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Biosynthesis of secondary metabolites in aromatic and medicinal plants in response to abiotic stresses: A review

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ABSTRACT

Climate change has massive consequences on non-living factors in the environment, resulting in irregular precipitation, fluctuating atmospheric temperature, and variations in humidity. These changes cause biotic and abiotic stresses; plants must have defense mechanisms to survive. Therefore, plants divert some synthesized energy towards producing numerous plant secondary metabolites (PSMs), *viz*., flavonoids, alkaloids, and essential oils. These compounds act as protections for the plants, helping them to survive under stressful conditions. Medicinal and aromatic plants (MAPs) are sessile organisms that are not immune to harmful consequences of various abiotic stresses in which the PSMs have an important role in acting against the adverse effects. In this regard, the MAPs have a coherent defense mechanism for abiotic stresses. The secondary metabolites produced by these plants are useful as medicines and aromatic products for humans. However, not all stresses produce high secondary metabolites, as their production is highly specific to certain stresses. This review provides a comprehensive understanding of secondary metabolite production under various stressful conditions, including extreme temperature, drought, water logging, salinity, harmful radiation, elevated levels of ozone and CO_2, heavy metals, and agrochemicals on MAPs. Additionally, the production of these compounds can be modified by subjecting plants to various stressors. Many authors have reported on PSMs in MAPs, which need to be well documented and exploited for humankind.

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1 Introduction

Since time immemorial, plants have provided food, medicine and shelter for mankind. These generate a diverse kind of valuable primary and secondary metabolites. The primary metabolites have a vital role in the growth and development of plants, while the secondary metabolites participate in defense mechanisms against biotic and abiotic stresses. Climate change mainly, water stress, and heat stresses are found to affect plant morphology and physiology (Rodrigues et al. 2021), where the medicinal and aromatic plants are much more vulnerable to adverse conditions as per their biodiversity (Qaderi et al. 2023; Rahman et al. 2023). Human anthropogenic activities like rapid urbanization, industrialization, deforestation, automobiles, etc., lead to extreme changes in climatic conditions, resulting in the prevalence of unseasonal rainfall, extreme temperature, high wind, heavy snowfall, inundation of sea water, flood, drought, and rising pests population posing a significant risk for many plant species on earth including medicinal and aromatic plants (Figure 1). A defense response is evolved in plants by producing secondary metabolites (PSMs) to avoid cell and tissue injury (Yeshi et al. 2022). PSMs like terpenoids, alkaloids, and phenolic biochemicals form the major PSM group. It is reported that the medicinal and aromatic plants, as the sessile group of plants, are most evolved with the production of PSMs under even mild abiotic stresses without adversely impacting growth and development, while in some cases, the plant's performance may improve (Jampílek and Kráľová 2023). PSMs evolution may increase or decrease as per the intensity of environmental stresses (Liu et al. 2023). Secondary metabolite production was increased in *Thymus vulgaris*, *Rosmarinus officinalis,* and *Mentha pulégium* with the increase in temperature and water stress up to 50%, while further extreme temperature and water pressure at 70% the levels of the compound depleted in plants (Laftouhi et al. 2023). The findings explained that the MAPs generate secondary metabolites (SMs) under non-living stresses to avoid interruption in the physiological process and damage to cells and tissues, though the extreme environment is quite detrimental. The growth and productivity of MAPs are strongly interrelated with the change in external climatic factors. Various researchers reported that plants have various responses like gene expression, physiological manipulation, architectural modification, and production of SMs to tackle the harmful effects of biotic and abiotic stresses (Mareri et al. 2022; Balfagón et al. 2022). The MAPs produce diverse secondary metabolites in low molecular weight such as alkaloids, flavonoids, phenolic compounds, steroids, terpens, and anthocyanins, which are important for adaption, protection, and environment adjustment (Wink 2003). The production of these biochemical compounds is the main way they adapt to their environment (Figure 2) (Verma and Shukla 2015).

Medicinal and aromatic plants are cultivated for roots, leaves, bark, seeds, flowers, and stems, which are rich in secondary metabolites used for medicine, neutraceutical, perfumes, food flavour, soap, or cosmetics. As per the Food and Agriculture Organization (FAO), 60% of the world's population depends on these herbs for wellbeing and beauty (Mahajan et al. 2020), leading to huge exploitation. In addition, the alarming climate change has a dangerous impact on plant morphology and physiology of MAPs, which may cause their extinction. So, it is critical to study the impact of abiotic stressors on MAPs and to draw the attention of research personnel for its sustainable use in the future. This article elaborates on critical secondary metabolites in medicinal and aromatic plants and their synthesis under different abiotic stresses.

