



Impact of Various Environmental Factors on Secondary Metabolism of Medicinal Plants



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Article Synopsis

Medicinal plants constitute main resource base of almost all the traditional healthcare systems. Most of the herbal drugs produced currently in majority of the developing countries lack proper quality specification and standards. Herbal drugs used in traditional medicine may contain a single herb or combinations of several different herbs believed to have complementary and/or synergistic effects. Both the raw drugs and the finished herbal products manufactured contain complex mixtures of organic compounds, such as fatty acids, sterols, alkaloids, flavonoids, polyphenols, glycosides, saponins, tannins, terpenes etc. The quality of the finished product is based on the quality of the raw materials, which is again depends on mineral composition of soil, geographical area etc. As many as 35% of the medicinal plants used in Indian systems of medicine are highly cross pollinated which indicate the existence of a wide range of genetic variability in the populations of these medicinal plant species which in turn reflected in the variations in the composition of secondary metabolites. Ecological and edaphic as well as seasonal variations also cause changes in the chemical composition of medicinal plants. These facts have to be considered while developing quality parameters standards of medicinal plants and their finished products.

Abstract

Plants are unrivaled in the normal world in both the number and multifaceted nature of optional metabolites they create, and the pervasive phenylpropanoids and the heredity explicit glucosinolates speak to two such extensive and artificially various gatherings. Advances in genome-empowered organic chemistry and metabolomic innovations have incredibly expanded the comprehension of their metabolic systems in various plant species. There likewise has been some advancement in illustrating the quality administrative systems that are vital to their amalgamation, amassing and work. Auxiliary metabolites have critical resistance and flagging jobs, and they add to the general nature of creating and maturing organic products. Particularly, light conditions and temperature are exhibited to have a noticeable job on the arrangement of phenolic mixes. The present survey centers around the examinations on instruments related with the control of key auxiliary metabolites, principally phenolic mixes, in different plants. are a helpful cluster of characteristic items as well as a vital piece of plant barrier framework against pathogenic assaults and natural burdens with noteworthy natural exercises, plant SMs are progressively utilized as drug fixings and sustenance added substances for helpful, fragrant and culinary purposes. Different hereditary, ontogenic, morphogenetic and natural elements can impact the biosynthesis and gathering of SMs. As per the writing reports, for instance, SMs amassing is unequivocally subject to an assortment of natural factors, for example, light, temperature, soil water, soil richness and saltiness, and for most plants, an adjustment in an individual factor may modify the substance of SMs regardless of whether different components stay steady. Here, we survey with accentuation how every one of single variables to influence the gathering of plant optional metabolites and lead a similar examination of pertinent characteristic items in the pushed and unstressed plants. Eagerly, this narrative audit will plot a general picture of ecological components in charge of variance in plant SMs, give a down to earth approach to get steady quality and high amount of bioactive mixes in vegetation, and present a few recommendations for future innovative work.

Purpose of the study

An illustrated review of factors that influence secondary metabolism of plants and their impacts on therapeutic efficacy changes along with environmental factors.

Findings: Traditional plants are used from ancient time for various human well-being, both as life-saving and lifestyle drugs. A careful observation may explore facts behind therapeutic efficacy of these plants.

Materials and Methods: A comprehensive literature review, consulting books, technical newsletters, herb magazines, journals, and many other sources. Health professionals like qualified doctors, herbal specialists, folk healers, alternative medicine specialists given their valuable suggestions.

Research limitations: The limitation lies with the unlimited information about traditional medicines. Validity of those are very hard to prove. Only data obtained from books, newsletters, national and international research-based articles are given here along with surrounding facts mostly visible. A few many plant medicine books consulted earlier but article has fewer scope to add from them.

Practical Implication: The article is based on plant medicine which is a specialized topic. Students, researchers and professionals may acquire much from this article.

