Pr. Mirabilis			Inhibit 52% of biofilm formation	
	Se. marcescens			Inhibit 76% of biofilm formation	
Cymbopogon flexuosus	MSSA	0.06% (v/v)	0.06% to 0.125% (v/v)	Inhibit biofilm formation completely	(Adukwu et al., 2012)
	Two strains of MRSA				
Cymbopogon nardus	*S. aureus*	0.5 mg/mL	0.125 mg/mL	Inhibit 61% of biofilm formation	(Pontes et al., 2019)
			0.25 mg/mL	Inhibit 72.7% of biofilm formation	
Eugenol	EHEC	> 0.1% (v/v)	0.005% (v/v)	Inhibit >75% of biofilm formation, >80% of biomass and mean thickness	(Kim et al., 2016)
	S. aureus	0.237 mg/mL (MIC90%)	0.106 mg/mL	Inhibit 52.8% of biofilm formation on polystyrene surface, 19.6% of biofilm formation on stainless steel surface	(Budri et al., 2015)
	S. aureus ATCC 29213	0.04% (v/v)	0.5 MIC	Inhibit >50% of biofilm biomass	(Yadav et al., 2015)
Geraniol	*S. aureus*	0.25 mg/mL	0.125 mg/mL	Inhibit 84.2% of biofilm formation	(Pontes et al., 2019)
Hexanal	*P. fluorescens*	0.313 to 0.625 mg/mL	0.1 mg/mL	Inhibit 20.18% of biofilm formation, 17.65% of EPS production	(Zhang et al., 2018)
	Er. carotovora			Inhibit 25.86% of biofilm formation, 54.52% of EPS production	

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
Lemon	*Sc. mutants* UA159	4.5 mg/mL	0.125 MIC	Inhibit 72.65% of biofilm formation	(Sun et al., 2018)
			0.5 MIC	Inhibit 97.87% of biofilm formation	
	Multidrug resistant *K. pneumoniae*		170 μL/mL	Inhibit 48.3% of biofilm formation	(Sahal, Avcioglu, & Bilkay, 2016)
	Multidrug resistant *K. rhinoscleromatis*			Inhibit 83.4% of biofilm formation	
Limonene	*Sc. mutans* UA159	21 mg/mL	0.125 MIC 0.5 MIC	Inhibit 46.62% of biofilm formation	(Sun et al., 2018)
				Inhibit 94.88% of biofilm formation	
	MRSA	5,000 μL/L	200 μL/L	Inhibit 80% of biofilm formation	(Espina et al., 2015)
	Sc. pyogenes SF370 and five clinical isolates, *Sc. mutans* UA159, *Sc. Mitis* ATCC 6249		400 μg/mL (no antibacterial activity)	Inhibit 75% to 95% of biofilm inhibition	(Subramenium et al., 2015)
Oregano and thyme red oil	UPEC	0.1% (v/v)	0.01% (v/v)	Inhibit 60% of biofilm formation, >80% of biomass, mean thickness, and substratum coverage	(Lee, Kim, & Lee, 2017)
Origanum heracleoticum	*Sa. enteritidis*	0.078 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	(Cabarkapa et al., 2019)
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
Origanum vulgare	*Sa. enteritidis*	0.156 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
	10 stains of *P. fluorescens*	10 to 40 μL/mL	0.5 μL/mL	Inhibit 85.57% to 95.51% of biofilm formation	(Rossi et al., 2018)
Origanum vulgare, *Salvia officinalis*, cloves, and ginger	*Sc. pyogenes* ATCC 19615 and ATCC 49399	0.25 to 1.0 mg/mL	Sub-MICs	Inhibit biofilm formation in a dose-dependent manner	(Wijesundara & Rupasinghe, 2018)
Peppermint	*S. aureus* ATCC 25923	0.5 mg/mL	0.125 mg/mL	Inhibit 50% of biofilm formation	(Kang et al., 2019)
Plectranthus amboinicus	12 strains of oxacillin- and vancomycin-resistant *S. aureus*	0.5 mg/mL	0.062 to 0.5 mg/mL	Inhibit biofilm formation in a dose-dependent manner	(Vasconcelos et al., 2017)
Salicylic acid	*P. fluorescens*	0.625 mg/mL	0.1 mg/mL	Inhibit 37.61% of biofilm formation	(Zhang et al., 2018)
	Er. carotovora			Inhibit 47.24% of biofilm formation	

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
Syzygium aromaticum	*S. aureus*	0.392 mg/mL (MIC90%)	0.106 mg/mL	Inhibit 69.4% of biofilm formation on polystyrene surface, 63.6% of biofilm formation on stainless steel surfaces	(Budri et al., 2015)
Thymol	*Sa. enteritidis*	0.156 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	(Cabarkapa et al., 2019)
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
	S. aureus, *S. epidermidi*, *P. aeruginosa*	0.125 to 0.5 μL/mL	0.125 MIC	Inhibit <12.5% of biofilm formation	(Ceylan & Ugur, 2015)
			0.25 MIC	Inhibit <23.2% of biofilm formation	
			0.5 MIC	Inhibit 11.4% to 48.9% of biofilm formation	
			MIC	Inhibit 20.1% to 68.6% of biofilm formation	
	UPEC	0.05% (v/v)	0.01% (v/v)	Inhibit >80% of biomass and mean thickness	(Lee et al., 2017)
	Er. carotovora	0.313 mg/mL	0.1 mg/mL	Inhibit 47.24% of biofilm formation	(Zhang et al., 2018)
Thymus serpyllum	*Sa. enteritidis*	0.323 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	(Cabarkapa et al., 2019)
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
Thymus sipyleus BOISS. subsp. *sipyleus* BOISS. var. *davisianus*	*S. aureus*, *S. epidermidi*, *P. aeruginosa*	5 to 50 μL/mL	0.125 MIC	Inhibit <24.9 of biofilm formation	(Ceylan & Ugur, 2015)
			0.25 MIC	Inhibit <37.6% of biofilm formation	
			0.5 MIC	Inhibit 8.2% to 43.9% of biofilm formation	
			MIC	Inhibit 23.5% to 67% of biofilm formation	
Thymus vulgaris	*Sa. enteritidis*	0.156 μL/mL	0.25 MIC	Inhibit 40% to 50% of biofilm formation	(Cabarkapa et al., 2019)
			0.5 MIC	Inhibit 60% to 70% of biofilm formation	
	Four *Sa. enteritidis* strains	0.156 μL/mL	0.5 MIC	Inhibit 70.1% to 77.7% of biofilm formation	(Cabarkapa et al., 2015)
			MIC	Inhibit 88.4% to 91.4% of biofilm formation	

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
Eradication of preformed biofilm					
Achillea millefolium	*L. monocytogenes* and *L. innocua* isolates	3.13% (v/v)	MIC	Inhibit 28.7% to 52.2% of 6 hr old biofilm (1 hr treatment)	(Jadhav et al., 2013)
			2 MIC	Inhibit 50% to 65% of 6 hr old biofilm (1 hr treatment)	
Allicin	*Pr. mirabilis* ATCC 12453	64 μg/ mL		BIC = 256 μg/mL (18 hr old biofilm, 24 hr treatment), BEC = 512 μg/mL (18 hr old biofilm, 72 hr treatment)	(Ranjbar-Omid et al., 2015)
Carvacrol	*E. coli* O157:H7 ATCC 35150, *S. aureus* ATCC 43387, *En. faecalis* ATCC 29212		0.1% (v/v)	Inhibit 49.4% to 65.2% of 4 days old biofilm (30 s treatment), 63.6% to 100% of 4 days old biofilm (5 min treatment), 69.4% to 100% of 4 days old biofilm (15 min treatment)	(Campana & Baffone, 2018)
	S. aureus LPMA63		5 μL/mL	Reduce the sessile cells counts in 24 and 72 hr old biofilm to <1 log CFU/cm^2 (15 min treatment)	(Rodrigues et al., 2018)
	12 strains of *Sa. typhimurium*	64 to 512 μg/mL	13.7 to 166.4 μg/mL	Inhibit 50% of 24 old biofilm (24 hr treatment)	(Miladi et al., 2017)
Cinnamaldehyde	MRSA	0.0625% to 0.125% (v/v)	0.5 MIC	Inhibit 40% to 70% of 24 hr old biofilm (24 hr treatment)	(Jia, Xue, Duan, & Shao, 2011)
			MIC	Inhibit 60% to 80% of 24 hr old biofilm (24 hr treatment)	
			2.5 MIC	Inhibit 70% to 90% of 24 hr old biofilm (24 hr treatment)	
			5 MIC	Inhibit 95% to 100% of 24 hr old biofilm (24 hr treatment)	
	P. aeruginosa	11.8 mM	11.8 mM	Inhibit 77.9% of 6 hr old biofilm (3 hr treatment)	(Topa et al., 2018)
Cinnamomum aromaticum	*P. aeruginosa* PAO1 and *P. putida* KT2440	0.2 % (v/v)	0.2% (v/v)	Kill the vast majority of cells within the 24 hr old biofilm (2 hr treatment)	(Kavanaugh & Ribbeck, 2012)
Coriandrum sativum	Two reference strains and three clinical isolates of *A. baumannii*	1 to 4 μL/mL	0.125 MIC to 4 MIC	Inhibit 7.98% to 24.16% of 24 hr old biofilm, 8.42% to 67.98% of 48 hr old biofilm (24 hr treatment)	(Duarte, Ferreira, Oliveira, & Domingues, 2013)

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
				Inhibit 30.62% to 78.82% of 24 hr old biofilm, 25.98% to 96.33% of 48 hr old biofilm (24 hr treatment)	
				Inhibit 46.34% to 94.12% of 24 hr old biofilm, 58.77% to 97.14% of 48 hr old biofilm (24 hr treatment)	
				Inhibit 75.41% to 94.22% of 24 hr old biofilm, 66.73% to 96.32% of 48h old biofilm (24 hr treatment)	
Eugenol	12 *Sa. typhimurium* strains	128 to 512 μg/mL	15.3 to 1,402 μg/mL	Inhibit 50% of 24 old biofilm (24 hr treatment)	(Miladi et al., 2017)
	43 strains of MRSA and 29 strains of MSSA	0.01% to 0.04%	2 MIC	Inhibit >50% of 24 hr old biofilm (6 hr treatment)	(Yadav et al., 2015)
Lavender	*P. aeruginosa* PAO1 and *P. putida* KT2440	>5% (v/v)		MBEC > 5% (v/v) (24 hr old biofilm, 2 hr treatment)	(Kavanaugh & Ribbeck, 2012)
Linalool	Five *A. baumannii* strains	2 to 8 μL/mL	4 MIC	Inhibit 55% to 86% of 24 hr old biofilm (24 hr treatment)	(Alves et al., 2016)
Macelignan, from *Myristica fragrans* Houtt.	*Sc. sanguis*		10 μg/mL	Inhibit 80% of 12 hr old biofilm (30 min treatment), 38% of 24 hr old biofilm (5 min treatment), 50% of 24 hr old biofilm (30 min treatment)	(Yan, Rukayadi, Kim, & Hwang, 2008)

(Continues)

TABLE 4 (Continued)

