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# Microbial Effector Proteins: Green Inducer for Systemic Acquired Resistance in Plants

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***Abstract:***
*Systemic acquired resistance (SAR) is considered as a "whole-plant" barrier response that has been been expressed by the plant following the localized exposure to phytopathogens. This defense mechanism is controlled by a line pathway of either interaction of one or more signaling compounds such as salicylic acid (SA) and jasmonic acid (JA) with the help of regulatory protein known NPR1. Upon challenged by phytopathogen and in response to other environmental stimulants, the host plant responds by developing an increased SAR that navigates itself to remote tissues and determines a regulated resistance in distal, the healthy tissues to encourage defense against pathogen to besiege. For decades, the phenomenon of SAR via plant resistance inducers application in the laboratory has been described by several researchers. However, the progress towards understanding SAR and the application of SAR in open fields remain limited. Therefore, this review discusses the significant knowledge of SAR mechanisms and its application in the field as parts of plant disease control strategies.*

***Key Word****: Systemic Acquired Resistance; Microbial effector protein; Virulence factor; Field application; Plant defense mechanism.*

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## I. Introduction

The Agricultural sustainability is the ultimate aim of any agricultural production systems. This should enable current and the future generations to satisfy their needs in addition to enhancing environmental quality and natural resources. According to the United Nations Food and Agriculture Organization (FAO), a minimum 50% increase in agricultural food production by that time is required to meet the demand in a scenario of moderate economic growth. Considering the limited availability of arable land, the key emphasis is to increase the return per area and lower yield losses to cope with this in-creasing food demand[1,2]. Therefore, the efficiency of plant disease management contribution to the global food production is essential[3].

Currently, plant disease control includes predominantly preventive steps, mostly covering cultural activities such as disease-resistant cultivars and crop rotation[4,5]. Contradictory to organic pesticides, chemical pesticides or industrial pesticides are utilized for both pre-emptive and curing disease approaches[5,6,7]. In current agriculture practices, chemical usage for plants crucially improves the crop yield and quality, food safety and optimizing shelf-life[8]. In spite of the positive contributions of pesticides in controlling plant diseases and pests, concerns have raised about the adverse effects of chemical pesticides on human health and their environmental impact including soil pollution, water pollutions, and toxicity to beneficial organisms[9,10.11,12]. As depicted by neonicotinoid-resistant insects and fungi being unresponsive towards broad-spectrum strobilurin or azole fungicides, it significantly demonstrates pests' insusceptible development and disease to the all-out usage of chemical pesticides[13,14,15].

Therefore, higher dosages and the desire to find alternative pesticides with specific methods are appropriate[16,17]. Other greener ways for achieving sustainability in food production without harming consumers, depleting soil fertility, and destroying the environment's quality have been suggested.

New strategies have been put in place with greater dependency on biological technology to use integrated disease control programs efficiently. The application of plant resistance inducers (PRIs) or elicitors or effectors of plant defense activators appears to be the promising green option to encounter the pest and disease attack from the traditional agricultural practices and phytosanitary issues[18,19]. Such agents provide a variety of chemical or biological stimulators that are capable of exogenously activate plant defenses[20,21]. In nature, plants defense mechanisms comprise MAMP-triggered immunity (MTI), effector-triggered immunity (ETI), and systemic acquired resistance (SAR). Of all layers of defense strategies, SAR is the inducible, broad-spectrum protection providing a long-term efficient defense system that remains weeks, months, and in some situations, it occurs throughout the crop's entire season[22]. When the pathogen is targeted, plants de-fend themselves by triggering defense mechanisms through pathogenesis-related (PR) proteins' expression. The release of the PR proteins or genes can increase pathogen resistance[23,24]. Exposing plants to virulent, avirulent and non-pathogenic microbe of volatile molecules can successfully induce and activate these PR proteins[25]. The inducing resistance of SAR by external inducers has been studied over the past years and this includes tobacco[26], *Arabidopsis thaliana*[27], cucumber[28], and papaya[29].

