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Antibacterial activity of ginger essential oil derived nanobactericide against the growth of phytopathogenic bacteria - A Review

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ABSTRACT

Phytopathogenic bacteria infect various plants, causing economic losses, negative environmental consequences, and harming agricultural development. The most currently available antimicrobial agents for agriculture were potentially toxic, non-biodegradable, and cause significant harm to the ecosystem. As a result, novel, effective, safe, user-friendly, and alternative methods were urgently needed. Essential oils (EOs) have great potential in managing plant bacterial diseases because they successfully destroy various pathogenic bacteria. Ginger essential oil (GEO) is more widely used because it contains a diverse mixture of volatile substances, such as phenolic compounds, terpenes, polysaccharides, lipids, and organic acids. The antibacterial activity of the EO against phytopathogenic bacteria is significantly improved when it is converted into nanoparticles. Nanoparticles (NPs) that were derived from EOs have a considerable antibacterial action resulting from increased chemical solubility and consistency, minimal rapid evaporation, and slow depletion of the effective substances of EO. Ginger EOs were encapsulated in chitosan as a nanogel to improve the antibacterial effects and the consistency of the oils against pathogenic bacteria. Nanogel had been shown to amplify the antibacterial effect of EOs against pathogenic bacteria by enhancing their potential to disturb the integrity and permeability of the cell membranes. This paper focuses on three major parts of ginger essential oils: the antibacterial efficacy to control plant pathogenic bacteria, the possible mechanisms of action of essential oils as nanobactericides, and more importantly, the fabrication of bactericide nanoformulation.

Keywords: antibacterial activity, essential oil, ginger, nanobactericide, nanogel, Phytopathogenic bacteria

INTRODUCTION

Plant pathogenic bacteria are the cause of a wide variety of plant diseases worldwide. Among them, plant bacterial diseases caused devastating crop damage and significant economic losses (Mansfield et al., 2012). It is found that of 7100 categories of bacteria, about 150 species are accountable for diverse plant diseases (Kannan et al., 2016). There are a limited number of compounds available for plant bacterial pathogen management. Bacterial diseases in plants can be managed using an integrated approach. The use of plant host resistance or the development of less susceptible cultivars, as well as treatment with chemical and/or biological controls and cultural practices aimed at inoculum decline, is typically the best basic approach for efficient and sustainable disease management. Consequently, plant pathogenic bacteria have developed resistance to conventional pesticides. Similarly, there is a limitation to the application of chemically synthesized pesticides and antibiotics due to their specific toxicity and harm to both yield and the environment. The development and implementation of management techniques for combating and destroying plant pathogenic bacteria, including preventing methodologies for survival, is crucial for world food security.

Plant species naturally develop a broad range of molecules known to function in the protection of plant pathogens (Hancock et al., 2015). Nowadays, the usage of plant-based natural active ingredients, especially EOs in the agriculture field, had become dominant (Mohammadi et al., 2015). Various EOs have recently been broadly investigated for their antibacterial characteristics and behavior against most plant pathogenic bacteria (Popovic et al., 2018). Biopesticides, such as EOs, have certain benefits where the bacterial pathogens are unlikely to produce resistance to them, have little or no toxic effects on mammals, and also are not accumulated in soils. In addition, it also served to inhibit bacterial cell growth and prevent the development of toxic bacterial metabolites (Nazzaro et al., 2013). EOs are known to have the capability for interactions with such cell membranes, influencing the potential of the membranes and the permeability of ions and nutrients (Pavoni et al., 2019).

Historically, ginger had been globally known as an herbal medicine and spice (Mao et al., 2019; Nas et al., 2018). The roots of the ginger plant are used to extract the ginger EO. Ginger EOs consist of phenols, flavonoids, gingerol, shogaol, and zingerone, several pungent and biologically active compounds (Ha et al., 2012). These substances contain a high concentration of bioactive chemicals, which may offer an alternative to the existing use of synthetic pesticides. Antimicrobials have diverse modes of action depending on the kind of EOs or microorganism strains. Ginger EOs may be used to suppress the development of phytopathogens as an antimicrobial agent and as potential alternatives to synthetic bactericides (Abdullahi et al., 2020). Nanobactericides have been developed and formed enormously due to their smaller size properties. Opposing from macroparticles, these nanosized bactericides are more active (Wang et al., 2013). The antibacterial efficacy of EOs against bacteria is greatly improved when it is converted into a nanoparticle. Nanobactericide also offers improved physical stability, improves the lipophilic drugs' solubility, provides greater absorption due to small-sized droplets, and requires less energy. Among several procedures, ionic gelation is an organic solvent-free, slight, and simple technique identified for the development of effective nano-sized particles (Hasheminejad et al., 2018). Nanogels gained more attention as flexible nanocarriers used in encapsulation as well as a medium of transport for bioactive components (Neamtu et al., 2017). Nanogels were mainly prepared by a small particle size, which offers a large surface area with good surface properties (Tiwari et al., 2015). A non or biodegradable, synthetic, and natural polymer that can be used to prepare the nanogels. Polymers such as chitosan can be used in the preparation. Chitosan is one of the most abundant naturally available amino polysaccharides extracted from insects and crustaceans’ exoskeleton and fungal cell walls (Katiyar et al., 2014). It had appeared as the most impressive polymer for the effective transportation of micronutrients and agrochemicals to nanoparticles (Kashyap et al., 2015).

Natural compounds such as EOs can be an ideal source of substitute groups of natural bio-pesticides that can serve as the templates for novel and more effective compounds in the management of plant bacterial pathogens. Ginger EOs have been studied considerably with particular attention to their antioxidant, antifungal, and antibacterial properties, as well as their potential use as a food preservative (Ju et al., 2018). Other studies found that applying ginger EOs to the leaves could extend their lifetime and increase their visual quality after harvest (Teerarak et al., 2019). However, only limited studies have been conducted to investigate the effects of ginger EOs on plant pathogenic bacteria management and antibacterial mechanisms. Although the chemical compounds and antimicrobial properties of EOs have been well documented, the information on the evaluation of their chemical components utilizing different extraction methods and the associated primary antibacterial processes is scarce and warrants further investigations. Therefore, this review discusses and emphasizes the antibacterial potentials of EOs extracted from ginger, followed by their possible mechanisms involved in the reticence of plant pathogenic bacteria and, lastly the production of bactericide nanoformulation.

PHYTOPATHOGENIC BACTERIA

Plant microbial pathogens were accountable for significant losses in crop production although the majority of crops were prone to bacterial disease, and in certain crops, the diseases of bacteria have become a major reason for the decline of yield (Gakuubi et al., 2016). Plant pathogenic bacteria were classified into three families such as Xantomonadaceae, Pseudomonadaceae, and Enterobacteriaceae. The most crucial Gram-negative genera of phytopathogenic bacteria were *Agrobacterium*, *Erwinia*, *Pseudomonas*, and *Xanthomonas*, while Gram-positive bacterial plant pathogens were the most important members of four genera, namely *Arthrobacter*, *Clavibacter*, *Curtobacterium*, and *Rhodococcus* (Gakuubi et al., 2016). Almost all of these bacteria were capable of causing a variety of damaging diseases and/or total yield loss. They were responsible for a variety of crop diseases such as leaf spots, blight, necrosis, canker, wilt, rot, galls and tumours, dwarfing, discolouration of plant parts, and so on. Among plant bacterial diseases, bacterial wilt damage was one of the most common. *Ralstonia* spp., *Pseudomonas* spp., and *Burkholderia* spp. were phytopathogenic b-proteobacterium that infect different kinds of plants and cause bacterial wilt (Mansfield et al., 2012).

The bacteria present two major phenotypes, viable but non-culturable (VBNC) and persistent. The VBNC cell population does not recover, while the persistent cells recover after stress (Ayrapetyan et al., 2015; Kim et al., 2018). A wide range of plants was affected by bacterial diseases, causing significant damage to crops and, therefore loss of yield and crop quality (Raveau et al., 2020). Bacteria have a diverse approach to survival and success in the environment and the plant hosts (Martins et al., 2018). Thus, plant bacterial disease management was a key task due to numerous reasons, such as inadequate availability of bactericides (Kokoskova et al., 2011) and the change in microbial resistance to currently available chemical pesticides (Badawy et al., 2014). The most effective management techniques for phytopathogenic bacteria include using seeds and seedlings that were disease-free, and resistant to varieties, antibiotics, and copper sprays. Copper compounds and antibiotics were currently being used as bactericide spray treatments for plant bacterial disease management. However, spraying antibiotics and copper mixtures to control bacterial diseases was usually optional (Kotan & Dadaso, 2013). Recently, heavy metal copper-based pesticides have received low social acceptance due to their toxicity, causing excessive risk to human health, animals, and the ecosystem. Green pesticides, which were composed of natural active compounds extracted from plants, were thus the ideal solution for preventing the spread of plant bacterial diseases.

