

Ginkgo biloba as a Forest-Derived Natural Product: Systematic Review of Bioactive Compounds and Processing Technologies

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ABSTRACT: *Ginkgo biloba* L. is a forest-derived natural product whose leaves, seeds, and exocarp contain bioactive compounds with potential relevance to neurodegenerative diseases. However, variation in raw-material characteristics and processing conditions can affect phytochemical composition, extraction efficiency, and product quality. Here, we systematically reviewed extraction, processing, and analytical technologies used to obtain and characterize *G. biloba*-derived bioactive compounds relevant to Alzheimer's disease, Parkinson's disease, and dementia. A Scopus-based search following PRISMA 2020 identified 436 records, supplemented by citation tracking, with 33 studies meeting the eligibility criteria for qualitative synthesis. The evidence shows that standardized solvent processing, green and subcritical-water extraction, and cell or organ culture are the principal approaches for producing bioactive fractions, while HPLC, UPLC-MS/MS, and LC-MS/MS dominate compound quantification, chemical fingerprinting, authentication, and quality control. Leaves were the predominant raw material, whereas seeds and exocarp represented comparatively underutilized resource fractions with potential for valorization. Raw-material heterogeneity associated with leaf age, harvest source, season, and tree characteristics emerged as a major challenge for reproducible phytochemical profiles. These findings position *G. biloba* as a forest-derived natural product whose development for neurodegenerative applications depends on integrating resource utilization, processing, phytochemical characterization, and analytical standardization. This perspective links forest resources with product quality.

KEYWORDS: *Ginkgo biloba*; forest-derived natural product; bioactive compounds; processing technologies; neurodegenerative diseases

1. INTRODUCTION

Neurodegenerative conditions, particularly Alzheimer's disease (AD), Parkinson's disease (PD), and dementia syndromes more broadly, remain among the leading contributors to disability in ageing populations, and the demand for safer, multi-target adjunct therapies has renewed scientific interest in tree-derived natural products [1]. Among these, extracts of *Ginkgo biloba* L. leaves are consistently reported to modulate oxidative stress, mitochondrial dysfunction, and neuroinflammatory pathways implicated in AD and PD pathophysiology [2,3], which has sustaining a large and still-growing body of chemical and technological research on this species over the past three decades [4].

Beyond its pharmacological reputation, *G. biloba* is first and foremost a forest tree species: a living-fossil member of a monotypic order that is cultivated and harvested worldwide as a non-timber forest product (NTFP), with leaves, seeds, and exocarp all entering commercial value chains [5,6]. Historically, the foliage and seeds have been used in East Asian traditional medicine for millennia before being industrially standardized in the twentieth century into leaf extracts such as EGb 761, which remain among the best-characterized plant extracts in the world [7,8]. This dual identity, a forest biomass resource on one hand and a pharmaceutical-grade phytochemical product on the other, means that the scientific and industrial value of *G. biloba* is inseparable from the forest-product technology used to convert raw foliage and seed biomass into a chemically defined, reproducible extract [9].

The technological challenge is substantial. The concentration of the two principal bioactive fractions, the terpene trilactones (ginkgolides A, B, C and bilobalide) and the flavonol glycosides, varies considerably with

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leaf age, harvest season, geographic provenance, and even the sex of the tree, so that raw forest material collected at different times or locations is chemically heterogeneous before any processing begins [10]. Converting this heterogeneous biomass into a standardized product therefore requires an integrated technological chain: post-harvest handling, solvent or green extraction, purification, and rigorous analytical quality control, most of which parallels the processing chain used for other non-timber forest products such as essential oils, resins, and tannin extracts [11].

Although numerous narrative reviews have summarized the pharmacology and clinical evidence for *G. biloba* in AD, PD, and dementia, comparatively few have systematically synthesized the literature from a forest-product-technology perspective, that is, focusing on how the raw biomass is sourced, processed, extracted, and analytically standardized, rather than on downstream pharmacological outcomes alone. To date, no systematic review has specifically mapped the extraction, processing, and analytical technologies applied across the leaf, seed, and exocarp fractions of *G. biloba* in the context of neurodegenerative-disease-relevant bioactive compounds. This review therefore aims to systematically evaluate the forest-product processing and analytical technologies applied to *G. biloba*-derived ginkgolides, bilobalide, and flavonoids, with emphasis on extraction methods, quality-control platforms, and raw-material/resource-utilization aspects relevant to Alzheimer's disease, Parkinson's disease, and dementia research.

2. MATERIALS AND METHODS

2.1. Material

This systematic literature review was conducted using bibliographic and computational resources without laboratory experimentation. Literature records were retrieved from the Scopus database (Elsevier). Reference management and deduplication were performed using Mendeley Reference Manager, and data extraction and tabulation were carried out in Microsoft Excel. All searching, screening, and synthesis activities were performed on a standard laptop computer with internet access to the institutional Scopus subscription.

