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Environmental Challenges and Medicinal Plants

Sustainable Production Solutions under Adverse Conditions

Springer

Environmental Challenges and Solutions

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Tariq Aftab
Editor

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Sustainable Production Solutions under Adverse Conditions

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This book is dedicated to

Sir Syed Ahmad Khan
(October 17, 1817–March 27, 1898)

Sir Syed Ahmad Khan, one of the architects of modern India, was born on October 17, 1817, in Delhi and started his career as a civil servant.
The 1857 revolt was one of the turning points in Syed Ahmed's life. He clearly foresaw the imperative need for the Muslims to acquire proficiency in the English language and modern sciences, if the community were to maintain its social and political clout, particularly in Northern India.

He was one of those early pioneers who recognized the critical role of education in the empowerment of the poor and backward Muslim community. In more than one way, Sir Syed was one of the greatest social reformers and a great national builder of modern India. He began to prepare the road map for the formation of a Muslim University by starting various schools. He instituted Scientific Society in 1863 to instil a scientific temperament into the Muslims and to make the Western knowledge available to Indians in their own language.

The Aligarh Institute Gazette, an organ of the Scientific Society, was launched in March 1866 and succeeded in agitating the minds in the traditional Muslim society. Anyone with a poor level of commitment would have backed off in the face of strong opposition but Sir Syed responded by bringing out another journal, Tehzibul Akhlaq which was rightly named in English as "Mohammedan Social Reformer."

In 1875, Sir Syed founded the Madarsatul Uloom in Aligarh and patterned the MAO College after Oxford and Cambridge universities that he went on a trip to London. His objective was to build a college in line with the British education system but without compromising its Islamic values. He wanted this College to act as a bridge between the old and the new, the East and the West. While he fully appreciated the need and urgency of imparting instruction based on Western learning, he was not oblivious to the value of oriental learning and wanted to preserve and transmit to posterity the rich legacy of the past. Dr. Sir Mohammad Iqbal observes:

"The real greatness of Sir Syed consists in the fact that he was the first Indian Muslim who felt the need of a fresh orientation of Islam and worked for it—his sensitive nature was the first to react to modern age."

The aim of Sir Syed was not merely restricted to establishing a college at Aligarh but at spreading a network of Muslim Managed educational institutions throughout the length and breadth of the country keeping in view this end, he instituted All India Muslim Educational Conference that revived the spirit of Muslims at national level. The Aligarh Movement motivated the Muslims to help open a number of educational institutions. It was the first of its kind of such Muslim NGO in India, which awakened the Muslims from their deep slumber and infused social and political sensibility into them.

Sir Syed contributed many essential elements to the development of the modern society of the subcontinent. During Sir Syed's own lifetime, The Englishman, a renowned British magazine of the nineteenth century, remarked in a commentary on November 17, 1885: 'Sir Syed's life "strikingly illustrated one of the best phases of modern history." He died on March 27, 1898, and lies buried next to the main mosque at Aligarh Muslim University.

Preface

Plants have evolved an incredible arrangement of metabolic pathways leading to molecules/compounds capable of responding promptly and effectively to challenging situations imposed by biotic and abiotic factors. Medicinal plants supply the ever-growing needs of humankind for natural chemicals, such as pharmaceuticals, nutraceuticals, agrochemicals, and chemical additives. Medicinal plants are used in traditional medicine to cure various ailments, and several studies have highlighted the therapeutic properties and biological activities of medicinal plants. These plants contain bioactive secondary metabolites which possess antimalarial, anthelminthic, anti-inflammatory, analgesic, antimicrobial, antiarthritic, antioxidant, antidiabetic, antihypertensive, anticancer, antifungal, antispasmodic, cardioprotective, antithyroid, and antihistaminic properties. Secondary metabolites play a major role in the adaptation of plants to the changing environment and stress conditions as they are affected by both biotic and abiotic stress.

Humans rely on medicinal plants for various needs since ancient times, and their population still seems enough for fulfilling our demands. But in the foreseeable future we will be forced to think about the accessibility of resources for the generations to come. For these reasons, we must look for alternative sustainable options of resources which can protect these immensely important medicinal plants from various stresses induced by the challenging environment. Moreover, we need to understand current advancements of molecular mechanisms of cross talk in relation to plant abiotic stress in order to create climate resilient medicinal plants which can survive under stress combinations. Evolving eco-friendly methodologies and mechanisms to improve these plants' responses to unfavorable environmental circumstances is important in creating significant tools for a better understanding of plant adaptations to various abiotic stresses and sustaining the supply of pharmaceuticals as global climate change intensifies.

One of the great challenges in the near future will be the sustainable production of medicinal plants in growing climate changes. A combination of adverse demographic factors and climatological perturbations is expected to impact food and pharmaceutical production globally. Despite the induction of several tolerance mechanisms, medicinal plants often fail to survive under environmental extremes.

To ensure their sustainable production under adverse conditions, multidisciplinary approaches are needed, and useful leads are likely to emerge. However, improving plants' performance under restrictive growth conditions requires a deep understanding of the molecular processes that underlie their extraordinary physiological plasticity. Therefore, this book aims to review and analyze the studies that investigate impacts of environmental challenges on medicinal plants and the possibilities for increased sustainable production. This book reviews the emerging importance of medicinal plants and how their production and sustainability is affected by environmental factors and provides eco-friendly solutions for the production of medicinal plants under challenging environmental conditions.