GINGER ESSENTIAL OIL

Essential oils were aromatic volatile materials derived from numerous parts of the plant (Wang et al., 2020). EOs were generally a complex mix of organic volatile substances that were biosynthesized as supplementary metabolites to determine the specific aroma, flavors, and fragrance of plants (Moghaddam et al., 2017). EOs could be found in over 2000 plant varieties from approximately 60 families. Asteraceae, Pinaceae, Rutaceae, Zingiberaceae, Apiaceae, Umbelliferae, Poaceae, Lamiaceae, and Myrtaceae were plant families which were mostly rich in EOs (Kocic-Tanackov et al., 2013). The use of EOs had certain constraints, for example, the low molecular weight of their compounds, the EOs were highly volatile and therefore have low environmental persistence (Mahdavi et al., 2018). Since then, these instability problems could lead to a decrease or loss of efficacy. Further, EOs' chemical compositions and yield were highly varied as a result of numerous parameters based on the plant development and growth conditions, such as the weather patterns, the site of cultivation, and the time of harvesting (Bhat et al., 2016). Using different extraction methods, EOs could be extracted from different plant parts (Pires et al., 2019). The most commonly used method for the extraction of natural products was the traditional method, such as steam distillation and extraction with organic solvents (Azmir et al., 2013). EOs could be soluble in organic solvents with a density particularly less than that of water. Hydrodistillation is another convenient way to produce EOs. The main advantage was using water as a solvent, which consequently does not produce any harmful residues after the extraction process (Souza et al., 2020).

Ginger (*Zingiber Officinalis* Roscoe) was a member of the Zingiberaceae family, the rhizome of the perennial monocotyledonous plant. It was a kind of perennial herb which originated in the tropical regions of southeast Asia (Alsherbiny et al., 2019). Ginger was commonly consumed as a food and dietary substitute and, its been utilized in traditional medicine throughout the world. Ginger EOs have been widely studied, with particular emphasis on their antioxidant, antifungal, and antibacterial properties, and also their expanding use in preserving food (Ju et al., 2018). Ginger had a distinct flavour that comes from both non-volatile and volatile oils. Ginger rhizome EOs contain aromatic and pungent compounds and were pale yellow to light amber in colour. Depending on the nature of the crop, ginger EOs could be extracted with a yield of up to 3.0% (De Barros et al., 2016). Ginger EOs were vulnerable to chemical transformation or reactions of degradation including was omerization, oxidation, polymerization, and rearrangement, depending primarily on the environmental parameters (Turek et al., 2013). Furthermore, ginger EOs' antibacterial activity was similar to or even more efficient than other various plant-driven EOs (Sharifi-rad et al., 2017). The most common ginger EO extraction techniques, major chemical compounds, and concentrations were mentioned in Table 1.

Characteristics and Bioactive Compounds of Ginger

Ginger comprises a combination of biologically active and pungent compounds (Ha et al., 2012). Fresh ginger had normally been comprised of 80.8% water, 12.3% carbohydrates, 2.4% fibers, 2.3% proteins, 1.2% minerals, and 0.9% lipids (Beristain-Bauza et al., 2019). Ginger chemical analysis indicated that it comprises more than 400 active chemical ingredients, the primary constituents of ginger rhizomes being 50–70 % carbohydrate, 3–8 % lipids, terpenes, and phenolic compounds. Ginger EO chemical compositions were influenced by cultural practices, storage conditions, source of rhizome, freshness, or dryness, and the methods of extraction (Mahboubi, 2019). Using several analytical methods such as high-performance liquid chromatography (HPLC), gas chromatography-mass spectroscopy (GC-MS), gas chromatography (GC), flame ionization detection (GC-FID), and liquid chromatography-mass spectrometry (LC-MS), each chemical compounds of ginger EOs were characterized and could be identified. The rhizome of ginger was high in secondary metabolites such as phenolic compounds, volatile sesquiterpenes, and monoterpenoids (Grace et al., 2017).

Ginger was a unique group of numerous bioactive substances, which include bioactive phenols (gingerols, zingerones, and shogaols) (Kieliszek et al., 2020) as presented in Figure 1. Chemically separated ginger ingredients were characterized by pungent and flavouring compounds. Gingerols, shogaols, zingerones, and capsaicin were all pungent ingredients of ginger and the flavouring compounds were categorized as volatile and sesquiterpene. Zingiberene, pine, camphene, cumene, borneol, bisabolene, and zingiberol were volatile ingredients, while sesquiterpene and zingiberol belong to the sesquiterpene class (Choi et al., 2018). The EOs consist of mainly terpenoids, monoterpenes (C_{10}), and sesquiterpenes (C_{15}) although they could also be available with diterpenes (C_{20}). Monoterpenes ($C_{10}H_{16}$) and sesquiterpenes ($C_{15}H_{24}$) were the most common terpenes, but longer chains including such diterpenes ($C_{20}H_{32}$), triterpenes ($C_{30}H_{40}$), and some others exist. The spectrometric studies exhibited the occurrence of monoterpenes (such as α-pinene, camphene, myrcene, and α-phellandrene), oxygenated monoterpenes (geranial, citronellal, neral, linalool, borneol, and α-terpineol), and sesquiterpenes (α-and β-farnesene, ar-curcumin, zingiberene, zingiberol, copaene, or cadinene) (Koch et al., 2017).

Table 1. Different extraction methods of ginger essential oil, chemical composition, identification method, and their percentage title of table

Extraction Method	Major compound	Percentage	Identification Method	Reference
Hydrodistillation. (Bentong Variety. Malaysia)	camphene	16.93	GC-MS	Abdullahi et al. 2020
	Bisacurone epoxide	16.35		
	Eucalyptol	14.90		
	β-phellandrene	11.60		
	α-zingiberene	7.17		
Hydrodistillation (Indian species)	α-Zingiberene	28.25	GC and GC/MS	Amiri et al., 2016
	β-Sesquiphellandrene	15.65		
	α-Curcumene	15.23		
	trans-γ-Cadinene	11.88		
Hydrodistillation (Chinese species)	α-Zingiberene	35.67	GC and GC/MS	Amiri et al., 2016
	β-Sesquiphellandrene	15.27		
	trans-γ-Cadinene	9.25		
	E-Citral	6.0		
Supercritical Fluid Extraction	α-Zingiberene	16.98	GC-MS	Azhari et al. 2017
	α-Farnesene	12.67		
	α-Curcumene	8.75		
	β-Sesquiohellandrene	8.02		
	Zingiberone	7.96		
	Citral	7.66		
Soxhlet extraction	Zingiberone	18.21	GC-MS	Azhari et al., 2017
	α-Zingiberene	13.74		
	α-Farnesene	11.01		
	β-Sesquiohellandrene	8.41		
	α-Curcumene	8.03		
Hydrodistillation	α-Zingiberene	26.0	GC-MS	Feng et al., 2018
	β-Sesquiphyllandrene	8.10		
	α-Bergamotene	7.99		
	α-Curcumene	7.99		
	β-Bisabolene	7.47		
Hydrodistillation	α-Zingiber	23.85	GC-MS, NMR	Ferreira et al., 2018
	Geraniale	14.16		
	α-farnesene	9.98		
	canfene	8.43		
	β-phellandrene	8.23		
	neral	7.47		
	β-Sequiphellandrene	7.04		
Hydrodistillation	Eudesmol	8.19	GC-MS	Lopez et al., 2017
	γ-terpinene	7.88		
	α-curcumene	2.28		
	alloaromadendrene	6.56		
Hydrodistillation	a-Zingiberene	24.96	GC-MS	Ferreira et al., 2018
	b-sesquiphellandrene	12.74		
	Sesquisabinene hydrate	6.19		
Hydrodistillation	Zingiberene	28.57	GC-MS	Oforma et al., 2020
	Ar-Curcumene	14.21		
	geranyl acetate	13.28		
	geranial	9.16		
Hydrodistillation	α-zingiberene	16.1	GC-MS	Silva et al., 2018
	geranial	14.4		
	(Z)-citral	9.2		
	β-cedrene	8.6		
	geranyl acetate	8.4		
Hydrodistillation	Comphene	11.5	GC/EIMS	Snuossi et al., 2016
	β-Phellandrene	10.7		
	1,8-cineal	10.4		
	α-Zingiberen	6.9		
Supercritical CO_2 Extraction	Zingiberene	37.55	GC-MS	Wang et al., 2020
	α-Curcumene	10.22		
	Zingiberone	6.59		
Steam Distillation	Zingiberene	35.65	GC-MS	Wang et al., 2020
	α-Curcumene	12.04		
	Zingiberone	9.02		