2.2. Study Design

This review was designed and reported as a systematic literature review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines, adapted for a technology-and-resource-focused (rather than purely clinical) synthesis of non-timber forest product literature.

2.3. Literature Search Strategy

A single comprehensive search was performed in Scopus using the following Boolean query, applied to titles, abstracts, and keywords (TITLE-ABS-KEY): ("Ginkgo biloba" AND (Alzheimer* OR Parkinson* OR dementia) AND (ginkgolide* OR bilobalide OR flavonoid* OR "bioactive compound*" OR phytochemical*)) The search was performed on the Scopus database and refined stepwise using document-type, language, source-type, publication-stage, and publication-year filters. The refinement process and the corresponding number of records retrieved at each step are summarized in Table 1. The final refined query retrieved 436 records, published between 1998 and 2025, and served as the identification pool for this review.

Table 1. Stepwise Boolean-Query Refinement in Scopus and Resulting Number of Retrieved Records.

Search string / refinement step (Scopus)	Records (n)
TITLE-ABS-KEY("Ginkgo biloba" AND (Alzheimer* OR Parkinson* OR dementia) AND (ginkgolide* OR bilobalide OR flavonoid* OR "bioactive compound*" OR phytochemical*))	567
+ PUBYEAR > 1989 AND PUBYEAR < 2026	538
+ LIMIT-TO DOCTYPE ("re" OR "ar")	462
+ LIMIT-TO LANGUAGE ("English")	439
+ LIMIT-TO SRCTYPE ("j")	437
+ LIMIT-TO PUBSTAGE ("final"); PUBYEAR > 1997 AND PUBYEAR < 2026	436

2.4. Eligibility Criteria

Studies were selected based on predefined inclusion and exclusion criteria.

Inclusion criteria were:

- (1) original research articles or review articles;
- (2) studies addressing *G. biloba*-derived bioactive compounds (ginkgolides, bilobalide, flavonol glycosides, or related phytochemicals) in relation to Alzheimer's disease, Parkinson's disease, or dementia;
- (3) studies reporting a forest-product-technology component, namely extraction or processing methods, analytical/quality-control platforms, raw-material or resource-utilization characterization (leaf, seed, or exocarp), or biotechnological production of the bioactive fraction; and
- (4) articles published in English with accessible full text.

Exclusion criteria were:

- (1) studies reporting only clinical efficacy or safety outcomes without any chemical, extraction, or analytical technology component;
- (2) studies focused exclusively on silvicultural or agronomic cultivation practices (e.g., planting density, breeding, orchard management) without a processing or analytical dimension;
- (3) conference abstracts, editorials, letters, and non-full-text records; and
- (4) records that substantially duplicated the dataset or content of an already-included study.

2.5. Study Selection Process

Records retrieved from Scopus ($n = 436$) were supplemented with records identified through reference-list and citation-tracking searches ($n = 14$), yielding 450 records. After removal of duplicates ($n = 8$), 442 records were screened by title and abstract against the eligibility criteria, of which 361 were excluded for being unrelated to the technological/analytical aspects of *G. biloba* bioactive compounds, unrelated to AD/PD/dementia, or purely clinical/agronomic in focus. The remaining 81 full-text articles were assessed for eligibility; 48 were excluded (no technological or analytical data, $n = 19$; exclusive focus on silvicultural cultivation, $n = 11$; insufficient methodological detail, $n = 10$; duplicated dataset/content, $n = 8$). A final set of 33 studies was included in the qualitative synthesis. The complete selection process is summarized in the PRISMA flow diagram (Figure 1).

2.6. Data Extraction

A standardized extraction form was used to record, for each included study:

- (1) author(s) and year of publication;
- (2) the forest-derived raw material or plant part investigated (leaf, seed, exocarp/fruit, or cell/organ culture biomass);
- (3) the extraction, processing, or analytical technology applied;
- (4) the bioactive compound class identified or quantified; and
- (5) the main technological objective and, where reported, its stated relevance to neurodegenerative-disease application.

2.7. Data Synthesis and Quality Assessment

A qualitative descriptive synthesis was performed, focusing on trends in raw-material sourcing, extraction and processing technology, and analytical/quality-control methodology. Because of substantial heterogeneity in raw material, technology, and reported outcomes, quantitative meta-analysis was not performed. Methodological quality was appraised using a framework adapted from QUADAS-2 for non-clinical analytical and processing studies, covering: (1) clarity and representativeness of the forest raw-material description; (2) appropriateness of the extraction/processing technology to the stated objective; (3) transparency of analytical conditions and parameters; and (4) confidence of compound identification, categorized where applicable according to the Metabolomics Standards Initiative (MSI) reporting levels (Level 1, confirmed by reference standard, to Level 4, unknown compound detected by mass only).

