



Elicitors and Secondary Metabolite Production: Review on Mechanisms, Applications, and Perspectives

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ABSTRACT

Secondary metabolites are essential for plant defense, ecological interactions, and human health. *In vitro* seed and embryo cultures provide a controlled environment for studying these compounds. This manuscript examines the effects of elicitors on secondary metabolite production in such cultures. It highlights the significance and application of secondary metabolites, introduces the concept of elicitors, and explains their role in enhancing metabolite production. Elicitors are categorized into biotic and abiotic types, with their mechanisms described in detail. The manuscript includes case studies and experimental data demonstrating the impact of elicitors on various cultures, emphasizing benefits such as increased yield, enhanced bioactivity, and improved quality. Challenges, such as cytotoxicity and response variability, are also discussed. It conveys the need for further research to optimize elicitor-based strategies for maximizing secondary metabolite production. This work serves as a valuable source of info for researchers who explore the role of elicitors in plant biotechnology.

Introduction

Importance of secondary metabolites in plants

Secondary metabolites are a diverse class of specialized organic compounds that, although not directly involved in plant growth, development, or reproduction, are indispensable for plant survival and ecological adaptation. Their biosynthesis is typically induced by biotic and abiotic stressors, including herbivory, pathogen invasion, extreme temperatures, and drought (Al-Khayri et al., 2023). Functionally, these metabolites mediate a wide array of ecological processes, from chemical defense against herbivores and pathogens to facilitating pollination and competitive interactions with neighboring species. Despite considerable advances in elucidating their biosynthetic pathways and ecological roles, substantial knowledge gaps persist,

particularly concerning the molecular mechanisms regulating their production and their broader contributions to plant resilience under shifting environmental conditions.

Defense is one of the primary roles of secondary metabolites. Alkaloids, such as nicotine in tobacco, act as potent neurotoxins deterring herbivory, while phenolic compounds like tannins disrupt microbial physiology, thereby limiting pathogen proliferation (Divekar et al., 2022; Lobiuc et al., 2023). Yet, although the chemical diversity of these compounds has been extensively catalogued, the regulatory networks coordinating their synthesis remain poorly characterized. The dynamic interplay between secondary metabolite pathways and hormonal signaling cascades, such as jasmonic acid–salicylic

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acid cross-talk, exemplifies an area of incomplete understanding. Furthermore, the metabolic trade-offs between investment in secondary metabolite production and allocation to primary processes—growth, reproduction, and yield—require systematic exploration, especially in the context of crop improvement.

Beyond defense, secondary metabolites underpin vital ecological interactions. Volatile compounds and floral pigments attract pollinators, ensuring reproductive success, while root-derived exudates facilitate symbioses with mycorrhizal fungi, enhancing nutrient acquisition and stress tolerance (Sharma et al., 2023; Noceto et al., 2021). Despite these established roles, critical questions remain unresolved. How will environmental change, including elevated atmospheric CO₂ concentrations and rising global temperatures, alter both the quantity and efficacy of these compounds? Are there yet-undiscovered metabolites that govern plant–microbe and plant–pollinator interactions in ways not currently appreciated? Addressing such questions is essential for predicting plant community dynamics and ecosystem stability under future climate scenarios.

Although prior research has provided significant insights, much of the field remains fragmented, with studies often confined to isolated compounds or individual stress responses. A comprehensive systems-level understanding—integrating molecular, physiological, and ecological dimensions—is still lacking. Moreover, the reliance on a narrow set of model plants constrains generalization, obscuring the species-specific metabolic adaptations that may carry substantial agricultural or ecological importance. Moving forward, multi-omics approaches that integrate genomics, transcriptomics, proteomics, and metabolomics hold promise for uncovering hidden regulatory mechanisms and identifying novel bioactive compounds. Equally important are field-based experiments that validate laboratory findings and assess their ecological relevance in complex natural settings. By bridging these gaps, future research can advance a holistic understanding of secondary metabolites, enabling the development of strategies to enhance crop resilience, promote sustainable agriculture, and support ecosystem restoration in the face of global change.

Potential applications of secondary metabolites

Secondary metabolites synthesized by plants represent a versatile reservoir of bioactive compounds with broad applications across multiple disciplines. Owing to their structural diversity and biological activities, many of these metabolites possess considerable pharmaceutical potential,

serving as a foundation for drug discovery and therapeutic innovation (Aware et al., 2022). Alkaloids such as morphine and vincristine exemplify this potential, functioning as powerful analgesics and anticancer agents, respectively (Varela et al., 2023). Likewise, terpenoids and flavonoids exhibit diverse pharmacological properties, including antioxidant, anti-inflammatory, and antimicrobial activities (Varela et al., 2023), underscoring their utility in the development of novel treatments for a wide spectrum of diseases.

In agriculture, secondary metabolites contribute significantly to plant protection and crop productivity. Numerous plant-derived compounds are being investigated as natural alternatives to synthetic pesticides and fungicides, offering environmentally sustainable solutions for pest and disease management (Fernandes et al., 2023). Furthermore, certain metabolites, such as gibberellins and cytokinins, function as plant growth regulators, promoting development and enhancing yield (Asif et al., 2022; Zahid et al., 2023). These applications highlight the growing importance of secondary metabolites in advancing sustainable agricultural practices.