One of the most potential PRIs is proteins and virulence factors, collectively described as pivotal for their host plants' pathogenesis and colonization[30]. Effector proteins are expressed to counteract signals that are essential for innate plant immunity. Beyond being effectors, specific effectors such as harpins and recombinant proteins are recognized to evoke plant defense mechanisms and SAR inductions[31,32,33,34]. Another good result involves reducing diseases caused by *Phytophthora infestans* and *Botrytis cinerea* in tomato because of HrpN harpin proteins treatment[35] and Hpa1 HRp protein promoting strong resistance to *Xanthomonas oryzae pv. oryzae* and *Magnaporthe grisea*[36]. Although the protection effect designed by PRIs is partially strong as expected, PRIs are appreciated as a promising approach in view of the growing understanding of the need to reduce the usage of pesticides. Many factors significantly affect their accomplishment, including genotype, environment, crop nutrition, and prior induced state in the field. Optimizing PRIs protein utilization and enhance control efficiency in an open field remain on-going[19]. In this review, relevant chronological descriptions on SAR research over the years will be overviewed including discussions on the roles of effector proteins in SAR activation, factors rendering their success in open field application and explanation on how these effector proteins act as promising tools to achieve agriculture sustainability.

## II. Effector Protein – Paratrooper in Pathogen Battlefield

A few years back, manifold exemplary reviews have addressed the notion of the evolutionary arms race between plants and pathogenic substances and how it configures the relationship between host and pathogens[37,38,39]. Amid the evolutionary process, both host and microbes create a state-of-art operationalization of their gene collection up-on tailoring the alterations in encircling both facets. This modification fruit heterogeneity of molecular participants which involves in regulating and intensifying the plant's defense mechanism. The events of plant-microbe interactions are often expressed by specific and typical players molecularly on the host and pathogen.

The outcome of the host-plant interplay is mainly dependent on the effectors (Figure 1). As the name suggests, effectors are star molecules capable of changing the host's cell structure and function, facilitating infection (virulence factors and toxins) and or triggering defense reaction (avirulence factors; Avr). Effectors can be classified into two groups based on their target sites in host plants[40,41]. Apoplastic effectors are secreted into the plant apoplast interacting with the extracellular targets and surface receptors whereas cytoplasmic effectors are transferred inside the plant cell[42,43,44,45]. Despite effector variability, successful infection events rely on efficient effector deliberation. This part is explained in the next section. For example, bacterial effector protein.

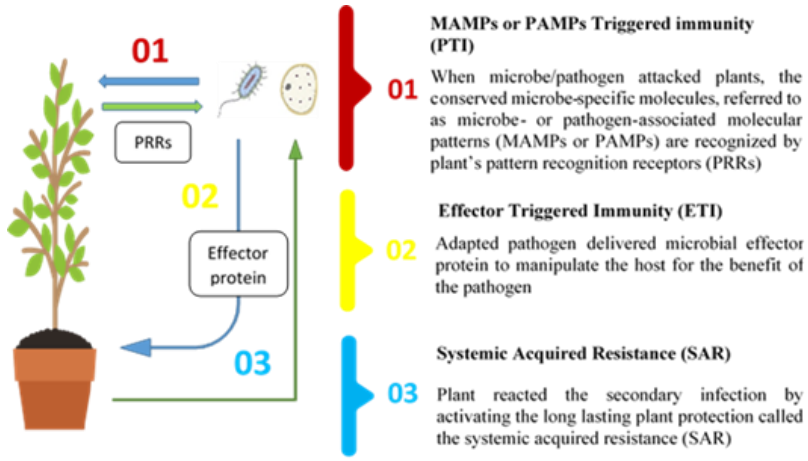


FIGURE 1: Three-layers of plant defense mechanism against phytopathogen infections

Although effector proteins are seen as the exquisite tools for microbial interaction, to date, the exact mechanism of plant pathogenesis and host defense activation via these communities remains rudimentary. In a review article by Snelders et al.[46], the roles of effector proteins are clouded by the overlapping functionalities with host, making it difficult to pinpoint the explicit key features exhibited by the effectors. However, effector proteins are classified into three groups as follows:

- Plant-targeting effectors (1) solely promotes manipulation to the host organism. Such group induces host resistance or susceptibility by gene-for-gene interaction between effectors and the hosts suppressing the plant-associated molecular pattern-triggered immunity (PTI). These roles of effectors in multiple host manipulation are recognized in the literature such as SnTox1 effector from *Parastagonospora nodorum*[47].
- Three-way interactions (effectors, plants and microbial community) (2). As the interaction implies, proteins are the one responsible in controlling the physiological processes in both plants and microbes. Zt6 effector from Zymoseptoria tritici exhibit this feature where the effector protein associated with self-defense against antimicrobial compounds is either secreted by the plant hosts or competing microbes[48].
- Microbe-targeting effectors (3), predominantly exhibited by endophytic and saprophytic microbes which are eminently specialized proteins that indirectly disrupt specific microbes by targeting analogous processes in plants. For example, these effectors first interrupt the connection between host and other microbes, like enacting local nutrient deprivation. The pathogens secrete effectors to enroll more symbiotic microbes to either aid the colonization or bid the host's protection against potential microbial rivalry.