3. RESULTS

3.1. Study Selection and Characteristics of Included Studies

Following the PRISMA-guided selection process (Figure 1), 33 studies published between 1998 and 2025 were included in the qualitative synthesis. The included literature originated from journals spanning natural product chemistry, ethnopharmacology, plant biology, analytical/physical chemistry, and food composition science, including the *Journal of Ethnopharmacology*, *Frontiers in Pharmacology*, *Plants*, *Plant Biology*, *Molecules*, and the *Russian Journal of Physical Chemistry B*, reflecting the inherently cross-disciplinary character of forest-product bioactive-compound research. Twenty-six of the 33 studies (79%) were published between 2019 and 2025, consistent with accelerating interest in green extraction, high-resolution analytical fingerprinting, and forest-biomass valorization technologies over the last technology cycle [12,13].

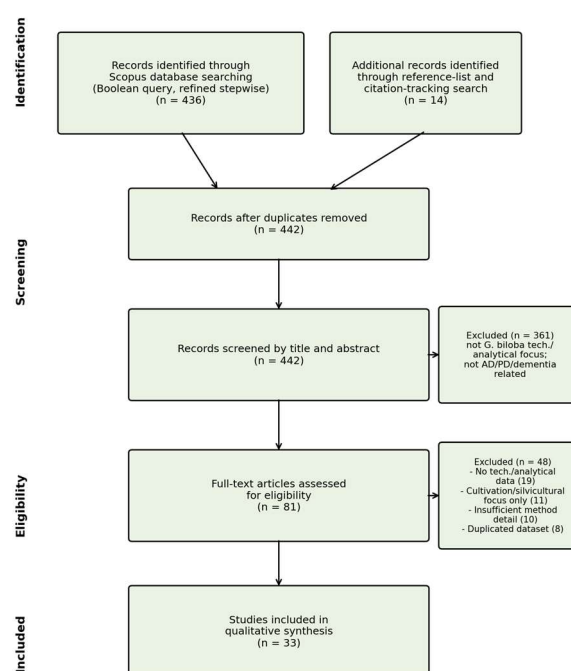


Figure 1. PRISMA 2020 Flow Diagram of The Study Selection Process.

The forest raw material investigated across studies was predominantly leaf biomass (24 studies), followed by seed/kernel material (5 studies), exocarp or fruit tissue (3 studies), and in vitro cell or organ culture biomass (1 study). Extraction- and processing-related technologies were reported in 13 studies, analytical/quality-control technologies in 15 studies, and combined phytochemistry-plus-bioactivity studies bridging both domains in 5 studies. General characteristics of all 33 included studies are summarized in Table 2.

Table 2. General Characteristics of The 33 Studies Included in The Qualitative Synthesis, Ordered by First Citation Appearance in The Text.

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Li et al. (2020) [1]	Leaf-derived compounds	Narrative review	Ginkgolides	Immune/inflammatory mechanism synthesis
Park et al. (2025) [2]	Purified compound (leaf- derived)	In vivo (5xFAD mouse) mechanistic study	Ginkgolide A	Downstream bioactivity of standardized compound
Praveen et al. (2024) [3]	Purified compound (leaf- derived)	In vivo (MPTP mouse) mechanistic study	Ginkgolide B	Downstream bioactivity of

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Shareena & Kumar (2022) [4]	Leaf (general)	Historical/technology timeline review	Terpene trilactones, flavonoids	standardized compound Functional-food ingredient transformation overview
Shahrajabian et al. (2022) [5]	Leaf, seed (general)	Ethnobotanical/nutritional review	Full phytochemical spectrum	Historical NTFP-use overview
Liu et al. (2022) [6]	Leaf, seed, exocarp	Comprehensive resource- utilization review	Full phytochemical spectrum	Cross-fraction resource utilization synthesis

Table 2. Continue

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Van Beek et al. (1998) [7]	Leaf (general)	Comprehensive phytochemical & pharmacological review	Terpene trilactones, flavonoids	Foundational compound-class characterization
Dubey et al. (2004) [8]	Leaf / EGb 761	Narrative review of standardized extract	Flavonol glycosides, terpene lactones	Overview of standardization rationale
Kulić et al. (2022) [9]	Leaf / EGb 761	Product-by-process standardization review	Terpene trilactones, flavonol glycosides	Processing- standardization framework
Yao et al. (2012) [10]	Leaf (age/source/sex comparison)	HPLC comparative quantification	Flavonol glycosides, terpene lactones	Raw-material heterogeneity characterization
Wang & Zhang (2019) [11]	Seed	Detoxification processing review	Carbohydrates, phenolics, ginkgotoxin-related	Seed processing for functional food use
Murthy et al. (2024) [12]	Cell/organ culture biomass	In vitro biotechnological production	Terpene trilactones	Biosynthesis technology independent of harvest cycle
Wang et al. (2025) [13]	Leaf (general)	Function/regulation/extraction review	Flavonoids	Extraction-technology and biosynthesis regulation review
Alishir & Kim (2021) [14]	Fruit / exocarp	Phytochemical isolation & structure elucidation	Phenylpropanoid glycosides (incl. novel ginkgopanoside)	Byproduct-fraction resource characterization
Khizrieva et al. (2022) [15]	Leaf	Subcritical water extraction	Polyphenols	Green extraction technology development
Iwamoto et al. (2019) [16]	Leaf extract + lipid carrier	Co-formulation/bioavailability study	Ginkgolide A	Formulation technology for bioavailability enhancement

