

Review

Bacterial elicitors of the plant immune system: An overview and the way forward[☆]

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ABSTRACT

A wide variety of root-associated bacterial mutualist species sensitize plant defenses to counteract pathogen infections. These beneficial bacteria produce myriad molecules that induce systemic resistance (ISR) in plants. Here, we review pioneering and recent studies describing the role of different ISR elicitors, including quorum sensing molecules, lipids, oligosaccharides, proteins, iron-chelating molecules, and volatiles. The concepts and differences between ISR and other plant immune responses, such as Localized Acquired Resistance (LAR) and Systemic Acquired Resistance (SAR) are also explored. We also highlight the necessity of understanding plant responses to such a wide chemical diversity of molecules. Finally, we discuss the urgency of using such elicitors to develop more sustainable agriculture by helping plant crops defend themselves from invading pathogens.

1. Introduction

Plants are sessile organisms surrounded by a great diversity of macro- and micro-organisms, where they may have beneficial, neutral, or pathogenic relationships. In the latter case, plant pathogens, which usually include viruses, bacteria, nematodes, fungi, and insects, can damage the plant and cause various symptoms that damage its health and even cause death (Besset-Manzoni et al., 2018; Lemanceau et al., 2017). In the case of vegetable crops, pathogens can cause huge economic losses, which can be counted in billions of dollars. In some cases, up to 70% of crops are lost (Savary et al., 2019; Syed Ab Rahman et al., 2018). Clearly, this is an area of opportunity to improve plant production in a sustainable way, since the first option to reduce or eliminate diseases in crops includes the use of toxic agrochemicals (Shailendra Singh, 2015). Therefore, understanding plant-microorganism interactions (whether pathogenic or beneficial) is urgent, both economically and environmentally.

Upon detection of potential phytopathogens, plants activate their systemic acquired resistance (SAR), among a plethora of defense

responses, a complex process that triggers a series of reactions that turn on the plant's immune system (Henry et al., 2013). In this way, the pattern recognition receptors (PPR) of plant cells recognize various pathogen-associated molecular patterns (PAMPs), thus are one of the first filters for the recognition of a potential pathogen (Henry et al., 2012; Macho and Zipfel, 2014). The second filter is the NOD-like intracellular immune receptor (NLR). These receptors recognize (directly or indirectly) virulence effectors secreted by pathogens into plant host cells, where effector molecules can subsequently trigger the immune system of the plant host. Understanding of pathogen recognition mechanisms and the molecular responses and defense signals that plants develop when encountering pathogens has come a long way in recent years, owing to molecular techniques and the generation of mutants (Cheng et al., 2017; Rodriguez et al., 2019; Yu et al., 2021); however, the discovery of some receptors has been left behind, and only a few have been characterized in a few plant species (Chen et al., 2020).

Plants can also recognize non-pathogenic microorganisms that could interact with them and provide benefits through mutualistic or symbiotic processes. Thus, plants detect microbe-associated molecular

Abbreviations: SAR, systemic acquired resistance; ISR, induced systemic resistance; CLPs, Cyclic lipopeptides; DAMPs, damage-associated molecular patterns; LAR, Localized Acquired Resistance; MAMPs, microbe-associated molecular patterns; PPR, pattern recognition receptors; PAMPs, pathogen-associated molecular patterns.