This comprehensive volume emphasizes the recent updates about the current research on the medicinal plants covering different aspects related to challenges and opportunities in the concerned field. This book is an attempt to bring together global researchers who have been engaged in the area of stress signaling, cross talk, and mechanisms of medicinal plants. The book will provide a direction toward the implementation of programs and practices that will enable sustainable production of medicinal plants, resilient to challenging environmental conditions. I believe that this book will instigate and commence readers to state-of-the-art developments and trends in this field. Moreover, I hope to have disseminated the chapters of this book in a way that will be novel for the readers and can be readily adopted as references for newer and further research.

I am highly grateful to all our contributors for accepting our invitation for not only sharing their knowledge and research but for venerably integrating their expertise in dispersed information from diverse fields in composing the chapters and enduring editorial suggestions to finally produce this venture. I also thank the Springer Nature team for their generous cooperation at every stage of the book production.

Lastly, thanks are also due to well-wishers, research students, and editor's family members for their moral support, blessings, and inspiration in the compilation of this book.

Aligarh, India Tariq Aftab

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About the Editor

Tariq Aftab received his Ph.D. in the Department of Botany at Aligarh Muslim University, India, and is currently Assistant Professor there. He is the recipient of a prestigious Leibniz-DAAD fellowship from Germany, Raman Fellowship from the Government of India, and Young Scientist Awards from the State Government of Uttar Pradesh (India) and Government of India. After completing his doctorate, he has worked as Research Fellow at the National Bureau of Plant Genetic Resources, New Delhi, and as Postdoctorate Fellow at Jamia Hamdard, New Delhi, India. Dr. Aftab also worked as Visiting Scientist at Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany, and in the Department of Plant Biology, Michigan State University, USA. He is a member of various scientific associations from India and abroad.

He has edited 12 books with international publishers, including Elsevier Inc., Springer Nature, and CRC Press (Taylor & Francis Group), coauthored several book chapters, and published over 70 research papers in peer-reviewed international journals. His research interests include physiological, proteomic, and molecular studies on medicinal and crop plants.

Chapter 1
Current Status of Medicinal Plants in Perspective of Environmental Challenges and Global Climate Changes

Mohammad Javad Ahmadi-Lahijani and Saeed Moori

Abstract The elevation in [CO_2] since the industrialization era has become a severe problem in plant physiology and human life. The level of CO_2 emission has drastically increased during the past 40 years mainly due to anthropogenic activities, which created a significant environmental challenge for plants. The expected behavior of plants is influenced by the climatic changing factors, which finally impact the morphophysiological traits and secondary metabolites (SMs) of pharmaceuticals. Medicinal plant SMs have been utilized to discover new drugs in the alleviation of many diseases over the past two decades. Medicinal plants possibly are able to adapt to their changing environment; hence, metabolic elasticity may impact metabolite production, which is the basis for their medicinal values. Primary metabolites such as the SMs are also impacted by climatic change. Medicinal plant growth, biomass production, and SMs are influenced by climatic fluctuations, e.g., temperature and [CO_2], due to alterations in the metabolic pathways, which regulate plant signaling, physiology, biochemistry, and defense mechanisms. The population of plant species including medicinal plants may be threatened by the elevated [CO_2], extreme temperatures, changing precipitation regimes, increases in pests and pathogens, and anthropogenic habitat fragmentation. Nevertheless, the potential effects of the abrupt climate change on medicinal plants have not been elucidated in-depth yet. The current status of medicinal plants under climate change, emphasizing its consequences, i.e., elevated [CO_2], drought, and extreme temperatures, is discussed in this chapter.

Keywords Biomass · Cold stress · Drought · Elevated [CO_2] · Global warming · Heat stress · Secondary metabolites

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1.1 Introduction

Medicinal and aromatic plant usage have dramatically been increased in recent years (Mishra 2016; Anand et al. 2019). The demand for medicinal plants has been increasing worldwide as the natural products have fewer or perhaps no side effects, and their accessibility and affordable costs might impact their demand for cultivation. Medicinal and aromatic plants are cultivated for their essential oils and cut flower marketing. Pharmacy, cosmetology, perfumes, and the food industry utilize their products. There are about half a million medicinal plant species worldwide with a promising future since most of their pharmaceutical effects have not been discovered yet and would be in demand of future studies.

Medicinal plants, particularly endemic medicinal plants, are precious for human life (Dewick 2002). According to the World Health Organization (WHO), approximately 21,000 plant species are being used for medicinal purposes (WHO 2013). Around 80% of the developing countries' population and 60% of the world's population depend on traditional medicines derived from plants (WHO 2013). However, the worldwide anthropogenic climate changes have adversely influenced medicinal plants. Further increases in the temperature from 1.4 to 5.8 °C are expected by 2100. There would be extreme and unpredictable weather incidents by 2033, for instance, warmer summers, stronger and more frequent storms, high winds, and more frequent and heavier rainfall (Cleland et al. 2012; Field et al. 2014).

Climate change has various adverse effects to not only melting polar ices but also changing in seasons and overall weather scenario, new plant disease occurrence, and frequent occurrence of floods. Climate change adversely affects every day human life, agriculture, forestry, biodiversity, and whole ecosystem functions (Lepetz et al. 2009). The increasing global human population, rapid industrialization, and vast amounts of chemical fertilizers and pesticide utilization in the agricultural section are some important factors causing climate change. Carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), sulfur dioxide (SO_2), nitrogen oxides (NO_x), and secondary pollutants like ozone (O_3) are among the greenhouse gases leading to the global warming. Simultaneously with the warming up of the climate, other climatic and environmental factors, i.e., the temperatures, [CO_2], drought, and rainfall patterns, are also changing. Figure 1.1 summarizes some of the major consequences of climate change.