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Eldalawy et al. (2024) [17]	Leaf	Microscopy + phytochemical + LC/MS profiling	Flavonoids, terpenoids	Raw-material authentication & fingerprinting
Pi et al. (2022) [18]	Ginkgo ketoester tablet (processed product)	UPLC-MS/MS multi-component quantification	38 active constituents	Multi-matrix quality/distribution analysis
Zhao et al. (2015) [19]	Extract formulations (leaf-derived)	LC-MS/MS pharmacokinetic-analytical method	Ginkgolide B	Formulation comparison via analytical quantification
Li et al. (2025) [20]	Purified compound (leaf-derived)	LC-MS/MS pharmacokinetic-analytical method	Ginkgolide B	Analytical method validation for PK study
Rossi et al. (2009) [21]	Phospholipid complex (leaf-derived)	LC/APCI-MS analytical-PK method	Bilobalide	Analytical method for complexed-formulation PK
Zhang et al. (2023) [22]	Leaf (in multi-herb formula)	Online SPE-LC-MS/MS multiplex quantitation	17 drug-derived marker components	Multi-botanical simultaneous quantification
Czigle et al. (2019) [23]	Leaf	GC-based volatile-constituent analysis	Volatile terpenoids	Volatile fraction profiling
Czigle et al. (2018) [24]	Commercial leaf extract products	Pharmacopoeial quality-control survey	Flavonol glycosides, terpene lactones	Market adulteration/QC assessment

Table 2. Continue

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Patel & Patel (2021) [25]	Leaf (ginkgetin)	Analytical/pharmacological review	Biflavone (ginkgetin)	Minor-constituent analytical characterization
Schäfer (2015) [26]	Leaf (biosynthesis)	Chemistry/biosynthesis review	Ginkgolides, bilobalide	Biosynthetic pathway characterization
Niu et al. (2022) [27]	Leaf-derived compounds	Mechanistic narrative review	Ginkgolides, bilobalide	Mechanism-of-action synthesis
Lu et al. (2021) [28]	Leaf (bilobalide)	Pharmacology/PK/toxicity review	Bilobalide	Compound-specific safety/PK characterization
Suárez-González et al. (2023) [29]	Leaf extract	Antioxidant assay + in silico docking	Kaempferol, quercetin, luteolin	Bioactivity-technology linkage (target prediction)
Morató et al. (2024) [30]	Leaf / EGb 761	Narrative pharmacodynamic-clinical review	Terpene trilactones, flavonoids	Translational link: extract composition to clinical outcome
Xie et al. (2014) [31]	Leaf / EGb 761	Quantitative HPLC analysis	Flavonoid glycosides, terpene trilactones	Compound quantification & A β -inhibition linkage

Author (Year) [Ref.]	Forest raw material	Technology / method	Bioactive compound class	Technological objective
Sharma et al. (2024) [32]	Leaf (in polyherbal blend)	Quality-control & toxicological evaluation	Multi-herb marker compounds	QC/toxicology of processed polyherbal product
Xia et al. (2024) [33]	Leaf extract	In vivo (rat AD model) mechanistic study	<i>G. biloba</i> extract (GBE)	Extract-level bioactivity assessment

3.2. Forest Biomass Sources and Raw-Material Heterogeneity

The reviewed literature confirms that *G. biloba* leaves, seeds, and exocarp represent chemically distinct forest-derived fractions that require separate processing strategies. Leaves remain the principal industrial raw material and are the almost-exclusive source of the standardized terpene trilactone-flavonol glycoside extract [9], whereas seeds are traditionally consumed as food after a detoxification step that removes cytotoxic ginkgotoxin- and ginkgolic-acid-related constituents, and are increasingly investigated as a source of carbohydrate-, protein-, and phenolic-rich functional-food ingredients [11]. The exocarp and fruit pulp, historically treated as processing waste, have been shown to contain distinctive antioxidant phenylpropanoid glycosides, including a previously unreported compound (ginkgopanoside), indicating an underexploited resource-valorization opportunity for a byproduct that is otherwise discarded during seed processing [14].