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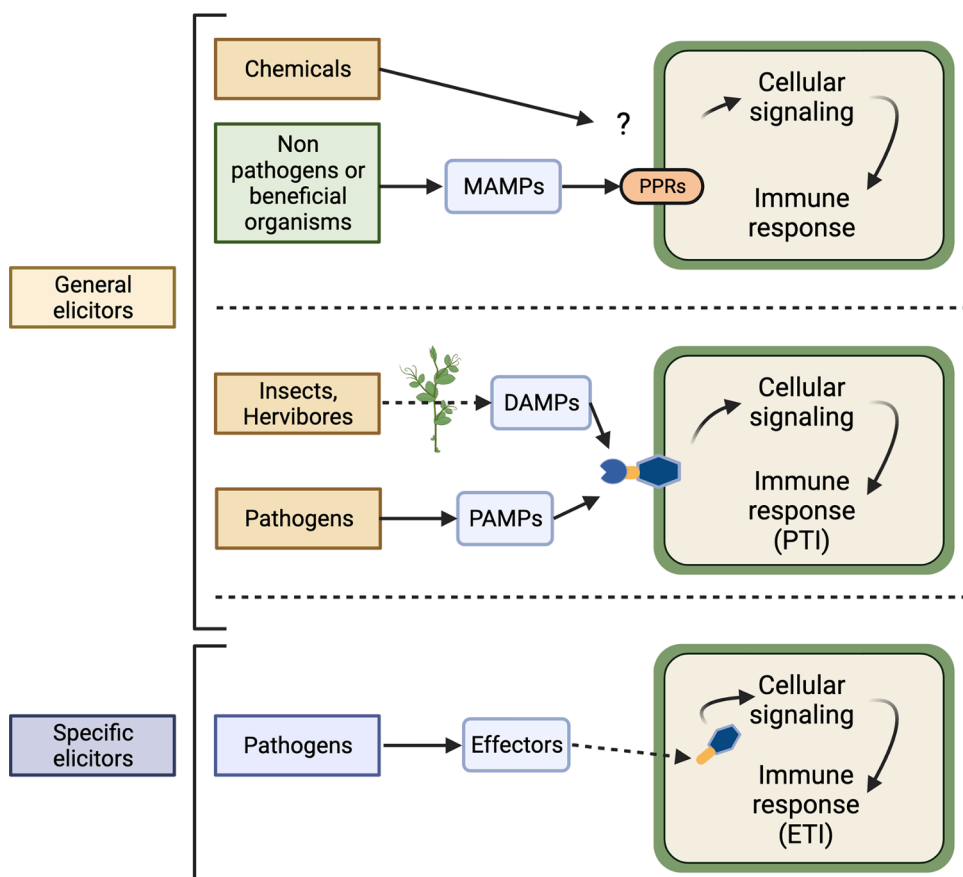


Fig. 1. Description of functionality of general and specific elicitors produced by diverse macro and microorganisms, pathogenic and non-pathogenic (beneficial microbes). Chemicals are recognized by unknown receptors, while PPRs are receptors of MAMPs. MAMPs: Microbe-Associated Molecular Patterns; DAMPs: Damage-Associated Molecular Patterns; PAMPs: Pathogen-Associated Molecular Patterns; PPRs: Pattern Recognition Receptors; PTI: PAMP-Activated Immunity; ETI: Effector Triggered Immunity. Adapted and redrawn from (Henry et al., 2012).

patterns (MAMPs), to which they respond by activating signaling pathways to activate their immune system, a process better known as induction of systemic resistance or ISR (Olanrewaju et al., 2019; Wu et al., 2014; Yu et al., 2019). Therefore, the ISR can be triggered by a series of quorum sensing molecules, rhamnolipids, protein patterns, antibiotic compounds, among others, which are usually produced by beneficial microorganisms (Klopper et al., 2004; Pršić and Ongena, 2020), including bacteria.

Elicitors can be classified as general or specific (Fig. 1). The general elicitors are chemical compounds produced by non-pathogenic microorganisms, as well as MAMPs themselves. However, non-specific elicitors can also be PAMPs or Damage-Associated Molecular Patterns (DAMPs) resulting from signals caused by the action of a pathogenic agent, such as insects or some herbivores (Thoms et al., 2021). The perception by a plant of general elicitors triggers different reactions in the plant, activating the so-called basal resistance or PAMP-Activated Immunity (PTI). Eventually, secondary innate immunity or effector-triggered immunity (ETI) responds to specific elicitors produced by pathogens that produce effector proteins called avirulence proteins (Avr) (Dodds et al., 2009). This specificity is provided by the R proteins of plants that recognize attacker-specific effectors (Choudhary et al., 2007).

2. Localized acquired resistance (LAR), systemic acquired resistance (SAR) and induced systemic resistance (ISR)

The SAR and ISR are two parallel processes that differentiate on the chemical nature of the elicitor which triggers a "signal" to give a systemic defense response at a point other than where the plant is infested by the pathogen. When resistance is established in the tissue surrounding the site of the initial infection, a type of resistance called Localized Acquired Resistance (LAR) is recognized (Henry et al., 2012). Further, the

production of enzymes, such as chitinases and glucanases, by pathogens triggers the SAR response, mainly inducing the synthesis of pathogenesis-related (PR) proteins (Astha et al., 2019; Bhardwaj et al., 2021). On the other hand, beneficial organisms are known not to trigger such PR protein production. In addition, pathogens trigger SAR through signals that involve hormones such as salicylic acid (SA), while ISR responds through jasmonic acid (JA) and ethylene. Downstream, the participation of the protein NPR1 (an ankyrin-repeat family protein) is important for transmitting the signal where both signaling pathways coincide, whether they are SAR or ISR (Chen et al., 2020). According to Dong (2004), a redox change transforms NPR1 oligomers into monomers under the influence of SA. Subsequently, these NPR1-derived monomers are transported from the cytoplasm to the nucleus, where they interact with transcription factors (TGA) specific for the expression of PR genes. Thus, the NPR1 protein is a key regulatory factor found in pathways where multiple defense pathways coincide, such as SAR and ISR. During previous studies, it has been proposed that some pathogens can activate plant host defenses through cross-linked pathways depending on their trophic state, whether bio- or necrotrophic (Glazebrook, 2005). A general view of the SAR and ISR responses is provided in Fig. 2.