GC/MS: Gas chromatography/mass spectrometry; NMR: nuclear magnetic resonance

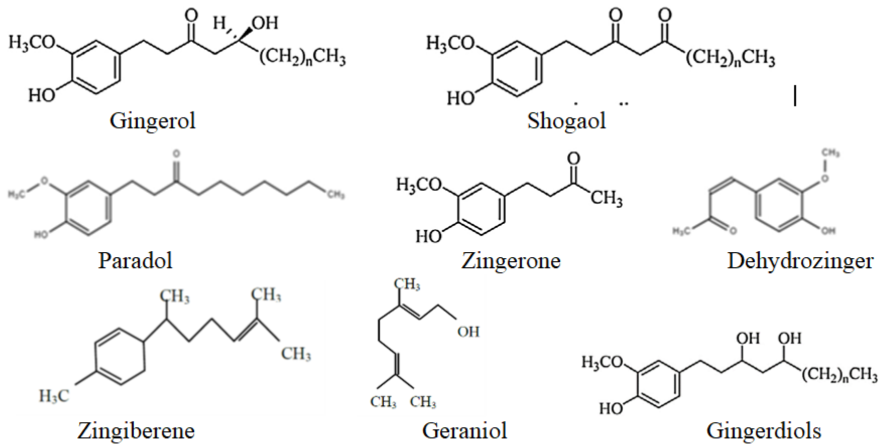

Figure 1. The structure of major chemical compounds derived from ginger essential oil

The major components of ginger EOs were quite a few terpene compounds in ginger, including β-bisabolene, α-curcumin, zingiberene, α-farnesene, and β-sesquiphellandrene. Intensive work indicated that the α-zingiberene was the most prevalent compound ranging from 17.4% to 25.4% in ginger EOs (Sharifi-rad et al., 2017). Furthermore, Gingerols were the most available pungent substances in fresh root systems due to their low molecular weight, and ginger comprises numerous gingerols of different carbon chain lengths (n 6 to n10), the most common of which was 6-gingerol (Ha et al., 2012). However, 6-gingerol was unstable in the existence of light, air, heat, and extended storage (Uthumpa et al., 2013).

Gingerols were primarily responsible for ginger pungency and were converted into corresponding shogaols with heat treatment or dehydration processes and long-term storage. Shogaols could be further converted into paradols after hydrogenation. Shogaols, a dehydrated type of gingerol, were present in the fresh root only in limited amounts and mainly in the dried and heat-treated roots. Commonly, all such key components were determined by the biological properties of the EOs. The chemical structure of EOs influences their mechanism of action in their antibacterial activity. The several EOs and their constituents were already evaluated for antibacterial action for the pathogens.

Antibacterial Activity of Ginger

Currently, the management of plant pathogenic bacteria was challenged since only a few bactericides were available, and there was a high chance of resistance development. To address the heavy losses in agriculture, the recognition of new active ingredients against new targets was a major concern (Masniari, 2011). EOs were volatile aromatic materials created by the secondary metabolism processes of plants that have medicinal properties which could be utilized as natural antimicrobial agents. As antimicrobial agents, EOs and their biologically active components were becoming more and more interesting in terms of safety and efficiency (Cui et al., 2018). The antibacterial properties of EOs were usually explained by toxic effects on membrane structure and activity.

A series of bioactive compounds contained in EOs could prevent or delay the growth of fungi, yeasts, and bacteria. EOs were considered to have a bactericidal rather than a bacteriostatic impact on growth cells. Chemical ingredients and the amount of the major single compounds of EOs were mostly affected by their antibacterial properties (Nazzaro et al., 2013). Several research reveal that the phenolic component in the EOs was the primary molecule held accountable for the antibacterial activities (Vahedikia et al., 2019). EOs, especially oils high in phenolics, could pass through the phospholipid bilayer of the bacterial cell membranes, bind to proteins, and prevent them from conducting their normal functions (Nazzaro et al., 2013). Despite the special antibacterial properties of EOs against pathogenic microorganisms, the real practical application of its often limited by vulnerability to chemical degradation reactions. The antibacterial activity could be determined by using various bioassay techniques including the agar or broth dilution methods and well or disk-diffusion methods (Balouiri et al., 2016). Table 2 showed the effectiveness of ginger extract and essential oil in inhibiting the growth of important bacterial pathogens in vitro. The Agar diffusion method was one of the most commonly used and was represented by its simplicity and cost-effectiveness. These dilution methods were the most acceptable bioassays for the estimation of the minimum inhibitory concentration (MIC) value. In addition, these bioassay methods provide an opportunity to estimate the concentration of the antibacterial agents in either agar (agar dilution) or broth medium (macro dilution or micro-dilution) (Chouhan et al., 2017).

Bactericidal activity was the most common technique to determine the minimum bactericidal concentration. MBC had represented the level of concentration that causes the kill of the initial inoculum at 99.9% and more (Canillac et al., 2001). It had been demonstrated that the antibacterial activity of ginger EOs, extracts, and oleoresins was highly dependent on their chemical composition, extraction solvent, extraction methodology, and procedures used. Beristain-Bauza et al. (2019) Ginger EOs may be effective against a wide range of phytopathogenic microorganisms, including non-phytotoxic substances (Beristain-Bauza et al., 2019).

Saad et al. (2013) indicated that geraniol activity was superior to geranyl acetate against certain bacterial strains. Previous studies have shown the antibacterial efficacy of ginger EOs against spoilage and pathogenic bacteria associated with food, such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, and *Bacillus subtilis* (Aghazadeh et al., 2016; Rahmani et al., 2014).

MODE OF ACTION OF GINGER ESSENTIAL OIL

The mode of action by antibacterial agents was selective which acts toward targeted pathogens without affecting the host function. The antibacterial activities of EOs contribute to a series of reactions that affect the whole bacterial cell. The action of EOs on bacterial cells had been explained by a variety of mechanisms. Many research indicated that the antibacterial mechanism of action in EOs and their components depends on their chemical constituent as well as the number of individual components (Nazzaro et al., 2013). For their actions, EOs and their constituents may also have a single target or even multiple targets. EOs may inhibit bacterial (bacteriostatic) growth or may kill bacterial cells (bactericidal) (Swamy et al., 2016).

Moreover, surface interference may be the possible mechanism for the bactericidal properties. EOs cause functional and structural damage to the membrane of the bacterial cell, both in the outer cell envelope and in the cytoplasm (Shaaban, 2020). In most cases, EOs induce antibacterial action by disrupting membranes and cell walls, leading to cell lysis and leaking of cell contents. The lysis could also be attributed to a cell wall weakening and, subsequently, a breakage of the cytoplasmic membrane resulting from osmotic pressure (Kerekes et al., 2015). Previous research had shown that bioactive compounds existing in EOs could be attached to the cell surface and entered the phospholipid bilayer of the cell membrane (Chouhan et al., 2017). The phenolic compounds were responsible for cytoplasmic membrane disruption, proton driving force, electron flow, active transport, and cell content coagulation. (Dhifi et al., 2016) Furthermore, the existence and position of active groups in a molecule may also affect its antibacterial activity.

Gram-positive bacteria's cell walls were mainly composed of peptidogly could linked to certain molecules known as proteins or teichoic acid (O'Bryan et al., 2015). Gram-negative bacteria have a hydrophilic lipopolysaccharide outer membrane that protects them from hydrophobic compounds like those identified in EOs (Shakeri et al., 2014).

Table 2. Effectiveness of ginger extraction and essential oil in suppressing the growth of important bacterial pathogens in in-vitro

