Journal of Agricultural Sciences (Tarim Bilimleri Dergisi) 2022, 28 (3) : 351 - 362 DOI: 10.15832/ankutbd.999117

Journal of Agricultural Sciences
(Tarim Bilimleri Dergisi)

J Agr Sci-Tarim Bili
e-ISSN: 2148-9297
jas.ankara.edu.tr

JAS

Environmental Abiotic Stress and Secondary Metabolites Production in Medicinal Plants: A Review

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ARTICLE INFO
Review Article
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Received: 24 September 2021 / Revised: 11 May 2022 / Accepted: 11 May 2022 / Online: 01 September 2022

Cite this article
PUNETHA A, KUMAR D, SURYAVANSHİ P, PADALİA R C, VENKATESHA K T (2022). Environmental Abiotic Stress and Secondary Metabolites Production in Medicinal Plants: A Review. *Journal of Agricultural Sciences (TarimBilimleriDergisi),* 28(3):351-362. DOI: 10.15832/ankutbd.999117

ABSTRACT
Medicinal plants that produce various secondary metabolites are quite useful to us owing to their anti-microbial properties, presence of huge amounts of anti-oxidants, cytotoxic nature, and various other medically significant properties. Medicinal plants, therefore, serve as raw materials for modern pharmaceutical medicines and several herbal medical supplements. Expansion and advancement of growing medicinal plants on large scale has flourished over the last few years. However, prolonged environmental changes have made medicinal plants susceptible to numerous abiotic stresses. On being exposed to abiotic stresses chiefly light (quality and quantity), extreme temperature conditions, water stress (drought or flooding), nutrients available, presence of heavy metals and salt content in the soil, medicinal plants undergo several changes physiologically and their chemical composition also gets altered. To combat the effects of abiotic stress, several mechanisms at morphological, anatomical, biochemical, and molecular levels are adapted by plants, which also include a change in the production of the secondary metabolites. However, plants cannot cope with extreme events of stress and eventually die. Several strategies stress such as the use of endophytes, chemical treatment, and biotechnological methods have therefore been introduced to help the plants tolerate the period of extreme stress. Moreover, nano bionics is also being developed as new technology to help plants survive stressful conditions.

Keywords: Biochemical, Biotechnological, Nanobionics, Strategies, Technology

1. Introduction

For thousands of years, medicinal plants have served as a source of treatment in local communities across the globe. Medicinal plants function as storehouses of secondary metabolites (SMs) i.e., they have evolved to produce a wide spectrum of SMs that are not implicated straightforwardly in primary processes of plant growth and development, and are produced in response to some kind of stress. SMs comprise of a group of bioactive compounds that are chiefly formed from primary metabolites and are not directly responsible for growth of plant and its development (Kumar et al. 2022). SMs differ from one plant to another and one species to another and generally their levels rise during periods of high stress (Taiz & Zeiger 2006). A number SMs produced by medicinal plants are beneficial to us owing to their anti-microbial properties, presence of huge amounts of anti-oxidants, cytotoxic nature, and other properties that are medically quite significant.

Several modern pharmaceutical medicines and several herbal medical supplements that are obtained from medicinal plants are based on these SMs. Plants that belong to families like Apiaceae, Rutaceae, Asteraceae, Hypericaceae, Papaveraceae, Ginkgoaceae, Lamiaceae, Zingiberaceae, Rhamnaceae, Rubiaceae, and Solanaceae produce rich SMs that provide the majority of pharmaceutical medicines (Gurib-Fakim 2006). Table 1 shows the secondary metabolites produced by a few medicinal plants and their uses. SMs produced by medicinal plants play several roles in plants such as being exclusive sources for pharmaceuticals, like food supplements, flavoring agents, and other industrial materials.

Many phenolic compounds like flavonoids are effective antioxidants and can also serve as free radical scavengers. Some phenolics like quercetin and silybinare known for their anti-inflammatory and anti-hepatotoxic properties respectively, while a few like genistein and daidzein possess phyto-estrogenic activity, and some such as naringenin are insecticidal (Goławska et al. 2014). Alkaloids also exhibit a wide range of pharmacological properties such as stimulator of respiration and relaxation, analgesic, local anesthesia, vasoconstriction, muscle relaxation, hyper and hypotensive. Many alkaloids are severely toxic and can be used as insecticides for instance nicotine and anabasine (Hoffmann 2003). Few saponins also exhibit antitumor, spermicidal, sedative, and analgesic properties while some saponins show anti-inflammatory properties. Monoterpenes and other volatile terpenes also have several medicinal uses. For instance, camphor and menthol are used as counter-irritants analgesics and anti-itching agents.