Spice essential oils Inhibition of biofilm formation	Bacteria	MIC	Concentrations used	Antibiofilm effects	References
Mentha pulegieum L.	Multidrug-resistant *A. baumannii*	0.6 to 2.5 μL/ mL		MBEC > 10 μL/ mL	(Tutar, Celik, Karaman, Atas, & Hepokur, 2016)
Mentha spicata L.	*V. cholerae* ATCC 9459 and *V. alginolyticus* ATCC 33787	0.023 mg/mL	0.092 mg/mL	Inhibit >50% of 24 old biofilm (3 hr treatment)	(Snoussi et al., 2015)
Origanum vulgare	*S. aureus* LPMA11 and *S. aureus* LPMA63		10 μL/mL	Inhibit ≥2 log CFU/cm ^{2} of sessile cells counts in 24 and 72 hr old biofilm (10 min treatment)	(Rodrigues et al., 2018)
Origanum vulgare and *Salvia officinalis*	*Sc. pyogenes* ATCC 19615 and ATCC 49399	0.5 mg/mL	0.5 mg/mL	Inhibit 24 hr old biofilm completely	(Wijesundara & Rupasinghe, 2018)
Syzygium aromaticum	*P. aeruginosa* PAO1 and *P. putida* KT2440	0.5% to 1.3% (v/v)		MBEC = 1.1% to 5% (v/v) (24 hr old biofilm, 2 hr treatment)	(Kavanaugh & Ribbeck, 2012)
Syzygium aromaticum and *Mentha spicata*	*L. monocytogenes*		1 mg/mL	Reduce the biomass of 6 hr old biofilm to 0.09 (18 hr treatment)	(Leonard et al., 2010)
Thymol	Twelve *Sa. typhimurium* strains	16 to 128 μg/mL	10.5 to 697.6 μg/mL	Inhibit 50% of 24 hr old biofilm (24 hr treatment)	(Miladi et al., 2017)
Thymus vulgaris	Four strains of *Sa. enteritidis*	0.156 μL/mL	0.5 MIC	Inhibit 18.5 to 27.8% of 48 hr old biofilm (30 min treatment), 22.5%% to 38.4% of 48 hr old biofilm (60 min treatment)	(Cabarkapa et al., 2015)
			MIC	Inhibit 35.5% to 51.8% of 48 hr old biofilm (30 min treatment), 41.7%% to 54% of 48 hr old biofilm (60 min treatment)	

Abbreviations: *A.*, *Acinetobacter*; *E.*, *Escherichia*; EHEC, Enterohemorrhagic *E. coli; En.*, *Enterococcus*; *Er.*, *Erwinia*; *K.*, *Klebsiella*; *L.*, *Listeria*; MIC, minimum inhibitory concentration; MBIC, biofilm inhibitory concentration; MBEC, minimum biofilm eradication concentration; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus; P.*, *Pseudomonas*; *Pr.*, *Proteus*; *S.*, *Staphylococcus*; *Sa.*, *Salmonella*; *Sc.*, *Streptococcus*; *Se.*, *Serratia*; UPEC, Uropathogenic *E. coli; V.*, *Vibrio.*

components, and the minor compounds, such as terpenoids, aldehydes, and ketones, may have a synergistic effect with major bioactive compounds of essential oils (Oral et al., 2010). Moreover, increasing concentrations of essential oils, extending incubation time, as well as modifying experimental conditions, like increasing temperature and changing pH, can also help to optimize the ultimate biofilm-eradicating effects (Rodrigues et al., 2018; Vidács et al., 2018).

Spice essential oils contain various volatile compounds, which can easily diffuse through the polar polysaccharide matrix of the biofilm. Although the influence of chemical structures of spice oil components on their bactericidal effects is not fully understood, studies have proved that hydroxyl (-OH), methoxy (-OCH_3), and olefinic bonds play quite important roles, since compounds such as carvacrol, thymol, cinnamaldehyde, and eugenol possessing these structural characteristics show prominent bactericidal activities (Castillo-Lopez, Gutierrez-Grijalva, Leyva-Lopez, Lopez-Martinez, & Heredia, 2017). Besides, the general hydrophobicity feature of essential oil compounds promotes their specific interaction with the lipid bilayers of cell cytoplasmic membranes. With the accumulation of compounds, the membranes disintegrate and increase their permeability, causing the leakage of intracellular components and ultimately leading to homeostatic imbalance and cell death (Saviuc et al., 2015). The extent of membrane damage is linked to intrinsic hydrophobicity of individual compounds in essential oils, which can be reflected by the log *p*-value. A compound with log *p*-value greater than 3 is defined to have a high membrane affinity, such as carvacrol and thymol, with log *p*-values of 3.62 and 3.30, respectively (Nostro et al., 2007). Additionally, these bioactive compounds can also act as direct bactericidal agents by disturbing membrane-related proteins, interfering with DNA synthesis, inhibiting ATPase activities, and blocking the electron transfer chains (Budri et al., 2015; Chueca, Pagan, & Garcia-Gonzalo, 2014). It is generally believed that lipophilic essential oil compounds show a stronger ability to eradicate preformed biofilm of Gram-positive bacteria. However, the hydrophilic lipopolysaccharide structure on the membrane of Gram-negative bacteria may hinder the penetration of these compounds.

Treatment of sub-MIC spice essential oils and their compounds can also induce the biofilm dispersal by modulating a secondary messenger molecule, bis-(3′–5′)-cyclic dimeric guanosine monophosphate (c-di-GMP). c-di-GMP can transform from the planktonic to the sessile state to establish biofilm formation and promote the production of other virulence factors (Krasteva, Giglio, & Sondermann, 2012). Treatment with carvacrol at 1.5 mM (0.125 MIC) reduces 47.3% of preformed biofilm and 66.2% of c-di-GMP expression in *P. aeruginosa* PAO1, without evident killing of biofilm matrix-embedded cells (Topa et al., 2018).

5 | BACTERIAL MOTILITY

Flagellae, the main motor organ system of bacteria, and their motility, the simplest biological behavior, are prerequisites for adhesion and invasion, playing important roles in the early stage of infection (Salehi et al., 2017). With the help of flagella, bacteria can enter an advantageous environment and travel toward the surface of epithelial cells through the viscous mucus barrier (Rivera-Chavez et al., 2013). Flagellae and their motility also play important roles in biofilm formation and are closely related to the secretion of other bacterial virulence factors (Duan et al., 2012). Flagella-regulated motility is critical for the pathogenesis of several bacteria, including *Proteus mirabilis*, *P. aeruginosa*, *Sa. enteritidis*, *Helicobacter pylori*, *L. monocytogenes*, and enteropathogenic *E. coli* (Kao et al., 2014).

Bacterial motility can be divided into flagella-mediated and nonflagella-mediated motility. Flagella-mediated movement includes swimming and swarming. Swimming refers to the linear or tossing movement of bacteria in a liquid or viscous environment by the impetus of polar or circumferential flagella (Deditius et al., 2015). Swarming migration refers to a complex process, in which short and vegetative cells differentiate into swarm cells assembled with flagella, facilitating the spread from the inoculation point to the periphery on a semisolid medium (Kearns, 2010). The twitching motion is a form of flagella-independent bacterial translocation and is powered by the extension and contraction of type IV pili located at one or both terminals of the cell (Burrows, 2012; Murray & Kazmierczak, 2008). The movement of bacteria toward the target surface is usually mediated by swimming motility, and subsequent colony adhesion and diffusion are mainly mediated by swarming and twitching.

5.1 | Inhibition of bacterial motility by spice essential oils

The effective strategies of inhibiting bacterial motility and subsequent serious infections include the use of spice essential oils and corresponding effective compounds, and the related studies are summarized in Table 5. The inhibitory effects of spice essential oils on motility vary due to the differences among the diverse compounds in spice essential oils and their targeted pathogens. Some spice essential oils can affect one or two forms of motility, and others can obstruct all three kinds of motility, leading to the inhibition of adhesion and subsequent invasion of pathogens in the host.

5.2 | Mechanisms of inhibiting bacterial motility by spice essential oils

The mechanisms by which essential oils inhibit bacterial motility, especially flagella-mediated motility, can be

TABLE 5 Inhibitory effects of spice essential oils and their major compounds on bacterial motility

Spice essential oils	Bacteria	MIC	Tested concentration	Motility inhibitory effects	References
Carvacrol	*Ca. jejuni* strains 108 (129108, 108WT)		0.2 mM	No motility observed under time-lapse microscopy Inhibit 45.6% of invasion to INT-407 cells	(van Alphen et al., 2012)
	Ca. jejuni strains 8116		0.25 mM	No motility observed under time-lapse microscopy	
	Sa. typhimurium DT104	2 mM	1 mM	Inhibit motility and the invasion to porcine intestinal epithelial cells significantly	(Inamuco et al., 2012)
	Ca. jejuni S-8		0.001% to 0.002% (no growth inhibition)	Reduce zone of motility from 5 to <4 cm	(Upadhyay et al., 2017)
	L. monocytogenes	0.75 mM	0.5 and 0.65 mM	Reduce zone of motility from 6 to <2.5 cm Inhibit 20% to 30% of attachment and invasion to human colon adenocarcinoma (Caco-2) and human brain microvascular endothelial cells (HBMECs)	(Upadhyay et al., 2012)
Cinnamaldehyde	*L. monocytogenes*	0.9 mM	0.5 and 0.75 mM		
	Ca. jejuni S-8		0.05% to 0.01% (no growth inhibition)	Inhibit >70% of motility Reduce zone of motility from 5 to <1 cm	(Upadhyay et al., 2017)
	Four strains of *Sa. enterica*		0.01% (no cell reduction)	Inhibit 3.7% to 7.15% of motility, 28.8% to 43.5% of invasion to avian intestinal epithelial cells	(Kollanoor-Johny et al., 2012)
Thymol	*L. monocytogenes*	0.6 mM	0.33 and 0.5 mM	Reduce zone of motility from 6 to <2.5 cm Inhibit 20% to 30% of attachment and invasion to human colon adenocarcinoma (Caco-2) and human brain microvascular endothelial cells (HBMECs)	(Upadhyay et al., 2012)
Eugenol	Four strains of *Sa. enterica* *Ca. jejuni* S-8		0.04% (no cell reduction) 0.005% to 0.01% (no growth inhibition)	Inhibit 3.8% to 5.3% of motility, 14.3% to 27.8% of invasion to avian intestinal epithelial cells Reduce zone of motility from 5 to <3 cm Inhibit the attachment from 4.2 to 1-1.5 log CFU/mL	(Kollanoor-Johny et al., 2012)

(Continues)

TABLE 5 (Continued)

Spice essential oils	Bacteria	MIC	Tested concentration	Motility inhibitory effects	References
					(Upadhyay et al., 2017)
Cinnamic acid	*P. fluorescens*		0.1 mg/mL	Inhibit 69.2% of swarming motility	(Naik, Wahidullah, & Meena, 2013)
Citral	*Er. carotovora*	2.5 mg/mL	0.1 mg/mL	Inhibit 52.4% of swarming motility, 56.5% of swimming motility	(Zhang et al., 2018)
	P. fluorescens	5 mg/mL	0.1 mg/mL	Inhibit 92.3% of swarming motility, 80.8% of swimming motility	
	Cr. sakazakii ATCC 29544		0.02 mg/mL	Inhibit 41.7% of swarming motility, 8.3% of swimming motility	(Shi et al., 2017)
Cinnamomum zeylanicum	*R. solanacearum*		1 ppm (approximately 1 μg/mL)	Inhibit swimming and twitching motility completely Reduce the diameter of swarming zone from 78 to 20 mm	(Hosseinzadeh, Shams-Bakhsh, & Hosseinzadeh, 2013)
Thymus vulgaris				Inhibit swimming and twitching zone completely Reduce the diameter of swarming zone from 78 to 4 mm	
Lavandula Angustifolia				Reduce the diameter of swimming zone from 64 to 28 mm Reduce the diameter of swarming zone from 78 to 11 mm Reduce the diameter of twitching zone from 12 to 8 mm	
Clove	*P. aeruginosa* PAO1		0.01% to 1% (no growth inhibition)	Inhibit 59.5% of swarming motility, 24% of twitching motility	(Jayalekshmi et al., 2016)

(Continues)

TABLE 5 (Continued)

Spice essential oils	Bacteria	MIC	Tested concentration	Motility inhibitory effects	References
Curcumin	*Sa. enterica*		20 μM (no growth inhibition)	Reduce 65% to 80% of the diameter of swim and swarm colony	(Marathe et al., 2016)
	E. coli	192 μg/mL	100 μg/mL	Reduce the diameter of swimming zone from 45.8 to 4.3 mm Reduce the diameter of swarming zone from 24 to 5.9 mm	(Packiavathy et al., 2014)
	P. aeruginosa PAO1			Reduce the diameter of swimming zone from 46.1 to 6.6 mm Reduce the diameter of swarming zone from 22.3 to 4.4 mm	
	Pr. mirabilis			Reduce the diameter of swimming zone from 43.4 to 20.8 mm Reduce the diameter of swarming zone from 43.7 to 7.8 mm	
Pelargonium graveolens	*Pr. mirabilis*		8.96 mg/mL (sub-MIC)	Inhibit 50% of swarming ability	(Malik et al., 2015)
Piperine	*Pylori*	125 μM	100 μM	Inhibit 40% of attachment	(Tharmalingam et al., 2014)
Rosemarinus officinalis L.	*P. aeruginosa*	5 to 25 μL/mL (MIC90)	Sub-MICs	Alter twitching, swarming, and swimming ability	(Araby & El-Tablawy, 2016)
Syzygium aromaticum	*Ca. jejuni*	200 μg/mL	50 μg/mL	Inhibit swarming ability	(Kovacs et al., 2016)
	P. aeruginosa ATCC 15692		1% (v/v)	Inhibit 59.5% of swimming motility, 35% of swarming motility, 24% of twitching motility	(Jayalekshmi et al., 2016)
Salicylic acid	*Er. carotovora*		0.1 mg/mL	Inhibit 52.5% of swarming motility, 55.7% of swimming motility	(Lemos et al., 2014)
	B. cereus			Inhibit 16.8% of swarming motility, 72.8% of swimming motility	
	P. fluorescens			Inhibit 82.4% of swarming motility	

Abbreviations: *B.*, *Bacillus*; *Ca.*, *Campylobacter*; *Cr.*, *Cronobacter*; *E.*, *Escherichia*; *Er.*, *Erwinia*; *H.*, *Helicobacter*; *L.*, *Listeria*; *P.*, *Pseudomonas*; *Pr.*, *Proteus*; *R.*, *Ralstonia*; *Sa.*, *Salmonella*.

generally divided into three types, including destroying the basic function of flagella without affecting their synthesis, inhibiting the formation of flagella, and degrading the formed flagella.

