

IMPACT OF GEOGRAPHICAL LOCATION ON PHYTOCHEMICAL COMPOSITION AND QUALITY OF MEDICINAL PLANTS AND FOOD CROPS: A COMPREHENSIVE REVIEW

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ABSTRACT

The therapeutic, nutritional and commercial value of medicinal plants and food crops are largely dependent on their phytochemical composition. This review provides a comprehensive synthesis of the role that geographical location plays in determining these bioactive compounds. Environmental factors stimulate considerable differences in the production of essential compounds, such as alkaloids, phenolics, flavonoids and terpenoids by modulating plant physiological processes and specialized secondary metabolic pathways. This chemical plasticity is usually a direct result of plants adaptation to local ecological stresses and ecological variation. The article discusses the mechanistic role of geography by outlining the importance of responses to stress and certain ecological interactions to broad phytochemical diversity. It highlights case studies of high-value medicinal species such as ginseng, *Artemisia annua* L. (Asteraceae), *Cryptolepis sanguinolenta*

(Lindl.) Schltr (Apocynaceae) and *Catharanthus roseus* (L.) G. Don (Apocynaceae), as well as food crops including *Camellia sinensis* (L.) Kuntze (Theaceae), *Vitis vinifera* L. (Vitaceae) and *Oryza sativa* L. (Poaceae) to demonstrate these multifaceted effects. Furthermore, it evaluates the importance of advanced analytical techniques such as chromatography, spectroscopy and high-throughput metabolomics in assessing, tracing and quantifying these geographical variations. Finally, the review examines implication of these variations to

pharmaceutical standardization, agricultural optimization and food science. The article identifies future research directions, which include the integration of genomics, metabolomics and climate modeling to ensure high quality and sustainable utilization of plant resources in a rapidly changing global environment.

KEYWORDS: Geographical diversity, phytochemical composition, medicinal plants, food crops.

1. INTRODUCTION

The therapeutic and nutritional value of medicinal plants and food crops are linked to their phytochemical quality, a complex composite, which include the concentration, diversity and interaction of bioactive secondary metabolites.^[1] In both clinical pharmacology and functional food science, it is assumed that the biological activity of a plant is remains as constant across different growing conditions. However, recent studies demonstrate the plant metabolome is highly plastic and is heavily dependent on its growth condition.^[1] The critical factor of such chemical plasticity is the geographical origin, which is a complex influence of the abiotic and biotic stressors.^[2] Plants of the same species that are grown in different geographic locations characterized by different latitudes, longitudes and altitudes often have considerably different chemical fingerprinting, despite being genetically identical.^[1] Such variability presents a significant challenge in the standardization and reproducibility of herbal medicine, because the same species can have different pharmacological potential based on its provenance.^[3]

Geographical location determines a number of important environmental factors, such as changes in temperature, precipitation, and soil composition, all of which can influence the levels of secondary metabolites.^[4] For instance, altitude is a significant cause of phytochemical changes, elevated altitudes tend to expose plants to higher amount of ultraviolet radiation and atmospheric pressure leading to accumulation of protective phenolics and essential oils.^[4,5] One example is *Salvia officinalis*, in which altitudinal differences cause changes of the metabolic pattern from predominance in sesquiterpenes at low altitude to monoterpenes at high altitude.^[4] Similarly, the interaction between local microclimates with variation in soil fertility and mineral content are used to define the suitability zoning of a crop that is required to maximize yields.^[3]

These metabolic changes are not just accidental but evolutionary changes that are designed to guarantee survival in the face of local environmental stress.^[1] Other stress factors such as water shortage or lack of nutrients in certain landscapes can prime metabolic pathways, leading to an increase in the concentration of health-promoting antioxidants and alkaloids.^[3,5] However, existing literature is disjointed, concentrating on individual aspects, instead of the totality of the terroir influence of geographic location. This review focuses on bringing together existing literature on the effect of geographic location on the quality of medicinal plants and food crops. The review will capture the mechanisms of adaptation to the environment and emphasize the role geographical traceability plays in determining the consistency, safety and effectiveness of plant-based products.

2. METHODOLOGY

An extensive review of published materials was conducted in PubMed, Scopus, Web of Science, google scholar, research gate, Elsevier, SciFinder, ACS using combination of search key words and strategy: geographical location, phytochemical composition or secondary metabolites, medicinal plants, food crops, environmental factors or climate or soil or altitude and plant quality or bioactive compound. The predefined inclusion criteria were used to evaluate full-text articles after eliminating duplicates and filtering titles and abstract. The inclusion criteria were that studies should be peer-reviewed, written in English and report the influence of environment or geographical location on the phytochemical composition or plant quality. A total of 114 articles were selected and critically analyzed in this review. The review flow chat is illustrated in **Figure 1**.

