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The Metabolomic Profiles and Therapeutic Potential of Selected Medicinal Plants: A Comprehensive Review

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Abstract

This review provides a comprehensive evaluation of the metabolomic profiles and therapeutic potential of five medicinal plants: *Ginkgo biloba*, *Digitalis purpurea*, *Zingiber officinale*, *Glycyrrhiza glabra*, and *Curcuma longa*. Using advanced analytical techniques such as GC-MS, LC-MS, HPLC-MS and UHPLC-MS/MS. The unique metabolite profiles of each plant are elucidated, linking specific compounds to therapeutic applications such as anti-inflammatory, cardioprotective, and neuroprotective effects. Clinical and laboratory studies underscore the efficacy of these plants in conditions ranging from cancer to cardiovascular disease. This review highlights plant metabolomics as a promising frontier in drug discovery and paves the way for future integrative research in alternative medicine.

1. Introduction

Metabolomics is a growing field that study changes in body metabolites due to internal and external influences. The approach employs untargeted, semi-targeted, and targeted techniques to detect noteworthy alterations in widely used metabolic pathways. However, because there are so many different types of plant metabolites and it can be difficult to identify them, plant metabolomics is still relatively new and difficult. [1][2]. It is difficult for metabolomics to provide thorough coverage because the platforms available today only detect about 10% of the small molecule complement in a cell. [3] This emphasizes the necessity of more developments and inventions. Understanding the processes involved in producing metabolites related to nutrition and health in plants is essential for high-quality and safe food, as is understanding their impact on human health due to potential biohazards. This is why plant metabolomics is important in research on plant development and stress responses [4].

Despite the large number of undiscovered metabolites, biological genomics has accelerated the development of metabolomics [5]. Understanding plant physiology and improving plant performance—particularly under stressed conditions—are greatly aided by metabolomics. It is anticipated to play a crucial role in functional genomics [6]. The variety of metabolites and how they react to environmental changes, however, presents difficulties [7].

In order to tackle these issues, mass spectrometry (MS) is an essential tool for gathering large amounts of data. Metabolomics examines small-molecule metabolites in

conjunction with proteomics and genetics [8]. Common methods used in plant metabolomics that are combined with statistical analysis include nuclear magnetic resonance (NMR) and liquid/gas chromatography-mass spectrometry (LC/GC-MS). The tools utilized to identify metabolomic studies are shown in Fig. 1.

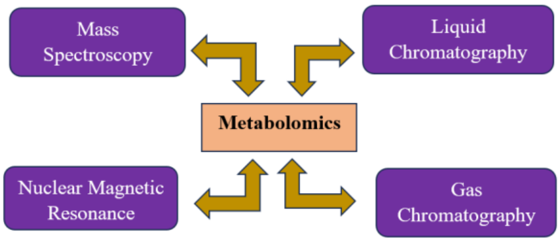

Figure 1:Illustration of the relationship between metabolomics and various analytical techniques

2. *Curcuma longa*

2.1. Lab exploration:

The herb *Curcuma longa*, well known for its culinary and therapeutic uses, has attracted a lot of interest in science. An examination into the chemical makeup of *Curcuma longa* was carried out by Salem *et al.* (2022), with a special emphasis on the effects of drying procedures. Using metabolomic analysis of fresh and dehydrated *Curcuma longa*, they found 161 possible drying indicators, including terpecurcumins and curcuminoids [9] . Ye *et al.* (2022) conducted a study that investigated five Curcuma species that are utilized in traditional Chinese herbal medicine. The analysis revealed 432 metabolites, with *C. longa* displaying unique metabolic profiles, particularly in terms of curcuminoid levels [10]. Furthermore, different metabolite profiles were found in the rhizomes and essential oils of different Curcuma cultivars, highlighting the metabolite diversity and health benefits of Curcuma species [11]. A study comparing the geographic origins and species differentiation of *Curcuma aromatica* and *Curcuma longa* from South Korea was conducted. Though geography had no effect, the two species' metabolite profiles differed significantly, especially in terms of curcuminoid levels [12]. Researchers identified important chemical markers for quality control and differentiation by characterizing the essential oil compositions of various Curcuma species using gas chromatography-mass spectrometry (GC-MS) [13]. Additionally, curcumin's ability to reduce hyperlipidemia was investigated, and 35 biomarkers suggesting improvements in metabolism were found [14] .