Retaining the flagella-mediated motility but interfering with their normal function is considered the first way to inhibit the pathogenicity of bacteria. For instance, *Ca. jejuni* loses its motility in the presence of 0.2 mM of carvacrol, associated with the blocking of flagellar function rather than inhibition of flagellar formation (van Alphen, Burt, Veenendaal, Bleumink-Pluym, & van Putten, 2012). Similarly, 1 mM of carvacrol does not inhibit the bacterial growth of *Sa. typhimurium*, but completely inhibits the bacterial motility, without significant changes in flagellin density (Inamuco et al., 2012). However, research to date is limited to the observed phenomena, and the interpretation at the molecular level, such as through genes and proteins, is not well understood and needs further study.

The synthesis of flagellin requires a large quantity of energy (Tremblay, Aklujkar, Leang, Nevin, & Lovley, 2012). Once bacteria are under adverse conditions such as exposure to essential oils, it is a feasible survival strategy to inhibit flagella production and to store energy for other physiological functions of cells (Burt et al., 2007). The introduction of 1 mM of carvacrol inhibits the synthesis of flagella in *E. coli* at the early stage of its growth (Burt et al., 2007). The inhibition of flagella synthesis is primarily caused by inhibiting related genes. Clove essential oil and piperine, the main compound of black pepper essential oil, are able to downregulate the expression of flagellar synthesis genes *flhB* in *Ca. jejuni*, and both *flhA* and flagellar hook gene *flgE* in *H. pylori* at sub-MICs (Kovacs et al., 2016; Tharmalingam et al., 2014). Besides, the sub-MIC (0.01%) of *trans*-cinnamaldehyde and eugenol also reduce the motility and infection of *Sa. enteritidis*, and the expression of *motA*, a gene that regulates flagellar assembly, and *flhC*, a gene that regulates flagellin production, are significantly downregulated (Kollanoor-Johny et al., 2012).

Spice essential oils can also induce the degradation of existing flagella. Marathe et al. (2016) report that 0.2 μM of curcumin decreases the number of flagellated bacteria from 84% to 59%, without significant change in the expression of flagellin synthesis-related genes, such as *flhD*, *fliC*, and *fljB*. Fluorescence binding and computational analysis predict that curcumin can bind to the conserved amino acid residues in the core area and the outer surface of flagellar filaments, increasing the torsional stress and making the flagellin fragile enough to be easily broken into small fragments (Marathe et al., 2016). In addition, the binding site of curcumin on *Sa. typhimurium* flagellin is somewhat conserved among other bacteria, it is predicted that curcumin can inhibit the bacterial motility in other pathogenic bacteria.

It must be mentioned that while flagellar degradation can destroy bacterial motility and reduce corresponding adhesive and infective abilities, the disappearance of flagella may also cause undesirable changes. Flagellin contains a pathogen-associated molecular pattern that initiates a signal transduction cascade. It activates mitogen-activated protein kinase and nuclear factors-κB signaling pathway by binding to a toll-like receptor 5 on epithelial cells, allowing the host to obtain an adaptive immune response (Yoon et al., 2012). This property is very important for the host to recognize pathogens. If the flagella of bacteria degrade in the exposure of essential oils, this might cause problems for the host immune system to recognize and remove pathogenic bacteria. Therefore, this issue should be considered in planning for the use of essential oils.

6 | CONCLUSIONS AND PERSPECTIVES

Virulence properties, including toxins, QS system, biofilm, and motility, are all important in the pathogenesis of bacteria in various infections. Spice essential oils can be appealing and promising to control pathogens by targeting their virulence factors rather than killing bacteria, leading to reduced selection pressure and chances of developing drug resistance. Current research mainly focuses on some effective spice essential oils and compounds that have been discovered, such as thymol, carvacrol, and cinnamaldehyde. Further studies should be undertaken to discover new antivirulence essential oil compounds, which can be potential antibiotic alternatives with promising applications. In addition, although many spice essential oils have been revealed to exhibit inhibitory effects on multiple virulence factors, the in-depth validation and interpretation of the molecular mechanisms for the effectiveness of the compounds are still limited and need more investigation. Besides, nanotechnology can be used to improve the properties of essential oils, such as their solubility, stability, odor, and efficacy. For instance, a delivery system can be used to transfer and release the active compounds at the site of action directly, thus reducing their loss. EPS degrading enzymes such as DNase I and dispersin B for biofilm eradication can be combined with essential oil nanoparticles, improving the antibiofilm activity of essential oils. Therefore, better antivirulence effects of such compounds can be expected, based on advanced nanotechnology. Moreover, the biological activity and toxicity studies of spice essential oils are limited under *in vivo* conditions and clinical tests; thus, further studies should be conducted in appropriate animal models and human to assess the efficacy, therapeutic value, and safety of spice essential oils.

ACKNOWLEDGMENTS

This work was supported by the National Key R&D Program of China (No. 2017YFC1600100), the Shanghai Basic and Key Program (No. 18JC1410800), the Shanghai Pujiang

Talent Plan (No. 18PJ1404600), the Agri-X Interdisciplinary Fund of Shanghai Jiao Tong University (No. Agri-X2017004), and the Shanghai Agricultural Science and Technology Key Program (NO. 18391900600). We thank Ms. Qiong-Qiong Yang, Ying-Ying Ge, and Gowoon Kim for proofreading the manuscript.

AUTHOR CONTRIBUTIONS

Dan Zhang, Ren-You Gan, and Harold Corke conceived this paper; Dan Zhang and Ren-You Gan wrote the draft; and Ren-You Gan, Jia-Rong Zhang, Arakkaveettil Kabeer Farha, Hua-Bin Li, Fan Zhu, Xiao-Hong Wang, and Harold Corke edited and revised this paper. The final version was approved by all authors.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Ren-You Gan https://orcid.org/0000-0002-4162-1511
Hua-Bin Li https://orcid.org/0000-0003-2332-8554
Fan Zhu https://orcid.org/0000-0003-3344-7741

REFERENCES

Abdel-Hameed, E.-S. S., Salman, M. S., Fadl, M. A., Elkhateeb, A., & Hassan, M. M. (2018). Chemical composition and biological activity of *Mentha longifolia* L. essential oil growing in Taif, KSA extracted by hydrodistillation, solvent free microwave and microwave hydrodistillation. *Journal of Essential Oil Bearing Plants*, *21*(1), 1–14. Retrieved from https://10.1080/0972060X.2018.1454343

Abdullah, Asghar, A., Butt, M. S., Shahid, M., & Huang, Q. (2017). Evaluating the antimicrobial potential of green cardamom essential oil focusing on quorum sensing inhibition of *Chromobacterium violaceum*. *Journal of Food Science and Technology-Mysore*, *54*(8), 2306–2315. Retrieved from https://10.1007/s13197-017-2668-7

Adukwu, E. C., Allen, S. C., & Phillips, C. A. (2012). The anti-biofilm activity of lemongrass (*Cymbopogon flexuosus*) and grapefruit (*Citrus paradisi*) essential oils against five strains of *Staphylococcus aureus*. *Journal of Applied Microbiology*, *113*(5), 1217–1227. Retrieved from https://10.1111/j.1365-2672.2012.05418.x

Ahmad, A., Viljoen, A. M., & Chenia, H. Y. (2015). The impact of plant volatiles on bacterial quorum sensing. *Letters in Applied Microbiology*, *60*(1), 8–19. Retrieved from https://10.1111/lam.12343

Ahmed, S., Rudden, M., Smyth, T. J., Dooley, J. S. G., Marchant, R., & Banat, I. M. (2019). Natural quorum sensing inhibitors effectively downregulate gene expression of *Pseudomonas aeruginosa* virulence factors. *Applied Microbiology and Biotechnology*, *103*(8), 3521–3535. Retrieved from https://10.1007/s00253-019-09618-0

Al-Fatimi, M. (2018). Volatile constituents, antimicrobial and antioxidant activities of the aerial parts of *Origanum majorana* L. from Yemen. *Journal of Pharmaceutical Research International*, *23*(4), 10. Retrieved from https://10.9734/JPRI/2018/35932

Allen, H. K., Levine, U. Y., Looft, T., Bandrick, M., & Casey, T. A. (2013). Treatment, promotion, commotion: Antibiotic alternatives in food-producing animals. *Trends in Microbiology*, *21*(3), 114–119. Retrieved from https://10.1016/j.tim.2012.11.001

Al-Shabib, N. A., Husain, F. M., Ahmad, I., & Baig, M. H. (2017). Eugenol inhibits quorum sensing and biofilm of toxigenic MRSA strains isolated from food handlers employed in Saudi Arabia. *Biotechnology & Biotechnological Equipment*, *31*(2), 387–396. Retrieved from https://10.1080/13102818.2017.1281761

Alvarez, M. V., Ortega-Ramirez, L. A., Gutierrez-Pacheco, M. M., Bernal-Mercado, A. T., Rodriguez-Garcia, I., Gonzalez-Aguilar, G. A., … Ayala-Zavala, J. F. (2014). Oregano essential oil-pectin edible films as anti-quorum sensing and food antimicrobial agents. *Frontiers in Microbiology*, *5*, 699. Retrieved from https://10.3389/fmicb.2014.00699

Alves, S., Duarte, A., Sousa, S., & Domingues, F. C. (2016). Study of the major essential oil compounds of *Coriandrum sativum* against *Acinetobacter baumannii* and the effect of linalool on adhesion, biofilms and quorum sensing. *Biofouling*, *32*(2), 155–165. Retrieved from https://10.1080/08927014.2015.1133810

Araby, E., & El-Tablawy, S. Y. (2016). Inhibitory effects of rosemary (*Rosemarinus officinalis* L.) essential oil on pathogenicity of irradiated and non-irradiated *Pseudomonas aeruginosa*. *Journal of Photochemistry and Photobiology B-Biology*, *159*, 24–32. Retrieved from https://10.1016/j.jphotobiol.2016.02.024

Arzanlou, M., & Bohlooli, S. (2010). Inhibition of streptolysin O by allicin - An active component of garlic. *Journal of Medical Microbiology*, *59*(9), 1044–1049. Retrieved from https://10.1099/jmm.0.019539-0

Arzanlou, M., Bohlooli, S., Jannati, E., & Mirzanejad-Asl, H. (2011). Allicin from garlic neutralizes the hemolytic activity of intra- and extra-cellular pneumolysin O *in vitro*. *Toxicon*, *57*(4), 540–545. Retrieved from https://10.1016/j.toxicon.2010.12.009

Azmi, K., Qrei, W., & Abdeen, Z. (2019). Screening of genes encoding adhesion factors and biofilm production in methicillin resistant strains of *Staphylococcus aureus* isolated from Palestinian patients. *BMC Genomics*, *20*(1), 578. Retrieved from https://10.1186/s12864-019-5929-1