The food industry also benefits substantially from secondary metabolites, which shape the sensory qualities and nutritional value of plant-derived products. Terpenoids and phenolic compounds confer the characteristic flavors, aromas, and pigmentation of fruits, herbs, and spices (Abbas et al., 2023; Maleš et al., 2022). Increasingly, these compounds are being utilized as natural substitutes for synthetic flavorings and additives. Moreover, polyphenols, widely recognized for their health-promoting effects, are incorporated into functional foods and dietary supplements to support human well-being (Banwo et al., 2021; Petropoulos, 2023). Beyond nutrition, secondary metabolites have secured a prominent role in cosmetics and personal care industries. Essential oils enriched in terpenoids are extensively used in perfumes, skincare, and hair care formulations, while polyphenols and carotenoids are valued for their antioxidant and anti-aging properties (Kouassi et al., 2022; Michalak, 2022). Their natural origin and bioactivity position them as attractive alternatives to synthetic compounds in cosmetic innovation.

Industrial and environmental applications of secondary metabolites further emphasize their versatility. Renewable compounds such as lignin and tannins are employed in paper manufacturing, bioplastics, and wastewater treatment (Mujtaba et al., 2023). Additionally, their potential as precursors for biofuels and bio-based chemicals offers sustainable alternatives to fossil fuel-derived resources (Narisetty et al., 2023; Wang et al., 2023). This manuscript presents a comprehensive overview of the multifaceted roles of secondary metabolites,

ranging from their ecological functions in plant defense, pollinator attraction, and symbiotic interactions to their practical applications in medicine, agriculture, nutrition, cosmetics, and industry. By integrating these perspectives, it underscores the critical importance of secondary metabolites as mediators of both plant survival and human innovation. Expanding our understanding of their biosynthesis, regulation, and functionality not only advances fundamental plant science but also provides a foundation for translational applications that promote health, sustainability, and environmental resilience.

Elicitors and their role in secondary metabolite production

Definition and concept of elicitors

Elicitors are defined as molecules or signals that trigger specific biological pathways in living organisms, particularly in plants (Humbal and Pathak, 2023). They may be derived endogenously from the plant itself or introduced exogenously, where they activate key defense mechanisms. By stimulating the biosynthesis of secondary metabolites such as phytoalexins, elicitors play a central role in strengthening plant defense responses (Shah and Gupta, 2023). Their mode of action relies on the plant's innate capacity to perceive external threats or internal damage and initiate corresponding protective strategies. Upon recognition, plants undergo complex biochemical and physiological adjustments, including reprogramming of gene expression, activation of signaling cascades, and accumulation of defensive compounds (Meena et al., 2022; Kumar et al., 2023).

Elicitors are broadly categorized into two classes: pathogen-associated molecular patterns (PAMPs), which include conserved microbial structures such as bacterial flagellin or fungal cell wall components, and damage-associated molecular patterns (DAMPs), released by plant cells upon wounding or stress (Shah and Gupta, 2023). In addition to these, certain beneficial microorganisms, such as mycorrhizal fungi, can function as elicitors by inducing systemic resistance and enhancing plant defense capacity.

The application of elicitors in agriculture and plant sciences has attracted growing interest due to their potential to enhance disease resistance, improve plant health, and increase crop productivity in an eco-friendly manner. Beyond practical applications, elicitors provide critical insights into plant immunity and contribute to a deeper understanding of the dynamic interactions between plants and their biotic and abiotic environments (Iula et al., 2022).

Mechanisms of action of elicitors

Elicitors activate plant defense responses through multiple, tightly regulated mechanisms. They are first perceived by pattern recognition receptors (PRRs) located on the plant cell surface, which recognize conserved molecular signatures such as pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) (Abdul Malik et al., 2020) (Fig. 1). This recognition event initiates a cascade of intracellular signaling processes that orchestrate defense activation. Among these, the mitogen-activated protein kinase (MAPK) cascade is one of the most extensively characterized pathways, modulating transcription factors that govern the expression of defense-related genes (Nandi and Aroeti, 2023).

Downstream responses include the enhanced biosynthesis of defense-related molecules, notably secondary metabolites such as phytoalexins, as well as antimicrobial peptides and hydrolytic enzymes that directly contribute to pathogen inhibition (Shah and Gupta, 2023). These compounds either suppress pathogen growth or reinforce plant tissues against biotic and abiotic stress. Another hallmark response is the rapid accumulation of reactive oxygen species (ROS), including hydrogen peroxide, which act not only as antimicrobial agents but also as critical secondary messengers that amplify defense signaling (Benchlih et al., 2023).

Elicitors also contribute to the activation of systemic acquired resistance (SAR), a durable defense mechanism that provides broad-spectrum protection against subsequent pathogen attacks (Urban et al., 2022). This process is mediated primarily through salicylic acid (SA) signaling, which primes distal tissues for enhanced defense responses (Joshi et al., 2022). Beyond SAR, elicitors modulate the levels and signaling dynamics of key phytohormones, including SA, jasmonic acid (JA), and ethylene (ET), which collectively coordinate defense strategies against biotrophic and necrotrophic pathogens (Li and Ahammed, 2023; Cox Jr, 2022).