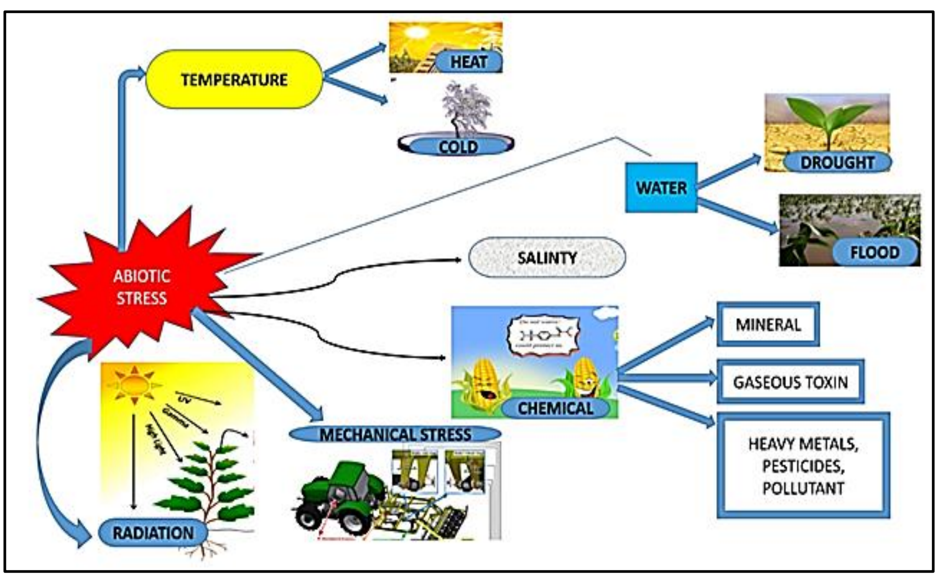

Figure 1 Various abiotic stresses affecting the growth and development of the plant

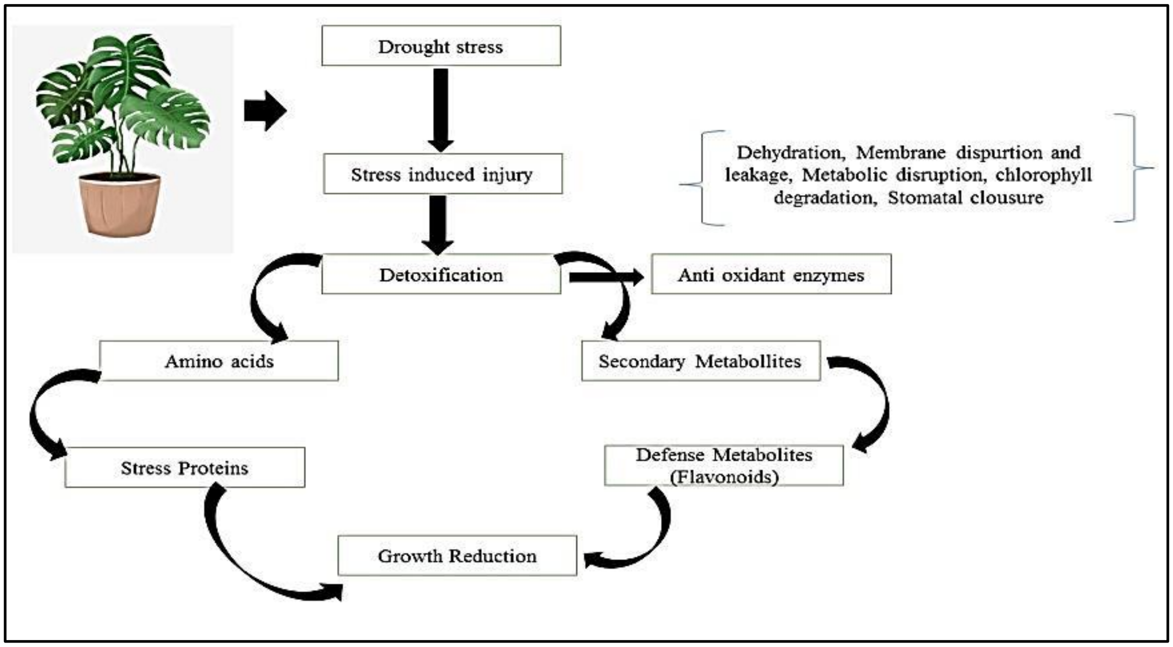

Figure 2 Illustrations of the effect of stress on plants growth and development

2 Secondary Metabolites and their Importance in Plants

Secondary metabolites (SMs) present in plants are among the most extensively studied chemicals due to their significant role in health, food, and beauty. The SMs have a direct correlation with morphological and physiological processes in plants. The plant is stunted under adverse conditions, which can be recovered by secondary metabolites generated in the plant body (Punetha et al. 2022). Several primary metabolites are produced in plants and can be easily extracted and crystallized, while the secondary metabolites are generated in extremely small quantities, and their extraction is complex and energy-intensive. Antibiotics and hormones are examples of secondary metabolites that are crucial for plant survival and growth. Plant secondary metabolites play more than one role in the plant metabolism process (Pagare et al. 2015). These metabolites impart a protection system when plants suffer biotic and abiotic stressors. Phenyl amides are formed, and polyamines are accumulated in beans and tobacco under abiotic stresses, explained the phytochemicals act as antioxidants to protect plants (Edreva et al. 2000). Likewise, accumulation of anthocyanin is observed in plants under the influence of drought, high light intensity, UV, wounds, disease attack, blue light expose, sugar and nutrient deficiencies (Winkel-Shirley 2001). The SMs are also crucial in plant pollination, chemical defense activities, molecule signaling, adaptation, seed dispersal, protection from insects, diseases, herbivores, and allelopathic injury (Pandita and Pandita 2021). The production and concentration of SMs are significantly affected by biotic factors, including insect and disease attacks (Taiz and Zeiger 2006). Plant secondary metabolites can also protect against various organisms, including fungi, bacteria, viruses, nematodes, and insects (Tak and Kumar 2020). Examples of antimicrobial secondary metabolites plants use to defend against invaders include phytoalexins and phytoanticipins.

3 Use of SMs as medicine

In the present-day scenario, a large percentage of the global population still uses traditional medicine practices based on herbal medicines, which rely on the therapeutic qualities of plants (WHO 2013; Hosseinzadeh et al. 2015). Many plant-derived polyphenolic nutraceuticals or pharmaceuticals undergo initial transformations in the intestine via microbiota and enterocyte enzymes before being absorbed at the level of colonocyte and enterocyte. This process confers a broad range of consumer benefits, such as substantial protection against various pathogens, including bacteria and protozoa (Marin-Bruzos and Grayston 2019; Marin et al. 2015). This shows that the intricate relationship between secondary metabolites and human health underscores the continued importance of exploring their multifaceted roles in plant biology and therapeutic applications.

