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Does abiotic stresses enhance the production of secondary metabolites? A review

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Abstract
Plants are the backbone of traditional systems of medicine and are also revered for their contribution to development of modern drugs. The therapeutic potential of plants depends on the quality and quantity of phytoconstituents present. Plant growth and the biosynthesis of plant metabolites are greatly influenced by biotic and abiotic factors. Scientific investigations have shown that various abiotic stresses including salt stress, flooding, drought, fertilization, shade, soil types etc. influence plant growth and formation of active constituents. Thus, optimization of abiotic stresses may help in increasing levels of plant metabolites and thus enhancing the bioactivity. The present review summarizes the importance of various abiotic stresses on plant growth and production of bioactive constituents. Literature shows that plants respond to abiotic stresses by modifying their morphology, physiology and phytochemical nature. Changes in plant growth and their bioactive metabolites are reported with alteration in abiotic stresses. This knowledge however is not translated to the fields during cultivation of valuable medicinal plants. From this review the authors conclude that, alteration of environmental factors during growth/cultivation of medicinal plants may ensure supply of plants with increased marker content which ensures better activity.

Keywords: Abiotic stress; plant growth; plant metabolites; secondary metabolites

1. Introduction

Medicinal plants are the mainstay for both traditional as well as modern system of medicine (Mehta *et al*., 2011) [73]. The World Health Organization states that 80% of the world population relies on traditional medicine that is derived mainly from plants. Moreover 30% of conventional drugs are of natural origin (WHO, 1999) [114]. The trend towards use of herbal medicines is increasing and thus the demand for medicinal plants is increasing in developing as well as developed countries. This has led to an increase in the number of herbal drug manufactures (Mehta *et al*., 2011) [73]. For the herbal drug industry regular supply of good quality raw material is necessary. Cultivation is one way of ensuring regular supply of uniform quality medicinal plants. The quality and medicinal properties of plants are attributed to the presence of different phytoconstituents present therein (Brinkhaus *et al*., 2000; Mukherjee *et al*., 2007) [17, 83]. The amount of bioactive constituents i.e. the secondary metabolites, present in plant is often low and they play a major role in adaptation of plants during stress conditions (Bannett and Wallsgrove, 1994; Bartwal *et al*., 2013; Murthy *et al*., 2014) [13, 12, 85]. The biosynthesis of plant metabolites is influenced by biotic and abiotic factors. The production of plant metabolites gets altered by variations in environmental factors or stresses (Akula and Ravishankar, 2011) [4].

Environmental factors that affect the growth as well as biochemical expression of plants are termed as stress (Lichtenthaler, 1996) [63]. Any change in environmental factors produces change in the plant growth, morphology or biochemistry of plants. These factors or stresses may be biotic or abiotic. Biotic stresses include effect of living organisms e.g. fungi, insects, viruses, bacteria, herbivores, weeds etc. (Mittler, 2006) [78]. Abiotic stresses are environmental and non-biological in nature e.g. climate [rainfall (e.g. annual rainfall and distribution; floods/drought), temperature (heat, cold, chilling), light (day length, shade, high light intensity)] and soil conditions [i.e. physical properties (particle size, water holding capacity), chemical nature (pH, salinity, organic and inorganic nutrients (fertilizers) and microbiological properties (e.g. nitrogen fixing bacteria)]. Figure 1 summarizes major factors that affect plant growth and metabolism.

Literature shows that these affect the plant growth and production of plant metabolites (Chinnusamy *et al*., 2004; Cramer *et al*., 2011) [23]. Change in concentration, (increase/decrease) of secondary metabolites in response to stress such as light, salinity, cold, drought, flooding shade, metal, fertilization etc. is well documented. The question arose in our minds that can we alter abiotic stresses during cultivation of medicinal plants with a view to increase the production of secondary metabolites. If we understand which environmental factor/stress enhances the production of secondary metabolites, that particular factor may be altered during cultivation thereby producing plants with increased amount of secondary metabolites. Hence we examined the available literature on effect of various environmental factors on medicinal plants. This review summarizes the effect of various abiotic factors on the plant growth and production of secondary metabolites and also suggests how these factors may be used during medicinal plant cultivation.