Recent studies have further clarified the molecular basis of elicitor perception. Receptor proteins embedded in the plant cell membrane, such as pattern-recognition receptors (PRRs) with leucine-rich repeat (LRR) and nucleotide-binding site (NBS) domains, recognize conserved molecular signatures derived from pathogens or herbivores (Bhaskar et al., 2022). These include pathogen-associated molecular patterns (PAMPs), microbe-associated molecular patterns (MAMPs), damage-associated molecular patterns (DAMPs), and herbivore-associated molecular patterns (HAMPs) (Khaliq et al., 2023). Recognition of these signals initiates intracellular defense cascades that converge on two principal branches of plant immunity: pattern-triggered immunity (PTI) and effector-triggered immunity (ETI) (Fig. 2).

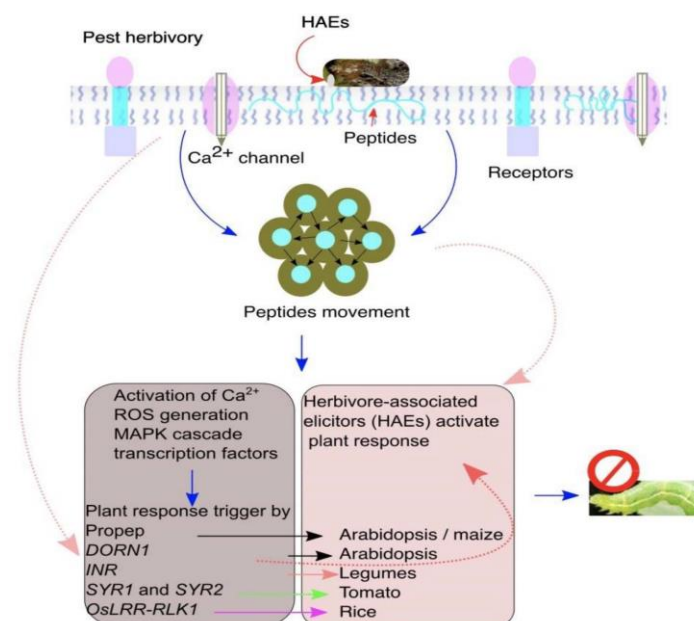


Fig. 1. The plant pattern-recognition receptors (PRRs) recognize herbivore-associated elicitors (HAEs) to elicit plant responses against insect herbivory (Malook et al., 2022).

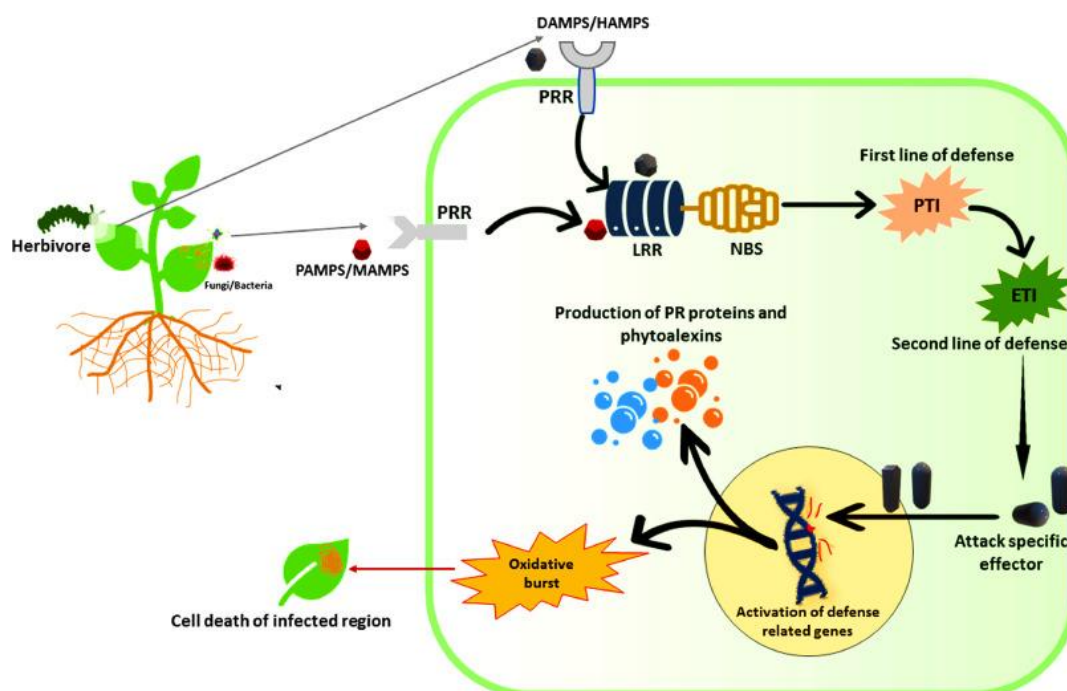


Fig. 2. Schematic presentation of defensive mechanism of elicitors (Meena et al., 2022).