Loon (2007) proposed another way to define induced resistance, either SAR or ISR, by alluding to the induced state as the "enhanced defensive capacity (EDC)" of the plant. In this state, the plant faces a series of challenges that allows it to defend itself and survive the attack of pathogens; thus, knowledge of the mechanisms and elicitor molecules produced by beneficial microorganisms could have a great impact on the suppression of plant related and sustainable agriculture.

3. Elicitors by beneficial bacteria

Bacteria that promote the growth, development, or health of plants

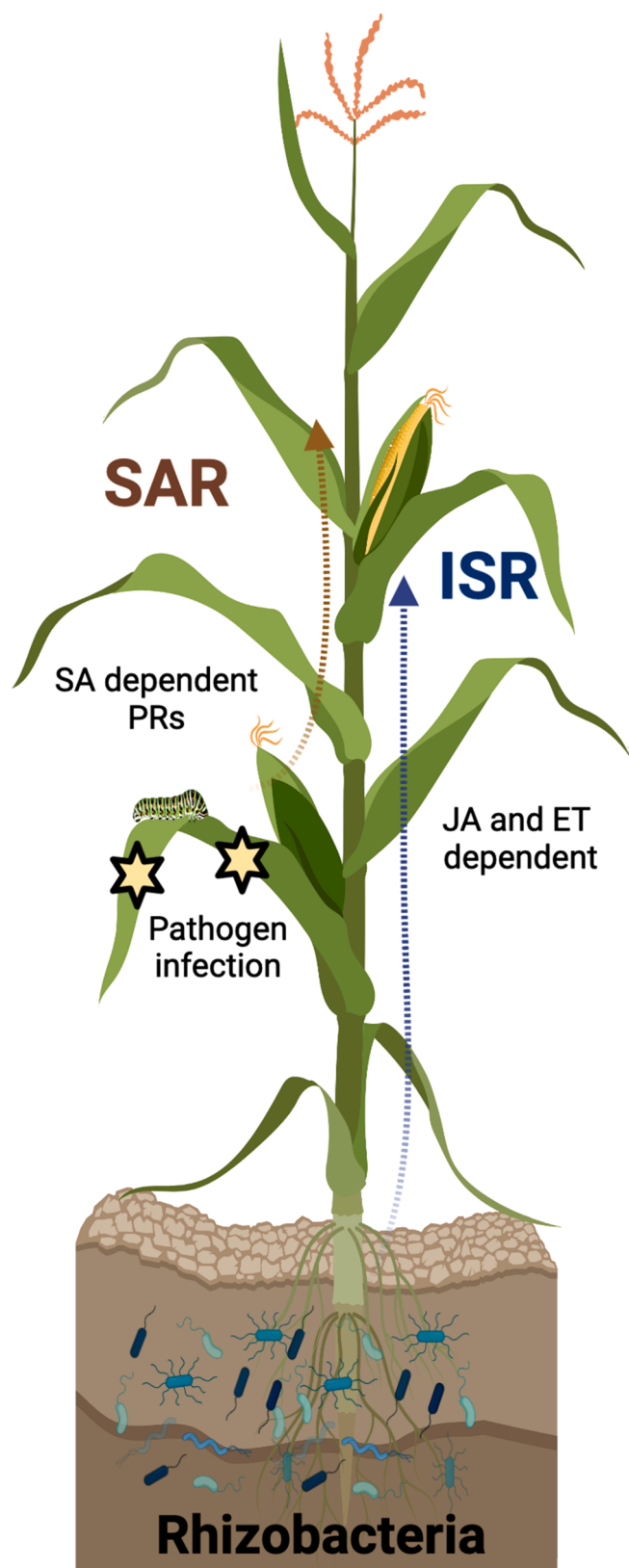


Fig. 2. A general overview of the systemic acquired resistance and induced systemic resistance mechanisms. Adapted from (Syed Ab Rahman et al., 2018).