Due to above multifariousness, it is challenging for researchers to identify the specific role of effector proteins in microbiota manipulation. However, across the timeline, explicit effector recognition of gene expression during host colonisation by various omics and technique approaches is fruitful. The reviews of Golics et al.[49] and Kanja and Hammond-Kosack[50] chronologically discussed the perspective of finding and identifying putative effectors along with their functionalities. Among the techniques, bioinformatics pipelines are currently favourable because of the lack of conservation of amino acid sequence, especially in fungi[51]. Integrating these methods often prioritized the precision of plant pathogenicity effector proteins towards pan-genomics. One of the current works by Carreon-Anguiano et al.[52] introduces EffHunter, a pipeline developed to in-corporate SignalP 4.1[53], Phobius[54], TMHMM 2.0[55] and WolFPSORT[56] together with Perl/Bioperl scripts for refining protein size and cysteine content. EffHunter is a user-friendly, amenable, and robust tool with greater accuracy and lower false positives. EffHunter can be a potential and fast track pipeline for effector protein prediction and characterization. Still many novel roles, locations, interplay and generic fundamental matter need to be discovered.

## III. Orchestrating Effector Protein in Plant-Induced Immunity

The principle of plant immunity relies on a layered protection mechanism to preserve plants from infection. PRIs identify pathogen-associated molecular patterns (PAMPs) and initiate pathogen-triggered immunity (PTI)[37]. This outcome led to the development of reactive oxygen species (ROS), the phosphorylation of mitogen-activated protein kinases (MAPKs), reorganization of transcription, and callose deposition on the cell wall[57]. Advance plant pathogens are able to resolve PTI by entering host cells and delivering effector proteins, both of which result in induced host susceptibility. In this regard, plants have developed the ability to track the presence or actions of

effectors by intracellular immune receptors, known as the R (resistance proteins) and result in effector-triggered immunity (ETI)[37]. ETI starts with hypersensitive reaction (HR), programmed cell death at primary site of the disease[58], thereby limiting pathogen dissemination inside infected tissue. This local pathogen attack often restricts the intake of secondary infections in un-failingly uninfected sections of plants. This type of increased resistance is referred to as systemic acquired resistance (SAR)[59]. The infection mechanism is complex and it involves long distance signaling to induce SAR. Defense hormone such as salicylic acid (SA) is said to be essential to SAR establishment because they increase the activity of non-ex-presser of PR genes1 (NPR1), a transcriptional coactivator[59]. It has been demonstrated that pipecolic acid, other signalling metabolites also play an important role in establishing SAR[60].

Indubitably, the successful defense system relies partially on effectors. In the past decade, many studies have demonstrated the role of effector proteins from bounties phytopathogens in boosting virulence in pathogen as well as stimulating plant aegis. However, inauguration and perpetuation of auspices reaction upon repertoire of effectors on these eukaryotic pathways involves a twain de no-vo synthesis of regulatory proteins and enzymes and coordinated degradation. Owing to maintain an efficient reaction to exogenous changes, tailoring a strong degree of proteomic plasticity during labyrinthine molecular processes of plant defense mechanism is pivotal.

Imperatively, the cellular variability during defenses is regulated by an essential component of plant biosynthesis called the ubiquitin-proteasome system (UPS) and autophagy. As one of the major protein degradation systems of eukaryotic cells, UPS and autophagy regulate various cellular pathways through selective destruction of short-lived regulatory proteins[61] (Figure 2). It is conceded that UPS governs numerous plant homeostasis processes comprising plant's progression, cell expansion and division, plant hormones responses and also abiotic and biotic stress tolerances[62,63,64]. There is a laudable compilation of evidence regarding protein turnover through UPS. This system manages various plant immunity features, including pathogen identification, receptors accumulation and downstream defense signaling[63,65]. Therefore, many effector proteins capitalize on the proteolytic deterioration curbing plant immunity system to augment the plant's impact because hampering the ubiquitin gene may dampen the plant's development and, consequently, drive to plant lethality[66].