Bagci, Y., Kan, Y., Dogu, S., & Celik, S. A. (2017). The essential oil compositions of *Origanum majorana* L. cultivated in Konya and collected from Mersin-Turkey. *Indian Journal of Pharmaceutical Education and Research*, *51*(3), S463–S69. Retrieved from https://10.5530/ijper.51.3s.68

Bai, A. J., & Vittal, R. R. (2014). Quorum sensing inhibitory and anti-biofilm activity of essential oils and their *in vivo* efficacy in food systems. *Food Biotechnology*, *28*(3), 269–292. Retrieved from https://10.1080/08905436.2014.932287

Banerjee, G., & Ray, A. K. (2017). Quorum-sensing network-associated gene regulation in Gram-positive bacteria. *Acta Microbiologica et Immunological Hungarica*, *64*(4), 439–453. Retrieved from https://10.1556/030.64.2017.040

Brackma, G., Defoirdt, T., Miyamoto, C., Bossier, P., Calenbergh, S. V., Nelis, H., & Coenye, T. (2008). Cinnamaldehyde and cinnamaldehyde derivatives reduce virulence in *Vibrio* spp. by decreasing the DNA-binding activity of the quorum sensing response regulator LuxR. *BMC Microbiology*, *8*(1), 149. Retrieved from https://10.1186/1471-2180-8-149

Brackman, G., Celen, S., Hillaert, U., Van Calenbergh, S., Cos, P., Maes, L., … Coenye, T. (2011). Structure-activity relationship of cinnamaldehyde analogs as inhibitors of AI-2 based quorum sensing and their effect on virulence of *Vibrio* spp. *PLoS One*, *6*(1), e16084. Retrieved from https://10.1371/journal.pone.0016084

Budri, P. E., Silva, N. C. C., Bonsaglia, E. C. R., Fernandes, A., Araujo, J. P., Doyama, J. T., … Rall, V. L. M. (2015). Effect of essential oils of *Syzygium aromaticum* and *Cinnamomum zeylanicum* and their major components on biofilm production in *Staphylococcus aureus* strains isolated from milk of cows with mastitis. *Journal of Dairy Science*, *98*(9), 5899–5904. Retrieved from https://10.3168/jds.2015-9442

Burrows, L. L. (2012). *Pseudomonas aeruginosa* twitching motility: Type IV pili in action. *Annual Reviews of Microbiology*, *66*, 493–520. Retrieved from https://10.1146/annurev-micro-092611-150055

Burt, S. A., Ojo-Fakunle, V. T., Woertman, J., & Veldhuizen, E. J. (2014). The natural antimicrobial carvacrol inhibits quorum sensing in *Chromobacterium violaceum* and reduces bacterial biofilm formation at sub-lethal concentrations. *PLoS One*, *9*(4), e93414. Retrieved from https://10.1371/journal.pone.0093414

Burt, S. A., van der Zee, R., Koets, A. P., de Graaff, A. M., van Knapen, F., Gaastra, W., … Veldhuizen, E. J. (2007). Carvacrol induces heat shock protein 60 and inhibits synthesis of flagellin in *Escherichia coli* O157:H7. *Applied and Environmental Microbiology*, *73*(14), 4484–4490. Retrieved from https://10.1128/AEM.00340-07

Cabarkapa, I., Colovic, R., Duragic, O., Popovic, S., Kokic, B., Milanov, D., & Pezo, L. (2019). Anti-biofilm activities of essential oils rich in carvacrol and thymol against *Salmonella enteritidis*. *Biofouling*, *35*, 361–375. Retrieved from https://10.1080/08927014.2019.1610169

Cabarkapa, I., Skrinjar, M., Levic, J., Blagojev, N., Kokic, B., & Suvajdzic, L. (2015). Effect of *Thymus vulgaris* on initial cell attachment and preformed biofilm of *Salmonella enteritidis*. *Journal of Pure Applied Microbiology*, *9*, 123–129.

Campana, R., & Baffone, W. (2018). Carvacrol efficacy in reducing microbial biofilms on stainless steel and in limiting regrowth of injured cells. *Food Control*, *90*, 10–17. Retrieved from https://10.1016/j.foodcont.2018.02.029

Castillo-Lopez, R. I., Gutierrez-Grijalva, E. P., Leyva-Lopez, N., Lopez-Martinez, L. X., & Heredia, J. B. (2017). Natural alternatives to growth-promoting antibiotics (Gpa) in animal production. *Journal of Animal and Plant Sciences*, *27*(2), 349–359.

Ceylan, O., & Ugur, A. (2015). Chemical composition and antibiofilm activity of *Thymus sipyleus* BOISS. subsp *sipyleus* BOISS. var. *davisianus* RONNIGER essential oil. *Archives of Pharmacal Research*, *38*(6), 957–965. Retrieved from https://10.1007/s12272-014-0516-0

Chang, C. Y., Krishnan, T., Wang, H., Chen, Y., Yin, W. F., Chong, Y. M., … Chan, K. G. (2014). No-antibiotic quorum sensing inhibitors acting against N-acyl homoserine lactone synthase as druggable target. *Scientific Reports*, *4*, 7245. Retrieved from https://10.1038/srep07245

Chatterjee, S., Zahid, M. S., Awasthi, S. P., Chowdhury, N., Asakura, M., Hinenoya, A., … Yamasaki, S. (2016). *In vitro* inhibition of cholera toxin production in *V. cholerae* by methanol extract of sweet fennel seeds and its components. *Japanese Journal of Infectious Diseases*, *69*(5), 384–389. Retrieved from https://10.7883/yoken.JJID.2015.421

Chiarot, E., Faralla, C., Chiappini, N., Tuscano, G., Falugi, F., Gambellini, G., … Bensi, G. (2013). Targeted amino acid substitutions impair streptolysin O toxicity and group a streptococcus virulence. *mBio*, *4*(1), e00387–12. Retrieved from https://10.1128/mBio.00387-12

Chueca, B., Pagan, R., & Garcia-Gonzalo, D. (2014). Differential mechanism of *Escherichia coli* inactivation by (+)-limonene as a function of cell physiological state and drug's concentration. *PLoS One*, *9*(4), e94072. Retrieved from https://10.1371/journal.pone.0094072

Cui, H., Li, W., Li, C., Vittayapadung, S., & Lin, L. (2016). Liposome containing cinnamon oil with antibacterial activity against methicillin-resistant *Staphylococcus aureus* biofilm. *Biofouling*, *32*(2), 215–225. Retrieved from https://10.1080/08927014.2015.1134516

Daly, S. M., Elmore, B. O., Kavanaugh, J. S., Triplett, K. D., Figueroa, M., Raja, H. A., … Hall, P. R. (2015). *ω*-Hydroxyemodin limits *Staphylococcus aureus* quorum sensing-mediated pathogenesis and inflammation. *Antimicrobial Agents and Chemotherapy*, *59*(4), 2223–2235. Retrieved from https://10.1128/AAC.04564-14

Deditius, J. A., Felgner, S., Sporing, I., Kuhne, C., Frahm, M., Rohde, M., … Erhardt, M. (2015). Characterization of novel factors involved in swimming and swarming motility in *Salmonella enterica* serovar Typhimurium. *PLoS One*, *10*(8), e0135351. Retrieved from https://10.1371/journal.pone.0135351

De Falco, E., Roscigno, G., Landolfi, S., Scandolera, E., & Senatore, F. (2014). Growth, essential oil characterization, and antimicrobial activity of three wild biotypes of oregano under cultivation condition in Southern Italy. *Industrial Crops and Products*, *62*, 242–249. Retrieved from https://10.1016/j.indcrop.2014.08.037

Defoirdt, T. (2018). Quorum-sensing systems as targets for antivirulence therapy. *Trends in Microbiology*, *26*(4), 313–328. Retrieved from https://10.1016/j.tim.2017.10.005

de Oliveira, M. M. M., Brugnera, D. F., Cardos, M. D., Alves, E., & Piccoli, R. H. (2010). Disinfectant action of *Cymbopogon* sp. essential oils in different phases of biofilm formation by *Listeria monocytogenes* on stainless steel surface. *Food Control*, *21*(4), 549–553. Retrieved from https://10.1016/j.foodcont.2009.08.003

de Souza, E. L., de Barros, J. C., de Oliveira, C. E., & da Conceicao, M. L. (2010). Influence of *Origanum vulgare* L. essential oil on enterotoxin production, membrane permeability and surface characteristics of *Staphylococcus aureus*. *International Journal of Food Microbiology*, *137*(2–3), 308–311. Retrieved from https://10.1016/j.ijfoodmicro.2009.11.025

Dhanawade, N. B., Kalorey, D. R., Srinivasan, R., Barbuddhe, S. B., & Kurkure, N. V. (2010). Detection of intercellular adhesion genes and biofilm production in *Staphylococcus aureus* isolated from bovine subclinical mastitis. *Veterinary Research Communications*, *34*(1), 81–89. Retrieved from https://10.1007/s11259-009-9326-0

Dickey, S. W., Cheung, G. Y. C., & Otto, M. (2017). Different drugs for bad bugs: Antivirulence strategies in the age of antibiotic resistance. *Nature Reviews Drug Discovery*, *16*(7), 457–471. Retrieved from https://10.1038/nrd.2017.23

Djebir, S., Ksouri, S., Trigui, M., Tounsi, S., Boumaaza, A., Hadef, Y., & Benakhla, A. (2019). Chemical composition and acaricidal activity of the essential oils of some plant species of *Lamiaceae* and *Myrtaceae* against the vector of tropical bovine theileriosis: *Hyalomma scupense* (syn. *Hyalomma detritum*). *Biomed Research International*, *2019*, 7805467. Retrieved from https://10.1155/2019/7805467

Duan, Q., Zhou, M., Zhu, X., Bao, W., Wu, S., Ruan, X., … Zhu, G. (2012). The flagella of F18ab *Escherichia coli* is a virulence factor that contributes to infection in a IPEC-J2 cell model *in vitro*. *Veterinary Microbiology*, *160*(1–2), 132–140. Retrieved from https://10.1016/j.vetmic.2012.05.015

Duarte, A. F., Ferreira, S., Oliveira, R., & Domingues, F. C. (2013). Effect of coriander oil (*Coriandrum sativum*) on planktonic and

biofilm cells of *Acinetobacter baumannii*. *Natural Product Communications*, *8*(5), 673–678.

El Euch, S. K., Hassine, D. B., Cazaux, S., Bouzouita, N., & Bouajila, J. (2019). *Salvia officinalis* essential oil: Chemical analysis and evaluation of anti-enzymatic and antioxidant bioactivities. *South African Journal of Botany*, *120*, 253–260. Retrieved from https://10.1016/j.sajb.2018.07.010

Eris, R., & Ulusoy, S. (2013). Rose, clove, chamomile essential oils and pine turpentine inhibit quorum sensing in *Chromobacterium violaceum* and *Pseudomonas aeruginosa*. *Journal of Essential Oil Bearing Plants*, *16*(2), 126–135. Retrieved from https://10.1080/0972060X.2013.794026

Espina, L., Berdejo, D., Alfonso, P., García-Gonzalo, D., & Pagán, R. (2017). Potential use of carvacrol and citral to inactivate biofilm cells and eliminate biofouling. *Food Control*, *82*, 256–265. Retrieved from https://10.1016/j.foodcont.2017.07.007

Espina, L., Pagan, R., Lopez, D., & Garcia-Gonzalo, D. (2015). Individual constituents from essential oils inhibit biofilm mass production by multi-drug resistant *Staphylococcus aureus*. *Molecules*, *20*(6), 11357–11372. Retrieved from https://10.3390/molecules200611357

Etcheverria, A. I., & Padola, N. L. (2013). Shiga toxin-producing *Escherichia coli*: Factors involved in virulence and cattle colonization. *Virulence*, *4*(5), 366–372. Retrieved from https://10.4161/viru.24642

Farouk, A., Ali, H., Al-Khalifa, A. R., Mohsen, M., & Fikry, R. (2018). Aroma volatile compounds of parsley cultivated in the Kingdom of Saudi Arabia and Egypt extracted by hydrodistillation and headspace solid-phase microextraction. *International Journal of Food Properties*, *20*, S2868–S2877. Retrieved from https://10.1080/10942912.2017.1381707