Raw-material heterogeneity is itself a major technological variable. A comparative characterization of leaves collected at different tree ages, from different cultivation/harvest sources, and from male versus female trees demonstrated significant differences in total flavonol glycoside and terpene lactone content, and specifically highlighted that late-season leaves from older fruit-bearing trees, ordinarily discarded after fruit harvest, retain bioactive-compound levels comparable to the conventionally harvested young leaves used industrially [10]. This finding reframes a substantial fraction of forest residue as a potentially recoverable bioactive resource rather than waste, an issue of direct relevance to sustainable non-timber forest product management.

3.3. Extraction and Processing Technologies

Standardized organic-solvent extraction, formalized in the so-called "product-by-process" concept underlying the EGb 761 extract, was identified as the reference industrial processing route; this framework explicitly links extract composition and reproducibility to the harvest region, the raw-material handling protocol, and the sequence of processing steps applied to the leaf biomass, rather than to the leaf material alone [9]. Alternative green-extraction routes were also reported: subcritical water extraction (100-200 °C) of leaf biomass produced polyphenol-rich extracts with acetylcholinesterase-inhibitory activity comparable to conventional solvent extracts while avoiding organic-solvent residues, illustrating a viable low-toxicity processing pathway for leaf-derived bioactive fractions [15].

Biotechnological production offers a complementary route that decouples bioactive-compound supply from forest harvest cycles: cell and organ (adventitious root, embryogenic callus) culture systems have been used to biosynthesize terpene trilactones in vitro, although reported yields to date remain lower than those obtained from field-harvested leaves, underscoring the continued reliance on forest biomass as the primary feedstock [12]. For the seed fraction, detoxification processing (removal of ginkgotoxin and related alkylphenolic acids through heat treatment, soaking, or solvent washing) was identified as the key technological step enabling the safe conversion of Ginkgo seeds into functional-food ingredients [11]. Downstream formulation technology, such as co-processing leaf extract with lipid carriers (sesame extract and turmeric oil), was reported to substantially enhance the brain bioavailability of ginkgolide A, indicating that post-extraction formulation engineering is an additional technological lever for improving the functional performance of the processed forest product [16].

3.4. Analytical and Quality-Control Technologies

High-resolution liquid chromatography coupled with mass spectrometry emerged as the dominant analytical platform for characterizing and quality-controlling *G. biloba*-derived extracts. Combined microscopical, phytochemical, and LC/MS profiling of leaf material enabled simultaneous morphological authentication and chemical fingerprinting of the raw biomass [17], while UPLC-MS/MS methods have been

developed to simultaneously quantify dozens of active constituents (up to 38 compounds in one reported method) across multiple biological or product matrices, reflecting the multi-component nature of the standardized extract [18]. Complementary LC-MS/MS methods have also been validated for the pharmacokinetic-analytical quantification of individual terpene trilactones such as ginkgolide B and bilobalide in biological matrices, supporting both quality control and downstream bioavailability assessment of processed extracts [19-21].

Beyond single-species quantification, multiplexed SPE-LC-MS/MS methods have been applied to fixed multi-herb preparations containing *G. biloba* alongside other botanicals, allowing simultaneous tracking of ginkgo-derived and co-formulated plant markers in complex products [22]. Volatile-constituent profiling by gas chromatography-based methods has additionally characterized the terpenoid and aromatic fraction of the leaf, complementing the polar-compound-oriented LC-MS methods typically used for flavonol glycosides and terpene lactones [23]. Importantly, quality-control surveys of commercial *G. biloba* food supplements sold on the European market found that a substantial proportion of sampled products failed to meet pharmacopoeial composition criteria, revealing adulteration and under-standardization as persistent, unresolved problems in the forest-product-to-consumer value chain [24]. Analytical characterization of the biflavone ginkgetin, a minor but pharmacologically relevant constituent, further illustrates that quality-control technology must extend beyond the two headline compound classes (terpene trilactones and flavonol glycosides) to capture the full phytochemical complexity of the raw material [25].