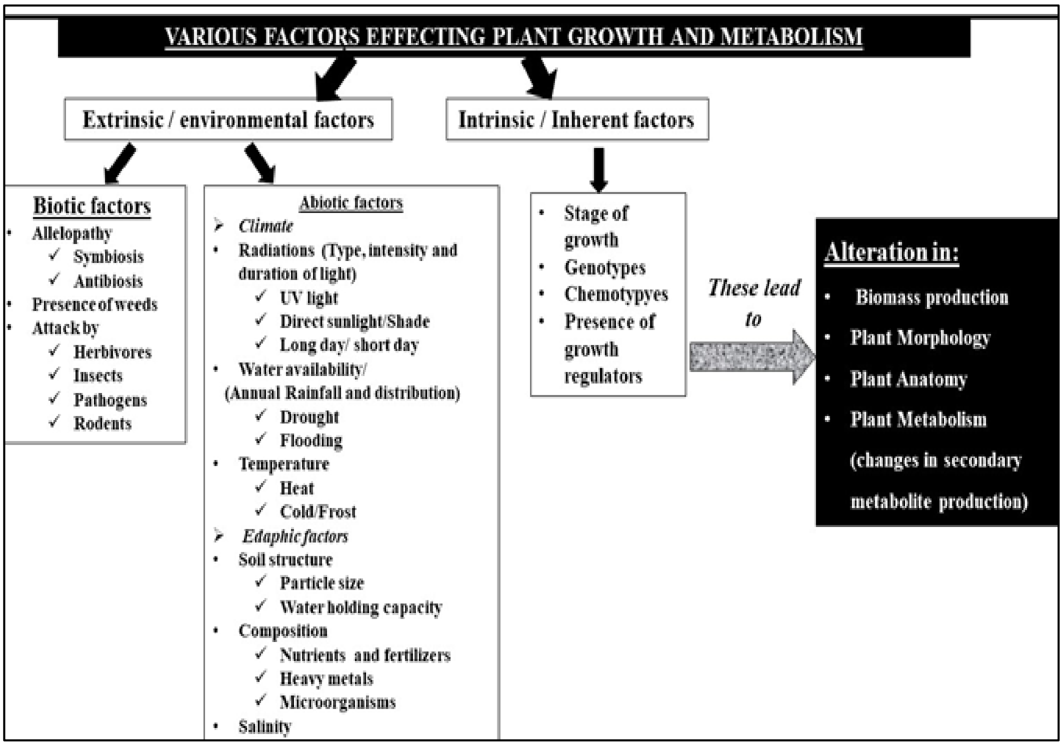

Fig 1: Various factors that influence plant responses

2. Method

Review of literature was prepared by using online searching on Google scholar, PubMed, Science direct, www.manybooks.net, http://www.pharmatext.org, www.getfreebooks.com etc. from 2000 to 2019.

3. Effect of abiotic stress on plants

Plants produce secondary metabolites to cope or adapt with any change or stress. Secondary metabolite production is often enhanced under stress. The emphasis of this review is to understand how environmental factors influence plant growth as well the nature and quantity of phytoconstituents. Effect of some abiotic factors influencing plant growth and metabolism are discussed below:

3.1. Climatic factors

Climate is a primary feature influencing plant growth and metabolism. Climatic conditions cannot be controlled or changed completely, but it is possible to select suitable climate for cultivation of a particular plant. Though plants grow best in their native environment, they adapt to altered environment and can exist in a range of external conditions by modifying their morphology, anatomy or biochemical response. Moreover these days using greenhouses for growing plants provide controlled conditions since greenhouses provide cover for crops and the amount of water and sunlight the plants receive can be controlled.

Water availability, temperature and day length/ light intensity are critical components of climate.

3.1.1. Water availability

Excess or lack of water can lead to change in plant growth and survival. Water deficit leads to decreased photosynthesis in plants and hence decreased productivity (Zlatev and Lidon, 2005) [121]. Water scarcity leads to slowing down of root and leaf growth, delays flowering and fruit set and fall in seed number, size and viability. Water scarcity also triggers production of secondary metabolites (Kumar and Sharma, 2018) [59].