Plant species are threatening by climate change. The endemic plant species are considered more vulnerable to climate change and facing a high risk of extinction as their narrow edaphic niches limit their possibilities to adapt through migration (Panchen et al. 2012). As for other species, medicinal species are also threatened by changing temperature and precipitation regimes, disruption of commensal relationships, pest and pathogen increases, and anthropogenic habitat fragmentation. Additionally, medicinal species are often harvested unsustainably, and the combination of those pressures may push many plant species to extinction. Besides, some species may respond to environmental stresses not only through a decline in biomass

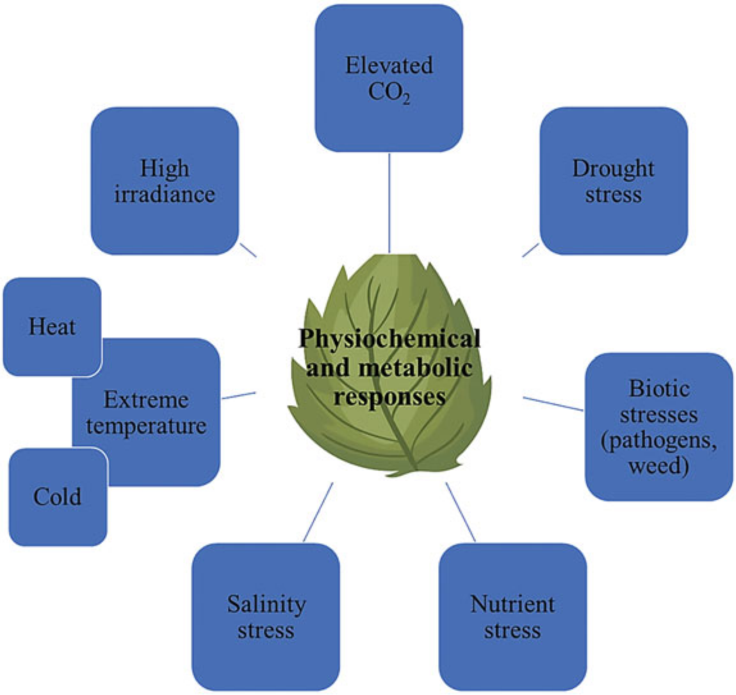

Fig. 1.1 Potential environmental stressors affecting the plant physiochemical and metabolic traits under climate change

production but also with changes in biochemical content and composition, potentially affecting the quality or even safety of medicinal products.

It is important to study the climate change effects on medicinal plants due to their dual use as medicine and food. High temperatures have been reported to reducing the oil content and unsaturated fatty acids of some oil-bearing crops, leading to declining their nutritional quality and ability to ameliorate chronic diseases (Canvin 1965; Mozaffarian et al. 2010; Dawczynski et al. 2015). Climatic changes are expected to make plant species more sensitive to pests and pathogens such as mycotoxin-producing fungi leading to reducing their quality and long-term food security (Chakraborty and Newton 2011; Magan et al. 2011; Bebber et al. 2013; Van der Fels-Klerx et al. 2016). Undoubtedly, anthropologically environmental changes will affect medicinal plants like other plant species, especially in higher altitude ecosystems, where endemic medicinal plants mainly grow (Applequist et al. 2020). Nevertheless, studies to evaluate the effects of climate change and its consequences, i.e., elevated [CO_2], higher or lower temperatures, and water stress, on medicinal plants and their physiology, biochemistry, and SMs need to be conducted in-depth. Limited and sporadic perceptions on the impacts of climate change and global warming on plant growth and development, physiology, biochemistry, and primary and secondary metabolites exist. In the present chapter, the impacts of changing climatic