are commonly called plant growth-promoting bacteria (PGPB) (Adeleke et al., 2021; Massa et al., 2022). Plant growth-promoting bacteria can associate with plants and form part of their beneficial microbiome with different points of interaction, mainly the phyllosphere, endosphere, or rhizosphere. Depending on the microecosystem inhabited, they can be classified as phyllospheric bacteria, endophytes, or rhizobacteria (del Barrio-Duque et al., 2019; Schlechter et al., 2019; Srivastava et al., 2021). Mechanisms for stimulating plant growth can be classified as direct or indirect. In the direct case, bacteria produce a series of hormones or compounds that improve the acquisition of nutrients in the plant. An indirect way of improving plant growth and health involves inhibiting the damaging effects of pathogens, either by restricting their growth through the production of antibiotic compounds or by stimulating the plant's immune system. (Bhattacharyya and Jha, 2012; Nascimento et al., 2020).

3.1. Cyclic lipopeptides

Cyclic lipopeptides (CLPs) are molecules with antibiotic activity that are produced as a part of the secondary metabolism of a wide variety of bacteria. Species from genera such as *Actinomyces*, *Streptomyces*, *Bacillus*, and *Pseudomonas* have been widely studied for their production of such metabolic molecules (Saravanakumar et al., 2019; Villa-Rodriguez et al., 2021). According to Schneider et al. (2014), CLPs are composed of a lipid tail attached to a short oligopeptide that cyclizes to form a lactam or lactone-type ring, either between an amino acid and an amino group or hydroxyl containing a fatty acid residue or between two amino acids in the amino acid chain.

Previous study enlisted different CLPs produced mainly by *Bacillus* and *Pseudomonas* (Pršić and Ongena, 2020). For example, strains of *B. amyloliquefaciens* produce surfactin, mycosubtilin, fengycin, and iturines, which induce protection in crops such as tomato, strawberry, cotton, and chilli pepper, against pathogens such as *Colletotrichum gloeosporioides*, *Botrytis cinerea*, *Magnaporthe* or *Phytophthora cinnamomi*. Other strains of *Pseudomonas* produce CLPs such as entolysin, lokisin, sessilin, orfamide, and massetolide A, which are involved in the protection of plants such as beans and rice against pathogenic species such as *Rhizoctonia solani* and *Phytophthora infestans*, etc. Some of these cyclic lipopeptides, and others with novel architectures, can be completely or semi-synthesized (Gao et al., 2022), which provides a great opportunity for their application in agriculture as a method of direct plant protection against pathogens, but also as part of turning on the immune system of crops.

3.2. Cyclodipeptides

Other elicitors of ISR in plants include cyclodipeptides (CDPs), which are formed from two amino acids by cyclodehydration, are produced by various beneficial bacteria and/or potentially pathogenic strains, such as *Pseudomonas aeruginosa*, and these have also been characterized as ISR elicitors (Solis-Ortiz et al., 2022). For example, Wu et al. (2017) reported that cyclo (l-Pro-l-Pro) and cyclo (d-Pro-d-Pro) could induce defense responses and systemic resistance in plants such as *Nicotiana benthamiana*, and reduce symptoms of infection caused by *Phytophthora nicotianae* and tobacco mosaic virus (TMV). Here also observed that the application of cyclodipeptides involved the possible participation of SA in the signaling pathway, as well as increasing the expression levels of proteins such as PR-1 α and PR-1a. Other CDPs, such as cyclo (l-Pro-l-Val), cyclo(l-Pro-l-Phe), and cyclo(l-Pro-l-Tyr) produced by *Pseudomonas aeruginosa* have also been associated with the stimulation of the growth of *Arabidopsis thaliana* (Ortiz-Castro et al., 2011). Recently found CDPs can stimulate defense responses in *Arabidopsis*, including by the induction of genes such as LOX2, which are associated with JA production. This result indicated the possible signaling pathway that induces the *Arabidopsis* immune system through CDPs is JA-dependent (Solis-Ortiz et al., 2022).

3.3. Quorum sensing molecules and organic volatile compounds

The metabolic process known as quorum sensing deals with the coordinated regulation of different genes in a bacterial population, where small chemicals or peptides play a significant role. In microorganisms such as *Pseudomonas aeruginosa* and *Vibrio fischeri* (gram-negative bacteria), molecules such as acyl homoserine lactones (AHLs) can regulate processes of biofilm formation or bioluminescence (Cellini et al., 2020; Laj et al., 2022). Likewise, AHLs are part of the interkingdom dialogue, and not solely part of bacteria-bacteria communication (Laj et al., 2022; Schikora et al., 2016), so that they can regulate plant growth stimulation processes, in addition to participating as immunity elicitors.