One of the untouched potent natural sources of antibacterial drugs is secondary plant metabolites. However, merely an insignificant fraction (< 1%) of tropical plant species on the planet has been subjected to phytochemical and pharmacological screening (Keita et al. 2022). Several bioactive secondary metabolites and their derivatives are produced by plants which have immense potential to be used as medications for the treatment of many disorders, such as cancer and neurological conditions, bacterial, fungal, and viral infections, and showed encouraging outcomes in the battle against the spread of antibiotic-resistant bacteria (Lahlou 2013). Many of these metabolites have already been released onto the market or are currently being evaluated in clinical trials. Berberine, a natural compound obtained from plants, including *Rhizoma coptidis*, is effective against methicillin-resistant *Staphylococcus aureus* (MRSA) by preventing the formation of biofilms. Additionally, berberine has beneficial synergistic effects when taken with other antibiotics (Zuo et al. 2012; Chu et al. 2016; Zhang et al. 2020). Sulfur-containing allicin has been discovered to have wide antibacterial activity in contrast to gram +ve and -ve bacteria, *Streptococcus* sp., *E. coli*, MRSA, and *Salmonella enterica* (Barbieri et al. 2017). It is a derivative of raw garlic (*Allium sativum*). S-allylmercap to alteration of thiol-containing proteins by allicin reasons a reduction in glutathione levels, the progress of protein aggregation, and the deactivation of critical enzymes in bacteria (Wallock-Richards et al. 2014; Müller et al. 2016; Nakamoto et al. 2020). Piperine is an alkaloid found in the Piper species, such as *Piper longum* and *P. nigrum*, and has strong antimicrobial activity against both Gram+ve (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-ve bacteria (*Escherichia coli* and *Salmonella* sp.). It is an efflux pump inhibitor in Staphylococcus aureus when administered with ciprofloxacin (Hikal 2018). Ajoene, an organo-sulfur compound found in oil-macerated garlic, demonstrates antibacterial activity against various gram +ve and -ve bacteria (Bhatwalkar et al. 2021), and its mechanism of action is like allicin (Han et al. 2011). Eugenol, a hydroxyphenyl propene found in essential oils from the Lauraceae, Lamiaceae, Myristicaceae, and Myrtaceae families, exhibits various modes of action, such as disrupting the cell membrane of *Salmonella typhi*, inhibiting biofilm formation and enterotoxin production in *Streptococci*, and decreasing gene expression related to *S. aureus* contamination (Yadav et al. 2015). Moreover, eugenol hinders the synthesis of bacterial virulence agents like pyocyanin, violacein, and elastase (Marchese et al. 2017; Mak et al. 2019). Several plant species, including bananas, groundnuts, grapevines, pines, beans, pomegranates, and soybeans, contain resveratrol, a naturally occurring polyphenolic antioxidant with antibacterial properties against various Gram-negative and Gram-positive foodborne bacteria (Keita et al. 2022). Resveratrol inhibits toxin production, suppresses gene expression, impedes biofilm formation, interferes with motility, and disrupts quorum sensing in various fungal, bacterial, and viral species (Ma et al. 2018). Continued research into these natural compounds could lead to new treatments for infectious diseases and help address challenges posed by antimicrobial resistance.

4 Influence of Abiotic Stresses on Secondary Metabolites (SMs) Production

The ability of plants to produce and aggregate (i.e., accumulate) phytochemicals is profoundly influenced by abiotic stresses such as temperature, soil, light intensity, and humidity (Radušienė et al. 2012). In addition, the production of plant secondary metabolites (SMs) can be influenced by minerals, radiation, heavy metals, and gaseous toxins (Akula and Ravishankar 2011). In order to adapt to varying environmental conditions, plants require acclimatization and adaptation, which leads to molecular, biochemical, physiological, and morphological responses. These responses may alter plant metabolic activity to decrease or repair damage caused by stress. This mechanism aims to safeguard the species' continual survival against certain growth conditions (Kapoor et al. 2020). In response to adverse environmental conditions, plants commonly produce reactive oxygen species (ROS), which are the final products of all stresses, such as superoxide (O_2^-), hydroxyl radical (OH^-), and hydrogen peroxide (H_2O_2) (Sharma et al. 2021). These can lead to cell damage by initiating an oxidative chain reaction called oxidative stress. As a countermeasure, plants employ secondary metabolism and other enzymatic and non-enzymatic processes to produce and store defensive chemicals. In nature, the intricate strategies employed by plants in response to environmental stresses highlight their remarkable capacity to adapt and survive through the synthesis and accumulation of protective phytochemicals.

Plants have limited mobility and a weak defense system, so they either change their orientation by moving or producing chemicals to defend themselves against environmental stress. When plants are under various environmental stresses, they typically produce and use more enzymes that help protect themselves, synthesizing secondary metabolite compounds. Chalcone synthase (CHS) and phenylalanine ammonia-lyase (PAL) are the enzymes that are essential in the synthesis of flavonoids. PAL (EC 4.1.3.5) plays a pivotal function in the defensive mechanisms of plants by producing phenol and lignin, while CHS (EC 2.3.1.74) is primarily responsible for the synthesis of flavonoids (Blanco-Ulate et al. 2015) (Figure 3).