2.2. Clinical exploration

Entering the realm of clinical investigation, a study conducted on the ingestion of dried *C. longa* extract exposed urine composition to metabolic alterations, including the presence of curcumin and its metabolites. This demonstrated the anti-inflammatory qualities of curcuma as well as the functions of the gut and liver bacteria in curcumin absorption and metabolism [15] . In their investigation into the potential therapeutic benefits of *Curcuma* in avoiding diabetes, lowering inflammation, and boosting anti-aging effects, Budhathoki *et al.* (2023) identified 30 compounds in organic extracts derived from the rhizome of *C. longa* [16]. Furthermore, Segneanu *et al.* (2022) investigated the antioxidant characteristics of *Curcuma longa*, detecting 80 metabolites and emphasizing its potential in methods for neurological treatment [17]. Zhou *et al.* (2019) investigated the anti-cancer properties of *Curcuma longa* and found that it inhibited the growth of cancer cells and changed 25 metabolites that were engaged in several pathways. Because of their synergistic effects, multi-curcuminoids were found to be more effective [18]. Another study examined the antioxidant activity of curcuminoids by giving rats extract from *Curcuma longa*. The results showed changes in sulfur-containing compounds and urine indicators of oxidative stress, suggesting possible antioxidant effects [19]. Find comprehensive insights into the metabolic pathway, biomarker compounds, and disease conditions linked to *Curcuma longa* by referring to Table 1

Table 1: List of Biomarker Compounds of Curcuma longa and their Associated Disease Conditions

S. No.	**Biomarker Compound**	**Disease Condition**	**Ref.**
1	Curcuminoids, Germacrone, Curdione, Epicurzerenone, Curzerenone	Hyperlipidemia	[14]
2	Curcumin, Ar-turmerone	Inflammation	[15]

3	Diarylheptanoids, Bisabolocurcumin ethers, Sesquiterpenoids, Fatty acid derivatives, Cinnamic acid derivatives	Various Therapies	[16]
4	Various metabolites from secondary metabolite categories	Neurodegenerative Diseases	[17]
5	Curcuminoids	Cancer	[18]
6	Curcumin	Oxidative Stress	[19]

3. *Glycyrrhiza glabra*

3.1. Lab exploration:

The flavonoid- and saponin-rich herb glycyrrhiza has drawn interest for its antibacterial, anti-inflammatory, and antioxidant qualities. Researchers have discovered twenty putative biomarkers linked to important metabolic pathways and flavonoids from Glycyrrhiza that may be used as therapeutic benefits for a range of inflammatory disorders using urine metabolomics [20]. Another study examined the effectiveness of *Salvia miltiorrhiza* and *Glycyrrhiza uralensis* in treating liver fibrosis using an integrated method of untargeted metabolomics and network pharmacology. The results emphasized the importance of such approaches in comprehending traditional Chinese medications by highlighting the management of inflammation, collagen production, and metabolic processes [21].

The goal of additional study was to examine the metabolomes of *Glycyrrhiza glabra L.* and *Glycyrrhiza uralensis* Fisch. ex-DC for liquiritigenin (F) and its isomer isoliquiritigenin (C). The investigation contributed to the standardization of licorice botanicals by revealing consistent F and C compositions and ratios among the many isolates [22]. Furthermore, the quality of *Glycyrrhiza glabra* was evaluated by the use of untargeted metabolomics, which revealed notable differences between samples and investigated models of geographical discrimination [23]. Well-known herbal supplement has a number of compounds that may have therapeutic benefits, such as antiviral and anticancer capabilities. Extensive metabolic profiling has revealed important molecules like glycyrrhizin and liquiritigenin/isoliquiritigenin glycosides, providing light on the chemical makeup of the many species in the *Glycyrrhiza* genus, despite the paucity of investigations on these species [24] [25].