It has recently been proposed that some AHLs produced by beneficial bacterial endophytes can induce responses in the plant's defense system through the activation of defense-related genes. By activating ISR, the plant can cause structural hardening through callose production, preventing easy access to potential pathogens (Pathak et al., 2022).

The previous study identified a molecule related to the regulation of quorum sensing, the rhizobacterial volatile N,N-dimethylhexadecylamine (DMHDA), and its role in the induction of defense genes in *Medicago truncatula* (Montejano-Ramírez et al., 2020). DMHDA is a volatile compound found in some beneficial rhizobacteria, such as *Arthrobacter* spp. UMCV2, *Sinorhizobium meliloti* 1021, and *Pseudomonas fluorescens* UM270, having different biocontrol roles against pathogenic fungi and acting as a plant growth stimulator (del Carmen Orozco-Mosqueda et al., 2013; Hernández-León et al., 2015; Martínez-Cámara et al., 2019). However, it was interesting to note that this volatile could also turn on defense genes, such as MtMYC2, MtPR4, and MtDef2.1, those are players in the ISR pathway. Interestingly, the JA pathway is not involved in plant responses (Montejano-Ramírez et al., 2020). Thus, DMHDA, which is a lipochitose structurally related to bacterial quorum sensing signals (Chung et al., 2016), is involved in ISR induction and is also a relevant compound mediating enhanced plant growth by improving nutrient acquisition (e.g., iron uptake).

Other volatile organic compounds (VOCs) produced by bacteria that act as elicitors include 2,3-butanediol (2,3-BD), which is produced by *Bacillus* and *Pseudomonas* strains (D'Alessandro et al., 2014; Park et al., 2018). This volatile compound was one of the first compounds described as a plant growth promoter, and it has recently been reported as an immune response elicitor (ISR) in plants. However, 2,3-BD can also activate SAR, as shown by the work of (Park et al., 2018), who evaluated the effect of 2,3-BD and observed an upregulation of genes involved in ROS detoxification and overexpression of PR-3, PR-4b, PR5 (TLP), PR5 (OSM), PR6, and the non-expressor of PR1 (NPR1). During this study it was evaluated the role of *Paenibacillus polymyxa* DSM 365 in mitigating the cell damage caused by the plant pathogen *Phytophthora parasitica* var. *Nicotianae* through inoculation in leaves. Other volatile compounds such as tridecane or hexadecane, also produced by *P. polymyxa* but evaluated in their pure form, have been shown to be elicitors of systemic resistance in *Arabidopsis* (Park et al., 2013). Tridecane may induce an ISR response in plants but has a negative effect on plant growth (Ali et al., 2015).

3.4. Rhamnolipids

Rhamnolipids are biosurfactant molecules (surface-active molecules of microorganisms) with various industrial applications (Varjani et al., 2021). They are produced naturally (mainly) by *Pseudomonas aeruginosa*, although it has also been reported that *Pseudomonas chlororaphis* and certain species of *Burkholderia* can occasionally produce them (Soberón-Chávez et al., 2021). Because *P. aeruginosa* is a potential pathogen of humans and plants in some environmental situations, its production and application as a bioinoculant in plant research may be limited. However, the production of rhamnolipids as ISR elicitors has great potential, since its application of the pure compound has managed to protect *Brassica napus* plants against the gray mold pathogen, *Botrytis*

cinerea. Even *B. napus* seedlings overexpressed defense genes, such as BnPR1, BnPR4, and BnPDF1.2, which were homologous to AtPR1, AtPR4, and AtPDF1.2, in *A. thaliana*. Additionally, it was found callous deposits and stomatal closure to be efficient structural protections against the pathogen *B. cinerea* (Monnier et al., 2018); that was also considered one of the ten most injurious in plant research and the cause of millions of dollars' worth of economic losses in crops such as strawberries and winemaking (Dean et al., 2012).

3.5. Lipopolysaccharides, exopolysaccharides and flagellin

Lipopolysaccharides (LPSs) form an important part of the outer membrane of gram-negative bacteria (Sumayo et al., 2013). The function of LPSs is to provide integrity and functionality to the membrane, which allows them to form a barrier against various environmental factors and interact with plant roots in the rhizosphere. Lipopolysaccharides have three functionally distinct domains: a lipophilic moiety, core oligosaccharide, and O-specific polysaccharide (Hernández-Esquivel et al., 2021).