Polyphenolic compounds, including flavonoids, proanthocyanidins, phenolic acids, and anthocyanins, can effectively reduce the harmful effects of salinity (Hichem and Mounir, 2009). This is because phenolic compounds possess antioxidant properties and function as ROS hunters. The production of these compounds typically occurs in response to biotic or abiotic stresses (D'Souza and Devaraj 2010). The synthesis and deposition of secondary metabolites are controlled by specific genes activated during the transcription stage. Certain transcription factors regulate the production and accumulation of these metabolites, with the total quantity depending on the expression of these genes. This process can produce numerous secondary metabolites through bioregulators and elicitors (Verma and Shukla 2015). This understanding enhances our knowledge of plant adaptation strategies and holds promise for applications in biotechnology and agriculture through controlled metabolite production (Table 1).

Table 1 Compilation of certain secondary metabolites and their respective roles

TERPENES		
Quinone	Helps in oxidation-reduction reaction	Yang et al. 2022
Pyrethroids	Highly toxic to insects	Meijar et al. 2024
β- pinene, α-pinene, limonene and myrcene	Toxic to numerous insects and serious pests of conifers	Nikolić et al. 2024
Gossypol	Repellent to herbivores in cotton	Xie et al. 2024
Abscisic acid	A PGR, Stomatal closure, dormancy, abscission	Kumar et al. 2024
Abietic acid	Powerful new anticancer drug	Ahmad et al. 2024
Gibberellins	One of the major groups of phytohormones, role in seed germination	Hussain et al. 2024
Phorbol	Toxic to herbivorous mammal	Medina-Rodelo et al. 2024
Sterols	Components of cell membrane; Retard the permeability of small molecules by retarding the motion of fatty-acid chain	Samanta et al. 2024
Limonoids	Anti-herbivore compounds	Rzyska et al. 2024
Azadirachtin	Highly toxic to insects	Sarkar et al. 2024
Cardenolites	Used in the treatment of heart diseases	Akanmu et al. 2021
Saponins	Act as fungicide	Morcia et al. 2022
Yamogenin	Used in making birth control pills	Vishwakarma et al. 2022
Carotene and xanthophylls	Significant role in light-harvesting and shielding chlorophyll molecules against photo-oxidation	Sachdev et al. 2021
Rubber	It is a polyterpene from the latex of *Hevea brasiliensis*	Tran et al. 2023
PHENOLIC COMPOUNDS		
Protocatechuic acid and catechol	Protect onion bulbs against Smudge disease	Nag et al. 2024
Coumarins	Inhibit the growth of micro-organisms; with scopoletin are inhibitors of seed germination and cell elongation; stimulate the IAA oxidase	Wang et al. 2023
Lignin	Most abundant organic substance in plants, distributed in cell walls, tracheid, and vessels elements of the xylem, provides tensile strength and cementing of cell walls	Ghorbani et al. 2024
Anthocyanin	Get dissolved in the cell sap of epidermal cells and impart a bright color to flowers	Yoshida 2024
Quercetin	Bright yellow color of lemon juice	Tahosin et al. 2024
Flavonoids (flavones and flavanols)	Distributed in epidermal cells of green leaves and stems, they serve as UV-absorbing pigments, i.e., harmful to cells; legumes and nitrogen-fixing symbionts interact through substances excreted into the soil by legume roots	Guo et al. 2024
Tannins	A second large category of plant phenolics and astringent in taste, distributed in the cell sap, cell walls, barks, and leaves, accumulate in dead tissues; rich in unripe fruits; protect the plant against desiccation, decay, and injury by animals and microbes attack	Hameed et al. 2020
ALKALOIDS		
Anabasine	Synthesized in shoot of *Nicotiana glauca*	Zenkner et al. 2019
Ricine	Found in castor seeds	Yadav et al. 2022
Cocaine- atropine	Natural cocaine	Zamarripa et al. 2024
Reserpine	Collected from *Rauwolfia serpentine* and used for curing hypertension	Bankar et al. 2024
Strychnine	Obtained from *Strychnousnux-vomica;* used as a poison for rats	Sadhunavar et al. 2015
Cinchonine and quinine	Extracted from the bark of Cinchona and used as a drug against malaria	Parveen et al. 2024
Colchicines	Inhibit the formation of spindle fiber formation during cell division; used in polyploidy formation	Ramirez-Castillo et al. 2024
Glycosinolates	Characteristic smell and taste of the members of the family Brassicaceae;	Raffo et al. 2024
Porphyrins	Constituent of chlorophyll and phytochrome	Ko et al. 2024