Pathogen	Formulation	MIC	DIZ (mm)	MBC (mg/mL)	Inhibitory Mechanism	Reference
Bacillus cereus	GEO	-	19.4 ± 0.22	-	NR	Ashraf et al., 2017
Bacillus subtilis ATCC6633	GEO Subcritical water extraction	39.10 ± 0.1 µg/ml		-	NR	Svarc-Gajic et al., 2017
Candida albicans ATCC10231	GEO Subcritical water extraction	39.10 ± 0.5 µg/ml		-	NR	Svarc-Gajic et al., 2017
Citrobacter freundii	GEO	-	15.8 ± 0.61	-	NR	Ashraf et al., 2017
Clostridium perfringens	GEO	-	7.1 ± 0.62	-	NR	Ashraf et al., 2017
Cronobacter sakazakii	GEO	-	12.7 ± 0.72	-	NR	Ashraf et al., 2017
Enterobacter aerogenes	GEO	-	19.4 ± 0.33	-	NR	Ashraf et al., 2017
Enterococcus faecalis	GEO	-	15.3 ± 0.25	-	NR	Ashraf et al., 2017
Enterococcus hirae	GEO	-	21.9 ± 0.37	-	NR	Ashraf et al., 2017
Escherichia coli	GEO	-	22.9 ± 0.16	-	NR	Ashraf et al., 2017
Escherichia coli ATCC25922	GEO Subcritical water extraction	39.10 ± 0.5 µg/ml			NR	Svarc-Gajic et al., 2017
E. coli 0157:H7 NCTC 12900	GEO hydro distillation	2.3 µl/ml	19.0 ± 1.2	4.7 µl/ml	NR	Silva et al., 2018
Escherichia coli	GEO	2.0 mg/mL	12.3	4.0	Disruption of the bacterial cell membrane	Wang et al., 2020
Klebsiella pneumoniae	GEO	1250 µg/ml		-	Inhibition for mrkD gene expression	Abozahra et al., 2020
Klebsiella pneumonia	GEO	-	12.5 ± 0.61	-	NR	Ashraf et al., 2017
Klebsiella pneumoniae ATCC13883	GEO Subcritical water extraction	156.25 ± 0.8 µg/ml	-	-	NR	Svarc-Gajic et al., 2017
Klebsiella pneumoniae	Nanostructured lipid carrier-ginger oil	625 µg/ml	-	-	Inhibition for mrkD gene expression	Abozahra et al., 2020
Klebsiella pneumoniae	Ginger oil loaded chitosan nanoparticles	156 µg/ml	-	-	Inhibition for mrkD gene expression	Abozahra et al, 2020
Lactococcus garvieae (FP5245)	GEO	1:1 dilution	13	4% (V/V)	NR	Hossain et al., 2019
Listeria monocytogenes	GEO water extraction	-	8.66 ±0.72	-	NR	Mesomo et al., 2013
L. monocytogenes ATCC 766	GEO hydro distillation	2.3 µl/ml	37.0 ± 1.2	4.7 µl/ml	NR	Silva et al., 2018
Micrococcus luteus	GEO	-	24.2 ± 0.24	-	NR	Ashraf et al., 2017
Proteus vulgaris ATCC13315	GEO Subcritical water extraction	156.25 ± 0.8 µg/ml	-	-	NR	Svarc-Gajic et al., 2017
Proteus mirabilis ATCC 14153	GEO Subcritical water extraction	156.25 ± 0.8 µg/ml	-	-	NR	Svarc-Gajic et al., 2017
Pseudomonas aeruginosa	GEO	-	16.2 ± 0.47	-	NR	Ashraf et al., 2017
P. aeruginosa ATCC 15443	GEO hydro distillation	9.4 µl/ml	13.0 ± 2.0	18.7 µl/ml	NR	Silva et al., 2018
Rhodococus equi	GEO	-	17.2 ± 0.31	-	NR	Ashraf et al., 2017
Salmonella enterica	GEO	-	16.9 ± 0.34	-	NR	Ashraf et al., 2017
Salmonella typhi	GEO	-	18.1 ± 0.36	-	NR	Ashraf et al., 2017
S. typhimurium ATCC 14028	GEO hydro distillation	9.4 µl/ml	15.0 ± 3.2	18.7 µl/ml	NR	Silva et al., 2018
Shigella	GEO	-	11.5 ± 0.38	-	NR	Ashraf et al., 2017
Staphylococcus aureus +	GEO water extraction	-	8.15 ±0.92	-	NR	Mesomo et al., 2013
Staphylococcus aureus	GEO	-	17.9 ± 0.31	-	NR	Ashraf et al., 2017
Staphylococcus aureus ATCC25923	GEO Subcritical water extraction	78.13 ± 0.7 µg/ml	-	-	NR	Svarc-Gajic et al., 2017
S. aureus ATCC25923	GEO hydro distillation	4.7 µl/ml	19.0 ± 1.2	9.4 µl/ml	NR	Silva et al., 2018
Staphylococcus aureus	Ginger ethanol extract	10 mg/ml	15.4 ± 0.23	-	NR	Mostafa et al., 2018
Staphylococcus aureus	GEO	1.0 mg/mL	17.1	2.0	Disruption of the bacterial cell membrane	Wang et al., 2020
Streptococcus iniae (S131)	GEO	1:1 dilution	23	4% (V/V)	NR	Hossain et al., 2019
S. iniae (S186)	GEO	1:1 dilution	19	4% (V/V)	NR	Hossain et al., 2019
S. iniae (S530)	GEO	1:1 dilution	18	4% (V/V)	NR	Hossain et al., 2019
S. iniae (FP5228)	GEO	1:1 dilution	13	4% (V/V)	NR	Hossain et al., 2019
Streptococcus parauberis (FP3287)	GEO	1:1 dilution	13	4% (V/V)	NR	Hossain et al., 2019
Xanthomonas oryzae pv.oryzae-strain A	GEO water extraction	400-500 µl/ml	20.66 - 22.66	-	Irregular shape with sunken surfaces	Abdullahi et al., 2020

MBC- Minimum Bacterial Concentration, MIC- Minimum Inhibitory Concentration, NR - Not Report, ZOI- Zone of Inhibition

The outer layer rich in lipopolysaccharides, gram-negative bacteria, was assumed to be less susceptible to EOs, which control direct interaction between both the EOs and the cytoplasmic membrane (Seow et al., 2014). Several researchers have also suggested the EO mode of action to their potential to enter the inner parts of cells via bacterial cell membranes and cytoplasmic membranes and thus break down cellular structures, creating them far more permeable to the surrounding EOs. Microbial organisms are almost certainly killed since the cytoplasmic membrane was interrupted or permeated by an inhibitory effect of interfacial contact that happened on the microspheres' surface (Li et al., 2019). In some cases, the EOs affect the enzymes responsible for the energy production or the synthesis of structural compounds in a cell (Amiri & Morakabati, 2017). The cell membrane was known to be the primary target site, when there was a significant amount of cell substance leakage from bacteria, they are prone to cell death. The interaction of EOs and microbial cell envelopes had also been investigated by scanning electron microscope to assess structural changes (Zhang et al., 2017).

Permeability of Bacterial Cell Membrane

The cytoplasmic membrane was responsible for preventing small ions from entering the cell and maintaining proper metabolism, as well as solute transport, turgor pressure control, and motility. The antibacterial function was also achieved by altering the permeability and morphology, and many antibacterial substances work by inhibiting bacterial growth by targeting the bacterial membrane (Li et al., 2019). As the membrane was permeabilized, the phenolic components are the most active and responsible. Protein denaturants, such as phenolic compounds, may alter cell permeability, causing swelling and rupture (Kerekes et a.l, 2015). Fluorescence-based assays which include fluorescence spectroscopy, confocal laser scanning microscopy (CLSM), and flow cytometry could also be used to examine changes in cell membrane permeability.

Essential oils could improve the membrane permeability of bacteria, because of this intracellular material leakage. One of the most important effects of EOs was to change the permeability of cell membranes, resulting in the leakage of ingredients of cells or the introduction of several other compounds into the cell. Proton, phosphate, and potassium leakage were all caused by increased membrane permeability, which disrupts pH balance and inorganic ion equilibrium (Kerekes et al., 2015). The leaking into the extracellular space of potassium could be seen as an indicator of increased membrane permeability and, eventually, the cell's death. The key feature of EOs was their hydrophobicity, which allows them to divide the bacteria's cellular membranes into lipids, interrupt the structure, and make it much more permeable. The permeability barrier supplied by cell membranes was essential for numerous cellular activities, such as the maintenance of cellular energy status, membrane-coupled energy-transducing activity, solute transport, and metabolic function. EOs primarily disrupt cellular architecture, resulting in membrane integrity breakdown and increased permeability, which adversely affects numerous cell functions, such as energy generation (membrane-coupled), membrane transport, and many other metabolic regulatory mechanisms (Swamy et al., 2016). The assessment of extracellular DNA, RNA, and protein content analysis was conducted to see how EOs affected bacterial cell membrane permeability. The mechanism of the antibacterial effect of EOs was associated with their hydrophobic nature, which causes the penetration of these materials into phospholipids of the bacterial cell membrane, causing disruption in the structure and an increase in permeability (Amiri & Morakabati, 2017).

Ginger EOs could prevent bacterial activity in a variety of ways. Initially, the antibacterial mechanism of ginger EOs indicated that the action was on the cell membrane, by interrupting the structure of the cell membrane, after that enhancing the permeability of the cell membrane, allowing bacteria to start losing their initial structural mechanisms and, at a certain concentration, potentially cause bacterial cell death (Wang et al., 2020). Ginger EOs altered the membrane permeability, causing the leaking of certain macromolecular compounds (nucleic acids and proteins) as well as the disruption of energy metabolism. Many research findings have highlighted the antimicrobial mechanism of ginger EOs in all these compounds (zingiberene, α-farnesene, 6-gingerol, and α-curcumin), arguing that by attacking cell membranes and cell walls, they could influence intracellular component permeability and release (Wang et al., 2020). As a result, even slight changes in the framework of the membrane could have a significant impact on cell metabolic processes and result in death.

The Impact on the Integrity of Cell Membranes

The cell membrane makes an efficient barrier between the external and internal transfer of major compounds and chemicals across the cell membrane (Abdullahi et al., 2020). During the growth of bacteria, the bacterial cell plasma membrane's integrity was important. The integrity of the cell membrane was important for bacteria survival, as it was a critical component of the essential biological activities that occur within the cells (Nazzaro et al., 2013). Any slight alterations to the cell membrane's structural integrity could interrupt the bacterial cell's regular metabolic function, resulting in incomplete lysis. Bacterial membranes were rich in enzyme systems that carry out a variety of critical metabolic functions, providing bacterial life activities with a relatively stable internal environment. It also serves as a material barrier and a site for specific transport of material and performs biological tasks, for example, hormonal action, enzyme response, cell recognition, and electronic transmission. When it comes to cellular structure and genetic material, nucleic acids and proteins are vital important macromolecules for cells. Gram-negative bacteria have a bilayer of lipids that provides additional protection against antimicrobial substances (Beristain-Bauza et al., 2019) and behave as an absorption barrier that inhibits macromolecules as well as hydrophobic compounds from entering the target cellular membranes (Li et al., 2019).