On the other hand, exopolysaccharides (EPSs) are carbohydrates that were secreted by various species of bacteria, as well as other groups of microorganisms (Abdalla et al., 2021). In the case of some pathogenic bacteria, EPSs can be virulence factors (Cassin and Tseng, 2019), whereas in plant growth-promoting bacteria, mainly those that inhabit the rhizosphere (Plant Growth-Promoting Rhizobacteria), the EPSs produced were relevant for rhizosphere colonization. Some species that produce LPSs include *Pseudomonas*, *Agrobacterium*, and *Rhizobia* (Santoyo et al., 2021).

Lipopolysaccharides and EPSs have been recognized as elicitors of immune responses in plants for decades (Ranf, 2016). In 2008, Park et al. (2008) determined that EPSs produced and purified from the rhizobacterium *Burkholderia gladioli* strain IN26 stimulated an ISR response in cucumber plants during infection with the fungal pathogen *Colletotrichum orbiculare*. Likewise, LPSs of beneficial strains of *Pseudomonas* manage to activate the immune system of radish plants, thereby reducing the harmful effects of *Fusarium* wilt. This study involved the generation of a mutant in the antigenic-O side chain of the lipopolysaccharide, which was characterized by a greenhouse bioassay (Leeman et al., 1995). During previous studies on the role of LPSs as ISR inducers have been conducted in tomato, *Arabidopsis*, radish, and carnation plants, where it was shown resistance against pathogens such as *Fusarium* spp. (Meziane et al., 2005). More recently, LPSs from the bacterium *Ochrobactrum lupini* KUDC1013 was shown to induce systemic resistance (ISR) in tobacco plants to soft rot caused by the pathogen *Pectobacterium carotovorum*. Further, flagellins from the same strain produced a similar effect (Sumayo et al., 2013). There is urgent requirement to make studies on the specific role of LPSs, including deletion of domains in genes important for the synthesis of LPSs and other components (apart from the region of the O-antigen), on the stimulation of the ISR. Whereas in other studies had focused on the role of LPSs as a plant growth stimulator (Sigida et al., 2020).

Flagellin and LPS from *P. fluorescens* strain WCS358 have also been characterized as effective inducers of resistance in *Arabidopsis*; however, both determinants were not equally effective, or their activity as elicitors was null in tomato and pea plants (Meziane et al., 2005). A previous study explored on the mechanism of activation of the ISR response in plants and the connection between flagellin and the mode of recognition by plant receptors in a two-step model (Meindl et al., 2000). The authors reported that the N-terminal region of flagellin is important in the first step of receptor recognition and binding, where the C-terminal is the one that gives the "message" of activation and the start of signaling.

Recently, it has been reported that the flagellin of *Bacillus amyloliquefaciens* is also capable of activating defense responses in chili plants (*Capsicum annum* L.) and ameliorating the effects of the groundnut bud necrosis virus (GBNV). Overexpression of the transcription factors WRKY33 and NPR1, PAL, PO, and SAR8.2, which are SA-sensitive