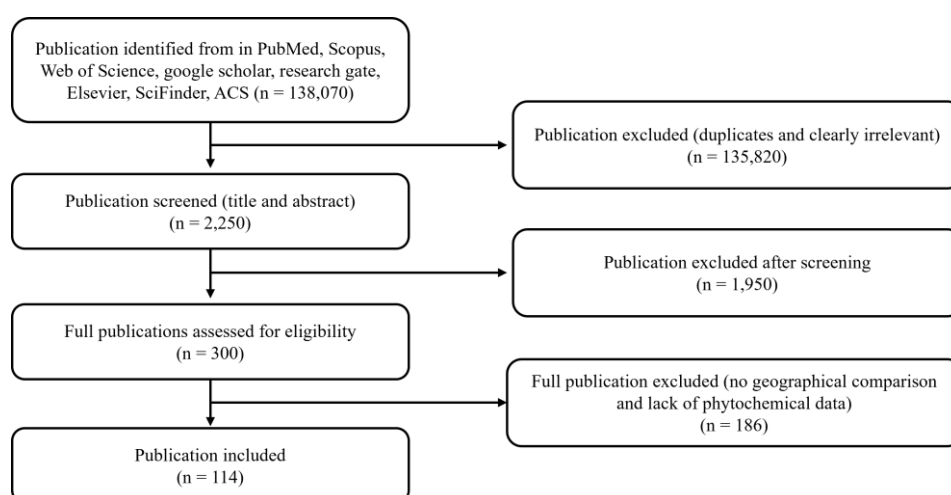


Figure 1: A flow chart illustration of literature search, screening and selection of relevant publication.

3. Conceptual framework

3.1. Primary and Secondary metabolites

Plant metabolome has traditionally been divided into primary and secondary metabolites, though the activity delimiting these domains is becoming more recognized to be dynamic.^[6] Carbohydrates, lipids and amino acids are primary metabolites that ensure the survival of the plant, support its basic function, such as respiration and growth.^[1] Secondary metabolites include alkaloids, phenolics, and terpenoids, these metabolites do not play a crucial role in plant survival but are important in adapting to the environment and providing defense.^[1,7]

Recent studies suggest that the secondary metabolites are the main agents of therapeutic activity and nutritional value of a plant.^[3] Synthesis of secondary metabolites can be influenced by environmental signals, where the plant diverts energy used in primary growth to protective pathways.^[3] According to this metabolic trade-off, stressful condition of growth are frequently associated with increased level of bioactive fractions than those of optimized growth conditions.^[7]

3.2. Plant and Environmental interaction

Metabolic plasticity is the interaction between a plant and the environment, where geographical origin acts as a combination of holistic abiotic and biotic selective pressure.^[1,2] The terroir effect determines the unique chemical fingerprint, or chemotype of a plant population.^[1] Since secondary metabolites are the chemical interface between the plant and the environment, their synthesis is extremely sensitive to local environmental changes.^[8]

Geographical origin is a determinant of the chemical variability because it can provide certain triggers, including extremes in temperature, water and sun radiation patterns, which can influence certain metabolic pathways.^[2] The relationship between geographical location, plant physiological processes and phytochemical response is summarized in **Figure 2**. For instance, a species cultivated in different location can have identical genetic blueprint but produce significantly different pharmacological characteristics when it is adaptively regulated by specialized metabolism.^[1,3]

3.3. Geographical location

Geographical location is a multidimensional measure of the phytochemical quality control that has been characterized by latitude, longitude and altitude.^[4] Latitude and longitude give a coordinates of larger climatic regions and seasonal photoperiods and altitude is a specialized

proxy of a set of eco-physiological stressors.^[9] Altitude is considered as the most significant geographical variable known to have an impact on plant chemistry.^[4] Low temperature, reduced atmospheric pressure, and increased UV-B radiation are some features of high-altitude environment, which have been demonstrated to cause the buildup of protective antioxidants such as phenolics and flavonoids.^[4,5] Furthermore, geographic location comprises of specific soil composition (pedology) location, the presence of soil minerals and nutrients in the interaction with the climate determines the ultimate density and quality of plant-derived bioactive compounds.^[3,5] This interaction of the spatial and environmental factors forms a suitability zone, which are essential for the standardization of medicinal plants and food crops.^[3]