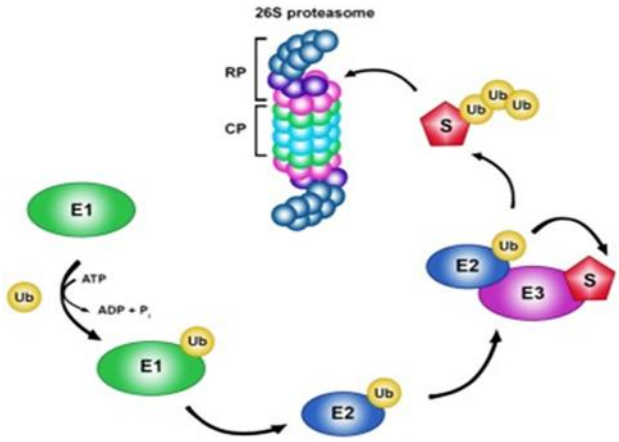


FIGURE 2: The ubiquitin-proteasome system (UPS) and its role during plant-pathogen interactions. Ubiquitin-proteasome cascade. Activated ubiquitin binds to E1 and is transferred to the ubiq-ui-tin-conjugating enzyme (E2). The E2 carries the activated ubiquitin to the ubiquitin ligase (E3), which facilitates the transfer of the ubiquitin from the E2 to a lysine residue in the target protein (S). Poly-ubiquitinated target proteins are degraded by the 26S proteasome, consisting of a 19S regulatory Particle (RP) and 20S core subunit (CP)[67].

However, how this intricate molecular mechanism is involved in defense responses and how host proteasome act as the prevailing strategy in plant pathogen is still poorly understood even if there are numerous studies discussing over this event. Fundamentally, ubiquitination is a firmly coordinated system that is regulated by three-step enzyme cascade associating E1 (ubiquitin-activating enzyme), an E2 (ubiquitin-conjugating enzyme) and an E3 (ubiquitin ligase)[68]. Among all enzymes, E3 possess the ability to interact with both substrate proteins and E2-ubiquitin complexes. Depending on their subunit architecture and mode of actions, E3 can be categorized into four main subfamilies: Homologous to E6-associated protein Carboxyl Terminus (HECT), Really Interesting New Gene

(RING), and U-Box and culling-RING ligases[69]. The ubiquitin chains linked by Lys48 target substrates to a multi-subunit protease is the notable and classical mechanism designated as proteasome for degradation. Compared with most post-translational modifications, ubiquitination is changeable events by an action of removal of ubiquitin being catalyzed by enzymes called deubiquitinating or deubiquitinating[70,71,72]. Considering these features in many studies, effector proteins from different pathogens advantageously target host protein ubiquitylation during infection via distinct array of ubiquitin ligases.

## IV. Sparking of SAR in Plants Attributable to Microbial Effector Proteins

Similar to animal-pathogenic bacteria, gram-negative plant-pathogenic bacteria exhibit a prominent secretion protein system during pathogenesis[73]. Of the multiple mechanisms, type III secretion system (T3SS) is a well-characterized secretory pathway where protein features are encoded by pathogenicity (hrp) genes and hypersensitive response (HR)[74]. The hrp-conserved (hrc) is the notable conserved genes in hrp group, congregating each other as the integral element in T3SS regulatory proteins delivering virulence factors from bacteria to the host cells[75,76,77]. In addition, several genes featured two classes of secreted proteins (1) distribution of effector proteins in host cells and (2) extracellular accessary proteins including harpins[78]. Although harpins as cell-free HR elicitors are acknowledged in over two decades, their functions or underlying mechanisms in host plants are not well understood[79,80].

Even so, there are compelling evidences demonstrating the role of harpins as trans-locator or server proteins of effector proteins at host plasma membrane. Harpins are characterized as unique proteins carrying distinct features where they: (1) have a comparatively large amount of glycine and serine residues, (2) possessed few α-helices, (3) having lower pH (very acidic) according to their theoretical isoelectric points, excluding HopAK1 and Hpaxm (Table 1), and (4) low tertiary structures making them heat stable. The ability to withstand the heat enables the purification of these proteins to produce cell-free elicitor as harpins HR elicitor activity consistently active even after boiling for 15 min[79,81]. Another precursor for the HR elicitation relies on the domains attaching to the harpins. HrpW-group hold particular N-terminal domains which exhibit role in eliciting the HR[82,83].