Keywords: Medicinal Plants; Organic Compounds; Secondary Metabolite; Biosynthesis

Abbreviations: SMs: Secondary Metabolites; CoA: Coenzyme A; ADP: Adenosine Diphosphate; ATP: Adenosine Triphosphate; NADP: Nicotinamide Adenine Dinucleotide Phosphate; Acetyl-CoA: Acetyl Coenzyme A

Introduction

While in food plants our main interest is the carbohydrate/sugars, proteins, fats and other vitamins, in medicinal plants we look for therapeutically useful chemicals which are generally termed as secondary metabolites which are not that essential for the normal growth and development of the plants/organisms. Plants synthesize these compounds to protect themselves i.e. to adjust, adapt or defend/ offend, from the hostile organisms or diseases or the environment. SMs that are useful in medicine are mostly polyphenols, alkaloids, glycosides, terpenes, flavonoids, coumarins, tannins etc. The production of secondary metabolites although controlled by genes but their specific expression is greatly influenced by various factors including biotic and abiotic environments such as climate and edaphic factors or other associated living organisms. During the course of evolution plants have evolved various physical and chemical mechanisms to protect themselves from the vagaries of nature (drought, heat, rain, flood, etc.) and also to defend or offend the predators or to protect from predators and pathogens. The most successful adaptation

of plants while developing various physiological mechanisms is through the production of a variety of phytochemicals by which they were able to face both biotic and abiotic stresses and threats.

In this process of defense/ offence from abiotic stress or the invading diseases causing organisms or the predators (animals, birds, insects and herbivorous animals), the plant synthesize a variety of chemical compounds. Apparently, plants produce many antioxidants for protecting themselves from the oxidative stress. These compounds are in general stored in the leaves or other parts such as, bark, hardwood, fruits, etc., so that the predators or the disease-causing organisms can be either knocked down or paralyzed or even get killed. In many cases, the production of the secondary metabolites in plant also depends on the association of other living organisms, more particularly, the plant or soil microbes. Such differential expressions of therapeutically active principles in plant on account of the above said factors appears to have known and well understood by the ancient scholars, when they gave specific instructions in the procurement of medicinal plants.

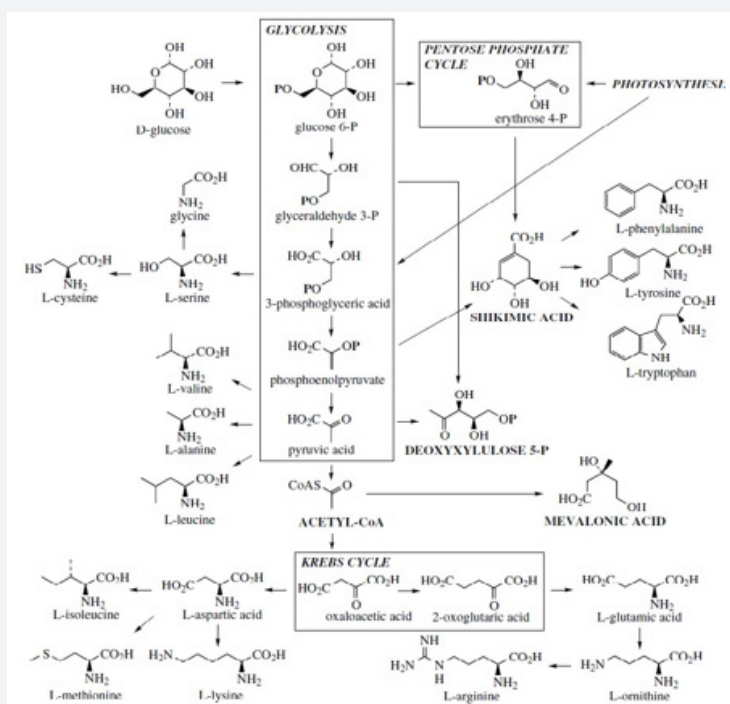


Figure 1. Biosynthesis scheme of plants secondary metabolites [8].