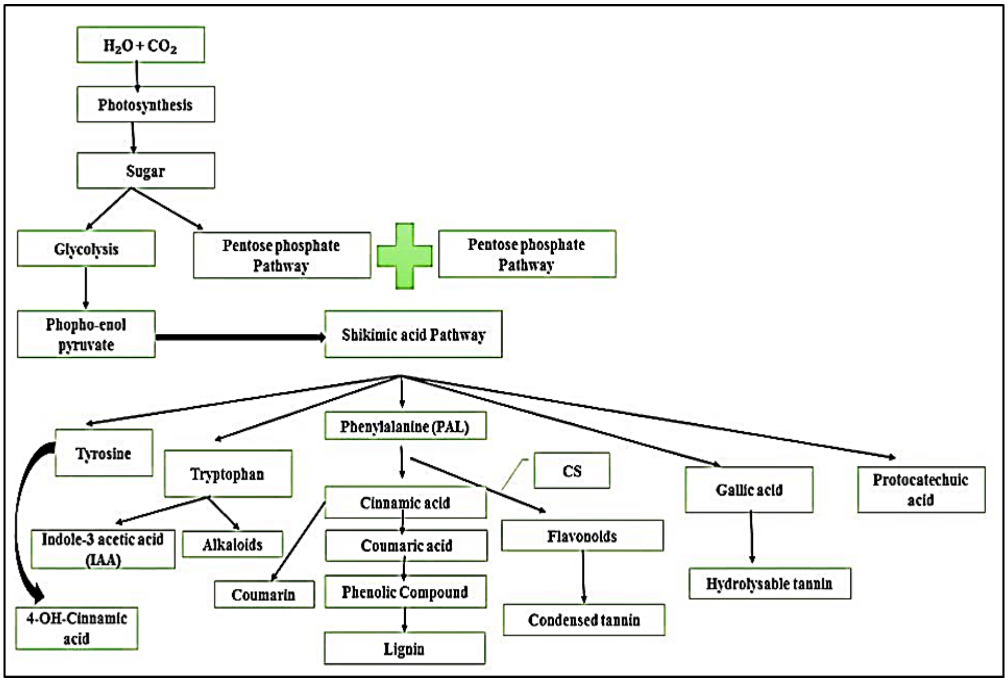

Figure 3 The concept of the Shikimic acid pathway

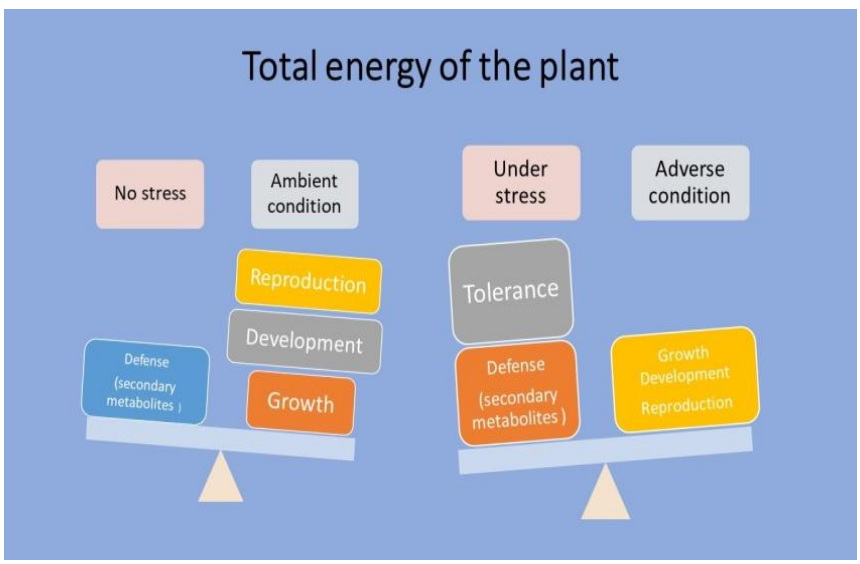

Figure 4 Secondary metabolites and the source sink balance hypothesis

4.1 CO_2 concentration and its influence on SMs

The concentration of CO_2 in the air has a substantial influence on how plants utilize energy and develop. The equilibrium of carbon and nutrients, especially nitrogen, influences multiple growth, development, and differentiation processes. The alterations influence the relationship between the source-sink systems in the proportion of carbon allocated to growth, carbon-based secondary or structural components, and total non-structural carbohydrates (Figure 4). In the current climate change scenario, greenhouse gases, mainly CO_2, are rising sharply. Consequently, the C:N ratio is inappropriate, harming growth over time. Depiction of Figure 4 revealed that the allocation of resources between sources and sinks is influenced by the rise in CO_2 levels and the limited availability of nitrogen. Further, CO_2 influences source strength more than sink strength, while nutrient stress affects sink strength more. However, both are anticipated to boost the quantity of carbon-based secondary products in plant tissue. Some studies suggest that CO_2 can directly or indirectly influence *Taxus bacatta*, *H. perforatum*, and *Echinacea purpurea* to produce more secondary metabolites

