

## Review

# Effective Biotic Elicitors for Augmentation of Secondary Metabolite Production in Medicinal Plants

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**Abstract:** Plants are an essential component of our daily diet, and their nutritional value has been thoroughly studied for many years. The ability of plants to adapt to changing environmental conditions through signaling systems is an essential component of their survival. Plants undergo an array of physiological alterations to respond to stress from biotic sources. Secondary compounds frequently accumulate in crops that are sensitive to stress, particularly those with several eliciting agents or signaling molecules. Plants contain various types of bioactive compounds, including phytosterols, alkaloids, glycosides, and polyphenols, which make them valuable for the food and pharmaceutical industries. The increased production of secondary metabolites via elicitation has opened up a new field of study with the potential to provide substantial financial gains for the pharmaceutical and nutraceutical industries. These elicitors are pharmacological compounds that activate specific transcription factors and up-regulate genes to activate metabolic pathways. Thus, the current review discusses the mechanism of biotic elicitation and various elicitation techniques using biotic (proteins, carbohydrates, rhizobacteria, fungi, and hormones) elicitors that may increase the yield of secondary metabolites, particularly in medicinal plants, which is advantageous to the agrochemical and therapeutic industries.

**Keywords:** secondary metabolites; biotic elicitor; signal molecules; phytochemicals; medicinal plants



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## 1. Introduction

Plant parts have been an integral component of our daily food intake and have been extensively researched for their biochemical properties. Primary metabolites, including lipids, glucose, and protein are necessary for life [1]. Plants also produce a wide range of secondary metabolites such as flavonoids, alkaloids, pigments, steroids, quinones, and terpenoids that are utilized as nutritional supplements, colors, flavors, biological pesticides, scents, and agricultural chemicals [2,3]. On the other hand, they do not significantly influence how plants' fundamental life cycles are regulated. Still, they are considered defensive chemicals in the relationship between plants and their habitats [4]. They also play a vital role in protecting plants from insects, phytopathogens, rodents, herbivores, and plant adaptation to the environment. With a dry mass of less than 1%, the processing of these

compounds is incredibly low and largely dependent on the metabolic and development stages of the plant [5,6].

If an elicitor is added to a living system in small amounts, it plays a significant role in adapting plants to stressful conditions by improving the particular biosynthesis compound [4]. They are chemical substances for both abiotic and biotic factors that can promote stress responses in plants and aid in the improved production and agglomeration of secondary metabolites to guarantee that they survive in adverse circumstances, i.e., water scarcity, salinity, and low/high temperature [7].

To increase the synthesis of the aimed secondary metabolite, adding an elicitor also results in the development of a novel compound. This will ultimately result in the creation of innovative chemical models for pharmaceuticals [8]. For instance, only in SA-treated cells, *Catharanthus roseus* suspension produces 2,5-dihydroxybenzoic-5-O-glucoside [9]. After being treated with MeJA and CuSO<sub>4</sub>, the hairy roots of *Hyoscyamus albus* produced four novel solavetivone compounds. It is essential to comprehend the elicitation mechanism at the genetic and proteome levels to achieve targeted improvement in secondary metabolite production by elicitation [10].

These days, several biotechnological tools are used to increase plant productivity. In order to produce massive amounts of data indicating both biotic and abiotic stress, high-throughput technologies, such as next-generation sequencing, microarrays, high-resolution mass spectroscopy combined with high-resolution chromatography and nuclear magnetic resonance (NMR) instruments, etc., are rapidly evolving [11].

In addition to increasing productivity, elicitation uses plant cell/tissue culture as a model system for regulating metabolic and biochemical pathways through stress induction. This technique may be used to characterize and comprehend the effects of different types of stress on plants [12].

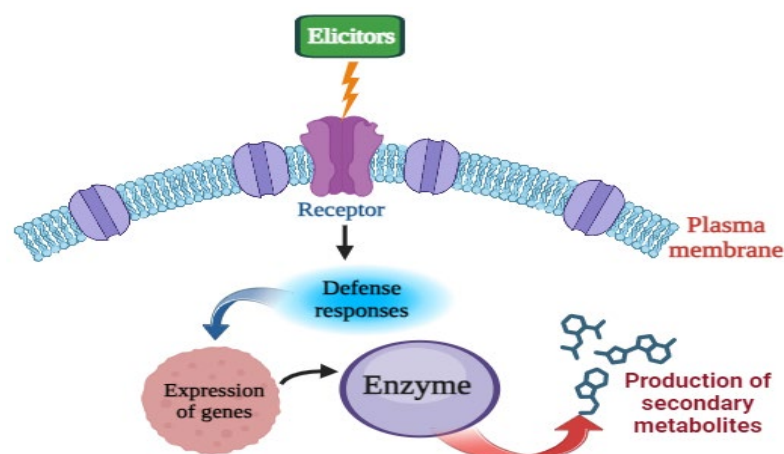
However, it is believed that elicitation is the best method for boosting the creation of advantageous secondary compounds from the activities within cells and organs [13]. Thus, this review aims to discuss the effect of different types of biotic elicitors on the production of secondary compounds of pharmaceutical importance.

## 2. Mode of Action of Elicitors

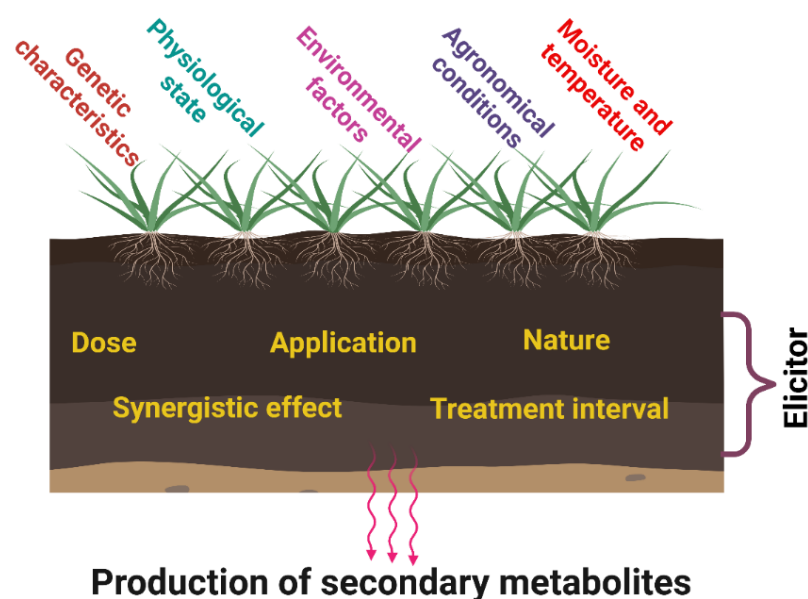
The first phase of the plant's reaction to eliciting agents involves the detection of the stimuli by receptors located in the plasma membrane of plant cells, such as protein kinases (Figure 1). A variety of elicitors may be localized within cells to initiate signaling mechanisms that trigger plant defenses by various mechanisms, such as the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), hypertensive reactions, the expression of defense-related genes, the stimulation and de novo biosynthesis of transcription factors, alterations to the potential of plasma membrane cells, the induction of pathogenesis-related proteins and enzymes involved in oxidative stress protection, increased ion fluxes (Cl<sup>-</sup> and K<sup>+</sup> efflux and Ca<sup>2+</sup> influx), fast cell death, problems with protein phosphorylation, lipid oxidation, and protective barriers in the structure. They control the activity of proteins associated with the synthesis of secondary compounds directly [14–16].

