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Effect of Abiotic Stress Conditions on Alkaloid Metabolism: A Bibliometric Analysis

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Abstract

Alkaloids are nitrogen-containing secondary metabolites that play essential roles in plant defense, stress adaptation and pharmaceutical applications. Increasing climatic variability has intensified the exposure of plants to abiotic stresses such as drought, salinity, temperature extremes and ultraviolet (UV) radiation, thereby influencing alkaloid biosynthesis and accumulation. This study aimed to synthesize current knowledge on the physiological, biochemical and molecular mechanisms regulating alkaloid metabolism under abiotic stress. While, providing a comprehensive bibliometric assessment of global research trends in this field. A systematic bibliometric analysis was conducted using the Web of Science Core Collection database and the retrieved records were analyzed through VOSviewer to evaluate publication trends, leading contributors, collaboration networks and emerging research themes. The findings revealed that abiotic stresses significantly alter alkaloid metabolism through phytohormonal signaling, transcriptional regulation and metabolic reprogramming. Key stress-responsive pathways involving jasmonic acid, abscisic acid, reactive oxygen species and transcription factors such as AP2/ERF, WRKY and MYB were identified as major regulators of alkaloid biosynthesis. Bibliometric analysis demonstrated a substantial increase in research output over recent decades, with China and the United States emerging as the most productive countries. The Chinese Academy of Sciences, China Agricultural University and the University of Calgary were among the leading research institutions. Industrial Crops and Products, Molecules and Plant Physiology were identified as influential journals. While, Elsevier dominated as the leading publisher in this research domain. Keyword analysis highlighted a shift from fundamental alkaloid biosynthesis studies toward climate resilience, stress adaptation and multi-omics approaches. Future research should integrate genomics, transcriptomics, metabolomics, artificial intelligence and genome-editing technologies to accelerate the development of climate-resilient medicinal plants with stable alkaloid profiles under changing environmental conditions.

Keywords: *Climate resilience, Secondary metabolite biosynthesis, Plant stress signaling, Multi-omics integration, Medicinal plant biotechnology and VOSviewer.*

Introduction

Alkaloids are a structurally diverse group of naturally occurring nitrogen-containing secondary metabolites synthesized by plants, fungi and some microorganisms. These compounds include well-known examples such as nicotine, morphine, quinine and caffeine, each characterized by distinct heterocyclic nitrogen structures and significant pharmacological activities (Samanta & Manna, 2025; Ushie et al., 2023). In plants, alkaloids function primarily as chemical defense molecules that protect against herbivores, insects and pathogenic microorganisms through their toxic, deterrent or antimicrobial properties (Divekar et al., 2022). Beyond ecological significance, alkaloids possess considerable economic and medicinal value, serving as important sources of pharmaceuticals, stimulants, analgesics and anticancer agents (Hashim et al., 2025). Recent studies have demonstrated that alkaloid biosynthesis is highly responsive to environmental fluctuations, particularly abiotic stress conditions such as drought, salinity, extreme temperatures and ultraviolet (UV) radiation (Yeshi et al., 2022). Stress-induced metabolic reprogramming often alters carbon and nitrogen allocation within plants. Thereby, influencing secondary metabolite accumulation (Khan et al., 2026). Two major theoretical frameworks, namely the Carbon/Nutrient Balance Hypothesis (CNBH) and the Growth-Differentiation Balance Hypothesis (GDBH), explain these responses in FIGRE 1. The CNBH proposes that environmental stress modifies the relative availability of carbon and nutrients, leading to enhanced production of carbon-rich secondary metabolites under nutrient-limited conditions (Zhang, 2022). Conversely, the GDBH suggests that plants under moderate stress divert metabolic resources from growth processes toward differentiation and defense-related pathways, including alkaloid biosynthesis in FIGRE 1. These adaptive responses enable plants to enhance stress tolerance through antioxidant activity, osmotic regulation and protective signaling mechanisms (Choudhary et al., 2023; Mishra et al., 2023). The objective of this study was to comprehensively evaluate the effects of major abiotic stress factors, including drought, salinity, temperature extremes and UV radiation on alkaloid metabolism in plants. The paper also aimed to synthesize current knowledge on the physiological, biochemical and molecular mechanisms regulating stress-induced alkaloid biosynthesis. While, identifying emerging research trends, technological advances and future opportunities through bibliometric analysis.

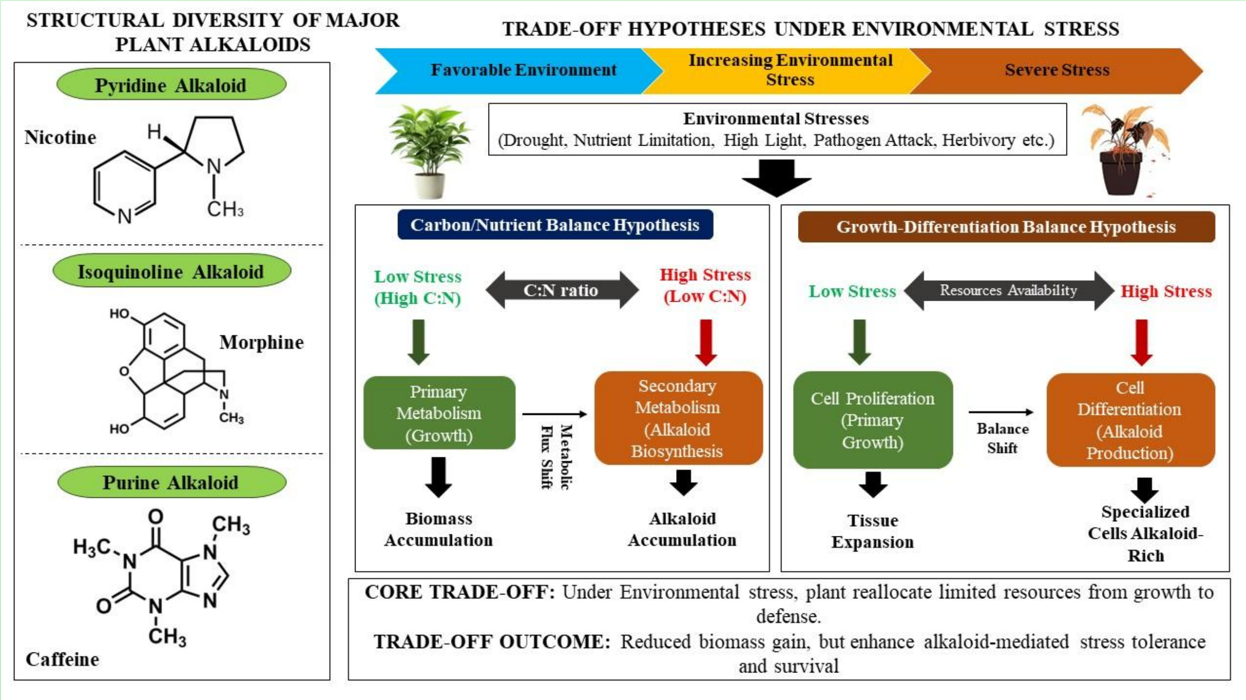

Figure 1. Structural diversity of major plant alkaloids and the trade-off hypotheses under environmental stress.

Influence of Specific Abiotic Stresses on Alkaloid Metabolism

Abiotic stress conditions profoundly influence plant secondary metabolism, particularly the biosynthesis and accumulation of alkaloids. Environmental stressors such as drought, salinity, temperature fluctuations and ultraviolet (UV) radiation trigger complex physiological and molecular responses that reprogram carbon and nitrogen allocation within plant tissues (Shoaib et al., 2024). Since alkaloids are nitrogen-containing defense compounds, their production is often closely associated with stress adaptation mechanisms. Under adverse environmental conditions, plants frequently divert metabolic resources from growth-related processes toward the synthesis of protective secondary metabolites, including alkaloids (Mishra et al., 2025; Salam et al., 2023). The extent and direction of these metabolic changes depend on stress intensity, duration, plant species and developmental stage.

Drought and Water Deficit

Drought stress is one of the most extensively studied abiotic factors affecting alkaloid metabolism. Water deficit generally reduces plant biomass and cellular expansion, leading to a phenomenon known as the “concentration effect,” where alkaloid levels increase due to reduced dilution within plant tissues (He et al., 2026; Y. Sun et al., 2023). However, drought-induced alkaloid accumulation is not solely a passive consequence of reduced growth. It is also actively regulated through stress-responsive metabolic pathways (Arif et al., 2025).

Under drought conditions, plants experience oxidative stress, stomatal closure and disruption of primary metabolism, which collectively stimulate secondary metabolite production (Sattar et al., 2024). Several medicinal plants such as *Nicotiana tabacum*, *Catharanthus roseus* and *Datura stramonium*, exhibit enhanced alkaloid accumulation during moderate water stress (Amirifar et al., 2022). In tobacco plants, drought stress has been associated with increased nicotine biosynthesis due to elevated activity of putrescine N-methyltransferase (PMT), a key enzyme involved in pyrrolidine alkaloid formation (Yin et al., 2025). PMT catalyzes the methylation of putrescine, representing an important regulatory step in nicotine biosynthesis. Increased jasmonic acid signaling during drought further activates transcription factors that enhance alkaloid biosynthetic gene expression (Bhushan et al., 2023; Ma et al., 2026). Additionally, drought-induced accumulation of alkaloids may contribute to osmotic adjustment and antioxidant defense. Certain alkaloids stabilize cellular membranes and help scavenge reactive oxygen species (ROS), thereby protecting plant cells from oxidative damage (Haghpanah et al., 2024; Ikram et al., 2025). Nevertheless, severe or prolonged drought may eventually inhibit alkaloid production due to excessive impairment of photosynthesis and energy metabolism (Amirifar et al., 2022).

Salinity Stress

Salinity stress affects plants through osmotic imbalance, ion toxicity and nutrient disturbances, particularly alterations in nitrogen metabolism. Excessive sodium and chloride ions disrupt cellular homeostasis, impair enzyme activities and induce oxidative stress (Farhan et al., 2024). To cope with these adverse effects, plants often enhance the synthesis of protective secondary metabolites (Yeshi et al., 2022). Salt stress has been shown to stimulate alkaloid accumulation in several medicinal species such as *Catharanthus roseus*, *Hyoscyamus muticus* and *Atropa belladonna* (Wen et al., 2023). In *Catharanthus roseus*, salinity enhances the accumulation of terpenoid indole alkaloids through the upregulation of tryptophan decarboxylase (TDC) and strictosidine synthase (STR), two key enzymes in alkaloid biosynthesis (Sharma et al., 2018). These metabolic adjustments are believed to strengthen antioxidant defenses and reduce oxidative injury caused by excessive ROS generation under saline conditions (Rao et al., 2025).

Furthermore, salinity-induced alkaloids may function in osmotic regulation by contributing to intracellular solute balance. Some alkaloids also interact with stress-responsive signaling pathways mediated by abscisic acid (ABA) and jasmonates, which coordinate adaptive metabolic responses (Akhtar et al., 2026). However, the relationship between salinity and alkaloid biosynthesis is highly species-specific. Moderate salt stress often enhances alkaloid production, whereas extreme salinity may suppress metabolic activity and reduce overall secondary metabolite accumulation due to impaired growth and cellular toxicity (Debbagh-Nour et al., 2026).

Temperature Extremes

Temperature is another critical environmental factor regulating alkaloid metabolism. Both heat stress and cold stress significantly affect enzymatic activities, precursor availability, membrane stability and gene expression associated with secondary metabolism, in Table 1.

Heat Stress

High temperatures can destabilize proteins and enzymes involved in alkaloid biosynthesis, resulting in altered metabolic fluxes. Heat stress often accelerates respiration and disrupts photosynthetic efficiency (Sharma et al., 2022). Thereby, reducing the availability of carbon skeletons required for secondary metabolite production. In some plant species, elevated temperatures decrease alkaloid accumulation due to degradation of biosynthetic precursors and suppression of enzyme activity (Yeshi et al., 2022). For example, excessive heat has been reported to reduce morphine accumulation in Papaver somniferum by affecting the activity of enzymes such as codeinone reductase (COR), which participates in benzylisoquinoline alkaloid biosynthesis (Tilkat et al., 2024). Heat stress also enhances ROS production, leading to oxidative damage that may impair metabolic pathways. Nevertheless, mild heat stress may occasionally stimulate alkaloid synthesis as part of an adaptive defense response, particularly when stress signaling pathways involving heat shock proteins and jasmonates are activated (Wu et al., 2026).

Cold Stress

Cold stress induces significant physiological and biochemical changes that often promote the accumulation of protective metabolites. Low temperatures slow down metabolic processes and may trigger the synthesis of specific alkaloids that function as cryoprotectants (He et al., 2023). These compounds help stabilize cellular membranes, preserve protein integrity and reduce oxidative damage during chilling or freezing conditions (Grgac et al., 2022). In certain medicinal plants, cold exposure enhances alkaloid accumulation through activation of stress-responsive transcription factors and secondary metabolic pathways (Alami et al., 2024). For instance, low temperatures can increase tropane alkaloid levels in species such as Datura and Hyoscyamus. Cold-induced alkaloids may also contribute to ROS scavenging and osmotic protection, thereby improving stress tolerance (Luo et al., 2025). However, prolonged freezing conditions can ultimately impair biosynthetic machinery and reduce overall metabolite production.

Light Intensity and UV Radiation

Light is an essential environmental regulator of plant metabolism, influencing photosynthesis, development and secondary metabolite biosynthesis. Variations in light intensity and exposure to ultraviolet radiation, particularly UV-B radiation (280-315 nm), strongly affect alkaloid production (Wang et al., 2025). UV-B radiation acts as an abiotic elicitor that stimulates defense-related metabolic pathways. Exposure to UV-B induces oxidative stress and DNA damage, leading to activation of signaling cascades involving reactive oxygen species, jasmonates and transcription factors (Mmbando, 2023). Consequently, plants enhance alkaloid biosynthesis as a protective mechanism against photo-oxidative stress (Ashraf et al., 2024).

In *Catharanthus roseus*, UV-B exposure increases the accumulation of vindoline and catharanthine through upregulation of genes associated with terpenoid indole alkaloid biosynthesis (Tang et al., 2022). Similarly, caffeine accumulation in tea and coffee plants has been linked to light intensity and UV exposure. Alkaloids produced under UV stress may function as UV-absorbing compounds, antioxidants or deterrents against stress-weakened herbivore attacks (Liu et al., 2023). However, excessive radiation can damage chloroplast structures and inhibit primary metabolism, ultimately reducing biosynthetic efficiency. Therefore, optimal levels of light and UV exposure are critical for maintaining balanced alkaloid production in medicinal plants (Alyas et al., 2023).

Table 1. Differential impacts of specific abiotic stresses on alkaloid accumulation, key enzymatic triggers and adaptive functions.

Representative Plant Species	*Major Alkaloid Affected*	*Key Enzyme/Gene Regulated*	*Direction of Alkaloid Accumulation*	*Physiological/Adaptive Function*	*Proposed Mechanism Under Stress*	*References*
Abiotic Stress: Drought / Water Deficit						
Nicotiana tabacum	Nicotine	Putrescine *N*-methyltransferase (PMT), Quinolinate phosphoribosyltransferase (QPT)	Increased	Antioxidant defense, herbivore deterrence, osmotic adjustment	Water deficit enhances jasmonic acid signaling, activating nicotine biosynthetic genes and concentrating alkaloids due to reduced biomass	(Selmar & Kleinwächter, 2013)
Catharanthus roseus	Vincristine, Vinblastine, Catharanthine	Tryptophan decarboxylase (TDC), Strictosidine synthase (STR)	Increased	ROS scavenging and stress adaptation	Drought induces terpenoid indole alkaloid pathway through ABA and JA-mediated transcriptional regulation	(Isah, 2019)
Datura stramonium	Tropane alkaloids (Atropine, Scopolamine)	Tropinone reductase I (TRI)	Moderate increase	Maintenance of cellular homeostasis	Enhanced nitrogen allocation toward secondary metabolism during stress	(Wink, 2010)
Abiotic Stress: Salinity Stress						
Catharanthus roseus	Ajmalicine, Vindoline	TDC, STR	Increased	Oxidative stress protection and osmotic regulation	Salt stress induces ROS production and activates alkaloid biosynthesis through ABA-dependent pathways	(Isah, 2019; Khashan & Al-Athary, 2016)
Hyoscyamus muticus	Hyoscyamine	Hyoscyamine 6β-hydroxylase (H6H)	Increased	Ion homeostasis and ROS detoxification	Salinity alters nitrogen metabolism and stimulates tropane alkaloid synthesis	(Jangpangi et al., 2025)
Atropa belladonna	Scopolamine	Putrescine decarboxylase (PDC)	Slight increase	Osmotic balance and membrane protection	Accumulation linked with stress-induced nitrogen remobilization	(Facchini, 2001)
Abiotic Stress: Heat Stress						
Papaver somniferum	Morphine, Codeine	Codeinone reductase (COR)	Decreased under severe heat	Protection against oxidative injury	High temperature destabilizes biosynthetic enzymes and reduces precursor availability	(Hasanuzzaman et al., 2021)
Catharanthus roseus	Catharanthine	Deacetylvindoline acetyltransferase (DAT)	Variable	Cellular defense under moderate heat	Mild heat may stimulate secondary metabolism, whereas severe heat suppresses biosynthetic activity	(Akula & Ravishankar, 2011)
Rauvolfia serpentina	Reserpine	Strictosidine β-glucosidase (SGD)	Reduced	Stress signaling regulation	Heat-induced metabolic imbalance suppresses alkaloid biosynthesis	(Yang et al., 2018)
Abiotic Stress: **Cold Stress**						
Datura inoxia	Scopolamine	Tropinone reductase II (TRII)	Increased	Cryoprotection and ROS scavenging	Low temperature activates stress-responsive genes and membrane stabilization pathways	(Wink, 2010)
Hyoscyamus niger	Hyoscyamine	H6H	Increased	Maintenance of membrane integrity	Cold-induced oxidative signaling stimulates tropane alkaloid metabolism	(Isah, 2019)
Camellia sinensis	Caffeine	Caffeine synthase (CS)	Slight increase	Antioxidant and stress mitigation role	Cold stress enhances purine alkaloid accumulation for metabolic protection	(Ashihara et al., 2008)
Abiotic Stress: UV-B Radiation / High Light Intensity						
Catharanthus roseus	Vindoline, Catharanthine	STR, Geraniol 10-hydroxylase (G10H)	Significant increase	UV shielding and antioxidant activity	UV-B acts as an elicitor, activating ROS-mediated signaling and secondary metabolism	(Akula & Ravishankar, 2011)
Coffea arabica	Caffeine	Xanthosine methyltransferase (XMT)	Increased	Photo-protection and defense enhancement	Increased light intensity stimulates purine alkaloid biosynthesis	(Mazzafera, 1999)
Nicotiana tabacum	Nicotine	PMT	Moderate increase	Photo-oxidative stress protection	UV exposure activates JA-responsive pathways involved in nicotine synthesis	(Shoji et al., 2010)
Abiotic Stress: Combined Stress Conditions						
Catharanthus roseus	Terpenoid indole alkaloids	TDC, STR, ORCA3 transcription factor	Strong increase under moderate combined stress	Enhanced stress tolerance and metabolic plasticity	Crosstalk among ABA, JA, and ROS signaling pathways coordinately regulates alkaloid metabolism	(El-Sayed & Verpoorte, 2007)
Nicotiana tabacum	Nicotine	PMT, A622 gene	Variable depending on stress intensity	Integrated defense response	Combined drought and heat alter carbon–nitrogen balance affecting nicotine biosynthesis	(Shoji et al., 2010)

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Physiological and Molecular Mechanisms Regulating Stress-Induced Alkaloid Biosynthesis.