To date, all harpins reported are able to activate HR with exceptional to XopA of X. *campestris pv. Vesicatoria*[84] and truncated HrpZ1 of *Pseudomonas syringae pv. Tabaci*[85]. Originally, harpins' ability to promote HR was first identified in tobacco plants[79,81]. Years afterwards, there are evidences revealing specific regions on several harpins contributing to HR activation (Table 1). Although the mechanism of HR elicitation is not known, there are several predictions explaining the HR process that are outlined which backed with empirical research. Among the harpin group of chemical compounds, some disrupt membrane physiology to cause cell death. Secondly, HrpN can hamper ATP synthesis which excluded the oxidative bursts by lessening the mitochondrial electron transport in tobacco cells[86]. Furthermore, treatment of Arabidopsis cells with HrpZ1 contributes to release of cytochrome C via mitochondria resulting in uptick in reactive oxygen species[87]. This suggests the in-direct effect by both HrpN and HrpZ1 in perplexing the mitochondria functionality and mitochondria-dependent cell death program induction in plants. Third, Hin1, the other HR-related genes inauguration by HrpZ1 which at the same time initiates the protein kinases such as AtMPK6 in Arabidopsis and its ortholog, SIPK, in tobacco[88,89,90]. These evidences demonstrate harpin features recognition in surrounding leaf cells.

**TABLE 1 :** List of harpin proteins functionally characterization in gram-negative plant-pathogenic bacteria

| **Name** | **Source bacteria** | **Bacterial virulence-related features** | | **Functional features** | |
|---|---|---|---|---|---|
| | | Severity | Effector | HR | Defense |
| HrpN group | | | | | |
| HrpN | *Erwinia amylovora* | + | + | + | + |
| HrpN | *E. pyrifoliae* | … | … | … | … |
| HrpN | *E. chrysanthemi* | … | … | … | … |
| HrpN | *E. carotovora subsp. carotovora* | … | … | … | … |
| HrpZ1 group | | | | | |
| HrpZ1 | *Pseudomonas syringae* pv. *tomato* | ND | + | + | + |

| | | | | | |
|---|---|---|---|---|---|
| HrpZ | *P. syringae* pv. *phaseolicola* | … | … | … | … |
| HrpZ | *P. syringae* pv. *syringae* | … | … | … | … |
| HrpZ | *P. syringae* pv. *glycinea* | … | … | … | … |
| HrpZ[i] | *P. syringae* pv. *tabaci* | … | … | … | … |
| HrpW1 group | | | | | |
| HrpW1 | *P. syringae pv. tomato* | - | + | + | + |
| HrpW | *E. amylovora* | … | … | … | … |
| PopW | *Ralstonia solanacearum* | … | … | … | … |
| HopAK1 | *P. syringae pv. tomato* | … | … | … | … |
| HrpW[k] | *Rhizobium etli* | … | … | … | … |
| Hpa1 group | | | | | |
| Hpa1 | *Xanthomonas pryzae* pv. *oryzae* | + | ND | + | + |
| Hpa1 | *X. oryzae* pv. *oryzicola* | … | … | … | … |
| Hpa1 | *X. axonopodis* pv. *citri* | … | … | … | … |
| HpaG | *X. axonopodis* pv. *glycines* | … | … | … | … |
| XopA | *X. campestris* pv. *pelargonii* | … | … | … | … |
| HreX | *X. campestris* pv. *pelargonii* | … | … | … | … |
| Others | | | | | |
| PopA1 | *R. solanacearum* | ND | ND | + | + |
| HopP1 | *P. syringae* pv. *tomato* | ND | + | + | ND |
| $Hpa_{xm}$ | *X. citri* subsp. *malvacearum* | ND | ND | + | ND |

ND : Not detected

Unlike bacteria, fungi do not exhibit specific analogous system in secretion to the host. However, secretion on host targeting through N-terminal translocation domains is considered to be the most common theme system in fungi which located after general secretory signal peptide. The understanding of effector movement process begins from oomycete pathogens employing same infection system in fungi[91]. Nonetheless, definition of the cell entry for the N-terminal signal motifs is uncertain for most fungi because it is express highly in oomycetes rather than fungi. For example, there is lack of direct evidence on the development of cerato-platanin protein (CPPs) in secretion mechanism and defense system in fungal-plant interaction in spite of the efforts to unravel their functions. CPPs are novel preserved proteins containing signal peptide and they are readily found in culture filtrates of fungi[92,93,94]. The only plausible way for their expression is through carbohydrate-binding or carbohydrate-loosening as CPPs was predominantly found in fungal cell wall of B. cinerea and Ceratocystis platani[94,95]. In many studies, CPPs are acknowledged as virulence factor[96,97], elicitors, promoting synthesis of reactive oxygen species, inducing local HR in plant leaves[93,98]. Many CPPS exhibit defense system either by inducing cell death, necrosis and HR (Table 2).