## 3. Parameters Affecting Elicitors

Elicitation is a complicated process that is influenced by several variables (Figure 2), including the concentration and specificity of the elicitor, its length, overall time course, development stage, growth regulation, soil type, and nutrient composition. Plant genetics (species and cultivars) influence defensive mechanisms more than the characteristics of an elicitor in terms of how plants respond to them. Secondary metabolite synthesis is significantly influenced by elicitor concentration [17,18].



**Figure 1.** General mechanism of plasma membrane receptor-mediated signaling for secondary metabolite production in plants. When the elicitor molecule binds to the receptor, a signal cascade initiates the activation of key enzymes that catalyze the synthesis of secondary metabolites in the plant's defense.



**Figure 2.** Factors influencing bioactive compounds in plant responses.

#### 4. Biotic Elicitors and Their Classification

Elicitors are natural and synthetic chemicals, and their discovery has led to a better understanding of plant signaling pathways, which led to the identification of natural and synthetic compounds that stimulate defensive responses in plants comparable to those generated by infection with a pathogen [19]. Biotic elicitors are compounds of biological origin produced either by pathogens or by the plant itself. Damage-associated molecular patterns (DAMPs) are elicitors [20]. These DAMPs act as endogenous elicitors and frequently manifest as danger cues to activate innate defenses in the apoplast [21].

Furthermore, exogenous elicitors, such as bacteria, viruses, infections of herbivores, and fungi, cause plants to produce compounds at the location of a pathogen or herbivore attack. They have receptor-related actions and can activate or deactivate various enzymes or ion channels [10]. Numerous bacterial and fungal diseases produce digestive enzymes, such as polygalacturonase, pieces of a cell wall, and peptides that may hinder or dissolve

physical obstacles in plant tissues, such as the central lamella. Gene-specific elicitors are generated by the pathogen's virulence-related genes [22].

#### 4.1. Proteins

In plant cell cultures, proteins and enzymes serve as biotic elicitors and set off defense responses (Table 1).

**Table 1.** Role of protein and carbohydrates in the production of secondary metabolites in plants.

| Plant Species                     | Elicitor                           | Compound                      | References                       |
|-----------------------------------|------------------------------------|-------------------------------|----------------------------------|
| <b>Protein</b>                    |                                    |                               |                                  |
| <i>Nicotiana tabacum</i>          | Cellulose                          | Phytoalexins                  | Threlfal and Whithead, 1988 [23] |
| <i>Plantanus acerifolia</i>       | Glycoprotein                       | Coumarin                      | Alami et al., 1998 [24]          |
| <i>Eschscholzia californica</i>   | Yeast cell                         | Benzophenanthridine           | Farber et al., 2003 [25]         |
| <b>Carbohydrates</b>              |                                    |                               |                                  |
| <i>Glycine max</i>                | Carbohydrates                      | Phytoalein                    | Sharp et al., 1984 [26]          |
| <i>Lithospermum erythrorhizon</i> | Oligogalacturonic acid             | Naphthoquinone hikonin        | Fukui et al., 1983 [27]          |
| <i>Panax ginseng</i>              |                                    | Saponin                       | Hu et al., 2003 [28]             |
| <i>Plumbago rosea</i>             |                                    | Plumbagin                     | Komaraiah et al., 2003 [29]      |
| <i>Ruta graveolens</i>            |                                    | Fluoroquinolone alkaloids     | Orlita et al., 2008 [30]         |
| <i>Vitis vinifera</i>             |                                    | Trans-resveratrol, viniferins | Taurino et al., 2015 [31]        |
| <i>Hypericum adenotrichum</i>     | Oligogalacturonic acid and sucrose | Hypericin                     | Omer and Bengi, 2013 [32]        |
| <i>Nicotiana tabacum</i>          | Chitosan                           | Phytoalexins                  | Brodelius et al., 1989 [33]      |
| <i>Eschscholzia californica</i>   |                                    | Indirubin                     | Radman et al., 2003 [34]         |
| <i>Curcuma longa</i> L.           |                                    | Isoflavonoids, Genistein      |                                  |
| <i>Lupines albus</i>              |                                    | Anthracene                    |                                  |
| <i>Polygonum tinctorium</i>       |                                    | Curcumin                      | Sathiyabama et al., 2016 [35]    |
| <i>Rheum palmatum</i>             | Sucrose and Chitson                | Withania A                    | Gorelick et al., 2015 [36]       |
| <i>Withania somnifera</i>         |                                    | Bacoside A                    | Naik et al., 2010 [37]           |
| <i>Bacopa monnieri</i>            | Sucrose                            | Bacoside A                    | Naik et al., 2010 [37]           |

Proteins exploit ion channels in the membranes of plant cells to propagate signals that are activated by external stimuli [38]. Plants use proteins that bind to carbohydrates, such as lectins or agglutinins, to defend themselves against other plant species. *Phytophthora drechleri*, a pathogenic fungus, secretes protein elicitors that induce tobacco leaf necrosis [39]. In plant cell membranes, ionic fluxes play a role in ion channel regulation in response to external stimuli, where protein elicitors are used. According to Zimmermann et al. (1998), the *Nicotiana tabacum* cell membrane contains the cell wall-degrading enzyme pectolyase, as well as a powerful inducer and membrane depolarizer (chloride efflux). Another enzyme released by *Phytophthora cryptogea* is called cryptogein [40]. The membrane becomes depolarized as a result. According to many researchers, the fungus *Pythium oligandrum* secretes a low-molecular-weight protein called oligandrin that makes *Lycopersicon esculentum* plants resistant to *Phytophthora parasitica* [41].

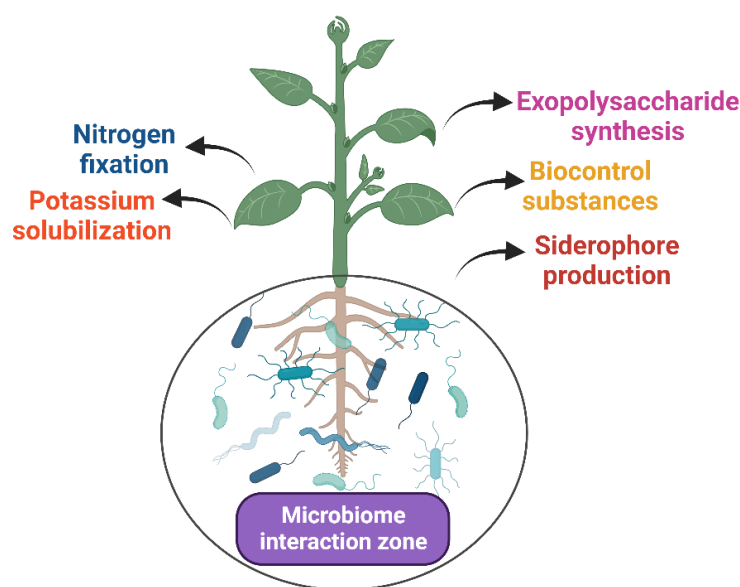
#### 4.2. Carbohydrates

Different types of carbohydrates, such as oligogalacturonides (OGAs) and pectic polysaccharides, also serve as elicitor molecules (Table 1). During the development of *Glycine max* cotyledons and defensive interactions with *Nicotiana tabacum*, OGAs aid in

the production of phytoalexins. Chitin, an essential element of fungal cell walls, functions as a potent trigger signal in several plant-based systems [42]. In addition, they participate in the overproduction of secondary compounds in vegetative cell cultures. Using specific carbohydrate elicitors, Ebel et al. (1986) investigated phytoalexin synthesis in cultured soybean cells [43].