Drought stress occurs when the available water in the soil is reduced to critical levels and an atmospheric condition adds to continuous loss of water i.e. water deficit, usually accompanied by high temperatures and intense solar radiation (Xu *et al*., 2011) [115]. Drought is considered a major abiotic factor affecting plants. It is well documented that exposure of plants to drought leads to enhanced secondary metabolite production (Isah, 2019) [50]. Drought causes oxidative stress and is reported to increase the amount of flavonoids and phenolic acids in willow leaves. Drought stress influenced changes in the ratio of chlorophyll a and b and carotenoids. Plant tissues containing anthocyanins are usually resistant to drought but anthocyanins are reported to accumulate under drought stress at cold temperatures (Chalker - Scott, 1999; Akula and Ravishankar, 2011) [19, 4].

Excess water or flooding is tolerated by some plants and not by others. Excessive moisture reduces oxygen levels and impedes respiration in the roots; leads to buildup of CO_2, CH_4 and N_2 gases as well as toxic compounds (Armstrong *et al*., 1994) [8]. Plant become more prone to microbial attack (Heath,

2000) [44]. If leaves and stems are submerged it leads to inhibition of photosynthesis (Liao and Lin, 2001; Caudle and Maricle, 2012) [62, 18]. Extent of damage by flooding depends on the time of the year and age of plants. Very young and old plants are more sensitive. During winters plants are not actively growing hence they are more tolerant to flooding (Colmer and Voesenek, 2009; Rapacz *et al*., 2014; Kosová *et al*., 2018) [26, 96, 56].

3.1.2. Temperature variations
Temperature strongly influences metabolic activity and plant ontology i.e. anatomy, morphology, growth and development of plant. Temperature is a key factor in regulating physiological processes.

High temperatures can disrupt functional integrity of the photosynthetic apparatus at the chloroplast level (Allakhverdiev *et al*., 2008) [6]. It can induce premature leaf senescence. Very high temperatures lead to water stress heading to nutrient deficiency. Several studies have examined the effects of increased temperatures on secondary metabolite production of plants. Temperature variations have multiple effects on the metabolic regulation, permeability, and rate of intracellular reactions in plant cell cultures. Elevated temperatures increase leaf senescence and root secondary metabolite (ginsenosides) concentrations in the herb *Panax quinquefolius*. Temperatures elevated by 5°C reduced photosynthesis and biomass production of *P. quinquefolius* (Jochum *et al*., 2007) [53].

Low temperature is one of the most harmful abiotic stresses affecting temperate plants. These species have adapted to variations in temperature by adjusting their metabolism during autumn, increasing their content of cryoprotective compounds to maximize their cold tolerance. Low temperatures or cold environment causes reduction in permeability of root surface membranes; delays stomatal opening thus lowering daily photosynthesis. Cold stress increases production of phenolics and subsequently they are incorporated into the cell wall as suberin/lignin, acting as a water barrier and increase resistance to the cold (Akula and Ravishankar, 2011) [4]. In apple tree adaptation to cold climate was found to be associated with a high level of chlorogenic acid (Zhao *et al*., 2011) [117]. The effect of cold stress on polyamime accumulation was reported. When leaves of *Triticum aestivum* L. are exposed to a cold temperature, accumulation of putrescine (6–9 times), increased (Kovacs *et al.*, 2010). Lower soil temperatures cause an increase in levels of steroidal furostanol and spirostanol saponins (Szakiel *et al*., 2011) [108].

3.1.3. Light
It is well known that light is a physical factor which can affect plant physiological processes and metabolite production. A positive correlation between increasing light intensity and levels of phenolics has been reported in *in-vitro* as well as in field studies (Chalker - Scott, 1999) [19]. Autotrophs depend on light for survival. Photoperiod (duration of light), intensity and quality of light change their primary metabolic processes thereby changing production of primary and subsequently secondary metabolites. With increasing light intensity, uptake of oxygen, phosphorus and potassium is increased. Decreased light is a limiting factor in plant growth. Shading leads to reduced rate of photosynthesis (Gordon, 1969) [37].

Long day conditions and direct sunlight enhance the flavor and production of volatile oil in *Mentha* species (Clark and Menary, 1980) [24]. It is reported that phenols and flavonols accumulate in the skin and leaves of fruits as their biosynthesis is stimulated by light (Treutter, 2006) [110]. UV-B is shown to induce the production of flavonols in Norway spruce, silver birch and grape leaves (Fischbach *et al*., 1999; Tegelberg *et al*., 2004) [32, 109]. UV (300–400 nm) increased flavonoids in the roots of pea plants (Akula and Ravishankar, 2011; Siipola *et al*., 2015; Shiozaki *et al*., 1999) [4, 102, 100]. *Catharanthus roseus* plants exposed to UV-B light show significant increases in the production of vinblastine and vincristine. In apples, UV light from 280–320 nm synergistically stimulates anthocyanin synthesis when it was combined with red light (Binder *et al*., 2009) [14].