The activation of PTI and ETI leads to extensive transcriptional reprogramming and the induction of genes associated with the biosynthesis of phytoalexins, antimicrobial proteins, and a wide range of bioactive metabolites. A central signaling route in this process is the octadecanoid pathway, which culminates in jasmonic acid (JA) biosynthesis and the subsequent production of defensive compounds that enhance resistance to biotic stressors (Pršić and Ongena, 2020). Through these

mechanisms, elicitors integrate localized and systemic signaling networks, thereby reinforcing plant immunity at multiple biological levels.

Elicitors have shown remarkable potential in enhancing the biosynthesis of high-value secondary metabolites. For instance, bacterial elicitors such as *Rhizobium rhizogenes* increased genistein production by 94%, while *Escherichia coli* elicitation resulted in a 9.1-fold increase in diosgenin accumulation (Pršić and Ongena, 2020). Similarly,

fungal elicitors demonstrate strong efficacy; treatment with *Aspergillus niger* enhanced thiophene production by 85%, whereas *Botrytis* species induced a striking 26-fold increase in sanguinarine levels. Algal-derived elicitors have also proven effective: extracts from *Haematococcus pluvialis* stimulated a 2.28-fold rise in betalain biosynthesis, while extracts from *Botryococcus braunii* elevated the production of vanillin, vanillylamine, and capsaicin by 3-fold, 6-fold, and 2.3-fold, respectively (Pršić and Ongena, 2020).

These findings highlight the substantial potential of elicitors to amplify secondary metabolite yields, opening new opportunities for applications in medicine, agriculture, and food science. The strategic use of elicitors not only offers an avenue to reduce dependence on synthetic agrochemicals but also enables the development of more resilient crop varieties and improved agricultural productivity (Kandoudi and Németh-Zámboiné, 2022) (Table 1).

Table 1. Mechanisms of action of elicitors.

| <i>Mechanisms of action</i> | <i>Key findings</i> | <i>References</i> |
|-----------------------------|--|--|
| Physiological | Initiate systemic acquired resistance or induced systemic resistance | (del Carmen Orozco-Mosqueda et al., 2023; Vallad and Goodman, 2004; Yu et al., 2022) |
| Biochemical | Accumulation of phytohormones that regulate downstream special metabolites | (Malook et al., 2022; L. Sharma et al., 2023; Zhai et al., 2017) |
| Molecular | Triggering the expression of stress-responsive genes | (Ahmad et al., 2019; Garstecka et al., 2023) |

Insect herbivores display a wide range of life cycles and feeding behaviors, forming complex interactions with their host plants. These interactions can often compromise the plants' defensive responses (Erb and Reymond, 2019). Plants perceive and respond to herbivory through molecular signals called herbivore-associated elicitors (HAEs). These elicitors are found in insect oral secretions, frass (the excrement of insect larvae), and egg-laying fluids, which activate plant defense mechanisms (Malook et al., 2022). Upon recognition by pattern-recognition receptors (PRRs) in the plant, HAEs enable plants to differentiate between herbivore feeding and other types of physical damage (Arias-Porras et al., 2023). This recognition triggers both localized and systemic defense responses tailored to the specific feeding arthropods. The interaction between HAEs and PRRs initiates significant alterations in plant metabolism and transcriptional activity, enhancing resistance to herbivory. Early signaling events include calcium influx, reactive oxygen species (ROS) production, and the activation of mitogen-activated protein kinases (MAPKs), forming the basis of the plant's coordinated response (Malook et al., 2022). In the molecular signaling model of plant response to insect herbivory, HAEs from the herbivores' oral secretions (OS) are detected by receptors located in the plant's plasma membrane. This detection initiates a rapid defense mechanism, often within minutes of herbivore feeding. Early signaling molecules such as ROS, calcium ions (Ca^{2+}), and MAPK signaling cascades are activated, alongside membrane depolarization (V_m). These early events stimulate the biosynthesis of jasmonate-

isoleucine (JA-Ile), a key signaling molecule. JA-Ile binds to the SCFCOII complex, leading to the degradation of JAZ proteins, which subsequently activates downstream defense responses in the plant (Fig. 3).

Types of elicitors: biotic and abiotic

Elicitors can be classified into two broad categories based on their origin and nature: biotic elicitors and abiotic elicitors (Alcalde et al., 2022). Biotic elicitors: Biotic elicitors are derived from living organisms or components of living organisms, such as pathogens or beneficial microorganisms. These elicitors are also of various types such as Pathogen-Associated Molecular Patterns (PAMPs), which are molecular patterns or compounds that are conserved among a particular group of pathogens (Zehra et al., 2021). These patterns are recognized by plant pattern recognition receptors (PRRs) and activate defense responses. Examples of PAMPs include bacterial flagellin, fungal chitin, and viral double-stranded RNA. Damage-Associated Molecular Patterns (DAMPs) are the other types of biotic electors which are endogenous molecules released by damaged plant cells or as a result of physical injury. DAMPs can act as danger signals, alerting the plant to the presence of potential threats. Examples of DAMPs include oligogalacturonides (OGs) released from pectin in cell walls, ATP, and peptides (Tanaka and Heil, 2021). The other types of biotic elicitors are called Induced Plant Volatiles. They can induce the release of volatile organic compounds (VOCs) from plants. These VOCs can act as signals to neighboring plants, triggering defense responses and preparing

them for potential threats. For example, herbivore-induced plant volatiles (HIPVs) can attract natural enemies of herbivores or induce defense responses in nearby plants (Ali et al., 2023).