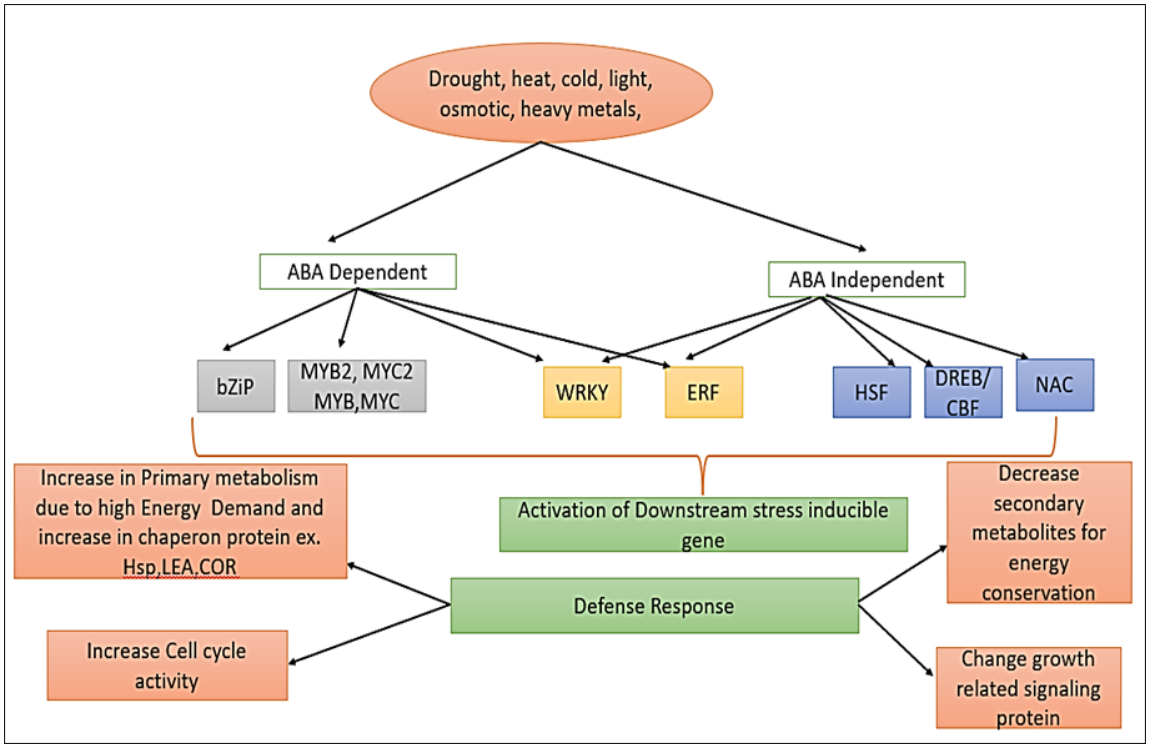

Figure 5 Effect of drought, heat, cold, light, osmotic, and heavy metal stress on secondary metabolite production

like phenols, flavonoids, lignins, nicotine, and coumarins (Savé et al. 2007). Further, Ibrahim et al. (2017) reported that elevated CO_2 levels increase phenol and flavonoid content in *Labisia pumila* plants. Similarly, lignins, nicotine, coumarins, and phenylpropanoids accumulate in tobacco plants after elevated CO_2 treatment (Li et al. 2018; Matros et al. 2006). Rising atmospheric CO_2 levels significantly influence how plants utilize energy and develop, impacting their carbon and nutrient balance. These changes highlight the intricate relationship between environmental shifts and plant biochemistry, with implications for ecological systems and agriculture.

4.2 Impacts of Drought on SM Production

Plant morphology is directly affected by soil water content. A rain or soil water deficiency leads to drought stress, which decreases the plant's water potential and leaf turgidity. This, in turn, triggers or adjusts various biochemical and morpho-physiological components and wide-ranging genetic feedback based on the cultivar or species (Zhou et al. 2017). In order to survive, water-limited vegetation may postpone glucose accumulation and use carbon for secondary metabolism (Herms and Mattson 1992). Furthermore, drought increases the levels of isoprinoid abscisic acid in the leaf apoplastic area (Liu et al. 2005). Studies have shown that abscisic acid (ABA) treatment induces *Orthosiphon stamineus* to produce reactive oxygen species and secondary metabolites as a defence mechanism (Khan et al. 2011). Plants generally produce bioactive chemicals such as phenolic compounds in response to water scarcity (Khan et al., 2011). Sampaio et al. (2016) found that water deprivation decreases the photosynthesis rate and increases ROS production and accumulation, resulting in increased phenolic compound production as a plant defence mechanism (Figure 5). Under mild water stress, *Labisia pumila* has more total flavonoids, anthocyanins, and phenolics than under severe stress (Jaafar et al. 2012). *Pisum sativum* cv. *meteor* under water deficit stress had higher anthocyanin and flavonoid content than well-watered controls (Nogués et al. 1998). Jaleel et al. (2007) observed that drought-induced oxidative stress enhanced the total alkaloid content in both the shoot and root of *Catharanthus roseus*. Further, drought stress also raised glycine betaine content in the *C. roseus* plant.

4.3 Impacts of Salinity Stress on SMs Production

Salt stress causes plant ionic and osmotic stressors, which increase or reduce secondary metabolites. Antioxidant secondary metabolites help plants balance their oxidative state. Salt stress causes many metabolic changes in plants. Plants produce more suitable osmolytes (neutral, soluble organic compounds) to deal with salt stress (Nelson et al. 1998). Salinity stress raises sodium levels and causes cytoplasmic potassium imbalances. It creates ROS and inactivates and unsaturates numerous enzymes (Luo et al. 2005). Further, salt stress also increases proline aggregation

Table 2 Secondary Metabolite Production in Response to Salinity Stress in a Range of Species

S. N.	Plant species	Compounds	References
1.	*M. chamomilla*	Increase in phenolic acids, including chlorogenic, caffeic, and protocatechuic acid	Said-Al Ahl and Omer (2011); Abd El-Azim and Ahmed (2009)
2.	*Nigella sativa*	Increase in Phenols	Bourgou et al. (2008)
3.	*Mentha pulegium*	Increase in Phenols	Oueslati et al. (2010)
4.	*Matricaria reutita* *Satureja hartensis* *Salvia officinalis*	Increase in essential oil	Said-Al Ahl and Omer (2011)
5.	*Thymus maroccanus* *Origanum vulgare* *Mentha piperita* *Majorana hartensis* *Salvia officinalis* *M. chamomilla*	Decrease in essential oil	Said-Al Ahl and Omer (2011)
6.	*Plantago ovata*	Increase in proline, flavonoids, and saponins	Haghighi et al. (2012)