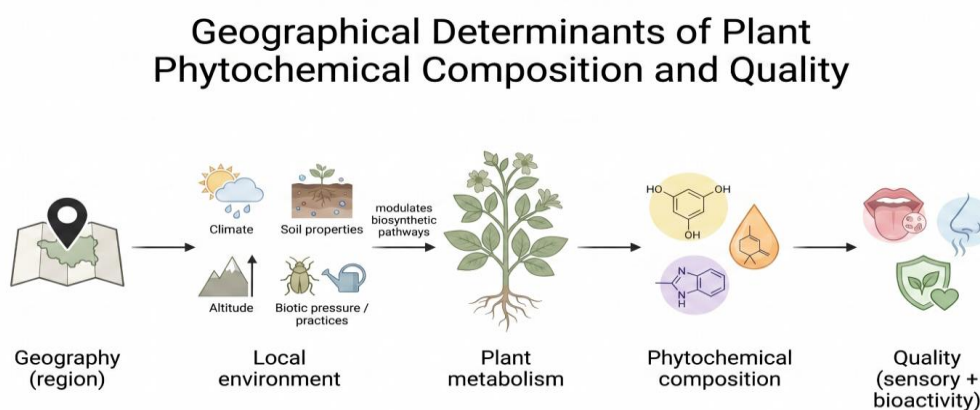


Figure 2: Summary of the relationship between geographic influences, plant physiological processes and phytochemical responses.

4. Geographical factors that influence the quality of plants

4.1. Climate

Temperature

Temperature is a basic geographical determinant that influences the speed of metabolic and enzymatic activities. Plants in geographical areas vulnerable to drastic changes in temperature are exposed to severe abiotic stress, which potentially causes low yield and changing chemical composition.^[10] In particular, growth may not occur in some high-latitude regions due to low temperatures, which disrupts nutritional cycle. Some studies have demonstrated that the plants in these areas have to reprogram their rhizosphere to modulate nitrogen-cycling as an adaptive response.^[11] In addition, thermal stress influences the capability of the plant to sustain cellular homeostasis and in many cases, stimulate protective responses to reduce the impact of oxidative stress.^[10]

Water Regime and Rainfall

A significant source of phytochemical differences is geographical variation in precipitation patterns. Areas with unpredictable precipitation or extended dry periods cause drought stress, which is especially destructive at the seed filling stage, as seen in crops such as soybeans.^[12] Drought also affects the physiological balance of plants, which greatly decreases the rate of carbon assimilation and weight of grain.^[12] Conversely localized water regime intensity defines the natural tolerance of a plant because the geographical area determines the occurrence of osmotic stress that plants endure by the activation of certain tolerance genes.^[13]

Light Intensity and Solar Radiation

The photoperiod and the intensity of solar radiation are both dependent on geographical location. Photo-inhibition may occur when intensity of light is high, commonly in certain latitude or plateaus with high altitude.^[14] Plants adapt to these geographical radiation levels by modulating their photosynthetic efficiency and accumulating protective pigments, often bioactive compounds with medicinal properties.^[10,14]

4.2. Soil characteristics

Nutrient Availability

The supply of the necessary minerals is directly related to the pedological history of a region. In most geographical areas, nitrogen is usually the most crucial limiting nutrient and its shortage can seriously decimate seedling development.^[15] The physical location of soil with lack of nitrogen compels the plants to alter their physiological reactions to the absorption of the nutrients to sustain productivity.^[16] Furthermore, it is the interplay between the root system and the local soil nutrient profile that defines the ability of the plant to utilize nutrients, which varies across cultivation sites.^[16]

Soil Microbes and Organic Matter

The quality of the soil is directly linked with the ecological health of the geographic region. Beneficial microbial communities are distributed and activated by the soil organic matter, thus increasing the nutrient uptake and enzyme activities.^[17] These soil microbial structures may be remodeled by geographical stressors and form either favorable or unfavorable environment to promote or hinder plant growth.^[18] The abiotic stresses (salinity or heat) typical in certain locations also differentially alter bacterial and fungal communities.^[19] The quality of soil in certain environmental sites contribute to the recruitment of beneficial bacteria to form a friendly rhizosphere, which then contributes to the health of plants and the

accumulation of secondary metabolites.^[20] The changes in microbes are not accidental, but a direct evidence of the selective pressure of the environment, which determines the rhizosphere composition and further influence its effect on plant development.^[19,21]

Chemical Protection and Pests

Chemical controls are required in most locations due to the existence of pests and diseases. Nevertheless, the presence of fungicides or pesticides may cause increased stress in plants.^[22] Geographical sites which utilize chemical management require elevated amount of internal protective mechanisms to maintain plant growth and keep metabolic quality during chemical strain.^[22]

5. Effect on phytochemical composition

5.1. Alkaloids

Alkaloids, which are synthesized by approximately 20% of vascular plant species, are essential defense metabolites and growth regulators.^[23] The synthesis of these alkaloids is tightly regulated by environmental factors, for instance, high temperature and certain level of precipitations can stimulate the metabolism, which will increase alkaloidal levels in plants such as *Anisodus tanguticus*.^[24] The quality of light is crucial in *Catharanthus roseus*, light exposure was found to induce the activity of N-methyltransferase, a key enzyme in approximately 30% alkaloid biosynthesis.^[25] Furthermore, the presence of high level of nitrogen and increased level of carbon dioxide has been found to significantly increase alkaloid synthesis, highlighting the synergistic interactions between atmospheric factors and soil nutrient status.^[25]