Plants respond to abiotic stress through highly coordinated physiological and molecular mechanisms that regulate secondary metabolite production such as alkaloid biosynthesis (Sana et al., 2025). Environmental stresses such as drought, salinity, extreme temperatures, and ultraviolet radiation trigger complex signaling networks involving phytohormones, transcription factors and intracellular transport systems (Rabeh et al., 2025). These adaptive responses enable plants to modulate alkaloid metabolism for enhanced survival under adverse environmental conditions (Leite Dias & D'Auria, 2025).

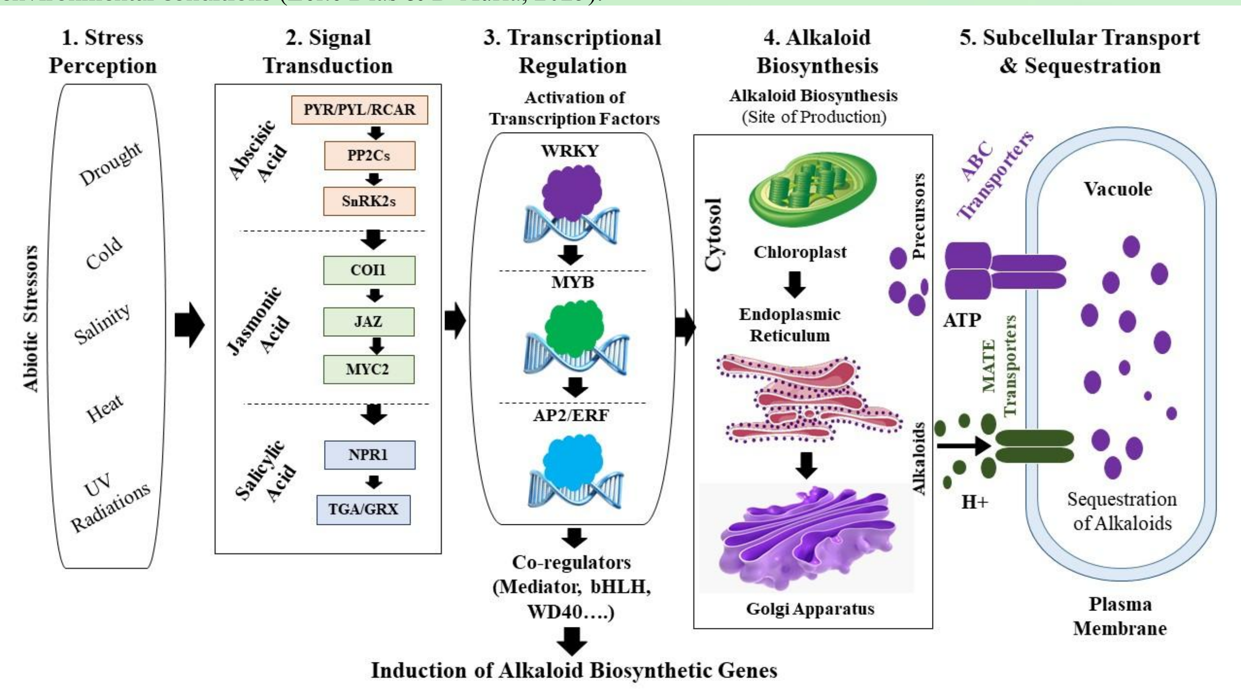

Figure 2. Molecular signaling cascade regulating stress-induced alkaloid biosynthesis and subcellular transport.

Signal Transduction and Phytohormonal Regulation

Phytohormones play central roles in mediating stress-responsive alkaloid biosynthesis, in **Figure 2.** Among these, jasmonic acid (JA), salicylic acid (SA) and abscisic acid (ABA) are considered major signaling molecules that coordinate plant defense and metabolic reprogramming during abiotic stress (Verma et al., 2025). Jasmonic acid is one of the most important elicitors of alkaloid biosynthesis. Under stress conditions, JA signaling activates genes associated with secondary metabolism, particularly those involved in nicotine, terpenoid indole alkaloid and tropane alkaloid pathways (Jeyasri et al., 2023). In *Nicotiana tabacum*, drought or wounding induces JA accumulation, which subsequently stimulates the expression of putrescine N-methyltransferase (PMT) and quinolinate phosphoribosyltransferase (QPT), key enzymes in nicotine biosynthesis (Lei et al., 2025). Similarly, in *Catharanthus roseus*, JA enhances the transcription of tryptophan decarboxylase (TDC) and strictosidine synthase (STR), leading to increased production of vinblastine and vincristine precursors (Guedes et al., 2024).

Abscisic acid is primarily associated with drought and salinity responses. Stress-induced ABA accumulation regulates stomatal closure, osmotic balance, and antioxidant defense while also influencing secondary metabolism (Sheuli et al., 2025). ABA interacts synergistically with JA signaling pathways to activate stress-responsive genes involved in alkaloid biosynthesis. Furthermore, salicylic acid contributes to stress tolerance by modulating reactive oxygen species (ROS) signaling and activating defense-related metabolic pathways (Lukan & Coll, 2022). SA-mediated signaling often enhances antioxidant alkaloid accumulation under oxidative stress conditions (Upadhyay et al., 2025).

Role of Transcription Factors

Stress-responsive transcription factors function as molecular switches that regulate alkaloid biosynthetic pathways. Among the most significant transcription factor families are WRKY, MYB and AP2/ERF proteins, which bind to promoter regions of biosynthetic genes and modulate their expression under stress conditions (Ma et al., 2026). The AP2/ERF family is particularly important in jasmonate-mediated alkaloid regulation. In tobacco, ERF transcription factors such as ORC1 and ERF189 activate nicotine biosynthetic genes, including PMT and A622, during drought and herbivory stress (Chen et al., 2026; Nie & Wang, 2023). In *Catharanthus roseus*, the AP2/ERF transcription factor ORCA3 positively regulates terpenoid indole alkaloid biosynthesis by activating TDC and STR genes in response to jasmonate signaling (Rai et al., 2022).

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WRKY transcription factors also play crucial roles in stress-induced secondary metabolism. These proteins are involved in ROS-responsive signaling and defense regulation (Wu et al., 2022). Several WRKY proteins enhance alkaloid accumulation by activating genes associated with phenylpropanoid and alkaloid pathways during environmental stress (Rai et al., 2022). Likewise, MYB transcription factors regulate carbon allocation and secondary metabolic flux, influencing alkaloid synthesis under stress-induced metabolic reprogramming (Imran et al., 2025). The coordinated action of these transcription factors ensures rapid metabolic adaptation to environmental stress while balancing growth and defense responses.

Subcellular Compartmentation and Alkaloid Transport

Subcellular compartmentation is another critical aspect of alkaloid metabolism during stress conditions. Alkaloids are often synthesized in specific tissues such as roots or young leaves and subsequently transported to storage compartments including vacuoles, laticifers, or epidermal cells (S. Sun et al., 2023). Stress conditions significantly influence this transport process by regulating membrane transporters and intracellular trafficking systems (Ahmed et al., 2026). ATP-binding cassette (ABC) transporters and multidrug and toxic compound extrusion (MATE) proteins are major transport systems involved in alkaloid sequestration and translocation (Kar et al., 2022). In nicotine-producing plants, nicotine is synthesized in roots and transported through the xylem to leaves, where it accumulates in vacuoles. Under stress conditions, enhanced transporter activity increases alkaloid compartmentation to minimize cytotoxicity and maximize defensive efficiency (Xiao et al., 2025). Vacuolar sequestration also protects cellular organelles from alkaloid toxicity while maintaining intracellular osmotic balance during abiotic stress. Additionally, compartmentation facilitates rapid remobilization of nitrogen-containing alkaloids when stress conditions subside (Saleem et al., 2022). Therefore, stress-regulated alkaloid transport and storage represent essential adaptive strategies that contribute to plant survival and metabolic homeostasis (Gillani et al., 2026).

Functional Role of Alkaloids in Stress Tolerance

Alkaloids are multifunctional secondary metabolites that play crucial roles in plant adaptation and survival under adverse environmental conditions. Beyond their classical defensive functions against herbivores and pathogens, alkaloids actively contribute to abiotic stress tolerance through antioxidant protection, osmotic regulation and nitrogen storage (Divekar et al., 2022). Environmental stresses such as drought, salinity, heat, cold and ultraviolet radiation frequently disrupt cellular homeostasis and trigger oxidative damage, thereby necessitating protective metabolic responses. Under such conditions, plants enhance alkaloid biosynthesis as part of an integrated defense strategy aimed at maintaining physiological stability and cellular integrity (Shoaib et al., 2024).

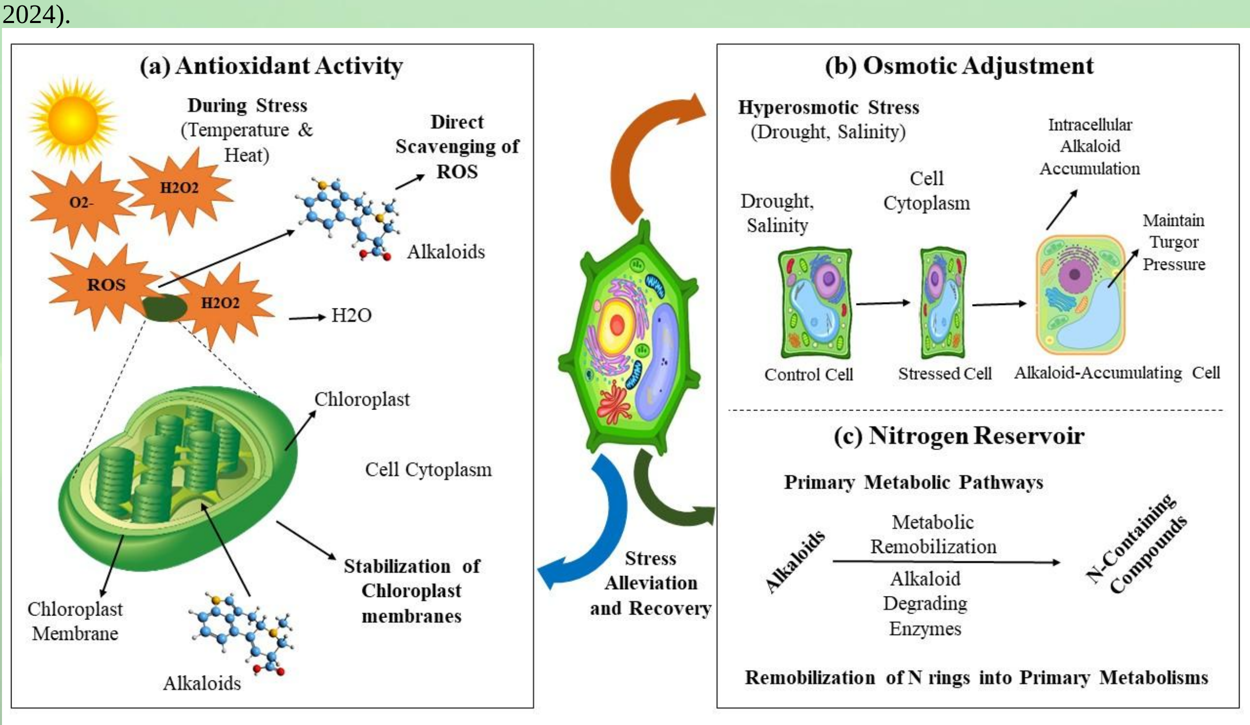

Figure 3. Tripartite protective mechanism of alkaloids during environmental stress.

Antioxidant Activity and Reactive Oxygen Species (ROS) Scavenging

One of the primary functional roles of alkaloids during abiotic stress is their involvement in antioxidant defense systems, in Figure 3. Environmental stresses commonly induce excessive production of reactive oxygen species (ROS), including superoxide radicals (O_2^-), hydrogen peroxide (H_2O_2) and hydroxyl radicals (OH) (Jomova et al., 2023). Although ROS serve as signaling molecules at moderate concentrations, their excessive accumulation damages proteins, lipids, nucleic acids and cellular membranes, ultimately impairing plant growth and metabolism (Kesawat et al., 2023). Several alkaloids possess strong antioxidant properties that help neutralize ROS and reduce oxidative injury. Nicotine, caffeine, berberine and various indole alkaloids have been reported to stabilize membrane structures and limit lipid peroxidation under stress conditions (Verma et al., 2026). *In Catharanthus roseus*, stress-induced accumulation of terpenoid indole alkaloids contributes to enhanced antioxidant capacity by scavenging free radicals generated during drought and salinity stress. Similarly, caffeine in tea and coffee plants functions as an antioxidant molecule that mitigates photo-oxidative stress caused by excessive light and UV radiation (Saleem et al., 2022). Alkaloids also interact with enzymatic antioxidant systems such as superoxide dismutase (SOD), catalase (CAT) and peroxidases (POD), thereby strengthening the overall cellular defense network (Raza et al., 2022). Through these mechanisms, alkaloids help maintain redox homeostasis and protect vital metabolic processes during environmental stress.

Osmotic Adjustment and Maintenance of Cellular Turgor

Abiotic stresses such as drought and salinity reduce cellular water availability and disrupt osmotic balance. Under these conditions, plants accumulate compatible solutes and osmoprotective compounds to maintain cell turgor and prevent dehydration (Guru et al., 2025). Certain alkaloids contribute significantly to osmotic adjustment by acting as nitrogen-containing osmolytes that stabilize cellular structures and regulate intracellular osmotic potential (Haghpanah et al., 2024). Tropane alkaloids, nicotine and related compounds have been associated with improved osmotic regulation during water-deficit stress. These metabolites accumulate within vacuoles and cytoplasmic compartments, where they help retain water and preserve membrane stability (Chada et al., 2023). In saline environments, alkaloid accumulation may also counterbalance ionic toxicity caused by excessive sodium and chloride ions. This protective mechanism supports cellular hydration, enzyme functionality and metabolic continuity under stressful conditions (Gul et al., 2022).

Moreover, alkaloids can interact with membrane lipids and proteins to enhance membrane integrity during dehydration stress (Khan, 2025). Their accumulation often coincides with increased levels of abscisic acid (ABA), which coordinates osmotic stress responses and promotes stress acclimation. Consequently, alkaloid-mediated osmotic adjustment represents an important adaptive strategy that improves plant resilience under fluctuating environmental conditions (Zambelli et al., 2025).

Alkaloids as Nitrogen Reservoirs

Because alkaloids contain substantial amounts of nitrogen, they also function as temporary nitrogen storage compounds within plant tissues. Nitrogen is an essential macronutrient required for amino acids, proteins, nucleic acids and chlorophyll synthesis (Farhan et al., 2024). Yet, its availability is often limited during environmental stress. Under unfavorable conditions, plants may divert excess nitrogen into alkaloid biosynthesis as a means of conserving and safely storing nitrogen resources (Alami et al., 2024). This storage function is particularly important during stress recovery. When environmental conditions improve, nitrogen incorporated within alkaloid structures can be remobilized and redirected toward primary metabolism, growth and tissue repair (Salam et al., 2023). Such metabolic flexibility allows plants to maintain nutrient balance while simultaneously enhancing defense capacity during stress exposure. In addition, nitrogen-rich alkaloids may help regulate carbon-nitrogen balance during abiotic stress by preventing accumulation of toxic nitrogen intermediates (Li et al., 2025). This adaptive strategy supports metabolic homeostasis and enables plants to optimize resource allocation between growth and defense pathways. Therefore, alkaloids serve not only as protective metabolites but also as dynamic reservoirs that contribute to nutrient recycling and long-term stress adaptation (Prashar et al., 2025).