(Cardoso et al. 2019). Similarly, Akula and Ravishankar (2011) also suggested that salt stress can increase or reduce plant secondary metabolite levels through osmotic and ionic stress. Adaptation to stress involves alteration in proline metabolism. Proline dehydrogenase and 1-pyrroline-5-carboxylate dehydrogenase catalyze two dehydrogenation processes in proline catabolism. Mitochondrial matrix NAD+-dependent dehydrogenase raises NAD+ PAL and converts this into polyphenols and antioxidants. Benjamin et al. (2019) found that NaCl increases flavonoids and other phenolic compounds in *S. brachiate* but decreases them in *S. portulacastrum*, which accumulates carotenoids, fighting ROS and aiding photosynthesis. Usually, shoots have more ricinine alkaloid content than roots and underground stems. Said-Al Ahl and Omer (2011) found that salt stress increases *Rouvolfia tetraphylla* reserpine and *Catharanthus roseus* shoot vincristine alkaloids. Numerous investigations are supported by current reviews and outlined in Table 2. Salt stress significantly impacts plant metabolism and secondary metabolite production through ionic and osmotic stress mechanisms. However, there remains a research gap in understanding the specific regulatory pathways and genetic mechanisms governing the differential responses of plants to salt stress, particularly to secondary metabolite synthesis under varying environmental conditions.

4.4 Impact of Temperature on SMs Production

Global warming and disruptive seasonal events may reduce secondary metabolite production in medicinal and aromatic plants (MAPs), affecting livelihoods and biodiversity. Timely interventions are needed to avert biodiversity loss (Das et al. 2016). Low and high temperatures alter plant cell proteins, enzymes, and lipids, affecting membrane integrity. Thakur et al. (2019) suggested low and high temperatures affect plant secondary metabolite synthesis. Human activity has raised the average global temperature by 0.74°C, and the temperature is anticipated to increase by 0.2°C each decade. As a supplementary defence against high temperatures, plants manufacture SMs (Isah 2019). Wahid and Close (2007) state that ROS from temperature stress harms plant cells.

Plants produce flavonoids and phenylpropanoids to deal with high temperatures. Table 3 illustrates the effects of elevated and reduced temperature stresses on producing various secondary metabolites in plants. Global warming and seasonal disruptions threaten secondary metabolite production in medicinal and aromatic plants (MAPs), impacting biodiversity and livelihoods. Extreme temperature alters plant cellular processes and membrane integrity, affecting secondary metabolite synthesis. As temperatures rise, plants increasingly rely on secondary metabolites like flavonoids and phenylpropanoids as a defence. However, further research is needed to fully understand and mitigate the effects of climate change on these vital plant compounds. Global warming and seasonal disruptions threaten secondary metabolite production in medicinal and aromatic plants (MAPs), impacting biodiversity and livelihoods. Extremes temperature may also alter plant cellular processes and membrane integrity, affecting secondary metabolite synthesis. As temperatures rise, plants increasingly rely on secondary metabolites like flavonoids and phenylpropanoids as a defence. However, further research is needed to fully understand and mitigate the effects of climate change on these vital plant compounds.

4.5 Effect of Light Irradiation on SMs Production

Growth and metabolism in plants are significantly impacted by solar radiation. Research has shown that fluctuations in solar radiation levels can cause plants to produce and accumulate secondary metabolites to adapt to their environment (Yang et al. 2018). The length of the light period is one of the critical factors

Table 3 Secondary Metabolite Production in Response to Temperature Stress in a Range of Species

S. N.	Temperature	Plant species	Compounds	References
1	Low	*Melastoma malabathricum*	Anthocyanin	Chan et al. (2010)
2	Low	*Rhodiola crenulata*	Melatonin	Zhao et al. (2011)
3	High	*Ribes nigrum*	Delphinidin-3-O- glucoside, Delphinidin-3-O-rutiniside, Myricetin-3-O-glucoside	Zheng et al. (2012)
4	Low	*Glycine max*	Genistein, Diazein, Genistin	Janas et al. (2002)
5	High	*C. accuminata*	10- hydroxycampothecin	Zu et al. (2003)
6	High	*Lupinus angustifolius*	Alkaloids	Jansen et al. (2009)
7	High	*C. roseus*	Vindoline, Catharanthine, Vinblastine	Guo et al. (2007)
8	High	*Picea abies*	Piperidine	Virjamo et al.(2014)
9	High	*Betula pendula* *Populus tremula*	Terpenoid	Ibrahim et al.(2010)

associated with irradiation that can impact the levels of secondary metabolites in plants. Studies have demonstrated that longer photoperiods can increase the levels of secondary metabolites, which can help plants resist the effects of light exposure. Conversely, shorter day-length conditions have been shown to reduce coumarin content in stems and leaves, while longer day-length periods have significantly increased coumarin content (de-Castro et al. 2007).

Light quality is a critical factor that significantly impacts the levels of secondary metabolites in plants. The escalation of ultraviolet radiation has been attributed to the diminution of the ozone layer, which had a detrimental effect on living organisms. Consequently, plant cells produce reactive oxygen species and accelerate the production of secondary metabolites that can absorb UV radiation (dos Santos Nascimento et al. 2015). Furthermore, it promotes antioxidant activity to minimize and correct oxidative harm (Takshak and Agrawal 2014). Park et al. (2007) demonstrated that the biosynthesis of anthocyanins is enhanced by the increased expression of genes responsible for producing proteins and enzymes, including dihydroflavonol reductase (DFR), flavanone 3-hydroxylase (F3H) and chalcone synthase. UV-B radiation leads to heightened activity of enzymes like cinnamyl alcohol dehydrogenase, phenylalanine ammonia-lyase (PAL), chalcone-flavanone isomerase, dihydroflavonol reductase (DFR), and 4-coumarate CoA ligase, along with increased levels of flavonoids, anthocyanins, and tannins in *Withania somnifera* (Takshak and Agrawal 2014). According to Ma et al. (2016), the effects of UV-B radiation on the phytochemical constituents of *Chrysanthemum* flowers, specifically chlorogenic acid and flavonoids, were investigated. These phytochemicals are the primary components that impart the healing properties of the flowers.

