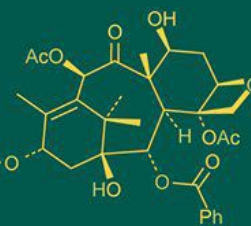
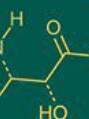
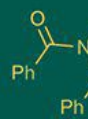
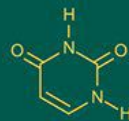
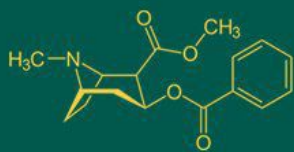


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Bioprospecting secondary metabolites from forest trees: Ecological roles, molecular regulation, and sustainable applications

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Abstract

Plant secondary metabolites (PSMs) are structurally diverse specialized compounds that mediate plant-environment interactions and play central roles in defense, communication, competition, and stress adaptation. Forest trees, characterized by long lifespans and complex ecological interactions, possess particularly rich and distinctive metabolite profiles, yet remain comparatively underexplored relative to agricultural species. This review synthesizes current advances in the bioprospecting of PSMs from forestry species, integrating knowledge of their major classes, biosynthetic pathways, regulatory mechanisms, and ecological functions. It further highlights recent progress in analytical, metabolomic, and genomic approaches that enable discovery, characterization, and functional interpretation of these compounds. Emerging applications in sustainable forestry are discussed, including plant-derived pest management agents, metabolite-based selection of stress-resilient genotypes, ecological restoration strategies, and the valorization of forest biomass for industrial and pharmaceutical uses. Key challenges such as limited chemodiversity exploration, scalability constraints, data integration, and ethical considerations are also outlined, together with future research priorities emphasizing multi-omics integration, sustainable production systems, and interdisciplinary collaboration. Overall, forest-derived secondary metabolites represent a critical interface between ecological function and applied innovation, offering substantial potential for advancing sustainable forestry and bio-based economies.

Keywords: Plant secondary metabolites, forest trees, bioprospecting, metabolomics, sustainable forestry, bioactive compounds

Introduction

Plants are master chemists capable of synthesizing an extraordinary diversity of organic compounds not directly required for basic growth and development, collectively termed plant secondary metabolites (PSMs) (Fraenkel, 1959) [25]. Unlike primary metabolites essential for cellular maintenance, PSMs function as dynamic biochemical mediators that regulate plant interactions with their biotic and abiotic environment, forming a critical interface for defense, competition, signaling, and adaptation (Hartmann, 2007; Erb & Kliebenstein, 2020) [35, 21]. The global scale of plant chemodiversity is extraordinary, with estimates exceeding 200,000 distinct metabolites distributed across plant taxa, reflecting evolutionary innovation driven by ecological pressures (Afendi *et al.*, 2012) [3]. Major groups such as terpenoids, phenolics, and alkaloids contribute to herbivore and pathogen resistance, competitive interactions, and tolerance to abiotic stress, thereby shaping plant fitness and ecosystem functioning (Harborne, 1993; Züst & Agrawal, 2024) [34, 81]. Recent advances in genomics and epigenetics further demonstrate that secondary metabolite biosynthesis is dynamically regulated by environmental cues and genetic architecture, underscoring their adaptive significance (Boycheva *et al.*, 2024) [11].

Despite substantial progress in model and crop plants, forest trees remain comparatively underexplored sources of specialized metabolites, representing a major gap given their ecological dominance and evolutionary longevity (Theis & Lerdau). Long life spans and continuous exposure to herbivores, pathogens, and climatic variability have driven trees to evolve sophisticated chemical defense systems and structurally unique metabolites, particularly evident in conifers and other woody taxa (Keeling & Bohlmann, 2006; Whitehill *et al.*, 2023) [43, 74]. These chemical traits are increasingly relevant in the context of global environmental change, which is intensifying pest outbreaks and stress pressures on forest

ecosystems while simultaneously driving demand for renewable bio-based resources (Jansson *et al.*, 2021; Kessler & Kalske, 2025) [41, 45]. Advances in analytical technologies, including high-resolution metabolomics and spatially resolved chemical imaging, now enable precise characterization and localization of metabolites within plant tissues, accelerating discovery and functional interpretation (Wolfender *et al.*, 2019; Dong *et al.*, 2024) [77, 18].

Understanding the ecological functions of PSMs provides the conceptual basis for their translational application in forestry. Naturally occurring defensive compounds can be harnessed as eco-friendly pest management agents, while durable heartwood extractives that confer decay resistance offer models for sustainable wood protection strategies (Mithöfer & Boland, Salem & Böhm, 2022) [61]. Accordingly, this review synthesizes current knowledge on the bioprospecting of plant secondary metabolites from forest species by integrating insights into their diversity and biosynthesis, examining their ecological roles in forest ecosystems, outlining modern approaches for their identification and functional analysis, and evaluating their potential applications in sustainable forestry and environmental management.

2. Classification and biosynthesis of secondary metabolites

A fundamental understanding of the chemical diversity and biosynthetic origins of plant secondary metabolites (PSMs) is essential before exploring their ecological roles and applications. This section provides an overview of the major

classes of PSMs found in forest trees, outlines the primary biosynthetic pathways responsible for their production, and discusses the key genetic and environmental factors that regulate their accumulation (Fig 1).

2.1 Major classes of secondary metabolites

2.1.1 Alkaloids: Alkaloids constitute a structurally diverse group of nitrogen-containing compounds typically derived from amino acids such as lysine, tyrosine, and tryptophan (Ziegler & Facchini, 2008). These metabolites often exhibit potent biological activity, particularly against herbivores, because many target nervous system receptors or metabolic enzymes. In woody plants and forest-associated taxa, alkaloids frequently function as feeding deterrents or toxins, illustrating their defensive significance in long-lived species (Wink, 2018) [76].