3.2. Edaphic factors
These are abiotic factor relating to the physical or chemical composition of the soil found in a particular area. Different plants have different soil and nutritive requirements. Soil properties vary from one place to another in terms of type of soil particles, pore spaces, water holding capacity, pH, presence of lime, inorganic nutrients (e.g. N, P, K, Mg, Ca, S, Cu etc.), humus content, heavy metals and salinity.

Fine soil, rich in inorganic nutrients and humus with a permeable substratum, pH range 6.5-7.5 and a good degree of moisture is favorable for growth of most plants. Specific pH, nutrient deficiency/ supplementation may elicit a response in plants in terms of altered secondary metabolite production.

3.2.1. Nutrients
Nitrogen, phosphorus and potassium are the primary nutrients necessary for plant growth. Nitrogen fertilizers improve plant vigor, water utilization, number of seeds, size of leaves and stems, number of roots. Nitrogen supplementation increases volatile oil production in *Mentha piperita* but there a decrease in menthol content (Marotti *et al*., 1994; Singh *et al*., 1989) [71, 103]. Physical size as well as alkaloid content of *Datura stramonium* is proportional to nitrogen supplied. In opium poppy similar results were obtained. A deficiency of nitrogen and phosphorus results in increased production of phenolics which are a part of the chemical defense of the plants. Phenolic compound biosynthesis is also increased by shortage of potassium, sulfur and iron (Mogren *et al*., 2006; Alizadeh *et al*., 2010) [79, 5].

3.3. Metal stress
Heavy metal application may effect the composition of chemical constituents in plants. Quality and efficacy of the natural plant products is seriously altered in many medicinal plants (Nasim and Dhir, 2010; Lizhong and Cullen, 1995) [87, 66]. Plants exposed to heavy metal stress show differential responses in synthesis and accumulation of pharmacologically active molecules. Usage of heavy metals in optimum concentration acts as abiotic elicitors that improve the biosynthesis of specific bioactive compounds (Namdeo, 2007) [86]. It is reported that heavy metals treatment increases the biosynthesis of secondary metabolites in many plant species.

3.4. Salinity/Salt stress
Plant metabolomic studies show varied responses of plants to salinity. Salt stress is a condition in which osmotic forces are exerted on plants by applying excessive salt solutions in soils, due to which the plant growth rate may be decreased but content of secondary metabolites increases significantly. Salt environment leads to cellular dehydration, which causes

osmotic stress and removal of water from the cytoplasm resulting in a reduction of the cytosolic and vacuolar volumes, this leads to increased accumulation of osmolytes like proline, glycine betaine, soluble sugars etc which elicit production of secondary metabolites. Salt stress also triggers ionic stress and leads to enhanced production of reactive oxygen species (ROS); in response to these changes plants produce enhanced amounts of antioxidant phenolic compounds, alkaloids, tannins (Sytar *et al*., 2018) [106]. For example, increase in polyphenol content in different plant parts under salinity has been reported in a number of plants eg. *Cakile maritima* (Asteraceae), *Mentha pulegium* L. (Labiatae) (Dixon *et al*., 1995; Ksouri *et al*., 2007; Oueslati *et al*., 2010) [29, 58, 92].
Numerous studies have been carried out, in the last 2 decades, to study the effect of different abiotic stresses on plant growth and production of secondary metabolites, and their outcomes are summarized in Table 1.

Table 1: Summary of studies demonstrating the effect of abiotic stresses on plant growth and secondary metabolites *in situ*.