3.5. Bioactive Compound Classes and Their Reported Relevance to Neurodegenerative Application

Across the included literature, three main bioactive-compound classes were consistently identified and linked, at a mechanistic or compositional level, to neurodegenerative-disease-relevant activity: the terpene trilactones (ginkgolides A, B, C, and bilobalide), the flavonoids (including flavonol/flavone glycosides and biflavones such as ginkgetin), and, in fruit/exocarp tissue, phenylpropanoid glycosides [7,26]. Ginkgolide-class compounds have been reported to modulate autophagy and amyloid- β accumulation in Alzheimer's disease models [2], to improve mitochondrial electron-transport-chain function and reduce neuroinflammation in Parkinson's disease models [3], and to exert broader anti-inflammatory immune effects relevant to neurological disease more generally [1,27]. Bilobalide has separately been the subject of a dedicated pharmacology-and-safety review describing its water solubility, favorable pharmacokinetic profile, and multi-target neuroprotective, antioxidative, and anti-inflammatory activity [28]. Flavonoid-class constituents, meanwhile, have been linked through in silico and antioxidant-activity studies to inhibition of central-nervous-system enzyme targets implicated in AD [29], and a dedicated 2025 review specifically addressed the regulatory biosynthesis and extraction technology of *G. biloba* flavonoids as a class, reinforcing the continued convergence of phytochemical function and extraction-technology research [13]. Clinical-pharmacodynamic evidence for the standardized EGb 761 extract, and its constituent phytochemical fractions, provides the translational anchor connecting the forest-product-technology chain summarized above to reported cognitive outcomes in Alzheimer's disease [30], while broader narrative overviews confirm the consistency of this compound-class-to-application mapping across the wider literature [4,5,8,31-33].

Representative chemical structures of the principal leaf-derived compound classes are presented in Figures 2 and 3. Ginkgolides A, B, and C are diterpene trilactones, whereas bilobalide is a sesquiterpene

trilactone (Figure 2). These compounds were used as chemical markers in the comparative leaf analysis by Yao et al. [10].

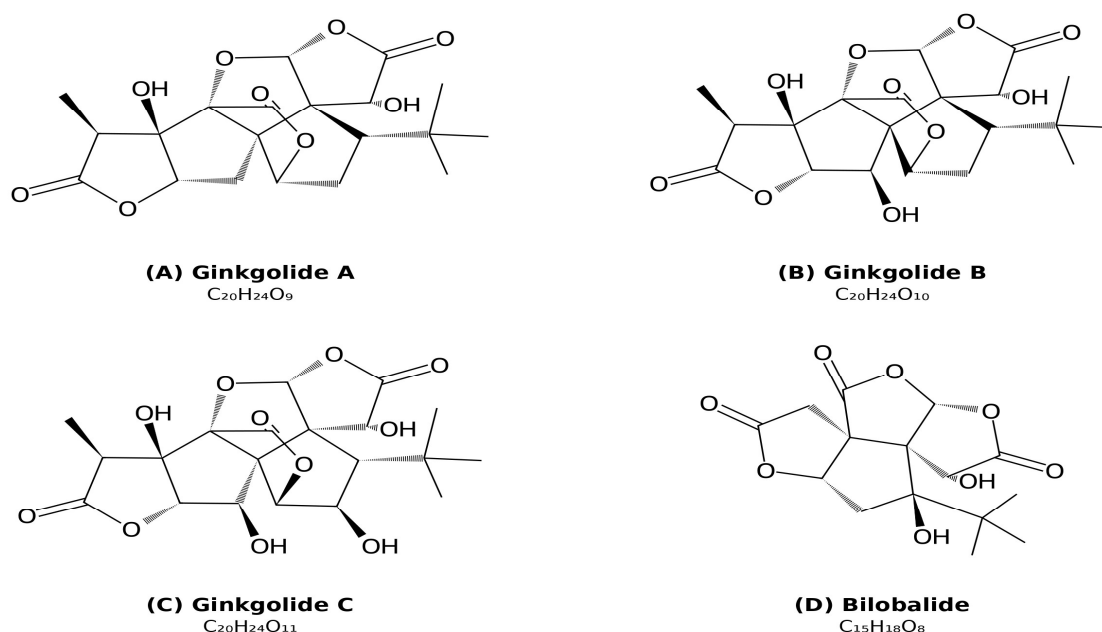


Figure 2. Chemical structures of representative terpene trilactones of *Ginkgo biloba*: (A) ginkgolide A, (B) ginkgolide B, (C) ginkgolide C, and (D) bilobalide. Structures were redrawn from PubChem records (CIDs 9909368, 6324617, 9867869, and 73581, respectively) [34].

Figure 3 distinguishes the flavonol aglycones quercetin, kaempferol, and isorhamnetin, which are used in flavonol-glycoside analysis [10], from the intact glycoside rutin (quercetin 3-O-rutinoside), isolated and characterized from *G. biloba* leaf extract by Xie et al. [31]. Ginkgetin is shown separately as a biflavone. This distinction clarifies the structural forms represented by the flavonoid markers discussed in the extraction and quality-control sections.