2.1.2 Terpenoids (Isoprenoids)

Terpenoids represent the largest class of plant secondary metabolites, with tens of thousands of known structures derived from the universal C₅ precursors isopentenyl diphosphate and dimethylallyl diphosphate (Gershenzon & Dudareva, 2007) [27]. They are classified according to the number of isoprene units (e.g., mono-, sesqui-, di-, and triterpenes). In forest ecosystems, terpenoids play especially prominent roles; for example, conifer oleoresin contains monoterpenes and diterpenes that repel bark beetles, inhibit pathogens, and seal wounds, thereby providing both chemical and physical defense (Keeling & Bohlmann, 2006; Whitehill *et al.*, 2023) [43, 74].

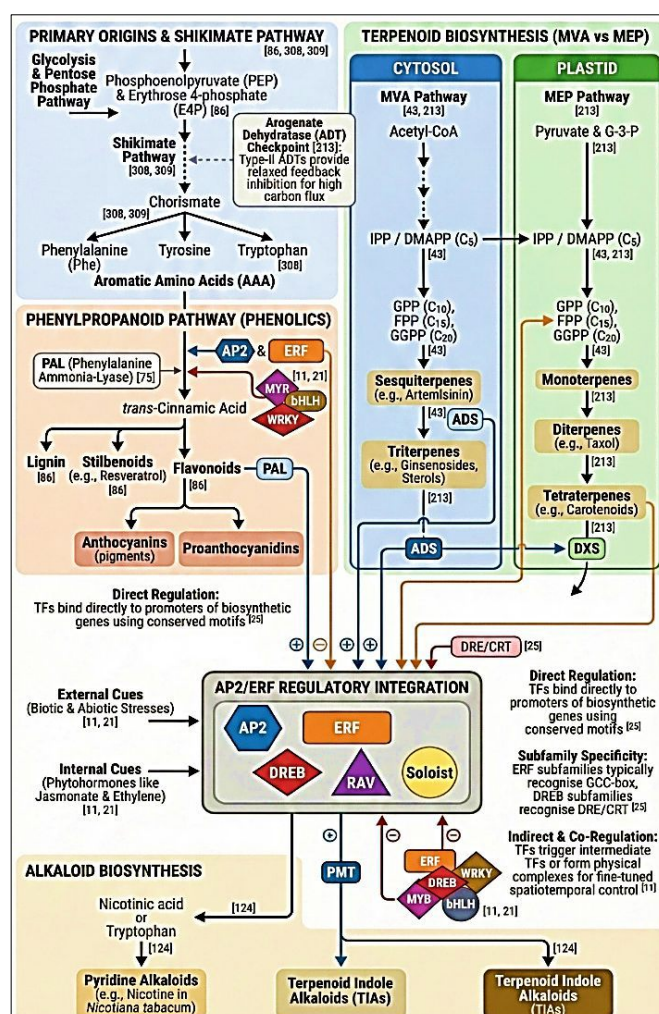


Fig 1: Integrated regulation of plant specialised metabolic pathways

2.1.3 Phenolics and flavonoids

Phenolic compounds are characterized by aromatic rings bearing hydroxyl groups and range from simple phenolic acids to complex polymers such as lignin (Cheynier *et al.*). Flavonoids, a major phenolic subclass, contribute to pigmentation, UV protection, and pathogen defense, while also mediating ecological interactions with pollinators and dispersers (Ferreira *et al.*, 2021) [22]. In trees, polymeric flavonoids such as condensed tannins accumulate in bark and foliage, where they reduce palatability and inhibit herbivory.

2.1.4 Saponins and glycosides

Saponins are glycosylated metabolites, usually triterpenoid or steroid derivatives, known for their membrane-disrupting properties and broad antimicrobial activity (Augustin *et al.*). Many other secondary metabolites also occur as glycosides, where attachment of sugar moieties modifies stability, solubility, transport, and toxicity. Such glycosylation can act as a reversible activation mechanism triggered by tissue damage or herbivory (Morant *et al.*, 2008) [52].

2.1.5 Tannins and lignans

Tannins and lignans represent structurally complex phenolic derivatives with major ecological importance in forest systems. Tannins influence litter decomposition rates and nutrient cycling by binding proteins and inhibiting microbial enzymes, thereby shaping soil processes and ecosystem productivity (Hättenschwiler & Vitousek, 2000) [36]. Lignans, formed by oxidative coupling of phenylpropanoid units, accumulate in woody tissues where they enhance resistance to fungal decay and contribute to heartwood durability (Suzuki & Umezawa, 2007) [67].

2.2 Biosynthetic pathways of secondary metabolites

Although structurally diverse, most secondary metabolites originate from a relatively small set of conserved biosynthetic routes that redirect primary metabolic intermediates into specialized pathways.

2.2.1 The shikimate pathway

The shikimate pathway generates aromatic amino acids phenylalanine, tyrosine, and tryptophan which serve as precursors for numerous phenolics, alkaloids, and lignin polymers (Maeda & Dudareva, 2012) [49]. A key regulatory step is catalyzed by phenylalanine ammonia-lyase (PAL), which converts phenylalanine into cinnamic acid, initiating phenylpropanoid biosynthesis.

2.2.2 The MVA and MEP isoprenoid pathways

Terpenoid formation depends on two compartmentalized pathways that produce the same universal precursors. The cytosolic mevalonate (MVA) pathway primarily supplies substrates for sesquiterpenes and triterpenes, whereas the plastidial methylerythritol phosphate (MEP) pathway generates precursors for monoterpenes, diterpenes, and other plastid-derived isoprenoids (Vranová *et al.*, 2013). Enzymes such as HMGR in the MVA pathway and DXS in the MEP pathway function as key regulatory control points governing carbon flux into terpenoid biosynthesis.

2.2.3 Enzymatic diversification and transcriptional regulation

Structural diversification of PSMs is largely driven by enzyme superfamilies, particularly cytochrome P450 monooxygenases and specialized transferases that catalyze

oxidation, glycosylation, methylation, and other modifications (Hamberger & Bak, 2013) [33]. Regulation of these pathways occurs through coordinated transcriptional control, where transcription factors such as MYB, bHLH, and WRKY regulate multiple biosynthetic genes simultaneously, allowing plants to rapidly adjust metabolite production in response to developmental or environmental stimuli (Patra *et al.*, 2013; Erb & Kliebenstein, 2020) [57, 21].