**TABLE 2 :** Fungal protein effectors inducing cell death, necrosis, HR and SAR during interaction with various plants

| **Family** | **Protein** | **Fungi** | **Plant** |
|---|---|---|---|
| Cerato-platanins | Sm1 (small protein 1), Sm2 (small protein 2)[99,100,101,102] | *Trochoderma virens* | Tomato and maize |
| | Ep11 (eliciting plant response-like)[101] | *T. atroviride* | Tomato |
| | VdCP1 (cerato-platanin-first) and PevD1[103] | *Verticilium dahlia* | Cotton |
| | HaCPL2 (cerato-platanin-like protein 2)[104] | *Heterobasidion annosum* | Tobacco and scots pine |

| | | | |
|---|---|---|---|
| | CmCP[105] | *Ceratocystis manginecans* expressed in *Pichia pastoris* | Tobacco |
| | FocCP1 (cerato-platanin-first)[106] | *Fusarium oxysporum* | Tobacco |
| Glycoside-hydrolases | Thph1 and Thph2 (cellulose-like protein)[107] | *T. harzianum* | Maize |
| | Cellulases[108] | *T. longibrachiatum* | Melon |
| | ThPG1[109] | *T. harzianum* | Tomato |
| | Eix (xylanase)[110] | *T. viride* | Tobacco |
| Hydrophobins | Hytlo1[111,112] | *T. longibrachiatum* | Several plants |
| | Tvhydii1[113] | *T. virens* | Tomato |
| | HFB2-4[114] | *T. asperellum* | PdPap poplar seedling |
| | ThHyd1[115] | *T. harzianum* | Maize |
| Short-chain dehydrogenase | PeBA1 (protein effector-like)[116] | *Bacillus amyloliquefaciens* expressed in *Escherichia coli* | Tobacco |

Apart from CPPs, another filamentous fungus related protein namely hydrophobins are invariably elicits the defense mechanism in plants. Hydrophobins are small surface-active hydrophobic proteins featured with eight conserved cysteine (Cys) residues forming four disulfide bonds[117,118]. All reported hydrophobins found in *Trichoderma* express genes and are associated with auxin signal transduction, reduction of reactive oxygen species and induction of SAR (Table 2).

## V. Possible Factors Influencing the Progression of SAR in Agriculture Field Application

There are reports on effector proteins inoculation inducing resistance in plants. Out of the considered elicitors, it is evident that although there are incidences where inducers yield a high level of resistance on crops against disease, there also are incidences where induced resistance does not attain desired results. There are cases where induced resistance due to inducers does not work in providing control of pathogenic diseases[119] especially when it comes to test the efficacy of these inducers in open field.

Ostensibly, protection against virulent pathogens (especially to necrotrophic pathogen and generalist chewing insects) can also be induced by infection and colonization of mycorrhizal[120]. Fungal and bacterial endophytes, insects, in addition to avirulent nematode species induced defense in plants[121,122,123,124,125]. As such, because the efficacy of target resistance is based on the ability of the plant to respond to the induced resistance agents, it is apparent that there are range of factors that play significant roles in influencing the effectiveness of resistance in plants besides microbial effector proteins themselves. These factors raise questions because of to the feeble performances displayed by plants in field compared with the grown plants under controlled environments.

## VI. Advance Induction in Plant Resistance

Do plants in open fields exhibit advance in plant resistance prior to induction? This question was pointed out by Walters et al.[19] due to the astonishing results reported by Pasquer et al.[126] where there were no differences in gene expression were shown be-tween treated and untreated wheat due to probable elevation in gene expression prior to induction. Likewise, three tomato cultivars exhibited an advance expression in gene even before the treatment of acibenzolar-S-methyl (ASM) under field conditions[127]. At this point, if it is true, will advancement in resistance jeopardize plant's progression in inducing resistance afterward? Herman et al.[127] provide an answer by reporting that the gene expression was further elevated following ASM treatment. Walters et al.[128], on the other hand, reported the contrary. Although it appears unlikely for the plant to exhibit resistance beforehand the inducer was applied, these evidences suggest that biotic and abiotic factors control the performance of plants in stimulating defense mechanism upon induction.

## VII. Host Genotype and Environmental Factors

One of the closest keys for the differential expression of induced plant resistance is host genotype[129,130,131,132]. In studying combination of resistance inducers, as an example, it was established that the spring barley exhibited a considerable range of expression of induced resistance across different varieties[133]. The researchers found that some varieties did not express induced resistance with a dissociation between plants ability to induce resistance and the resistance rating of barley. In different studies, the effect of resistance was not always regarded to plant accession. Sharma et al.[134] proclaimed degree of resistance induction may due to multiple factors, indicating an effect of acropetal systemic of BABA (DL- 3- amino butyric acid)[135]. All aspects contributing variation in defense system in different plants are summarized in Table 3.