3.2. Clinical Exploration:

Glycyrrhiza glabra, a traditional treatment, has been shown in clinical study to include a variety of chemicals with potential pharmacological effects, enriched in pathways linked to signaling kinases, cell cycle regulation, and inflammatory management [26] . Additionally, the study on the toxicity of triptolide (TP) and the protective effects of *Glycyrrhiza glabra* water extraction (LWE) highlighted metabolic pathways influenced by LWE treatment, suggesting that LWE treatment has interventional effects on TP toxicity, and identified possible biomarkers associated with TP toxicity [27] . Refer to Table 2 for a detailed overview of the metabolic pathway, biomarker compounds, and disease conditions attributed to Glycyrrhiza glabra.

Table 2:List of Biomarker Compounds of Glycyrrhiza glabra and their Associated Disease Conditions

S.No	**Biomarker Compound**	**Disease Condition**	**Reference**
1	Flavonoids	Acute inflammation, chronic inflammation, inflammatory pain	[20]
2	Glycyrrhizin, 4 hydroxyphenyl acetic acid, glycosidic conjugates of liquiritigenin/isoliquiritigenin	Chronic inflammatory diseases, antiviral and anticancer properties	[24] [25]

3	Terpenoids, alkaloids, flavonoids, quercetin glucosides, beta-carotene, dopamine, serotonin, acetylcholine neurotransmitter receptors	Control of cell cycle, inflammatory processes, growth factor receptors, and signaling kinases	[26]
4	Triptolide (TP), tryptophan, pantothenic acid, porphyrin	Rheumatoid arthritis, TP toxicity	[27]

4. *Zingiber officinale*

4.1. Lab exploration:

In order to address chemotherapy resistance, the work starts with a thorough focus on the metabolomics examination of Raji cells treated with *Zingiber officinale* extract i*n-vitro*. By identifying changed metabolites and impacted pathways, the study reveals substantial cytotoxic effects on Raji cells that impair protein synthesis, amino acid metabolism, and glucose metabolism [28]. With a smooth transition, the review explores the metabolomic profiling of different cultivars of *Zingiber officinale* using LC-MS, stressing the extensive therapeutic potential of *Zingiber officinale* by identifying acetylated gingerol derivatives as important pharmacological indicators [29].

Increasing its reach, the study adds dried *Zingiber officinale* samples from several geographic locations, exposing metabolite differences and alarming concentrations of heavy metals impacting the metabolome [30]. Turning now to therapeutic uses, metabolomics studies how *Zingiber officinale* extract affects Blood Stasis Syndrome (BSS) in rat models, providing important information on changed metabolites and pathways and providing a whole picture of *Zingiber officinale*'s potential for metabolomic therapy [31]. The study explores the antibacterial characteristics of *Zingiber officinale* flower oil and highlights its potential applications in the food and pharmaceutical industries by extracting it with subcritical carbon dioxide using metabolomics profiling [32].

The investigation continues with a metabolomic examination of three varieties of *Zingiber officinale*: fresh, dried, and charcoal. This research outlines the primary components of each variety and offers insightful information for evaluating quality using sophisticated analytical methods. The research highlights 6- gingerol, 6-shogaol, and zingerone as important therapeutic compounds and names gingerol and diphenyl heptanes as the main differential components[33]

4.2. Clinical Exploration:

Metabolomics studies are investigating the possibility of using *Zingiber officinale* lozenges to lessen nausea and vomiting caused by chemotherapy in children diagnosed with acute lymphoblastic leukemia during the clinical exploratory phase of the disease. Promising recovery rates, accuracy, and consistency are demonstrated by the approach, indicating its potential for *Zingiber officinale* compositional analysis and quality control [33]. Clinical metabolomics research compares the effectiveness of loratadine and *Zingiber officinale* extract in treating allergic rhinitis, finding that both are equally effective with fewer side effects. This finding highlights the ability of dietary libraries with LC-MS/MS spectra to identify potential biomarkers and link food intake to health benefits [34].