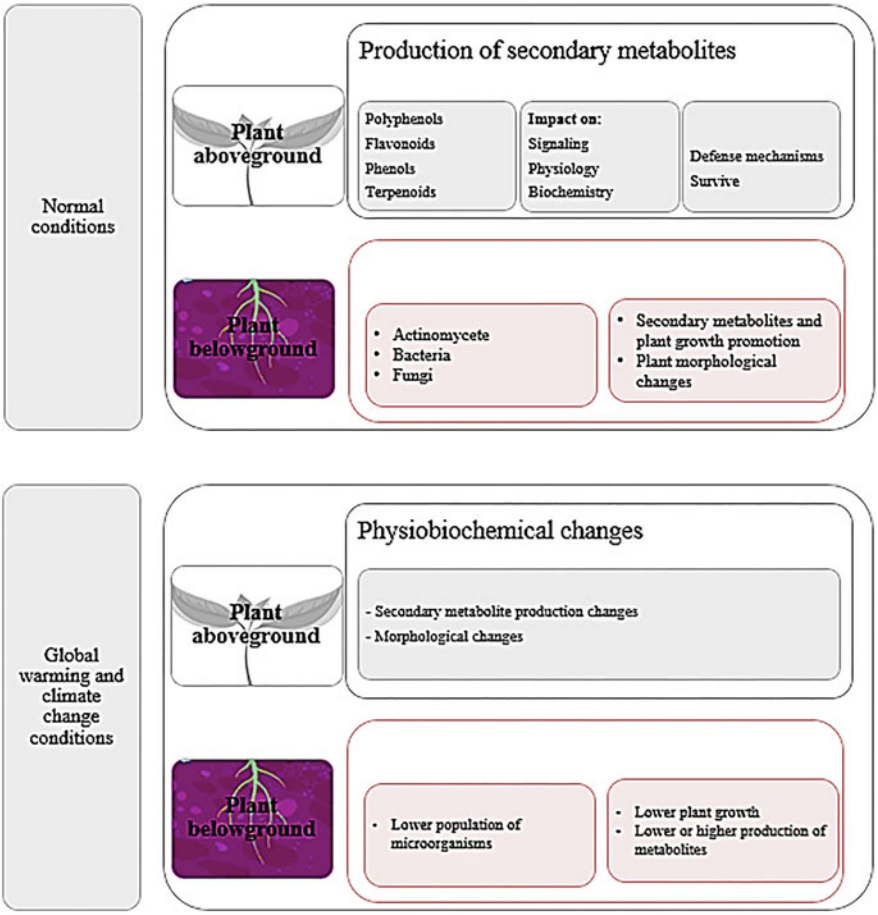

Fig. 1.2 An overview of medicinal plant status under climate change conditions

conditions on medicinal plants, with an emphasis on the main consequences of climate change, i.e., elevated [CO_2], high and low temperatures, and drought, and the current status of medicinal plants under a changing climate are discussed (Fig. 1.2).

1.2 Medicinal Plants' Availability and Population Extinction Under a Changing Climate

It seems many plant species are expected to be locally or globally extinct in the near future (Applequist et al. 2020). Almost 600 plant species have been extinct during the last hundred years (Humphreys et al. 2019). Research indicated that the world species of wild plants is threatened mainly by human activities such as habitat destruction (Skole and Tucker 1993; Riitters et al. 2002; Harper et al. 2007; Haddad et al. 2015). On the other hand, unsustainable and uncontrolled medicinal plant harvesting has made the situation even worse. The American ginseng (*Panax quinquefolius* L.), an important nourishing herb, for instance, has been harvested in large and uncontrolled quantities for commercial purposes, and illegal harvesting due to the great demand has become a serious problem in which their distribution and abundance have dramatically decreased (McGraw 2001; Case et al. 2007; Souther and McGraw 2014; Applequist et al. 2020). Similar situations have also been reported for the slow-growing medicinal herbs, goldenseal (*Hydrastis canadensis* L.) and snow lotus (*Saussurea laniceps* Hand. -Mazz.) (Mulligan 2003; Zedan 2004; Law and Salick 2005). In worse cases, habitat destruction and irregular and commercial harvesting may result in species distinction, as happened to the North African herb, *silphium Ferula* sp., which was extinct a thousand years ago (Parejko 2003; Kiehn 2007).

Even without climate changes, their isolated and small populations are endangered locally. However, environmental conditions change due to climate change will alter plant habitats, making them no longer survivable or optimum for plants. Due to global warming and a rise in the air temperature, many plant distributions have shifted toward higher latitudes, hence increasing competition between the species, leading to vanishing some of the species (Applequist et al. 2020). Nevertheless, some medicinal species, such as arnica (*Arnica montana* L.), chamomile (*Matricaria chamomilla* L.), and bush tea (*Athrixia phylicoides* DC.), are more adaptable and potent when grown at higher altitudes (Ganzera et al. 2008; Spitaler et al. 2008; Turner et al. 2011; Nchabeleng et al. 2012). This habitat fragmentation and phenological changes may also lead to disruption in the plant-pollinator relationship. Although human activities have reduced the pollinator populations, climate change will worsen these situations (Applequist et al. 2020). Medicinal plants are not exempted from these situations. Predictions showed that the ecological distribution of some medicinal herbs, e.g., *Rhodiola quadrifida*, will become smaller; however, it would be varied depending on the species (You et al. 2018).

1.3 Medicinal Plant Physiology, Biochemistry, and SMs in a Changing Climate

In addition to affecting their distribution, climate change may influence, either negatively or positively, the productivity and quality of medicinal plants and their chemical compositions. The climate change consequences, i.e., weather extremes, disturb the growth and development of unadapted plants to such conditions, resulting in reduced sustainable harvest and productivity (IPCC 2014). Nevertheless, the responses will be inconsistent within plant species and their metabolisms. Mild drought stress often stimulates bioactive compound production by enhancing the actual metabolite production or decreasing plant biomass. The effects of climate change factors, solely or in combination with other environmental stimuli, on the morphology, physiology, and biochemistry of some medicinal plant species are summarized in Table 1.1.

The SMs are the bioactive compounds producing autogenously or by endophytic symbionts; however, SMs might be altered by environmental factors. Those alterations may also impact human health since the medicinal plants are mainly consumed to derive health benefits from their bioactivities. The changes in chemical compositions of SMs might be unnoticed by the new-generation customers without chemical testing, leading to the loss of the effectiveness of medicinal plants. Although plant SMs are increased in some species to compensate for the biomass reduction under stressful conditions, this is not always desired and safe. The locally used medicinal plants may contain toxic levels of the compounds, which may be used by susceptible individuals or harmful with excessive consumption. For example, toxic metabolites such as pyrrolizidine alkaloids in *Senecio* species have been reported to increase under drought stress (Briske and Camp 1982; Kirk et al. 2010). Therefore, the geographical shifting and phenological changes due to climate change force may result in undesired alteration in the quality and composition of the SMs, leading to the medicinal plants' toxicity or unusability as a medicine.