**TABLE 3:** All contributors influencing variation in defense mechanism in different plants

| Main contributor | Sub-factor | Plant | Descriptions |
|---|---|---|---|
| Host genotype | Variety[36] | Rice | Variation in resistance induction across variety of rice |
| | Cultivars[136] | Bean | Wild accessions of beans induced higher resistance than modern cultivars |
| | Pathogen isolated[134] | Tomato | Genotypes of tomato varied in their expression of BABA-induced resistance against *Phytophthora infestans* |
| | Leaf age[119,142] | Tomato | Resistance decreased with increasing leaf age |
| Environments | Nutrient[119,142] | Wheat and Arabidopsis | Wheat incurred higher allocation costs under nitrogen-limiting conditions |
| | Water stress[137] | Barley | Water stress enhanced resistance towards powdery mildew |
| | Osmotic and proton stress[138] | Barley | Stresses on osmotic and proton induce active defenses against powdery mildew (dependent on intensity of stress) |
| | Climate change[139] | Wheat | Cold hardening of winter wheat increased resistance to the snow mould pathogens *Typhula incarnata* and *Microdochium nivale* |

In different perspectives, plant resistance is appreciably costly, creating a predicament for the plant for either to grow or defend[140]. Heil et al.[141] notes that if, as re-search has established, plants resistance is dependent on the resources diversion toward defense, then any environmental fact that leads to diversion of these factors for other purposes leads to constraints on resources. Therefore, constraints on resources is responsible for shortage of the resources that are set aside to aid in controlling disease through improving resistance. Höfte and Bakker[142] acknowledged that costs associated with inducing resistance will have an impact on the resources that cater for plant resistance. In a study about the use of ASM on wheat resistance, Miles et al.[143] found that in incidences where nitrogen supply was available, the effectiveness of the resistance had significant impact on the target farms. In cases where chitinase, chitosanase, and peroxidase and levels of chitinase and peroxidase were low (causing lowering of nitrogen in the plants), the rate of resistance was low. Although there is little evidence on how chitosanase influences induced plants, the effects of enzymes on plants are influenced by nitrogen levels.

In a study testing the influence of protein induced treatments of plants for disease control, results indicated that total soluble protein content decreased significantly in the first 12 h following ASM treatment[144]. This improved control of disease indicates that the fundamental metabolism may be of critical impact when controlling the effects of induced resistance in plants. In recent studies, this issue has been championed. Miles et al.[143] states, "Arabidopsis plants treated with ASM exhibited a growth reduction during the week following induction." Further, studies show that SAR resistance is often inhibited especially if the primary infection occurs in the absence of light. All these studies show that increased metabolism facilitate the level of resistance among crops.

## VIII. SAR Mechanism is Equivocal

Based on the current state of information, defense in plant comprises two typical and successive roadblocks against pathogen attacks. PTI served as front-liner and ETI as the second defender which and it known as the gene-for-gene resistance or upright resistance. These two defensive lines seemingly have a major superposition in their

transcriptomics, considering their sequential implications, and stressing that ETI may contain amplified elements of PTI. This aspect was observed by *A. thaliana* expressing resistance identical to SAR, but without secreting tissue HR-associated necrosis. In other words, the frontline defense (PTI) following sensing the MAMPs is able to induce resistance mimicking SAR with typical effects like cell wall enhancement, ROS production, and callose deposition.

In this present review, the conspicuous questions are as follows: How come the typical SAR can be promptly re-induced upon pathogen infection in plants? and does the above statements support the occurrence of resistance being already induced in open field? What are the actual mechanisms involved when the exogenous inducers success-fully alert the plant to respond immediately against pathogen? Gozzo and Faoro[145] compiled evidences to explain the SAR occurrence. The labyrinth pathways of entire phenomenon might have centered on two developmental stages known as priming for defenses and their activation upon pathogen attacks. The first phase is believed to be essential and greatly elusive although the PR-1 expression, the most predictable actor of SAR is not completely responsible for the barrier of resistance. Regardless, it is presumed that tissues in the physiological state can be altered rapidly to be usable by the time pathogen initiate their attack into host cells signify number of genes in priming phase ought to be conserved in pre-transcriptional state[146,147] (Figure 3). Two feasible models which explain the pre-transcriptional stages are as follows:

- Dormant defense regulatory proteins termed mitogen-activated protein kinases (MPKs) are believed solves resolve priming in greater amount which only activated at secondary post-translational stage to act upon a subsequent attack of pathogen. Furthermore, accumulation of transcription factors of defense gene may have suggested to alleviated in primed plant[148].
- Second possible aspect is focusing on chromatin as the probable substrate of memory in SAR. It is believed that gene SAR activation is related to histones serving as anchoring ground for transcriptional coactivator proteins[149,150]. With this belief, Conrath et al.[148] clearly proved the transcription coactivator gene WRKY 20 being expressed following application of BTH which highly related to histone chemical clarifying the hypothesis provided by Kanno et al.[149] and Ruthenburg et al.[150].