Biosynthesis

The pathways of biosynthesis are responsible for the occurrence of both primary and secondary metabolites illustrated in Figure 1. Biosynthetic reactions are energy consuming, fueled by the energy released by glycolysis of carbohydrates and through

the citric acid cycle. Oxidation of glucose, fatty acids and amino acids results in ATP formation, which is a high-energy molecule formed by catabolism of primary compounds. ATP is recycled in fuel anabolic reactions involving intermediate molecules on the pathways. Whereas, catabolism involves oxidation of starting

molecules, biosynthesis or anabolism involves reduction reaction. Hence, the need of reducing agent or hydrogen donor, which is usually the NADP. These catalysts are known as coenzymes and the most widely occurring is CoA made up of ADP and pantetheine phosphate. The most common pathways taken for biosynthesis are performed through the pentose for glycosides, polysaccharides; shikimic acid for phenols, tannins, aromatic alkaloids; acetate-malonate for phenols and alkaloids and mevalonic acid for terpenes, steroids and alkaloids. As showed in the Fig. 1, the scheme outlines how metabolites from the process of photosynthesis, glycolysis and Krebs cycle are tapped off from energy-generating process to provide biosynthetic intermediates. By far, the important building blocks employed in the biosynthesis of secondary metabolites are derived from Acetyl-CoA, shikimic acid, mevalonic acid and 1-deoxyulose 5-phosphate [1-7] [Figure.1]

Expression of Secondary Metabolites

The presence of or absence of certain secondary metabolites in medicinal plants are influenced by a variety of factors [8], which include climate/ season, edaphic conditions or the association of other plants and other living organisms [9]. Another factor that influenced the production of secondary metabolites in plants are the inter relationship between plants and the insect flora. It is now generally accepted that the flora and the insect flora in a tropical ecosystem have been co-evolving and co-adapting. Many of the medicinal plants are cross-pollinated and they need the help of pollinators. In an open area the wind could do the function, but in a canopied forest many of the shrubs and herbs growing under the big trees cannot get wind to pollinate. These plants are thus heavily depending upon the insects or even the birds to pollinate them. To attract the insects or birds the plants develop pleasant aroma (essential oils) and provide honey and pollen as food to these pollinators. Many flowers contain honey or pollen, which are the normal food of many insects and birds [10,11]. The insects like bees and butterflies visit flowers after flowers and take honey or pollen or both. During this process they also carry pollen on their body part, which then help in pollinating while visiting other plants. Many flowers have structurally evolved flower parts to affect such pollinations by insects.

These insects also multiply on plants. They lay millions of eggs and the larvae that emerge from these eggs then feed on leaves of the plants, sometimes destroying the plants altogether by over feeding. During the course of evolution, the plants began to synthesize certain toxic substance so that a good percentage of the feeding larvae could be killed [12-14]. The insect on the other hand began to develop resistance so that many of the larvae could survive. The plants on the other hand again counteracted. It is synthesizing more and more toxic compounds. This was something like the love and hate relationship between plants and the insects, which during the course of millions of years of evolutions have resulted in the synthesis of innumerable chemical compounds, mostly the secondary metabolites in plants as well as

in insects [15,16]. The variability in living organisms is indeed the insurance for survival. The evolutionary origin of cross breeding was indeed a nature's device for reshuffling of genes so that new variants could be produced. Similarly, the abiotic conditions also exerted certain influence in the plants and the plants responded by developing various chemicals [17]. In extreme drought conditions the desert exerts a kind of stress on the plants and the plants evolve by synthesizing chemicals that would help them to protect from stress induced by the desert conditions.

An excellent example for this is the plant *Commiphora wightii*; an important medicinal plant used extensively as complimentary medicine named 'Guggul'. The medicinal part of the plant is the gum exudates from the stem bark of living plants. This gum is traditionally collected from the desert regions of Rajasthan, Gujarat and even Afghanistan. To everyone's surprise the chemical data of this gum revealed that it does not contain most of the active compounds. A logical explanation may be that this plant growing in a warm humid tropical forest region. It has no desert like conditions and therefore there is no question of any drought induced stress. The same plant when growing in desert has to confront drought induced stress and the plant synthesizes the stress beating chemicals. There are many similar cases that demonstrate that certain specific climatic conditions and edaphic situations are extremely important in the production of therapeutically desirable medicinal compounds. Sandalwood is another classical example. The specific aroma of sandalwood is due to the presence of certain essential oil chemicals, mostly monoterpenes and sesquiterpenes. The production of the specific aroma chemicals is fully expressed only in those sandalwood trees that grow in certain forest regions of Karnataka. The sandalwood growing in other places in India or elsewhere in the world do not have the same kind of aroma with the corresponding chemical constituents [18-20].