Additionally, the study investigates how different signaling pathways and transcription factors, including NF-κB, p38 mitogen-activated protein kinase, and PI3K/Akt signaling, may enhance *Zingiber officinale*'s neuroprotection in Parkinson's disease. This emphasizes the potential of *Zingiber officinale* as a neuroprotective therapeutic agent [35].

5. *Digitalis purpurea*:

5.1. Lab exploration:

The investigation of the metabolomic composition of *Digitalis purpurea* commences with an emphasis on genetic insights obtained from genome sequencing utilizing long-read sequencing. This method reveals the red-flowering *Digitalis purpurea* plant's amazing assembly continuity and completeness, illuminating structural genes involved in the generation of anthocyanins and variances in white flowering plants. Moving on to more useful uses, research assesses the plant's biological potential by looking at its capacity to bioconvert hydroquinone into arbutin, demonstrating

Digitalis purpurea's resistance to elevated hydroquinone concentrations and its bioconversion potential [36].
Major regulators of secondary metabolite synthesis were identified by Amiri *et al.* using multi-omics data analysis, which allowed them to delve deeper into the molecular pathways underpinning the therapeutic advantages of *Digitalis purpurea.* This thorough method clarifies the complex pathways through which cardiac glycosides are biosynthesised in *Digitalis purpurea*, offering a thorough comprehension of its metabolic processes [37]. Adding to the historical and medicinal applications, Passi *et al*. emphasize the long-standing reputation of *Digitalis purpurea* for treating obesity-related cardiac issues, highlighting its cardiotonic properties and the importance of digitoxin in enhancing muscle contractions and enhancing nutrient absorption [38].

Additional metabolomic studies concentrate on free radical scavenging and phytochemical screening, revealing a range of physiologically significant phytochemicals in *Digitalis purpurea*. This demonstrates its ability to provide pharmaceutical remedies and offer information on the eradication of sickness. Examining how methyl jasmonate affects the synthesis of cardiac glycosides in the presence of water stress provides useful information on how the plant reacts to environmental stresses [39]. Furthermore, studies have examined the induction of somatic embryogenesis in tissue culture, the impact of ethylene antagonist and biogenic polyamines that counteract senescence on flower longevity, and the results have shown that these factors have a major influence on the lifespan of Digitalis flowers as well as the genetic stability between *in vitro* clones and mother plants [40] [41]

5.2. Clinical Exploration:

Before addressing clinical research, it is important to note the historical context *of Digitalis purpurea's* therapeutic use in the treatment of congestive heart failure as well as its cytotoxic, antioxidant, and wound-healing qualities. *Digitalis purpurea* plants' adaptive responses to oxidative stress are elucidated by low-dose γ-irradiation effects, which may have significance for plant metabolomics in the future[42]. A unique case study that highlights the poisonous effects of drinking *Digitalis purpurea* tea suicidally serves as a reminder of the risks that might arise from misusing medicinal herbs as the review comes to a close [43] . Refer Table 3 for details on the metabolic pathway, biomarker compounds, and disease conditions associated with *Digitalis purpurea*.