Emerging Trends and Technologies in Alkaloid Research

Rapid advances in plant biotechnology, systems biology and environmental analytics have significantly transformed the study of alkaloid metabolism under abiotic stress conditions (Khan et al., 2025). Traditional approaches focused mainly on biochemical characterization of individual pathways. Whereas, modern technologies now enable large-scale exploration of stress-responsive metabolic networks at genomic, transcriptomic, proteomic and metabolomic levels (Satrio et al., 2024). These emerging tools are improving our understanding of how environmental stress regulates alkaloid biosynthesis and are facilitating the development of climate-resilient medicinal plants with stable phytochemical profiles, in **Table 2**.

Omics Integration and Systems Biology Approaches

The integration of omics technologies, particularly transcriptomics and metabolomics, has become a powerful strategy for studying stress-induced alkaloid metabolism (Yan et al., 2024). Transcriptomics enables comprehensive analysis of gene expression patterns under environmental stress, helping researchers identify biosynthetic genes, transcription factors, signaling molecules and regulatory pathways involved in alkaloid production (Huang et al., 2024). Simultaneously, metabolomics provides detailed profiling of alkaloid composition and metabolic fluxes within plant tissues. Combined omics approaches allow researchers to map complex stress-responsive metabolic networks and uncover interactions between primary and secondary metabolism

(Varadharajan et al., 2025). In medicinal plants such as *Catharanthus roseus*, transcriptomic analyses have identified key stress-responsive genes including tryptophan decarboxylase (TDC), strictosidine synthase (STR) and AP2/ERF transcription factors that regulate terpenoid indole alkaloid biosynthesis during drought and salinity stress (Gupta et al., 2023). Metabolomic studies further reveal dynamic changes in alkaloid accumulation associated with environmental fluctuations.

Multi-omics integration also enhances understanding of signaling pathways mediated by jasmonic acid, salicylic acid and abscisic acid under stress conditions. Advanced bioinformatics and network analysis tools are increasingly used to correlate transcriptomic data with metabolite profiles, enabling prediction of regulatory hubs and metabolic bottlenecks (Sanches et al., 2024). Such systems-level approaches provide valuable insights into stress adaptation mechanisms and facilitate targeted improvement of medicinal plant productivity (Lv & Fan, 2026). Moreover, next-generation sequencing (NGS), RNA sequencing (RNA-Seq) and mass spectrometry-based metabolomics have accelerated the discovery of novel alkaloid biosynthetic genes and unknown intermediate metabolites (Singh et al., 2025). These technologies are particularly valuable for non-model medicinal species lacking complete genomic information.

Metabolic Engineering and Climate-Smart Medicinal Plants

Metabolic engineering has emerged as a promising approach for enhancing alkaloid production and developing “climate-smart” medicinal plants capable of maintaining stable bioactive compound profiles under environmental stress (Das et al., 2023). Conventional cultivation of medicinal plants is highly sensitive to climatic variability, which often causes fluctuations in alkaloid content and pharmaceutical quality. Modern genetic engineering techniques aim to overcome these limitations by manipulating biosynthetic pathways and stress-responsive regulatory networks (Khalid et al., 2026). One major strategy involves overexpression of rate-limiting enzymes such as PMT, TDC and STR to enhance alkaloid biosynthesis. Genetic modification of transcription factors, particularly AP2/ERF and WRKY families, has also been used to improve stress-responsive secondary metabolism (Su et al., 2025). For example, overexpression of ORCA3 in *Catharanthus roseus* significantly enhances terpenoid indole alkaloid accumulation under stress conditions (Rai et al., 2022).

The development of CRISPR/Cas9 genome-editing technology has further revolutionized alkaloid engineering. CRISPR-based approaches enable precise editing of biosynthetic genes, transporter proteins and regulatory elements associated with alkaloid metabolism (Rynjah et al., 2025). These technologies offer opportunities to improve stress tolerance, optimize carbon-nitrogen allocation and stabilize alkaloid yield despite drought, salinity or temperature fluctuations (Ullah et al., 2026). Additionally, synthetic biology approaches are increasingly used to reconstruct alkaloid biosynthetic pathways in microbial hosts such as yeast and bacteria for sustainable production of pharmaceutically important compounds (Qin et al., 2025). Such innovations may reduce dependence on environmentally sensitive medicinal plant cultivation while ensuring consistent alkaloid supply.

Geospatial Influence and Environmental Chemotyping

Geographical and climatic conditions strongly influence alkaloid composition in wild and cultivated medicinal plants. Variations in altitude, temperature, precipitation, soil characteristics, solar radiation and seasonal patterns create distinct environmental pressures that shape plant metabolic responses (Yadav et al., 2024). Consequently, medicinal plants collected from different regions often exhibit unique chemical fingerprints or chemotypes characterized by quantitative and qualitative differences in alkaloid profiles (Noviana et al., 2022). Geospatial analysis combined with environmental monitoring has become an important tool for understanding regional variability in medicinal plant chemistry (Nagavi et al., 2024). Climatic factors such as drought frequency, UV radiation intensity and temperature extremes can significantly alter secondary metabolite accumulation by regulating stress-responsive biosynthetic pathways (Khan, 2025). For example, high-altitude medicinal plants frequently accumulate greater concentrations of protective alkaloids due to increased UV exposure and low-temperature stress (Kumar et al., 2026).

Modern geographic information systems (GIS), remote sensing technologies and ecological modeling are increasingly applied to predict alkaloid distribution patterns across different climatic zones (Tiwari et al., 2023). These approaches help identify optimal cultivation regions for medicinal plants with superior phytochemical quality. Furthermore, geospatial metabolomics can support conservation strategies for wild medicinal species threatened by climate change and habitat degradation (Borthakur et al., 2026). Understanding environmental chemotyping is also important for pharmaceutical standardization because climatic variability directly affects the consistency, efficacy and safety of plant-derived bioactive compounds (Alum et al., 2025). Therefore, integrating geospatial analytics with metabolomic and genomic studies represents a promising direction for future medicinal plant research and sustainable phyto-pharmaceutical production (Tekade & Saraf, 2026).

Table 2. Applications of multi-omics integration and metabolic engineering in optimizing alkaloid profiles.

Approach	Medicinal Plant Species	Target Alkaloid(s)	Omics/Engineering Strategy	Key Genes/Pathways Identified	Stresses	Major Outcomes and Applications	References
Transcriptomics Integration	*Catharanthus roseus*	Vinblastine, Vincristine, Catharanthine	RNA-Seq analysis under drought and salinity stress	*TDC*, *STR*, *DAT*, *ORCA3*	Drought, salinity	Identification of stress-responsive terpenoid indole alkaloid (TIA) pathways and regulatory transcription factors	(Khalkho et al., 2024; Ngara & Shavrukov, 2026)
Metabolomics Profiling	*Nicotiana tabacum*	Nicotine	LC-MS/MS and GC-MS metabolic fingerprinting	Nicotine biosynthetic pathway	Drought and UV stress	Quantification of stress-induced nicotine accumulation and metabolic flux reprogramming	(Shoji et al., 2010)
Integrated Transcriptomics & Metabolomics	*Papaver somniferum*	Morphine, Codeine, Thebaine	Combined RNA-Seq and metabolite network analysis	*COR*, *SalAT*, *T6ODM*	Heat and drought stress	Mapping of stress-regulated benzylisoquinoline alkaloid pathways and identification of metabolic bottlenecks	(Facchini, 2001)
Proteomics-Assisted Metabolic Mapping	*Rauvolfia serpentina*	Reserpine	Stress-responsive proteome analysis	Secondary metabolite regulatory proteins	Temperature stress	Identification of enzyme stability mechanisms controlling alkaloid biosynthesis	(Yang et al., 2018)
CRISPR/Cas9 Genome Editing	*Catharanthus roseus*	Vinblastine precursors	CRISPR-mediated editing of regulatory genes	AP2/ERF transcription factors, *ORCA3*	Multiple abiotic stresses	Enhanced alkaloid biosynthesis and improved stress resilience in engineered lines	(Giri et al., 2025)
Overexpression of Rate-Limiting Enzymes	*Nicotiana tabacum*	Nicotine	Genetic overexpression of biosynthetic enzymes	Putrescine *N*-methyltransferase (*PMT*), *QPT*	Drought and herbivory stress	Increased nicotine accumulation and enhanced defense capability	(Shoji et al., 2010)
Transcription Factor Engineering	*Catharanthus roseus*	Terpenoid indole alkaloids	Overexpression of transcription factors	*ORCA3*, WRKY, MYB proteins	Salinity and drought	Improved activation of alkaloid biosynthetic pathways under stress	(El-Sayed & Verpoorte, 2007)
Synthetic Biology Platforms	Yeast (*Saccharomyces cerevisiae*) engineered with plant genes	Morphinan alkaloids	Reconstruction of alkaloid biosynthetic pathways in microbial systems	Multi-enzyme benzylisoquinoline pathways	Climate-independent production	Sustainable production of pharmaceutical alkaloids independent of environmental variability	(Galanie et al., 2015)
Metabolite Network Modeling	*Hyoscyamus niger*	Hyoscyamine, Scopolamine	Computational metabolomic network analysis	Tropane alkaloid biosynthetic pathways	Salinity and cold stress	Prediction of pathway regulation and optimization of alkaloid yield	(Ashihara et al., 2008)
Epigenomics and Stress Memory Studies	*Arabidopsis thaliana* (model system for medicinal plant stress studies)	Indirect alkaloid-related secondary metabolism	DNA methylation and chromatin remodeling analysis	Stress-responsive epigenetic regulators	Recurrent drought stress	Identification of heritable stress-adaptive metabolic responses	(Selmar & Kleinwächter, 2013)
Geo-Metabolomics and Environmental Chemotyping	*Camellia sinensis*	Caffeine	GIS-linked metabolomics and climatic profiling	Purine alkaloid pathways	Altitude, UV radiation, temperature variation	Identification of regional alkaloid chemotypes and optimal cultivation zones	(Ashihara et al., 2008)
Remote Sensing-Assisted Precision Cultivation	*Cannabis sativa*	Cannabinoid alkaloid-like compounds	Integration of environmental sensors with metabolomic data	Secondary metabolite stress pathways	Heat and drought stress	Development of climate-smart cultivation systems with stable metabolite profiles	(Chandra et al., 2017)
Transporter Engineering	*Nicotiana tabacum*	Nicotine	Manipulation of vacuolar transport proteins	ABC and MATE transporters	Combined stress conditions	Improved alkaloid sequestration and reduced cellular toxicity	(Yazaki, 2005)
Multi-Omics Assisted Breeding	*Withania somnifera*	Withanolide alkaloids	Integration of genomics, transcriptomics and metabolomics	Stress-responsive biosynthetic genes	Drought and salinity	Selection of elite climate-resilient medicinal genotypes with stable bioactive yields	Kumar et al., 2022
Machine Learning and AI-Assisted Metabolic Prediction	Multiple medicinal plant species	Diverse alkaloids	AI-based predictive metabolic modeling	Integrated stress-metabolic networks	Variable climatic stress	Prediction of stress-responsive alkaloid accumulation and optimization strategies	(Yang et al., 2018)

Materials and Methods (Bibliometric Approach)

Two of the most comprehensive and internationally recognized transdisciplinary citation databases the Web of Science Core Collection (WoS) and Scopus, were used as the primary data sources for this bibliometric analysis. These databases were selected due to their extensive coverage of peer-reviewed literature in environmental sciences, plant biology and physiology and agricultural sciences. Thereby ensuring a robust and representative dataset for research on alfalfa production systems. The Clarivate Analytics Web of Science (WoS) is one of the most widely used platforms for academic citation searches and bibliometric analyses and constitutes one of the largest scientific databases worldwide. It encompasses a broad range of high-impact scholarly publications (Pranckutė, 2021). Publication records were retrieved from the WoS Core Collection. This including the indices such as Science Citation Index Expanded (SCI-EXPANDED, 1975-2026) with 82 papers, Conference Proceedings Citation Index-Science (CPCI-S, 1975-2026) with 4 papers, Book Citation Index-Science (BKCI-S, 1975-2026) with 4 papers and the Emerging Sources Citation Index (ESCI, 1975-2026) with 8 papers. Data collection was completed on May 10, 2026, to minimize potential database update bias.

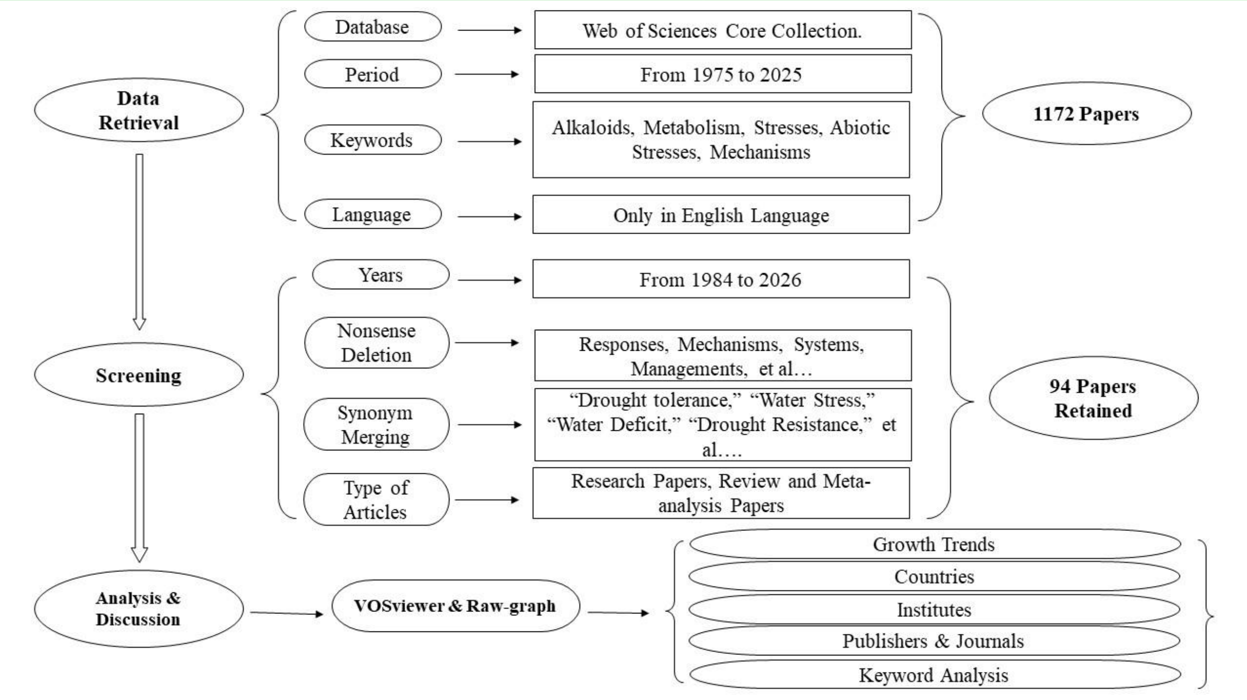

Figure 4. PRISMA flowchart for article selection based on WoS criteria.

The search was conducted using the topic-based keyword alkaloid metabolites, biosynthesis and abiotic stresses in plants. In total, 94 publications related to the title of the study "Effect of Abiotic Stress Conditions on Alkaloid Metabolism" were identified. All records were exported in "full record and cited references" format and saved as RIS, EndNote, and tab-delimited files. The retrieved data were subsequently imported into VOSviewer for further bibliometric visualization and network analysis in Figure 4.

VOSviewer

The datasets obtained from this search were analyzed and visualized using VOSviewer, a user-friendly and freely available bibliometric visualization software. This tool was selected due to its wide range of analytical capabilities, its ability to process large volumes of data, and its capacity to generate intuitive visual representations that facilitate data interpretation (McAllister et al., 2022; Van Eck & Waltman, 2010). In the present study, VOSviewer was employed to examine the level of international collaboration among authors, institutions, and countries, as well as to identify research trends through keyword analysis. The software was also used to perform cluster and network analyses. All analyses were conducted using the default parameters provided by VOSviewer (Suryantoro et al., 2023). In the network visualizations, items are represented by circles, with the size of each circle reflecting the relative weight or importance of the item. Different colors indicate clusters of related elements. The spatial distance between items represents the strength of their relationships, with items positioned closer together indicating stronger associations.

Results of the bibliometric analysis

Type of document and publication language

A total of 1172 papers on effect of abiotic stress conditions on alkaloid metabolism were published between 1975 and 2026 and identified through keyword-based searches. The publications were indexed in several Web of Science databases, including the Science Citation Index Expanded (SCI-EXPANDED; 904 records), Conference Proceedings Citation Index–Science (CPCI-S; 860 records), Book Citation Index-Science (BKCI-S; 167 records), Emerging Sources Citation Index (ESCI; 63 records), Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH; 14 records), Social Sciences Citation Index (SSCI; 7 records), Arts & Humanities Citation Index (A&HCI; 2 records) and Book Citation Index-Social Sciences & Humanities (BKCI-SSH; 2 records). Regarding publication language, the vast majority of the papers (91) were published in English. A limited number of publications were written in other languages, including Chinese, French and German (1 paper in each).