5.2. Phenolic compounds

Phenolic compounds (flavonoids and phenolic acids) are often produced as a defense mechanism against abiotic stress factors such as UV radiation and extreme temperatures.^[24,26] Cold stress as a potential inducer, for instance in *Glycine max* roots subjected to low temperature has shown increased levels of isoflavonoids such as genistein and daidzein within 24 hours.^[27] Light spectrum is also known to affect phenolic profiles with some studies reporting that blue light enhances the accumulation of total phenolics and flavonoids in *Rhodiola imbricata* more than other light treatment.^[27] Additionally, elevated altitudes with more UV-B radiation and cooler climate tend to have a positive correlation with high flavonoid content in wild plant population.^[28]

5.3. Terpenoids and essential oils

Terpenoids constitute the largest class of secondary metabolites, with about 25000 known compounds derived from a five-carbon precursor isopentenyl diphosphate.^[26] They are commonly produced in response to salinity and oxidative stress and serve as an adaptation and resistance mechanism.^[29,30] The composition of essential oils is also variable, moderate environmental stresses, such as water and light intensity may act as the triggering factor that induce the expression of control genes in the terpenoid indole alkaloids biosynthesis.^[3,31] However, hormesis can boost production of metabolites but severe or undesirable conditions might hamper biomass growth and decrease the level of these active constituents.^[3]

5.4. Integrated phytochemical responses

Environmental factors are not independent of the plant response, instead, they undergo integrative phytochemical changes in complex signaling cascades.^[29,31] Factors such as soil properties, altitude and moisture interact to fine-tune the entire metabolome, which commonly involves a cross-talk between signaling molecules to cope with oxidative stress.^[24,29] For instance, a higher amount of carbohydrates could be used as a marker for increased synthesis of several classes of secondary metabolites at once to enhance the overall quality of plant medicine.^[32] This synchronized action implies that phytochemical diversity is an outcome of the plant's holistic adaptation to the eco-climatic zone.^[27]

Table 1: Influence of location on physiological response and phytochemical composition in plants.

Geographical Factor	Environmental Condition	Plant Response	Affected Phytochemicals	Mechanism	Ref
Temperature	High/low temperature	Stress response, enzyme modulation	Phenolic, flavonoid	Alters enzyme kinetic and ROS production	[33]
Soil	Rich/poor Nutrients	Nutrient uptake variation	Alkaloids, terpenoid	Influences precursor availability	[34, 35]
Altitude	High UV, low oxygen	Increased protective metabolism	Phenolic, flavonoid	UV-induced phenylpropanoid activation	[36]
Water	Drought/excess water	Osmotic stress	Alkaloids, phenolics	ABA signaling, oxidative stress	[37]
Biotic Factor	Pathogens	Defense activation	phenolic, flavonoid	JA/SA signaling pathways	[38]

5.5. Quality and standardization implications

Standardization of herbal medicine remains a global challenge due to inherent variability of phytochemicals as a result of geographical and climatic influence as demonstrated in **Table 1**.^[1,39] The variation in the environmental conditions surrounding cultivation sites might cause disproportions in the active ingredients of otherwise similar preparation, which further hinders therapeutic activity and safety.^[40,41] Current standardization of herbal products are performed on the basis of a single marker compound, which does not always represent the complete bioactivity of the plant.^[42] To ensure reproducible quality of herbal products, strict quality control parameters are needed that account for the influence of the cultivation region, seasonal variation, and processing of the harvested plant on the chemical fingerprint.^[3,42]

6. Case study: Effects of geographic region on medicinal plants and food crops

6.1. Medicinal plants

Ginseng

Ginsenosides are the main active compounds of the *Panax ginseng* and *P. quinquefolius*, the biosynthesis of which is highly sensitive to both the diurnal temperature and soil moisture.^[43,44] In *P. quinquefolius*, a constant diurnal range of 25 °C/25 °C has been reported to significantly enhance the total ginsenoside content as compared to a fluctuating range of 25 °C/15 °C.^[44] In China's geographical origin (Shandong, Beijing, and Jilin), the plant as demonstrated significant differences in ginsenoside makers such as Rg1 and Re, with moderate water stress and cooler temperature promoting the accumulation of ginsenoside.^[43,45] However, heat may reduce the chemical composition, which can be attributed to lower biomass.^[46]

Artemisia annua L. (Asteraceae)