Importance of Secondary Metabolites

Secondary metabolites, which are a characteristic feature of plants, are especially important and can protect plants against a wide variety of microorganisms (viruses, bacteria, fungi) and herbivores (arthropods, vertebrates). As is the situation with all defense systems of plants and animals, a few specialized pathogens have evolved in plants and have overcome the chemical defense barrier. Secondary metabolites, including antibiotics, are produced in nature and serve survival functions for the organisms producing them. Secondary metabolites serve:

- As competitive weapons used against other bacteria, fungi, amoebae, plants, insects, and large animals;
- As metal transporting agents;
- As agents of symbiosis between microbes and plants, nematodes, insects, and higher animals;
- As sexual hormones; and
- As differentiation effectors.

Although antibiotics are not obligatory for sporulation, some secondary metabolites (including antibiotics) stimulate spore formation and inhibit or stimulate germination. Formation of secondary metabolites and spores are regulated by similar factors. Thus, the secondary metabolite can:

- a. Slow down germination of spores until a less competitive environment and more favorable conditions for growth exist.
- b. Protect the dormant or initiated spore from consumption by amoebae; or
- c. Cleanse the immediate environment of competing microorganisms during germination [21-24].

Environmental Stress and Secondary Metabolites in Plants

Environmental factors significantly affect plant growth and biosynthesis of SMs. Plant growth and productivity is negatively affected by temperature extremes, salinity, and drought stress. Plant SMs are compounds that play an essential part in the interaction of plants with abiotic stresses [25]. In addition, plant growth and development are also largely mediated by the endogenous levels of these SMs. A wide range of SMs are produced from primary metabolites such as amino acids, lipids, and carbohydrates in higher plants. Particular colors, tastes, and odors of plants are associated with SMs. Plant SMs also serve as essential sources of industrially important chemicals, flavors, food additives, and pharmaceuticals [26]. Plants accumulate such compounds in response to different signaling molecules. SM production is influenced by various environmental stresses. Environmental factors determine the synthesis and subsequent accumulation of SM. Alteration in any one factor triggers perturbations in the biosynthesis of plant SMs [27].

Differential Responses of Plants to Biotic Stress

Plants contribute a lot to this universe, but they have to face many stresses of biotic or abiotic nature. Biotic stress is a severe environmental constraint to the plant's productivity. Biotic stress induces loss in crop yield probably more than the cumulative losses from all other factors. In any stress, the type and duration are critical for plant growth [28]. Plants use various defensive strategies to tolerate these adverse factors. Of the various defensive mechanisms, one is the production of reactive oxygen species. These defensive mechanisms against biotic stress are generated as a result of the continuous interaction between plant and pathogen [29]. Plants' responses to biotic stress are not only the alteration in anatomical features, such as formation of a waxy cuticle, trichome, setae, and spines, but also the production of various secondary metabolites. Such types of plant responses have been observed against bacteria, fungi, and pests. These secondary metabolites trigger different plant defense mechanisms in the form of ascorbic acid, antioxidative enzymes (peroxidase, polyphenol oxidase, lipoxygenases), salicylic acid, jasmonic acid, and Ca²⁺ against biotic stress and also act as toxins (terpenes, alkaloids, and phenolic compounds) against plant pathogens [30].