Abiotic elicitors: abiotic elicitors are derived from non-living factors or environmental stressors. These elicitors can include various physical or chemical stimuli that induce defense responses in plants (Rani et al., 2023). Examples of abiotic elicitors include: heat, cold, and drought stress: exposure to high or low temperatures, water deficit, or drought conditions can induce defense responses in plants. These stressors can trigger the production of heat

shock proteins, osmoprotectants, and other defense-related compounds (P. Habibi et al., 2022).

UV Radiation: ultraviolet (UV) radiation can cause damage to plant cells and DNA. In response, plants can activate defense mechanisms, such as the production of flavonoids and other UV-absorbing compounds, to protect themselves from UV-induced stress (Emus-Medina et al., 2023). **Heavy metals and chemicals:** exposure to heavy metals, pollutants, or toxic chemicals can elicit defense responses in plants. This includes the activation of detoxification pathways, the production of antioxidant enzymes, and changes in gene expression to cope with the stress (Maleki et al., 2017).

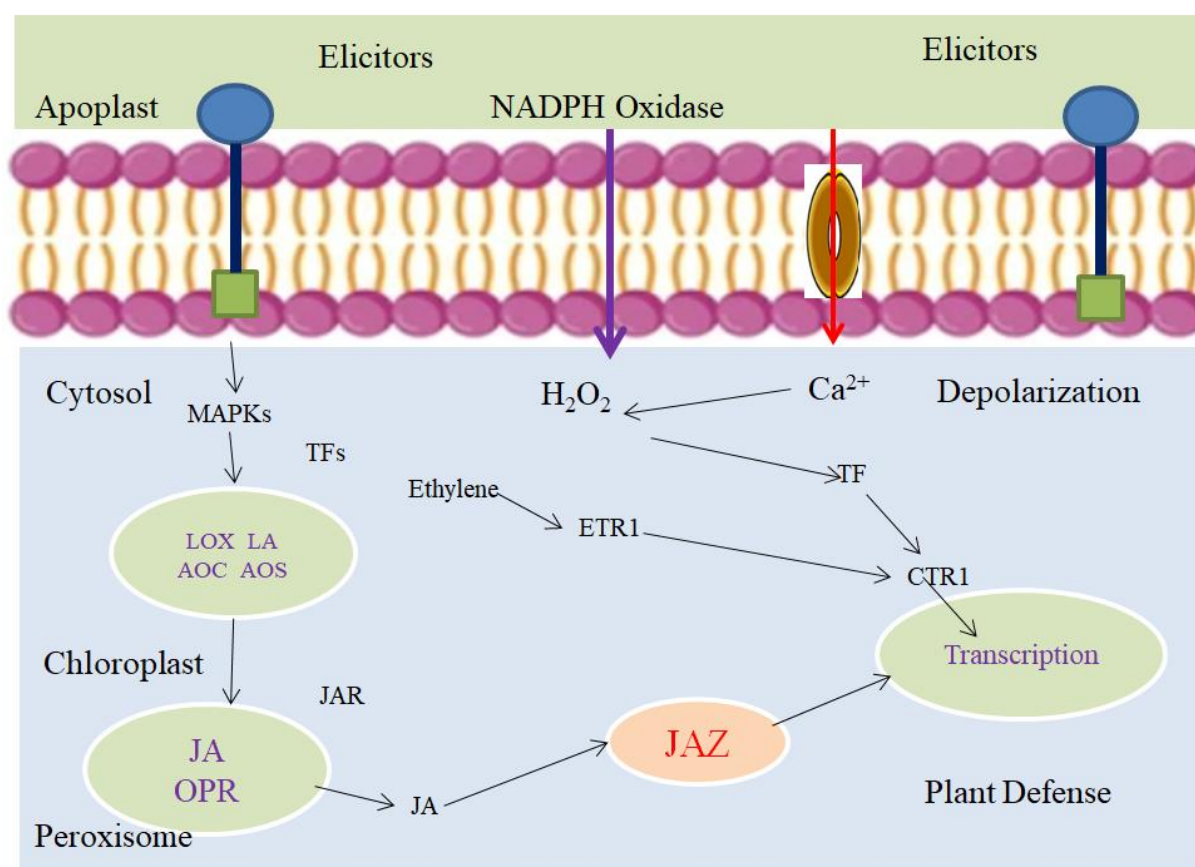


Fig. 3. The molecular signaling model of plant response to insect herbivory (modified from Malook et al., 2022).