Galloway, W., Hodgkinson, J. T., Bowden, S. D., Welch, M., & Spring, D. R. (2011). Quorum sensing in Gram-negative bacteria: Small-molecule modulation of AHL and Al-2 quorum sensing pathways. *Chemical Reviews*, *111*(1), 28–67. Retrieved from https://10.1021/cr100109t

Gokalsin, B., Aksoydan, B., Erman, B., & Sesal, N. C. (2017). Reducing virulence and biofilm of *Pseudomonas aeruginosa* by potential quorum sensing inhibitor carotenoid: Zeaxanthin. *Microbial Ecology*, *74*(2), 466–473. Retrieved from https://10.1007/s00248-017-0949-3

Gottardi, D., Bukvicki, D., Prasad, S., & Tyagi, A. K. (2016). Beneficial effects of spices in food preservation and safety. *Frontiers in Microbiology*, *7*, 20. Retrieved from https://10.3389/fmicb.2016.01394

Grandclement, C., Tannieres, M., Morera, S., Dessaux, Y., & Faure, D. (2016). Quorum quenching: Role in nature and applied developments. *FEMS Microbiology Reviews*, *40*(1), 86–116. Retrieved from https://10.1093/femsre/fuv038

Grumann, D., Nubel, U., & Broker, B. M. (2014). *Staphylococcus aureus* toxins–Their functions and genetics. *Infection Genetics and Evolution*, *21*, 583–592. Retrieved from https://10.1016/j.meegid.2013.03.013

Guo, Q., Kong, W., Jin, S., Chen, L., Xu, Y., & Duan, K. (2014). PqsR-dependent and PqsR-independent regulation of motility and biofilm formation by PQS in *Pseudomonas aeruginosa* PAO1. *Journal of Basic Microbiology*, *54*(7), 633–643. Retrieved from https://10.1002/jobm.201300091

Gupta, P., Sarkar, S., Das, B., Bhattacharjee, S., & Tribedi, P. (2016). Biofilm, pathogenesis and prevention - A journey to break the wall: A review. *Archives of Microbiology*, *198*(1), 1–15. Retrieved from https://10.1007/s00203-015-1148-6

Gutierrez-Pacheco, M. M., Gonzalez-Aguilar, G. A., Martinez-Tellez, M. A., Lizardi-Mendoza, J., Santana, T. J., Bernal-Mercado, A. T., … Ayala-Zavala, J. F. (2018). Carvacrol inhibits biofilm formation and production of extracellular polymeric substances of *Pectobacterium carotovorum* subsp. carotovorum. *Food Control*, *89*, 210–218. Retrieved from https://10.1016/j.foodcont.2018.02.007

Halicioglu, O., Astarcioglu, G., Yaprak, I., & Aydinlioglu, H. (2011). Toxicity of *Salvia officinalis* in a newborn and a child: An alarming report. *Pediatric Neurology*, *45*(4), 259–260. Retrieved from https://10.1016/j.pediatmeurol.2011.05.012

Harjai, K., Kumar, R., & Singh, S. (2010). Garlic blocks quorum sensing and attenuates the virulence of *Pseudomonas aeruginosa*. *FEMS Immunology and Medical Microbiology*, *58*(2), 161–168. Retrieved from https://10.1111/j.1574-695X.2009.00614.x

Hashemi, S. M. B., Nikmaram, N., Esteghlal, S., Khaneghah, A. M., Niakousari, M., Barba, F. J., … Koubaa, M. (2017). Efficiency of Ohmic assisted hydrodistillation for the extraction of essential oil from oregano (*Origanum vulgare* subsp. *viride*) spices. *Innovative Food Science & Emerging Technologies*, *41*, 172–178. Retrieved from https://10.1016/j.ifset.2017.03.003

Hayat, S., Sabri, A. N., & McHugh, T. D. (2018). Chloroform extract of turmeric inhibits biofilm formation, EPS production and motility in antibiotic resistant bacteria. *Journal of General Applied Microbiology*, *63*(6), 325–338. Retrieved from https://10.2323/jgam.2017.01.004

Hosseini, S. S., Nadjafi, F., Asareh, M. H., & Rezadoost, H. (2018). Morphological and yield related traits, essential oil and oil production of different landraces of black cumin (*Nigella sativa*) in Iran. *Scientia Horticulturae*, *233*, 1–8. Retrieved from https://10.1016/j.scienta.2018.01.038

Hosseinzadeh, S., Shams-Bakhsh, M., & Hosseinzadeh, E. (2013). Effects of sub-bactericidal concentration of plant essential oils on pathogenicity factors of *Ralstonia solanacearum*. *Archives of Phytopathology and Plant Protection*, *46*(6), 643–655. Retrieved from https://10.1080/03235408.2012.749698

Howyzeh, M. S., Noori, S. A. S., & Shariati, J. V. (2018). Essential oil profiling of Ajowan (*Trachyspermum ammi*) industrial medicinal plant. *Industrial Crops and Products*, *119*, 255–259. Retrieved from https://10.1016/j.indcrop.2018.04.022

Husain, F. M., Ahmad, I., Khan, M. S., Ahmad, E., Tahseen, Q., Khan, M. S., & Alshabib, N. A. (2015). Sub-MICs of *Mentha piperita* essential oil and menthol inhibits AHL mediated quorum sensing and biofilm of Gram-negative bacteria. *Frontiers in Microbiology*, *6*, 42. Retrieved from https://10.3389/fmicb.2015.00420

Inamuco, J., Veenendaal, A. K. J., Burt, S. A., Post, J. A., Tjeerdsma-van Bokhoven, J. L. M., Haagsman, H. P., & Veldhuizen, E. J. A. (2012). Sub-lethal levels of carvacrol reduce *Salmonella typhimurium* motility and invasion of porcine epithelial cells. *Veterinary Microbiology*, *157*(1–2), 200–207. Retrieved from https://10.1016/j.vetmic.2011.12.021

Iversen, H., L'Abee-Lund, T. M., Aspholm, M., Arnesen, L. P. S., & Lindback, T. (2015). Commensal *E. coli* Stx2 lysogens produce high levels of phages after spontaneous prophage induction. *Frontiers in Cellular and Infection Microbiology*, *5*. Retrieved from https://10.3389/fcimb.2015.00005

Jadhav, S., Shah, R., Bhave, M., & Palombo, E. A. (2013). Inhibitory activity of yarrow essential oil on *Listeria* planktonic cells and biofilms. *Food Control*, *29*(1), 125–130. Retrieved from https://10.1016/j.foodcont.2012.05.071

Jafri, H., Ansari, F. A., & Ahmad, I. (2019). Prospects of essential oils in controlling pathogenic biofilm. In Khan, M. S. A., Ahmad, I., & Chattopadhyay, D. (Ed.)., *New look to phytomedicine: Advancements in herbal products as novel drug leads* (pp. 203–236). Cambridge, CA, USA: Academic Press.

Jaramillo-Colorado, B., Olivero-Verbel, J., Stashenko, E. E., Wagner-Dobler, I., & Kunze, B. (2012). Anti-quorum sensing activity of essential oils from Colombian plants. *Natural Product Research*, *2*(12), 1075–1086. Retrieved from https://10.1080/14786419.2011.557376

Jayalekshmi, H., Omanakuttan, A., Pandurangan, N., Vargis, V. S., Maneesh, M., Nair, B. G., & Kumar, G. B. (2016). Clove bud oil reduces kynurenine and inhibits *pqs*: A gene expression in *P. aeruginosa*. *Applied Microbiology and Biotechnology*, *100*(8), 3681–3692. Retrieved from https://10.1007/s00253-016-7313-2

Jia, P., Xue, Y. J., Duan, X. J., & Shao, S. H. (2011). Effect of cinnamaldehyde on biofilm formation and *sarA* expression by methicillin-resistant *Staphylococcus aureus*. *Letters in Applied Microbiology*, *53*(4), 409–416. Retrieved from https://10.1111/j.1472-765X.2011.03122.x

Joshi, J. R., Khazanov, N., Senderowitz, H., Burdman, S., Lipsky, A., & Yedidia, I. (2016). Plant phenolic volatiles inhibit quorum sensing in pectobacteria and reduce their virulence by potential binding to ExpI and ExpR proteins. *Scientific Reports*, *6*, 38126. Retrieved from https://10.1038/srep38126

Kang, J. M., Jin, W. Y., Wang, J. F., Sun, Y. Y., Wu, X. X., & Liu, L. (2019). Antibacterial and anti-biofilm activities of peppermint essential oil against *Staphylococcus aureus*. *LWT-Food Science and Technology*, *101*, 639–645. Retrieved from https://10.1016/j.lwt.2018.11.093

Kao, C. Y., Lin, W. H., Tseng, C. C., Wu, A. B., Wang, M. C., & Wu, J. J. (2014). The complex interplay among bacterial motility and virulence factors in different *Escherichia coli* infections. *European Journal of Clinical of Microbiology & Infectious Diseases*, *33*(12), 2157–2162. Retrieved from https://10.1007/s10096-014-2171-2

Kavanaugh, N. L., & Ribbeck, K. (2012). Selected antimicrobial essential oils eradicate *Pseudomonas* spp. and *Staphylococcus aureus* biofilms. *Applied and Environmental Microbiology*, *78*(11), 4057–4061. Retrieved from https://10.1128/AEM.07499-11

Kearns, D. B. (2010). A field guide to bacterial swarming motility. *Nature Reviews Microbiology*, *8*(9), 634–644. Retrieved from https://10.1038/nrmicro2405

Khan, M. S., Zahin, M., Hasan, S., Husain, F. M., & Ahmad, I. (2009). Inhibition of quorum sensing regulated bacterial functions by plant essential oils with special reference to clove oil. *Letters in Applied Microbiology*, *49*(3), 354–360. Retrieved from https://10.1111/j.1472-765X.2009.02666.x

Khatibi, S. A., Misaghi, A., Moosavy, M. H., Basti, A. A., Mohamadian, S., & Khanjari, A. (2018). Effect of nanoliposomes containing *Zataria multiflora* Boiss. essential oil on gene expression of Shiga toxin 2 in *Escherichia coli* O157:H7. *Journal of Applied Microbiology*, *124*(2), 389–397. Retrieved from https://10.1111/jam.13641

Kim, H. S., Lee, S. H., Byun, Y., & Park, H. D. (2015). 6-Gingerol reduces *Pseudomonas aeruginosa* biofilm formation and virulence via quorum sensing inhibition. *Science Reports*, *5*, 8656. Retrieved from https://10.1038/srep08656

Kim, Y. G., Lee, J. H., Kim, S. I., Baek, K. H., & Lee, J. (2015). Cinnamon bark oil and its components inhibit biofilm formation and toxin production. *International Journal of Food Microbiology*, *195*, 30–39. Retrieved from https://10.1016/j.ijfoodmicro.2014.11.028

Kim, Y. G., Lee, J. H., Gwon, G., Kim, S. I., Park, J. G., & Lee, J. (2016). Essential oils and eugenols inhibit biofilm formation and the virulence of *Escherichia coli* O157:H7. *Science Reports*, *6*, 36377. Retrieved from https://10.1038/srep36377

Kitao, T., Lepine, F., Babloudi, S., Walte, F., Steinbacher, S., Maskos, K., … Rahme, L. G. (2018). Molecular insights into function and competitive inhibition of *Pseudomonas aeruginosa* multiple virulence factor regulator. *mBio*, *9*(1), 13. Retrieved from https://10.1128/mBio.02158-17

Koch, W., Kukula-Koch, W., Marzec, Z., Kasperek, E., Wyszogrodzka-Koma, L., Szwerc, W., & Asakawa, Y. (2017). Application of chromatographic and spectroscopic methods towards the quality assessment of ginger (*Zingiber officinale*) rhizomes from ecological plantations. *International Journal of Molecular Sciences*, *18*(2), 452. Retrieved from https://10.3390/ijms18020452

Kollanoor-Johny, A., Mattson, T., Baskaran, S. A., Amalaradjou, M. A., Babapoor, S., March, B., … Venkitanarayanan, K. (2012). Reduction of *Salmonella enterica* serovar Enteritidis colonization in 20-day-old broiler chickens by the plant-derived compounds *trans*-cinnamaldehyde and eugenol. *Applied and Environmental Microbiology*, *78*(8), 2981–2987. Retrieved from https://10.1128/AEM.07643-11