#### 4.3. Plant Growth-Promoting Rhizobacteria (PGPR)

The production of secondary compounds can be increased by the pharmacological effects of pathogenic microorganisms or other biological elicitors (Figure 3; Table 2). Plant rhizosphere-colonizing bacteria can stimulate plant growth under both standard and unfavorable conditions via different pathways [44,45]. PGPR can also be categorized as an extracellular growth promoter of rhizobacteria in plants. In the rhizosphere, or root cortex, there is an intercellular plant growth promoter (iPGPR) that depends on its interaction with plants [46]. In the biosynthetic processes of secondary metabolites associated with plant defense responses to pathogenic agents, PGPR act as the main catalysts for key enzymes [47]. PGPR also encourage jasmonic acid biosynthesis in plants, which act as a signal pathway transducer that lead to aggregation in the production of secondary plant metabolites. Investigators have tried many methods, including hormone-dependent tests, medium structure, and penetration of light, to improve plant tissue crops [48,49].



**Figure 3.** A schematic representation of plant micro biome interactions in the rhizosphere. PGPR are interacting with the plant in the root zone of the plant, beneficial for plant growth and productivity.

**Table 2.** Role of PGPR in the production of secondary metabolites in plant.

| Plant Species               | Compound                                                 | References                                             |
|-----------------------------|----------------------------------------------------------|--------------------------------------------------------|
| <i>Catharanthus roseus</i>  | Ajmalicine and serpentine                                | Jaleel et al., 2007, 2009; Namdeo et al., 2002 [50–52] |
| <i>Hyoscyamus niger</i>     | Scopolamine, hyoscyamine                                 | Ghorbanpour et al., 2013 [53]                          |
| <i>Ocimum basilicum</i>     | $\alpha$ -terpineol, eugenol                             | Banchio et al., 2008, 2009 [54,55]                     |
| <i>Origanum majorana</i> L. | $\alpha$ -terpineol                                      |                                                        |
| <i>Pisum sativum</i>        | Gallic acid, ferulic acid, cinnamic                      | Bahadur et al., 2007 [56]                              |
| <i>Salvia miltiorrhiza</i>  | Tanshinone                                               | Zhao et al., 2010 [57]                                 |
| <i>Salvia officinalis</i>   | Cis-thujone. Camphor                                     | Ghorbanpour et al., 2014 [58]                          |
| <i>Solanum viarum</i>       | Orthodihydroxy, tannins, flavonoids, Saponins, alkaloids | Hemashenpagam and selvaraj, 2011 [59]                  |
| <i>Stevia rebaudiana</i>    | Stevioside                                               | Vafadar et al., 2014 [60]                              |
| <i>Targetes minuta</i>      | Monoterpenes, phenolic compounds                         | Cappellari et al., 2013 [61]                           |

#### 4.4. Parasites

Plants engage in distinct defensive processes in response to the specific kind of pathogen encountered [62]. Necrotrophic pathogens seem to start reactions that depend on jasmonic acid and ethylene, while biotrophic pathogens trigger reactions that depend on salicylic acid. The processes responsible for this differential identification and reaction may include crosstalk between jasmonic acid, ethylene, and salicylic acid signal transduction pathways [63]. When a parasite is detected in a plant, its immune system responds by inducing a complex array of defensive responses by interacting with elicitor molecules [64]. Host-specific resistance and non-host-specific resistance are the two categories used to classify resistance in plant species. Interactions between certain genotypes of the host and the pathogen are necessary for host-specific resistance to develop, which then results in pathogen race-specific resistance [65].

#### 4.5. Virus

Viruses are parasites that need an organism's host body to replicate. The interaction between the host and the virus leads to the development of several tactics to boost the plant's defensive system [66]. The factors that contribute to plant illnesses, such as the environment, plant host, and pathogen, may all be influenced by biocontrol agents. Several countries worldwide have produced and registered numerous bio-control medications with effective phytopathogen inhibitory activity to reduce plant damage and promote plant growth and development. The use of biocontrol agents includes the natural or purposeful exploitation of living creatures (microorganisms) that interact with phytopathogens [67].

These interactions have the potential to change the conditions of the soil and significantly impact the health of the plants in numerous ways. Plants have undergone evolutionary processes in response to their specific environmental circumstances, and they engage in ongoing interactions with other microorganisms. Hypersensitive response induction in plants is related to the proliferation of necrotic or chlorotic lesions and aberrant development, which seems to increase ethylene biosynthesis. The interaction between viruses and hosts influences the production and level of auxin in plants. In addition, viral infections alter the endogenous levels of cytokinins (CK) in plants [68,69].

#### 4.6. Bacteria

Bacterial elicitation is the process of inducing a physiological or biochemical response in plants by using bacteria and their biological components (Table 3). Since bacteria already exist in the soil, plants confront enormous obstacles in the environment, which encourages the creation of secondary metabolites as a defensive strategy. Similar to this, live bacteria cultures may be able to stimulate the production of secondary metabolites in the absence of oxygen [70,71]. Comparatively, bacterial elicitors have a shorter growing time and fewer preparatory procedures than other biotic elicitors [72].

#### 4.7. Fungal Elicitation

Fungal association with the plant root, such as arbuscular mycorrhizal fungi (AMF), helps the plant contain nitrogen, sulfur, phosphorus, and micronutrients required for growth and development. This symbiosis improves plant water uptake while preventing harmful fungi, microorganisms, and nematode parasites from entering the plant via the roots [81].

Fungal elicitors (free-living and endophytic) are the most significant and often employed biotic elicitors for the synthesis of industrial compounds (Table 4). Because of the hypersensitive reactions brought on by the interaction between fungi and plants, phytoalexins are increased, and secondary metabolite production is more efficiently stimulated [82]. Pure fungal cultures are frequently made using the hyphal tip culture. Water-soluble extracts of *Aspergillus niger*, *Aspergillus flavus*, *Penicillium notatum*, and *Fusarium oxysporum*, among others, were utilized to stimulate the formation of anthocyanins in *D. carota* L. In contrast to *P. notatum* and *F. oxysporum* treatments, mycelial extracts of *A. flavus* provided

the greatest elicitation through a double rise in anthocyanin synthesis [83]. In a different experiment, *A. niger* increased the production of thiophene in *T. patula* L. by 85% in comparison to a control [84]. In comparison to earlier non-biological elicitation techniques, the use of *A. niger* as an elicitor enhanced menthol production in *Mentha piperita* L. cell cultures to a level of 140.8 mg/L [85].