Publications Trend

An integrated meta-analysis of the chronological data reveals a distinct evolutionary trajectory within this research field, characterized by a foundational surge in publication volume that subsequently catalyzed long-term citation impact, in Figure 5. The field achieved its absolute historical peak in production during 2010, yielding the maximum number of annual publications. This is driven heavily by core pioneering institutions like the University of Calgary and foundational researchers such as Facchini. In contrast, the peak for scientific impact lag-shifted significantly, with the maximum number of citations recorded years later in 2015. This temporal gap directly illustrates a classic bibliometric citation delay model. The immense volume of high-quality primary literature established during the 2010 production boom required a multi-year gestation period to be thoroughly absorbed, integrated and cited by the global scientific community. Following this 2015 citation zenith, the overlay trends show that while the total volume of new papers from the original core nucleus tapered off. It successfully sparked a decentralized wave of modern, highly collaborative studies between 2020 and 2025. Consequently, the publication trends act as a leading indicator of field maturity, transitioning from high-volume institutional output to widespread, global citation diffusion. The 94 papers analyzed from 1975 to 2026 had an h-index of 30 and received a total of 3281 citations during the study period, with an average of 36.73 citations per publication.

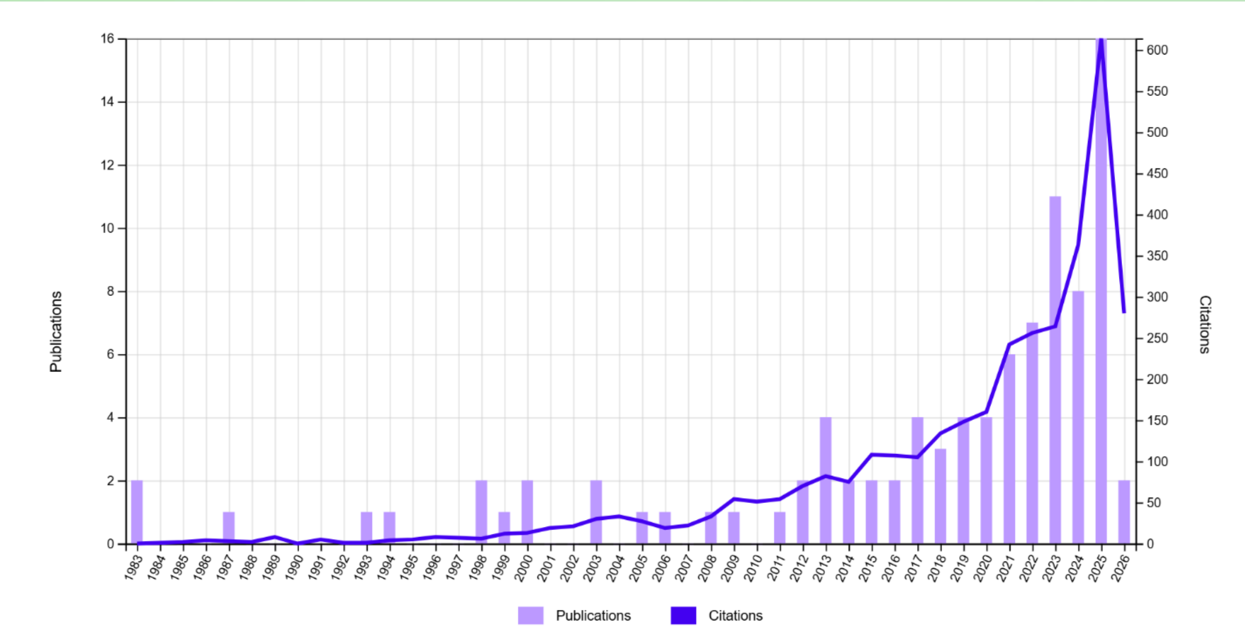

Figure 5. Scholarly article publication trends concerning the effect of abiotic stress conditions on alkaloid metabolism between 1992 and 2025.

Web of Science Categories, Research Areas and Sustainable Development Goals

A bibliometric meta-analysis of literature published between 1975 and 2026 reveals critical trends regarding the “Effect of Abiotic Stress Conditions on Alkaloid Metabolism”, in **Figure 6**. Within the broader disciplinary landscape, the dataset spans 21 distinct research areas and 31 Web of Science (WoS) categories, heavily anchored in plant biology and chemistry. Plant Sciences stands as the predominant domain with 57 publications, followed closely by Biochemistry & Molecular Biology (15 papers in research areas; 14 in WoS categories). Other foundational disciplines driving this meta-analysis include Agriculture (9 papers), Chemistry (9 papers) and Environmental Sciences & Ecology (9 papers), alongside targeted contributions from Biotechnology & Applied Microbiology (5 papers) and Pharmacology & Pharmacy (4 papers). When mapped against global sustainability frameworks, this scientific output aligns dynamically with 6 core Sustainable Development Goals (SDGs), reflecting a total of 112 strategic alignments. Research is overwhelmingly concentrated in SDG 03: Good Health and Well-Being (35 papers) and SDG 13: Climate Action (34 papers), illustrating how understanding stress-induced alkaloid variations directly connects to both medicinal resource discovery and climate resilience. Additionally, SDG 02: Zero Hunger accounts for 30 papers, highlighting the profound impact of abiotic stress on agricultural productivity and food security. The ecological dimension is captured by SDG 15: Life on Land (11 papers), with marginal representations in SDG 06 (Clean Water and Sanitation) and SDG 12 (Responsible Consumption and Production), each holding a single paper. Together, these metrics map a highly specialized yet interdisciplinary research cluster bridging environmental pressure, plant biochemistry and sustainable health solutions.

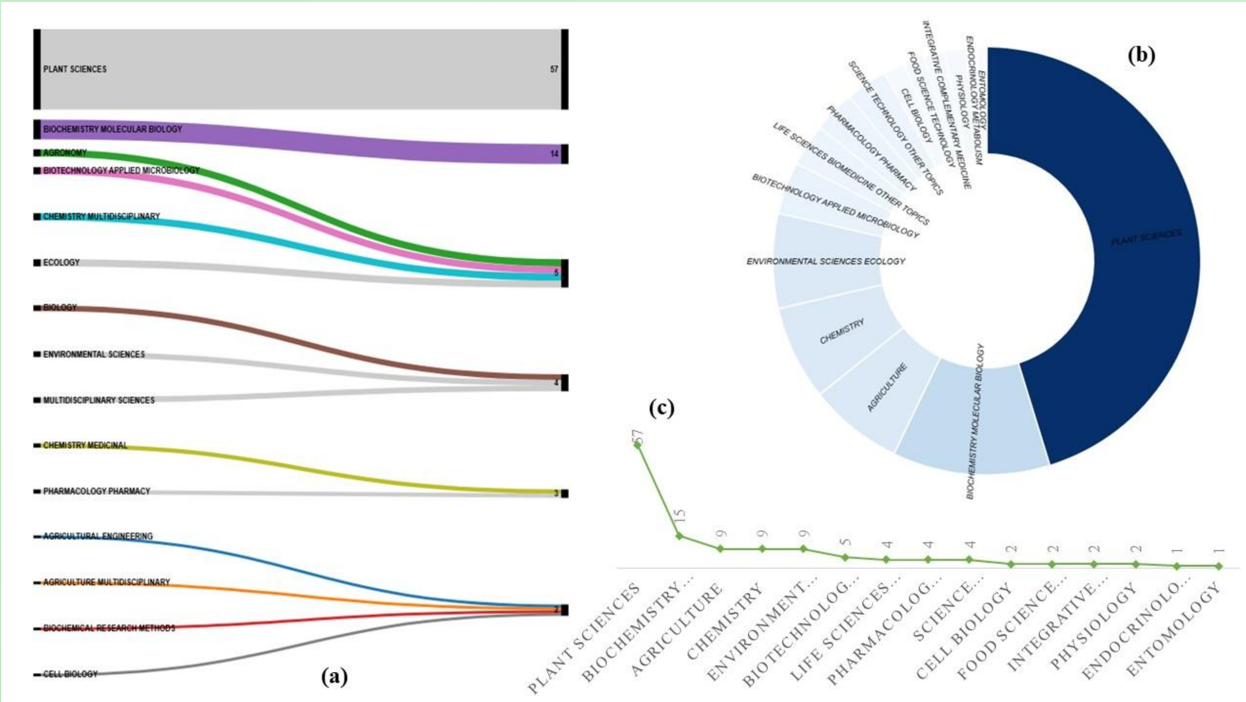

Figure 6. The most important Web of Sciences Categories, Research and SDGs are demonstrated in this field.

Core Journals and Publishers

These are the most prominent publishing avenues and intellectual hubs driving research on the Effect of Abiotic Stress Conditions on Alkaloid Metabolism, in **Figure 7, 8 and 9**. When analyzing the core data across the top-performing journals, distinct leaders emerge based on total publication volume and overall citation impact. *Industrial Crops and Products* stands out as a premier venue, striking an exceptional balance by topping both productivity and impact metrics, which emphasizes its role in translating stress-induced chemical shifts into industrial and agricultural applications. Following closely in publication frequency are authoritative plant science and molecular biology journals, including *Molecules*, *Phytochemistry*, *Journal of Agricultural and Food Chemistry*, *Plant Physiology and Biochemistry*. These platforms consistently document how environmental stressors like drought, salinity and temperature fluctuations trigger complex metabolic pathways to alter secondary metabolite profiles. However, when evaluating the intellectual weight through citation counts, journals like *Plant Physiology*, *Frontiers in Plant Science* and the *Journal of Experimental Botany* command significant scientific influence. Despite publishing fewer total papers relative to the high-volume leaders. These high-impact journals accumulate substantial citations, proving that they serve as foundational references for mechanistic insights into plant stress responses. Collectively, this journal ecosystem reveals a highly integrated research network where high-volume chemical analysis perfectly complements high-citation physiological studies, shaping the global understanding of how crops adapt to a changing climate.

Similarly, a wide range of publishers contribute to publications across different research fields. Among these publishers, the field is supported by emerging contributions from Taylor & Francis, Frontiers Media and Wiley. Higher-volume output is driven by MDPI and Springer Nature. While, Elsevier clearly dominates as the premier publishing house for this domain, in Figure 10.

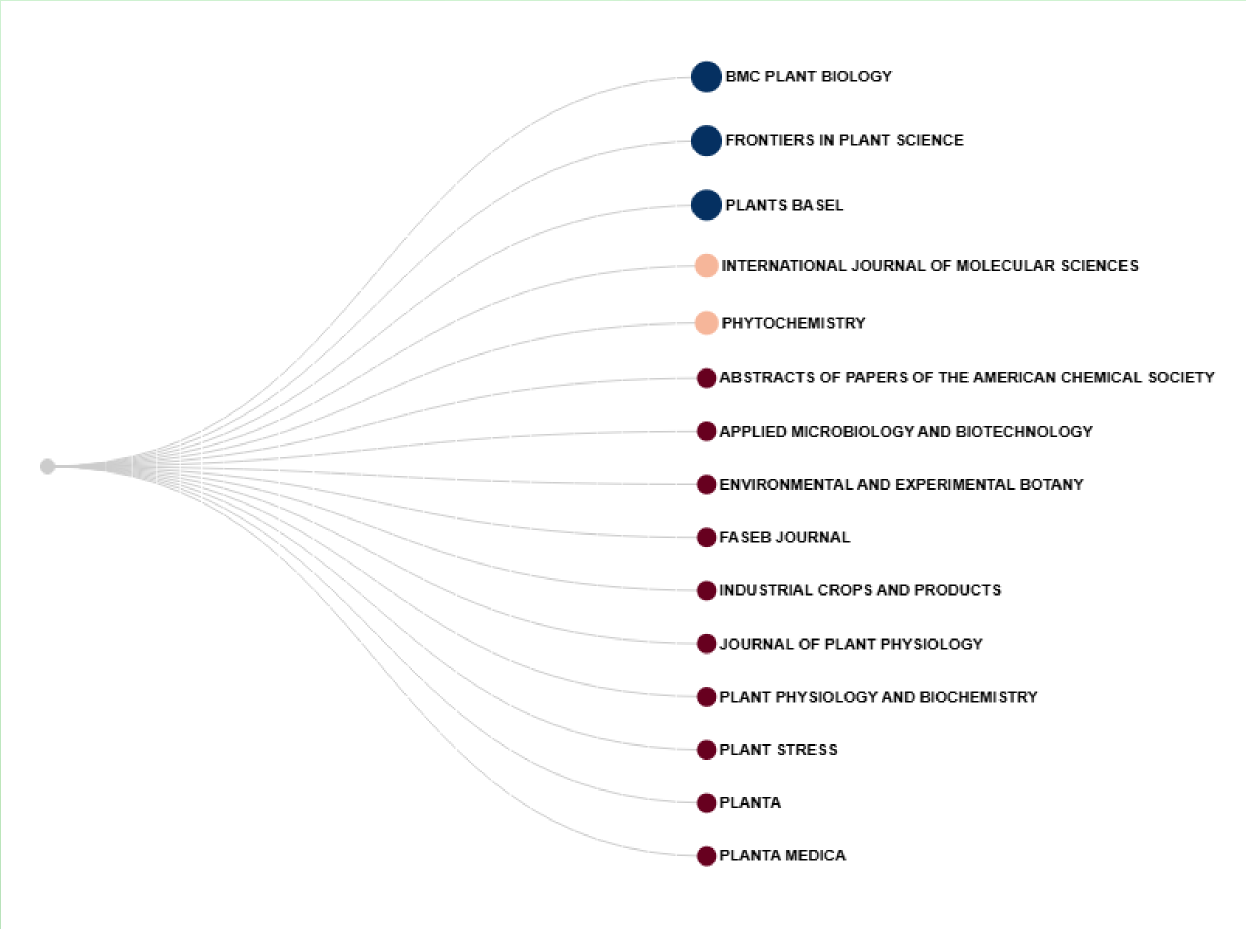

Table 7. List of the 15 most important journals pertaining to plant alkaloid metabolites.

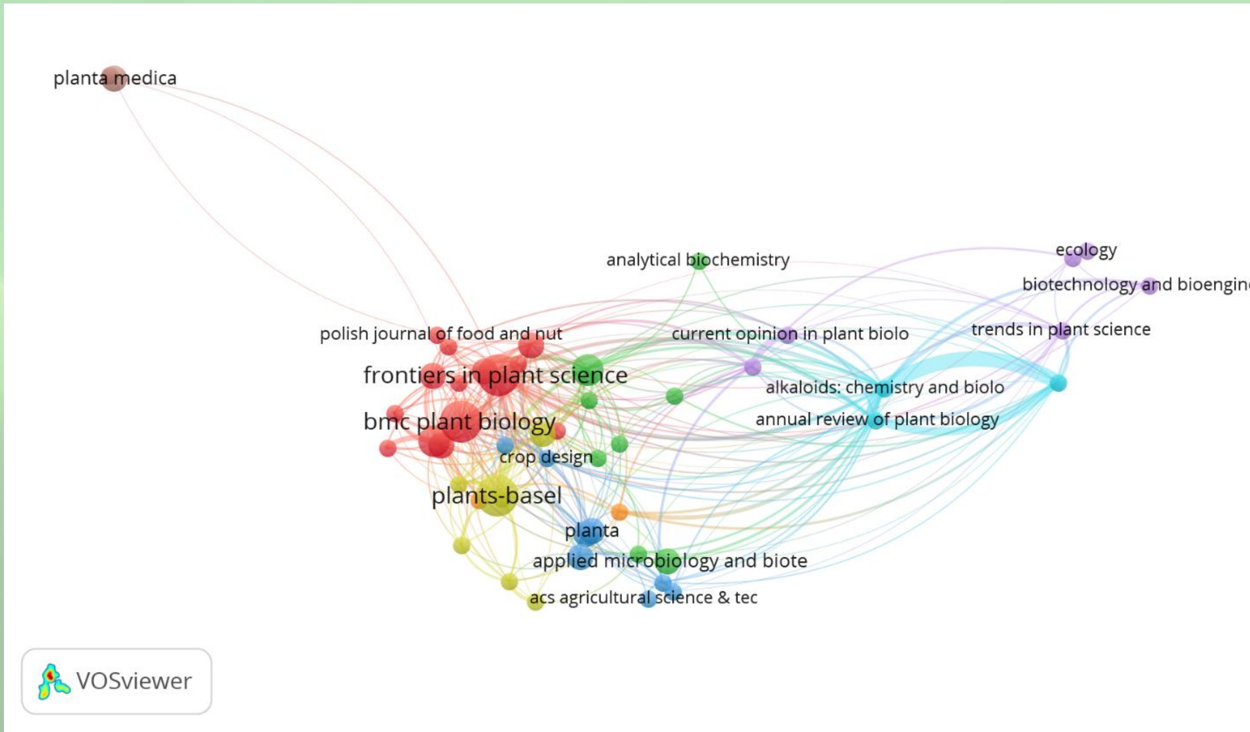

Figure 8. Most highly rated journals in which the most papers were cited with an average citation.