Therefore, for drug development, numerous SMs are being taken into account (Sanchita & Sharma 2018). Concomitantly, the introduction, expansion, and advancement of research on herbal substances have flourished over the last few years. To date, millions of people across the globe devour herbal medicines for several medical problems. However, prolonged environmental changes have made medicinal plants susceptible to numerous abiotic stresses. The most significant abiotic stresses are drought, temperature extremes, heavy metal toxicity, salinity, light intensity, UV radiation, nutrient deficiency, etc. On being exposed to environmental stresses, medicinal plants undergo several changes physiologically and their chemical composition also gets altered. Abiotic stresses induce detoxification systems of plants which include enhanced production of the antioxidant enzymes like superoxide dismutase, catalase, ascorbate peroxidase and glutathione peroxidase (Hasanuzzaman et al. 2012). Phenolic compounds like flavonoids and lignin precursors are found to accumulate in plants as a reaction to abiotic stresses and are therefore considered as the basic mechanisms of scavenging Reactive Oxygen Species (ROS). Plants on being exposed to environmental stresses also begin synthesizing SMs, which a have significant role in adaptive during conditions of stress. In this review, we have summarized the information on the defense mechanism adopted by medicinal plants at the time of stress, a consequence of abiotic stresses on secondary metabolites made by plants, and approaches to overcome environmental stress in plants.

Table 1- Secondary metabolites produced by few medicinal plants and their uses

S.No	*Medicinal plant*	*Metabolites produced*	*Medicinal properties*	*Reference*
1	*Acanthospermum hispidum*	Acanthospermolgalactoside, β-caryophyllene. cafeic acid, cis-cis-germacranolides, flavones, melampolides,	Anti-cancer, anti-microbial, anti-inflammatory, anti-allergic.	Edewor & Olajire (2011)
2	*Alpinia officinarum*	Diarylheptanoids Alpinoids, officinaruminane, officinin A	Tooth decay, abnormal mensuration, abdominal pain, flatulence, inflammation	Abubakar et al. (2018)
3	*Artemisia annua L.*	Artemisinin, artemetin, , cirsilineol, casticin, chrysoplenetin	Anti-malarial, anti-inflammatory, anti-cancer	Weathers & Towler (2012)
4	*Atropa belladonna L.*	Atropine, hyoscyamine, hyoscine	Anti-spasmodic, mydriatic	Okigbo et al. (2008)
5	*Cymbopogon flexuosus*	Citral, β-myrcene	Anti-inflammatory, anti-fungal, analgesic	Boukhatem et al. (2014)
6	*Foeniculum vulgare* Mill	Furocoumarins, isopimpinellinkaempferol, psoralen, quercetin, xanthotoxin	Antioxidants, cardiac stimulant, digestive, vermifuge	Nassaret al. (2010)
7	*Matricaria chamomilla*	Herniarin, umbelliferone	Anti-inflammatory, spasmolytic, anti-biotic	Eliasova et al. (2004)
8	*Mentha piperita* Linn.	Hesperidin, menthone, menthol, didymin, buddleoside, diosmin	Anti-tumour, carminative, spasmolytic, anti-diabetic	Zhao et al. (2018)
9	*Ocimum sanctum*	Eugenol, rosmarinic acid, carvacrol, oleanolic acid	Anti-cancer, antio-xidants anti-diabetic, cardio protective, analgesic, anti-spasmodic	Prakash & Gupta (2005)
10	*Origanumonites*	Carvacrol and thymol	Antifungal, antimicrobial, antioxidant, insecticidal, hepatoprotective, and cytotoxic activity	Spyridopoulou et al. (2019)
11	*Panax ginseng*	Ginsenosides	Anti-tumour, anti-inflammatory and antioxidant properties, and anti-apoptotic	Razgonova et al. (2019)
12	*Plantago lanceolata*	Alkaloids, fatty acids, flavonoids, glycosides, polyphenols, tannins, terpenoids, iridoid, and polysaccharides	Wound healing, inflammation, cancer, respiratory system disorder, blood circulation, reproductive system, and digestive organs	Abate et al. (2022)
13	*Piper nigrum* Linn	Piperine	Anti-inflammatory, anti-thyroids, antihypertensive, hepato-protective, anti-allergic, appetizer, anti-histaminic, anti-flatulant	Damanhouri & Ahmad (2014)
14	*Scutellaria orientalis*	Baicalin, baicalein, wogonin, melatonin, serotonin, viscidulin	Used to treat epilepsy, insomnia, hysteria, anxiety, delirium tremens, bronchitis, hepatitis, jaundice, diarrhea, dysentery, thrombosis, hypertension and cancer	Sherman et al. (2022)
15	*Thymus vulgaris*	Carvacrol, geraniol, linalool terpineol, thymol,	Respiratory diseases, especially chronic cough, bronchitis, and asthma, vascular problems, diseases of the urinary tract, teeth pain and indigestion	Hossain et al. (2022)
16	*Withania somnifera*	Withanine, withanolides, withananine, somnine, somniferine,	Anti-oxidant, amnesia, anti-inflammatory, anti-neoplastic, anti-fibrotic, cardiovascular	Brant (2016) ; Bharti et al. (2016)