The concept of priming suggests an intrinsic system in plant enacted as memory "bank" storing all previous stresses to encounter next attacks. In fact, priming superior to direct induction because priming requires is not expensive[151].

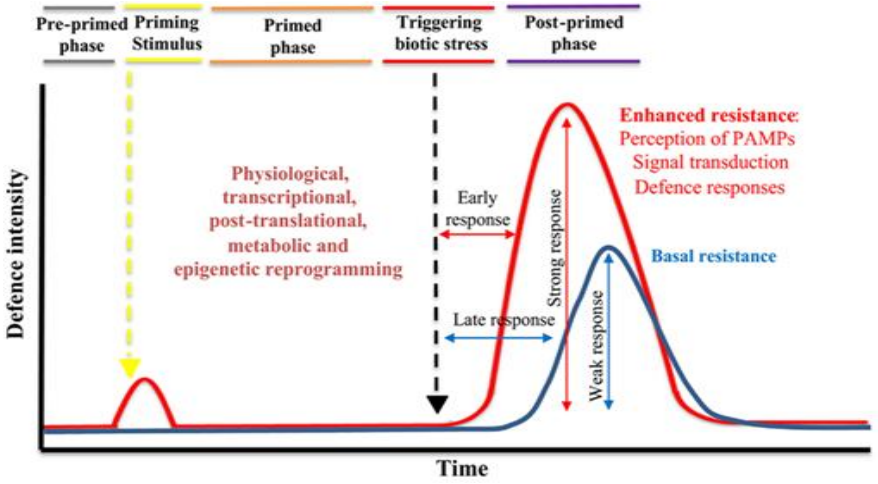


FIGURE 3: This model of a basic priming system with an elicitor or inducer as 'priming agent'. The primulas stimulus (e.g: chemical or natural priming agents) acts on a primed organism leading to a 'primed phase' and precedes the stress response induced by triggering stimulus (e.g: pathogen infection). The 'post-primed' plant demonstrates a stronger and prompter defense response following pathogen attack (stress trigger) subsequently leads to an enhanced resistance against various stresses[152,153].

## IX. Conclusion

Studies of effector proteins involved in SAR activation have created a wealth of knowledge in many areas of agriculture especially in plant protection, both at molecular and organismal levels. Different methods or approaches of effector proteins have been adopted in farming systems to enhance plant immunity against pests and diseases. However, there are significant gaps in understanding and application regarding advancement in identification of the vastness of the gene repertoires and the effectiveness of these effector proteins application in

open field. As previously mentioned, the reputed roles of effector proteins in SAR interactions are played out elusively. Different effector proteins are expressed in different ways toward the host plant, directly or indirectly. Further studies by proposing good host models are undoubtedly obligatory to shed light on many speculations. With breakneck growth of novel and sophisticated next-generation sequencing platforms, many roles of pathogen effectors in manipulating of microbiota can be revealed. This adds on to the knowledge on improving crop productivity. In this present review the section on elicitors or effectors either fungal or bacterial effector proteins shed multiples feeler questions which could enlighten re-searchers to unlocking the mystery in the near future.

Despite the potential application of the effector proteins in inducing disease resistance in field trials, the potency of this practice can be perplexed by host genotypes and changeable in environmental conditions suggesting that single-handed effectors may be irregular and poorly performed compared to the chemical pesticides. Practically, the pre-sent crop dis-ease control is greatly dependent on the synthetic fungicides and bactericides compared to biological inducers. Chemical based pesticides are more accepted by the majority farmers worldwide because of their effectiveness, accessible, and affordable prices of the chemical pesticides. These facts challenge researchers worldwide in convincing farmers to adopt biological inducers in their farm practices. Integrated pest management approaches feasibly offer new perspective for farmers. Combination of chemical and biological agents could provide wide spectrum of plant defenses against various pests and diseases thus improving and sustaining their economical yields. A more extensive progress is required to be done before effector proteins can be fully included as regular crop protection practices. Throughout this review, we are hoping that we can portray a glimpse of small picture of microbial effector proteins involvement in augmenting SAR in agricultural production system.

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