Al-Gabbiesh et al. (2015) and Selmar and Kleinwächter (2013) reported increases in the bioactive compound concentrations, including essential oils, simple and complex phenolics, alkaloids, terpenes, and glucosinolates, in a variety of species exposed to drought stress. For instance, *Vitellaria paradoxa* Gaertn. active metabolites were increased under a drier region (Maranz and Wiesman 2004). Drought stress, therefore, may increase the potency of some medicinal plants. A decrease in plant biomass, however, due to severe drought stress (Ahmadi-Lahijani and Emam 2016) would outweigh any increases in the secondary metabolite concentrations. On the other hand, although drought may enhance the SMs' concentrations, higher temperature due to stomatal closure and lower transpiration rate reduces the concentration of SMs, as it was observed in *Rehmannia glutinosa* (Chung et al. 2006). Due to reduced biomass production, high temperatures like water stress could enhance the concentration of SMs (Jochum et al. 2007). However, it should be considered that lower biomass production would ultimately lead to enhanced harvest level unsustainability and severe economic harm.

Water scarcity decreases the CO_2 entrance into leaves by reducing the stomatal aperture, which in turn lessen the energetic molecules, i.e., ATP and NADPH, consumed by the Calvin cycle, resulting in more ATP and NADPH provided to the production of SMs. Elevated levels of [CO_2], despite a reduction in the stomatal aperture due to a greater [CO_2] availability to the plant (Ahmadi-Lahijani et al. 2018, 2021), reduce ATP and NADPH redirected toward the SMs' production pathways (Applequist et al. 2020). For instance, Nowak et al. (2010) found that the reduction capacity arising from drought stress pushed metabolic activity toward the biosynthesis of the SMs in sage (*Salvia officinalis* L.) monoterpenes here, but elevated [CO_2] decreased the monoterpene concentration. However, those observations were not found in all tested species. The CO_2 concentration and duration of exposure to

Table 1.1 Impact of climate change on the morphology, physiology, biochemistry, and secondary metabolites on a number of medicinal plant species

Medicinal plant species	Environmental stimuli	Level of treatment	Environmental conditions	Morpho-physiochemical and metabolic changes	References
Labisia pumila	Enriched [CO_2] × light intensity	(400, 800, and 1200 μmol/mol) (225, 500, 625, and 900 μmol/m^2/s)	Glasshouse	↑Flavonoids ↑Phenolics	Ibrahim et al. (2014)
Isatis indigotica Fort	Enriched [CO_2]	Ambient and 550 ± 19 μmol/mol	Free-air carbon dioxide enrichment (FACE)	↑Net photosynthetic rate ↑Water use efficiency ↑Maximum rate of electron transport (J_{max}) ↓Stomatal conductance ↓Transpiration ratio ↓Maximum velocity of carboxylation (Vc_{max}) ↑Efficiency of PSII (F_v'/F_m') ↑Quantum yield of PSII (Φ_{PSII}) ↓Non-photochemical quenching (NPQ) ↑Starch grains ↑Yield	Hao et al. (2013)
Catharanthus roseus	Enriched [CO_2]	600 and 900 ppm	Open top chambers	↑Phenolics ↑Flavonoids ↑Tannins ↑Alkaloids	Saravanan and Karthi (2014)
Zingiber officinale	Enriched [CO_2]	400 to 800 μmol/mol	Growth chamber	↑Flavonoids ↑Phenolics ↑DPPH ↑Photosynthesis ↑Plant biomass ↓Stomatal conductance ↑Water use efficiency ↑Soluble carbohydrates and starch ↑Antioxidant activities	Ghasemzadeh and Jaafar (2011) Ghasemzadeh et al. (2010)

(continued)

Table 1.1 (continued)

Medicinal plant species	Environmental stimuli	Level of treatment	Environmental conditions	Morpho-physiochemical and metabolic changes	References
Catharanthus roseus	Enriched [CO_2] × nitrogen supply	375 ± 30 ppm and 560 ± 25 ppm	Open top chambers	↑Phenolics ↑Flavonoids ↑Tannins ↑Alkaloids	Singh and Agrawal (2015)
Artemisia annua	Enriched [CO_2]	378–374 (ambient) and 570–577 (elevated) μmol/mol	Free-air [CO2] enrichment (FACE)	↑Artemisinin ↑C:N	Zhu et al. (2015)
Ginkgo biloba	Enriched [CO_2] × [O_3]	Ambient and doubled	Open top chambers	↓Tannins ↑Quercetin aglycon ↓Kaempferol aglycone ↓Isorhamnetin ↓Bilobalide	Huang et al. (2010)
Ginkgo biloba	Enriched [CO_2] × [O_3]	40 and 80 nmol/mol	Open top chambers	↓Tannins ↑Quercetin aglycon ↓Kaempferol aglycon ↓Isorhamnetin ↓Bilobalide	Xingyuan et al. (2009)
Papaver setigerum	Enriched [CO_2]	(300, 400, 500, and 600 μmol/mol)	Controlled environment chambers	↑Morphine ↑Codeine ↑Papaverine ↑Noscapine ↑Leaf area ↑Above-ground biomass ↑Capsules ↑Capsule weight ↑Latex	Ziska et al. (2008)