2. Biochemical mechanisms adopted by plants for abiotic stresses tolerance

Plants react to abiotic stress at morphological, anatomical, biochemical, and molecular levels. Some mechanisms are adopted by plants to overcome the period of stress (Figure 1). Biochemical mechanisms involve the formation of metabolites such as proline, polyamines, terpenes, carbohydrates. As a part of biochemical response, they synthesize several secondary metabolites to survive unfavorable environmental conditions. The most common secondary metabolites produced by medicinal plants as a part of their mechanism to adapt to periods of stress are:

a) Terpenes: Terpenes are one of the many species of SMs that are involved in the different biological processes undergoing in plants. During stress, terpenes reduce the consequences of oxidative stress by two mechanisms: a) reacting directly with oxidants intercellularly and b) altering ROS signaling. Amongst the various kinds of terpenes, the membrane stabilization and direct antioxidant effects of isoprene and monoterpene minimize abiotic stress in several plant species. In addition to having antioxidant effects, isoprenes and monoterpenes also react quickly with ozone, thereby reducing its toxicity. Being amphipathic, isoprene can improve hydrophobic interactions that occur between membrane proteins and lipids (Sharkey & Yeh 2001) which results in the prevention of membrane and protein disintegration.

b) Phenylpropanoids: Phenylpropanoids are a highly diversified chemical class of metabolites that play a chief role in abiotic stress management in plants. These act as chief constituents in structure formation of the secondary cell wall, protect plants from harmful UV rays, help in ROS scavenging, act as signaling compounds, and are modulators of auxin transportation in plants (Cheynier et al. 2013). Phenolic compounds like flavonoids or coumarins are phenylpropanoids having one or more phenolic rings. Phenolic substances are very crucial for plants since they are major constituents of secondary cell walls, provide antioxidant properties to plants, help in signaling and also act as phytoalexins (Arbona & Gómez-Cadenas 2015). Phenolics have been studied to exhibit activity in response to high intensity of light and UV-B rays. Flavonoids are a type of phenolic compounds that serve as outstanding protectants against UV rays (Schenke et al. 2011).

c) Carotenoids: Carotenoids also serve as vital substances in diverse processes of plants and act as potential antioxidants during the period of stress. They harvest light, quench and scavenge chlorophyll in triplicate state and singlet oxygen species, scatter surplus of harmful energy and stabilize membrane during stress. The production of these metabolites increases excessively at the time of abiotic stress (Espinoza et al. 2013) and might also be related to possessing a protective role and stabilization of the lipids present in thylakoid membranes (Volkova et al. 2009). Additionally, carotenoids also absorb excessive light or UV radiation (Pateraki & Kanellis 2010).