2.3 Factors influencing secondary metabolite biosynthesis

The accumulation of PSMs is not static but reflects a dynamic interaction between genetic programming, developmental processes, and environmental conditions.

2.3.1 Genetic and developmental regulation

The capacity to synthesize specific metabolites is genetically encoded, defining species-specific chemical profiles. Variation within species often produces distinct chemotypes that differ in metabolite composition and abundance (Moore *et al.*). Developmental stage further influences metabolite allocation: young tissues commonly exhibit higher concentrations of defensive compounds, whereas specialized tissues such as heartwood accumulate extractives including tannins, lignans, and terpenoids that confer long-term structural protection and decay resistance (Taylor *et al.*, 2002) [69].

2.3.2 Environmental modulation

Environmental factors exert strong influence on secondary metabolism. Light intensity and UV radiation commonly stimulate phenolic and flavonoid production, enhancing photoprotection, whereas drought and salinity stress can increase synthesis of protective metabolites that mitigate oxidative damage (Selmar & Kleinwächter, 2013; Züst & Agrawal, 2024) [64, 81]. Such stress-induced metabolic plasticity is particularly relevant for forestry applications because controlled environmental manipulation can enhance yields of valuable compounds. Integrative approaches combining metabolomics, transcriptomics, and ecological analyses are increasingly used to unravel these complex regulatory networks and to optimize metabolite production (Erb & Kliebenstein, 2020) [21].

3. Ecological roles of plant secondary metabolites in forest ecosystems

The extraordinary diversity of plant secondary metabolites (PSMs) reflects millions of years of evolutionary refinement that has shaped these compounds into precise biochemical tools mediating plant interactions with their environment. In forest ecosystems, where trees must survive for decades or centuries while exposed to persistent biotic and abiotic pressures, chemical strategies are particularly critical. Rather than serving a single function, PSMs operate as multifunctional mediators linking plant physiology with ecological processes such as defense, communication, competition, stress tolerance, and symbiosis. Understanding these ecological roles is essential for interpreting the adaptive significance of secondary metabolism in forestry species and for identifying compounds with potential applied value.

3.1 Defense against herbivores and pathogens

3.1.1 Antifeedant, toxic, and deterrent functions

The most widely recognized ecological role of PSMs in forest trees is defense against herbivores and pathogens.

Long-lived woody plants have evolved complex chemical arsenals that deter feeding, reduce digestibility, or directly poison attackers. Alkaloids, phenolics, and terpenoids frequently act as antifeedants or toxins; for example, quinolizidine alkaloids present in certain leguminous trees deter herbivory through bitterness and neurotoxicity (Wink, 2018)^[76]. A classic forestry example is conifer oleoresin, a terpene-rich secretion released upon bark beetle attack. This resin simultaneously seals wounds, traps invading insects, and delivers volatile toxins and antifungal diterpenes that inhibit associated pathogens (Keeling & Bohlmann, 2006; Whitehill *et al.*, 2023)^[43, 74]. Similarly, condensed tannins in oak leaves reduce herbivore performance by binding dietary proteins and digestive enzymes (Salminen & Karonen, 2011)^[62].

3.1.2 Constitutive and induced chemical defense systems

Tree defenses may be constitutive or inducible. Constitutive defences such as stored resins, phenolic-rich bark, or lignified tissues provide immediate protection, whereas inducible defenses are activated only after attack, reducing metabolic costs (Mithöfer & Boland). Induction is controlled by complex phytohormone signaling networks. Jasmonic acid (JA) regulates responses to chewing insects and necrotrophic pathogens, while salicylic acid (SA) mediates resistance to biotrophic pathogens, and ethylene (ET) modulates both pathways through synergistic or antagonistic interactions (Howe & Jander, 2008; Pieterse *et al.*, 2012)^[38, 59]. Genomic studies in forest genera such as *Populus* demonstrate that these signaling networks are conserved yet flexible, enabling species-specific defensive strategies shaped by ecological context (Jansson *et al.*, 2021)^[41].

3.2 Plant-pollinator and seed disperser interactions

Although defense is critical, many PSMs facilitate beneficial ecological interactions necessary for reproduction. Forest trees often depend on animals for pollination and seed dispersal, and these interactions are largely mediated by volatile secondary metabolites. Floral volatile organic compounds (VOCs) including terpenes, benzenoids, and phenylpropanoids serve as long-distance attractants guiding pollinators to reproductive structures (Raguso). Specific scent blends can promote pollinator fidelity and specialization, thereby enhancing reproductive success and contributing to plant diversification. Likewise, volatile compounds emitted by ripe fruits signal nutritional rewards to frugivores, ensuring effective seed dispersal (Rodríguez *et al.*, 2013)^[55]. The evolution of these signals illustrates a key principle of chemical ecology: the same metabolites that deter antagonists may simultaneously attract mutualists, depending on concentration, context, and receiver perception (Kessler & Kalske, 2025)^[45].

3.3 Allelopathy and competitive interactions

Forest trees compete intensely for resources such as light, water, and nutrients, and many employ chemical interference as a competitive strategy. Allelopathy involves the release of metabolites that inhibit neighboring plant growth through volatilization, litter leachates, or root exudates. A classic example is black walnut (*Juglans nigra*), which releases the naphthoquinone juglone from roots and litter, suppressing sensitive understory species (Willis, 2000)^[75]. Similarly, monoterpenes from conifer litter and

phenolic-rich residues from *Eucalyptus* species can inhibit seed germination and alter soil microbial communities, influencing forest succession and community composition (Zhang *et al.*, 2010; Hättenschwiler & Vitousek, 2000)^[79, 36]. Such chemically mediated competition is increasingly recognized as a major driver of plant community dynamics in forest ecosystems.