Engineering of Biomass Accumulation and Secondary Metabolite Production

Plants are the source of valuable secondary metabolites that are commonly used in pharmaceutical, food, agricultural, cosmetic, and textile industries [31]. Plant cell and tissue culture technologies can be established routinely under sterile conditions from explants, such as plant leaves, stems, roots, and meristems for both the ways for multiplication and extraction of secondary metabolites. In vitro production of secondary metabolite in plant cell suspension cultures has been reported from various medicinal plants, and bioreactors are the key step for their commercial production. Based on this line of thought, the present review is aimed to cover phytotherapeutic application and recent advancement for the production of some important plant pharmaceuticals [32]. The increasing commercial importance of secondary metabolites has resulted in a great interest in research focusing on secondary metabolism and finding alternative ways for secondary metabolite production. Plant cell and tissue cultures are branches of plant biotechnology and they have been introduced as alternative ways for the production of valuable secondary metabolites. Plant technology provides a continuous and reliable source for pharmaceutical phytochemicals and can easily be scaled up [33]. Therefore, plant cell and tissue cultures have a great potential to be used as an alternative to traditional agriculture for the industrial production of secondary metabolites [34,35].

Response to Secondary Metabolism to Light Irradiation

The key factors related light radiation include photoperiod (duration), intensity (quantity), direction and quality (frequency or wavelength). In response to light radiation, plants are able to adapt to the changes of circumstances by the release and accumulation of various secondary metabolites including phenolic compounds, triterpenoids and flavonoids, and many of them, have high economic and utilization value due to the well-known antioxidant property [36]. (Table 1) Camptothecin (CPT) class of compounds has been demonstrated to be effective against a broad spectrum of tumors. Their molecular target has been firmly established to be human DNA topoisomerase I (topo I). The medicinal plant *Centella asiatica* (L.) Urban contains mainly ursane-type triterpene saponins, the most prominent one is asiaticoside. It is now firmly established that the major bioactivities of *C. asiatica* leaf extracts are due to these saponins, including memory improvement, wound and vein healing, antihistaminic, antiulcer and antilepsy treatments, as an antidepressant, and as antibacterial, antifungal, and antioxidant agents [37-45]. As a familiar indole alkaloid, the SM camptothecin can respond to environmental stresses and its accumulation rate can change with light irradiation conditions. It is known that overshadowing can induce biochemical changes in plants, particularly in leaves, and heavy shading of only 27% full sunlight, for example, can elevate the concentration of camptothecin in leaves of *Camptotheca acuminata*, whereas substantially reduce that in the lateral roots of this tree (Table 2).

Table 1: Photoperiod change on the content of various plant SMs [37-41].

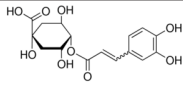
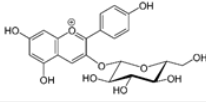
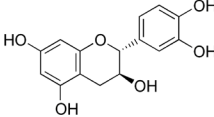
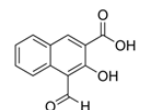
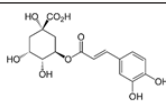
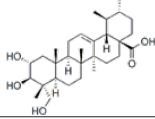
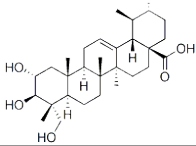
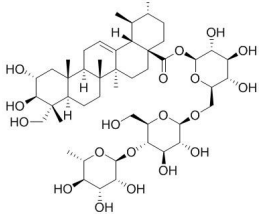
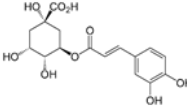
Metabolite Class	Metabolite Name	Structural Image	Environment Factor	Concentration Change	Plant Species
Phenols	Caffeoylquinic acids		Short day of light	Decrease	<i>X. pensylvanicum</i>
Phenols	Pelargonidin		Short day of light	Decrease	<i>P. contorta</i>
Phenols	Catechins		Long day of light	Increase	<i>I. batatas</i>
Phenols	Hydroxybenzoic acids		Long day of light	Increase	<i>I. batatas</i>
Phenols	Chlorogenic acid		Long day of light	Increase	<i>V. myrtillus</i>

Table 2: Light intensity changes on the content of various plant SMs [42-45].