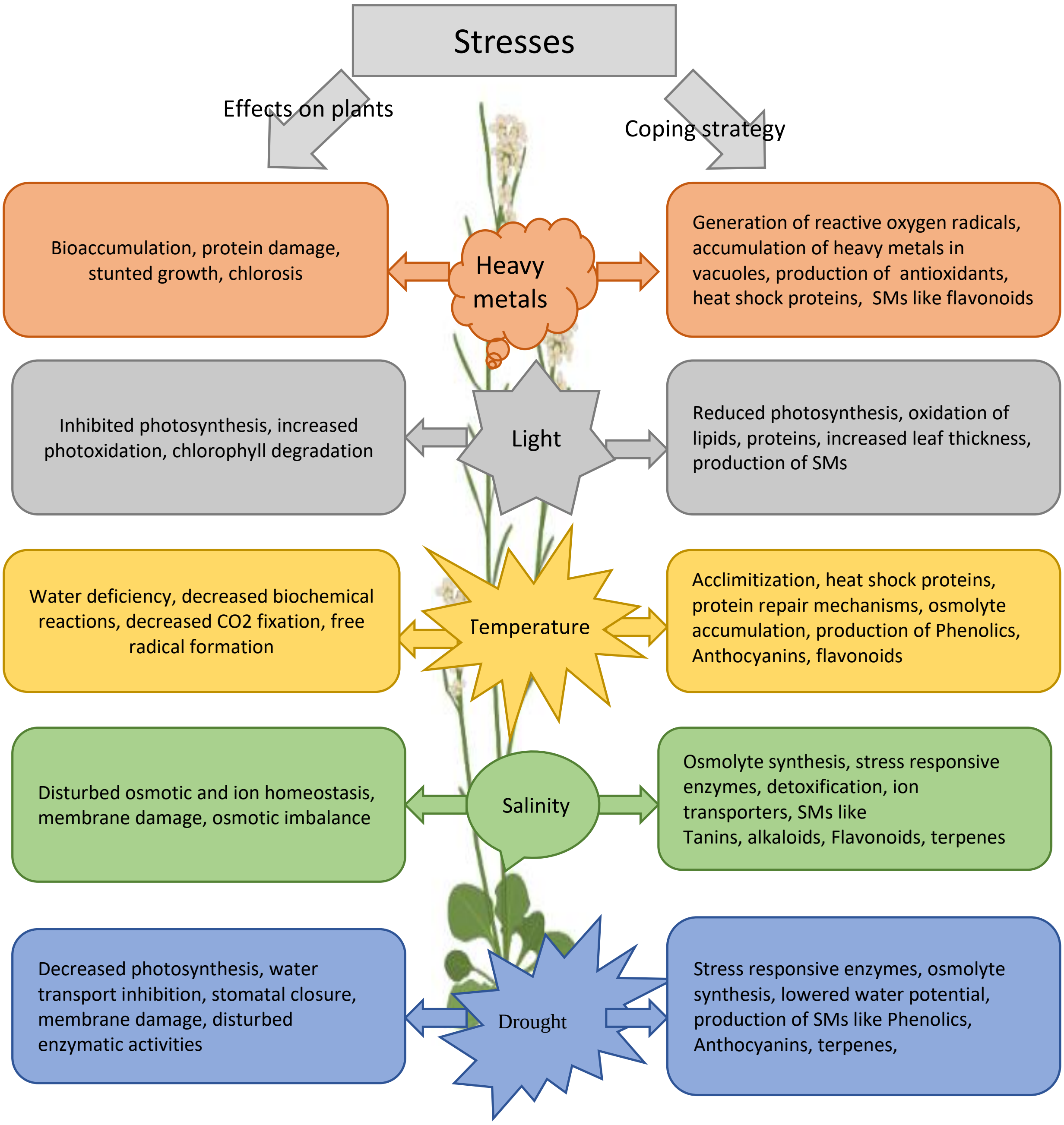

Figure1- Effects of various abiotic stresses on plants and coping strategies adopted by them

3. Influence of abiotic stress on secondary metabolite formation by medicinal plants

The chemical interaction that takes place among plants and their surroundings is primarily conciliated through secondary metabolite formation that helps plants to adapt during adverse environmental conditions (Table 2). Plants being influenced by different kinds of stresses regulate the synthesis of SMs (Verma & Shukla 2015). Abiotic stresses, chiefly light (quality and quantity), extreme temperature conditions, water stress (drought or flooding), nutrients available, presence of heavy metals, and salt content in soil are known to extensively persuade the amount and composition of SMs produced by plants (Khan et al.2016; Sampaio et al. 2016).

i. **Temperature stress:** Temperature serves as a key physical factor severely affecting the growth and development of plants. Extreme temperature stress that occurs in the form of excessive heat or cold affects basic processes of medicinal plants at biochemical, physiological as well as molecular levels. Temperature stress results in leaf senescence damages the membrane of cells, promotes chlorophyll degradation and results in protein degradation (Pradhan et al. 2017). Medicinal plants can also produce SMs in response to high temperatures (Verma & Shukla 2015). Though some plants have shown an increase in the production of SMs due to high temperatures (Naghiloo et al. 2012), few studies have reported a decrease in the production of SMs (Shibata et al. 1988). It can therefore be said that the production of SMs is dependent on plants and their species. Several studies report the outcome of temperature stress on the content of SMs like phenolics and terpenoids. Loreto &

Schnitzler 2010 reported that terpenes are emitted at a higher amount from plants with an increase in temperature. These terpenes help in the stabilization of thylakoid membranes present in chloroplasts and also possess great antioxidant activity. The ratio of formation of flavonoids namely quercetin: kaempferol has been found to increase with a decrease in temperature in *Arnica Montana* plants. The roots of *Panax quinquefolius* were found to have an increased amount of ginsenoside during elevated temperatures (Jochum et al. 2007). Soufi et al. (2015) demonstrated an increase in the content of chlorophyll and carotenoid in plants of *Stevia rebaudiana* which were exposed to high temperature than control plants that were grown at lower temperatures. Vashisth et al. (2018) demonstrated that exposure of *Artemisia annua* to cold stress improved the accretion of artemisinin as a result of up regulation of genes that are concerned in its biosynthesis. Chan et al. (2010) studied how temperature affects anthocyanin production by *Melastoma malabathricum* and reported that higher amounts got accumulated when the temperature was low (20±2 °C) than in higher temperature conditions (26±2 °C and 29±2 °C).