3.4 Adaptation to abiotic stress

In addition to biotic interactions, PSMs contribute to tree survival under environmental stress. Abiotic stresses such as drought, high light, salinity, and temperature extremes often trigger oxidative stress through accumulation of reactive oxygen species. Many phenolics and flavonoids act as antioxidants that scavenge these molecules and stabilize cellular structures (Agati *et al.*, 2012)^[4]. Flavonoids can also function as UV filters, accumulating in epidermal tissues to absorb harmful radiation while allowing photosynthetically active light to penetrate (Ferreira *et al.*, 2021)^[22]. Under drought or salinity stress, plants frequently increase production of protective metabolites that stabilize membranes and proteins, enhancing tolerance (Selmar & Kleinwächter, 2013)^[64]. Volatile isoprenoids such as isoprene and monoterpenes further protect photosynthetic membranes against thermal and oxidative damage, highlighting their importance under climate warming scenarios (Sharkey & Monson). The capacity of trees to dynamically adjust their metabolite profiles under stress is therefore a key determinant of resilience (Züst & Agrawal, 2024)^[81].

3.5 Symbiotic interactions and chemical communication

Beyond defense and competition, secondary metabolites mediate beneficial symbioses that are fundamental to forest ecosystem functioning. Most tree species form associations with mycorrhizal fungi that enhance nutrient and water uptake. Establishment of these symbioses depends on chemical signaling; for example, root-secreted strigolactones stimulate hyphal branching in arbuscular mycorrhizal fungi, facilitating colonization (Akiyama *et al.*, 2005)^[5]. Similarly, flavonoids released by leguminous trees induce nodulation genes in rhizobia, initiating nitrogen-fixing symbiosis (Oldroyd). Root exudates also contain complex mixtures of metabolites that shape rhizosphere microbial communities, selectively promoting beneficial microorganisms while suppressing pathogens (Bais *et al.*, 2006)^[8]. Advances in spatial metabolomics now allow visualization of these compounds within plant tissues, providing new insights into how chemical signals structure plant-microbe interactions (Dong *et al.*, 2024)^[18].

4. Analytical techniques for isolation and characterization

The progression from understanding the ecological roles of plant secondary metabolites (PSMs) to harnessing their potential applications relies critically on robust analytical methodologies. The ability to efficiently extract, purify, and structurally characterize these compounds is fundamental to bioprospecting from forest species. This section provides an overview of the key techniques employed in PSM analysis, from classical extraction methods to cutting-edge metabolomics and chemoinformatics approaches, with an emphasis on their application to woody plant material.

4.1 Extraction and purification strategies

4.1.1 Conventional solvent-based extraction

Extraction is the foundational step determining metabolite recovery and integrity. Traditional solvent extraction remains widely used because solvent polarity can be tailored to target specific metabolite classes. Nonpolar solvents efficiently extract lipophilic compounds such as terpenoids, whereas polar solvents are more suitable for phenolics, alkaloids, and glycosides (Azmir *et al.*, 2013) [7]. Soxhlet extraction, which repeatedly cycles solvent through plant material, is often employed as a reference method due to its high efficiency, although it is time-consuming and solvent-intensive (López-Bascón & De Castro, 2020) [48].

4.1.2 Supercritical fluid extraction

Supercritical CO₂ extraction represents an advanced alternative that combines gas-like diffusion with liquid-like solvation capacity, enabling efficient extraction of volatile and thermolabile compounds (Herrero *et al.*, 2006) [37]. Because CO₂ evaporates after depressurization, extracts are solvent-free, making this method particularly valuable for isolating terpenoids and essential oils from forest biomass.

4.1.3 Green and intensified extraction technologies

To improve sustainability and efficiency, several environmentally friendly extraction approaches have been developed. Microwave-assisted extraction and ultrasound-assisted extraction enhance cell disruption and mass transfer, reducing processing time and solvent usage (Chenat *et al.*, 2020; Kumar *et al.*, 2021) [14, 46]. Pressurized liquid extraction further improves recovery by maintaining solvents in a liquid state at elevated temperature and pressure (Nieto *et al.*, 2023) [55]. Such methods are especially relevant for forestry applications requiring large-scale processing of plant material (Salem & Böhm, 2022) [61].

4.2 Chromatographic separation techniques

4.2.1 Liquid chromatography systems

High-performance liquid chromatography (HPLC) is the principal separation technique for nonvolatile or thermally unstable metabolites, including flavonoids, alkaloids, and saponins (Sasidharan *et al.*). Advances in ultra-high-performance liquid chromatography (UHPLC) have improved resolution and sensitivity, enabling faster and more precise metabolite profiling (Guillarme & Veuthey, 2022) [31].

4.2.2 Gas chromatography for volatile metabolites

Gas chromatography (GC) is ideally suited for volatile and semi-volatile compounds such as monoterpenes and sesquiterpenes characteristic of conifer resins and floral emissions. Its high resolving power and reproducibility make it a standard method for profiling volatile metabolites in forest species (Adams, 2017; Keeling & Bohlmann, 2006) [2, 43].

4.2.3 Hyphenated chromatographic techniques

Coupling chromatography with mass spectrometry has transformed natural product analysis. LC-MS and GC-MS systems allow simultaneous separation, detection, and tentative identification of metabolites within complex extracts, greatly enhancing analytical efficiency (Wolfender *et al.*, 2019) [77]. High-resolution mass analyzers provide accurate mass measurements that facilitate molecular

formula determination and trace-level detection (Forcisi *et al.*, 2021) [24].

4.2.4 Preparative chromatography

For compound isolation, preparative techniques such as preparative thin-layer chromatography or preparative HPLC enable purification of individual metabolites for structural analysis or bioactivity testing (Sasidharan *et al.*).

4.3 Spectroscopic and spectrometric characterization

4.3.1 Nuclear Magnetic Resonance (NMR) spectroscopy

NMR spectroscopy is the most definitive technique for structural elucidation because it reveals detailed information about molecular connectivity, stereochemistry, and functional groups. One- and two-dimensional experiments allow complete structural determination, and recent microscale methods have reduced sample requirements (Claridge, 2016; Molinski, 2022) [16, 51].

4.3.2 Mass spectrometry and fragmentation analysis

Mass spectrometry provides molecular mass and elemental composition, while tandem MS generates diagnostic fragmentation patterns that serve as structural fingerprints for compound identification (Dunn *et al.*, 2021) [19].