Brassica oleracea	Enriched [CO_2]	[430–480] ppm [685–820] ppm	Greenhouse	↑Glucoiberin ↑Methylsulfinylalkyl glucosinolates Glucoraphanin ↓Indole glucosinolates ↓Glucobrassicin ↓4-Methoxyglucobrassicin ↓N/S ratio ↑qN ↑qP	Schonhof et al. (2007)
Hypericum perforatum L.	Enriched [CO_2] × light intensity	100, 300, and 600 μmol/m^2/s (PPF) 500, 1000, and 1500 μmol/mol [CO_2]	Controlled environment chambers	↑Hypericin ↑Pseudohypericin ↑Hyperforin	Mosaleeyanon et al. (2005)
Quercus ilicifolia	Enriched [CO_2]	Ambient and 350 ppm above ambient	Open top chambers	↑Tannins ↑Phenolics ↓Herbivore abundance ↑Relative consumption rates ↑Development time ↑Total consumption ↓Relative growth rate ↓Conversion efficiency ↓Pupal weight ↑Biomass ↑C/N ratio ↓Nitrogen	Stiling and Cornelissen (2007)
Hypericum perforatum L.	Enriched [CO_2]	Ambient and 950–1050 μmol/mol	Closed controlled environment system (CCES)	↑Hypericin ↑Pseudohypericin ↑Hyperforin ↑Growth parameters ↑Biomass	Zobayed and Saxena (2004)

(continued)

Table 1.1 (continued)

Medicinal plant species	Environmental stimuli	Level of treatment	Environmental conditions	Morpho-physiochemical and metabolic changes	References
Panax ginseng	Enriched [CO_2]	(1%, 2.5%, and 5%)	Bioreactor	↑Phenolics ↑Flavonoids ↑DPPH ↑Fresh weight ↑Dry weight ↑Growth ratio	Ali et al. (2005)
Pseudotsuga menziesii	Enriched [CO_2] × temperature	Ambient and + 179 μmol/mol [CO_2] Ambient and +0.3.5 °C	Controlled environment chambers	↓Monoterpenes	Snow et al. (2003)
Digitalis lanata	Enriched [CO_2]	Ambient and 1000 ppm	Greenhouse	↑Cardenolide ↑Digoxin	Stuhlfauth and Fock (1990)
Hymenocallis littoralis	Enriched [CO_2]	400 and 700 ppm	Open top enclosures	↑7-Deoxy-trans-dihydronarciclasin ↑Pancratistatin ↑7-Deoxynarciclasine	Idso et al. (2000)
Digitalis lanata	Enriched [CO_2]	Ambient and 1000 ppm	Greenhouse	↑Cardenolide ↑Digoxin	Stuhlfauth et al. (1987)
Salvia officinalis	Enriched [CO_2] × drought	Normal and 70% of the optimal water supply 385 ppm or 700 ppm		↑Monoterpenes (cineole, camphor, and α-β-thujone) under drought ↓Monoterpenes exposed to enriched [CO_2]	Nowak et al. (2010)
Labisia pumila	Drought	Evapotranspiration replacement (100%, 75%, 50%, and 25%)	Glasshouse	↑Phenolics ↑Flavonoids ↑Anthocyanin ↑Phenylalanine ammonia-lyase ↓Net photosynthesis ↓Quantum yield ↓f_v/f_m ↓Dark respiration	Jaafar et al. (2012)

Petroselinum crispum	Drought	Soil water potentials (0–10%, 30–45%, and 45–60% of field capacity)	Greenhouse and outdoors	↑Monoterpenes ↓Foliage and root weight ↓Leaf number ↑Essential oil	Petropoulos et al. (2008)
Hypericum brasiliense	Drought × temperature		Greenhouse	↑Phenolic compounds ↑Reallocation of carbon ↓Growth	de Abreu and Mazzafera (2005)
Arnica montana L. *cv. ARBO*	Low temperature and ultraviolet (UV)-B radiation	5 °C	Climate chamber	↑Ortho-diphenolics	Albert et al. (2009)
Salvia sclarea	Low temperatures	Altitudes, 305, 1730, and 3505 msl	Field	↑Essential oils ↑Linalool ↑Sclareol ↑Antioxidants	Kaur et al. (2015)
Origanum dictamnus L.	Low temperatures	Natural conditions	Field	↑Proline ↑Soluble sugar ↑The antioxidative enzyme ↓Stomata and peltate hairs ↓Sclerenchymatous fibers ↓Vacuoles with phenolics ↓Chloroplasts ↓Grana and starch grains ↑Plastoglobuli ↓Net photosynthetic rate ↓Chlorophyll content ↑p-Cymene ↑Carvacrol ↑γ-Terpinene ↑Borneol ↑Antioxidant essential oils secreted ↑Glandular hairs	Lianopoulou and Bosabalidis (2014)

(continued)

Table 1.1 (continued)