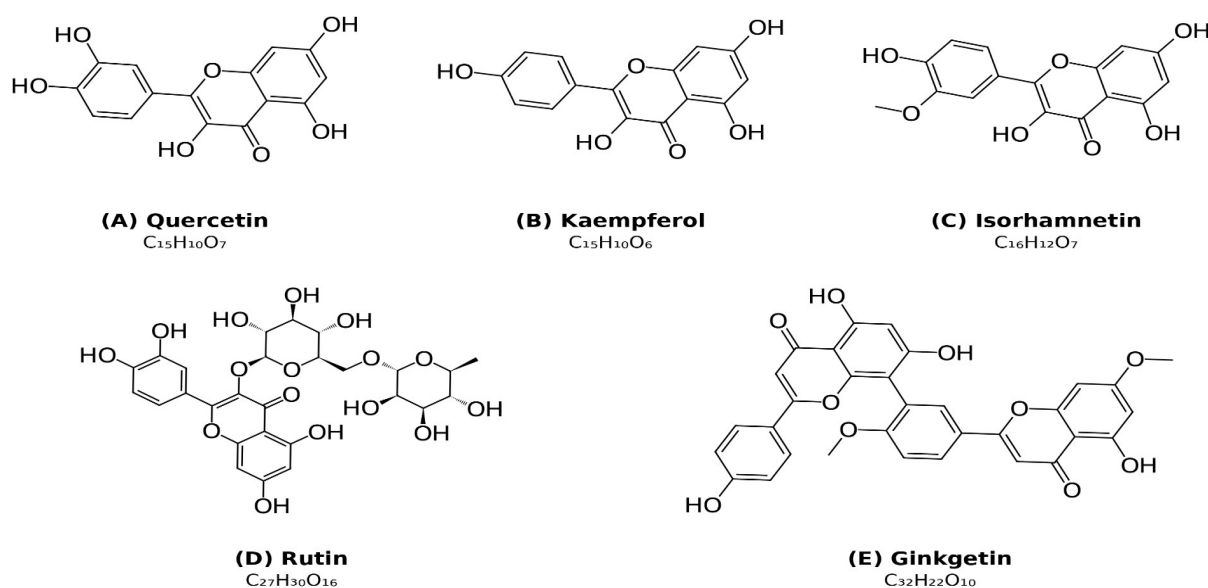


Figure 3. Chemical structures of selected *Ginkgo biloba* flavonoids: (A) quercetin, (B) kaempferol, (C) isorhamnetin, (D) rutin, and (E) ginkgetin. Panels A-C show aglycones without sugar residues; panel D shows an intact flavonol glycoside, and panel E shows a biflavone. Structures were redrawn from PubChem records (CIDs 5280343, 5280863, 5281654, 5280805, and 5271805, respectively) [34].

A summary of extraction, processing, and analytical technology categories identified across the included studies, together with their principal advantages and limitations, is presented in Table 3.

Table 3. Extraction, Processing, and Analytical Technology Categories Identified Across The Included Literature.

Technology category	Representative technique / principle	Main technological function	Main advantage	Main limitation	Ref.
Standardized solvent processing	Sequential organic-solvent extraction/purification under fixed harvest-region and process parameters ("product-by-process" model)	Establishes reference industrial extract (e.g., EGb 761) with reproducible terpene trilactone/flavonol glycoside ratio	Long-established, extensively validated, regulatory-recognized	Organic-solvent use; composition tied tightly to a fixed process, limiting flexibility	[7,8,9]
Green/subcritical extraction	Pressurized hot-water (subcritical, 100-200°C) extraction of leaf biomass	Solvent-free recovery of polyphenol-rich fractions with retained bioactivity	Avoids organic-solvent residues; lower environmental footprint	Yields and selectivity not yet benchmarked at industrial scale	[15]
Biotechnological (cell/organ culture) production	In vitro cell suspension or organ (adventitious root/callus) culture biosynthesis of terpene trilactones	Decouples bioactive-compound supply from seasonal forest-harvest cycles	Enables continuous, traceable, land-independent production	Currently lower yield than field-harvested leaf; scale-up needed	[12]

Table 3. Continue

Technology category	Representative technique / principle	Main technological function	Main advantage	Main limitation	Ref.
Seed detoxification processing	Heat treatment/soaking/solvent washing to remove ginkgotoxic and alkylphenolic acids	Converts otherwise toxic seed kernels into safe functional-food ingredients	Recovers an underused forest byproduct fraction	Detoxification efficiency and residual-toxin monitoring not standardized	[11]
Post-extraction formulation engineering	Co-processing of leaf extract with lipid carriers (e.g., sesame extract, turmeric oil)	Enhances brain bioavailability of terpene trilactones (e.g., ginkgolide A)	Improves functional performance without altering the core extract	Adds formulation-process complexity and cost	[16]
Multi-component LC-MS/UPLC-MS/MS quantification	Simultaneous chromatographic-mass-spectrometric quantification of tens of marker compounds across matrices	Enables comprehensive batch quality control and pharmacokinetic tracking	High specificity/sensitivity; suited to complex multi-component extracts	Requires costly instrumentation and method validation	[18,19,20,21, 22]
Chemical fingerprinting & morphological authentication	Combined microscopy, phytochemical screening, and LC/MS profiling of raw leaf material	Confirms raw-material identity and chemical profile prior to processing	Detects adulteration/substitution early in the value chain	Labor-intensive; needs reference chemical/morphological libraries	[17,23]
Market/pharmacopoeial quality-control auditing	Compliance testing of commercial products against pharmacopoeial composition standards	Detects under-standardization and adulteration in finished consumer products	Directly protects product quality/consumer safety	Reactive (post-market) rather than preventive	[24]