4.3.3 Vibrational and electronic spectroscopy

Complementary methods such as Fourier-transform infrared spectroscopy identify functional groups based on characteristic vibrational bands (Griffiths & De Haseth, 2007), whereas UV-visible spectroscopy detects conjugated systems typical of phenolics and flavonoids and can be used for quantitative analysis (Mabry *et al.*).

4.4 Metabolomics and computational approaches

4.4.1 Untargeted metabolite profiling

Modern phytochemical research increasingly employs untargeted metabolomics, which aims to detect as many metabolites as possible in a sample, providing a comprehensive chemical fingerprint (Fiehn, 2002) [23]. Using high-resolution LC-MS or GC-MS platforms, this approach allows comparison of metabolite profiles across species, tissues, or environmental conditions, facilitating discovery of novel compounds (Wolfender *et al.*, 2019) [77].

4.4.2 Molecular networking and data visualization

Molecular networking organizes MS/MS spectra based on structural similarity, grouping related metabolites into clusters and enabling rapid identification of known compounds while highlighting novel candidates (Wang *et al.*, 2016) [71].

4.4.3 Spectral databases and chemoinformatics

Databases such as METLIN and KNApSack provide curated spectral and metabolite-species information that accelerates compound annotation and dereplication (Afendi *et al.*, 2012; Guijas *et al.*, 2018) [3, 30]. Integration of these resources with computational tools allows prediction of chemical properties, biosynthetic relationships, and potential bioactivity, transforming phytochemical analysis into a data-driven discipline (Kessler & Kalske, 2025) [45].

5. Molecular and genomic insights

The remarkable diversity and ecological specificity of plant secondary metabolites (PSMs) are ultimately rooted in the

genome. Understanding the genes, enzymes, and regulatory networks that govern PSM biosynthesis is essential for harnessing their potential in forestry applications. Recent advances in genomics, transcriptomics, and other omics technologies have provided unprecedented insights into the molecular machinery underlying chemical diversity in forest trees. This section explores the key gene families involved in PSM biosynthesis, the transcriptional networks that regulate their expression, and the integration of multi-omics approaches to understand how trees deploy their chemical arsenals in response to environmental challenges (Table 01).

5.1 Gene families underlying secondary metabolite biosynthesis

Secondary metabolite production is driven by specialized enzyme systems belonging to large multigene families whose diversification is a major source of plant chemodiversity (Pichersky & Gang, 2000; Boycheva *et al.*, 2024)^[58, 11].

5.1.1 Cytochrome P450 monooxygenases

Cytochrome P450 enzymes constitute one of the most versatile catalytic systems in plants, performing oxidative transformations that generate structural complexity and biological activity in specialized metabolites (Hamberger & Bak, 2013)^[33]. These enzymes participate in phenylpropanoid, alkaloid, and terpenoid pathways and are particularly important in trees for lignin formation, tannin synthesis, and resin acid biosynthesis (Keeling & Bohlmann, 2006)^[74]. Expansion of lineage-specific P450 subfamilies is common in forest species; for instance,

members of the CYP720B clade catalyze successive oxidation steps in conifer diterpene resin acid biosynthesis (Whitehill *et al.*, 2023)^[43]. The genome of *Populus trichocarpa* alone encodes hundreds of P450 genes, reflecting the metabolic complexity of long-lived woody plants (Nelson & Werck-Reichhart).

5.1.2 Terpene synthases

Terpene synthases (TPSSs) generate the structural backbone of terpenoid diversity by cyclizing prenyl diphosphate substrates into diverse terpene skeletons (Chen *et al.*, 2011)^[13]. Conifers possess large TPS gene families, particularly within the TPS-d subfamily, which produces monoterpenes, sesquiterpenes, and diterpenes constituting oleoresin defenses (Keeling & Bohlmann, 2006)^[43]. The Norway spruce genome contains dozens of TPS genes, enabling production of complex terpene blends that deter herbivores and pathogens (Warren *et al.*, 2021)^[72].

5.1.3 Glycosyltransferases

UDP-glycosyltransferases (UGTs) catalyze glycosylation reactions that modify solubility, stability, storage, and bioactivity of specialized metabolites (Bowles *et al.*, 2006)^[10]. Glycosylated forms of phenolics, cyanogenic compounds, and terpenoids often function as inactive storage forms that are rapidly activated upon herbivore attack (Morant *et al.*, 2008)^[52]. Large UGT gene families in trees such as *Populus* underscore the importance of glycosylation in regulating metabolite accumulation across tissues and developmental stages (Louveau & Osbourn, 2019)^[47].

Table 1: Representative forest tree species, their major secondary metabolites, and associated ecological functions.

Tree Species (Common Name)	Major Secondary Metabolite Classes	Representative Compounds	Ecological Functions	Key References
Conifers (<i>Pinus</i> , <i>Picea</i> , <i>Abies</i>)	Terpenoids (mono-, sesqui-, diterpenes); Phenolics	α -Pinene, β -pinene, limonene; resin acids (abietic acid, levopimaric acid); stilbenes	Defense against bark beetles and fungal pathogens; constitutive and induced oleoresin production	Keeling & Bohlmann, 2006; Whitehill <i>et al.</i> , 2023 ^[43, 74]
<i>Populus</i> spp. (Poplar, Cottonwood)	Phenolics (salicinoids, flavonoids, tannins); Terpenoids	Salicin, tremulacin; catechin, quercetin; mono- and sesquiterpenes	Herbivore defense; signaling; UV protection	Jansson <i>et al.</i> , 2021; Tsai <i>et al.</i> , 2006 ^[41, 82]
<i>Quercus</i> spp. (Oak)	Phenolics (hydrolyzable & condensed tannins, flavonoids)	Ellagitannins (vescalagin, castalagin); proanthocyanidins	Anti-herbivore defense; nutrient cycling via litter chemistry	Salminen & Karonen, 2011 ^[62]
<i>Eucalyptus</i> spp. (Gum trees)	Terpenoids; Phenolics	1,8-Cineole; macrocarpals; essential oil components	Herbivore defense; allelopathy; antimicrobial activity	Zhang <i>et al.</i> , 2010; Goodger <i>et al.</i> , 2022 ^[79, 28]
<i>Acacia</i> spp. (Wattle)	Phenolics (tannins); Alkaloids; Cyanogenic glycosides	Profisetinidin tannins; pyridine alkaloids; prunasin	Herbivore deterrence; nitrogen storage; allelopathy	Seigler, 2003 ^[83]
<i>Juglans</i> spp. (Walnut)	Phenolics (naphthoquinones)	Juglone	Allelopathy; defense against herbivores and pathogens	Willis, 2000 ^[75]
<i>Taxus</i> spp. (Yew)	Alkaloids (taxane diterpenoids)	Paclitaxel (Taxol®)	Defense against herbivores and pathogens	Croteau <i>et al.</i> , 2006 ^[17]
<i>Betula</i> spp. (Birch)	Terpenoids (triterpenes); Phenolics	Betulin, betulinic acid; papyriferic acid; flavonol glycosides	Herbivore resistance; bark protection	Taipale <i>et al.</i> , 2021 ^[68]