Solar radiation significantly influences plant metabolism and secondary metabolite production. Fluctuations in radiation levels prompt plants to adjust secondary metabolite synthesis, with longer photoperiods enhancing their production. Additionally, UV radiation induces reactive oxygen species in plants, stimulating the biosynthesis of protective secondary metabolites like flavonoids and anthocyanins. Heavy metals such as chromium and cadmium disrupt plant metabolism, triggering oxidative stress and altering secondary metabolite profiles. Understanding these environmental impacts is crucial for optimizing plant-based bioactive compound production.

4.6 Effect of Heavy Metal on SMs Production

The term "heavy metal" describes metallic elements with a high-density level that can inflict harm even at low concentrations. Heavy metals, including chromium, cadmium, iron, zinc, and manganese, can potentially elevate ROS generation, causing an imbalance between ROS generation and detoxification. These metals can have a detrimental impact on plants by either directly binding to proteins, owing to their affinities for histidyl-, thioyl-, and carboxyl-groups that mark catalytic, structural, or transport locations in cells or eliciting the production of reactive oxygen species, potentially leading to oxidative stress (Table 4) (Kaczor-Kamińska et al. 2020). In addition, the presence of heavy metals can affect plants by displacing essential cations from specific binding sites (Sharma and Dietz 2009). Kovacik and Klejdus (2008) found that varying copper doses, like 120 and 60 µM, significantly boosted PAL activity, increasing lignin content and phenolic compound the day after treatment. This result reflects the response of the defence mechanism to metal entry. Reports are also available that higher artemisinin levels in *A. annua* were achieved by the application of arsenic-induced stress through two methods: converting dihydroartemisinic acid (monocarboxylic acid) to artemisinin via ROS breakage and promoting genes involved in artemisinin production (Rai et al. 2011a; Khare et al. 2020).

Table 4 Impact of heavy metal stress on the production of secondary metabolites by different species

S. N.	Heavy metal	Plant species	Compounds	References
1	$AgNO_3$	*Perovskia abrotanoides*	Tanshinone	Zaker et al. (2015)
2	Ag	*Salvia castanea*	Tanshinone	Li et al. (2016)
3	$AgNO_3$	*Datura metel*	Atropine	Shakeran et al. (2015)
4	Cd, Co, Ag	*Vitis vinifera*	Resveratrol	Cai et al. (2013)
5	Cu	*Bacopa monnieri*	Bacoside	Sharma et al. (2015)
6	Pb	*Mentha crispa*	Carvone	Sá et al. (2015)
7	Cu and Zn	*Mentha pulegium*	Pulegone Cineol Thymol	Lajayer et al. (2017)
8	Cd and Co	*Trigonella rogusum*	Diosgenin	De and De (2011)
9	Cr, Cd, Pb and Ni	*Ocimum basilicum*	Chavicol Cinalol	Prasad et al. (2011)
10	As	*Artemisia annua*	Artemisinin	Rai et al. (2011b)

The research gap lies in understanding the precise mechanisms by which different heavy metals individually and collectively influence secondary metabolite production in plants. Current studies often focus on specific metals like copper and arsenic, but comprehensive comparative analyses are limited across a broader spectrum of heavy metals. Additionally, there is a need to explore how varying concentrations and combinations of heavy metals affect different plant species' secondary metabolite profiles under realistic environmental conditions. This knowledge is crucial for developing strategies to mitigate heavy metal-induced stress and sustainably optimize plant-based bioactive compound production.

Conclusion

Plant cells are recognized as a significant source of biochemical compounds, encompassing primary metabolites like sugars, fatty acids, and amino acids alongside a diverse array of secondary metabolites, including alkaloids, terpenoids, phenols, and sulfur-containing complexes. These secondary metabolites serve various functions, such as providing defence protection or engaging in offensive/invasive tactics in response to environmental factors, including microbes, insect pests, herbivorous predators, and insects. Various environmental factors, including sunlight, temperature, soil fertility, soil water, and acidity/salinity largely impact the generation and accumulation of secondary metabolites in plants. To cope with these conditions, plants adjust their metabolism towards producing numerous secondary metabolites. During environmental challenges, the orientation of secondary metabolism in plants involves complex signal transduction pathways. The current review presents comprehensive and reliable reasons for the variation in the composition of secondary metabolites in different ecological circumstances. Acquiring knowledge about secondary metabolism and its instability in plants may benefit both agriculturalists and geneticists. As advancements in modern techniques continue to emerge, the significance of secondary metabolism in plant adaptation cannot be overstated. Furthermore, conducting extensive research into the physiological, molecular, and biochemical responses of plants and the primary genetic mechanisms involved can provide valuable insights and enhance adaptation to various environmental influences. By doing so, scientists may be able to strategically apply stress factors to increase the production of various secondary metabolites, ultimately benefiting humanity.

However, gaps remain in understanding the intricate signal transduction pathways and regulatory networks that govern secondary metabolism in response to diverse environmental challenges. Future research should unravel these complexities across various plant species and environmental conditions. Advancements in modern techniques, including omics technologies and gene editing tools, offer promising avenues to deepen our understanding of secondary metabolism. This knowledge could potentially enable agriculturalists and geneticists to manipulate plant metabolism strategically. By harnessing stress factors or enhancing genetic pathways, scientists may enhance the production of valuable secondary metabolites for medicinal, agricultural, and industrial applications, benefiting human health and sustainable agriculture practices.

Conflict of interest

The authors declare no conflicts of interest

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