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Physiological Regulation of Bioactive Compound Production in Medicinal Plants: A Comprehensive Review

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Abstract

Medicinal plants form the foundation of both traditional and modern healthcare systems owing to their ability to produce diverse bioactive compounds with significant therapeutic potential. The biosynthesis and accumulation of these metabolites are governed by complex physiological and biochemical processes that regulate both primary and secondary metabolism. Key physiological activities such as photosynthesis, respiration, transpiration, and nutrient assimilation not only sustain plant growth and development but also strongly influence the synthesis of pharmacologically active secondary metabolites including flavonoids, terpenoids, alkaloids, and phenolics. Plant growth regulators (PGRs)—such as auxins, cytokinins, gibberellins, jasmonic acid, and salicylic acid—play pivotal roles in modulating these physiological and metabolic pathways by mediating stress responses, cell differentiation, and secondary metabolite biosynthesis. Moreover, environmental and abiotic factors such as light, temperature, water availability and nutrient status further interact with PGR signaling networks, thereby shaping the metabolic outcomes and therapeutic quality of medicinal plants. This review synthesizes recent advances in understanding the physiological and hormonal regulation of bioactive compound production in medicinal plants, emphasizing the integration of metabolism, environmental adaptation, and signaling mechanisms. A comprehensive understanding of these processes can guide the development of improved cultivation practices, biotechnological interventions, and metabolic engineering strategies for the sustainable enhancement of medicinal plant resources.

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Introduction

The foundation of both conventional and modern health care systems worldwide has long been acknowledged to be medicinal plants. They are natural sources of bioactive substances with medicinal qualities that are the end result of complex physiological and biochemical reactions that take place in plant systems. All metabolic and regulatory processes that either directly or indirectly affect the quality, quantity, and effectiveness of medicinal compounds, including photosynthesis, respiration, transpiration, nutrient assimilation, and secondary metabolite biosynthesis, are included in the physiological activity of medicinal plants (Taiz *et al.,* 2015). In addition to supporting primary metabolism, which is necessary for growth and development, plant physiological processes also control secondary metabolism, which yields pharmacologically significant compounds such as flavonoids, terpenoids, phenolics, and alkaloids (Dewick, 2002). These secondary metabolites are important for plant defence mechanisms and have a variety of biological actions that are important for human health, including antibacterial, anti-inflammatory, and antioxidant properties (Wink, 2015).

The production and accumulation of these metabolites are significantly influenced by physiological and environmental parameters, including as temperature, light intensity, water availability, and nutritional status (Chaves *et al.,* 2009; Ramakrishna & Ravishankar, 2011). Understanding these physiological processes is therefore vital for optimizing the medicinal value of plants through cultivation practices, biotechnological interventions, and metabolic engineering. The goal of this review is to compile the most recent research on the ways in which physiological processes in plants affect the synthesis, control, and therapeutic potential of bioactive chemicals found in medicinal plants. It draws attention to the linkages among secondary metabolism, physiological processes, and environmental adaptation in order to lay the groundwork for further study and the sustainable use of medicinal plant resources.

Physiological Processes Influencing Medicinal Properties

Photosynthesis and Carbon Assimilation

Plant metabolism and growth are maintained by photosynthesis, a basic physiological mechanism that transforms light energy into chemical energy stored in carbohydrates. These carbohydrates act as the main building blocks for the primary metabolites (like sugars, lipids, and amino acids) and secondary metabolites (like flavonoids, terpenoids, alkaloids, and phenolic compounds), which are frequently in charge of plants' therapeutic qualities (Taiz *et al.,* 2015; Lichtenthaler *et al.,* 1998; Verpoorte *et al.,* 2000). As carbon dioxide (CO_2) is absorbed during photosynthesis, the Calvin–Benson cycle creates triose phosphates, which are then utilised to create starch and sucrose. These absorbed carbon compounds serve as building blocks for a variety of biosynthetic processes that result in the production of bioactive substances. The amount of carbon skeletons available for secondary metabolism can consequently be increased by increased photosynthetic efficiency (Caretto *et al.,* 2015). Light intensity, CO_2 concentration, temperature, and water availability are examples of environmental variables that significantly affect photosynthetic activity and, in turn, secondary metabolite biosynthesis. Higher light intensity, for instance, frequently promotes the buildup of flavonoids and phenolics, which act as defenses against photo oxidative stress (Kumar *et al.,* 2020). The production of carbon-based secondary metabolites such as terpenoids and phenolics can also be enhanced by greater CO_2 levels, which can encourage higher carbohydrate accumulation (Ghasemzadeh *et al.,* 2010). In medicinal plants, the link between secondary metabolism and photosynthesis is essential. Higher quantities of chemicals having pharmacological activity are directly correlated with increased carbon absorption. According to Jaleel *et al.,* (2007), for example, it has been demonstrated that increased photosynthetic activity in Catharanthus roseus increases the production of indole alkaloids like vincristine and vinblastine. The quality and production of metabolites that are relevant for medicine can therefore be enhanced by optimising photosynthetic efficiency by environmental or biotechnological treatments.