**Table 3.** Role of bacterial elicitor for the production of secondary metabolites in plant.

| Bacterial Elicitor                                         | Plant Species                  | Types of Elicitors                                                           | References                                                              |
|------------------------------------------------------------|--------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <i>Bacillus subtilis</i>                                   | <i>Gymnocma sylvestre</i>      | Acetoin, Surfactin, mycosubtilin, fengycin, iturines, 2,3-butanediol, StPep1 | Vatsa et al., 2011 [73]                                                 |
| <i>Helminthosporium victoria</i>                           | <i>Solanum tuberosum</i>       | Victorin                                                                     | Abdel-monaim et al., 2011 [74]                                          |
| <i>Magnaporthe grisea</i>                                  | <i>Oryza sativa</i> L.         | PemG1                                                                        | Ning et al., 2004 [75]                                                  |
| <i>Phytophthora</i> and <i>Pythium</i>                     |                                | $\beta$ -Glucans and chitin oligomers                                        | Abdel-monaim et al., 2011 [74]                                          |
| <i>Phytophthora infestans</i>                              | <i>Nicotiana tabacum</i>       | Glucans and eicosapentaenoic acid                                            | Ning et al., 2004; Vatsa et al., 2011 [73,75]                           |
| <i>Phytophthora sojae</i>                                  |                                | Glycoprotein                                                                 | Minami et al., 1996 [76]                                                |
| <i>Pseudomonas fluorescens</i> WCS374r                     | <i>Hypericum perforatum</i> L. | Pseudobactin                                                                 | Minami et al., 1996; Sanabria et al., 2010; Vander et al., 1998 [76–78] |
| <i>Pseudomonas syringae</i> pv. <i>tomato</i> (Pst) DC3000 | <i>Pinellia ternate</i>        | Coronatine                                                                   | Vander et al., 1998 [78]                                                |
| <i>Trichoderma harzianum</i>                               | <i>Triticum aestivum</i>       | C6 Zinc finger protein-like elicitor (Thc6)                                  | Day et al., 2014; Vander et al., 1998 [78,79]                           |
| <i>Arthrobacter</i> spp.                                   | <i>Oryza sativa</i> L.         |                                                                              |                                                                         |
| <i>Pseudomonas fluorescens</i>                             | <i>Hypericum perforatum</i> L. | N, N-Dimethyl hexadecyl amine                                                | Sanabria et al., 2010 [77]                                              |
| <i>Sinorhizobium meliloti</i>                              | <i>Medicago sativa</i>         |                                                                              |                                                                         |
| <i>Burkholderia gladioli</i>                               | <i>Panicum virgatum</i>        | Lipopolysaccharides                                                          | Schuhegger et al., 2006 [80]                                            |

*A. niger* produced nine times more gymnemic acid in *G. sylvestre* (Retz.) schult cultures than it did in those cultures [86]. *A. niger* and *Rhizopus stolonifera* produced 4.9 and 3.8 times more glycyrrhizin in *Abrus precatorius* L. cultures, respectively [87]. Commercial value can be found in the dye-producing plant *Oldenlandia umbellata* L. Elicitors such as *A. niger*, *Mucor prayagensis*, and *Trichoderma viride*, among others, were used to accelerate its growth. With 79 shoots and 47 roots, *A. niger*-treated cultures showed the greatest response [88].

*P. quinquefolius* L. suspension cells were employed to extract ginsenoside from *Trichoderma atroviride* and *T. harzianum* culture filtrates. *T. atroviride* produced ginsenoside (3.2 times more than the control) after a 5-day treatment. It was used to produce the simultaneous metabolite ginsenoside and anthocyanin in suspension-cultured cells of *P. sikkimensis* [89]. *T. harzianum* filtrate raised asiaticoside production on *Centella asiatica* L. cultures by 2.53 times. *Colletotrichum lindemuthianum* decreased asiaticoside production but increased biomass, and *F. oxysporum* inhibited shoot growth and produced poor asiaticoside yield [90].

After being treated with the cultures of *H. perforatum* L., the extracts of *F. oxysporum*, and *Botrytis cinerea* caused a decline in biomass and an immediate rise in phenylpropanoid and naphtho-dianthrones. Hypericin and pseudo-hypericin levels peaked early in the growth stage and then steadily declined. In contrast to the control, where only trace amounts of ajmalicine and 5.8 g/L catharanthine were found, *Micromucoris abellina* filtrates from cultures rapidly increased indole alkaloid biosynthesis in *Catharanthus roseus* (L.) G. Don. As a result, 400 g/L ajmalicine and 600 g/L catharanthine were produced [91].

To treat *Corylus avellane* L. cell suspension cultures, endophytic fungi like *Chaetomium globosum* and *Paraconiothyrium brasiliense* were obtained from *Taxus baccata* L. and *Corylus avellane* L., respectively. The highest level of elicitation was observed at 10% (v/v) of *C. globosum*, with a 4.1-fold increase in paclitaxel production on day 17 [92]. Table 4 lists the most frequent fungal stimuli for the production of secondary compounds.

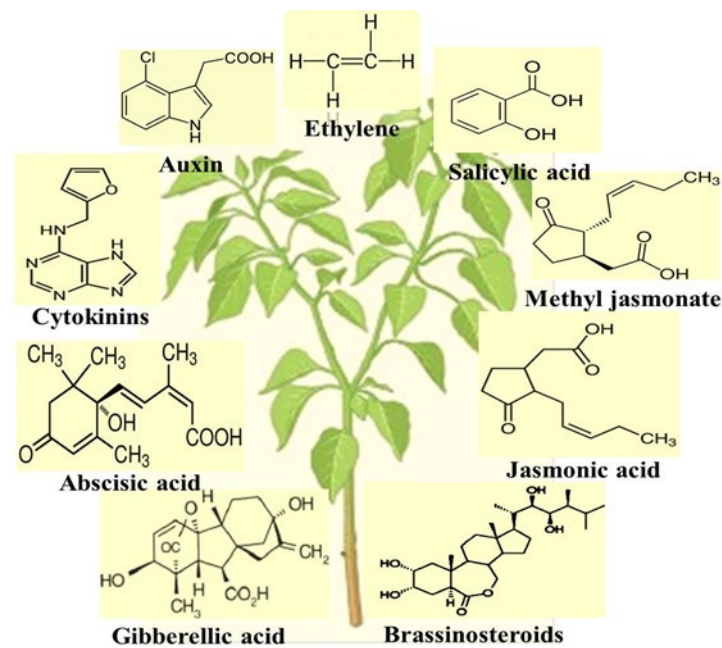
**Table 4.** Fungi elicitors used in the production of secondary metabolites with biological activities.