4. DISCUSSION

4.1. *Ginkgo biloba* as a Strategic Non-Timber Forest Product

The findings of this review reinforce that *G. biloba* functions simultaneously as a forest tree species and as a globally traded phytopharmaceutical raw material, a duality shared by other high-value non-timber forest products such as tannin-, resin-, and essential-oil-yielding species. Unlike timber, whose value is primarily structural, the commercial and scientific value of *G. biloba* biomass resides almost entirely in its secondary-metabolite content, making forest-product processing technology, rather than silvicultural yield alone, the decisive factor in realizing the resource's economic and therapeutic potential. This positions *G. biloba* as an instructive model for forestry and forest-product-technology programs seeking to develop other underexploited medicinal tree species into standardized, quality-assured bioactive products.

4.2. Extraction and Green Processing Technology Trends

The coexistence of the long-established organic-solvent "product-by-process" model [9] with emerging green-extraction routes such as subcritical water processing [15] and biotechnological cell/organ-culture biosynthesis [12] reflects a broader shift in forest-product technology toward more sustainable, lower-solvent-residue processing. However, the reviewed evidence also shows that green and biotechnological alternatives have not yet matched the reproducibility and yield of the conventional standardized process at industrial scale, meaning that near-term technology development should prioritize process intensification and yield optimization of green-extraction routes rather than complete replacement of the reference process.

4.3. Analytical Standardization and Quality Control as a Forest-Product-Technology Challenge

The recurring finding that raw-material composition varies substantially with leaf age, harvest source, tree sex, and season [10], combined with documented market-level adulteration and pharmacopoeial non-compliance of commercial products [24], indicates that analytical standardization is not a peripheral quality-assurance activity but a core forest-product-technology requirement. High-resolution LC-MS/MS-based multi-component quantification and fingerprinting methods [17,18,22] provide the necessary technical capacity to trace bioactive-compound content from raw biomass through to finished extract, and their wider adoption throughout the ginkgo supply chain, from forest or plantation harvest to processed product, would directly address the adulteration and batch-variability problems documented in this review.

4.4. From Forest Raw Material to Nutraceutical Value Chain: Byproduct Valorization

A consistent theme across the resource-utilization literature is that substantial fractions of harvested *G. biloba* biomass, late-season or older-tree leaves [10], seed processing residues [11], and exocarp/fruit pulp [14], remain underutilized or are discarded despite containing recoverable bioactive compounds. From a forest-product-technology standpoint, this represents an unrealized opportunity to extend resource-use efficiency and reduce processing waste, consistent with circular-economy principles increasingly applied to other non-timber forest product value chains. Systematic evaluation of detoxification and byproduct-recovery processes, of the kind demonstrated for Ginkgo seeds [11], could plausibly be extended to leaf residues and exocarp fractions currently treated as waste.

4.5. Limitations and Future Research Directions

This review is limited by its restriction to Scopus-indexed, English-language records and by the qualitative nature of the synthesis, which precluded formal meta-analysis given the heterogeneity of raw materials, technologies, and reported outcomes. Future research bridging forestry and forest-product technology with neuroscience application should prioritize: (1) harmonized, validated extraction protocols with documented raw-material traceability; (2) scale-up studies for green and biotechnological extraction routes; (3) systematic valorization studies for leaf, seed, and exocarp byproduct streams; and (4) integrated analytical fingerprinting frameworks capable of linking forest raw-material origin directly to the bioactive-compound profile of the finished, application-ready extract.

5. CONCLUSION

This systematic literature review demonstrates that the value of *Ginkgo biloba* as a source of ginkgolide-, bilobalide-, and flavonoid-based bioactive compounds relevant to Alzheimer's disease, Parkinson's disease, and dementia research is fundamentally dependent on forest-product processing and analytical technology.

Across the 33 studies synthesized, standardized solvent processing, emerging green and biotechnological extraction routes, and high-resolution LC-MS/MS-based analytical platforms together define the technological chain that converts heterogeneous forest biomass, leaves, seeds, and exocarp, into quality-assured, application-ready bioactive extracts. Persistent raw-material variability, market-level adulteration, and underutilized byproduct fractions were identified as recurring technological bottlenecks and resource-valorization opportunities. Continued development of harmonized extraction and quality-control protocols, explicitly linking forest raw-material characteristics to finished bioactive-compound quality, will be essential to fully realize the potential of *G. biloba*, and by extension other medicinal forest tree species, as a technologically robust non-timber forest product resource.

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