Metabolite Class	Metabolite Name	Structural Image	Environment Factor	Concentration Change	Plant Species
Alkaloids	Camptothecin		27% Full sunlight	Increase	<i>C. acuminata</i>
Phenols	Asiatic acid		70% Shade	Increase	<i>C. asiatica</i>
Phenols	Asiaticoside		Full sunlight	Increase	<i>C. asiatica</i>
Phenols	Chlorogenic acid		Full sunlight	Increase	<i>V. myrtillus</i>

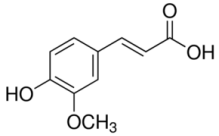
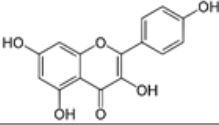
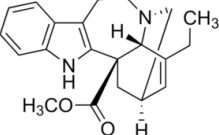
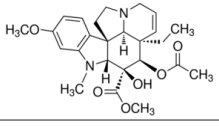
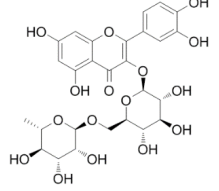
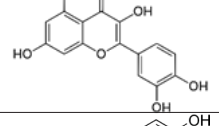
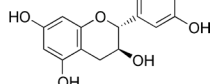
There has been considerable public and scientific interest in the use of phytochemicals derived from dietary components to combat human diseases. They are naturally occurring substances found in plants. Ferulic acid (FA) is a phytochemical commonly found in fruits and vegetables such as tomatoes, sweet corn and rice bran. It arises from metabolism of phenylalanine and tyrosine by Shikimate pathway in plants. It exhibits a wide range of therapeutic effects against various diseases like cancer, diabetes, cardiovascular and neurodegenerative [46-60] (Table 3) Kaempferol (3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one) is a flavonoid found in many edible plants (e.g., tea, broccoli, cabbage, kale, beans, endive, leek, tomato,

strawberries, and grapes) and in plants or botanical products commonly used in traditional medicine (e.g., Ginkgo biloba, Tilia spp, Equisetum spp, Moringa oleifera, Sophora japonica and propolis). Its anti-oxidant/anti-inflammatory effects have been demonstrated in various disease models, including those for encephalomyelitis, diabetes, asthma, and carcinogenesis. Moreover, kaempferol act as a scavenger of free radicals and superoxide radicals as well as preserve the activity of various anti-oxidant enzymes such as catalase, glutathione peroxidase, and glutathione-S-transferase. The anticancer effect of this flavonoid is mediated through different modes of action, including anti-proliferation, apoptosis (Table 4) induction, cell-cycle

arrest, generation of reactive oxygen species (ROS), and anti-metastasis/anti-angiogenesis activities [61-63]. (Table 5) Context *Catharanthus roseus* (L.) G. Don (Apocynaceae) is still one of the most important sources of terpene indole alkaloids including anticancer and hypertensive drugs as vincristine and vinblastine. These final compounds have complex pathway and many enzymes are involved in their biosynthesis [64]. Indeed, ajmalicine and catharanthine are important precursors their increase can lead

to enhance levels of molecules of interest. A direct coupling of catharanthine with vindoline to provide vinblastine is detailed along with key mechanistic and labeling studies. With the completion of a first-generation total synthesis of vindoline that was extended to a series of related analogues. The antioxidant effects of the flavonoids rutin and quercetin inhibit oxaliplatin-induced chronic painful peripheral neuropathy.

Table 3: Light quality change on the content of various plant SMs [46-51].

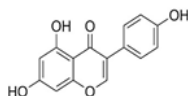
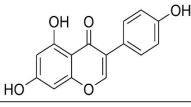
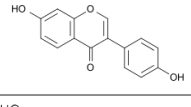
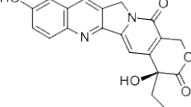
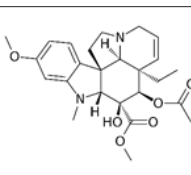
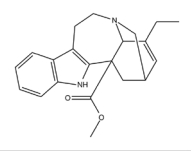
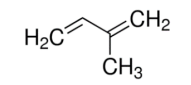
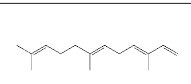
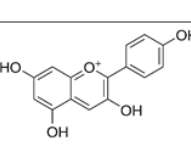
Metabolite Name	Structural Image	Metabolite Class	Environment Factor	Concentration Change	Plant Species
Ferulic acid		Phenols	Increase red light	Decrease	<i>L. sativa</i>
Kaempferol		Phenols	Increase red light	Decrease	<i>L. sativa</i>
Catharanthine		Alkaloids	UV-B	Increase	<i>C. roseus</i>
Vindoline		Alkaloids	UV-B	Increase	<i>C. roseus</i>
Rutin		Phenols	UV	Increase	<i>F. esculentum</i>
Quercetin		Phenols	UV	Increase	<i>F. esculentum</i>
Catechins		Phenols	UV	Increase	<i>F. esculentum</i>