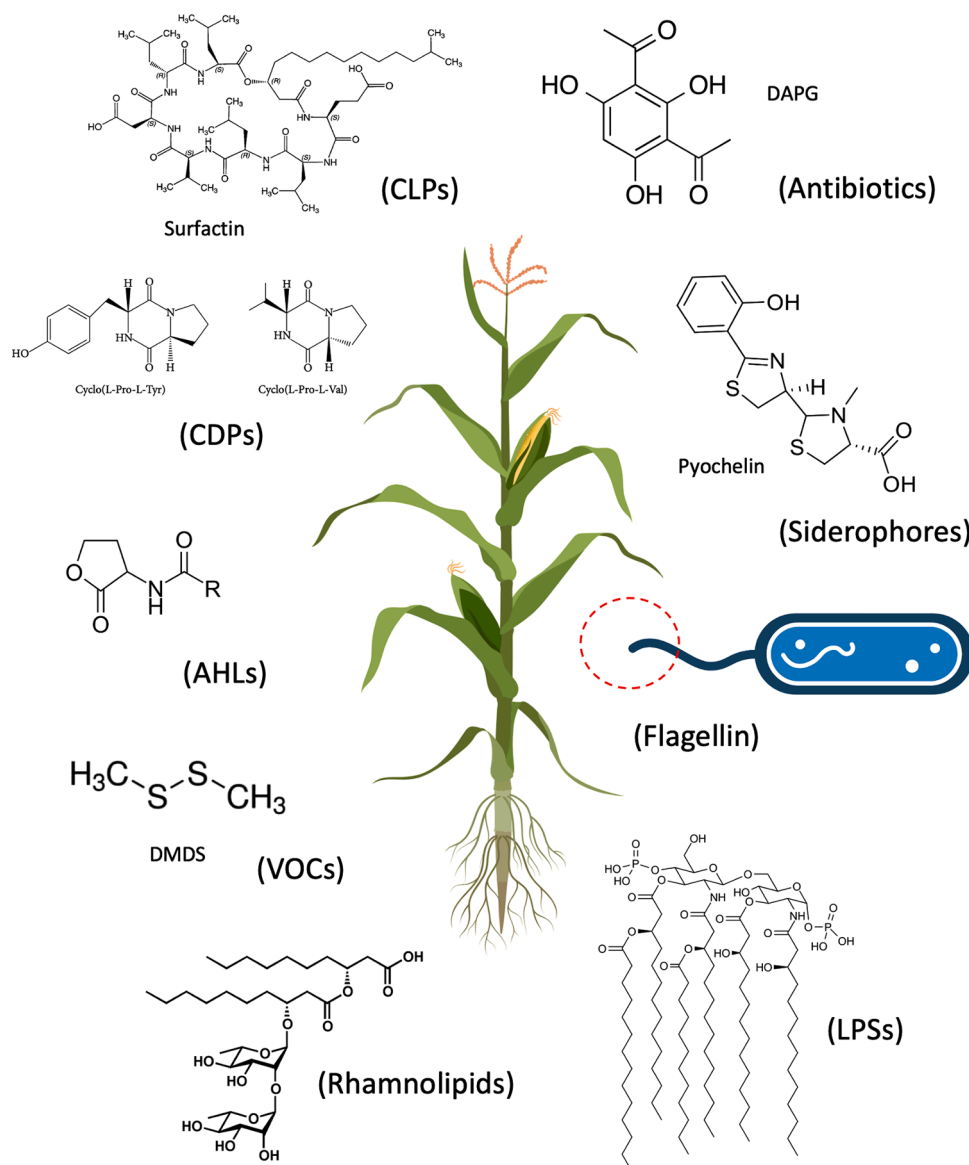


Fig. 3. Chemical and structural diversity of bacterial elicitors reviewed here. Made with information from multiple references cited in this work. CLPs: Cyclic lipopeptides; CDPs: cyclodipeptides; AHLs: Acyl homoserine lactones; VOCs: Volatile organic compounds; LPSs: Lipopolysaccharides; DAPG: 2,4-diacetylphloroglucinol.

defense genes, has been reported. However, the authors also found that JA-sensitive PDF and LOX genes were upregulated in pepper plants challenged with GBNV. It was observed that flagellin, recognized as a MAMP molecule of the bacterium *B. amyloliquefaciens* strain CRN9, can trigger innate immunity and restrict the growth of the virus in chilli through ISR as a response activated by both pathways SA and JA/ET signaling (Rajamanickam and Nakkeeran, 2020).

3.6. Siderophores

Siderophores, which are iron-chelating molecules, were produced by pathogenic and nonpathogenic microorganisms to obtain iron from the surrounding environment, either by freely inhabiting the soil, interacting with plants, or living within the host as endophytes (Gu et al., 2020). Siderophores were also efficient virulence factors, and in beneficial bacteria, the production and excretion of siderophores is a mechanism for deprivation of iron in pathogenic organisms (Alejandre-Castañeda et al., 2022; Saha et al., 2013). The role of siderophores as ISR elicitors has been recognized as the chemical diversity of siderophores is

surprising in beneficial bacteria, in communication and beneficial interactions with plant hosts. For example, there are carboxylate-type siderophores (e.g., Achromobactin and Citrate), hydroxamate (e.g., Ferrichrome and Desferrioxamine-E), catecholate (e.g., Enterobactin), phenolate (e.g., Pyochelin and Yersiniabactin), and mixed-type siderophores, such as Aerobactin and Pyoverdine, which are common in *Pseudomonas* species (Ghosh et al., 2020; Loper et al., 2012).

Although siderophores were widely studied molecules and one of the mechanisms pioneered for biological control of phytopathogens, the mechanism by which they trigger the ISR response in plants is poorly understood. Iron deprivation or elimination per se seems to be a novel mechanism of activation of immunity, which implies an alteration in the homeostasis of metals (Aznar and Dellagi, 2015). Previous studies on the use of animal models may help in the understanding of the role of microbial siderophores as triggers of plant immunity. Fig. 3 illustrates the chemical diversity of the bacterial elicitors.

Several other elicitors also identified that may be part of the bacterial cells and it can function as ISR elicitors; however, their function has studied earlier because of antimicrobial activities. These included the

Table 1
Examples of bacterial species and their ISR elicitors.