Kovacs, J. K., Felso, P., Makszin, L., Papai, Z., Horvath, G., Abraham, H., … Schneider, G. (2016). Antimicrobial and virulence-modulating effects of clove essential oil on the foodborne pathogen *Campylobacter jejuni*. *Applied and Environmental Microbiology*, *82*(20), 6158–6166. Retrieved from https://10.1128/AEM.01221-16

Kraker, M. E. A., Stewardson, A. J., & Harbarth, S. (2016). Will 10 million people die a year due to antimicrobial resistance by 2050? *PLoS Medicine*, *13*(11), e1002184. Retrieved from https://10.1371/journal.pmed.1002184

Krasteva, P. V., Giglio, K. M., & Sondermann, H. (2012). Sensing the messenger: The diverse ways that bacteria signal through c-di-GMP. *Protein Science*, *21*(7), 929–948. Retrieved from https://10.1002/pro.2093

Kumar, S., Kolodkin-Gal, I., & Engelberg-Kulka, H. (2013). Novel quorum-sensing peptides mediating interspecies bacterial cell death. *mBio*, *4*(3), e00314–13. Retrieved from https://10.1128/mBio.00314-13

Kumar, N. V., Murthy, P. S., Manjunatha, J. R., & Bettadaiah, B. K. (2014). Synthesis and quorum sensing inhibitory activity of key phenolic compounds of ginger and their derivatives. *Food Chemistry*, *159*, 451–457. Retrieved from https://10.1016/j.foodchem.2014.03.039

Kumar, L., Chhibber, S., Kumar, R., Kumar, M., & Harjai, K. (2015). Zingerone silences quorum sensing and attenuates virulence of *Pseudomonas aeruginosa*. *Fitoterapia*, *102*, 84–95. Retrieved from https://10.1016/j.fitote.2015.02.002

Kumara, S. M., Sayeed, A. M., & Rani, S. U. (2016). Antimicrobial properties of plant essential oils against human pathogens and their mode of action: An updated review. *Evidence-Based Complementary and Alternative Medicine*, *2016*, 1–21. Retrieved from https://10.1155/2016/3012462

Le, K. Y., & Otto, M. (2015). Quorum-sensing regulation in staphylococci - An overview. *Frontiers in Microbiology*, *6*, 8. Retrieved from https://10.3389/fmicb.2015.01174

Lee, J. H., Kim, Y. G., Ryu, S. Y., & Lee, J. (2016). Calcium-chelating alizarin and other anthraquinones inhibit biofilm formation and the hemolytic activity of *Staphylococcus aureus*. *Scientific Reports*, *6*, 19267. Retrieved from https://10.1038/srep19267

Lee, J. H., Kim, Y. G., & Lee, J. (2017). Carvacrol-rich oregano oil and thymol-rich thyme red oil inhibit biofilm formation and the virulence of uropathogenic *Escherichia coli*. *Journal of Applied Microbiology*, *123*(6), 1420–1428. Retrieved from https://10.1111/jam.13602

Lee, K., Lee, J. H., Kim, S. I., Cho, M. H., & Lee, J. (2014). Anti-biofilm, anti-hemolysis, and anti-virulence activities of black pepper, cananga, myrrh oils, and nerolidol against *Staphylococcus aureus*. *Applied Microbiology and Biotechnology*, *98*(22), 9447–9457. Retrieved from https://10.1007/s00253-014-5903-4

Lemos, M., Borges, A., Teodosio, J., Araujo, P., Mergulhao, F., Melo, L., & Simoes, M. (2014). The effects of ferulic and salicylic acids on *Bacillus cereus* and *Pseudomonas fluorescens* single- and dual-species biofilms. *International Biodeterioration & Biodegradation*, *86*, 42–51. Retrieved from https://10.1016/j.ibiod.2013.06.011

Leng, B. F., Qiu, J. Z., Dai, X. H., Dong, J., Wang, J. F., Luo, M. J., … Deng, X. M. (2011). Allicin reduces the production of alpha-toxin by *Staphylococcus aureus*. *Molecules*, *16*(9), 7958–7968. Retrieved from https://10.3390/molecules16097958

Leonard, C. M., Virijevic, S., Regnier, T., & Combrinck, S. (2010). Bioactivity of selected essential oils and some components on *Listeria monocytogenes* biofilms. *South African Journal of Botany*, *76*(4), 676–680. Retrieved from https://10.1016/j.sajb.2010.07.002

Lewis, K. (2007). Persister cells, dormancy and infectious disease. *Nature Review Microbiology*, *5*(1), 48–56. Retrieved from https://10.1038/nrmicro1557

Li, J., Dong, J., Qiu, J. Z., Wang, J. F., Luo, M. J., Li, H. E., … Deng, X. M. (2011). Peppermint oil decreases the production of virulence-associated exoproteins by *Staphylococcus aureus*. *Molecules*, *16*(2), 1642–1654. Retrieved from https://10.3390/molecules16021642

Li, T. T., Wang, D. F., Liu, N., Ma, Y., Ding, T., Mei, Y. C., & Li, J. R. (2018). Inhibition of quorum sensing-controlled virulence factors and biofilm formation in *Pseudomonas fluorescens* by cinnamaldehyde. *International Journal of Food Microbiology*, *269*, 98–106. Retrieved from https://10.1016/j.ijfoodmicro.2018.01.023

Liu, Q., Meng, X., Li, Y., Zhao, C. N., Tang, G. Y., & Li, H. B. (2017). Antibacterial and antifungal activities of spices. *International Journal of Molecular Sciences*, *18*(6), 62. Retrieved from https://10.3390/ijms18061283

Ma, Y. P., Hao, L., Ke, H., Liang, Z. L., Ma, J. Y., Liu, Z. X., & Li, Y. G. (2017). LuxS/AI-2 in *Streptococcus agalactiae* reveals a key role in acid tolerance and virulence. *Research in Veterinary Science*, *115*, 501–507. Retrieved from https://10.1016/j.rvsc.2017.07.032

Malik, T., Singh, P., Pant, S., Chauhan, N., Lohani, H., Kumar, V., & Swarup, S. (2015). Inhibition of swarming behaviour in *Proteus mirabilis* by *Pelargonium graveolens* essential oil. *Bangladesh Journal of Medical Science*, *14*(4), 384–388. Retrieved from https://10.3329/bjms.v14i4.20004

Marathe, S. A., Balakrishnan, A., Negi, V. D., Sakorey, D., Chandra, N., & Chakravortty, D. (2016). Curcumin reduces the motility of *Salmonella enterica* serovar Typhimurium by binding to the flagella, thereby leading to flagellar fragility and shedding. *Journal of Bacteriology*, *198*(13), 1798–1811. Retrieved from https://10.1128/JB.00092-16

Martin-Rodriguez, A. J., Ticona, J. C., Jimenez, I. A., Flores, N., Fernandez, J. J., & Bazzocchi, I. L. (2015). Flavonoids from *Piper delineatum* modulate quorum-sensing-regulated phenotypes in *Vibrio harveyi*. *Phytochemistry*, *117*, 98–106. Retrieved from https://10.1016/j.phytochem.2015.06.006

Miladi, H., Zmantar, T., Kouidhi, B., Chaabouni, Y., Mahdouani, K., Bakhrouf, A., & Chaieb, K. (2017). Use of carvacrol, thymol, and eugenol for biofilm eradication and resistance modifying susceptibility of *Salmonella enterica* serovar Typhimurium strains to nalidixic acid. *Microbial Pathogensis*, *104*, 56–63. Retrieved from https://10.1016/j.micpath.2017.01.012

Miller, L. C., O'Loughlin, C. T., Zhang, Z., Siryaporn, A., Silpe, J. E., Bassler, B. L., & Semmelhack, M. F. (2015). Development of potent inhibitors of pyocyanin production in *Pseudomonas aeruginosa*. *Journal of Medicinal Chemistry*, *58*(3), 1298–1306. Retrieved from https://10.1021/jm5015082

Mirzahosseini, S. M., Noori, S. A. S., Amanzadeh, Y., Javid, M. G., & Howyzeh, M. S. (2017). Phytochemical assessment of some native ajowan (*Therachyspermum ammi* L.) ecotypes in Iran. *Industrial Crops and Products*, *105*, 142–147. Retrieved from https://10.1016/j.indcrop.2017.04.052

Mith, H., Clinquart, A., Zhiri, A., Daube, G., & Delcenserie, V. (2015). The impact of oregano (*Origanum heracleoticum*) essential oil and carvacrol on virulence gene transcription by *Escherichia coli* O157:H7. *FEMS Microbiology Letters*, *362*(1), 1–7. Retrieved from https://10.1093/femsle/fnu021

Mossa, A. T. H., Afia, S. I., Mohafrash, S. M. M., & Abou-Awad, B. A. (2018). Formulation and characterization of garlic (*Allium sativum* L.) essential oil nanoemulsion and its acaricidal activity on eriophyid olive mites (Acari: Eriophyidae). *Environmental Science and Pollution Research*, *25*(11), 10526–10537. Retrieved from https://10.1007/s11356-017-0752-1

Murray, T. S., & Kazmierczak, B. I. (2008). *Pseudomonas aeruginosa* exhibits sliding motility in the absence of type IV pili and flagella. *Journal of Bacteriology*, *190*(8), 2700–2708. Retrieved from https://10.1128/JB.01620-07

Musthafa, K. S., & Voravuthikunchai, S. P. (2015). Anti-virulence potential of Eugenyl acetate against pathogenic bacteria of medical importance. *Antonie Van Leeuwenhoek International journal of General and Molecular Microbiology*, *107*(3), 703–710. Retrieved from https://10.1007/s10482-014-0364-4

Myszka, K., Schmidt, M. T., Majcher, M., Juzwa, W., Olkowicz, M., & Czaczyk, K. (2016). Inhibition of quorum sensing-related biofilm of *Pseudomonas fluorescens* KM121 by *Thymus vulgare* essential oil and its major bioactive compounds. *International Biodeterioration & Biodegradation*, *114*, 252–259. Retrieved from https://10.1016/j.ibiod.2016.07.006

Naik, D. N., Wahidullah, S., & Meena, R. M. (2013). Attenuation of *Pseudomonas aeruginosa* virulence by marine invertebrate derived *Streptomyces* sp. *Letters in Applied Microbiology*, *56*(3), 197–207. Retrieved from https://10.1111/lam.12034

Nielsen, C. K., Subbiahdoss, G., Zeng, G., Salmi, Z., Kjems, J., Mygind, T., … Meyer, R. L. (2018). Antibacterial isoeugenol coating on stainless steel and polyethylene surfaces prevents biofilm growth. *Journal of Applied Microbiology*, *124*(1), 179–187. Retrieved from https://10.1111/jam.13634

Nikolic, M., Glamoclija, J., Ferreira, I., Calhelha, R. C., Fernandes, A., Markovic, T., … Sokovic, M. (2014). Chemical composition, antimicrobial, antioxidant and antitumor activity of *Thymus serpyllum* L., *Thymus algeriensis* Boiss. and Reut and *Thymus vulgaris* L. essential oils. *Industrial Crops and Products*, *52*, 183–190. Retrieved from https://10.1016/j.indcrop.2013.10.006

Nostro, A., Roccaro, A. S., Bisignano, G., Marino, A., Cannatelli, M. A., Pizzimenti, F. C., … Blanco, A. R. (2007). Effects of oregano, carvacrol and thymol on *Staphylococcus aureus* and *Staphylococcus epidermidis* biofilms. *Journal of Medical Microbiology*, *56*(4), 519–523. Retrieved from https://10.1099/jmm.0.46804-0

Oral, N. B., Vatansever, L., Aydin, B. D., Sezer, C., Guven, A., Gulmez, M., … Kurkcuoglu, M. (2010). Effect of oregano essential oil on biofilms formed by staphylococci and *Escherichia coli*. *Kafkas University Veteriner Fakultesi Dergisi*, *16*, S23–S29. Retrieved from https://10.1638/2010-0026.1

Oscarsson, J., Kanth, A., Tegmark-Wisell, K., & Arvidson, S. (2006). *SarA* is a repressor of *hla* (α;-hemolysin) transcription in *Staphylococcus aureus*: Its apparent role as an activator of *hla* in the prototype strain NCTC 8325 depends on reduced expression of *sarS*. *Journal of Bacteriology*, *188*(24), 8526–8533. Retrieved from https://10.1128/JB.00866-06