Respiration and Energy Metabolism

Plant respiration is a vital physiological process in which carbohydrates generated through photosynthesis are oxidized to produce energy in the form of ATP and reducing equivalents (NADH and $FADH_2$). This energy is crucial for driving numerous biosynthetic reactions, including those involved in the formation of secondary metabolites such as alkaloids, flavonoids, terpenoids, and phenolic compounds, which are largely responsible for the medicinal properties of plants (Hopkins & Hüner, 2008; Taiz *et al.,* 2015). Respiration also provides carbon skeletons and intermediates such as pyruvate, acetyl-CoA, and oxaloacetate, which act as precursors for secondary metabolite biosynthesis. Environmental stresses, including drought, salinity, and temperature extremes, often trigger stress-induced changes in respiration, resulting in enhanced ATP production and altered metabolite fluxes. This stress-responsive respiration can modulate secondary metabolism, leading to increased accumulation of bioactive compounds that help plants adapt to adverse conditions (Fernie & Stitt, 2012; Nunes-Nesi *et al.,* 2010). Thus, respiration not only sustains plant growth and primary metabolism but also plays a central role in regulating the production of medicinally important compounds.

Water Relations and Transpiration

Water relations are essential for sustaining physiological processes in plants, including as nutrient transfer, cell turgidity, and primary and secondary metabolite production. Maintaining the flow of nutrients through the xylem and enabling carbon dioxide uptake for photosynthesis are two benefits of adequate water availability, which guarantees proper stomatal function. On the other hand, a series of physiological and biochemical reactions brought on by water scarcity or drought stress affect the synthesis of secondary metabolites that are significant for medicine. Under water-limiting situations, for example, plants frequently collect phenolic chemicals, terpenoids, and alkaloids as part of their adaptive response to stress, strengthening their defensive mechanisms and antioxidant capacity.

Osmotic adjustment and water potential modification brought on by drought can also increase the expression of genes linked to the manufacture of secondary metabolites, establishing a clear connection between increased phytochemical accumulation and water stress. Transpiration plays a dual role in this context: it regulates leaf temperature and turgor, while excessive water loss can intensify stress signals, thereby altering metabolite profiles. Thus, precise regulation of water balance is essential for both growth and the medicinal quality of plants (Chaves *et al.,* 2009; Taiz *et al.,* 2015; Farooq *et al.,* 2009).

Mineral Nutrition and Secondary Metabolism

Mineral nutrients are essential for medicinal plants' growth, development, and secondary metabolism. Key enzymes and co-factors involved in the production of secondary metabolites depend on macronutrients including nitrogen (N), phosphorus (P), and potassium (K), as well as micronutrients like iron (Fe), zinc (Zn), and manganese (Mn). According to Marschner (2012), nitrogen is especially important for the synthesis of nitrogen-containing substances like alkaloids since it supplies the amino groups needed for their production. Through the creation of ATP, phosphorus aids in energy metabolism and consequently promotes the synthesis of flavonoids and phenolic compounds (Taiz *et al.,* 2015). Potassium controls enzyme activity and osmotic balance, which indirectly affects the buildup of secondary metabolites. Iron is necessary for the activity of cytochrome enzymes in phenolic biosynthesis, for example. Micronutrients, despite being needed in smaller quantities, are crucial as co-factors for enzymes involved in redox reactions and secondary metabolic pathways (Marschner, 2012). In addition to improving plant growth, adequate mineral nutrition also dramatically affects the amount and calibre of bioactive compounds, highlighting its significance in the production of phytochemicals and medicinal plants (Fageria *et al.,* 2011).