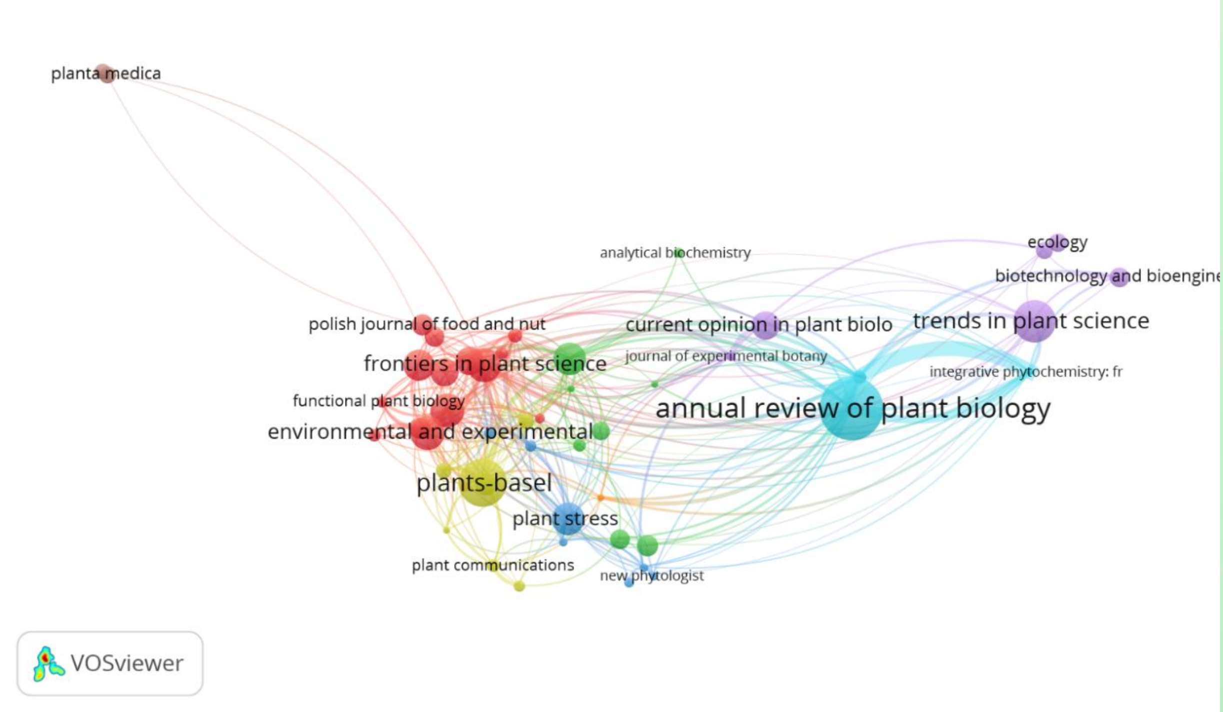

Figure 9. Most highly rated journals in which the most papers were cited with an average citation.

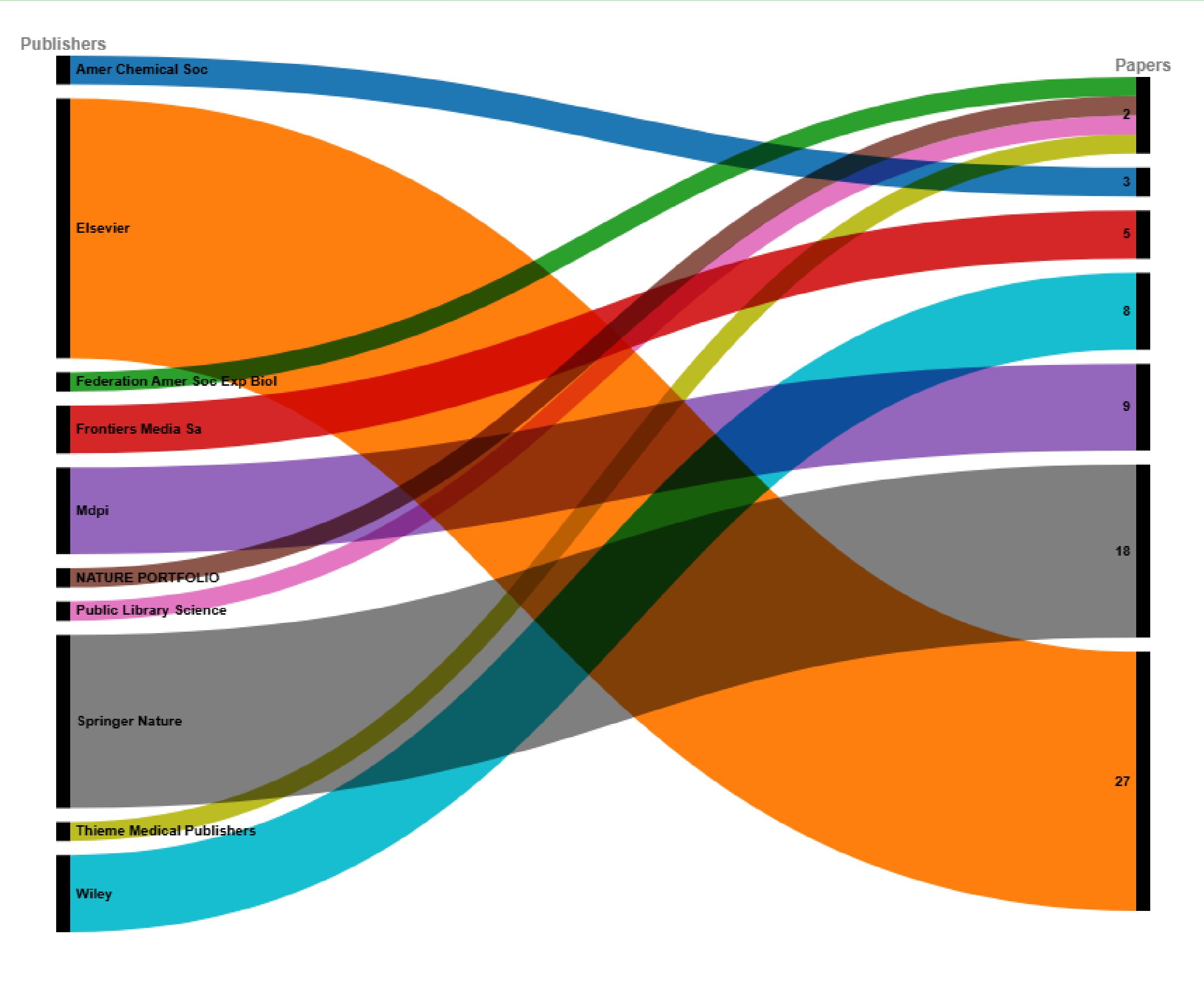

Figure 10. Top 10 publishers associated with the effect of abiotic stress conditions on alkaloid metabolism in plants.

Countries co-authorship analysis

A distinct geographical distribution in research exploring this field. Globally, China and the USA emerge as the primary titans of productivity out of the 34 countries, driving the vast majority of publications and establishing the foundational frameworks for how environmental pressures dictate plant chemical defense mechanisms, in Figure 11 and 12. Beyond these two dominant superpowers, significant research clusters thrive across Asia, Europe and the Middle East. Countries such as Iran, Germany, India, Japan and Brazil contribute substantial literature, illustrating a shared global priority to safeguard crop resilience against climate variations. Furthermore, the active participation of nations like Egypt, Turkey and South Korea underscores a diversified, transcontinental effort. This international research network effectively links regional agricultural challenges ranging from arid-zone salinity to temperature extremes with advanced global secondary metabolite research.

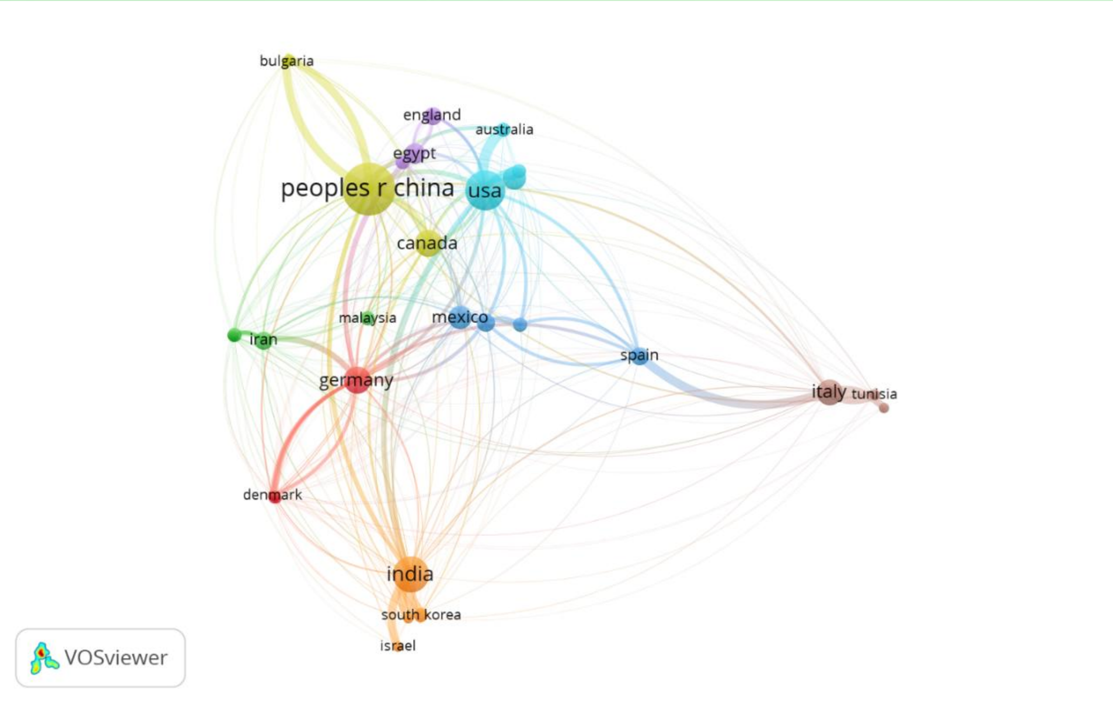

Figure 11. Countries working on Plant Alkaloid Metabolites on the bases of papers.

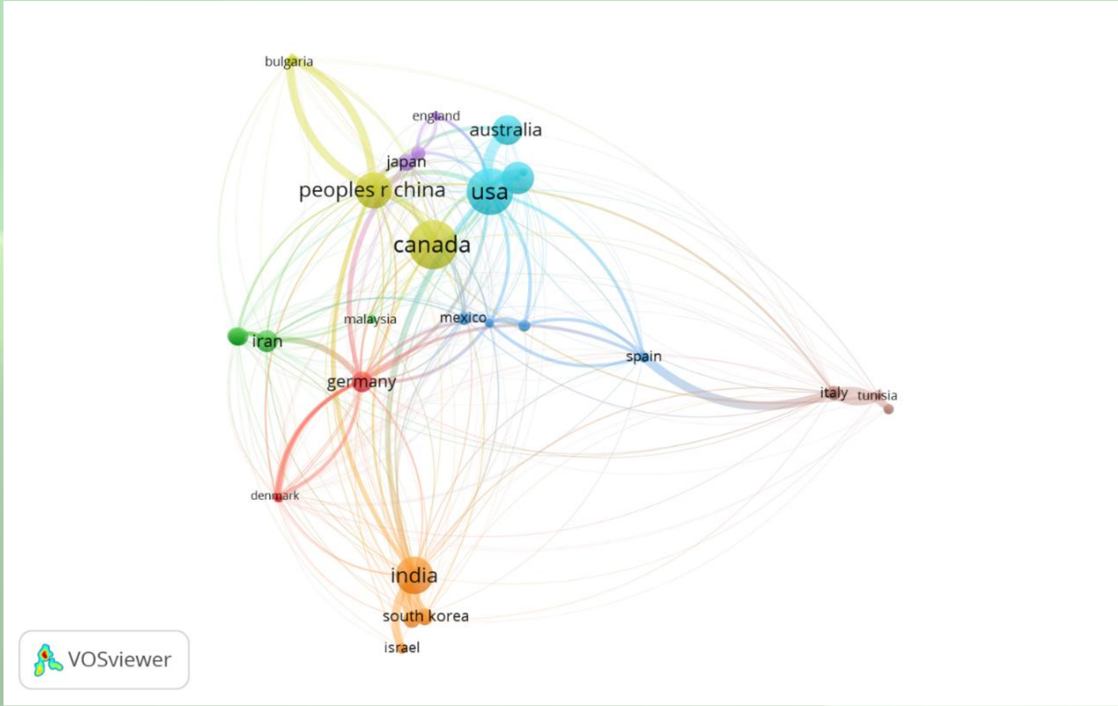

Figure 12. Countries working on Plant Alkaloid Metabolites with minimum 5 citations per paper.

Authors and co-authorship analysis

The researcher network highlights key contributors within this specialized scientific field, structured by publication volume, citation impact and chronological evolution. At the foundational core of this network stands Facchini, Peter J., who dominates the landscape as the top researcher, characterized by the largest node size and an intense heat signature indicating maximum citations and extensive collaborative links, in **Figure 13 and 14**. Moving upwards in an ascending analysis of the research cluster, peripheral and emerging scholars such as *Berni, Roberto*, *Lucini, Luigi* and *Cabrita, Ana R. J.* represent highly localized nodes. Each contributing minimal thresholds such as 1 paper and 5 citations acting as independent or newly integrated entry points into the field. Intermediates like *Parida, Asish Kumar*, *Jalmi, Siddhi Kashinath* and *Chaudhary, Talha* bridge the gap, showcasing growing citation metrics and tighter integration with the central hub. Chronologically, the overlay visualization reveals a clear temporal shift: legacy contributions centered around Facchini (predominantly pre-2015) have paved the way for recent. Modern developments (2020-2025) led by peripheral authors like *Gao, Yang-yang*, indicating a vibrant, evolving field that continues to expand outwards from its foundational authors.

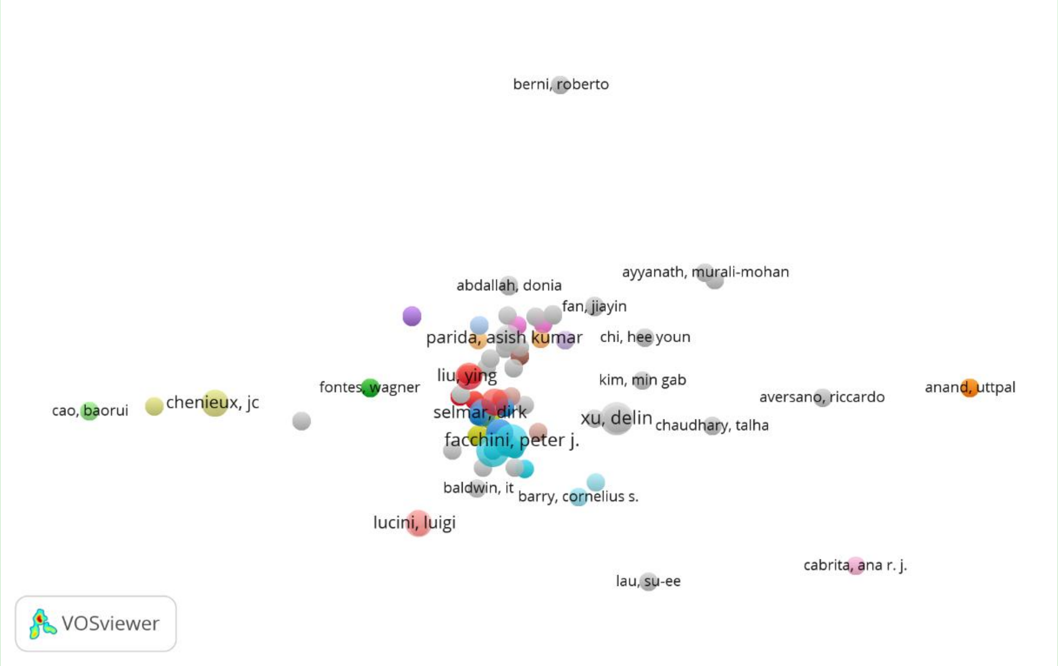

Figure 13. Network visualization map of the most prominent researchers throughout the world with more than 1 PAPER per author.

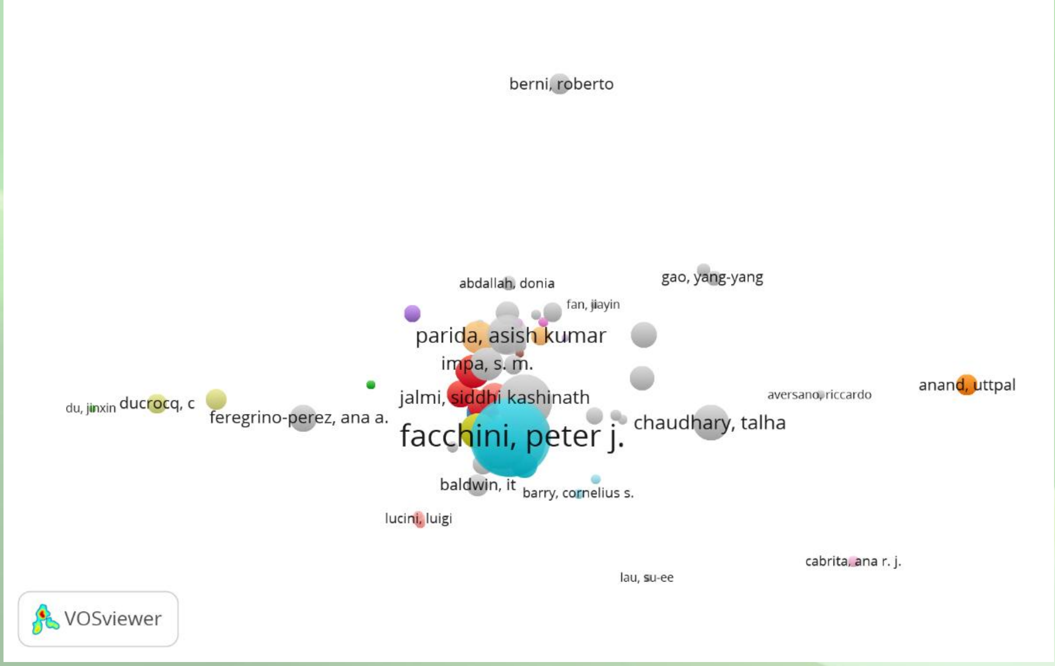

Figure 14. Network visualization map of the most prominent researchers throughout the world with more than 5 citations per author.