Plant Name	Abiotic stress	Observation	Reference
Achillea fragratissima L. (Asteraceae)	Salinity	Increase in tannin and alkaloid content	Abd *et al*., 2009
Artemisia annua L. (Asteraceae)	Drought	Water deficits of 38 and 62 hours increased leaf artemisinin content	Marchese *et al*., 2010
Atriplex hortensis (Amaranthaceae)	Heavy metals i.e. Cu, Ni, Pb, Zn	Decrease in growth rate of the roots and shoots of the plant	Kachout *et al*., 2009
Beta vulgaris L. (Amaranthaceae)	Salinity (150 and 500 mM Nacl for 12 days)	Activity of antioxidant enzymes i.e. Glutathione reductase, Ascorbate peroxidase was stimulated with NaCl treatment	Bor *et al*., 2003
Brassica juncea (Brassicaceae)	Metal (Copper chloride)	Level of Indole phytoalexins increased under the effect of $CuCl_2$	Mithofer *et al*., 2004
	Fertilizer (Nitrogen)	With nitrogen application glutathione reductase activity Increased, required to restore the oxidative balance of glutathione. Data also suggested that glutathione has role in defense mechanisms. Results suggest that the nitrogen fertilizer increased the *Brassica* biomass and by alleviating B-induced oxidative stress.	Giansoldati *et al*., 2012
Brassica napus L. (Brassicaceae)	Flooding	crop yield, the growth of seedlings unaffected by freshwater, but negatively affected by seawater	Hanley *et al*., 2019
Buplerum chinense DC. (Apiaceae)	Fertilizers (0.3 g N+ 0.4 g P_2O_5 kg^{-1})	Increase in saiko-saponin a and d	Zhu *et al*., 2009
Cakile maritima (Brassicaceae)	Salinity	Polyphenols content of the halophytes increases	Ksouri *et al*., 2007
Calendula officinalis L. (Asteraceae)	Fertilizer (180 kg N ha^{-1})	Yield of marigold was increased with nitrogen treatment	Moosavi *et al*., 2014
Camelia sinesis L. (Theaceae)	Drought	Increase in epicatechin content	Mello *et al*., 2006
		Increase in Caffeine level	Munivenkatappa *et al*., 2018
	Shade	Increase level of epicatechin and epigallocatechin in tea leaves	Hagiwara and Wright, 2015
Cassiope tetragona (Ericaceae)	Shade	Increase in myricetin content	Weijers *et al*., 2013
Catharanthus roseus L. (Apocynaceae)	Metal treatment with Cadmium (Cd) concentration ranging from 0.05 to 0.4mM	Increase in amount of Ajmalicine	Zheng and Wu, 2004
	Salinity	Increase in indole alkaloid content in leaves	Misra and Gupta, 2006
	Drought	Increase in ajmalicine content	Jaleel *et al*., 2008
Chrysanthemum boreale M. (Asteraceae)	Fertilizer($CaCO_3$)	At 1.5 ton $CaCO_3$ /hac terpene content was increased sesquiterpenes (30.4%) and monoterpenoids (9.5%), compared to the control.	Lee *et al*., 2005
Coriandrum sativum L. (Apiaceae)	Drought	Water deficit increased percentage of petroselinic, oleic and palmitic acids	Yeganehpoor *et al*., 2017
	Fertilizers	Nitrogen and phosphorus increased crop growth rate and leaf area index	Jamali, 2012
Cucumis sativus L. (Apiaceae)	Salinity	NaCl + Silicon treatment significantly increased the dry weight of shoots and roots	Zhu *et al*., 2004
Datura stramonium (Solanaceae)	Metal	Concentration of Lubimin, 3-OH-l-Lubimin is increased with $Cucl_2$ and $Cdcl_2$ treatment	Mithofer *et al*., 2004
Echinacea angustifolia DC (Asteraceae)	Fertilizers	Nitrate and ammonium in the molar ratio of 1:1 supplied to the plant, the concentrations of chlorogenic acid, echinacoside and caffeic acid were significantly higher in roots of the plant	Montanari *et al*., 2008
Echinacea purpurea (Asteraceae)	Drought	Increase in total phenol content	Gray *et al*., 2003
Elodea (Egeria) densa Planch (Hydrocharitaceae)	Metal	increase the level of chlorophyll and carotenoids in leaves with cadmium treatment	Melava *et al*., 2012
Eucalyptus globulus (Myrtaceae)	Metal	Inoculation of *Pseudomonas orientalis* and *Chaetomium cupreum* on the plant significantly increased plant growth and mitigated	Ortiz *et al*., 2019