Bioactive compounds existing in EOs may be attached to the surface of cells and then invade the phospholipid bacterial cell membrane. Furthermore, it had revealed that the activity of EOs on cell membrane integrity changes membrane permeability, as a result, the significant loss of important intracellular substances such as reducing sugars, proteins, ATP, and DNA, when preventing energy (ATP) production and related enzymes, resulting in cell damage and electrolyte leakage (Chouhan et al., 2017; Cui et al., 2018; Lakehal et al., 2016). The structural integrity of the cellular membranes had been affected by its accumulation, which could adversely affect cellular functions having cause cell death (Bajpai et al., 2013; Lv et al., 2011). The main activities and the possible mode of action against phytopathogens by ginger EOs were shown in Figure 2.

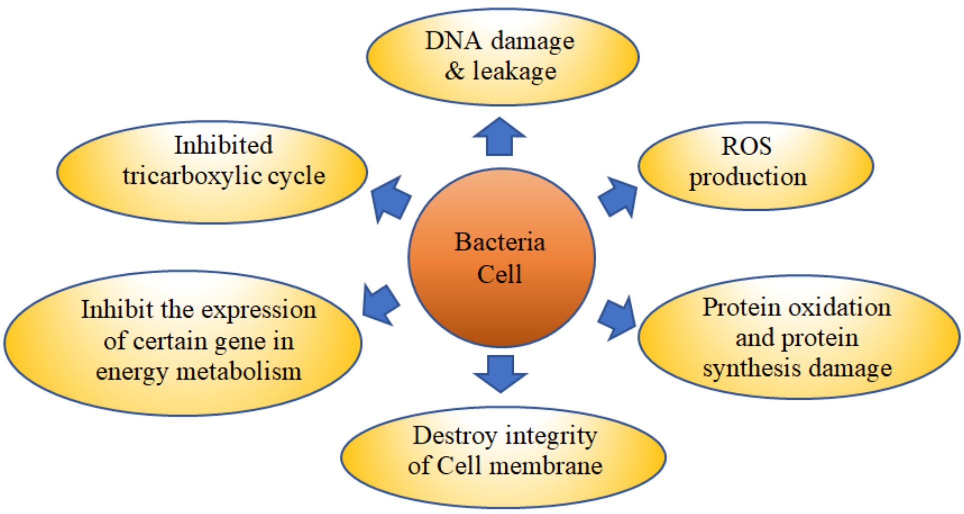

Figure 2. The possible antibacterial mechanism for the action of GEO

The Effect on Bacterial Gene Expression

When it comes to cellular structure and genetic material, nucleic acids and proteins were critical macromolecules for cells. The ginger EO treatment broke down the cell membranes, allowing nucleic acids to leak out of bacterial cells, it's also possible that this could lead to failure to take information on genetics and, ultimately, bacterial death (Wang et al., 2020). Some genes involved in bacterial energy metabolisms, such as alkaline phosphatase (ALPase), adenosine triphosphatase (ATPase), and β-galactosidase (β-GAL), were considerably reduced after treatment with ginger EOs (Wang et al., 2020). Furthermore, Citrate synthase (CS) and isocitrate dehydrogenase (ICDH) were also important catalytic reaction regulators in the TCA cycle. The loss of such proteins may have inhibited respiration and affected the TCA cycle, second, by interfering with the TCA cycle.

Ginger EOs may be able to suppress the bacterial strain's respiratory metabolism. Furthermore, the expression of several primary genes in the tricarboxylic acid (TCA) cycle pathway, and also some TCA cycle upstream genes, including citrate synthase (CS) and isocitrate dehydrogenase (ICDH), were also found to be considerably up regulated. Whereas downstream genes such as oxoglutarate dehydrogenase (OGDH), Dihydrolipoamide succinyl transferase (DLST), and dihydrolipoamide dehydrogenase (DLD) exhibited a trend toward downregulation. Upstream genes accumulated after ginger EOs treatment, while downstream genes were not expressed at all. The downregulation from these genes indicated that such ginger EOs treatment had caused damage to the cell membranes. Some genes, such as ATP-dependent clp protease (clpA, clpB), heat shock protein (GroE, GrpE), and small heat shock protein (IbpA, hslO), were significantly up-regulated. Additionally, genes involved in DNA metabolisms, such as DNA repair proteins (RecF and RecN) and DNA polymerase, were downregulated (holA) (Wang et al., 2020).

The Alteration of Protein Synthesis

Proteins were biological macromolecules located in bacterial cytoplasm and cell membranes that serve structural functions. The hydrophobicity of EOs prevents the formation of lipid membranes in bacteria. which involve the surface of the membranes with specific enzymes and proteins. This causes bacterial membrane permeability to increase and protein leakage in bacteria, both were linked in EOs with phenolic compounds (Wang et al., 2020). The release of proteins in the bacteria caused by Ginger EO disrupted the bacterial cell membrane, particularly for some proteins with a high molecular weight. Ginger EOs destroyed the bacterial cell membrane and protein leakage in the bacteria, especially in the case of large molecular weight proteins.

The ginger EO induced protein leakage by damaging the bacterial cell membrane, resulting in a decrease in bacterial cell protein level. The intercellular proteins in bacterial cells declined as the concentration of ginger EO increased a considerable downward trend (Wang et al., 2020). As a result, it functions as an antibacterial agent by interfering with the production of some proteins and enzymes, resulting in a reduction in protein expression in bacterial cells. These were some of the key causes that contribute to bacterial cell death after Ginger EO treatment, and a decrease in these enzymes could be one of them. EO treatment could reduce the action of β-galactosidase, ATPase, and ALP, which might be a major component of bacterial cell death. Ultimately, Ginger EOs had the potential to interrupt DNA metabolic processes by preventing DNA reproduction and the repair of important enzymes and proteins (Wang et al., 2020).

Effect on Cell Mitochondria Functioning

EOs could inhibit mitochondrial ATPase activity and decrease mitochondrial membrane potential in cells (Kerekes et al., 2015). Another possibility was will generate reactive oxygen species that oxidize and seriously damage lipids, proteins, and DNA (Li et al., 2019). Past studies have shown that phenolics contained in EOs could disturb the cell membrane, affect the mechanism of cellular energy (ATP) generation, and disturb the power of proton motivation, resulting in the leak of the cell's internal contents (Bajpai et al., 2012). There was a failure of membrane permeability as a result membrane permeability increased, resulting in a significant reduction in both ATP production and intracellular pH values. Ginger EO hydrophobic compounds bind to the lipophilic portion of the membrane and isolated mitochondria by destroying their function and integrity (Wang et al., 2020). Ginger EOs hydrophobic substances may also interact with isolated mitochondria with the lipophilic component of the membrane, interrupting its integrity and activity (nucleic acid, protein, metabolism of energy, and enzymatic activities) (Wang et al., 2020).

The Impact on the Membrane Potential

The role of MP in the metabolism of bacteria was a potential difference inside and outside the bacteria. The cell membrane structural damage may result in a reduction in MP bacteria (Cui et al., 2013). Cell membrane potential was used to perform essential life-saving activities, including the synthesis of enzymes, polysaccharides, nucleic acids, and some other cellular elements, cell maintenance and damage recovery, motility, and other mechanisms. Changes in the membrane potential MP play a vital role in bacterial metabolic activity (O'Bryan et al., 2015). The bacteria's surface behaves as a penetrating barrier, preventing macromolecules and hydrophobic substances from entering the cell membrane of the target cell. Research indicates that an EOs had an almost immediate reaction when an EOs affects a cell's membrane potential. Further, EOs caused an increase in electric conductivity leading to the fast leaking of tiny electrolytes, a protein and nucleic acid concentration in cell suspension, and a 3–5-fold decrease in bacterial metabolic action on membrane potential (Chouhan et al., 2017). Membrane potential loss is unfavourable to cell viability but it may occur as a result of membrane disruption. The depolarization of the cell membrane caused by the addition of ginger EOs results in decreased cell metabolism and bacterial death (Cui et al., 2018). Several findings have shown that other antibacterial substances affect cell membrane depolarization and subsequently lead to apoptosis; the effects were seen in the treated groups, which have a lower fluorescence intensity than the comparison group (Xu et al., 2019; Zhang et al., 2016).