Bacterial genera or species	Bacterial elicitor	Beneficiated plant or crop	Pathogen	References
<i>Bacillus</i> spp.	Surfactin, mycosubtilin, fengycin, iturines, 2,3-butanediol	Tomato, strawberry, cotton, and chilli pepper	<i>Colletotrichum gloesporioides</i> , <i>Botrytis cinerea</i> , <i>Magnaporthe oryzae</i> or <i>Phytophthora cinnamomi</i>	(Rodríguez et al., 2018; Le Mire et al., 2018; Rajamanickam and Nakkeeran, 2020)
<i>Pseudomonas</i> spp.	Lokisin, rhamnolipids, pyoverdine, salicylic acid, pyochelin, cyclodipeptides, acyl homoserine lactones, lipopolysaccharides; Flagellin	Rice, bean, grapevine, Arabidopsis, Tomato	<i>Magnaporthe oryzae</i> , <i>Botrytis cinerea</i>	(Omoboye et al., 2019; Solis-Ortiz et al., 2022; Chae et al., 2020; Monnier et al., 2018; Meziane et al., 2005)
<i>Arthrobacter</i> spp., <i>Sinorhizobium meliloti</i> , <i>Pseudomonas fluorescens</i>	N,N-dimethylhexadecylamine	Tomato <i>Medicago truncatula</i>	<i>Botrytis cinerea</i>	(Montejano-Ramírez et al., 2020)
<i>Paenibacillus polymyxa</i>	Tridecane	Arabidopsis	<i>Phytophthora parasitica</i> var. <i>nicotianae</i>	(Park et al., 2013)
<i>Enterobacter aerogenes</i>	2,3-butanediol	Maize	<i>Setosphaeria turcica</i>	(D'Alessandro et al., 2014)
<i>Ochrobactrum lupini</i>	Lipopolysaccharides	Tobacco	<i>Pectobacterium carotovorum</i>	(Sumayo et al., 2013)
<i>Burkholderia gladioli</i>	Lipopolysaccharides	Cucumber	<i>Colletotrichum orbiculare</i>	(Park et al., 2008)

volatile compounds hydrocyanic acid (HCN) (Shabanamol et al., 2017), dimethyl disulfide (Huang et al., 2012), or others such as 2,4-diacetylphloroglucinol (2,4-DAPG) (Chae et al., 2020), or phenazines (Patel and Archana, 2018; Weller et al., 2012). In contrast, other compounds such as N-alkylated benzylamine produced by non-pathogenic *Pseudomonas putida* bacteria function as ISR elicitors, but more study need to explore in interaction with plants (Pršić and Ongena, 2020). It is evident that the antibiotic functions of several elicitor compounds are very attractive for research, but their roles in the immune response of plants cannot be ignored. Some of the works reviewed in this work are listed in Table 1.

4. The way forward

Previous studies unravel the biochemical components participated in the signaling of the SAR and ISR pathways (Pieterse et al., 2014; Pršić and Ongena, 2020; Zehra et al., 2021). The present study reviewed the immense diversity of bacterial origin biomolecules that can function as elicitors of the ISR response, and non-pathogenic nature that can activate both SAR and ISR pathways. There must be more explored about the nature of the specific and general receptors for the plant cell. In addition, only a few genes that participate in the response and signaling of both the SAR and ISR pathways have been identified. Previous studies have also focused their research efforts on further evaluation, mainly by determining expression levels (e.g., qPCR, RT-PCR) and the roles of the same genes in responses to different species of beneficial bacteria. It is essential to further research to find out the different interactions of the products of these genes, for example, protein-protein interactions, in plants, including *Arabidopsis*.

On the other hand, the ISR response mediated by rhizobacteria has been studied; however, the role of other environmental factors and how they can regulate (or enhance) the action of certain elicitors has still need to be evaluated. Such as iron deficiency can play an important role in the overlapping regulation of ISR and responses to nutrient deficiency in plants (Montejano-Ramírez et al., 2020; Romera et al., 2019). However, given the importance of multiple abiotic factors (e.g., temperature, drought, salinity, etc.), many of these abiotic stresses may explore the plant-bacteria communication and interaction in the ISR response to plants. Finally, it is necessary to formulate novel bioinoculants that contain one or several bacterial elicitors, which together with microbial agents, prevent and reduce the negative effects of pathogens on crops. This would undoubtedly result in a more sustainable production.

Author contributions

MCOM and GS: conceived the ideas, collected the data, and

developed the manuscript. AF and OB provided professional input and critiqued the work. All authors approved the submitted version.

Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability

No data was used for the research described in the article.

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