| Fungi Elicitor                 | Plant Species                                                                       | Secondary Metabolites                           | Biological Activity                                                                                                                                                                                                                                 | References                                                               |
|--------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| <i>Phytophthora megasperma</i> | <i>Soybeans and capsicum annum</i>                                                  | Glyceollin                                      | Antiestrogen effect in breast cancers, anti-vasculogenesis, anti-inflammatory, anti-tumor, anti-septic, and osteoinductive activity                                                                                                                 | Akutagawa et al., 2019; Chamkhi et al., 2021 [93,94]                     |
| <i>Alternaria carthami</i>     | <i>Catharanthus Tinctorius</i> L.                                                   | Polyacetylenes                                  | Antiproliferative, anti-inflammatory, antifungal antimicrobial, insecticidal, and repellent activity                                                                                                                                                |                                                                          |
| <i>Alternaria tenuis</i>       | <i>Catharanthus roseus</i> (L.) G. Don                                              | Diosgenin                                       | Anti-diabetic, apoptotic, necrotic, and anti-proliferative, anti-Alzheimer, genotoxic, mutagenic, autoimmune encephalitis activity, and cardiovascular disorders                                                                                    | Banchio et al., 2008; Iman et al., 2016 [54,95]                          |
| <i>Fungal mycelia</i>          | <i>Panax Ginseng</i> C.A.                                                           |                                                 | Anti-tumor and immunomodulating activity                                                                                                                                                                                                            | Rokem et al., 1984 [96]                                                  |
| <i>Rhizopus arrhizus</i>       | <i>Morinda citrifolia</i> L.                                                        |                                                 |                                                                                                                                                                                                                                                     | Akutagawa et al., 2019 [93]                                              |
| <i>Aspergillus flavus</i>      | <i>Zea mays</i> L.                                                                  | Anthocyanin                                     | Antioxidant, anti-inflammatory, antioxidant, anticancer and anti-allergic activity                                                                                                                                                                  | Bahadur et al., 2007 [56]                                                |
| <i>Penicillium chrysogenum</i> | <i>Arabidopsis thaliana</i>                                                         | Artemisinin                                     | Anti-angiogenic, anti-tumoral, anti-inflammatory, antibacterial, osteoprotective, antiviral, antimalarial, antiparasitic, and antifungal activity                                                                                                   | Bahadur et al., 2007; Banchio et al., 2008 [54,56]                       |
| <i>Phytophthora parasitica</i> | <i>Nicotiana tabacum</i>                                                            | Coumarin                                        | Antioxidant, antibacterial, antiproliferative, aminudin $\alpha$ -glucosidase inhibitory activity                                                                                                                                                   | Akutagawa et al., 2019; Chen et al., 2003 [93,97]                        |
| <i>Protomyces gravis</i>       | <i>Ambrosia artemisiifolia</i>                                                      | Thiarubrine A                                   | Antibiotic, antiviral, and anti-HIV activity                                                                                                                                                                                                        | Chen et al., 2003 [97]                                                   |
| <i>Rhizoctonia solani</i>      | <i>Abrus precatorius</i> L.                                                         | Sesquiterpenes                                  | Anti-Alzheimer, anti-influenza A (H <sub>1</sub> N <sub>1</sub> ), Cytotoxic, allelopathic, and antibacterial activity                                                                                                                              | Banchio et al., 2008 [54]                                                |
| <i>Pythium aphanidermatum</i>  | <i>Nicotiana Tabacum</i> ,<br><i>Lycopersicon esculentum</i>                        | <i>p</i> -Hydroxy benzoic acid, rosmarinic acid | Anti-inflammatory, antifibrotic, anti-diabetic, antioxidant, anticancer, genotoxic, antimicrobial, hepatoprotective, allelochemical, immunotherapeutic, antifeedant, antibacterial, antifungal, molluscicide activity, and anti-convulsant activity | Bahadur et al., 2007; Banchio et al., 2008; Iman et al., 2016 [54,56,95] |
| <i>Aspergillus niger</i>       | <i>Abrus precatorius</i> L.,<br><i>Gymnema sylvestre</i> ,<br><i>Taxuschinensis</i> |                                                 |                                                                                                                                                                                                                                                     |                                                                          |
| <i>Rhizoctonia solani</i>      | <i>Phaseolus vulgaris</i> L.                                                        | Sesquiterpenes                                  | Anti-Alzheimer, anti-influenza A (H <sub>1</sub> N <sub>1</sub> ), Cytotoxic, allelopathic, and antibacterial activity                                                                                                                              | Banchio et al., 2008 [54]                                                |
| <i>Verticillium albo-atrum</i> | <i>Withania somnifera</i>                                                           | Phytoalexins                                    | Antimicrobial and anticancer activity                                                                                                                                                                                                               | Chamkhi et al., 2021 [94]                                                |

#### 4.8. Plant Growth Regulators

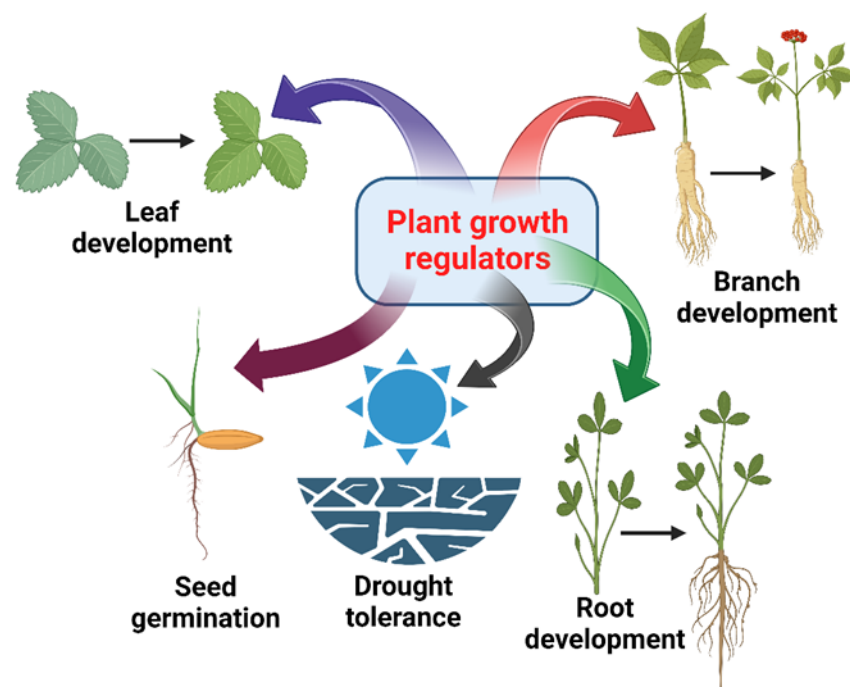
Hormones (chemical messengers) influence the capacity of the plant to react based on environmental conditions. Specific target tissues are identified with plant hormones and respond physiologically. On the other hand, some plant hormones (Figure 4) act as elicitors to influence the genetic expression of multiple photosynthetic pathway genes. Salicylic acid and jasmonic acid and their derivatives are essential in gene expression for signals. While abscisic acid is a stress hormone, it prompts a quick reaction to stress [46].

By regulating phytohormones in strawberry cell suspensions, researchers tried to increase anthocyanin aggregation in *Fragaria ananassa*, *Daucus carota*, *Oxalis reclinata*, and *Ipomoea batatas*. The impact of several growth-regulating agents is investigated on the biomass aggregation and anthocyanin content of batch crops of *Daucus carota* grown in liquid and solid states. At various levels where growth and production of the pigments were encouraged, growth regulators like 2,4-D and indole-3-acetic acid (IAA) were complementary. Therefore, when treated with methyl jasmonic acid (MeJA), the most substantial improvement was achieved in anthocyanin biosynthesis [98].



**Figure 4.** Different plant hormones as elicitors.

Calcium is a pervasive molecule active in the plant's signal transduction in different pathways. It has been demonstrated that the calcium ion inflow enhances the plant's stress-related reaction to light, salt, drought, and cold temperatures. Treatment of low-calcium *Daucus carota* cultures increased both the growth of the plant and the production of anthocyanin. It was recently demonstrated that exogenous calcium addition stimulates somatic embryogenesis in vitro in *Coffea canephora* culture. By stimulating endogenous production of IAA in the roots of etiolated seedlings of *Brassica juncea*, exogenously administered melatonin, and increasing root development [4]. Figure 5 shows various influences on the different aspects of plants.



**Figure 5.** Hormones influence the different aspects of plants in response to environmental conditions.

#### 4.8.1. Ethylene

The phytohormone ethylene has a significant impact on the entire plant life cycle, but it is especially important for the development of resistance to abiotic stress. Functional genomics has gradually characterized the action mechanism of ethylene in the growth of medicinal plant parts and fiber elongation [99]. It is an essential factor in the response of plants to microbial pathogens, including herbivorous insects, as well as in plant interactions with beneficial microorganisms and insects, as shown in Table 5 [100]. Ethylene also affects a variety of plant processes, including maturation and the process of aging [101,102].