The interplay between altitude, temperature and humidity has a significant effect on the content of artemisinin in *Artemisia annua* L.^[47] The artemisinin levels in plants grown under cooler temperatures conditions, for instance, plants grown in Kashmir demonstrate higher content (0.1%) than those found in subtropical climatic conditions such as Lucknow (0.06%).^[48] Low elevation and high temperature have been observed to reduce vegetative growth and artemisinin concentration by up to 3-4 times, while showing a positive correlation between relative humidity and the metabolite yield.^[47] Furthermore, artemisinin content in European population varies approximately (0.03 % to 0.05%) dry weight, highlighting the influence of the environment condition on metabolite production.^[49]

***Catharanthus roseus* (L.) G. Don (Apocynaceae)**

Light and temperature changes can influence the production of anticancer terpenoidal indole alkaloids.^[31,50] Although light activation can result in the biosynthesis of vindoline, catharanthine may be accumulated without the stimulation of light.^[50] It was found that low temperature (12° C) lead to an increase in root ajmalicine content by 3 times relative to control temperature of 25°C. Furthermore, UV-B promotes the expression of essential biosynthetic genes (tryptophan decarboxylase (TDC) and strictosidine synthase (STR)) that results in more metabolites being stored in special tissues.^[51]

***Cryptolepis sanguinolenta* (Lindl.) Schltr. (Apocynaceae)**

In the case of *C. sanguinolenta*, the planting density and availability of nutrients play a significant role in the root biomass and production of the alkaloid cryptolepine.^[52,53] Cryptolepine concentration can be increased to 2.08mg/100mg, when high-density planting (45 plants/1.8m²) is used.^[52] Management of agriculture is also an important fact, root biomass and alkaloidal yield can be increased by the use of nitrogen (through Urea or NPK), with a 9-month old plant typically becoming rich in cryptolepine.^[53] These findings highlight the suitability of agro-ecological specialties in maximizing the medicinal quality of this West African shrub.^[54]

6.2. Food crops***Camellia sinensis* (L.) Kuntze (Theaceae)**

Climate-driven changes in seasonality and water availability make tea quality quite vulnerable to secondary metabolites such as caffeine and catechins varying by up to 50%.^[55,56] In Yunnan, tea grown in the dry spring region has a distinct chemical composition of about 50 different compounds that are not the same as those of the ones harvested in monsoon summer.^[57] These changes are further increased by extreme weather conditions and agro-ecosystems, which affects the sensory and antioxidant properties of the end product.^[56,58]

***Vitis vinifera* L. (Vitaceae)**

The phenolic content of grapes such as anthocyanins and resveratrol increase at higher altitude due to increase in UV-B radiation.^[59,60] Berries growing at 1500 m above sea level have been found to have 17.6% higher content of polyphenols and 28.5% levels of anthocyanin than those at lower elevation, where there is less UV-B exposure. The temperature also negatively affects the flavonoid content, temperature higher than 40 °C may

inhibit several essential enzymes such as phenylalanine ammonia lyase, thus reducing the phenolic content of the fruit.^[61,62]

***Oryza sativa* L. (Poaceae)**

Light and temperature are factors that influence the quality of rice during a 45-day grain filling period.^[63] The presence of high-night temperature is particularly harmful, because it causes grains chalkiness, reducing rice quality.^[64] Furthermore, the environmental conditions such as temperature and water availability at the time of harvest play an important role in dictating final grain quality, such differences have significant implications on food security, nutrition and agricultural practices.^[65]

6.3. Comparative case studies

The case studies prove that environmental factors such as UV-B at high altitude or extreme temperature during growth has an influence on the phytochemical diversity of medicinal plants and food crops.^[56,60] Although these stressors induce protective metabolic responses that have the potential to improve the potency of medicinal plants such as *Panax* and *Artemisia*, they also can have a negative impact on the quality consistency of the plants.^[27] To achieve effective standardization, interaction between genotype and environment needs to be incorporated into cultivation to ensure the bioactivity and nutritional value remain similar across various geographical locations.^[66] **Table 2** highlights suitable geographical locations of some of the key medicinal plants and food crops.

Table 2: Geographic diversity of some key medicinal plants and food crops.

Species	Region	Key Compound	Variation	Environmental Stressor	Ref
<i>Cryptolepis sanguinolenta</i>	West Africa	Cryptolepine	Regional Variation	Soil, Rainfall	[67]
<i>Catharanthus roseus</i>	India, Madagascar	Vincristine	Increased Under Stress	Soil Nutrition	[68-70]
<i>Panax ginseng</i>	Korea/ China	Ginsenosides	High altitude	Temperature, soil	[71-73]
<i>Artemisia annua</i>	China/ Africa	Artemisinin	Variable yields	Light, temperature	[68-70]
<i>Vitis vinifera</i>	European Region	Polyphenols	Terroir dependent	Climate, soil	[68, 74]
<i>Camellia sinensis</i>	High/low altitude	Catechins	Higher in highland	UV radiation	[75, 76]

7. Analytical methods used in standardization of medicinal plants and food crops

7.1. Chromatographic techniques

High-Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS)