		the toxic effects of copper.	
Fragaria ananassa (Rosaceae)	Fertilizers	Increase in ellagic acid, quercetin and kaempferol	Anttonen *et al*., 2006
Glycine max L. (Fabaceae)	Shade	In shade tolerant soybean variety (Nandou 12) showed stiffer stems, higher lignin content, and greater gene expression level	Liu *et al*., 2018
		Structural and non-structural carbohydrates fluctuate significantly under shade stress	Liu *et al*., 2019
	Metal	Level of Glyceollins increased with $HgCl_2$ treatment	Mithofer *et al*., 2004
Glycyrrhiza uralensis (Fabaceae)	Shade	Increased accumulation of glycyrrhizic acid in the root with low light intensity	Hou *et al*.,2010
Gossypium hirsutum (Malvaceae)	Salinity	Inductive response on antioxidant enzyme by salt stress	Meloni *et al*., 2003
Helianthus annuus L. (Asteraceae)	Fertilizers	Total carbohydrate percentage and oil percentage increases significantly with N-P- Fertilizers	Ahmed *et al*., 2010
Hibiscus sabdariffa (Malvaceae)	Metal	Increase in the content of anthocyanins and Flavones	Aziz *et al*., 2007
Hordeum vulgare (Poaceae)	Salinity	Increase in content of Flavonoids	Gulzar *et al*., 2003
Hypericum brasiliense (Clusiaceae)	Flooding	The content of betulinic acid and phenolic compounds i.e. quercetin, rutin is increased	DeAbreu and Poulo, 2005
Ilex paraguariensis (Aquifoliaceae)	Shade	Decrease in Methylxanthine like caffeine, theobromine content with increasing shading.	Coelho *et al*., 2007
Labisia pumila (Myrsinaceae)	Fertilizers	Decrease total flavonoid and phenolics by nitrogen fertilization	Ibrahim *et al*., 2011
Lupinus albus (Fabaceae)	Metal	Level of genistein and 2-OH genistein increased with $CuCl_2$ treatment	Mithofer *et al*., 2004
Lycopersicon esculentum (Solanaceae)	Salinity	Increase in Sorbitol content	Shivajirao, 2010
Matricaria chamomilla (Asteraceae)	Metal	Plant yield was enhanced when treated with heavy metals i.e. Zn, Co, Pb & Ni	Nasim and Dhir, 2009
Mentha arvensis (Lamiaceae)	Metal	Co & Ni enhanced the uptake of essential elements and improve micro and macronutrient status	Aziz *et al*., 2007
Mentha peperita (Lamiaceae)	Fertilizers	Amount of menthol, Peppermint was increased with 75% vermi compost+25% urea application in sandy loam soil	Mohammad *et al*., 2017
Mentha pulegium L. (Labiatae)	Salinity	Increase of total polyphenol content in leaves	Oueslati *et al*., 2010
Origanum vulgare L. (Lamiaceae)	Flooding	Increasing water supply from 30% to 60% available soil moisture increased essential oil percentage and by increasing soil moisture significantly enhanced the fresh herb yield in both seasons.	Said-Al Ahl and Hussein, 2010
Ocimum basilicum (Lamiaceae)	Shade	Decrease total volatile oil with increasing shading, increasing shading decreases linalool and eugenol while increases methyl eugenol content in oil.	Chang *et al*., 2008
Ocimum tenuiflorum (Lamiaceae)	Metal	Increase in the content of Eugenol	Rai *et al*., 2004
Ononis arvensis (Fabaceae)	Metal	Increase the level of flavonoids	Tumova *et al*., 2011
Origanum vulgare L. (Labiatae)	Fertilizers	Fertilization responsible for raising the productivity of herb and the content and yield of essential oil	Said-Al Ahl *et al*., 2009
Oryza sativa L. (Poaceae)	Metal	Growth rate and yield of plant is affected when plant is treated with Cadmium and N	Aina *et al*., 2007
		Amount of volatile oils is effected when treated with $CuCl_2$	Mithofer *et al*., 2004
	Fertilizers	Increase in the level of active compounds	Fan *et al*., 2005
Oryza sativa L. (Gramineae)	Salinity	Inductive response on antioxidant enzyme by salt stress	Lee *et al*., 2001
Papaver somniferum (Papaveraceae)	Drought	Increase in Morphine alkaloids	Szabo *et al*., 2008
Phaseolus vulgaris (Leguminosae)	Shade	Shade stress increases the grain filling and grain weight	Hadi *et al*., 2006
Phyllanthus amarus (Phyllanthaceae)	Metal	Increase the content of Phyllanthin and Hypophyllanthin	Street, 2012
Pisum sativum (Leguminosae)	Metal	Level of Pisatin altered under the effect of $Hgcl_2$	Mithofer *et al*., 2004
	Salinity	Short term effect on antioxidant system	Hernandeza and Almansa, 2002
Populus nigra or Black poplar (Salicaceae)	Drought	Total biomass, leaf area, root mass increased and total phenolic glycosides increased in leaves by water deflict	Hale *et al*., 2005
Prunella vulgaris L. (Labiatae)	Drought	Drought stress with N application enhances the production of rosmarinic acid, ursolic acid and oleanolic acid	Chen *et al*., 2011
Rheum palmatum (Polygonaceae)	Metal	Amount of Anthracene derivatives increased with application of Cadmium chloride and Aluminium chloride	Kasparova and Siatka, 2004