Packiavathy, I., Priya, S., Pandian, S. K., & Ravi, A. V. (2014). Inhibition of biofilm development of uropathogens by curcumin - An anti-quorum sensing agent from *Curcuma longa*. *Food Chemistry*, *148*, 453–460. Retrieved from https://10.1016/j.foodchem.2012.08.002

Packiavathy, I. A., Sasikumar, P., Pandian, S. K., & Ravi, A. V. (2013). Prevention of quorum-sensing-mediated biofilm development and virulence factors production in *Vibrio* spp. by curcumin. *Applied Microbiology and Biotechnology*, *97*(23), 10177–10187. Retrieved from https://10.1007/s00253-013-4704-5

Poli, J. P., Guinoiseau, E., Serra, D. D., Sutour, S., Paoli, M., Tomi, F., … Lorenzi, V. (2018). Anti-quorum sensing activity of 12 essential oils on *Chromobacterium violaceum* and specific action of *cis-cis-p*-menthenolide from *Corsican mentha suaveolens* ssp. insularis. *Molecules*, *23*(9), 11. Retrieved from https://10.3390/molecules23092125

Pontes, E. K. U., Melo, H. M., Nogueira, J. W. A., Firmino, N. C. S., de Carvalho, M. G., Catunda, F. E. A., & Cavalcante, T. T. A. (2019). Antibiofilm activity of the essential oil of citronella (*Cymbopogon nardus*) and its major component, geraniol, on the bacterial biofilms of *Staphylococcus aureus*. *Food Science and Biotechnology*, *28*(3), 633–639. Retrieved from https://10.1007/s10068-018-0502-2

Qiu, J, Feng, H. H., Lu, J., Xiang, H., Wang, D. C., Dong, J., … Deng, X. M. (2010a). Eugenol reduces the expression of virulence-related exoproteins in *Staphylococcus aureus*. *Applied and Environmental Microbiology*, *76*(17), 5846–5851. Retrieved from https://10.1128/AEM.00704-10

Qiu, J., Luo, M., Dong, J., Wang, J. F., Li, H. G., Wang, X. L., … Deng, X. M. (2011a). Menthol diminishes *Staphylococcus aureus* virulence-associated extracellular proteins expression. *Applied Microbiology and Biotechnology*, *90*(2), 705–712. Retrieved from https://10.1007/s00253-011-3122-9

Qiu, J., Wang, D., Xiang, H., Feng, H., Jiang, Y., Xia, L., … Deng, X. (2010b). Subinhibitory concentrations of thymol reduce enterotoxins A and B and α;-hemolysin production in *Staphylococcus aureus* isolates. *PLoS One*, *5*(3), e9736. Retrieved from https://10.1371/journal.pone.0009736

Qiu, J., Zhang, X. R., Luo, M. J., Li, H. G., Dong, J., Wang, J. F., … Deng, X. M. (2011b). Subinhibitory concentrations of perilla oil affect the expression of secreted virulence factor genes in *Staphylococcus aureus*. *PLoS One*, *6*(1), e16160. Retrieved from https://10.1371/journal.pone.0016160

Raina, A. P., & Abraham, Z. (2017). Essential oil profiling of *Alpinia* species from southern India. *Indian Journal of Experimental Biology*, *55*(11), 776–781.

Ranjbar-Omid, M., Arzanlou, M., Amani, M., Shokri Al-Hashem, S. K., Amir Mozafari, N., & Peeri Doghaheh, H. (2015). Allicin from garlic inhibits the biofilm formation and urease activity of *Proteus mirabilis in vitro*. *FEMS Microbiology Letters*, *362*(9), fnv049. Retrieved from https://10.1093/femsle/fnv049

Rasko, D. A., & Sperandio, V. (2010). Anti-virulence strategies to combat bacteria-mediated disease. *Nature Reviews Drug Discovery*, *9*(2), 117–128. Retrieved from https://10.1038/nrd3013

Reen, F. J., Gutierrez-Barranquero, J. A., Parages, M. L., & O'Gara, F. (2018). Coumarin: A novel player in microbial quorum sensing and biofilm formation inhibition. *Applied Microbiology and Biotechnology*, *102*(5), 2063–2073. Retrieved from https://10.1007/s00253-018-8787-x

Rivera-Chavez, F., Winter, S. E., Lopez, C. A., Xavier, M. N., Winter, M. G., Nuccio, S. P., … Baumler, A. J. (2013). Salmonella uses energy taxis to benefit from intestinal inflammation. *PLoS Pathogens*, *9*(4), e1003267. Retrieved from https://10.1371/journal.ppat.1003267

Rodrigues, J. B. D., de Souza, N. T., Scarano, J. O. A., de Sousa, J. M., Lira, M. C., de Figueiredo, R. C. B. Q., … Magnani, M. (2018). Efficacy of using oregano essential oil and carvacrol to remove young and mature *Staphylococcus aureus* biofilms on food-contact surfaces of stainless steel. *LWT-Food Science and Teachnology*, *93*, 293–299. Retrieved from https://10.1016/j.lwt.2018.03.052

Rossi, C., Chaves-Lopez, C., Serio, A., Anniballi, F., Valbonetti, L., & Paparella, A. (2018). Effect of *Origanum vulgare* essential oil on biofilm formation and motility capacity of *Pseudomonas fluorescens* strains isolated from discoloured Mozzarella cheese. *Journal of Applied Microbiology*, *124*(5), 1220–1231. Retrieved from https://10.1111/jam.13707

Rudrappa, T., & Bais, H. P. (2008). Curcumin, a known phenolic from curcuma longa, attenuates the virulence of *Pseudomonas aeruginosa* PAO1 in whole plant and animal pathogenicity models. *Journal of Agricultural and Food Chemistry*, *56*(6), 1955–1962. Retrieved from https://10.1021/jf07259lj

Rutherford, S. T., & Bassler, B. L. (2012). Bacterial quorum sensing: Its role in virulence and possibilities for its control. *Cold Spring Harbor Perspectives in Medicine*, *2*(11), 25. Retrieved from https://10.1101/cshperspect.a012427

Sahal, G., Avcioglu, N. H., & Bilkay, I. S. (2016). Higher biofilm formation by multi-drug resistant *K. pneumoniae* and *K. rhinoscleromatis* strains and effects of lemon and ginger essential oils on biofilm formation. *Indian Journal of Pharmaceutical Education and Research*, *50*(2), S82–S88. Retrieved from https://10.5530/ijper.50.2.22

Salami, M., Rahimmalek, M., Ehtemam, M. H., Szumny, A., Fabian, S., & Matkowski, A. (2016). Essential oil composition, antimicrobial activity and anatomical characteristics of *Foeniculum vulgare* Mill. fruits from different regions of Iran. *Journal of Essential Oil Bearing Plants*, *19*(7), 1614–1626. Retrieved from https://10.1080/0972060X.2015.1117951

Salehi, S., Howe, K., Lawrence, M. L., Brooks, J. P., Bailey, R. H., & Karsi, A. (2017). *Salmonella enterica* serovar Kentucky flagella are required for broiler skin adhesion and Caco-2 Cell invasion. *Applied Environmental Microbiology*, *83*(2), e02115–16. Retrieved from https://10.1128/AEM.02115-16

Sandeep, I. S., Das, S., Nasim, N., Mishra, A., Acharya, L., Joshi, R. K., … Mohanty, S. (2017). Differential expression of *CURS* gene during various growth stages, climatic condition and soil nutrients in turmeric (*Curcuma longa*): Towards site specific cultivation for high curcumin yield. *Plant Physiology and Biochemistry*, *118*, 348–355. Retrieved from https://10.1016/j.plaphy.2017.07.001

Satyal, P., Craft, J. D., Dosoky, N. S., & Setzer, W. N. (2017). The chemical compositions of the volatile oils of garlic (*Allium sativum*) and wild garlic (*Allium vineale*). *Foods*, *6*(8), 63. Retrieved from https://10.3390/foods6080063

Saviuc, C. M., Drumea, V., Olariu, L., Chifiriuc, M. C., Bezirtzoglou, E., & Lazar, V. (2015). Essential oils with microbicidal and antibiofilm activity. *Current Pharmaceutical Biotechnology*, *16*(2), 137–151. Retrieved from https://10.2174/1389201016021501121515 49

Schuster, M., Sexton, D. J., Diggle, S. P., & Greenberg, E. P. (2013). Acyl-homoserine lactone quorum sensing: From evolution to application. *Annual Review of Microbiology*, *67*, 43–63. Retrieved from https://10.1146/annurev-micro-092412-155635

Seal, B. S., Lillehoj, H. S., Donovan, D. M., & Gay, C. G. (2013). Alternatives to antibiotics: A symposium on the challenges and solutions for animal production. *Animal Health Research Reviews*, *14*(1), 78–87. Retrieved from https://10.1017/S1466252313000030

Sepahi, E., Tarighi, S., Ahmadi, F. S., & Bagheri, A. (2015). Inhibition of quorum sensing in *Pseudomonas aeruginosa* by two herbal essential oils from *Apiaceae* family. *Journal of Microbiology*, *53*(1), 176–180. Retrieved from https://10.1007/s12275-015-4203-8

Shafreen, R. M. B., Selvaraj, C., Singh, S. K., & Pandian, S. K. (2014). *In silico* and *in vitro* studies of cinnamaldehyde and their derivatives against LuxS in *Streptococcus pyogenes*: Effects on biofilm and virulence genes. *Journal of Molecular Recognition*, *27*(2), 106–116. Retrieved from https://10.1002/jmr.2339

Sharma, A. K., Dhasmana, N., Dubey, N., Kumar, N., Gangwal, A., Gupta, M., & Singh, Y. (2017). Bacterial virulence factors: Secreted for survival. *Indian Journal of Microbiology*, *57*(1), 1–10. Retrieved from https://10.1007/s12088-016-0625-1

Sheng, L. N., Rasco, B., & Zhu, M. J. (2016). Cinnamon oil inhibits Shiga toxin type 2 phage induction and Shiga toxin type 2 production in *Escherichia coli* O157:H7. *Applied and Environmental Microbiology*, *82*(22), 6531–6540. Retrieved from https://10.1128/AEM.01702-16

Shi, C., Sun, Y., Liu, Z. Y., Guo, D., Sun, H. H., Sun, Z., … Xia, X. D. (2017). Inhibition of *Cronobacter sakazakii* virulence factors by citral. *Scientific Reports*, *7*, 43243. Retrieved from https://10.1038/srep43243

Shrikant, P., & Chandrajit, L. (2018). Quorum sensing: An imperative longevity weapon in bacteria. *African Journal of Microbiology Research*, *12*, 96–104. Retrieved from https://10.5897/AJMR2017.8751

Silva, L. N., Zimmer, K. R., Macedo, A. J., & Trentin, D. S. (2016). Plant natural products targeting bacterial virulence factors. *Chemical Reviews*, *116*(16), 9162–9236. Retrieved from https://10.1021/acs.chemrev.6b00184

Simonetti, O., Cirioni, O., Cacciatore, I., Baldassarre, L., Orlando, F., Pierpaoli, E., … Offidani, A. (2016). Efficacy of the quorum sensing inhibitor FS10 alone and in combination with tigecycline in an animal model of staphylococcal infected wound. *PLoS One*, *11*(6), e0151956. Retrieved from https://10.1371/journal.pone.0151956

Snoussi, M., Noumi, E., Trabelsi, N., Flamini, G., Papetti, A., & De Feo, V. (2015). *Mentha spicata* essential oil: Chemical composition, antioxidant and antibacterial activities against planktonic and biofilm cultures of *Vibrio* spp. strains. *Molecules*, *20*(8), 14402–14424. Retrieved from https://10.3390/molecules200814402

Solorzano-Santos, F., & Miranda-Novales, M. G. (2012). Essential oils from aromatic herbs as antimicrobial agents. *Current Opinion in Biotechnology*, *23*(2), 136–141. Retrieved from https://10.1016/j.copbio.2011.08.005

Souza, E. L., Oliveira, C. E. V., Stamford, T. L. M., Conceicao, M. L., & Neto, N. J. G. (2013). Influence of carvacrol and thymol on the physiological attributes, enterotoxin production and surface characteristics of *Staphylococcus aureus* strains isolated from foods. *Brazilian Journal of Microbiology*, *44*(1), 29–35. Retrieved from https://10.1590/S1517-83822013005000001