5.2 Transcriptional regulation and signaling networks

5.2.1 Master transcription factor families

Biosynthetic genes are coordinated by transcription factors that regulate entire pathways rather than individual enzymes (Patra *et al.*, 2013)^[57]. Among the most important regulators:

- **MYB proteins** control phenylpropanoid metabolism, including lignin, flavonoid, and tannin biosynthesis (Liu *et al.*, 2015)^[47]. In poplar, MYB134 regulates

proanthocyanidin synthesis in response to stress (Mellway *et al.*, 2009)^[50].

- **bHLH factors** frequently partner with MYB and WD40 proteins to form regulatory complexes controlling anthocyanins and tannins (Xu *et al.*, 2015)^[78].
- **WRKY proteins** integrate stress signaling with defense metabolite production and are strongly induced by pathogens and herbivores (Rushton *et al.*, 2010)^[60].

5.2.2 Hormonal crosstalk in metabolic regulation

Transcriptional control is tightly linked to phytohormone signaling. Jasmonic acid regulates defense responses against herbivores, salicylic acid mediates pathogen resistance, and ethylene and abscisic acid modulate stress responses (Karthik *et al.*, 2024; Howe & Jander, 2008; Pieterse *et al.*, 2012)^[42, 38, 59]. Crosstalk among these pathways enables trees to tailor metabolite production to specific environmental threats. Transcriptomic studies in conifers show that insect attack rapidly activates hundreds of biosynthetic genes and transcription factors involved in terpene and phenolic pathways (Whitehill *et al.*, 2023)^[74].

5.3 Multi-omics integration in forest metabolite research

5.3.1 Genomics

Sequenced genomes of major forest trees including *Populus trichocarpa*, *Eucalyptus grandis*, *Picea abies*, and *Pinus taeda* provide comprehensive catalogs of biosynthetic genes and reveal lineage-specific expansions linked to metabolite diversity (Tuskan *et al.*, 2006; Myburg *et al.*, 2014; Nystedt *et al.*, 2013; Neale *et al.*, 2014)^[70, 53, 56, 54] (table 2).

5.3.2 Transcriptomics

RNA-seq enables identification of genes induced during stress or development. Correlating transcript abundance with metabolite profiles allows discovery of candidate biosynthetic genes. For example, transcriptome analysis of Sitka spruce identified terpene synthase genes associated with induced resin production (Hall *et al.*, 2011)^[32].

5.3.3 Proteomics and metabolomics integration

Transcript levels do not always predict enzyme abundance or metabolite accumulation due to post-transcriptional regulation. Integrative multi-omics approaches combine transcriptomic, proteomic, and metabolomic data to construct functional metabolic networks (Fernie & Stitt). In *Populus*, integrated analyses have revealed coordinated shifts in phenylpropanoid metabolism during drought stress, illustrating how environmental cues reshape chemical pathways (Barros *et al.*, 2022)^[9]. Such systems-level approaches are emerging as powerful tools for identifying genetic determinants of metabolite traits relevant to forestry improvement (Boycheva *et al.*, 2024)^[11] (table 2).

Table 2: Molecular regulation of secondary metabolism in selected tree species and model woody plants

Tree species (Common name)	Gene family / regulatory system	Key findings	Ecological or applied significance	Key references
<i>Picea sitchensis</i> (Sitka spruce)	Terpene synthases (TPS-d); CYP720B P450s	Co-regulated genes identified during induced oleoresin formation; functional diterpene synthases characterized	Molecular basis of bark beetle resistance; targets for marker-assisted selection	Hall <i>et al.</i> , 2011; Whitehill <i>et al.</i> , 2023 ^[32, 74]
<i>Populus trichocarpa</i> (Black cottonwood)	MYB transcription factors (MYB134, MYB115)	Regulators of condensed tannin biosynthesis activated by wounding and herbivory	Improving constitutive and inducible phenolic defenses in plantation and bioenergy trees	Mellway <i>et al.</i> , 2009 ^[50]
<i>Populus tremula</i> × <i>alba</i> (Hybrid aspen)	Hormonal signaling (JA pathway)	Jasmonate signaling required for induced phenolic glycoside accumulation and resistance to herbivores	Basis for hormone-mediated pest resistance strategies in forestry	Ehrlich <i>et al.</i> , 2023 ^[20]
<i>Eucalyptus grandis</i>	Terpene synthase (TPS) gene family	Genome-wide expansion of TPS genes; cineole synthase genes identified	Breeding for enhanced essential oil production, pest resistance, and pharmaceuticals	Myburg <i>et al.</i> , 2014; Goodger <i>et al.</i> , 2022 ^[53, 28]
<i>Pinus taeda</i> (Loblolly pine)	Multi-omics integration (genomics, transcriptomics, metabolomics)	QTL-transcript-metabolite integration identified loci controlling resin composition and yield	Genomic selection for improved oleoresin production and defense traits	Westbrook <i>et al.</i> , 2020 ^[73]
<i>Vitis vinifera</i> (Grapevine*)	WRKY and MYB regulators of stilbene pathway	Coordinated transcriptional regulation of stilbene phytoalexins during pathogen attack	Model system for defense metabolite regulation relevant to woody perennials	Vannozzi <i>et al.</i> , 2018 ^[84]