Environmental and Abiotic Factors on Bioactive Compound Production in Medicinal Plants

Environmental and abiotic factors exert profound influence on the biosynthesis of secondary metabolites in medicinal plants. Light quality, intensity, and photoperiod regulate key enzymes such as PAL and CHS, stimulating phenolic and flavonoid accumulation, particularly under UV-B exposure (Zhang *et al.,* 2023; Llorente *et al.,* 2024). Temperature extremes trigger oxidative stress responses that elevate antioxidant metabolite production, though growth reduction can limit overall yield (Hasanuzzaman *et al.,* 2020).

Water scarcity and salinity stress both promote synthesis of ROS-scavenging compounds, osmoprotectants, and terpenoids as part of adaptive tolerance (Piwowarczyk *et al.,* 2023; Kamal *et al.,* 2025). Elevated CO_2 modifies carbon–nitrogen allocation, enhancing carbon-based secondary metabolite production while reducing nitrogen-based compounds (Zvereva & Kozlov, 2012). Similarly, nitrogen limitation favors phenolic and flavonoid accumulation at the expense of alkaloids (Herms & Mattson, 1992; Løvdal *et al.,* 2020). Overall, controlled abiotic stress management can strategically enhance bioactive compound production in medicinal plants.

Hormonal Regulation of Bioactive Compound Production in Medicinal Plants

Plant hormones play a central role in regulating the biosynthesis of bioactive secondary metabolites, acting as major controllers that integrate developmental and environmental signals to modulate metabolic pathways. Among these, jasmonic acid (JA) serves as a master regulator of defense-associated metabolites such as terpenoids, alkaloids, and phenolics. JA signaling, mediated through the COI1–JAZ–MYC2 module, activates a range of transcription factors including MYC2, MYB, and AP2/ERF, which enhance the expression of key biosynthetic genes such as phenylalanine ammonia-lyase (PAL), chalcone synthase (CHS), and terpene synthases (TPS).

Table.1 Influence of Environmental and Abiotic Factors on Bioactive Compound Production in Medicinal Plants.

Abiotic Factor	Effect on Secondary Metabolites	Mechanism / Key Observation	Representative References
Light (quality, intensity, photoperiod)	Increase in Phenolics, flavonoids, terpenoids	UV-B and blue light activate photoreceptors (UVR8, cryptochrome), upregulating phenylalanine ammonia-lyase (PAL) and chalcone synthase (CHS) genes involved in flavonoid biosynthesis.	Zhang *et al.,* 2023, *Front. Plant Sci.*, 14:1326218; Xu *et al.,* 2022, *Plant Growth Regul.*, 98:47–58; Llorente *et al.,* 2024, *Plants*, 13(8):1070
Temperature stress (high/low)	Moderate increase in phenolics/flavonoids; severe decrease in volatile terpenoids & growth	Both heat and cold induce oxidative stress, enhancing antioxidant metabolite synthesis, but extreme stress reduces photosynthetic carbon supply.	Hasanuzzaman *et al.,* 2020, *Front. Plant Sci.*, 10:1463; Wahid *et al.,* 2022, *Plant Stress Physiol.*, Elsevier
Water deficit (drought)	Increase in Phenolics, flavonoids, alkaloids, osmolytes	Drought elevates ROS and ABA, triggering antioxidant pathways (phenylpropanoid, alkaloid) for cellular protection.	Piwowarczyk *et al.,* 2023, *Front. Plant Sci.*, 14:1323085; Selmar & Kleinwächter, 2013, *Plant Cell Environ.*, 36:1663–1677
Salinity stress	Increase in Phenolics, flavonoids, terpenoids, proline	NaCl stress increases osmotic and oxidative stress, stimulating phenolic and terpene biosynthesis as osmoprotectants.	Kamal *et al.,* 2025, *Heliyon*, 11(1):e21038; Ashraf *et al.,* 2022, *Ind. Crops Prod.*, 183:114988
Elevated CO_2	Increase in Carbon-based metabolites (phenolics, tannins, flavonoids); decrease in N-based metabolites (alkaloids)	Increased C:N ratio shifts carbon allocation toward secondary metabolism; some metabolites act as excess carbon sinks.	Zvereva & Kozlov, 2012, *New Phytol.*, 195:727–736; Peñuelas & Staudt, 2010, *Trends Plant Sci.*, 15:684–691
Nitrogen limitation	Increase in Phenolics, flavonoids; decrease in Alkaloids	Reduced N availability limits protein synthesis, diverting carbon to phenylpropanoid pathways (C-based defense compounds).	Herms & Mattson, 1992, *Q. Rev. Biol.*, 67:283–335; Stewart *et al.,* 2011, *J. Exp. Bot.*, 62(2):519–529; Løvdal et al., 2020, *Front. Plant Sci.*, 12:613839
Combined stresses (e.g., drought + heat)	Variable but often synergistic increase in phenolics and flavonoids	Combined stress intensifies ROS generation, activating multi-pathway antioxidant responses.	Rivero *et al.,* 2022, *Environ. Exp. Bot.*, 194:104702; López et al., 2023, *Front. Plant Sci.*, 14:1282917