ii. **Drought stress:** This is a majorly significant abiotic stress that dramatically affects plant growth and yield. The condition of drought is a result of inadequate rainfall and constant loss of water through transpiration and evaporation as a result of which, the amount of available water in the soil decreases (Jaleel et al. 2007). Several studies report that drought stress affects the production of SMs in medicinal plants. Drastically increased concentration of betulinic acid, flavonoids, and phenolic substances was found in *Hypericum brasiliense* during conditions of drought (Azharet al. 2011). Yang & Li (2011) found raised amounts of anthraquinones, chlorogenic acids, and flavonoids in the leafy area of *Myrica lubra* during a situation of medium water stress condition. Liu et al. (2011) gave an account of the increased content of salvianolic acid B and decreased content of tanshinone IIA in the roots of the plant *Salvia miltiorrhiza*. The production of oleanolic, rosmarinic, as well as ursolic acids increases when *Prunella vulgaris* is exposed to moderately dry conditions (Chen et al. 2011). Disclosure to drought stress in a moderate amount might help the accumulation of baicalin in *Scutellaria baicalensis* (Cheng et al. 2018). Drought stress is also known to enhance the quality of SMs like artemisinin in plants of *Artemisia*. Betulinic acid, quercetin, and rutinare also produced in increased amounts in *Hypericum brasiliense* plants during drought conditions (Verma & Shukla, 2015). Increased production of SMs like phenolics, alkaloids, and terpenoids during stress prevents the production of ROS thereby protecting medicinal plants (Radasci et al. 2010). Thus, drought affected areas can be exploited for growing medicinal plants, which can provide dual benefits a) higher production of secondary metabolites, b) exploitation of drought pretentious land.

iii. **Salinity stress:** Soil salinity is a chief problem faced worldwide that severely affects plants (Jamil et al. 2006). The use of poor-quality water and excessive amounts of inorganic salts present in water used for irrigation are the major causes of salinity. Medicinal plants produce SMs as defense mechanisms to survive salt stress. *Plantago ovata* plants growing under saline conditions are known to have increased concentrations of alkaloids and tannins (Abd EL-Azim & Ahmed 2009), phenolics (Verma & Shukla 2015), flavonoids, proline, and saponins (Haghighi et al. 2012). The level of ricinine in shoots of *Ricinus communis* is significantly higher under saline conditions (Ali et al. 2008). The concentration of reserpine, solasodine, and vincristine accumulated in *Solanum nigrum, Catharanthus roseus, and Rauvolfia tetraphylla* respectively, was found to increase on exposure to salt stress (Bhat et al. 2008). Cik et al. (2009) found a considerable rise in the number of phenolics like caffeic, chlorogenic, and protocatechuic acids in *Matricaria chamomilla* during salinity stress. The concentration of phenolics has also been found to increase in plants of *Achillea fragratissima* (Abd El-Azim & Ahmed 2009), *Mentha pulegium* (Queslati et al. 2010), *Nigella sativa* (Bourgou et al. 2010), and *Stevia rebaudiana* (Rathore et al. 2014) on treating with salt. *Nigella sativa* plants grown in saline conditions have been found to have an increased concentration of apigenin, quercetin,and trans-cinnamic acid (Bourgouet al. 2010). Shahverdi et al. (2017) investigated the influence of salt stress on *Stevia rebaudiana* plants and observed an increased percentage of rebaudioside-A and stevioside. Phenolic compounds exhibit antioxidant properties that eradicate ROS produced through the condition of stress (Ksouri et al. 2007). The production of SMs is influenced by several regulatory genes and enzymes that are formed during salinity stress and the level production of SMs changes as per the plants require.

iv. **Light:** Light is a very crucial abiotic factor responsible for the formation of secondary metabolites by medicinal plants. Light quality (wavelength and color), quantity, and photoperiod severely influence the growth of the plant, its structure, time of flowering, and output (Casal & Yanovsky 2005). Some plants exhibit better growth and more production of SMs on being exposed to the higher irradiance (Zhang et al. 2015). For example, the leaves of *Erigeron breviscapus* developed in sunlight contain a higher amount of scutellarin than those developed in shade (Zhou et al. 2016). Several reports also suggest contradictory situations. For example, in *Flourensia cernua* plants grown at shade, the amount of borneo, b-pinene, bornyl acetate, camphene, sabinene, l, and Z-jasmone were elevated as compared to the ones grown under sunlight (Estell et al. 2016). Barbaloin, homonataloin, and nataloin increase in amounts in *Aloe mutabilis* when developed in shade conditions instead of directly available sunlight. Callus culture of *Zingiber officinale* was found to have more concentration of gingerol and zingiberene when grown in presence of light (Anasori & Asghari 2008). Ultraviolet (UV) radiation can naturally stimulate the synthesis of SMs however, in higher amounts UV-B severely damages the photosynthetic system, DNA or RNA, and proteins and also might cause cell damage (Pell et al. 1997). Flavonoids and phenolic acids were produced in a better amount under influence of UV-B radiation in *Chrysanthemum plants* (Ma et al. 2016). The outcome of UV light exposure on production SMs is helpful in most cases however higher doses negatively affect the rate of photosynthesis, subsequently affecting growth and development in plants (Katerova et al. 2017).