6. Applications in forestry and sustainable agriculture

The diversity, ecological relevance, and molecular regulation of plant secondary metabolites (PSMs) collectively position forest trees as a rich resource for sustainable technologies and bio-based innovations. Insights into metabolite biosynthesis, ecological function, and genetic control now enable translation of fundamental knowledge into applied forestry solutions. Bioprospecting of tree-derived metabolites supports environmentally compatible pest management, climate-resilient breeding programs, ecosystem restoration strategies, and industrial bioproduct development. The following sections synthesize current and emerging applications of PSMs across forestry and allied sectors.

6.1. Natural product-based pest and disease management

Concerns regarding pesticide resistance, environmental contamination, and non-target toxicity have stimulated interest in plant-derived pest control agents. Secondary metabolites evolved as natural defense compounds represent

a promising alternative to synthetic pesticides (Isman, 2006; Salem & Böhm, 2022)^[39] (table 3).

6.1.1. Botanical biopesticides

Plant-derived biopesticides include crude extracts, purified compounds, and essential oils. A widely recognized example is neem (*Azadirachta indica*), whose limonoid azadirachtin functions as an antifeedant, growth inhibitor, and reproductive disruptor against numerous insect pests (Schmutterer, 1990)^[63]. Essential oils from conifers and *Eucalyptus* species, rich in mono- and sesquiterpenes, exhibit insecticidal and repellent properties effective against bark beetles, defoliators, and aphids (Isman, 2020; Långström & Day, 2022)^[39, 85]. Their complex chemical composition often results in multi-target activity, which may reduce the likelihood of resistance development compared with single-compound pesticides (Isman, 2006)^[39].

6.1.2. Antifungal compounds for disease control

Forest pathogens cause substantial economic losses in plantations and nurseries. Many tree-derived metabolites function as natural antifungal agents. Heartwood extractives, including tropolones, lignans, and tannins, provide intrinsic decay resistance and have been investigated as eco-friendly wood preservatives (Taylor *et al.*, 2002; Singh & Singh, 2012) ^[69, 66]. Stilbenes synthesized by conifers in response to infection act as phytoalexins with strong antifungal activity and are being explored for nursery protection and plant health formulations (Chong *et al.*, 2009; Salem & Böhm, 2022) ^[15, 61].

6.2. Stress-resilient forest tree improvement

Climate change is intensifying abiotic and biotic stress pressures on forest ecosystems, making resilience a major breeding target. Because PSMs are directly involved in stress responses, their profiles can serve as functional biochemical markers for selecting tolerant genotypes.

6.2.1. Metabolites as biomarkers for stress tolerance

Metabolite-assisted breeding integrates metabolomic data into selection programs to identify stress-resilient individuals (Fernie & Schauer). For example, enhanced flavonoid and proanthocyanidin accumulation in *Populus* has been linked to drought tolerance through antioxidant activity (Barros *et al.*, 2022) ^[9]. Similarly, constitutive resin production and specific terpene profiles in conifers correlate with resistance to bark beetles and other pests, supporting their use as selection criteria in breeding programs for species such as *Pinus taeda* (Westbrook *et al.*, 2020) ^[73]. Integrating metabolomic and genomic data is expected to improve predictive breeding models for forestry species (Jansson *et al.*, 2021; Moran *et al.*, 2024) ^[51, 52].

6.3. Ecological restoration and soil health

Secondary metabolites influence not only individual plant defense but also ecosystem-level processes such as species interactions, soil chemistry, and microbial community composition.

6.3.1. Allelopathic vegetation management

Allelopathic trees can be strategically deployed to suppress invasive plants or manage competing vegetation in restoration projects. Chemical compounds released through litter, roots, or volatiles may inhibit germination or growth of neighboring plants, providing a natural weed control mechanism (Callaway & Ridenour, 2004; Lorenzo *et al.*,

2022) ^[12, 86]. Such approaches must be carefully evaluated to avoid unintended suppression of desirable native species.

6.3.2. Soil processes and nutrient cycling

Phenolic compounds, especially tannins, influence decomposition dynamics and nitrogen cycling by forming stable complexes with proteins and organic matter (Hättenschwiler & Vitousek, 2000; Adamczyk *et al.*, 2021) ^[36, 1]. Root-derived metabolites also shape rhizosphere microbial communities, selectively promoting beneficial microbes and suppressing pathogens (Bais *et al.*, 2006; Dong *et al.*, 2024) ^[8, 18]. Understanding these interactions can inform species selection and management practices aimed at enhancing soil fertility, carbon sequestration, and ecosystem stability.

6.4. Industrial and pharmaceutical prospects

Forest biomass residues including bark, needles, knots, and branches represent abundant renewable feedstocks for extracting high-value metabolites within a circular bioeconomy framework (Keegan *et al.*, 2022) ^[44].

6.4.1. Value-added bioproducts from forest biomass

Tree bark, often constituting up to one-fifth of stem volume, is rich in extractives such as polyphenols, tannins, triterpenes, and lignans (Feng *et al.*). These compounds support diverse industrial uses: tannins serve as adhesives and polymer precursors; terpenes are used in solvents, fragrances, and resins; and suberin derivatives contribute to advanced biomaterials and coatings (Gandini *et al.*, 2021; Silvestre & Gandini, 2020; Pizzi, 2021) ^[26, 65, 87]. Such valorization strategies enhance economic returns while reducing biomass waste.