Effects of elicitors on secondary metabolite production

There have been numerous case studies and experimental findings that demonstrate the effects of elicitors on the production of secondary metabolites in plants. For example, researchers found that treatment with various elicitors, including chitosan and yeast extract, significantly increased the production of phytoalexins, such as resveratrol and viniferins, in the grapevine cells (Lucini et al., 2018). In another independent investigation, it was revealed that treatment with methyl jasmonate (a plant hormone) significantly enhanced the production of

alkaloids, such as vincristine and vinblastine, in *Catharanthus roseus* (Madagascar periwinkle). Treatment with 100 μM methyl jasmonate (MeJA) significantly enhanced the production of alkaloids in *Catharanthus roseus* (Madagascar periwinkle). Specifically, the concentrations of vincristine and vinblastine increased to 0.9 $\mu\text{g g}^{-1}$ and 1.23 $\mu\text{g g}^{-1}$ fresh weight (FW), respectively, compared to control levels of 0.31 $\mu\text{g g}^{-1}$ and 0.5 $\mu\text{g g}^{-1}$ FW. This represents approximately a 190% increase in vincristine and a 146% increase in vinblastine content (Naeem et al., 2017). Similarly, researchers investigated the effects of various elicitors on the

production of essential oils in *Thymus vulgaris* (common thyme) and *Origanum vulgare* (oregano). They found that treatment with salicylic acid and methyl jasmonate significantly increased the yield and composition of essential oils in both herbs (Ghasemi Pirbalouti et al., 2014). Besides, different elicitors have impact on the production of flavonoids in soybean (*Glycine max*) suspension cultures (Devi et al., 2020).

Elicitors have also been shown to induce significant changes in the secondary metabolite profiles of plants. These changes can include alterations in the types and levels of secondary metabolites produced, as well as the activation of specific biosynthetic pathways (Humbal and Pathak, 2023). Elicitors can stimulate the production of phytoalexins, which are antimicrobial compounds synthesized by plants in response to pathogen attack or elicitor treatment (Jeandet et al., 2023). For example, treatment with chitosan, a biotic elicitor, has been shown to induce the production of phytoalexins such as resveratrol in grapevines and pisatin in pea plants (Shah and Gupta, 2023). Elicitors can also enhance the production of alkaloids, which are nitrogen-containing compounds with various biological activities. Elicitor treatment can also induce changes in terpenoid profiles. For

instance, treatment with methyl jasmonate has been shown to increase the production of terpenoids such as menthol and limonene in peppermint and lemon balm plants (Aqeel et al., 2023). Furthermore, elicitors can influence the composition of essential oils, which are complex mixtures of volatile secondary metabolites. For example, treatment with abiotic elicitors such as salicylic acid or jasmonic acid has been found to alter the composition of essential oils in herbs like thyme and oregano, leading to changes in the levels of specific compounds (Majdi et al., 2017). The change in composition is explained by Yadegari (2018), in such a way that foliar application of jasmonic acid (JA) and salicylic acid (SA) significantly influenced the essential oil composition of *Salvia officinalis* (sage). JA treatments notably increased the accumulation of compounds such as α -pinene, limonene, β -pinene, camphor, thymol, camphene, trans-thujone, cis-thujone, 1, 8-cineole, borneol, borneol acetate, carvacrol, α -humulene, and caryophyllene. The findings of different research works also reflect the increase in production of secondary metabolites due to effect of elicitors (Table 2).

Table 2. Effect of elicitors on production of secondary metabolites and their increase as compared to a control.

| Plant Species | Elicitor | Secondary Metabolites | Increase Compared to Control | Reference |
|----------------------------|--|---|---|-----------------------------|
| <i>Catharanthus roseus</i> | Methyl jasmonate | Vinblastine and vincristine | Vinblastine: 1.23 $\mu\text{g g}^{-1}$ FW (146% increase) Vincristine: 0.9 $\mu\text{g g}^{-1}$ FW (190% increase) | Naeem et al. (2017) |
| <i>Catharanthus roseus</i> | Methyl jasmonate | Vinblastine and vincristine | Vinblastine: 0.9 $\mu\text{g g}^{-1}$ FW (80% increase) Vincristine: 0.6 $\mu\text{g g}^{-1}$ FW (100% increase) | Karimi et al. (2018) |
| <i>Stevia rebaudiana</i> | Light (UV and spectral) | Steviol glycosides, phenolics, and flavonoids | Enhanced production of steviol glycosides, phenolics, and flavonoids in root cultures exposed to specific light conditions | Capataz-Tafur et al. (2020) |
| <i>Catharanthus roseus</i> | Methyl jasmonate and silver nanoparticles | Vincristine and vinblastine | Enhanced production of vincristine and vinblastine in tissue cultures treated with methyl jasmonate and silver nanoparticles | Shahin et al. (2021) |
| <i>Catharanthus roseus</i> | Methyl jasmonate and β -cyclodextrin | Vindoline, catharanthine, and ajmalicine | Significant enhancement in alkaloid production observed in cambial meristematic cells treated with MeJA and β -cyclodextrin | Zhong et al. (2015) |