Medicinal plant species	Environmental stimuli	Level of treatment	Environmental conditions	Morpho-physiochemical and metabolic changes	References
Teucrium polium	Low temperatures	Natural conditions	Field	↑Linalool ↑Terpinene-4-ol ↑Germacrene D ↑Spathulenol	Lianopoulou et al. (2014)
Withania somnifera	Low temperatures	4 °C	Controlled environment	↑Anolide (steroidal lactones) ↓Withanone ↑Superoxide anion and MDA ↑Enzymatic activities	Mir et al. (2015)
Withania somnifera	Low temperatures	25 °C and 8 °C	Growth chamber	↑Anolide ↑Withanolide A ↑Withanone	Kumar et al. (2012)
Picea abies (L.) Karst.	High temperatures × elevated UVB × fertilization	Natural conditions	Outdoor experiment	↑Piperidine alkaloids Catechins and acetophenones and bark flavonoids	Virjamo et al. (2014)
Aquilaria sinensis	High temperatures	50 °C for 30 min	Controlled environment	↑Jasmonic acid ↑Agarwood sesquiterpene	Xu et al. (2016)
Ribes nigrum L.	High temperatures	Natural conditions	Field	↑Delphinidin-3-O-glucoside ↑Delphinidin-3-O-rutinoside ↑Myricetin-3-O-glucoside	Zheng et al. (2012)
Cyanea acuminata	High temperatures	40 °C	Controlled environment	↑10-Hydroxycamptothecin	Zu et al. (2003)
Panax quinquefolius	High temperatures	25/20 or 30/25 °C (day/night)	Greenhouse	↑Ginsenoside ↓Photosynthesis ↑Leaf senescence ↓Carbon accumulation ↓Stomatal conductance ↓Root and total biomass	Jochum et al. (2007)

Catharanthus roseus	High temperatures	16 °C to 40 °C	Controlled environment	↓Alkaloids ↓Serpentine ↓Ajmalicine	Morris (1986)
Catharanthus roseus	High temperatures	Short-term heat shock at 30 °C and 40 °C Long-term heat at 20 °C, 25 °C, and 35 °C	Controlled environment	↑Vindoline ↑Catharanthine ↑Vinblastine	Guo et al. (2007)

CO_2 levels, which both either increased or decreased SMs' production, have been proposed depending on the species (Table 1.1). Many studies have also reported an enhanced biosynthesis of the SMs under elevated levels of [CO_2]. For instance, elevated [CO_2] levels increased the concentration of artemisinin in Sweet Annie (*Artemisia annua* L.) and phenolic and flavonoid compounds in ginger (*Zingiber officinale* Roscoe) rhizome under controlled conditions (Ghasemzadeh et al. 2010; Zhu et al. 2015).

1.4 The Climate Change Consequences on Medicinal Plants

Abiotic stresses reduce crop performance and yield. However, mild stresses may positively affect the quality of plant products, e.g., through the activation of the phenylpropanoid pathway and the accumulation of bioactive compounds (Imai et al. 2006). These can improve postharvest performance and enhance the nutritional quality of the products, which is particularly important for their consumers. Abiotic stresses must be continuously studied with multidisciplinary approaches, from the basic science to understand crop responses and their adaptation to the identification of practical agronomic solutions for alleviating the stressful effects and preserving crop productivity (Mariani and Ferrante 2017; Ferrante and Mariani 2018).

The interaction of plants with the biotic and abiotic environmental stimuli influences metabolite biosynthesis (Akula and Ravishankar 2011). The synthesis of metabolites is regulated by and restricted to specific vegetal tissues or development stages in response to environmental stimulation (van der Plas et al. 1995; Gargallo-Garriga et al. 2014). Plant SMs, besides participating in the pharmaceutical industry, play a significant role in plant survival, and their synthesis is induced by the plant-environment interaction (Radušienė et al. 2012). The plant primary and secondary metabolisms are closely related to each other (Kumar et al. 2017); the primary metabolites are utilized as substrates to plant SMs' biosynthesis. When a plant is affected by adverse environmental conditions, e.g., climate change, plant growth and the production of primary metabolites are influenced, which in turn affect the SMs' production (Table 1.1). As a survival strategy and to make diversity at the organism level, plant species are variable in their potentials of synthesizing SMs. There are even variations in the content of the chemical compounds within a species. These characteristics are possibly associated with genetic variability and the differences in the growth conditions (Radušienė et al. 2012; Mishra 2016).

Environmental parameters have direct effects on crop performance in different seasons and nutrient availability. Cultivation of two cultivars lettuce (*Lactuca sativa*) in different seasons with various nutrient availabilities showed that suboptimal growing conditions limited nutrient utilization and had adverse effects on biomass accumulation. Secondary metabolites involving the antioxidant capacity of lettuce were affected by the seasons through effects on the compositions and total concentrations of different flavonoids (Toscano et al. 1982; Sublett et al. 2018). Under stressful conditions, plants tend to come up with reactive oxygen species (ROS) like superoxide (O_2^-), H_2O_2, and hydroxyl radical ($OH^\bullet$), which might promote cellular damage by triggering off an oxidative chain reaction (Imlay 2003). Plants eliminate the ROS by producing defense compounds through enzymatic and non-enzymatic mechanisms, as some secondary metabolism compounds. For a balanced ROS level and not being harmful to cells, the combination of enzymatic and non-enzymatic mechanisms is fundamental (Shohael et al. 2006; Moori et al. 2012). Generally, under stressful conditions, plants tend to increase their enzymatic activity and synthesize secondary metabolite compounds. This accumulation is because of a rise in the enzymes such as phenylalanine ammonia-lyase and chalcone synthase activities (Heldt and Piechulla 2011), which are vital enzymes in the flavonoid synthesis pathway and might be affected by environmental stresses. The phenylalanine ammonia-lyase, by producing phenols and lignin, is the main enzyme in plant stress defense (Dixon et al. 1992). Medicinal plants may accumulate terpenes in the type of essential oils under stressful conditions. Terpenoids are the main constituents of the essential oils; however, phenylpropanoids would also contribute to the essential oil composition (Sangwan et al. 2001; Jaafar et al. 2012).