The Effects of Cell Morphology

Essential oils cause destruction to microorganism cell walls and membranes, affect morphology and cause cytoplasmatic material to coagulate. The EOs and their compounds also have a diverse range of characteristics, especially membranes and cytoplasm, and under certain conditions, they significantly change the morphology of the cells (Nazzaro et al., 2013). The action of EOs and their constituents have different effects based on the form of the bacteria being studied, with rod-shaped bacteria being more vulnerable to EOs than coccoid bacteria walls. On the other hand, the majority of bacteria treated with the EOs became shriveled and irregular to varying degrees (Li et al., 2019). The cell membrane surface had been shrunk and pitted with surface holes, Furthermore, bacterial aggregation was observed. The changes in bacteria were caused by the impact of EO, which could result in cell membrane destruction and intracellular material losses. Bacterial species were destroyed by an interfacial inhibiting influence that existed on the surface of the microsphere, which disturbed or permeated the cytoplasmic membrane (Li et al., 2019). In terms of bacterial cell surface physicochemical properties, the hydrophobicity and surface tension parameters of bacteria were altered by the selected EOs components (Lopez-Romero et al., 2015) (Figure 3).

The Inhibition of Biofilm Formation

A biofilm was a microbial matrix that forms on various surfaces and contains extracellular substances, such as polysaccharides, proteins, nucleic acids, and lipids compose this substance (Kerekes et al., 2015). It was a three-dimensional colony of microorganisms that was coated and embedded in an extracellular polymeric material matrix that was self-produced. This multicellular structure protects biofilm-surrounded cells from adversarial environments such as high salinity and pressure, excessive temperature and pH, poor nutrients, and antibiotics. In pathogenic bacteria, biofilm was one of the virulence factors that were critical for bacterial colonization and disease development. Bacteria in a biofilm were much more tolerant than bacteria in the stationary phase.

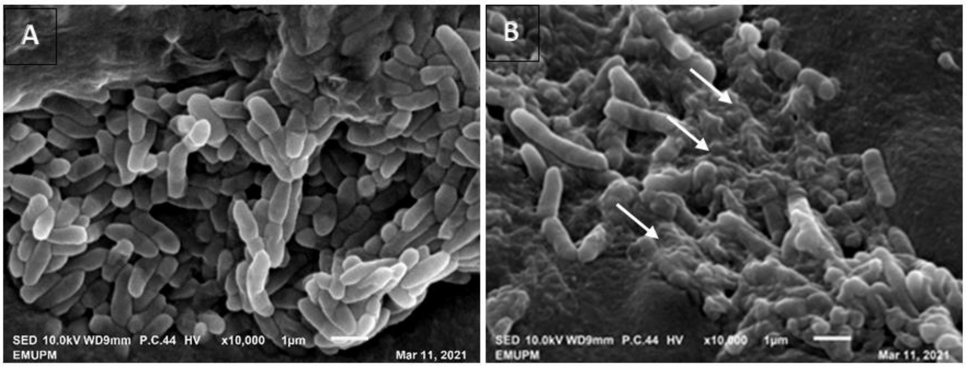

Figure 3. The effect of ginger essential oil on morphological changes of bacterial cells, which induces structural changes, is shown in this scanning electron microscopy. (A) Bacteria without essential oil treatment (control) show normal rod-shaped cells with smooth and regular cell surfaces. (B) Bacteria cells treated with ginger essential oils have an irregular shape with holes and were sunken on the surface.

(Mizan et al., 2020) Bacterial species were destroyed by an interfacial inhibition activity that existed on the surface of microspheres, which disturbed or permeated the cytoplasmic membrane. Biofilms were sessile microbial cell organizations that have a tight adherence to surfaces. Diverse gene expression could be caused by gradients in oxygen, nutrients, and electron acceptors during a biofilm. This communication was known as quorum sensing (QS) between these bacterial cells mediated the expression of genes and QS was important for biofilm formation, resistance, and virulence, as well as activated virulence factors (Kerekes et al., 2015).

Ginger influences membrane integrity and inhibits the formation of biofilms. The ginger extract inhibited biofilm formation by decreasing the level of bis-(30-50)-cyclic dimeric guanosine monophosphate (c-di-GMP) in *Pseudomonas aeruginosa* PA14 (Kim & Park, 2013). Furthermore, a crude extract and methanolic fraction of ginger blocked *Streptococcus mutans* biofilm formation, glucan synthesis, and adherence by downregulating virulence genes (Hasan et al., 2015). Attachment, microcolony formation, accumulation or maturation, and detachment or dispersal were the four primary phases of biofilm formation. EOs have quite a powerful anti-biofilm as well as anti-QS function (Szczepanski et al., 2013). The ability of certain EOs to suppress biofilm formation had received less attention; even so, several articles have indicated that they could be used as an effective inhibitor of virulence factors and biofilm formation. The major component of EOs could disrupt biofilm expansion in a variety of ways, including blocking the quorum-sense system, inhibiting flagellar gene transcription, and interfering with bacterial motility (Nazzaro et al., 2013).

NANOBACTERICIDE

Nanotechnology was the study of nanoscale (1–100 nm) substances defined when nanoparticles (NPs) have unique and new chemical, physical, and biological properties (Mishra et al., 2016). A lot of interest had been paid to nanomaterial applications in the farming sector (Mukhopadhyay et al., 2014: Sabir et al., 2014), as it provides a better delivery system for agricultural chemicals (Campos et al. 2014; Ghormade et al., 2011). Nanomaterials were the best approach to in-plant microbial pathogens management. These tiny materials also have many advantages compared to bulk materials, which could be improved effectiveness, reduced input, and eco-friendly. Nowadays, the synthesis of NPs through biotic means, either of microbial or plant basis was gaining popularity (Mishra et al., 2016). The mode of action of EOs against bacteria was significantly improved when it was converted into NPs, which was directly linked to the efficient entry of EOs into bacterial cells (Moghimi et al., 2016). Also, NPs could have been used to enhance the function and structure of pesticides by improving hydrolysing solubilities and resistance, optimizing photodecomposition, and offering more effective and controlled release to target pathogens (Grillo et al., 2016; Mishra et al., 2016). The growth and multiplication of pathogens were inhibited when the antimicrobial agents possess a bacteriostatic effect. More effective nano-bactericides have been developed owing to their advantage of having smaller sizes and superlative properties. Moreover, compared to macroparticles, these nanosized bactericides were more active sites available due to their smaller sizes (Wang et al., 2013).

Nanomaterials for the Generation of Nanobactericide

Various types of nanomaterials (NMs) have been produced to prevent microbial infections in agricultural applications. Metals, metal oxides, magnetic materials, and semiconductors were among the inorganic materials used to create nanobactericides. Some examples include SiO_2, ZnO, TiO_2, CaO, CuO, and Au (Balderrama-González et al., 2021). Mesoporous materials were inorganic nano-carriers that were widely utilized in drug delivery systems. The advantage of having a highly stable porous was fully utilized to load with bioactive cargo (Xu et al., 2019). Solid lipid NPs were spherical making them excellent candidates for lipophilic bioactive compound encapsulation. Carbon-based materials have recently gained more attention due to the existence of diverse allotropes of carbon, ranging from well-known allotropic phases such as amorphous carbon, graphite, and diamonds to newly discovered auspicious carbon nanotubes, graphene oxide, graphene quantum dots, and fullerene (Maiti et al., 2019). Organic compounds such as biobased polymers represent a sustainable and environmentally friendly substitute in agriculture. Organic-based NMs were made primarily of organic matter, as opposed to carbon-based or inorganic-based NMs. Organic NMs could be converted into desirable forms including dendrimers, micelles, liposomes, and polymer nanoparticles by using noncovalent interactions for molecular self-assembly and design. Micelles were spherical aggregates of surfactant molecules that spontaneously self-assemble, whereas Liposomes were spherical vesicles that contain at least one lipid bilayer. Dendrimer structures were made up of three parts: a focal core, dendrons, and cavities between dendrons (Safari et al., 2014). Biopolymers were polymers that were directly extracted/removed from biomass, or that were produced by the synthesis of monomers derived from renewable resources, microorganisms, or petroleum (Menossi et al., 2021). Nanogels were hydrophilic cross-linked networks of polymer chains that absorb large quantities of water. Surfactant-assisted homogeneous suspensions of nano-sized droplets of a dispersed phase in a continuous phase were known as nano-emulsions. They were all spherical and allow for the controlled release of cargo. Multiphase NPs and nanostructured materials with one phase on the nanoscale dimension were composite-based NMs. They could either combine NPs with other NPs or NPs combined with larger or bulkier materials (for example, hybrid nanofibers) or more complex structures, like metal-organic frameworks (Jeevanandam et al., 2018) (Figure 4).