**Table 5.** Role of ethylene, auxin, cytokine, and abscisic acid in the production of secondary metabolites in plants.

| Plant Species                      | Compounds                                                              | Reference                                                                             |
|------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| <b>Ethylene</b>                    |                                                                        |                                                                                       |
| <i>Fragaria ananassa</i>           | Anthocyanin                                                            | McSteen et al., 2008 [103]                                                            |
| <i>Daucus carota</i>               | Phenolic compounds                                                     | Heredia et al., 2009; Ke et al., 2018; Liang et al., 2013; Liu et al., 2016 [104–107] |
| <i>Camellia sinensis</i> L.        |                                                                        |                                                                                       |
| <i>Salvia miltiorrhiza</i>         |                                                                        |                                                                                       |
| <i>Catharanthus roseus</i>         |                                                                        |                                                                                       |
| <i>Vitis vinifera</i>              | Flavonoids, Phenolic acids, Stilbenes, and Flavonols                   | Ma et al., 2021 [108]                                                                 |
| <i>Rauwolfia serpentina</i>        | Alkaloids                                                              | Baharudin et al., 2023 [109]                                                          |
| <i>Catharanthus roseus</i>         |                                                                        |                                                                                       |
| <i>Arabidopsis</i> sp.             | Glucosinolate                                                          | Villarreal-García et al., 2016 [110]                                                  |
| <i>Pinophyta</i> sp.               | Terpenoids                                                             | Ninkuu et al., 2021 [111]                                                             |
| <b>Auxin</b>                       |                                                                        |                                                                                       |
| <i>Beeta vulgaris</i>              | Betalain                                                               | Taya et al., 1992 [112]                                                               |
| <i>Catharanthus roseus</i>         | Indole alkaloids                                                       | Moreno et al., 1993 [113]                                                             |
| <i>Chamomile recutita</i>          | $\alpha$ -Bisabolol oxide                                              | Çakmakçı et al., 2020 [114]                                                           |
| <i>Melissa officinalis</i> Lam     | Nerol and Geraniol                                                     | Da Silva et al. 2005 [115]                                                            |
| <i>Papaver somniferum</i>          | Thebaine                                                               | Jamwal et al., 2018 [116]                                                             |
| <i>Rauwolfia serpentine</i>        | Reserpine                                                              |                                                                                       |
| <i>Corydalis ambigua</i>           | Corydaline                                                             |                                                                                       |
| <i>Salvia moorcroftiana</i> L.     | Phenolic compound, and Flavonoid                                       | Bano et al., 2022 [117]                                                               |
| <b>Cytokinin</b>                   |                                                                        |                                                                                       |
| <i>Cocos nucifera</i>              | 1,3-Diphenylurea                                                       | GE, 2006 [118]                                                                        |
| <i>Nicotiana tabacum</i>           | Cytokinin 7 and 9-glucosides                                           | Vylicilova, 2020 [119]                                                                |
| <i>Triticum aestivum</i>           | trans-Zeatin                                                           | Babosha et al., 2009 [120]                                                            |
| <i>Oryza sativa</i>                | Isopentenyladenine                                                     | Akagi et al., 2014 [121]                                                              |
| <b>Absciscic acid</b>              |                                                                        |                                                                                       |
| <i>Vitis vinifera</i> L.           | Polyphenols                                                            | Ferrandino et al., 2014 [122]                                                         |
| <i>Aristotelia chilensis</i>       | Anthocyanins                                                           | Wang et al., 2021 [98]                                                                |
| <i>Malus hupehensis</i>            |                                                                        | González-Villagra et al., 2018 [123]                                                  |
| <i>Artemisia annua</i>             | Artemisinin                                                            | Lv et al., 2021 [124]                                                                 |
| <i>Orthosiphon stamineus</i> Benth | Phenolics, Flavonoids and Soluble sugars                               | Thakur et al., 2019                                                                   |
| <i>Salvia miltiorrhiza</i>         |                                                                        | Ibrahim et al., 2013 [125,126]                                                        |
| <i>Atractylodes lancea</i>         | Atractylone, $\beta$ -Eudesmol and Hinesol, Atractylodin, Volatile oil | Wang et al., 2015 [127]                                                               |

#### 4.8.2. Auxin

The hormone auxin appears to be essential for the survival of plants and is commonly found as IAA. It performs a crucial role in controlling cell development and mitosis. On a large morphological scale, auxin influences apical dominance and root dominance, as well as other processes such as elongation and lateral root development [128,129]. The IAA also affects fluorescence, photosynthetic activity, and the formation of pigments, the biosynthesis of different metabolites (Table 5), and the plant's ability to handle stress. Auxin also helps oilseed crops develop and grow seeds, which increases the amount of oil extracted from seeds [130].

Auxins are very important for keeping leaves and fruits from falling apart as they grow. In contrast, a reduction in auxin causes the petiole branch to split and the fruit stem to droop, resulting in the leaves and fruit falling to the ground. Also, using ROS together with auxin may give plants a way to improve their performance when they are under stress [131]. Research shows that *Melissa officinalis* grows better when IAA is used, having more branches, nodes, calluses, longer stems, new roots, and stems [114].

#### 4.8.3. Cytokinins

Stronger cytokinins exist, such as synthetic phenyl urea derivatives Thidiazuron hormone (TDZ) and forchlorfenuron (CPPU) activity, which are crucial for plant growth. As opposed to adenine-form cytokinins like kinetin KIN and BAA, they promote adventitious bud development [132]. TDZ has proven to be an effective stimulant for in vitro shoot regeneration in some plant species. Utilizing plant cell culture techniques, important secondary metabolites have been produced in great quantities from a variety of medicinal plants, adding to our vast understanding of the synthesis and utilization of secondary metabolites from plants (Table 5) [133].

#### 4.8.4. Absciscic Acid

Absciscic acid (ABA) is a phytohormone that accumulates in response to many environmental and biological events, functioning as a stress hormone. It is an essential phytohormone that controls the expansion, maturation, and tolerance of plants to stress. It also regulates physiological processes in plants, such as the closing of stomata, the buildup of cuticular wax, the aging of leaves, the dormancy of buds, the germination of seeds, and the regulation of osmosis [128].

Plants quickly build up ABA, which then triggers several stress responses in response to things like drought and salt (Table 5). The activation of many LEA-class genes, including EM6, RD29B, EM1, RAB18, AIL1, and other well-established ABA-responsive indicator genes, is considered to protect plants against the detrimental effects of dehydration [134,135]. Through regulation of gene expression, ABA plays a key role in speeding up leaf senescence. Two marker genes up-regulated during senescence, ASSOCIATED GENE12 (SAG12), ORESARA1 (ORE1), and SENESCENCE, are transcriptionally stimulated by ABA [136,137].

#### 4.8.5. Gibberellic Acid

Gibberellic acid (GA) is a well-known diterpene phytohormone that develops secondary metabolites as an important elicitor, as listed in Table 6 [106]. Geranylgeranyl diphosphate (GGPP), a natural precursor of the diterpenoid C<sub>20</sub>, is present in them, and regulates many biosynthetic processes of development and production, notably germination of seeds, stem lengthening, flowering, development of fruits, and transcription of the cereal substratum aleurone. It is produced not only by higher plants but also by bacteria and fungi [138].

The GA of fungal and bacterial origin serves as a signaling factor to determine the interplay with the host plants. Also, functional cDNA expression library screening or molecular genetic methods using dwarf mutants deficient in GA biosynthesis have established enzymes for coding genes [139]. The critical growth regulators are consistent with

GA's role as hormonal and environmental signals. These are examined by GA biosynthesis and deactivation pathways [140].

#### 4.8.6. Brassinosteroids

A group of vital agricultural hormones known as brassinosteroids (BS) have a variety of roles in the complex growth and development of plants. They first evolved from *Brassica napus* pollen and are distinguished by their polyhydroxylated sterol structure. According to studies, they have been demonstrated to control a wide range of physiological processes, including seed germination, elongation of cells, division of cells, senility, vascular differentiation, growth, root development, photomorphogenesis, etc. [141].