Glucosinolate's function may also be affected by climate change. Glucosinolates are a class of SMs that their biological activity, mainly in preventing cancer, has attracted attention (Schonhof et al. 2007). Studies have shown that the synthesis of glucosinolate compounds in *Brassicaceae* beyond the biotic factors was influenced by abiotic factors such as salinity, drought, extreme temperatures, nutrient deficiency, and soil acidity (low pH) (Steinbrenner et al. 2012). Aromatic amino acids are likely the main precursors of SMs contributing to plant stress defense. For instance, tryptophan is the precursor of alkaloids, phytoalexins, and indole glucosinolates. Phenylalanine is the main precursor of phenolic compounds such as flavonoids, tannins, and phenylpropanoids, and tyrosine is the precursor of isoquinoline alkaloids and quinones (Cheynier et al. 2013). The metabolic pathway of synthesis for these compounds is performed in three phases, where the chain elongation is affected by the stress (Ruelland et al. 2009; Holopainen and Gershenzon 2010; Khan et al. 2011).

1.5 Effects of Elevated [CO_2] on Medicinal Plants

The plant photosynthetic gas exchange is directly affected by elevated [CO_2], where it indirectly contributes to the global warming. The photosynthesis of many plant species is not fully saturated under the present [CO_2]; hence, its enrichment enhances the photosynthetic rate and stimulates crop growth and productivity (Reddy et al. 2010; Fleisher et al. 2014; Ahmadi-Lahijani et al. 2021). Accordingly, a higher photosynthetic rate was observed in the elevated [CO_2] compared with an ambient [CO_2] (Ainsworth and Long 2005; Hao et al. 2013; Ahmadi-Lahijani et al. 2018). Studies revealed that elevated [CO_2] enhanced photosynthetic carbon assimilation rates in some plant species (Ainsworth and Long 2005; Ahmadi-Lahijani et al. 2018, 2019, 2021). They also observed that the elevated [CO_2] increased the above-ground biomass and dry matter partitioning to the underground parts of the plants. The higher carboxylation rate and inhibition of the Rubisco oxygenation are responsible for the improvement in photosynthesis at elevated [CO_2], although its effects might be varied depending on the plant species, [CO_2], developmental stage, and environmental conditions (Hao et al. 2013). Higher photosynthesis of plants at elevated [CO_2] could also be due to adjustment of the photosynthetic apparatus, such as cellular fine structures, i.e., chloroplast and mitochondria number and size, to such conditions (Ainsworth and Long 2005; Hao et al. 2013; Ahmadi-Lahijani et al. 2018).

Nevertheless, long-term exposure to elevated [CO_2] might result in photosynthetic acclimation and a decrease in photosynthesis (Lawson et al. 2001; Katny et al. 2005). For instance, some research found a photosynthetic acclimation at elevated [CO_2] (Huang et al. 2003; Aranjuelo et al. 2011; Hao et al. 2012). However, Hao et al. (2013) did not observe a photosynthetic acclimation in *Isatis indigotica*, which is used for the clinical treatment of virus infection, tumor, and inflammation in Chinese traditional medicine, at elevated [CO_2] due to developing new carbon sinks. Elevated [CO_2] increased net photosynthetic rate, water use efficiency, and maximum rate of electron transport (J_{max}) of *Isatis indigotica* leaves, although stomatal conductance, transpiration ratio, and maximum velocity of carboxylation (Vc_{max}) were not altered. In addition, the efficiency (F_v'/F_m') and quantum yield (Φ_{PSII}) of PSII were significantly increased at elevated [CO_2], but leaf non-photochemical quenching (NPQ) was decreased. While *Isatis indigotica* yield was higher due to the improved photosynthesis at elevated [CO_2], the content of adenosine was not affected.

Medicinal plants are sources of SMs and show a wide range of plasticity to adapt to changing environments. The SMs may affect other metabolites, which are usually the basis for their medicinal properties (Stuhlfauth et al. 1987; Mishra 2016). It is predicted that an increase in the [CO_2] may increase plant carbon/nutrient ratio, leading to produce non-structural carbohydrates (NSCs) that incorporate in C-based SMs (Heyworth et al. 1998). For instance, elevated [CO_2] increased digoxin, a cardenolide glycoside that is used in heart diseases, by 3.5-fold in *Digitalis lanata* plants (Rahimtoola 2004). Another experiment indicated that although digoxin was enhanced under the elevated [CO_2], digitoxin, digitoxigenin, and digoxin-monodigitoxoside were declined (Stuhlfauth et al. 1987; Stuhlfauth and Fock 1990). The SMs may also be affected by the time of exposure to the elevated [CO_2]. For instance, the alkaloids (pancratistatin, 7-deoxynarciclasine, and 7-deoxy-trans-dihydronarciclasin) of the medicinal plant *Hymenocallis littoralis*, whose bulbs are used for their antineoplastic and antiviral effects, were increased by the first year exposure to the elevated [CO_2]; however, they were decreased in the subsequent year (Idso et al. 2000). Similarly, elevated [CO_2] and [O_3] increased quercetin aglycon up to 15% and decreased kaempferol aglycon by 10% in *Ginkgo biloba*, a traditional Chinese medicinal plant used in Alzheimer's disease (Huang et al. 2010; Weinmann et al. 2010).

It has been shown that elevated [CO_2] enhanced *Hypericum perforatum* phenolic compounds, hypericin, pseudohypericin, and hyperforin (Zobayed and Saxena