HPLC is essential in targeted phytohormone analysis and quantifying valuable secondary metabolites. It is commonly used to quantify the levels of metallothionein in plant tissue such as leaves and roots subjected to abiotic stress.^[77] LC-MS/MS is generally considered the most sensitive and specific method of determining melatonin in plants matrices.^[78,79] UPLC-based advanced system with High-Resolution Orbitrap Mass Spectrometry has further improved sensitivity and precision, achieving a recovery of over 96.4%, with a limit of detection of 0.03pg.^[80] Methodological rigor has improved with the introduction of isotope-labeled internal standard, e.g., MLT-d4 which is essential to balance the matrix effects and for accurate quantitative analysis across botanical samples.^[79] In medicinal plants, HPLC-ESI-Q-TOF-MS/MS is able to provide the mass accuracy necessary to quantify artemisinin and its biosynthetic precursor in *Artemisia annua*.^[81] Similarly, HPLC is used in the complex isolation and analysis of ginsenosides in *Panax* species.^[82]

Gas chromatography-mass spectrometry (GC-MS)

GC-MS is the main tool of untargeted metabolomics, specifically volatile and semi-volatile compounds. It provides detailed molecular fingerprint of extracts, which is essential in the identification of low-molecular-weight primary metabolites.^[83] This technique is effective in profiling organic and amino acids of the root exudates that are substrates of rhizosphere enzyme induction.^[83]

7.2. Spectroscopic methods

Nuclear magnetic resonance (NMR) Spectroscopy

NMR is a non-destructive method of structural identification, which can be used to provide in-depth stereochemical data missing from mass spectrometry.^[83] It enables the concomitant identification of a broad spectrum of metabolite classes (i.e., sugars, organic acids and alkaloids) without the need of extensive sample purification, thus making it an indispensable instrument in global metabolic profiling.^[83]

Ultraviolet-Visible spectroscopy

UV-Vis spectroscopy is indispensable in rapid, quantitative assay of nitrogen compounds and enzyme rates. In nitrogen quantification, salicylic acid method is often used to determine the content of nitrate (NO_3^-) at 410 nm, and the total nitrogen is typically determined through the

kjeldahl method involving $\text{H}_2\text{SO}_4\text{-H}_2\text{O}_2$.^[84] In enzymatic activity, spectrophotometric quantification of the main enzyme of metabolic processes, including urease and nitrate reductase are used to determine the rate of substrate conversion.^[84]

7.3. Multivariate analysis and chemometrics

In order to analyze the data sets produced by the methods above, researchers use sophisticated statistical models to detect biologically significant trends.

Principle component analysis (PCA)

PCA is a data dimensionality reduction that is an unsupervised exploratory tool. It enables the visualization of intrinsic groupings and trends, practically demonstrating whether the use of melatonin treatment has a significant effect on changing the global metabolic state of plants.^[83,85] For instance, PCA may cluster plant samples depending on environmental adaptive mechanism or treatment regime.^[86]

Partial least squares discriminant analysis (PLS-DA)

PLS-DA is a supervised technique which utilizes the group information to achieve maximum separation between classes. The method is mostly applied to detect discriminant metabolites or biomarkers, particularly molecules, whose concentrations are significantly altered by melatonin and cause a growth or stress-tolerance phenotype.^[85]

7.4. Integration with omics

Recent studies aim at integrating untargeted metabolomics with other layers of omics in mapping holistic interaction. For instance, metabolic fingerprints of root exudates can be combined with metagenomic analysis of soil microbial DNA to enable the association of chemical secretion induced by melatonin with the recruitment of specific microorganisms that recycle nitrogen.^[86] This integrative method provides the definitive link between the biochemical output of plant and its external rhizosphere environment.

7.5. Impact on quality control and authentication

The standardization and authentication of medicinal plants and food crops is largely dependent on the analytical rigor. To achieve quality control, innovative methods including two-dimensional coding to visually map the metabolomes have been applied on species such as *Ganoderma lucidum*.^[87] Furthermore, the use of MS/MS to establish unique metabolic fingerprints allows the authentication of plants across geographical region, ensuring enhanced

metabolic activity mediated by melatonin is translated into standardized pharmaceutical and nutritional quality.^[87]

8. Mechanistic insight

8.1. Stress signaling pathways

Plants react to environmental stimuli by using complex signaling network that translate stress perception into metabolic reprogramming.^[88] The accumulation of reactive oxygen species and activation of mitogen-activated protein kinase cascades are often the initial phases of these cascades.^[89] These signals regulate levels of phytohormones (abscisic acid, jasmonic acid and salicylic acid) which act as central regulators in triggering transcriptional activity of secondary metabolite biosynthesis in plants.^[88] Through this coordination, plant cells are able to stabilize cellular homeostasis and generate anti-stress agents that stabilize the cell structure in unfavorable conditions.^[30,90]