Salvia miltiorrhiza (Lamiaceae)	Fertilizers	Applying phosphorus and potassium fertilizers at different growth stages on root growth, production of bioactive compounds i.e. salvianolic acid B and total tanshinone increased	Lu *et al*., 2013
Salvia officinalis (Lamiaceae)	Salinity	Increase in thujone and camphor content	Hendawy and Khalid, 2005
	Fertilizers	Zinc application increased thujone and camphor content	Hendawy and Khalid, 2005
Scrophularia ningpoensis (Scrophulariaceae)	Drought	Increase in Glycosides	Wang *et al*., 2010
Silybumm arianum (Asteraceae)	Salinity	Increase in silymarin and silybin content	Ghavami and Ramin, 2008
Simarouba glauca (Simaroubaceae)	Drought	Increase in flavonoid, alkaloid tannin and polyphenol content	Awate *et al*., 2014
Simmondsia chinensis (Simmondsiaceae)	Salinity	Salt stress decreases the level of carotenoids in plants but in combination of potassium fertilizer and salt stress the plant yield and level of carotenoids increased	Hussein *et al*., 2014
Solanum lycopersicum L. (Solanaceae)	Drought	Water deficit elevates the amino acid content, especially proline, in leaves and roots of plant	Omena-Garcia *et al*., 2019
		biomass of plant was increased by regular estimating soil moisture content using proximal gamma-ray spectroscopy	Baldoncini *et al*., 2019
Stevia rebaudiana (Asteraceae)	Metal	Plant yield and growth is enhanced	Nasim and Dhir, 2009
Trifolium repens (Fabaceae)	Metal	Level of Medicarpin altered under the effect of $HgCl_2$	Mithofer *et al*., 2004
Triticum aestivum L. (Gramineae)	Salinity	Salt stress increased the contents of hydrogen peroxide (H_2O_2) and thiobarbituric acid reactive substances	Sairam and Srivastava, 2002
Triticum aestivum L. (Poaceae)	Fertilizers	Grain yield was increased with N application	Golbadi and Golkar, 2013
Triticum aestivum L. (Poaceae)	Drought	Grain yield was increased	Chandra *et al*., 2019
Ulmus pumila L. (Ulmaceae)	Salinity	salt stress effects the activity of superoxide dismutase	Song *et al*., 2006
Vicia faba L. (Leguminosae)	Shade	High yield of faba bean plants stress and enhanced grain filling period which led to the production of larger grains	Nasrullahzadeh *et al*., 2007
Vigna radiata L. (Fabaceae)	Drought	Protein and proline percentage increased with drought stress	Mahmoudi *et al*., 2016
Zea mays L. (Poaceae)	Drought	With drought stress and potassium fertilization seed yield is effected	Nejab *et al*., 2010
	Shade	Shade stress effects the yield of the plant	Gao *et al*., 2017

Production of secondary metabolites depends principally on the change in ecosystem in which plant grows. Several factors like climate change, soil type, water availability, salinity, temperature, light and various other adverse conditions have direct effect on the plant biomass and biomarker content. For an instance, it was noticed that under the shade stress the plant yield increased in plants i.e. *Glycine max* L., *Zea mays* L., *Vicia faba* L., *Phaseolus vulgaris* etc. while in *Ocimum basilicum*, total volatile oil content decreased with shade stress. Under the effect of salinity stress tannin and alkaloid content, polyphenol content, flavonoid content increased in *Achillea fragratissima* L., *Cakile maritima*, *Hordeum vulgare* respectively. In *Labisia pumila* plant total flavonoid content decreased with nitrogen fertilization but on other hand, in *Oryza sativa* L., *Origanum vulgare* etc. yield and phytoconstituents content increased under fertilization stress. It was found that, eugenol and flavonoid content increased in plants i.e. *Ocimum tenuiflorum*, *Oronis arvensis* with metal treatment.