Response of Plant SMs to Temperature

The modulation of temperature to alkaloids accumulation was reported, and high temperature preferable to induce the biosynthesis of alkaloids. The total accumulation of alkaloids (morphinane, phthalisoquinoline and benzyloisoquinoline) in dry *Papaver somniferum* was restricted at low temperature [65]. In contrast, the total level of phenolic acids and isoflavonoid (genistein, daidzein and genistin) in soybean (*Glycine max*) roots increased after the treatment at low temperature for 24h, and among which the highest increase of about 310% was observed in genistin after the treatment at 10 °C for 24h, in comparison to the

control [52,53]. In women, aging and declining estrogen levels are associated with several cutaneous changes, many of which can be reversed or improved by estrogen supplementation. Experimental and clinical studies in postmenopausal conditions indicate that estrogen deprivation is associated with dryness, atrophy, fine wrinkling, and poor wound healing. The isoflavone genistein binds to estrogen receptor β and has been reported to improve skin changes. In vitro data has shown that the soy isoflavones genistein and daidzein may even stimulate the proliferation of estrogen-receptor alpha positive (ER α +) breast cancer cells at low concentrations.

Table 4: Temperature change on the content of various plant SMs [50,54-58].

Metabolite Class	Metabolite Name	Structural Image	Environment Factor	Concentration Change	Plant Species
Alkaloids	Morphine		Low temperature	Decrease	<i>P. somniferum</i>
Phenols	Genistein		10 °C for 24 h	Increase	<i>G. max</i>
Phenols	Daidzein		10 °C for 24 h	Increase	<i>G. max</i>
Alkaloids	10-hydroxycamptothecin		40 °C for 2 h	Increase	<i>C. acuminata</i>
Alkaloids	Vindoline		Short-term heat	Increase	<i>C. roseus</i>
Alkaloids	Catharanthine		Long-term heat	Increase	<i>C. roseus</i>
Terpenes	Isoprene		High temperature	Increase	<i>Q. rubra</i>
Terpenes	α -farnesene		High temperature	Increase	<i>D. carota</i>
Phenols	Pelargonidin		Low temperature	Increase	<i>Z. mays</i>

10-Hydroxycamptothecin (10-HCPT), an indole alkaloid isolated from a Chinese tree, *Camptotheca acuminata*, inhibits the activity of topoisomerase I and has a broad spectrum of anticancer activity in vitro and in vivo. However, its use has been limited due to its water-insolubility and toxicity with i.v. administration. Isoprene is synthesized through the 2-C-methylerythritol-5-phosphate (MEP) pathway that also produces abscisic acid (ABA). Increases in foliar free ABA concentration during drought induce stomatal closure and may also alter ethylene biosynthesis. This first report on α -farnesene synthesis in *Y. lipolytica* lays a foundation for future research on production of sesquiterpenes in *Y. lipolytica* and other closest yeast species and will potentially contribute in its industrial production. Pelargonidin chloride is an anthocyanidin chloride that has pelargonidin as the cationic counterpart. It has a role as a phytoestrogen and a plant metabolite. It contains a pelargonidin.