Organizations co-authorship analysis

The institutional landscape driving research on the effect of abiotic stress conditions on alkaloid metabolism in plants, showcasing a powerful concentration of scientific output across elite global organizations, in Figure 15 and 16. Analyzing the contributing research institutes reveals that the Chinese Academy of Sciences (CAS) stands out as the global leader in productivity out of 200 organizations, anchoring a massive portion of the literature. This heavy contribution underscores China's strategic academic focus on dissecting how environmental constraints alter plant secondary metabolites. The institutional network expands through highly productive clusters, prominently featuring the University of California System and the United States Department of Agriculture (USDA), both of which serve as major Western pillars linking metabolic stress responses to agricultural resilience. Domestically, the academic momentum within China is further driven by specialized institutions like China Agricultural University, Zhejiang University and the Chinese Academy of Agricultural Sciences, establishing a dense, collaborative ecosystem focused on crop adaptability. On the global stage, foundational contributions from the University of London and Institut National de la Recherche Agronomique (INRA) add crucial European expertise in plant physiology and biochemical pathways. Together, these top organizations form an interconnected, intercontinental research network. Their collective publication volume demonstrates that decoding the intricate relationship between abiotic stress and alkaloid metabolism has become a highly prioritized, resource-intensive global scientific endeavor bridging advanced molecular biology with sustainable agricultural practices.

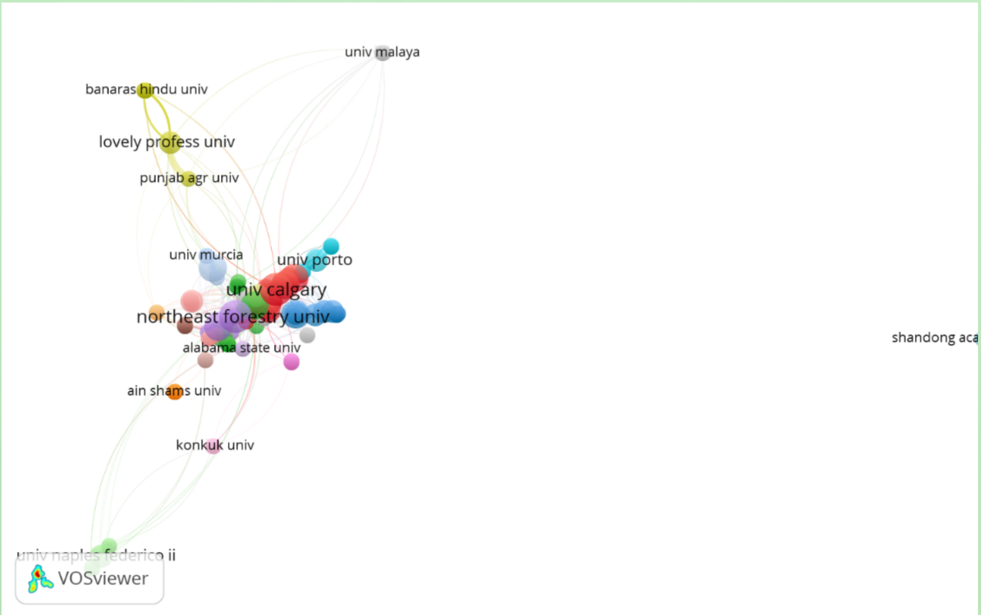

Figure 15. Research Institutes working on Alkaloid Metabolites on Paper bases.

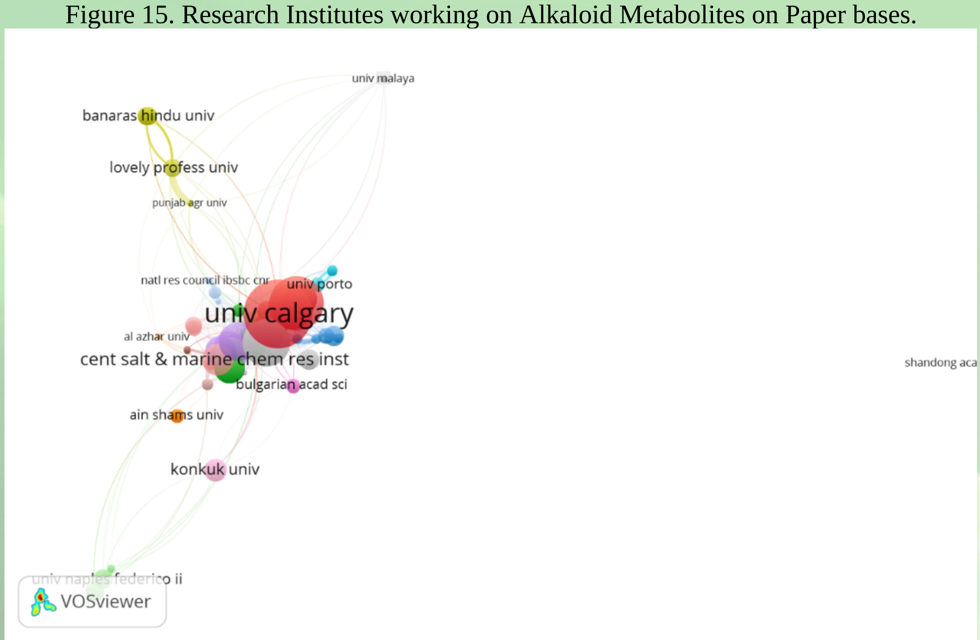

Figure 16. Research Institutes working on Alkaloid Metabolites with at least on Citation bases.

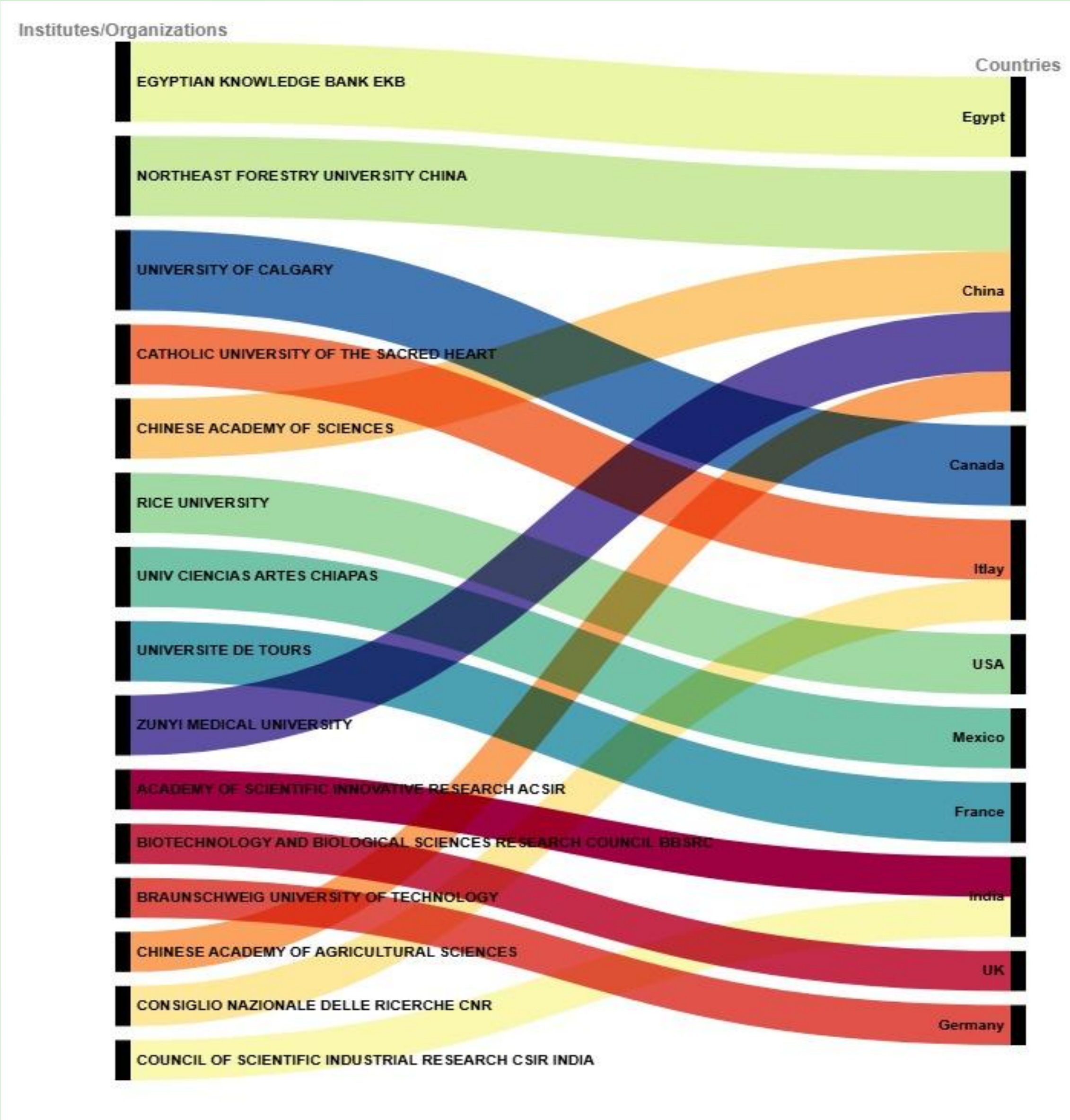

Figure 17. Top Research Institutes working on this topic.

The scientific domain deeply focused on plant specialized metabolism, benzylisoquinoline alkaloid biochemistry and synthetic biology is anchored by the University of Calgary, which stands as the absolute apex contributor with 23 published papers. *China Agricultural University* leads the intermediate tier with 6 papers, followed closely by a dense cluster consisting of the *Banaras Hindu University*, the *Chinese Academy of Agricultural Sciences* and *Southwest University*, each contributing 5 papers. Rounding out the baseline of the top 10 network are the *University of Porto*, *Università Cattolica del Sacro Cuore,* the *University of Natural Resources and Life Sciences Vienna* and *Purdue University* with 4 papers apiece, terminating at the *University of Delhi* with 3 papers. This distribution emphasizes a healthy research pipeline where a highly specialized primary nucleus drives the core bibliometric weight, in Figure 17. Supported, globally by Asian, European and American institutions expanding the field's peripheral scope.

All keywords co-occurrence analysis

The network of all-keyword co-occurrences in a specific botanical or plant biochemistry research domain, highlighting thematic clusters, research intensity and chronological evolution. Image 6 (the network visualization) reveals distinct color-coded clusters that represent specialized sub-fields of study. Central to this network are heavily weighted nodes such as biosynthesis, flavonoids, and abiotic stress, which exhibit the highest density of interconnections, underscoring their roles as the foundational pillars of this research. These core terms link outwards to specific physiological responses, such as water-stress, plant defense, and herbivory, as well as model organisms like arabidopsis-thaliana. Figure 18 further emphasizes this structural focus, showing a prominent center concentrated around the biosynthesis and flavonoids cluster, indicating a substantial volume of publications and intense scholarly focus in this core area. This chronological view reveals that earlier research focused on foundational topics like *periwinkle*, *tropane alkaloids* and *plant-cell cultures*. In contrast, more recent research frontiers have shifted prominently toward abiotic stress management, specific enzyme characterization and specialized pathways like *caffeine biosynthetic-pathway*. This is illustrating a dynamic research transition from basic secondary metabolite identification to climate-resilient crop stress responses, in Figure 18 and 19.

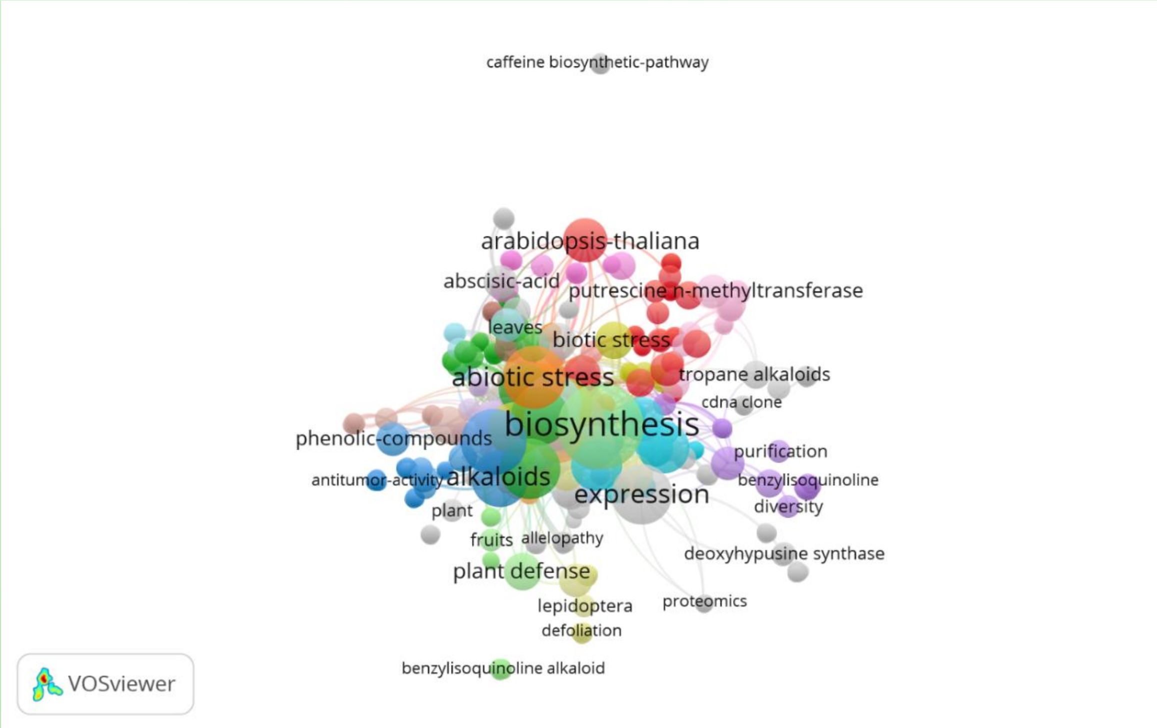

Figure 18. Co-occurrence network visualization diagram of the most frequently occurring keywords in full counting, pertaining to the effect of abiotic stress conditions on alkaloid metabolism in plants. Clusters of related terms are represented by nodes that share the same color.

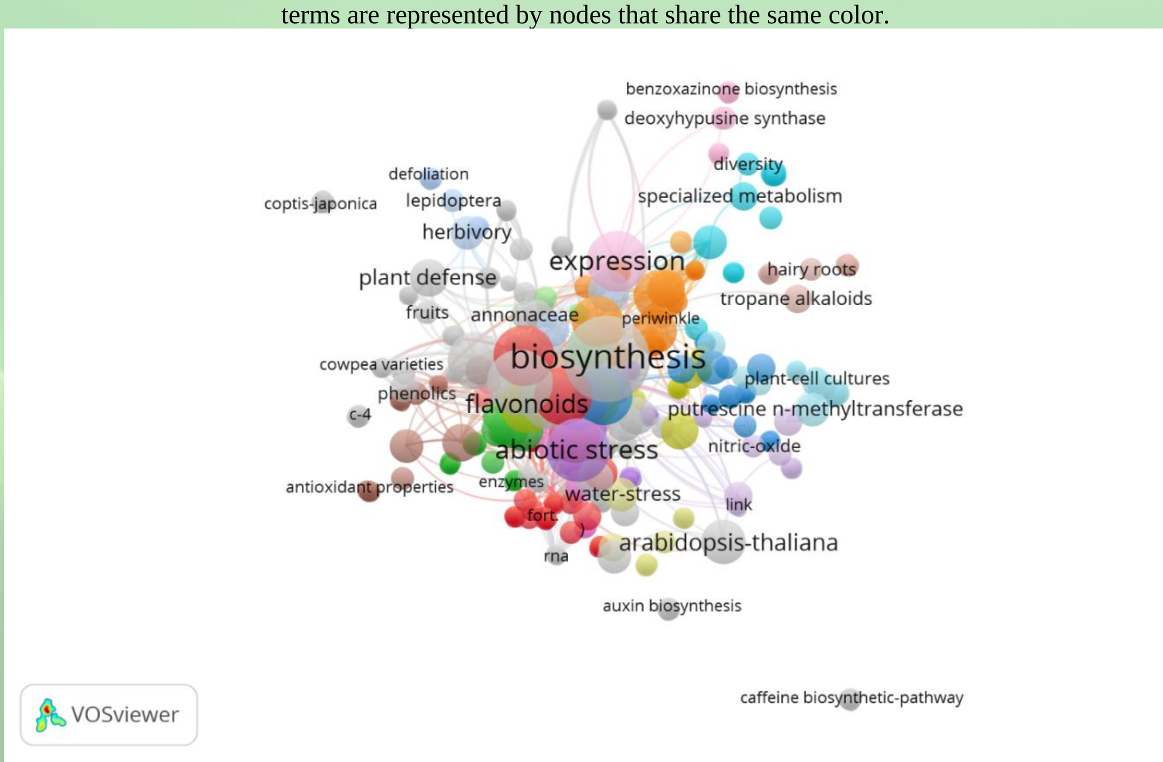

Figure 16. Co-occurrence network visualization diagram of the most frequently occurring keywords in binary counting pertaining to effect of abiotic stress conditions on alkaloid metabolism in plants, represented by clusters that share the same color.