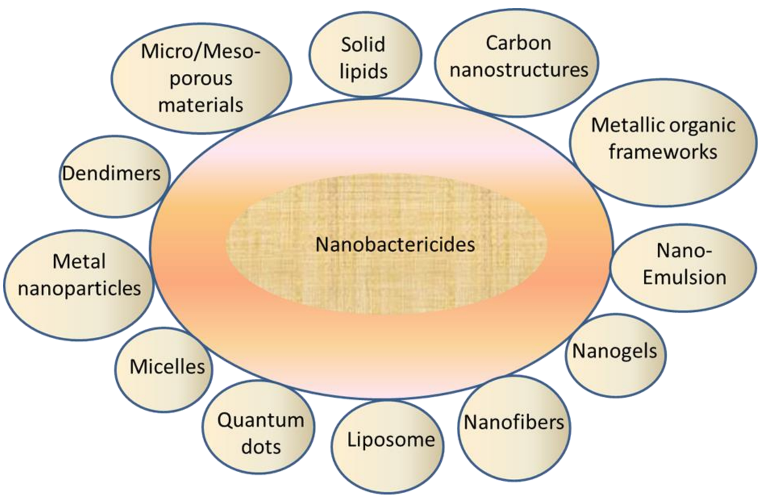

Figure 4. Synthesis of different nanobactericides utilizing different kinds of nanomaterials

Mechanism of Action of Nanobactericide

Nanobactericides were effective against a wide variety of bacteria. As a result, an NP derived from an inherently antibacterial material may possess multiple antibacterial mechanisms (Figure 5). Nanobactericides have the potential to damage the structure of bacteria cell membranes, causing the leakage of reducing sugars and the death of bacteria (Rajni et al., 2014). It affects the bacterial cell wall's surface integrity. Furthermore, tiny NPs (≤ 30 nm) could easily penetrate bacterial cell bodies. The cytoplasmic material was extruded from the cell, causing the cell to collapse. Increased membrane permeability through cell wall penetration. Nanobactericides cause harm when they interact with phosphorus and sulfur-containing compounds like DNA. Metal NPs have an affinity to interact with sulfur and phosphorus-containing biomaterials found in bacterial cells, such as DNA bases, and metal NPs could act on these soft bases and destroy the DNA, resulting in cell death.

It was reported that nanobactericides inhibit respiratory chain enzymes, interfere with membrane permeability, and interact with cytoplasmic and nucleic acids (Baker et al., 2019). Adsorption of NP to the surface of bacteria causes oxidative stress due to redox reactions, resulting in nanotoxicity. Nanotoxicity was caused by the formation of free radicals such as hydroxyl radicals, superoxide anions, and hydrogen peroxide. DNA replication, as well as amino acid synthesis, causes lipid peroxidation in bacterial cell membranes, compromising membrane semi permeability and suppressing oxidative phosphorylation. NPs furthermore exhibit antibacterial activity by either toppling the membrane potential and inhibiting ATPase activities to decrease the ATP level or by inhibiting the ribosome subunit from binding to tRNA. Both were equally able to inhibit producing ATP, forming pits that interrupt membrane integrity, and rupturing the cell membrane, resulting in pathogen death (Syed et al., 2018) NPs have been shown to influence bacterial signal transduction. The NPs dephosphorylate the peptide substrates on tyrosine residues, inhibiting signal transduction and bacterial growth (Rajni et al., 2014).

The Effect of Nanobactericide on Plant Physiology

Nanoparticle absorption and translocation have always been multifactorial and dependent on the properties of NPs, the dosages of NPs, the method of delivery, and the species of plants (Larue et al., 2012). Airborne NPs have the potential to associate the surface of the leaf as well as many other aerial plant parts. Biomagnifications of NPs take place frequently, contributing to changing physiological processes that influence plant development and growth (Wang et al., 2011). Plant cells interact with those NPs, causing changes in the expression of plant genes and, as a result, biological pathways, influencing plant development and growth (Nair et al., 2010). Even though the diameter of the cell wall was smaller in leaf tissue, those NPs could still penetrate and accumulate, through the efficacy of NP.

The NPs were affected by the catalytic, chemical, mechanical, or surface impact of plant physiology. The effectiveness of absorption and the impacts of numerous NPs on growth and physiological processes differ between plants (Nair et al., 2010). NPs also have an impact on plant physiology by mechanically blocking the structure of the cell. The spread of NPs into the environment was increasing the toxic effects on plants. The chemical impact in plant cells was induced by higher NP concentrations or collective intoxication at a particular location. The phytotoxic effect of NMs could be seen such as decreased root length, shoot length, biomass production enhanced genetic material disruption, and agglomeration observed by increasing concentrations of NPs. The NPs penetrate the plants via trichomes or through the stomata and a were then transported to the tissues of different plant systems. These NPs were observed to be toxic to plants at a much higher dosage only. NPs with their ultra-small size, unique shape, geometric structure, and superlative properties could have significantly improved the toxicity potential (Parthasarathi, 2011).

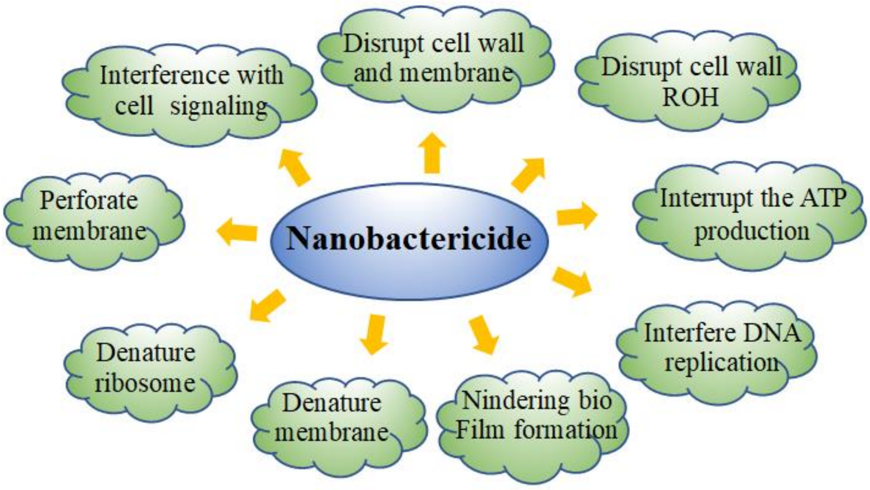

Figure 5. Mechanisms of nanobactericide antibacterial activity

NANOGEL FORMULATION OF GINGER ESSENTIAL OIL

Nanogels could be defined as sub-micron-sized, three-dimensionally crosslinked polymer networks, (Zhang et al., 2016). Polymeric networks were developed due to the internal crosslinking between the polymer chains (Wu et al., 2016). Nanogels were conventionally categorized as chemically or physically crosslinked nanogels, based on the crosslinking method. Nanogels could be synthesized using several methods. Chemical crosslinking facilitates the creation of covalent bonds during the polymerization of monomers with low molecular weight between both polymer chains or the crosslinking of polymer precursors. Although formed under mild reaction conditions, physically crosslinked systems were more unstable than covalently crosslinked counterparts. This was because they were stabilized by comparatively low relationships between polymer chains, such as hydrogen bonding, hydrophobic interactions, or ion interactions (Soni et al., 2016).

At very low concentrations, the bioactive nanogels displayed excellent bactericidal activity and exhibited mortality against bacterial strains. Moreover, nanogels were highly biocompatible with guest molecules and have a greater loading capacity (Chacko et al., 2012). As nanoscale carriers, nanogels offer numerous advantages, such as better delivery mechanisms, efficient storing, and slow-release characteristics. Consequently, nanogels typically have the potential to swell in water rather than dissolve due to the existence of cross-links in nanogels (Farag et al., 2013). Nanogels retain their structure, which was composed primarily of hydrophilic groups in polymers including such–OH, –CONH, –$CONH_2$, and SO_3H (Zhang et al., 2016). Furthermore, Excess water content was related to the properties of fluid-like transport properties of biologically active compounds that were considerably smaller than the size of gel pores (Neamtu et al., 2017).

Methods of Fabrication

It was known that the efficiency of bioactive compounds on plant-based products was reduced because of degradation and volatilization in field conditions (Borges et al., 2018). Nano-sized formulations have emerged as an effective possible answer to expand water dispersion and also protect EOs from destruction (Donsì et al., 2011; Acevedo-Fanietal et al., 2015). Another solution to overcome these limitations was by preparation of various formulations of biologically active plant compounds with polymers, stabilizers, plasticizers, and biodegradable antioxidants. Bioactive compound stability, adherence, or controlled release was frequently used based on the nature of formula polymers, emulsifiers, surfactants, solvents, stabilizers, defoamers, and other parts (Gasic et al., 2013).

Different kinds of NPs could be used to prepare nanocomplexes to improve the bactericidal action of EOs (Gomes et al., 2011). Natural and environmentally friendly polymer NPs have attracted a lot of interest in the encapsulation of EOs. Nano-encapsulation had recently emerged as an effective method to protect EOs from evaporation and oxidation (Beyki et al., 2014).