6.4.2. Pharmaceutical applications

Forest trees have historically yielded pharmacologically important compounds. The diterpenoid alkaloid paclitaxel, originally isolated from *Taxus brevifolia*, is a widely used anticancer drug and exemplifies the therapeutic potential of tree metabolites (Croteau *et al.*, 2006) ^[17]. Numerous other tree-derived compounds, including triterpenes, lignans, and alkaloids, show antimicrobial, anti-inflammatory, and anticancer properties and are currently under investigation for clinical development (Atanasov *et al.*, 2021) ^[6]. Continued integration of ethnobotanical knowledge with metabolomics-guided discovery is expected to accelerate identification of novel therapeutic molecules.

Table 3: Applications of tree-derived secondary metabolites in forestry and related sectors

Application area	Compound class / source	Example species	Practical application	Key references
Pest management	Limonoids (azadirachtin)	<i>Azadirachta indica</i>	Botanical insecticide	Schmutterer, 1990; Isman, 2020 ^[63, 39]
	Essential oils (terpenes)	<i>Pinus, Picea, Eucalyptus</i>	Repellents and insecticides	Isman, 2020; Långström & Day, 2022 ^[63, 85]
Disease control	Stilbenes	Conifers	Antifungal phytoalexins	Chong <i>et al.</i> , 2009 ^[15]
	Heartwood extractives	<i>Thuja, Acacia</i>	Natural wood preservatives	Taylor <i>et al.</i> , 2002 ^[69]
Tree improvement	Oleoresin metabolites	<i>Pinus, Picea</i>	Biomarkers for pest resistance	Westbrook <i>et al.</i> , 2020 ^[73]
	Phenolic glycosides	<i>Populus</i>	Drought and herbivore resistance markers	Barros <i>et al.</i> , 2022 ^[9]
Restoration	Allelochemicals	<i>Juglans, Eucalyptus</i>	Weed suppression	Lorenzo <i>et al.</i> , 2022
Industrial products	Tannins, terpenes	Multiple tree species	Adhesives, polymers, solvents	Pizzi, 2021; Silvestre & Gandini, 2020 ^[87, 65]
Pharmaceuticals	Taxanes, triterpenes	<i>Taxus, Betula</i>	Anticancer and therapeutic agents	Croteau <i>et al.</i> , 2006; Atanasov <i>et al.</i> , 2021 ^[17, 6]

7. Challenges, knowledge gaps, and future perspectives

Despite rapid progress in elucidating the diversity, ecological functions, and biosynthetic regulation of plant secondary metabolites (PSMs) in forest trees, significant barriers remain before this knowledge can be fully translated into sustainable applications. These challenges span biological, technological, and socio-economic dimensions and collectively define the research priorities that will shape the next phase of discovery and utilization.

7.1. Knowledge gaps in chemodiversity and ecological function

A major limitation is the uneven exploration of tree chemodiversity. While a few model or economically important genera have been intensively studied, the vast majority of tree species particularly those from tropical and subtropical forests remain chemically uncharacterized. This underexplored diversity represents both an opportunity for novel compound discovery and a challenge requiring systematic, strategically guided screening approaches. Equally important is the limited ecological validation of metabolite function. Many compounds show promising activity in laboratory assays, yet their real-world performance within complex forest ecosystems remains poorly understood. Interactions among multiple metabolites, environmental conditions, and biological communities can profoundly influence efficacy, specificity, and ecological safety. In addition, the role of the tree-associated microbiome in shaping chemical phenotypes is only beginning to be recognized. Endophytes, rhizosphere microbes, and symbiotic fungi may contribute directly or indirectly to metabolite biosynthesis, suggesting that tree chemistry should be viewed as a property of an integrated biological system rather than of the host plant alone.

7.2. Technical and translational constraints

Translating metabolite discovery into practical products remains a central bottleneck. Many bioactive compounds occur in low concentrations, making sustainable supply difficult and necessitating alternative production strategies such as cell culture systems, microbial biosynthesis platforms, or endophyte cultivation. Although modern extraction technologies have improved efficiency, scaling these methods for industrial processing of forestry biomass requires further optimization. Product development also faces formulation challenges, since many metabolites are volatile, unstable, or rapidly degraded under field conditions. Furthermore, the integration of multi-omics datasets linking genomic, transcriptomic, proteomic, and metabolomic information remains analytically demanding, and improved computational tools are needed to translate large datasets into predictive biological insight.

7.3. Socio-economic and ethical dimensions

Bioprospecting from forest resources operates within complex regulatory and ethical frameworks. Ensuring fair access, equitable benefit-sharing, and respect for traditional knowledge is essential for responsible research and innovation. Intellectual property considerations add further complexity, as balancing open scientific collaboration with commercialization incentives remains challenging. Addressing these issues requires interdisciplinary engagement that integrates legal, social, and policy perspectives alongside biological research.

7.4. Strategic directions for future research

Advancing the field will require coordinated efforts across several priority areas: systematic exploration of underinvestigated tree lineages; ecologically realistic validation of metabolite function through field-based experimentation; development of scalable and sustainable production platforms; integration of multi-omics data to model biosynthetic networks; characterization of microbiome contributions to tree chemistry; and innovation in formulation technologies that enhance stability and efficacy. Equally important is the adoption of ethical and transparent research practices that ensure long-term sustainability and equitable participation of source communities.

8. Conclusion

Plant secondary metabolites from forest trees constitute a vast and evolutionarily refined reservoir of chemical diversity that underpins ecological resilience and offers significant opportunities for sustainable innovation. This review highlights that these compounds, produced through specialized metabolic pathways and tightly regulated genetic networks, mediate critical ecological functions including defense, communication, and stress adaptation, while also providing a foundation for applications in pest management, climate-resilient tree improvement, ecological restoration, and bio-based industries. Advances in omics technologies, analytical chemistry, and bioinformatics have transformed our ability to characterize and utilize these metabolites, enabling integrative approaches that link molecular mechanisms with ecosystem processes and practical forestry solutions. Moving forward, effective bioprospecting will depend on interdisciplinary collaboration, sustainable production strategies, and responsible resource governance, particularly for underexplored tree taxa and their associated microbiomes. Harnessing the biochemical potential of forests thus represents not only a scientific frontier but also a pathway toward resilient ecosystems, green technologies, and a circular bioeconomy grounded in ecological stewardship.

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