About 70 brassinosteroids have been isolated, along with 24 metabolites and many conjugates. Epimerization, dehydrogenation, demethylation, acylation, esterification, hydroxylation, glycosylation, side-chain cleavage, and sulphonation are a few metabolic and catabolic processes that are involved in preserving the optimal levels of bioactive BS in the cell or tissue, as listed in Table 6. There are two categories of brassinosteroid metabolism, depending on the change in steroid conformation and side chains. They exhibit regulatory stress and growth-enhancing behavior. Elucidation of the biochemical and molecular impact of secondary metabolites and brassinosteroids has projected them as extremely promising and environmentally safe natural compounds ideal for wide use in plant defense and enhanced crop yield. Recent studies have also shown that BR biosynthesis can be regulated by external stimuli like salt, temperature, and stress [142].

**Table 6.** Role of gibberellic acid and brassinosteroids in the production of secondary metabolites in plants.

| Plant Species               | Compounds                                                                                          | References                   |
|-----------------------------|----------------------------------------------------------------------------------------------------|------------------------------|
| <b>Gibberellic acid</b>     |                                                                                                    |                              |
| <i>Salvia miltiorrhiza</i>  | Tanshinones                                                                                        | Yuan et al., 2018 [143]      |
| <i>Echinacea pupurea</i>    | Caffeic acid derivatives                                                                           | Abbasi, 2012 [144]           |
|                             | Caftaric and cichoric acid                                                                         | Jones et al., 2009 [145]     |
| <i>Artemisia annua</i>      | Artemisinin                                                                                        | Banyai et al., 2011 [146]    |
| <b>Brassinosteroids</b>     |                                                                                                    |                              |
| <i>Aegle marmelos</i>       | 24-Epibrassinolide                                                                                 | Sondhi et al., 2008 [147]    |
| <i>Brassica napus</i>       |                                                                                                    | Nolan et al., 2020 [148]     |
| <i>Helianthus annuus</i>    |                                                                                                    | Filová et al., 2013 [149]    |
| <i>Pisum sativum</i>        |                                                                                                    | Fedina et al., 2017 [150]    |
| <i>Raphanus sativus</i>     |                                                                                                    | Chaudhary et al., 2012 [151] |
| <i>Arabidopsis thaliana</i> | GSK-3/Shaggy, BKT1                                                                                 | Rozhon et al., 2014 [152]    |
| <i>Brassica campestris</i>  | 24-Epibrassinolide, brassinolide                                                                   | Ferrie et al., 2005 [153]    |
| <i>Solanum lycopersicum</i> | 28-Homobrassinolide, 24-epibrassinolide                                                            | Hayat et al., 2012 [154]     |
| <i>Cupressus arizonica</i>  | Teasterone, 28-homocastasterone, 3-dehydroteasterone, brassinolide, and dolichosterone             | Griffiths et al., 1995 [155] |
| <i>Equisetum arvense</i>    | Brassinolide, 24-epibrassinolide, ,                                                                | Vardhini et al., 2006 [156]  |
| <i>Thea sinensis</i>        | Brassinolide, castasterone, 28-norbrassinolide, brassinone, 24-ethylbrassinone, and dolichosterone | Ikekawa et al., 1984 [157]   |
| <i>Citrus sinensis</i>      | Castasterone                                                                                       | Motegi et al., 1994 [158]    |
| <i>Zea mays</i>             | 28-Norbrassinolide, 28-norcastasterone, 28-homocastasterone, and 28-homodolichosterone             | Tumova et al., 2018 [159]    |
| <i>Lilium elegans</i>       | Brassinolide, castasterone, typhasterol, and teasterone                                            | Suzuki et al., 1994 [160]    |

#### 4.8.7. Jasmonic Acid (JA)

Higher-growing plants contain jasmonic acid (JA; 3-oxo-2-20 -cis-pentenyl-cyclopentane-1-acetic acid), a natural growth-regulating compound. The jasmonate group of cyclopentanone chemicals, which includes JA and MeJA, modulates a variety of plant reactions and serves as an efficient elicitor to increase in vitro generation of secondary compounds, as listed in Table 7 [161]. It is commonly produced in selective plants as a stress hormone. It has an essential role in many cellular processes, such as signaling in plant defense systems for gene expression and regulating protein production by the octadecanoid pathway, which causes systemic metabolic changes to control resistance against pathogenic JA [162]. Stomatal opening, Rubisco biosynthesis inhibition, nitrogen and phosphorus uptake, and the transport of organic materials like glucose can all be affected by it [163].

Many signal transduction routes, including short-distance, long-distance, airborne, and vascular bundle transmission, are well-recognized concerning the production and transmission of JA. Plants' metabolic pathways trigger secondary substance formation in response to stressors from the environment [164]. According to Chung et al. (2016), JA elicitation enhances the levels of phenolic molecules, or antioxidants, in basil and lettuce leaves. *Origanum majorana* L. has a significant increase in carotenoids in response to JA elicitation. The *O. majorana* L. plant's antioxidant profile can increase the elicitation of yeast extracts, which guarantees a high concentration of ascorbic acid and chlorophyll [165].

**Table 7.** Role of Jasmonic acid in the production of secondary metabolites in plants.

| Plant Species                  | Compounds                                | References                                                |
|--------------------------------|------------------------------------------|-----------------------------------------------------------|
| <i>Celastrus paniculatus</i>   | Phenolics                                | Anusha et al., 2016 [166]                                 |
| <i>Glycyrrhiza glabra</i>      | Soyasaponin                              | Hayashi et al., 2003 [167]                                |
| <i>Hypericum perforatum</i>    | Phenyl propanoids                        | Gadzovska et al., 2007 [168]                              |
| <i>Mentha piperita</i>         | Rosmarinic acid                          | Krzyzanowska et al., 2012; Almagro et al., 2014 [162,169] |
| <i>Psoralea corylifolia</i> L. | Psoralen                                 | Siva et al., 2015 [170]                                   |
| <i>Vitis rotundifolia</i>      | Stilbene                                 | Nopo-olazabal et al., 2014 [171]                          |
| <i>Vitis vinifera</i>          | Anthocyanin, stilbene, trans-resveratrol | Curtin et al., 2003; Xu et al., 2015 [172,173]            |
| <i>Plumbago indica</i>         | Plumbagin                                | Gangopadhyay, 2011 [174]                                  |
| <i>Plumbago rosea</i>          |                                          | Silja, 2014 [175]                                         |

#### 4.8.8. Methyl Jasmonate

Methyl Jasmonate (MeJA) was first isolated from the essential oil of *Jasminum grandiflora* in 1962. The important signaling compounds suggested for the mechanism of elicitation, contribute to the hyperproduction of various secondary metabolites, e.g., JA, methyl ester, and MeJA [176]. It plays a vital role and demonstrates efficacy in improving secondary metabolite development in cell cultures, as listed in Table 8.

#### 4.8.9. Salicylic Acid (SA)

It induces several pathogens for systemic resistance, signals for defensive gene expression-regulating pathogens, and manages the tolerance of fungal, bacterial, and viral infections. The octadecanoid pathway, which is activated by JA, generates a variety of proteins (Table 9) that give plants immunity to insects. The triterpenoids, ginsenosides in ginseng, and glycyrrhizin in licorice are also caused to accumulate. According to recent research, SA at the right concentrations can also encourage the formation of monoterpenes [209–212]. Plants produce resistance to pathogenic bacteria when SA and JA are administered externally [213].