Table 2- Effect of abiotic stress on secondary metabolite production by few plants

Abiotic stress	*Plant*	*Metabolite formed*	*Effect*	*Reference*
UV-B	*Arnica montana*	Anthocyanins, lignin, tannins, Phenolic acids	Increase	Spitaler et al. (2006)
	Asparagus officinalis	Flavonol quercetin-4′-O-monoglucoside	Increase	Eichholz et al. (2012)
	Astragalus compactus	Anthocyanins, lignin, tannins, Phenolic acids	Increase	Naghiloo et al. (2012)
	Nasturtium officinale	Glucosinolate	Increase	Reifenrath & Müller (2007)
Light intensity	*Aloe vera*	Anthocyanin, aloin	Increase	Hazrati et al. (2016)
	Cassia angustifolia	Sennoside	Increase	Raju et al. (2013)
	Erigeron breviscapus	Scutellarin	Increase	Zhou et al. (2016)
	Hypericum perforatum	Naphthodianthrones and phenoliccompounds	Increase	Radusiene et al.(2012)
	Mahonia breviracema	Essential oil, Hexadecanoic acid	Increase	Li et al. (2018)
Drought	*Artemisia*	Artemisinin	Increase	Verma & Shukla (2015)
	H. brasiliense	Rutin, Quercetin, Betulinic acid	Increase	Verma & Shukla (2015)
	Labisia pumila	Total phenolics, anthocyanins	Increase	Jaafar et al. (2012)
	Salvia officinalis	Terpenes	Increase	Nowak et al. (2010)
	Scutellaria baicalensis	Baicalin	Increase	Cheng et al. (2018)
	Thymus vulgaris	Thymol	Decrease	Alavi-Samani et al. (2015)
	T. vulgaris	Thymol, carvacrol,γ-terpinene, and p-cymene	Increase	Mohammadi et al.(2018)
	Trachyspermum ammi	Total phenolics	Increase	Azhar et al. (2011)
High temperature	*A. compactus*	Phenolics	Increase	Naghiloo et al.(2012)
	Chrysanthemum	Anthocyanins, α-linolenic, Jasmonic acid	Decrease	Shibata et al. (1988)
	Eleutherococcus senticosus	Eleutherosides and chlorogenic acid	Increase	Shohael et al. (2006)
	H. perforatum	Naphthodianthrones and phenolics	Increase	Radusiene et al. (2012)
	H. perforatum	Hyperforin	Decrease	Radusiene et al. (2012)
	Polygonum minus	Flavonols	Increase	Goh et al. (2015)
Low temperature	*Artemisia annua*	Artemisinin	Increase	Yin et al. (2008)
	Artemisia tilesii	Flavonoids	Decrease	Havryliuk et al. (2017)
	Camellia japonica	Anthocyanins, α-linolenic, Jasmonic acid	Increase	Li et al. (2016)
Salinity	*Achillea fragratissima*	Tannin, Alkaloid	Increase	Abd EL-Azim & Ahmed (2009)
	Coriandrum sativum	Carvacrol, Octanal; Borneol; (E)-2-Nonenal	Increase	Neffati & Marzouk (2008)
	Coriandrum sativum	γ-trepine, α-Pinene; (Z)-Myroxide	Decrease	Neffati & Marzouk (2008)
	Origanum majorana	cis-Sabinene Hydrate; Linalyl acetate; Terpinene-4-ol	Increase	Baatour et al. (2010)
	Plantago ovata	Flavonoids, Saponins, Proline	Increase	Haghighi et al. (2012)
	Ricinus communis	Recinine alkaloids	Increase	Ali et al. (2008)

1. **Strategies enabling plants to tolerate the conditions of extreme stress**: Though plants can cope with the conditions of stress on their own using several mechanisms, however, extreme stress conditions severely affect the plants and lead to plant death. Therefore, to ensure plant survival at the time of stress, several strategies are being used to increase plant stress tolerance. Current efforts at increasing stress tolerance in plants include the use of microorganisms, chemical treatment, biotechnological and nano-technological approaches (Figure 2).

   i. **Biological:** This method of ensuring plant survival at the time of severe abiotic stress in plants includes the introduction of plants with endophytes. Endophytes are microbes that live in roots, stems, leaves, and seeds of healthy plants without showing any negative effects on physiological plant functions and also not resulting in any disease. Endophytes help plants in adapting to unfavorable conditions and during stress conditions that limit their growth. During severe conditions, plants develop symbiotic relationships with these microorganisms, which is helpful to both partners. The main functions of these microorganisms which confer resistance to stress in plants are hormone production such as cytokinins, gibberellins, indole-3-acetic acid (IAA), siderophore formation, phosphate solubilization, nutrient uptake, and antagonism to pathogens. Endophytes can stimulate chemical or physical modifications that confer plant protection. Several reports have confirmed that plant growth-promoting fungi (PGPF) can provide aid in escalating tolerance of plants against different environmental stresses such as cold, heat, drought, salinity, and heavy metals (Khan et al. 2012).