Discussion

The findings of this study demonstrate that abiotic stresses profoundly influence alkaloid metabolism through complex physiological, biochemical and molecular mechanisms. Drought, salinity, temperature extremes, and UV radiation consistently emerged as major environmental drivers capable of altering alkaloid biosynthesis and accumulation across diverse medicinal and crop species. These observations support previous reports indicating that environmental stress redirects carbon and nitrogen resources from primary growth processes toward the production of defensive secondary metabolites (Akula & Ravishankar, 2011; Yeshi et al., 2022). The enhanced accumulation of alkaloids under moderate stress conditions aligns with the Carbon/Nutrient Balance Hypothesis and the Growth-Differentiation Balance Hypothesis, which predict increased investment in defense-related compounds when growth becomes constrained by environmental limitations (Zhang, 2022). The reviewed literature further highlights the central role of stress-responsive signaling pathways involving jasmonic acid (JA), abscisic acid (ABA) and reactive oxygen species (ROS) in regulating alkaloid biosynthesis. Key biosynthetic enzymes, including putrescine N-methyltransferase (PMT), tryptophan decarboxylase (TDC) and strictosidine synthase (STR), were frequently upregulated under drought and salinity stress, resulting in enhanced production of nicotine, tropane alkaloids and terpenoid indole alkaloids (Guedes et al., 2024; Jeyasri et al., 2023). These metabolites contribute not only to plant defense but also to antioxidant protection, osmotic adjustment and nitrogen storage, thereby enhancing stress resilience (Divekar et al., 2022; Haghpanah et al., 2024).

The bibliometric analysis revealed a substantial increase in research output over the last two decades, reflecting growing scientific interest in understanding stress-induced metabolic reprogramming. China and the United States were identified as major contributors. While, Plant Sciences and Biochemistry & Molecular Biology represented the dominant research areas. Emerging technologies such as transcriptomics, metabolomics, CRISPR/Cas9 genome editing and artificial intelligence-assisted metabolic prediction are accelerating discoveries in alkaloid research and facilitating the development of climate-smart medicinal crops (Huang et al., 2024; Khalid et al., 2026). Future studies should focus on integrating multi-omics datasets with field-scale environmental monitoring to improve the predictability and stability of alkaloid production under changing climatic conditions.

Conclusion

Abiotic stress conditions, including drought, salinity, temperature extremes, and ultraviolet radiation, play a pivotal role in regulating alkaloid metabolism in plants. These environmental factors trigger complex physiological and molecular responses that reprogram carbon and nitrogen allocation, resulting in significant alterations in alkaloid biosynthesis and accumulation. Alkaloids not only function as defensive compounds but also contribute to stress tolerance through antioxidant activity, osmotic adjustment, and nitrogen storage. The evidence synthesized in this study highlights the critical involvement of phytohormones, transcription factors and stress-responsive genes in mediating these adaptive responses. Bibliometric analysis revealed a rapidly expanding research landscape, with increasing emphasis on multi-omics technologies, metabolic engineering, CRISPR/Cas9-based approaches and climate-smart crop development. Future research should focus on integrating genomics, metabolomics and environmental monitoring to better predict stress-induced metabolic changes and optimize alkaloid production. Such advances will support the development of resilient medicinal plants and sustainable phytopharmaceutical production under changing climatic conditions.

Data Availability Statement

All the data sources can be provided on demands.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Author Contributions

Muhammad Khizar Hayat and Muhammed Said Yolcu did a significant contribution to this work. In the conception, study design, execution and interpretation. Both of these authors took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published. Both of these authors are agreed on the conference to which the article has been submitted and agree to be accountable for all aspects of the work.

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References

Ahmed, N., Hussain, M., Hussain, Z., Ahmed, Z., Yang, Z., Khalique, A., Chachar, S., Chachar, Z., Bozdar, B., & Ali, A. (2026). Fulvic acids as biostimulants in plant–soil systems: mechanistic insights into nutrient chelation, transport, and stress tolerance. *Plant and Soil*, 1-27.

Akhtar, M. T., Noor, M., Lin, X., Lu, Z., & Jin, B. (2026). Flavonoids in Plant Salt Stress Responses: Biosynthesis, Regulation, Functions, and Signaling Networks. *Plants*, *15*(1), 171.

Akula, R., & Ravishankar, G. A. (2011). Influence of abiotic stress signals on secondary metabolites in plants. *Plant Signaling & Behavior*, *6*(11), 1720-1731.

Alami, M. M., Guo, S., Mei, Z., Yang, G., & Wang, X. (2024). Environmental factors on secondary metabolism in medicinal plants: exploring accelerating factors. *Medicinal Plant Biology*, *3*(1).

Alum, E. U., Manjula, V. S., Uti, D. E., Echegu, D. A., Ugwu, O. P.-C., Egba, S. I., & Agu, P. C. (2025). Metabolomics-driven standardization of herbal medicine: advances, applications, and sustainability considerations. *Natural Product Communications*, *20*(8), 1934578X251367650.

Alyas, J., Khalid, N., Ishaque, S., Fatima, H., Hashim, M., Hassan, S., Bukhari, S., Hano, C., Abbasi, B. H., & Anjum, S. (2023). Light (high light/UV radiation) modulates adaptation mechanisms and secondary metabolite production in medicinal plants. In *Medicinal plants: their response to abiotic stress* (pp. 363-390). Springer.

Amirifar, A., Hemati, A., Asgari Lajayer, B., Pandey, J., & Astatkie, T. (2022). Impact of various environmental factors on the biosynthesis of alkaloids in medicinal plants. *Environmental challenges and medicinal plants: sustainable production solutions under adverse conditions*, 229-248.

Arif, M., Helal, M. M. U., Bilal, M. S., Shi, W., Wang, Z., Xu, R., Ghorbani, A., Chen, M. X., & Li, L. (2025). Transcriptomic and metabolomic profiling reveal the close implication of alkaloid biosynthesis and ureide metabolism to drought stress tolerance in maize. *Journal of Agricultural and Food Chemistry*, *73*(24), 15416-15428.

Ashihara, H., Sano, H., & Crozier, A. (2008). Caffeine and related purine alkaloids: biosynthesis, catabolism, function and genetic engineering. *Phytochemistry*, *69*(4), 841-856.

Ashraf, M. V., Khan, S., Misri, S., Gaira, K. S., Rawat, S., Rawat, B., Khan, M. H., Shah, A. A., Asgher, M., & Ahmad, S. (2024). High-altitude medicinal plants as promising source of phytochemical antioxidants to combat lifestyle-associated oxidative stress-induced disorders. *Pharmaceuticals*, *17*(8), 975.

Bhushan, S., Sharma, D., Rakshant, Kaul, S., Dhar, M. K., & Sharma, M. (2023). Recent strategies to engineer alkaloid biosynthesis in medicinal plants. In *Medicinal plants: Their response to abiotic stress* (pp. 391-416). Springer.

Borthakur, U., Sarma, N., Basumatary, B. R., Phukan, S. G., Boro, K., Gogoi, S., Sikdar, N., Kundu, B. K., Kalita, B., & Tanti, B. (2026). Impacts of Climate Change on the Genetic and Phytochemical Diversity of Medicinal Plants in Biodiversity Hotspot Regions. In *Genetic Diversity in Medicinal Plants: Challenges, Threats, and Future Applications* (pp. 321-344). Springer.

Chada, S., Asiedu, S., Ofoe, R., & Abbey, L. (2023). An overview of plant morpho-physiology, biochemicals, and metabolic pathways under water stress. *Horticult Int J*, *7*(4), 115-125.

Chandra, S., Lata, H., ElSohly, M. A., Walker, L. A., & Potter, D. (2017). Cannabis cultivation: methodological issues for obtaining medical-grade product. *Epilepsy & Behavior*, *70*, 302-312.

Chen, Q., Li, N., Cui, X., & Ge, F. (2026). AP2/ERF transcription factors regulate the biosynthesis of terpenoids, phenolics, and alkaloids in plants. *Horticulture Research*, *13*(1), uhaf280.

Choudhary, S., Wani, K. I., Naeem, M., Khan, M. M. A., & Aftab, T. (2023). Cellular responses, osmotic adjustments, and role of osmolytes in providing salt stress resilience in higher plants: polyamines and nitric oxide crosstalk. *Journal of Plant Growth Regulation*, *42*(2), 539-553.

Das, D. R., Sarkar, M., & Paul, A. (2023). Tools and Approaches for Assessing Stress-Responsive Secondary Metabolites to Design Climate-Smart Crops. In *Biology and Biotechnology of Environmental Stress Tolerance in Plants* (pp. 305-370). Apple Academic Press.

Debbagh-Nour, H., Briache, F. Z., El Mouttaqi, A., Sabraoui, T., Ducousso, M., Boukcim, H., & Hirich, A. (2026). Secondary metabolites of desert and stress-adapted plants: adaptive responses toward salinity and drought stresses, and optimization tools and techniques. *Phytochemistry Reviews*, 1-25.

Divekar, P. A., Narayana, S., Divekar, B. A., Kumar, R., Gadratagi, B. G., Ray, A., Singh, A. K., Rani, V., Singh, V., & Singh, A. K. (2022). Plant secondary metabolites as defense tools against herbivores for sustainable crop protection. *International Journal of Molecular Sciences*, *23*(5), 2690.

El-Sayed, M., & Verpoorte, R. (2007). Catharanthus terpenoid indole alkaloids: biosynthesis and regulation. *Phytochemistry Reviews*, *6*(2), 277-305.

Facchini, P. J. (2001). Alkaloid biosynthesis in plants: biochemistry, cell biology, molecular regulation, and metabolic engineering applications. *Annual review of plant biology*, *52*(1), 29-66.

Farhan, M., Sathish, M., Kiran, R., Mushtaq, A., Baazeem, A., Hasnain, A., Hakim, F., Atif, S., Mubeen, M., & Iftikhar, Y. (2024). Plant nitrogen metabolism: balancing resilience to nutritional stress and abiotic challenges. *Phyton*, *93*(3), 581.

Galanie, S., Thodey, K., Trenchard, I. J., Filsinger Interrante, M., & Smolke, C. D. (2015). Complete biosynthesis of opioids in yeast. *Science*, *349*(6252), 1095-1100.

Gillani, S. W., Wang, M., Wang, L., Lu, X., Bai, Y., Song, Y., Meng, C., Jia, X., Li, Y., & Zhang, C. (2026). Temporal Transcriptomic and Metabolomic Reprogramming Unveils a Two-Phase Salt Tolerance Mechanism in Apocynum venetum. *International Journal of Molecular Sciences*, *27*(4), 1917.

Giri, A., Magnuson, A., & Kalia, S. (2025). *Designer Poultry Eggs: Innovations, Applications, and Future Outlook*. Academic Press.

Grgac, R., Rozsypal, J., Des Marteaux, L., Štětina, T., & Koštál, V. (2022). Stabilization of insect cell membranes and soluble enzymes by accumulated cryoprotectants during freezing stress. *Proceedings of the National Academy of Sciences*, *119*(41), e2211744119.

Guedes, J. G., Ribeiro, R., Carqueijeiro, I., Guimarães, A. L., Bispo, C., Archer, J., Azevedo, H., Fonseca, N. A., & Sottomayor, M. (2024). The leaf idioblastome of the medicinal plant Catharanthus roseus is associated with stress resistance and alkaloid metabolism. *Journal of Experimental Botany*, *75*(1), 274-299.

Gul, Z., Tang, Z.-H., Arif, M., & Ye, Z. (2022). An insight into abiotic stress and influx tolerance mechanisms in plants to cope in saline environments. *Biology*, *11*(4), 597.

Gupta, A., Gupta, K. K., Gupta, S. K., & Mishra, P. K. (2023). Transcriptional Regulation in Biosynthesis of Phytochemicals in Medicinal Plants Under Stress Conditions. In *Stress-responsive Factors and Molecular Farming in Medicinal Plants* (pp. 123-140). Springer.

Guru, A., Ranjan, D., Jaiswal, D., Hidangmayum, A., & Dwivedi, P. (2025). Role of Osmolytes in ROS-Scavenging and Maintaining Homeostasis Under Abiotic Stress. In *Plant Signaling Molecules in Regulation of ROS-Scavenging System: Adapting to Climate Change* (pp. 61-86). Springer.

Haghpanah, M., Hashemipetroudi, S., Arzani, A., & Araniti, F. (2024). Drought tolerance in plants: physiological and molecular responses. *Plants*, *13*(21), 2962.

Hasanuzzaman, M., Parvin, K., Bardhan, K., Nahar, K., Anee, T. I., Masud, A. A. C., & Fotopoulos, V. (2021). Biostimulants for the regulation of reactive oxygen species metabolism in plants under abiotic stress. *Cells*, *10*(10), 2537.

Hashim, S. E., Basar, N., Abd Samad, A., Jamil, S., Bakar, M. B., Jamalis, J., Abd-Aziz, N., Wagiran, A., Razak, M. R. M. A., & Samad, A. F. A. (2025). Advancing alkaloid-based medicines: medical applications, scalable production and synthetic innovations. *Phytochemistry Reviews*, *24*(5), 4653-4681.

He, J., Yao, L., Pecoraro, L., Liu, C., Wang, J., Huang, L., & Gao, W. (2023). Cold stress regulates accumulation of flavonoids and terpenoids in plants by phytohormone, transcription process, functional enzyme, and epigenetics. *Critical Reviews in Biotechnology*, *43*(5), 680-697.

He, X., Zhao, X., Li, Y., Liu, L., Qiu, C., & Xing, H. (2026). A Comprehensive Omics Study Revealed the Responses of Flax to Drought Stress and the Changes in Lignans. *Journal of Natural Fibers*, *23*(1), 2650804.

Huang, X., Rong, W., Zhang, X., Gao, Y., Zhou, Y., Su, J., Luo, H., Chu, G., & Wang, M. (2024). Transcriptome and metabolome analysis reveal the dynamic changes and biosynthesis pathways of alkaloids in Sophora alopecuroides L. under drought stress. *Industrial Crops and Products*, *212*, 118365.

Ikram, M., Batool, M., Ullah, M., Khalid, B., El-Badri, A. M., Mohamed, I. A., Zhang, L., Kuai, J., Xu, Z., & Zhao, J. (2025). Molecular alchemy: Converting stress into resilience via secondary metabolites and calcium signaling in rice. *Rice*, *18*(1), 32.

Imran, M., Wu, Q., Guanming, C., & Zhou, L. (2025). Multifaceted roles and regulatory mechanisms of MYB transcription factors in plant development, secondary metabolism, and stress adaptation: Current insights and future prospects. *GM Crops & Food*, *16*(1), 626-655.

Isah, T. (2019). Stress and defense responses in plant secondary metabolites production. *Biological Research*, *52*.

Jangpangi, D., Patni, B., Chandola, V., & Chandra, S. (2025). Medicinal plants in a changing climate: understanding the links between environmental stress and secondary metabolite synthesis. *Frontiers in plant science*, *16*, 1587337.

Jeyasri, R., Muthuramalingam, P., Karthick, K., Shin, H., Choi, S. H., & Ramesh, M. (2023). Methyl jasmonate and salicylic acid as powerful elicitors for enhancing the production of secondary metabolites in medicinal plants: an updated review. *Plant Cell, Tissue and Organ Culture (PCTOC)*, *153*(3), 447-458.

Jomova, K., Raptova, R., Alomar, S. Y., Alwasel, S. H., Nepovimova, E., Kuca, K., & Valko, M. (2023). Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. *Archives of toxicology*, *97*(10), 2499-2574.

Kar, D., Pradhan, A. A., Dutta, A., Bhagavatula, L., & Datta, S. (2022). The multidrug and toxic compound extrusion (MATE) family in plants and their significance in metal transport. In *Plant metal and metalloid transporters* (pp. 151-177). Springer.

Kesawat, M. S., Satheesh, N., Kherawat, B. S., Kumar, A., Kim, H.-U., Chung, S.-M., & Kumar, M. (2023). Regulation of reactive oxygen species during salt stress in plants and their crosstalk with other signaling molecules—Current perspectives and future directions. *Plants*, *12*(4), 864.

Khalid, B., Javed, M. U., Ikram, M., Ateeq, M., Ashraf, M. A., Riaz, T., Nawaz, S., & Maqbool, R. (2026). Precision Rewiring of Stress-Responsive Gene Networks Via CRISPR: Mechanistic Pathways Toward Climate-Smart Agriculture. *Journal of Crop Health*, *78*(1), 2.

Khalkho, J. P., Beck, A., Priyanka, Panda, B., & Chandra, R. (2024). Microbial allies: exploring fungal endophytes for biosynthesis of terpenoid indole alkaloids. *Archives of Microbiology*, *206*(8), 340.

Khan, A., Kanwal, F., Ullah, S., Fahad, M., Tariq, L., Altaf, M. T., Riaz, A., & Zhang, G. (2025). Plant secondary metabolites—Central regulators against abiotic and biotic stresses. *Metabolites*, *15*(4), 276.

Khan, N. (2025). Molecular insights into ABA-mediated regulation of stress tolerance and development in plants. *International Journal of Molecular Sciences*, *26*(16), 7872.

Khan, S., Korai, Z., Yang, L., Korai, S. K., Li, S., Zulfiqar, U., Alotaibi, M. S., Asadullaeva, D., Muminov, M., & Gururani, M. A. (2026). Metabolic reprogramming in plant defense: linking signaling networks to metabolomics-driven insights. *Plant Signaling & Behavior*, *21*(1), 2672221.

Khashan, K. T., & Al-Athary, M. A. (2016). Vinblastine and vincristine alkaloids production from callus of Catharanthus roseus (L.) G. Don under some abiotic factors. *Al-Kufa University Journal for Biology*, *8*(2), 9-24.