Table 3:List of Biomarker Compounds of *Digitalis purpurea* and their Associated Disease Conditions

S.No	Biomarker Compound	Disease Condition	Reference
1	Anthocyanin	Loss of anthocyanin pigment	[38]
2	Arbutin	Medicinal and cosmetic applications	[36]
3	Cardiac glycosides	Cardiac problems related to obesity	[43]
4	Cardiac glycosides, Saponins, Flavonoids	Potential pharmaceutical treatments, Disease eradication	[39]
5	Polyamines (Putrescine, Spermidine, Spermine)	Anti-senescence, Extended bloom duration	[41]

6. *Ginkgo biloba*

6.1. Lab exploration:

Ginkgo biloba (GB) has been a mainstay of herbal medicine due to its wide range of bioactive components, which have drawn interest from the traditional and modern healthcare sectors and prompted a great deal of scientific research [44] . Research has examined the physicochemical characteristics and chemical composition of *Ginkgo biloba* leaves (GBL) under different extraction techniques, with studies like Zhang CW *et al.*, 2016 indicating notable changes in components like proteins, carbohydrates, flavonoids, and fatty acids. The evaluation of *Ginkgo biloba* extract quality has been transformed by cutting-edge analytical methods including HPLC-MS and UHPLC-MS/MS, assuring uniformity and effectiveness in pharmaceutical and nutraceutical goods [45] [46] [47]. Studies on the metabolism of *Ginkgo biloba* have revealed how the plant responds to altitude, exhibiting changes in endophytic bacterial populations and flavonoid levels that point to a mechanism for adaptation to environmental stresses [48]. It is imperative to comprehend the metabolomic dynamics of various environmental circumstances in order to ensure sustainable utilization and conservation. The absorption, distribution, metabolism, and excretion of *Ginkgo biloba* components have been clarified by pharmacokinetic studies conducted in animal models. These studies have provided valuable information for forecasting clinical outcomes and modifying dosing regimens [47]. Furthermore, *ginkgo biloba* has demonstrated potential as a natural treatment for a number of illnesses, including heart disease and diabetes. It also shows promise in regulating glucose levels.

6.2. **Clinical exploration**

Ginkgo biloba has demonstrated a wide range of biological activity in clinical research, including anti-inflammatory, neuroprotective, cardioprotective, and antioxidant qualities [49] [50]. These results have been supported by clinical research, which shows that it is effective in lowering inflammation, strengthening cognitive function, and improving cardiovascular health [51] [52] . Future study aims to clarify the molecular mechanisms underlying *Ginkgo biloba's* therapeutic effects. The discovery of *Ginkgo biloba's* medicinal potential presents intriguing prospects for integrated medicine and disease prevention [46] [48].

7. Discussion:

Exploring the metabolomic intricacies of *Curcuma longa*, *Glycyrrhiza glabra*, *Zingiber officinale*, *Digitalis purpurea* and *Ginko biloba* unveils a rich tapestry of botanical complexity. In the laboratory, *Curcuma longa*'s diverse metabolite profiles showcase its geographic influences, therapeutic compounds, and applications in traditional medicine. *Glycyrrhiza glabra's* versatility in traditional Chinese medicine is illuminated through its influence on liver fibrosis and a spectrum of compounds with potential health benefits. *Zingiber officinale*'s metabolomic journey encompasses cytotoxic effects on cancer cells, therapeutic potential in reducing nausea, and impact on allergic rhinitis. *Digitalis purpurea*, a pharmaceutically significant plant, reveals its genomic intricacies and therapeutic potential in bioconversion and cardiovascular management. *Ginko biloba* offers intriguing insights for medicine and conservation due to its numerous bioactive components, medicinal potential, and adaptive responses to environmental conditions.

8. Conclusion:

This review underscores the significant therapeutic potential of *Ginkgo biloba*, *Digitalis purpurea*, *Zingiber officinale*, *Glycyrrhiza glabra*, and *Curcuma longa*, showcasing how their unique metabolomic profiles contribute to anti-inflammatory, cardioprotective, and neuroprotective applications. These findings emphasize the role of plant metabolomics in bridging traditional herbal medicine with modern pharmacology. Future studies should prioritize clinical trials to validate these findings, as well as investigate synergistic applications with current therapies. Ultimately, this review highlights plant metabolomics as an essential field in advancing personalized and integrative medicine.

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