This hormonal regulation is particularly evident under wounding, herbivory, or elicitor exposure, where methyl jasmonate treatment markedly increases the accumulation of artemisinin in Artemisia annua and indole alkaloids in Catharanthus roseus (Wasternack & Feussner, 2018; De Geyter *et al.,* 2012; Akula & Ravishankar, 2011). In contrast, salicylic acid (SA) is primarily associated with responses to biotrophic pathogens, modulating phenolic and phytoalexin biosynthesis through the NPR1–TGA–WRKY signaling cascade. SA frequently interacts synergistically or antagonistically with JA depending on the stressor and tissue context, influencing flavonoid and phenolic accumulation in medicinal species such as Ocimum sanctum (Vlot *et al.,* 2009; Yang *et al.,* 2019).

Ethylene (ET) further modulates secondary metabolism, often acting in concert with JA to regulate stress-induced compounds. Through EIN3/EIL1 and ERF transcription factors, ET enhances alkaloid and terpenoid biosynthesis, exemplified by JA–ET co-regulation of nicotine formation in Nicotiana tabacum (Broekaert *et al.,* 2006; Shoji & Hashimoto, 2011). Meanwhile, abscisic acid (ABA) plays a significant role under abiotic stress conditions, such as drought or salinity, where it stimulates the production of antioxidant phenolics and flavonoids via SnRK2-mediated activation of bZIP, MYB, and WRKY transcription factors. ABA has been shown to enhance glycyrrhizin content in Glycyrrhiza uralensis and anthocyanin accumulation in Arabidopsis thaliana under osmotic stress (Jiang & Zhang, 2002; Wang *et al.,* 2020).

In addition, gibberellins (GA) and cytokinins (CK) influence secondary metabolism through developmental regulation and hormonal cross-talk. GA typically antagonizes JA responses, prioritizing growth over defense, whereas CKs enhance metabolite biosynthesis by promoting the formation of glandular trichomes and secretory tissues that house essential oils and phenolics. CKs have also been linked to the activation of PAL and CHS enzymes, thereby enhancing phenolic accumulation in several medicinal plants (Unterholzner *et al.,* 2015; Guo & Gan, 2011; Sharma *et al.,* 2020). Collectively, these hormones form a complex regulatory network where JA and SA function as primary defense inducers, while ET, ABA, GA, and CK fine-tune the biosynthetic and developmental balance to optimize plant adaptation and secondary metabolite production.

In conclusion, the production of bioactive compounds in medicinal plants is a multifaceted process controlled by intricate interactions among physiological functions, environmental cues, and hormonal signaling pathways. Physiological processes such as photosynthesis, respiration, transpiration, and nutrient assimilation provide the fundamental energy and substrates required for both primary and secondary metabolism, ultimately determining the yield and quality of therapeutic metabolites. Plant growth regulators (PGRs) act as central mediators that fine-tune these physiological and metabolic pathways, influencing secondary metabolite biosynthesis under both optimal and stress conditions. A holistic understanding of the physiological and regulatory mechanisms governing secondary metabolism is essential for enhancing the medicinal value of plants through targeted cultivation strategies, elicitor applications, and metabolic engineering approaches. Integrating knowledge from plant physiology, biochemistry, and molecular biology will pave the way for sustainable production and conservation of medicinal plant resources. Ultimately, deciphering these complex regulatory systems can contribute to the development of more efficient, eco-friendly, and economically viable methods for producing high-quality phytopharmaceuticals.

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