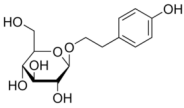
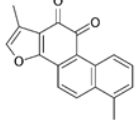
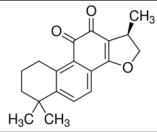
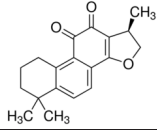
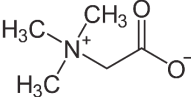
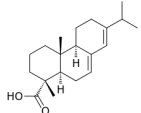
Response of Plant SMs to Soil Water

Water stress is one of the most important environmental stresses that can regulate the morphological growth and development of plants and alter their biochemical properties. Severe water deficit has been considered to reduce the plants growth, but several studies have demonstrated that water stress may be possible to increase the amount of SMs in a wide variety of plant species [59,60]. Salidroside is isolated from *Rhodiola rosea* and is one of the main active components in *Rhodiola* species. *Rhodiola rosea* has long been used as a medicinal plant and has been reported to have various pharmacological properties, including antifatigue and anti-stress activity, anticancer, antioxidant and immune enhancing and stimulating sexual activity, anti-inflammation, improvement of glucose and lipid metabolism, antiarrhythmic effect, and enhancement of angiogenesis [61-64]. Tanshinone IIA (Tan-IIA) is derived from the dried roots of *Salvia*

miltiorrhiza Bunge, a traditional Chinese medicine. Although *Salvia miltiorrhiza* has been applied for many years, the toxicity of the mono-constituent of *Salvia miltiorrhiza*, tanshinone IIA, is still understudied. Molecular evidence found with cryptotanshinone

for treatment and prevention of human cancer. Synthesis of the compatible solute glycine betaine confers a considerable degree of osmotic stress tolerance to *Bacillus subtilis*. Recent study reveals that abietic acid can be developed as a wound-healing agent.

Table 5: Soil water change on the content of various plant SMs [61-64].

Metabolite Class	Metabolite Name	Structural Image	Environment Factor	Concentration Change	Plant Species
Phenols	Salidroside		Soil moisture of 55-75%	Increase	<i>R. sachalinensis</i>
Phenols	Tanshinone		Severe drought	Increase	<i>S. miltiorrhiza</i>
Phenols	Cryptotanshinone		Severe drought	Increase	<i>S. miltiorrhiza</i>
Alkaloids	Codeine		Drought	Increase	<i>P. somniferum</i>
Alkaloids	Glycine betaine		Drought	Increase	<i>C. roseus</i>
Phenols	Abietic acid		Severe drought	Increase	<i>P. sylvestris</i>

Conclusion

SMs are the useful natural products that are synthesized through secondary metabolism in the plants. The production of some secondary metabolites is linked to the induction of morphological differentiation and it appears that as the cells undergo morphological differentiation and maturation during plant growth. It is observed that in-Vitro production of secondary metabolites is much higher from differentiated tissues when compared to non-differentiated or less -differentiated tissues. There are lots of advantages of these metabolites like there is recovery of the products will be easy and plant cultures are particularly useful in case of plants which are difficult or expensive and selection of cell lines for high yield of secondary metabolites will be easy. Many other examples could be presented with plant metabolic engineering as this research area is developing actively. Metabolic engineering is probably a large step forward but playing on the genes will not solve all the problems that have prevented the development of commercial success in the field of plant secondary metabolites. And Advances in plant cell cultures could provide new means for the cost-effective, commercial production of even rare or exotic plants, their cells, and the chemicals that they will produce. Knowledge of the biosynthetic pathways of

desired compounds in plants as well as of cultures is often still rudimentary, and strategies are consequently needed to develop information based on a cellular and molecular level. Because of the complex and incompletely understood nature of plant cells in-vitro cultures, case-by-case studies have been used to explain the problems occurring in the production of secondary metabolites from cultured plant cells. Advance research has succeeded in producing a wide range of valuable secondary phytochemical in unorganized callus or suspension cultures till to date; in other cases, production requires more differentiated micro plant or organ cultures.

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purpose from any authority, the experience was good enough to carry on research.

Compliance with Ethical Standards

a) Ethics approval and consent to participate

I. Animal and Human experiment: N/A

II. Human Data Submission Approval: N/A

b) Consent for publication

Consent to publish Individual Person's data: N/A

c) Availability of data and materials

Data sharing: Please contact author for data requests

D) Competing interests

The authors declare that they have no competing interests

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