   ii. **Chemical treatment:** Chemical treatment mostly involves seed priming. Priming is a technique where plant seeds are chemically treated to provide them protection from unfavorable situations. Chemical substances as priming agents came into use only after they were established to appreciably perk up the ability of plants to bear situations not favorable to them (Irani & Todd 2018). Chemical substances like hydrogen peroxide (H_2O_2), hydrogen sulfide (H_2S) and nitric oxide (NO) are generally used for priming and can provide abiotic stress resistance to plants (Jinet al. 2017; Liang et al. 2018). The seeds are treated with these chemicals before sowing which confers increased tolerance of plants to abiotic stress, without inhibiting plant development (Shi et al. 2014). These compounds might confer priming effects from their signaling functions at the cellular level and or from transcriptional and post-translational regulation (Savvides et al. 2016). Seed priming increases the percentage of seed germination, decreases the time taken by seeds to germinate and improves the growth of seeds during unfavorable environmental conditions.

iii. **Biotechnological:** Modifying the regulatory genes like protein kinases and phosphatase that protect plants from abiotic stress or bringing change in transcription factors is an approach that efficiently improves the capacity of plants to resist stress by modulation of stress signals and regulation of several downstream genes. The most suitable approach used to improve abiotic stress tolerance in plants requires strengthening the internal systems by interfering with the sensors and signaling/ regulative elements (i.e. kinases, phosphatases, transcription factors) or genes and effectors (e.g. antioxidant producing enzymes, heat-shock proteins, osmoprotectants synthesizing enzymes) (Reguera et al. 2012).In plants, several protocols have been proposed that develop abiotic stress resistance depending on the enzymes that can produce metabolites having solubility, serve as membrane lipid synthesizers, antioxidant producers, act as protein protectants, and transporters (Yang et al. 2018). For instance, Proline dehydrogenases (ProDH) and Δ1-pyrroline-5-carboxylate synthetases (P5CS) are known to confer stress tolerance to plants through regulation of the synthesis of proline. It is an important area of research to identify chief regulators or sensors that acclimatize stress upstream and tolerate abiotic stress.