8.2. Role of enzymes in biosynthetic pathways

Enzymes are the primary catalysts leading to the chemo-diversity of secondary metabolites such as alkaloids, terpenes and phenolics.^[91] The key enzymes of the phenylpropanoid pathway (phenylalanine ammonia-lyase, cinnamate-4-hydroxylase (C4H) and 4-coumaroyl: CoA-ligase (4CL)) are commonly activated in response to stress to promote the production of protective flavonoids and anthocyanins.^[92,93] Recent studies indicate that such enzymes tend to operate through metabolic channeling in plants, which enables them to be more efficient and specific than commonly observed *in vitro*.^[94] The characteristic expression of these proteins assists in determining whether a plant favors high energy or energy-saving pathways in reaction to specific stressors.^[95]

8.3. Gene expression and epigenetic regulation

The plant secondary metabolites (PSMs) regulation occurs at multiple layers, beginning with a more complex network of transcription factors that detect the presence of stress and activate the expression of downstream defense genes.^[96] Beyond genetic, epigenetic alteration such as DNA methylation, histone acetylation and small-RNA-based processes are vital in regulating metabolic outputs.^[96,97] For instance, DNA methylation induced by stress can silence or activate genes involved in the phenylpropanoid and terpenoid pathway, a process which can be involved in transgenerational stress memory.^[98] These inherited modification enables plants to set up their metabolic defenses in advance for future environmental challenges.^[98]

8.4. Metabolic flux and resource utilization

Plants are faced with a significant growth defense trade-off in which limited resources have to be divided between primary growth and secondary metabolism.^[99,100] Carbon and nitrogen are diverted under stress conditions from primary pathways like tricarboxylic acid (TCA) cycle and glycolysis to defensive product formation.^[93,101] Targets of rapamycin complexes often control this reallocation and serves as cellular fuel gauges that sense energy availability and adjust growth according to resource supply.^[99] For instance, flavonoids and lignin often compete for the same metabolic pathway, the plant must regulate these pathways to maintain cell integrity while ensuring antioxidant protection.^[100]

8.5. Omics integration

Metabolomics provides a comprehensive perspective of the plant's phytochemical cosmos by assessing changes in thousands of molecules.^[102] By integrating metabolomics, transcriptomics and genomics, researchers can determine the specific genes related to stress-related mechanisms such as anthocyanidin synthase (ANS) and UDA-glucose: flavonoid 3-O-glucosyltransferase (UFGT) that lead to the accumulation of anthocyanin in tea.^[92] This multi-omics method is essential in unravelling the function of genes at different levels of geographical conditions and understanding the complicated biochemical dynamics that lead to PSM production.^[30,103] Furthermore, prediction tools based on phylogenomics can now be used in identifying bioactive molecules by linking the genomic architecture with metabolic profile.^[102]

8.6. Impact on phytochemical variability

Genetic control and environmental stimuli contribute to a significant phytochemical diversity between population, genotype and even individual plant tissues.^[93,104] In addition, diurnal and circadian oscillations also affect variability by refining the time of defense chemical production.^[90] Establishing comprehensive chemical fingerprints through metabolite profiling has become the standard in identifying botanical authenticity and adulteration.^[104] Understanding this variability is essential to ecological adaptation and industrial production of quality plant-derived compounds.^[30,104]

9. Implication

9.1. Agricultural implication

In farming, it is recognized that plant quality is greatly influenced by geographical location, this has led to the adaptation of specific cultivation practice. To achieve high-quality

production, cultivation of specific plants relies on selecting of geo-authentic or native geographical region, for instance, *Panax ginseng* is considered to have medicinal quality only when grown in northeastern China and *Glycyrrhiza uralensis* is preferred in inner Mongolia.^[105]

Technology precision in agriculture such as remote sensing and geographic information system enable monitoring of environmental variables such as soil pH, rainfall and temperature, which are directly linked to the accumulation of active substances including podophyllotoxins in *Sinopodophyllum hexandrum*.^[105,106] Such tools enable agronomists to optimize production area by using geostatistical imaging and remote sensing to determine microclimates that promote secondary metabolism under moderate environmental stress; to implement specific intervention through adaptive site-specific irrigation and nutrient management to enhance antioxidant and phenolic content in specific cultivar; and to implement enhanced grazing management through using spatio-chemical analysis to map nutritional landscapes, in which the distribution of nutraceutical-rich vegetation is determined for sustainability of livestock production.^[3,107-110]