**Table 8.** Role of methyl jasmonate in the production of secondary metabolites in plants.

| Plant Species                    | Compounds                                       | References                                            |
|----------------------------------|-------------------------------------------------|-------------------------------------------------------|
| <i>Catharanthus roseus</i>       | Ajmalicine, serpentine, catharanthine, ajmaline | Ruiz-May et al., 2009 [177]                           |
| <i>Centella asiatica</i>         | Asiaticoside and centelloside                   | Kim et al., 2004; Gangopadhyay et al., 2011 [174,178] |
| <i>Hypericum perforatum</i>      | Flavonoids                                      | Wang et al., 2015 [127]                               |
| <i>Panax ginseng</i>             | Ginsenosides                                    | Kim et al., 2004; Corchete and Bru, 2013 [178,179]    |
|                                  | Ginsenosidea (Rg3)                              | Ali et al., 2005 [180]                                |
| <i>Ajuga bracteosa</i>           | Phenols, flavonoids, Phytoecdysteroids          | Saeed et al., 2017 [181]                              |
| <i>Andrographis paniculata</i>   | Andrographolide                                 | Sharma, 2015 [142]                                    |
| <i>Artemisia absinthium</i>      | Phenols and flavonoids                          | Ali et al., 2015 [180]                                |
| <i>Bacopa monnieri</i>           | Bacoside A                                      | Largia et al., 2015 [182]                             |
| <i>Thevetia peruviana</i>        | Phenolic compounds                              | Mendoza et al., 2018 [183]                            |
| <i>Persicaria minor</i>          | Sesquiterpenes                                  | Sellapan et al., 2018 [184]                           |
| <i>Gymnema sylvestre</i>         | Gymnemic acid                                   | Ajungla, 2009; Chodisetti et al., 2015 [185,186]      |
| <i>Salvia miltiorrhiza</i>       | Tanshinone                                      | Hao et al., 2015 [187]                                |
| <i>Portulaca oleracea</i>        | Dopamine, Non-adrenaline                        | Ahmadi et al., 2013, Pirian and Piri, 2012 [188,189]  |
| <i>Salvia officinalis</i>        | Diterpenoid                                     | Izabela and Halina, 2009 [190]                        |
| <i>Silybum marianum</i>          | Silymarin, tanshinone                           | Firouzi et al., 2003; Hao et al., 2015 [187,191]      |
| <i>Taverniera cuneifolia</i>     | Glycyrrhizic acid                               | Awad, 2014 [192]                                      |
| <i>Vitis vinifera</i>            | Stilbene, trans-resveratrol, anthocyanin        | Xu et al., 2015; Taurino, 2015 [31,173]               |
| <i>Withania somnifera</i>        | Withanolide A, withanone, withaferin A          | Sivanandhan et al., 2013 [193]                        |
| <i>Satureja khuzistanica</i>     | Rosmarinic acid                                 | Khojasteh et al., 2016 [194]                          |
| <i>Taxus baccata</i>             | Phenolic content                                | Ghobanpour et al., 2014 [60]                          |
| <i>Taxus cuspidate</i>           | Paclitaxel                                      | Pedapudi et al., 2000 [195]                           |
| <i>Taxus canadensis</i>          |                                                 |                                                       |
| <i>Hyoscyamus albus</i>          | Phytoalexins                                    | Kuroyanagi et al., 1998 [196]                         |
| <i>Medicago truncatula</i>       | Protein content                                 | Thatcher et al., [197]                                |
| <i>Rubia tinctorum</i>           | Anthraquinone                                   | Perassolo et al., 2011 [198]                          |
| <i>Eschscholtzia californica</i> | Benzophenanthridine alkaloid                    | Cho et al., 2008 [199]                                |
| <i>Origanum basilicum</i>        | Hydroxycinnamic acid derivatives                | Mathew and Sankar, 2012 [200]                         |
| <i>O. sanctum</i>                |                                                 |                                                       |
| <i>O. gratissimum</i>            |                                                 |                                                       |
| <i>Melastoma malabathricum</i>   | Anthocyanin                                     | Suan et al., 2011 [201]                               |
| <i>Glycyrrhiza glabra</i>        | Glycyrrhizin                                    | Shabani et al., 2009 [202]                            |
| <i>Drosera indica</i>            | Plumagin                                        | Thaweesak et al., 2011 [203]                          |
| <i>Arabidopsis thaliana</i>      | Anthocyanin                                     | Peng et al., 2011 [204]                               |
| <i>Fragaria ananassa</i>         |                                                 | Perez et al., 1977 [205]                              |
| <i>Vaccinium pahalae</i>         |                                                 | Fang et al., 1999 [206]                               |
| <i>Tulipa Gesneriana</i>         |                                                 | Saniewski et al., 2003 [207]                          |
| <i>Rubus idaeus</i>              |                                                 | Pedapudi et al., 2000 [195]                           |
| <i>Coleus blumei</i>             | Rosmarinic acid                                 | Szabo et al., 1999 [208]                              |

**Table 9.** Role of salicylic acid in the production of secondary metabolites in plants.

| Plant Species                   | Compounds                                  | References                                                      |
|---------------------------------|--------------------------------------------|-----------------------------------------------------------------|
| <i>Datura metel</i>             | Hyoscyamine and scopolamine                | Ajungla, 2009 [185]                                             |
| <i>Daucus carota</i>            | Chitinase                                  | Muller et al., 1994 [214]                                       |
| <i>Digitalis purpurea</i>       | Digitoxin                                  | Patil et al., 2013 [215]                                        |
| <i>Brumansia candida</i>        | Scopolamine (alkaloid)                     | Avancini et al., 2003 [216]<br>Pitta-alvarez et al., 2000 [217] |
| <i>Rubia cordifolia</i>         | Anthraquinone                              | Bulgakov et al., 2002 [218]                                     |
| <i>Gymnema sylvestre</i>        | Gymnemic acid                              | Chodisetti et al., 2013 [219]                                   |
| <i>Hypericum hirsutum</i>       | Hypericin and pseudohypericin              | Coste et al., 2011 [220]                                        |
| <i>Vitis vinifera</i>           | Stilbene, vinblastine and vincristine      | Xu et al., 2015 [173]                                           |
| <i>Withania somnifera</i>       | Withanolide A, withanone, and withaferin A | Sivanandhan et al., 2013 [193]                                  |
| <i>Aloe vera</i>                | Polysaccharides and phenolics              | Shukla and kiridena, 2016 [221]                                 |
| <i>Stephania venosa</i>         | Dicentrine                                 | Kitisripanya et al., 2013 [222]                                 |
| <i>Pilocarpus pennatifolius</i> | pilocarpine                                | Avancini et al., 2003 [216]                                     |
| <i>Glycyrrhiza glabra</i>       | Glycyrrhizin                               | Shabani et al., 2009 [202]                                      |

## 5. Conclusions

Numerous stressors, including the growth and production of secondary metabolites, have an impact on plants. The main benefit of elicitation is synthesizing bioactive metabolites with independence from the environment and soil conditions. Significant progress has been made in using elicitation techniques to manufacture chemicals and pharmaceuticals. Genetic alterations are used to control the formation of secondary metabolites that can improve the plant's potential by enhancing its natural defense mechanisms and can be influenced by both biotic and abiotic influences. The molecular understanding of the stress response can aid in the improvement of in-plant processes with enhanced adaptability and efficiency. Though elicitation increases secondary metabolism in plants or plant cells, the specific process of elicitation is unknown. Experts in plant science, pharmacognosy, microbiology, phytochemistry, biochemistry, molecular biology, and fermentation technology can work together to maximize the capacity of plant cells. This opens up the possibility of doing extensive research to use plant cells for the production of secondary metabolites for various applications. It can also help in developing eco-friendly agricultural practices and the production of healthier crops.

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