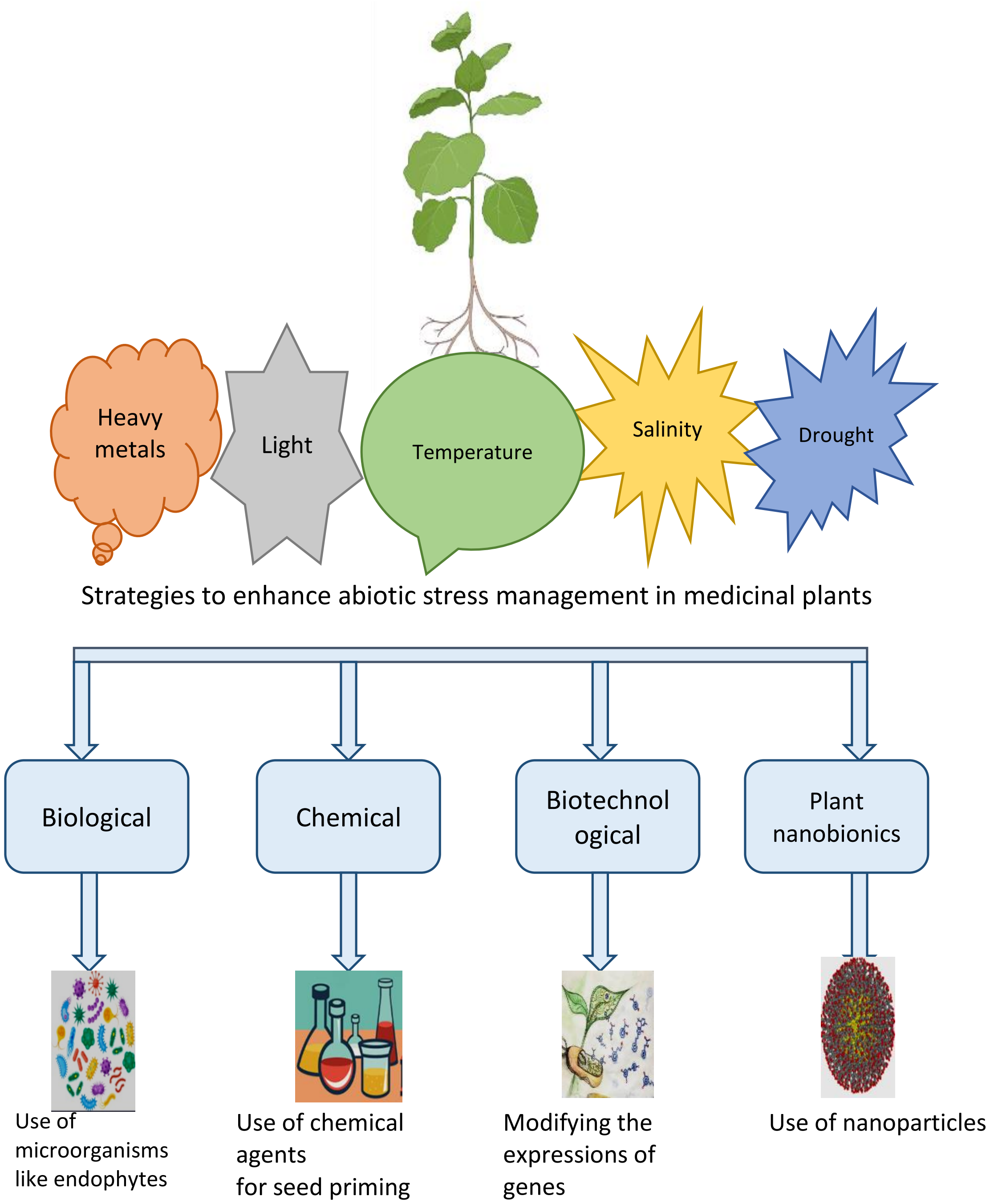

Figure 2- Strategies enhancing the ability of plants to tolerate abiotic stress

iv. **Plant Nanobionics:** Plant nanobionics is a field of plant science that investigates how nanoparticles (NPs) interact with plant systems to produce novel functions. NPs have sizes ranging from 1 to 100 nanometers and have a high surface energy and surface-to-volume ratio, which increases their reactivity and other biological activity thereby making them quite efficient for a number of purposes. NPs also have the potential to protect plants from a variety of abiotic stresses. Abiotic stresses make photosynthesis particularly sensitive; nevertheless, NMs have been shown to preserve the photosynthetic system and promote photosynthesis by reducing oxidative and osmotic stress (Siddiqui et al. 2014). NPs are also being intensively studied for their ability to help medicinal plants to accumulate valuable secondary metabolites (Paramo et al. 2020). Silver NPs (AgNPs) were observed to augment the ability to bear drought stress in *Thymus daenensis* and *Thymus vulgaris L.* along with enhanced germination and increased length of roots during 200 mM saline conditions (Ghavam 2019). Spraying Iron oxide (Fe_2O_3) NPs in plants of *Dracocephalum moldavica* L. under salt stress (100 mM of NaC1) noticeably improved the canopy, enhanced the rate at which SMs were formed and also improved the antioxidant enzymatic activities (Moradbeygi et al. 2020). Besides, for this plant, Fe_2O_3 NPs can also serve as a basis of Fe supply to this plant. Application of Fe_3O_4 NPs can also assuage toxicity induced by Cd and Pb in the leaves of coriander plants (Fahad et al. 2020). Titanium dioxide (TiO_2) NPs have also been studied for their effects on plants. *Verbascum sinuatum* plants on being treated with TiO_2 were able to alleviate negative effects of exposure to artificial drought and increased the number of pigments assimilated due to stimulation of antioxidant defence systems (Karamian et al. 2020). In contrast to this, the amount of pigments assimilated in the leaves of *Dracocephalum moldavica* plants were reduced significantly when treated with TiO_2 NPs of size 10 ppm (Mohammadi et al. 2016). Additionally, applying 10 ppm TiO_2 NPs on the leaves of *Dracocephalum moldavica* L. plants growing in drought conditions resulted in enhanced dry mass of the shoot and EO content. Plants growing in water deficient conditions in presence of 10 ppm TiO_2 NPs, showed higher concentrations of proline and lower amount of H_2O_2 signifying that TiO_2 NPs are capable of diminishing oxidative damages caused by water deficiency. Under salinity stress, the use of silicon nanoparticles has been demonstrated to have promising impacts on physiological and morphological aspects of basil vegetative properties. Treating basil with silicon nanoparticles and silicon fertilizer, showed a considerable improvement in growth metrics, chlorophyll content, and proline level under salt stress (Kaltech et al. 2014). Reduced Na+ ion concentration, possibly by lowering Na+ ion absorption by plant tissues, is a possible approach used by silica nanoparticles to ameliorate salinity stress in plants (Saxena et al. 2016).

4. Conclusions

For thousands of years, secondary metabolites produced by medicinal plants have served as raw materials for the production of pharmaceutical compounds and treatment of several diseases by local communities across the globe. Plants produce SMs as a defence mechanism to combat the conditions of environmental stress. Stresses might lead to change in the quality of the SMs produced by plants along with their quantity. The modification in the quantity and quality of SMs synthesized by plants during stress conditions varies from plant to plant. From the present overview it can be concluded that the production of secondary metabolites can be optimized in plants by exposing them to different kinds of stresses. However, it is extremely necessary to understand that plants can deal with stresses only to a certain extent and extreme stress events lead to the death of plants. Therefore, to protect the plants from the conditions of extreme stress, several biological, chemical and biotechnological methods can be used. In addition to these well known methods, plant nano bionics has also emerged as a new method that helps plants in tolerating or managing stresses. This field is still in its infancy and requires extensive research before being introduced to field conditions.

Acknowledgements

Authors are thankful towards CSIR and Scientist in Charge, CIMAP, Pantnagar

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