9.2. Pharmaceutical industry

The pharmaceutical sector faces challenge by the variability of phytochemical composition of medicinal plants. Geographical variations may cause inconsistency in active compounds concentration, directly affecting the effectiveness and safety of medicinal plants.^[39,111] For instance, marker compounds concentration such as ginsenosides Rg1, Rb1 and Rd are used to differentiate the quality of *Panax ntoginseng* based on 21 ecological factors including elevation and soil data.^[112] In order to provide reproducible therapeutic effect that is required per international standards (USP, Chinese pharmacopoeia), the industry is moving towards; chemical standardization by validating analytical procedures such as HPLC-DAD to determine the content of key makers like gallic acid and ellagic acid in different batches.^[1,113] The quality consistency through phytochemical fingerprinting and metabolic profiling to manage significant differences in medicinal plants compared to synthetic drugs has also been used^[111] Furthermore, controlled blending through systematic methods of different batches to achieve batch-to-batch consistency has been utilized, a technique pioneered for *Ginkgo biloba* leaves.^[111]

9.3. Food industry

Geographic variation in the food industry plays a critical role in determining nutritional value, flavor and quality of food crops. The concept *terroir*, which has traditionally been associated with *Vitis vinifera* and *Camellia sinensis* is now applied to a wide range of crops that are valued due to their geographical identity.^[114] Some studies have revealed that locally-adapted varieties including tomatoes, sweet cherries and onion can have significantly greater functional molecules than commercial varieties.^[115]

Understanding these differences provides the industry with some strategic opportunities. First, improve nutritional value by utilizing genotype environment interaction (latitude, altitude and UV exposure) to improve phenolic and antioxidant capacity.^[116] Secondly, improvement of processors by addressing the perennial issue to ensure reproducible phytochemical profile when using ingredients of different origins, which influence both flavor and shelf life.^[66] Finally, supporting the development of consumer instruments by authenticating low-cost tools such as reflectometers to determine nutrient changes across the food supply, assisting consumers and manufacturers authenticate fully-traceable functional foods.^[108]

10. Call for further research

10.1. Integrated multidisciplinary approaches

Future studies must focus on integrating multidisciplinary frameworks to decipher the complicated relationship between geographical location and plant quality. The priority should be integrating omics technologies with advanced climate modeling and machine learning tools. Recent studies have demonstrated that it is possible to predict the accumulation of secondary metabolites (nepetalactone and saponins) by using ML algorithms and geospatial analytics to identify primary environmental factors such as elevation and temperature gradients.^[117,118] This integration serves as an “encoder” of environment forcing upon phytochemistry, allowing for the screening of bioactive compounds and identifying structural changes induced by climate change.^[119] Furthermore, zoning schemes like the Ecological Suitability-Spatial Quality Zoning can outline high-quality ecological zones to improve predictive ability of niche models to guide precision agriculture.^[118,120]

10.2. Manage cultivation and practice sustainability

To reduce the natural variability of wild harvested plants, further research should explore controlled-environment cropping such as greenhouses, vertical farms and artificial-light plant factories. Such systems allow the accurate control of environmental characteristics, including

light intensity, CO₂ content and root zone temperature to enhance the uniformity, concentration and productivity of bioactive phytochemicals throughout the year.^[121,122] Alongside such technologies, sustainable agriculture such as organic farming and agroecology should be further researched. It has been revealed that organic production can enhance biosynthesis of potent compounds, improve soil stability and protect genetic variation while maintaining ecological balance.^[123-125] These regulated environments together with mycorrhizal treatment or other bio-stimulants are a promising prospect in stabilizing metabolite synthesis.^[126]

10.3. Standardization and international cooperation

Global quality assurance requires the development of standardized guidelines to be applied in each stage of the production lifecycle from cultivation to processing. Although WHO offers good agricultural and collection practice, the knowledge gap in growers largely relates to operational expenses.^[127] Further studies are recommended on the regulatory harmonization and development of international standards, including the international standard of sustainable Wild Collection of Medicinal and Aromatic plants, to ensure safety and prevent the risk of species depletion.^[128,129] Furthermore, to bridge the gaps between traditional practice and new regulations, the establishment of government certified raw-material supply centers and improved documentation are necessary.^[130] Coordinated management of these dimensions are essential in modernization and global recognition of medicinal plants.^[3]

11. CONCLUSION

In conclusion, geographical location is one of the key factors that influence the phytochemical profile and the overall quality of medicinal plants and food crops. The complex interaction between environmental factors is the force behind the metabolic mechanisms that result in the production of key bioactive compounds. These environmental stressors and conditions are not only external influences but are inherent in the development of alkaloids, phenolics and terpenoids that determine the therapeutic and nutritional potential of the plant. The main challenge lies in bridging the gap between metabolic variability and the requirement of standardized, high-quality plant production. Achieving such standards requires a transition towards multidisciplinary studies that integrate modern omics technology and sustainable agriculture. The reduction of variation induced by geographical changes can be achieved through the use of controlled cultivation conditions and standardized processing

guidelines. Finally, understanding the effects of location in plant chemistry is crucial in the safety, efficacy and sustainability of global medicinal plants and functional food industries.

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