Kumar, P., Kapoor, B., Negi, S., Deepika, Manikandan, E., Sharma, S., & Thakur, N. (2026). High-Altitude Resilience: Environmental Perturbations and the Medicinal Potential of Alpine Flora. In *Climate Resilience and Molecular Adaptation in Alpine Medicinal Plants: Ecophysiology, Metabolism and Plantomics* (pp. 67-90). Springer.

Lei, B., Mao, Y., Zhao, H., Yu, J., Wang, B., Li, P., & Hu, X. (2025). ABA-INSENSITIVE 4 promotes nicotine biosynthesis under high light in Nicotiana attenuata. *Plant Science*, *353*, 112416.

Leite Dias, S., & D'Auria, J. C. (2025). The bitter truth: how insects cope with toxic plant alkaloids. *Journal of Experimental Botany*, *76*(1), 5-15.

Li, J., Song, L.-Y., Guo, Z.-J., Xu, C.-Q., Zhang, L.-D., Wang, J.-C., Tang, H.-C., Dai, M.-J., Zhu, X.-Y., & Zheng, H.-L. (2025). Salinity affects C/N ratio through differential responses of carbon and nitrogen metabolism in mangrove

Avicennia marina leaves revealed by combined analysis of transcriptome and metabolome. *Plant and Soil*, *507*(1), 783-806.

Liu, Y., Singh, S. K., Pattanaik, S., Wang, H., & Yuan, L. (2023). Light regulation of the biosynthesis of phenolics, terpenoids, and alkaloids in plants. *Communications Biology*, *6*(1), 1055.

Lukan, T., & Coll, A. (2022). Intertwined roles of reactive oxygen species and salicylic acid signaling are crucial for the plant response to biotic stress. *International Journal of Molecular Sciences*, *23*(10), 5568.

Luo, D., Jia, Z., Ding, X., Zeng, L., Cheng, Y., Zou, X., Raza, A., & Lv, Y. (2025). Tropine alkaloid-driven panomic (transcriptome–metabolome) reprogramming delivers insights into cold stress tolerance in rapeseed (Brassica napus L.). *Plant Physiology and Biochemistry*, 110844.

Lv, Y., & Fan, G. (2026). Network-Driven Insights into Plant Immunity: Integrating Transcriptomic and Proteomic Approaches in Plant–Pathogen Interactions. *International Journal of Molecular Sciences*, *27*(3), 1242.

Ma, P., Chengcun, L., Airao, M., & Tengfei, Z. (2026). Plant Ornithine Decarboxylase: A Key Regulator of Polyamine Biosynthesis and Its Roles in Growth, Stress Response, and Secondary Metabolism. *Horticulturae*, *12*(3), 389.

Mazzafera, P. (1999). Chemical composition of defective coffee beans. *Food chemistry*, *64*(4), 547-554.

McAllister, J. T., Lennertz, L., & Atencio Mojica, Z. (2022). Mapping a discipline: a guide to using VOSviewer for bibliometric and visual analysis. *Science & Technology Libraries*, *41*(3), 319-348.

Mishra, A. K., Agrawal, S. B., & Tiwari, S. (2025). Unveiling oxidative stress: surface ozone triggers phenylpropanoid pathway shifts and metabolite rewiring in PBW-550 wheat. *Plant cell reports*, *44*(8), 185.

Mishra, N., Jiang, C., Chen, L., Paul, A., Chatterjee, A., & Shen, G. (2023). Achieving abiotic stress tolerance in plants through antioxidative defense mechanisms. *Frontiers in plant science*, *14*, 1110622.

Mmbando, G. S. (2023). The recent relationship between ultraviolet-B radiation and biotic resistance in plants: a novel non-chemical strategy for managing biotic stresses. *Plant Signaling & Behavior*, *18*(1), 2191463.

Nagavi, J. C., Shukla, B. K., Bhati, A., Rai, A., & Verma, S. (2024). Harnessing Geospatial Technology for Sustainable Development: A Multifaceted Analysis of Current Practices and Future Prospects. In *Sustainable Development and Geospatial Technology: Volume 1: Foundations and Innovations* (pp. 147-170). Springer.

Ngara, R., & Shavrukov, Y. (2026). Omics and Multi-Omics Insights into Plant Responses to Abiotic Stresses. In (Vol. 15, pp. 799): MDPI.

Nie, S., & Wang, D. (2023). AP2/ERF transcription factors for tolerance to both biotic and abiotic stress factors in plants. *Tropical Plant Biology*, *16*(3), 105-112.

Noviana, E., Indrayanto, G., & Rohman, A. (2022). Advances in fingerprint analysis for standardization and quality control of herbal medicines. *Frontiers in Pharmacology*, *13*, 853023.

Prashar, D. B., Sharma, M., Sharma, D., Mir, Z. A., Sood, H., & Sharma, M. (2025). Exploring the complexity of plant stress response: Role of metabolomics and signalling pathways in metabolic diversification. *Journal of Plant Biochemistry and Biotechnology*, *34*(4), 851-864.

Qin, K., Liu, F., Zhang, C., Deng, R., Fernie, A. R., & Zhang, Y. (2025). Systems and synthetic biology for plant natural product pathway elucidation. *Cell Reports*, *44*(6).

Rabeh, K., Hnini, M., & Oubohssaine, M. (2025). A comprehensive review of transcription factor-mediated regulation of secondary metabolites in plants under environmental stress. *Stress Biology*, *5*(1), 15.

Rai, S. K., Rai, K. K., Apoorva, Kumar, S., & Rai, S. P. (2022). functional genomics approaches for gene discovery related to terpenoid indole alkaloid biosynthetic pathway in Catharanthus roseus. In *The Catharanthus Genome* (pp. 155-173). Springer.

Rao, M. J., Duan, M., Zhou, C., Jiao, J., Cheng, P., Yang, L., Wei, W., Shen, Q., Ji, P., & Yang, Y. (2025). Antioxidant defense system in plants: reactive oxygen species production, signaling, and scavenging during abiotic stress-induced oxidative damage. *Horticulturae*, *11*(5), 477.

Raza, A., Salehi, H., Rahman, M. A., Zahid, Z., Madadkar Haghjou, M., Najafi-Kakavand, S., Charagh, S., Osman, H. S., Albaqami, M., & Zhuang, Y. (2022). Plant hormones and neurotransmitter interactions mediate antioxidant defenses under induced oxidative stress in plants. *Frontiers in plant science*, *13*, 961872.

Rynjah, D., Sandhanam, K., Bhattacharjee, B., Deka, B., Newar, A., Kalita, T., Nath, J., Ahmed, A. B., Sahu, R. K., & Das, T. (2025). CRISPR/Cas9 gene editing systems for enhancing secondary metabolite biosynthesis via reproductive tissue modification. *Discover Plants*, *2*(1), 245.

Salam, U., Ullah, S., Tang, Z.-H., Elateeq, A. A., Khan, Y., Khan, J., Khan, A., & Ali, S. (2023). Plant metabolomics: an overview of the role of primary and secondary metabolites against different environmental stress factors. *Life*, *13*(3), 706.

Saleem, S., Ul Mushtaq, N., Shah, W. H., Rasool, A., Hakeem, K. R., & Ul Rehman, R. (2022). Beneficial role of phytochemicals in oxidative stress mitigation in plants. In *Antioxidant defense in plants: molecular basis of regulation* (pp. 435-451). Springer.

Samanta, D., & Manna, O. (2025). Alkaloids: Exploring Their Diversity, Complexity and Applications. *Medicinal plants and Their uses: Basic to Field*, 73.

Sana, Aftab, T., Naeem, M., Jha, P. K., & Prasad, P. V. (2025). Production of secondary metabolites under challenging environments: understanding functions and mechanisms of signalling molecules. *Frontiers in plant science*, *16*, 1569014.

Sanches, P. H. G., de Melo, N. C., Porcari, A. M., & de Carvalho, L. M. (2024). Integrating molecular perspectives: strategies for comprehensive multi-omics integrative data analysis and machine learning applications in transcriptomics, proteomics, and metabolomics. *Biology*, *13*(11), 848.

Satrio, R. D., Fendiyanto, M. H., & Miftahudin, M. (2024). Tools and techniques used at global scale through genomics, transcriptomics, proteomics, and metabolomics to investigate plant stress responses at the molecular level. In *Molecular dynamics of plant stress and its management* (pp. 555-607). Springer.

Sattar, M., Shabbir, M., Ullah, G., Abbas, K., Hussain, A., Hayat, M. K., Sarfraz, B., & Usman, H. (2024). Molecular Mechanisms In Plant Physiology: Regulating Stomatal Development And Function Under Environmental Stress. *Frontiers in Health Informatics*, *13*(8).

Selmar, D., & Kleinwächter, M. (2013). Influencing the product quality by deliberately applying drought stress during the cultivation of medicinal plants. *Industrial Crops and Products*, *42*, 558-566.
Sharma, A., Verma, P., Mathur, A., & Mathur, A. K. (2018). Overexpression of tryptophan decarboxylase and strictosidine synthase enhanced terpenoid indole alkaloid pathway activity and antineoplastic vinblastine biosynthesis in Catharanthus roseus. *Protoplasma*, *255*(5), 1281-1294.
Sharma, N., Thakur, M., Suryakumar, P., Mukherjee, P., Raza, A., Prakash, C. S., & Anand, A. (2022). 'Breathing Out'under heat stress—respiratory control of crop yield under high temperature. *Agronomy*, *12*(4), 806.
Sheuli, S. A., Arafin, M. S., Sultana, S., Rabbi, M. A., & Ghosh, A. (2025). Exogenous salicylic acid, abscisic acid, and shikimic acid enhance drought tolerance in tea by modulating antioxidant defense and osmotic regulation. *PloS one*, *20*(10), e0331456.
Shoaib, N., Pan, K., Mughal, N., Raza, A., Liu, L., Zhang, J., Wu, X., Sun, X., Zhang, L., & Pan, Z. (2024). Potential of UV-B radiation in drought stress resilience: A multidimensional approach to plant adaptation and future implications. *Plant, cell & environment*, *47*(2), 387-407.
Shoji, T., Kajikawa, M., & Hashimoto, T. (2010). Clustered transcription factor genes regulate nicotine biosynthesis in tobacco. *The plant cell*, *22*(10), 3390-3409.
Singh, D., Mathur, S., Prasad, M., & Ranjan, R. (2025). Next-generation sequencing in medicinal plants: recent progress, opportunities, and challenges. *Journal of Plant Growth Regulation*, *44*(4), 1448-1464.
Su, Z.-L., Li, A.-M., Wang, M., Qin, C.-X., Pan, Y.-Q., Liao, F., Chen, Z.-L., Zhang, B.-Q., Cai, W.-G., & Huang, D.-L. (2025). The role of AP2/ERF transcription factors in plant responses to biotic stress. *International Journal of Molecular Sciences*, *26*(10), 4921.
Sun, S., Shen, X., Li, Y., Li, Y., Wang, S., Li, R., Zhang, H., Shen, G., Guo, B., & Wei, J. (2023). Single-cell RNA sequencing provides a high-resolution roadmap for understanding the multicellular compartmentation of specialized metabolism. *Nature Plants*, *9*(1), 179-190.
Sun, Y., Alseekh, S., & Fernie, A. R. (2023). Plant secondary metabolic responses to global climate change: a meta-analysis in medicinal and aromatic plants. *Global change biology*, *29*(2), 477-504.
Suryantoro, E., Udin, U., & Qamari, I. (2023). A bibliometric analysis using VOSviewer: Leadership in infection prevention and control. *Multidisciplinary Science Journal*, *5*(2).
Tang, W., Liu, X., He, Y., & Yang, F. (2022). Enhancement of vindoline and catharanthine accumulation, antioxidant enzymes activities, and gene expression levels in Catharanthus roseus leaves by chitooligosaccharides elicitation. *Marine drugs*, *20*(3), 188.
Tekade, R. K., & Saraf, S. (2026). *Biomolecular and Safety Considerations of Phytopharmaceuticals*. CRC Press.
Tilkat, E., Ayaz Tilkat, E., Akkaya, Ö., & Özden Çiftçi, Y. (2024). Metabolic engineering for overproduction of plant secondary metabolites: Alkaloids. *Innovative Methods in Horticultural Crop Improvement: Molecular Tools, Nanotechnology and Artificial Intelligence*, 297-328.
Tiwari, D., Kewlani, P., Gaira, K. S., Bhatt, I. D., Sundriyal, R., & Pande, V. (2023). Predicting phytochemical diversity of medicinal and aromatic plants (MAPs) across eco-climatic zones and elevation in Uttarakhand using Generalized Additive Model. *Scientific Reports*, *13*(1), 10888.
Ullah, A., Tariq, A., Zeng, F., Asghar, M. A., Noor, J., Javed, H. H., Kazmi, A., Sardans, J., & Peñuelas, J. (2026). Nitrogen Addition Optimizes Root-Leaf Coordination of Carbon-Nitrogen Metabolism and Osmolytes to Improve Drought Tolerance in Alhagi Sparsifolia. *Journal of Soil Science and Plant Nutrition*, *26*(1), 522-539.
Upadhyay, R., Saini, R., Shukla, P., & Tiwari, K. (2025). Role of secondary metabolites in plant defense mechanisms: A molecular and biotechnological insights. *Phytochemistry Reviews*, *24*(1), 953-983.
Ushie, O., Ochepo, E., Nkom, P., Ago, M., & Gani, J. (2023). Medicinal Uses of Nitrogen Group Containing Secondary Metabolites: A Review. *Tropical Journal of Science and Technology*, *4*(1), 71-82.
Van Eck, N., & Waltman, L. (2010). Software survey: VOSviewer, a computer program for bibliometric mapping. *scientometrics*, *84*(2), 523-538.
Varadharajan, V., Rajendran, R., Muthuramalingam, P., Runthala, A., Madhesh, V., Swaminathan, G., Murugan, P., Srinivasan, H., Park, Y., & Shin, H. (2025). Multi-omics approaches against abiotic and biotic stress—a review. *Plants*, *14*(6), 865.
Verma, K., Kumari, K., Rawat, M., Devi, K., & Joshi, R. (2025). Crosstalk of jasmonic acid and salicylic acid with other phytohormones alleviates abiotic and biotic stresses in plants. *Journal of Soil Science and Plant Nutrition*, *25*(2), 4997-5019.
Verma, S., Verma, S. S., Sharma, N., Kumar, J., Verma, A., & Gupta, P. C. (2026). Alkaloids as Antioxidants: Implications for Health and Disease Prevention. In *Alkaloids From Medicinal Plants and Their Transformative Applications* (pp. 184-200). CRC Press.
Wang, G., Sun, X., Li, Y., Wang, Y., & Jin, C. (2025). The Role of UV-B Radiation in Modulating Secondary Metabolite Biosynthesis and Regulatory Mechanisms in Medicinal Plants. *BioResources*, *20*(2).
Wen, Y., Liao, Y., Tang, Y., Zhang, H., Zhang, J., & Liao, Z. (2023). Metabolic effects of elicitors on the biosynthesis of tropane alkaloids in medicinal plants. *Plants*, *12*(17), 3050.
Wink, M. (2010). *Annual plant reviews, functions and biotechnology of plant secondary metabolites*. John Wiley & Sons.
Wu, J., Li, Y., Yin, H., Zhao, L., Xu, C., Fu, X., Shang, J., Liu, S., Guo, H., & Ma, F. (2026). Plant heat shock protein Hsp90 enhances stress resistance through integrating protein quality control, chloroplast protection, hormone signal network, and immune defense. *Journal of Experimental Botany*, *77*(4), 910-931.
Wu, Y., Li, X., Zhang, J., Zhao, H., Tan, S., Xu, W., Pan, J., Yang, F., & Pi, E. (2022). ERF subfamily transcription factors and their function in plant responses to abiotic stresses. *Frontiers in plant science*, *13*, 1042084.
Xiao, C., Zhou, G., He, T., & Li, C. (2025). Transport of secondary metabolites in plants: Mechanistic insights and transporter engineering for crop improvement. *Plant Communications*, *6*(12).
Yadav, A., Bohra, N., & Singh, H. (2024). Forest ecosystem adaptation to climate change: morphological and physiological responses. In *Forests and Climate Change: Biological Perspectives on Impact, Adaptation, and Mitigation Strategies* (pp. 269-289). Springer.

Yan, Q., Zhang, G., Zhang, X., & Huang, L. (2024). A review of transcriptomics and metabolomics in plant quality and environmental response: From bibliometric analysis to science mapping and future trends. *Metabolites*, *14*(5), 272.

Yang, L., Wen, K.-S., Ruan, X., Zhao, Y.-X., Wei, F., & Wang, Q. (2018). Response of plant secondary metabolites to environmental factors. *Molecules*, *23*(4), 762.

Yazaki, K. (2005). Transporters of secondary metabolites. *Current Opinion in Plant Biology*, *8*(3), 301-307.

Yeshi, K., Crayn, D., Ritmejerytė, E., & Wangchuk, P. (2022). Plant secondary metabolites produced in response to abiotic stresses has potential application in pharmaceutical product development. *Molecules*, *27*(1), 313.

Yin, Q., Feng, Z., Ren, Z., Wang, H., Wu, D., Jaisi, A., & Yang, M. (2025). Integrative physiological, metabolomic and transcriptomic insights into phenylpropanoids pathway responses in Nicotiana tabacum under drought stress. *Plant Stress*, *16*, 100815.

Zambelli, A., Nocito, F. F., & Araniti, F. (2025). Unveiling the multifaceted roles of root exudates: chemical interactions, allelopathy, and agricultural applications. *Agronomy*, *15*(4), 845.

Zhang, J. (2022). *Investigating Molecular Mechanisms Involved in Plant Defense Priming and Genotypic Variation in Defense Phenotype* ETH Zurich].