Stanojevic, L. P., Marjanovic-Balaban, Z. R., Kalaba, V. D., Stanojevic, J. S., Cvetkovic, D. J., & Cakic, M. D. (2017). Chemical composition, antioxidant and antimicrobial activity of basil (*Ocimum basilicum* L.) essential oil. *Journal of Essential Oil Bearing Plants*, *20*(6), 1557–1569. Retrieved from https://10.1080/0972060X.2017.1401963

Subramenium, G. A., Vijayakumar, K., & Pandian, S. K. (2015). Limonene inhibits streptococcal biofilm formation by targeting surface-associated virulence factors. *Journal of Medical Microbiology*, *64*, 879–890. Retrieved from https://10.1099/jmm.0.000105

Sun, Y. W., Chen, S. J., Zhang, C., Liu, Y., Ma, L., & Zhang, X. Y. (2018). Effects of sub-minimum inhibitory concentrations of lemon essential oil on the acid tolerance and biofilm formation of *Streptococcus mutants*. *Archives of Oral Biology*, *87*, 235–241. Retrieved from https://10.1016/j.archoralbio.2017.12.028

Tajkarimi, M. M., Ibrahim, S. A., & Cliver, D. O. (2010). Antimicrobial herb and spice compounds in food. *Food Control*, *21*(9), 1199–1218. Retrieved from https://10.1016/j.foodcont.2010.02.003

Tapia-Rodriguez, M. R., Hernandez-Mendoza, A., Gonzalez-Aguilar, G. A., Martinez-Tellez, M, A., Martins, C. M., & Ayala-Zavala, J. F. (2017). Carvacrol as potential quorum sensing inhibitor of *Pseudomonas aeruginosa* and biofilm production on stainless steel surfaces. *Food Control*, *75*, 255–261. Retrieved from https://10.1016/j.foodcont.2016.12.014

Tharmalingam, N., Kim, S. H., Park, M., Woo, H. J., Kim, H. W., Yang, J. Y., … Kim, J. B. (2014). Inhibitory effect of piperine on *Helicobacter pylori* growth and adhesion to gastric adenocarcinoma cells. *Infectious Agents and Cancer*, *9*, 43. Retrieved from https://10.1186/1750-9378-9-43

Toker, R., Gölükcü, M., & Tokgöz, H. (2017). Effects of distillation times on essential oil compositions of *Origanum minutiflorum* O. Schwarz Et. and P.H. Davis. *Journal of Essential Oil Research*, *29*(4), 330–335. Retrieved from https://10.1080/10412905.2016.1276026

Topa, S. H., Subramoni, S., Palombo, E. A., Kingshott, P., Rice, S. A., & Blackall, L. L. (2018). Cinnamaldehyde disrupts biofilm formation and swarming motility of *Pseudomonas aeruginosa*. *Microbiology-SGM*, *164*(9), 1087–1097. Retrieved from https://10.1099/mic.0.000692

Tran, T. H., Ha, L. K., Nguyen, D. C., Dao, T. P., Nhan, L. T. H., Nguyen, D. H., … Bach, L. G. (2019). The study on extraction process and analysis of components in essential oils of black pepper (*Piper nigrum* L.) seeds harvested in Gia Lai Province, Vietnam. *Processes*, *7*(2), 15. Retrieved from https://10.3390/pr7020056

Tremblay, P. L., Aklujkar, M., Leang, C., Nevin, K. P., & Lovley, D. (2012). A genetic system for *Geobacter metallireducens*: Role of the flagellin and pilin in the reduction of Fe(III) oxide. *Environmental Microbiology Reports*, *4*(1), 82–88. Retrieved from https://10.1111/j.1758-2229.2011.00305.x

Tutar, U., Celik, C., Karaman, I., Atas, M., & Hepokur, C. (2016). Antibiofilm and antimicrobial activity of *Mentha pulegium* L essential oil against multidrug-resistant *Acinetobacter baumannii*. *Tropical Journal of Pharmaceutical Research*, *15*(5), 1039–1211. Retrieved from https://10.4314/tjpr.v15i5.20

Upadhyay, A., Johny, A. K., Amalaradjou, M. A., Baskaran, S. A., Kim, K. S., & Venkitanarayanan, K. (2012). Plant-derived antimicrobials reduce *Listeria monocytogenes* virulence factors *in vitro*, and down-regulate expression of virulence genes. *International*

Journal of Food Microbiology, *157*(1), 88–94. Retrieved from https://10.1016/j.ijfoodmicro.2012.04.018

Upadhyay, A., Arsi, K., Wagle, B. R., Upadhyaya, I., Shrestha, S., Donoghue, A. M., & Donoghue, D. J. (2017). *Trans*-cinnamaldehyde, carvacrol, and eugenol reduce *Campylobacter jejuni* colonization factors and expression of virulence genes *in vitro*. *Frontiers in Microbiology*, *8*, 713. Retrieved from https://10.3389/fmicb.2017.00713

van Alphen, L. B., Burt, S. A., Veenendaal, A. K., Bleumink-Pluym, N. M., & van Putten, J. P. (2012). The natural antimicrobial carvacrol inhibits *Campylobacter jejuni* motility and infection of epithelial cells. *PLoS One*, *7*(9), e45343. Retrieved from https://10.1371/journal.pone.0045343

Vasconcelos, S. E. C. B., Melo, H. M., Cavalcante, T. T. A., Catunda, F. E. A., de Carvalho, M. G., Menezes, F. G. R., … Costa, R. A. (2017). *Plectranthus amboinicus* essential oil and carvacrol bioactive against planktonic and biofilm of oxacillin-and vancomycin-resistant *Staphylococcus aureus*. *BMC Complementary and Alternative Medicind*, *17*, 462. Retrieved from https://10.1186/s12906-017-1968-9

Venkadesaperumal, G., Rucha, S., Sundar, K., & Shetty, P. H. (2016). Anti-quorum sensing activity of spice oil nanoemulsions against food borne pathogens. *LWT - Food Science and Technology*, *66*, 225–231. Retrieved from https://10.1016/j.lwt.2015.10.044

Vestergaard, M., & Ingmer, H. (2019). Antibacterial and antifungal properties of resveratrol. *International Journal of Antimicrobial Agents*, *53*(6), 716–723. Retrieved from https://10.1016/j.ijantimicag.2019.02.015

Vidács, A., Kerekes, E., Rajkó, R., Petkovits, T., Alharbi, N. S., Khaled, J. M., … Krisch, J. (2018). Optimization of essential oil-based natural disinfectants against *Listeria monocytogenes* and *Escherichia coli* biofilms formed on polypropylene surfaces. *Journal of Molecular Liquids*, *255*, 257–262. Retrieved from https://10.1016/j.molliq.2018.01.179

Vigan, M. (2010). Essential oils: Renewal of interest and toxicity. *European Journal of Dermatology*, *20*(6), 685–692. Retrieved from https://10.1684/ejd.2010.1066

Wang, Y., Yi, L., Wang, S., Fan, H., Ding, C., Mao, X., & Lu, C. (2015). Crystal structure and identification of two key amino acids involved in AI-2 production and biofilm formation in *Streptococcus suis* LuxS. *PLoS One*, *10*(10), e0138826. Retrieved from https://10.1371/journal.pone.0138826

Wang, D. Y., Fan, W. C., Guan, Y. F., Huang, H. N., Yi, T., & Ji, J. M. (2018). Oxidative stability of sunflower oil flavored by essential oil from *Coriandrum sativum* L. during accelerated storage. *LWT-Food Science and Technology*, *98*, 268–275. Retrieved from https://10.1016/j.lwt.2018.08.055

Werber, D., King, L. A., Muller, L., Follin, P., Buchholz, U., Bernard, H., … Hohle, M. (2013). Associations of age and sex with the clinical outcome and incubation period of Shiga toxin-producing *Escherichia coli* O104:H4 infections, 2011. *American Journal of Epidemiology*, *178*(6), 984–992. Retrieved from https://10.1093/aje/kwt069

Wijesundara, N. M., & Rupasinghe, H. P. V. (2018). Essential oils from *Origanum vulgare* and *Salvia officinalis* exhibit antibacterial and anti-biofilm activities against *Streptococcus pyogenes*. *Microbial Pathogensis*, *117*, 118–127. Retrieved from https://10.1016/j.micpath.2018.02.026

Yadav, M. K., Chae, S. W., Im, G. J., Chung, J. W., & Song, J. J. (2015). Eugenol: A phyto-compound effective against methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* clinical strain biofilms. *PLoS One*, *10*(3), e0119564. Retrieved from https://10.1371/journal.pone.0119564

Yadav, M. K., Vidal, J. E., Go, Y. Y., Kim, S. H., Chae, S. W., & Song, J. J. (2018). The LuxS/AI-2 quorum-sensing system of *Streptococcus pneumoniae* is required to cause disease, and to regulate virulence- and metabolism-related genes in a rat model of middle ear infection. *Frontiers in Cellular and Infection Microbiology*, *8*, 138. Retrieved from https://10.3389/fcimb.2018.00138

Yan, T., Rukayadi, Y., Kim, K. H., & Hwang, J. K. (2008). *In vitro* anti-biofilm activity of macelignan isolated from *Myristica fragrans* Houtt. against oral primary colonizer bacteria. *Phytotherapy Research*, *22*(3), 308–312. Retrieved from https://10.1002/ptr.2312

Yang, X. L., Sha, K. H., Xu, G. Y., Tian, H. W., Wang, X. Y., Chen, S. Z., … Huang, N. (2016). Subinhibitory concentrations of allicin decrease uropathogenic *Escherichia coli* (UPEC) biofilm formation, adhesion ability, and swimming motility. *International Journal of Molecular Science*, *17*(7), 979. Retrieved from https://10.3390/ijms17070979

Yap, P. S., Krishnan, T., Yiap, B. C., Hu, C. P., Chan, K. G., & Lim, S. H. (2014). Membrane disruption and anti-quorum sensing effects of synergistic interaction between *Lavandula angustifolia* (lavender oil) in combination with antibiotic against plasmid-conferred multi-drug-resistant *Escherichia coli*. *Journal of Applied Microbiology*, *116*(5), 1119–1128. Retrieved from https://10.1111/jam.12444

Yoon, S. I., Kurnasov, O., Natarajan, V., Hong, M., Gudkov, A. V., Osterman, A. L., & Wilson, I. A. (2012). Structural basis of TLR5-flagellin recognition and signaling. *Science*, *335*(6070), 859–864. Retrieved from https://10.1126/science.1215584

Zhang, B. Z., Ku, X. G., Zhang, X. Q., Zhang, Y., Chen, G., Chen, F. Z., … He, Q. G. (2019). The AI-2/luxS quorum sensing system affects the growth characteristics, biofilm formation, and virulence of *Haemophilus parasuis*. *Frontiers in Cellular and Infection Microbiology*, *9*. Retrieved from https://10.3389/fcimb.2019.00062

Zhang, Y., Kong, J., Xie, Y., Guo, Y., Cheng, Y., Qian, H., & Yao, W. (2018). Essential oil components inhibit biofilm formation in *Erwinia carotovora* and *Pseudomonas fluorescens* via anti-quorum sensing activity. *LWT-Food Science and Technology*, *92*, 133–139. Retrieved from https://10.1016/j.lwt.2018.02.027

Zhao, L. P., Xue, T., Shang, F., Sun, H. P., & Sun, B. L. (2010). *Staphylococcus aureus* AI-2 quorum sensing associates with the KdpDE two-component system to regulate capsular polysaccharide synthesis and virulence. *Infection and Immunity*, *78*(8), 3506–3515. Retrieved from https://10.1128/IAI.00131-10

Zhou, L. M., Zheng, H. D., Tang, Y. D., Yu, W. G., & Gong, Q. H. (2013). Eugenol inhibits quorum sensing at sub-inhibitory concentrations. *Biotechnology Letters*, *35*(4), 631–637. Retrieved from https://10.1007/s10529-012-1126-x

How to cite this article: Zhang D, Gan R-Y, Zhang J-R, et al. Antivirulence properties and related mechanisms of spice essential oils: A comprehensive review. *Compr Rev Food Sci Food Saf*. 2020;19:1018–1055. https://doi.org/10.1111/1541-4337.12549