Benefits and potential applications of elicitor-based strategies

Increased yield and productivity of secondary metabolites

Increasing the yield and productivity of secondary metabolites remains a focal point of research due to their wide-ranging applications in pharmaceutical, agricultural, and industrial domains (de Oliveira et

al., 2023). Genetic engineering offers one major strategy to enhance metabolite production by overexpressing key biosynthetic genes or transcription factors that regulate their pathways. For example, overexpression of *CHS* (chalcone synthase) in *Arabidopsis thaliana* has been demonstrated to increase flavonoid accumulation, while overexpression of MYB transcription factors

in *Nicotiana tabacum* has been shown to stimulate alkaloid biosynthesis (Zhan et al., 2022). Such approaches can yield substantial improvements in the production of targeted metabolites. Moreover, suppressing genes that act as negative regulators of secondary metabolite biosynthesis provides another promising strategy for enhancing metabolite output. Beyond single-gene manipulations, metabolic engineering enables a more direct and systematic reconfiguration of cellular pathways to redirect metabolic flux toward secondary metabolite biosynthesis (Patel et al., 2023). This approach may involve modifying enzymatic activities, increasing precursor availability, or balancing co-factor supply through interventions such as gene knockouts, gene silencing, or the introduction of heterologous biosynthetic pathways (Bagal et al., 2023). While genetic modification affords precise control over metabolic flux, its application is constrained by regulatory hurdles, ecological concerns, and issues of consumer acceptance.

In contrast, elicitation strategies harness external stimuli to activate plant defense responses, thereby enhancing secondary metabolite accumulation (Rani et al., 2023). Elicitors—including jasmonates, salicylic acid, and microbial-derived molecules—represent a non-transgenic alternative that can be applied in both *in vitro* systems and field conditions. A key advantage of elicitation lies in its capacity to induce metabolite synthesis without altering the plant's genetic constitution. However, elicitor performance varies with plant species, elicitor concentration, and mode of application. Some studies report substantial increases in metabolite yield following elicitor treatment, whereas others document inconsistent or species-specific responses (Bagal et al., 2023). This variability underscores the need for further optimization and standardization before elicitor-based strategies can be reliably applied at large scale.

When compared, genetic modification provides long-term and stable improvements in metabolite production but is often encumbered by ethical, ecological, and regulatory challenges. Elicitation, by contrast, offers a more flexible and environmentally sustainable option, though its reproducibility and consistency remain significant obstacles. Advancing both approaches will require deeper insights into the molecular mechanisms underlying elicitor-mediated responses and the development of more precise, efficient strategies for elicitation.

Enhanced bioactivity and therapeutic potential

Elicitors play a crucial role in enhancing both the bioactivity and therapeutic potential of secondary metabolites. By stimulating their biosynthesis, elicitors increase the yield of bioactive compounds, thereby improving their availability for research, development, and application (Kandoudi and

Németh-Zámoriné, 2022). In addition, elicitors activate plant defense mechanisms closely associated with secondary metabolite production. These defense responses often involve the synthesis of phytoalexins, antimicrobial peptides, and other bioactive molecules that protect plants against pathogens and environmental stressors (Ramírez-Gómez et al., 2019). The induction of such pathways not only promotes the accumulation of secondary metabolites but also enhances their bioactivity and therapeutic efficacy.

Elicitor treatments can further induce the production of secondary metabolites that are not typically synthesized under standard physiological conditions (Reshi et al., 2023). These novel metabolites frequently exhibit unique chemical structures and distinctive bioactivities, thereby presenting valuable opportunities for therapeutic exploration. By expanding both the structural and functional diversity of secondary metabolites, elicitation broadens the spectrum of compounds available for drug discovery and related applications (Mehta and Degani, 2023).

Moreover, elicitors contribute to improving the stability and shelf life of secondary metabolites. Certain elicitors stimulate the biosynthesis of compounds with preservative properties, thereby protecting metabolites from degradation or microbial contamination. Enhanced stability ensures the retention of bioactivity and therapeutic potential during storage and transportation (dos S. Costa et al., 2022).

In summary, elicitors significantly influence the bioactivity, yield, and stability of secondary metabolites. By stimulating their synthesis, modulating their biochemical profiles, and promoting the formation of novel compounds, elicitors provide promising avenues for the discovery and development of bioactive metabolites with therapeutic potential.

Future directions and research opportunities

Exploring novel elicitors and elucidating their mechanisms of action represents a critical direction for future research, particularly in advancing innovative strategies to enhance secondary metabolite production. Nanotechnology offers one promising avenue, as nanoparticles can serve as carriers to improve the stability, bioavailability, and targeted delivery of elicitors, thereby increasing their effectiveness. For instance, nano-encapsulated elicitors can enable controlled release, ensuring prolonged exposure and optimized plant responses. Another emerging strategy involves the combination of multiple elicitors or the development of hybrid forms, such as conjugating microbial-derived molecules with plant hormones. These hybrid systems hold the potential to generate synergistic effects, amplifying metabolite biosynthesis beyond

the capacity of individual elicitors. Advances in CRISPR-based gene editing further extend these possibilities by enabling the fine-tuning of plant receptors, thereby increasing their responsiveness to specific elicitors and improving the precision and efficiency of elicitation. Collectively, these approaches expand the range of tools available for enhancing the bioactivity, therapeutic potential, and quality of secondary metabolites.