A range of polymers, such as alginate, chitosan, poly (vinyl alcohol), poly(ethylene), poly (ethylene oxide), poly (vinylpyrrolidone), (N-isopropyl acrylamide) could be used in nanogel formulations (Viswanathan et al., 2018). The emulsification-ionic gel method was also popular because it was non-toxic and one of several procedures used to create EOs loaded with chitosan nanoparticles (Hosseini et al., 2013; Shetta et al., 2019). Cross-linking such as chemical and physical cross-linking, were the key points of the nanogel production process. Ionic gelation is just a slight, easy, and organic solvent-free technique for the development of durable nano-sized particles among the many methods. Ionic gelation was caused by the connection between positively charged polymers including such chitosan and polyanions, including Penta sodium tripolyphosphate (TPP), which, without the use of high temperature and toxic crosslinking agents, contributes to the formation of inter-and intra-molecular cross-linkages (Hasheminejad et al., 2018; Keawchaoon et al., 2011; Woranuch et al., 2013). For EO encapsulation, various lipid-based and polymeric nanocarriers were used. Chitosan had recently received a huge amount of interest mostly in the encapsulation of bioactive compounds and EOs owing because of its non-toxicity, biocompatibility, biodegradability, and antibacterial activity, as well as its potential to construct gels, film, and particles (Keawchaoon et al. 2011; dos Santos et al., 2012; Wang et al. 2014). The encapsulation of EOs increases the antimicrobial action and its controlled release while protecting the EOs (Aghazadeh et al. 2016; Rahmani et al. 2014).

Advantages and Disadvantages

Nanoformulations and delivery have the potential to revolutionize sustainable and efficient agricultural practices, as well as make the agroindustry more environmentally friendly and secure. Nanoformulations were specifically designed to enhance the solubility of insoluble or poorly soluble active ingredients while also releasing the biocide in a controlled and targeted manner (Yadav et al., 2022). Nanogel-based carrier systems were highly biocompatible and biodegradable, they were a highly promising field these days. The biodegradability of nanogel makes these nanocarriers nontoxic. Nanogel systems have demonstrated their ability to deliver active ingredients (AIs) in a controlled, sustained, and targetable manner (Neamtu et al., 2017). The addition of a polymeric network to nanogels allows for controlled drug release from the formulation. Bio-nanostructured systems have several advantages, including durability, compatibility with EO molecules, low environmental impact, soil degradability, and lack of toxicity (Menossi et al., 2021). In addition to those certain advantages, bio-nano formulations could comprise trace amounts of EOs with pesticide properties, allowing them to be used as slow-release carriers for agrochemicals. The particle size of the formulation was also controlled by polymeric networks (Hickey et al., 2015). Nanogels have an advantage over macro-sized networks because their size allows them to interact with cells more specifically and even be internalized. They also behave differently than solid and self-assembled polymer-based AI delivery systems due to their soft nature. A small quantity of an AI per area was adequate for the application that may facilitate consistent delivery of AIs which were more efficient for longer durations. Interestingly, for controlled release nanoformulations remained inactive until the AIs were released. The use of a polymer matrix in nanoencapsulation may improve the dispersion of hydrophobic AIs in aqueous solutions, permitting slow release with high selectivity and without interfering with biocidal activity. Encapsulation technology was applied to agricultural applications because hydrophobic or hydrophilic bioactive compounds could be entrapped in controlled release formulations prepared using encapsulation technology. These could reduce the number of pesticides used, enhance the stability of the unsteady core materials, suppress the sharp odors of the released chemicals, and secure biocompatibility to carrier systems. Another benefit was that by reducing exposure to toxic chemical compounds, non-target surrounding or distant flora and fauna will be less affected.

However, nanogels, similar to other AI delivery systems, have limitations in terms of optimal biodistribution, degradation mechanisms, and component toxicity (Neamtu et al., 2017). An expensive technique was required to remove all solvents and surfactants at the end of the preparation process. There may be residual surfactant or monomer residues, which could have negative effects. A portion of the particles was in the micrometre range.

Opportunities and Challenges

Nanotechnology will be a key driver in the upcoming agro-based technical revolution, which assures a more sustainable, effective, and resilient agricultural system while also promoting food security. Nanogel bactericides reduce crop losses by improving crop disease management and increasing crop resistance. The agrochemical efficiency also could be further improved through targeted delivery. The most important property of a nanogel in an aqueous environment was its swelling. It was influenced by structural characteristics such as the chemical structure of the polymer matrix, the degree of cross-linking, the charge density in polyelectrolyte gels, and environmental variables as external triggers (Neamtu et al., 2017). Nano-delivery systems could improve pesticide controlled-release properties, active ingredient solubility, protection against premature degradation, and active ingredient stability. Due to their small size, nanobactericides could pass through biological barriers and diffuse into the plant's vascular system after being applied to the roots or leaves. Many of these nanomaterials were metastable, allowing for controlled release to promote plant disease resistance (Kah et al., 2019). Nanogel could significantly increase the effectiveness of pesticide application, mitigating the harmful effects on the environment and embodied energy losses.

Despite the numerous advantages that EO-loaded bio-nanomaterials present as potential nanotechnology applications in agriculture, a few challenges must be overcome before this technology could make significant contributions to agriculture. The major drawbacks were the industrial scalability of nano formulations and the EO extraction methods and their associated expenses. Other limitations of nanogels were poor drug loading efficiency and suboptimal drug release regulation. A strong interaction between drug and polymer could reduce the hydrophilicity of nanogels and lead the structure to collapse, entrapping the drug molecules irreversibly and increasing the hydrophilicity of the nanogel matrix (Sharma et al., 2014). Also, excessive amounts of surfactants or monomers in nanogel may harm the formulations. Furthermore, the technical constraints associated with the mass production of nano-carriers for agricultural use should be correlated with the economic boundaries that low production costs and configure potential revenues for producers. More research was required to properly evaluate not only the fate of nano-encapsulation materials and payloads, physical-chemical and biological performance but also the long-term environmental risks and economic viability.

CONCLUSION AND FUTURE PERSPECTIVES

Suboptimal lands, characterized by poor soil fertility, low organic matter content, water stress, and other environmental constraints, significantly influence the prevalence and severity of phytopathogenic bacterial infections. These conditions not only weaken plant health, making them more susceptible to bacterial pathogens, but also create favourable environments for certain bacterial populations to thrive. In such lands, factors like nutrient deficiencies, pH imbalance, and excessive soil moisture due to poor drainage contribute to plant stress, reducing their natural defences against microbial infections.

The impact of suboptimal land on bacterial disease management necessitates the development of novel, efficient, and environmentally friendly solutions. Conventional chemical bactericides may have limited effectiveness in these regions due to rapid degradation, leaching, or reduced bioavailability in extreme soil conditions. Furthermore, excessive reliance on synthetic pesticides could lead to soil toxicity, microbial imbalance, and long-term environmental degradation. Nanobactericides formulated with ginger essential oil (GEO) present a promising alternative for managing bacterial diseases in suboptimal lands. The nanoencapsulation of GEO enhances its stability, increases its solubility, and ensures a controlled release, making it more effective under challenging soil conditions. Unlike conventional bactericides, nanogels and nanoemulsions could improve adherence to plant surfaces, resist environmental degradation, and provide prolonged antibacterial activity. Additionally, chitosan-based nanoformulations contribute to plant growth promotion by enhancing nutrient uptake and inducing plant defence responses, which was particularly beneficial in nutrient-poor suboptimal lands.

The application of nanobactericides in suboptimal lands aligns with the principles of sustainable agriculture, as it minimizes chemical inputs while maximizing disease control efficacy. Future research should focus on optimizing nanoformulations to suit varying suboptimal soil conditions, ensuring their adaptability and long-term benefits in improving plant resilience and productivity in these challenging environments.

Phytopathogenic bacteria have a direct impact on a variety of crops worldwide as well as an adverse impact on agricultural production owing to their consequent economic damage and environmental effects. Nanotechnology had been an interesting approach with potential possible applications for plant protection. Plant essential oil was an important aspect of decreasing the adverse impacts of synthetic chemical pesticides. The essential oil could inhibit the growth of pathogens effectively, thereby possibly becoming a good alternative to synthetic antimicrobials. Ginger EOs were rich sources of volatile compounds formed as secondary metabolites in ginger that also were extensively used as a possible substitute for chemically synthesized antimicrobials and antioxidants. Essential oils obtained from ginger have excellent antimicrobial activity against numerous bacterial pathogens. Ginger had antimicrobial properties and contains bioactive compounds including gingerols, shogaols, and paradols. Essential oils have the potential to disturb the cell membrane of bacteria by improving membrane permeability, allowing intracellular ingredients to leak out, and disrupting the target pathogens' cell metabolism. Some of these antibacterial studies utilizing essential oils have failed to provide strong evidence of both their chemical properties and mode of action. For novel applications in agriculture, essential oils, it's necessary to better understand their mode of action. Therefore, more research should be needed to discover their active ingredients the molecular mechanisms of essential oils, and their potential toxicological effects to optimize their possible application. The pesticide industry requires environmentally friendly alternative molecules to handle plant diseases caused by bacterial pathogens. Therefore, ginger essential oils could be a potential source of alternative bacterial pathogens and could perform a significant role in the development of a new bactericide for the control of a wide variety of bacterial pathogens.

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