It is evident from the literature surveyed, that environmental factors have an impact on the plant growth and biosynthesis of secondary metabolites. Since secondary metabolites are produced in response to stress, if we understand which environmental factor triggers the production of bioactive constituents, that particular factor can be altered during cultivation. If production of bioactive constituents is enhanced there is a direct impact on the activity of the plant. This is very well understood however this knowledge is not translated into practice while cultivating medicinal plants.

It is well accepted all over the world that medicinal plants play a noteworthy role in maintaining health and in the treatment of diseases. These are largely procured from the wild sources. The availability of the plant materials from wild sources is greatly threatened due to deforestation, urbanization and increasing demand for herbal drugs. Cultivation of medicinal plants can insure conservation of environment, a regular sustainable supply as well as uniformity of content. Cultivation practices for many vital medicinal plants are documented. The authors recommend that while developing agrotechnology for medicinal plants it is important to lay emphasis not only on plant yield but also on the content of phytoconstituents. It is necessary to develop the cultivation conditions for optimum biomass yield and incorporate minor, inexpensive changes in the growth environment of the plants (e.g. giving water stress; adding saline once a month; shade stress) that can result in enhanced production of desired secondary metabolites. Once the factors and the changes necessary to elicit the production of the bioactive constituents are elaborated and demonstrated by agricultural/research institutes, knowledge transfer to the cultivators should ensue. Fig. 2 summarizes the application of modification of abiotic factors during cultivation of medicinal plants.

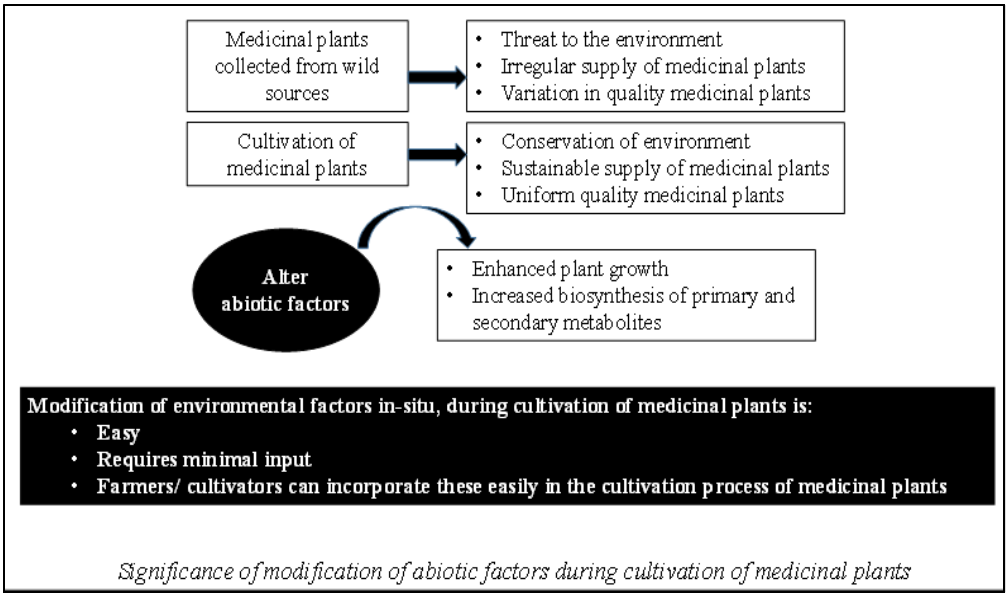

Fig 2: Application of modification of environmental factors during the medicinal plant cultivation.

4. Concluding remarks
The objective of this review was to highlight the influence of different abiotic stresses on the production of secondary metabolites. Based on the study it may be concluded that minor alteration of environment factors that lead to increased phytoconstituents biosynthesis can be easily incorporated during the cultivation of medicinal plants.

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6. Conflict of interest
There is no conflict of interest to declare.

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