A deeper understanding of the mechanisms by which elicitors activate secondary metabolite pathways remains central to optimizing their application. Investigating these molecular and physiological processes provides insights into plant defense and metabolic networks, which in turn can guide the design of targeted elicitation strategies for specific metabolites of interest. Importantly, elicitors also offer a sustainable and environmentally friendly alternative to conventional enhancement methods. By leveraging the natural defense systems of plants, elicitors reduce reliance on synthetic agrochemicals and promote eco-friendly cultivation practices, aligning with broader goals of sustainable production.

Equally important is the optimization of elicitation strategies to ensure their effectiveness and reproducibility. Research on novel elicitors can clarify the most effective concentrations, timing, and methods of application to maximize metabolite yield. Such refinements contribute not only to greater efficiency but also to the development of biotechnological tools for targeted production. Understanding elicitor mechanisms allows for the design of synthetic elicitors and genetic engineering interventions to upregulate key biosynthetic genes, thereby providing more precise and predictable modulation of secondary metabolite biosynthesis.

These scientific advances carry significant commercial implications. Effective elicitation strategies can facilitate the scalable and cost-efficient production of high-value secondary metabolites, with wide-ranging applications in pharmaceutical, nutraceutical, and agricultural industries. As such, the exploration of novel elicitors and their mechanisms of action represents not only a fundamental research priority but also a pathway toward sustainable innovation and industrial application.

The development of standardized protocols for elicitor application is essential to ensure consistency, reproducibility, and comparability of results across different studies. Such protocols should provide clear guidelines for selecting elicitors appropriate to the target secondary metabolite and plant species under investigation. Key factors, including elicitor concentration, timing, and mode of application, must be systematically defined. Protocols should also outline procedures for the preparation and formulation of elicitors to guarantee consistent and

accurate dosing. This includes specifications on solubility, storage conditions, and any required dilutions or adjustments to achieve the desired concentrations. Furthermore, standardized protocols should detail optimal dosing strategies and application methods, whether through foliar spraying, root application, or alternative delivery systems, including information on volume, frequency, and duration of application.

Beyond standardization, integrating elicitor-based strategies with other biotechnological approaches offers opportunities for synergistic effects that can significantly enhance secondary metabolite production. For example, elicitation can be combined with genetic engineering techniques to upregulate key genes involved in secondary metabolite biosynthesis. When such engineered plants are exposed to elicitors, their ability to accumulate desired metabolites is further amplified. Similarly, elicitor-based approaches can be integrated with metabolic engineering, which modifies metabolic flux to increase precursor availability and optimize biosynthetic pathways. In this context, elicitors can stimulate the expression of pathway-specific genes, while metabolic engineering fine-tunes the broader network to maximize metabolite yield (Perez-Matas et al., 2023; Zong et al., 2022).

Elicitor-based methods are also well suited for incorporation into bioreactor systems, which provide controlled environments optimized for large-scale secondary metabolite production. In such systems, elicitors may be applied continuously or periodically, ensuring sustained stimulation of biosynthesis (Mohaddab et al., 2022). Complementary to these approaches, omics technologies—including genomics, transcriptomics, proteomics, and metabolomics—offer powerful tools to dissect the molecular mechanisms underlying elicitor responses. The integration of elicitor treatments with omics analyses can reveal key genes, pathways, and regulatory elements involved in elicitation, thereby guiding the development of more precise and effective strategies (F. Habibi et al., 2024).

Advances in nanotechnology provide another frontier for enhancing elicitor efficiency. Nanoencapsulation, involving the encapsulation of elicitors within nanoscale carriers such as nanoparticles or liposomes, can protect elicitors from degradation, improve their stability, and facilitate targeted delivery to specific plant tissues. This technology not only prolongs the bioactivity of elicitors but also increases the precision and efficacy of secondary metabolite induction (Riseh et al., 2022). Together, these developments highlight the importance of standardization, integration, and technological innovation in advancing elicitor-based strategies. By combining rigorous protocols with

complementary biotechnological and nanotechnological approaches, researchers can optimize secondary metabolite production and accelerate their application in pharmaceutical, nutraceutical, and agricultural industries.

Conclusion

Elicitors have demonstrated considerable potential for enhancing secondary metabolite production in seed and embryo cultures *in vitro*. By stimulating the expression of key genes and activating biosynthetic pathways, they can significantly increase the accumulation of desired metabolites. Nonetheless, further research and optimization are essential to fully harness their potential. This entails identifying the most effective elicitors, determining optimal dosages, timing, and application methods, and tailoring strategies to specific plant species and target metabolites. Moreover, integrating elicitor-based approaches with complementary biotechnological techniques—such as genetic engineering and metabolic engineering—offers promising avenues to further amplify metabolite yield. Advancing research in this field will not only deepen our understanding of plant secondary metabolism but also enable the development of efficient, scalable, and sustainable methods for producing high-value metabolites with diverse pharmaceutical, nutraceutical, and agricultural applications.

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Author contributions

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Conflict of Interest

The authors indicate no conflict of interest in this work.

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