Industrial Development History of Ginkgo Biloba Extract

I. Tribute Section

Ginkgo biloba L., a relict gymnosperm of the Ginkgoaceae family, refers to the dried leaves of ginkgo, commonly known as duck-foot leaves, grandparent-grandchild tree leaves, or moth leaves. It is a classic medicinal and edible raw material with blood-activating and stasis-resolving effects covering six core global sectors: cardiovascular and cerebrovascular care, cognitive and memory improvement, ocular microcirculation repair, antioxidant anti-aging skincare, middle-aged and elderly dietary nutrition, and bulk APIs for traditional Chinese medicine compound prescriptions targeting cardiovascular and cerebrovascular disorders. This natural polyphenol and terpenolide raw material with dual active markers spans ten major fields: oral decoction among civilians in the Tang and Song dynasties, systematic documentation in officially compiled materia medicas of the Ming and Qing dynasties, industrialization of modern botanical drugs in Europe and America, separation and identification of standardized active fractions in East Asia, pharmacological analysis of flavonol glycoside and ginkgolide target mechanisms, low-temperature ethanol gradient extraction, membrane separation for removal of ginkgolic acid sensitizing impurities, simultaneous dual-component enrichment via macroporous resin, solvent-free refining by supercritical CO_2, stable encapsulation with nanocapsules, and full-resource recycling of the entire ginkgo plant.

Its development covers more than a thousand years of records on materia medica harvesting and processing; isolation and characterization of core marker compounds (standard 24% flavonol glycosides and standard 6% ginkgo terpenolides including ginkgolide A/B/C and bilobalide); establishment of standards for harvesting autumn green leaves to lock in active ingredients; hermetic low-temperature countercurrent extraction; ultrafiltration membrane removal of ginkgolic acid and macromolecular colloidal impurities; directional fractional enrichment of flavonoids and terpenolides via special resins; cyclodextrin encapsulation to boost oral bioavailability; and iteration of full-process vacuum low-temperature freeze-drying technologies. It has formed six core application sectors: cardiovascular and cerebrovascular prescription drugs, cognitive dietary supplements for middle-aged and elderly populations, soothing anti-aging cosmetics, eye-protecting functional beverages, bulk APIs for blood-activating TCM compound formulas, and clean-label antioxidant food additives. China has realized domestic mass production of pharmaceutical-grade standardized EGb761-type extracts, high-purity ginkgolide monomers, and highly water-soluble ginkgo flavonoid lyophilized powders, and built a global multi-category raw material grading, compliance and quality control system covering pharmaceuticals, health foods, cosmetics, beverages, feeds and dietary supplements. Scientific research teams worldwide have dedicated themselves to this field for over a millennium.

We pay sincere tribute to scholars and R&D teams worldwide who have achieved full-chain technological breakthroughs, including textual research on ginkgo leaf efficacy in

ancient materia medica classics, isolation and characterization of ginkgo flavonoid and terpenolide monomers, establishment of pharmacopoeia standards for simultaneous multi-component quantification by HPLC, low-temperature hermetic countercurrent extraction, membrane separation for removing sensitizing ginkgolic acid impurities, simultaneous enrichment of dual active components with macroporous resins, standardized harvesting and activity-locking processes for autumn green leaves, verification of platelet-activating factor (PAF) antagonism and molecular pathways for microcirculation protection, construction of domestic solvent-free green extraction production lines, and compliance registration with European and United States Pharmacopoeias. Based on principles of industry competition and enterprise privacy protection, no corporate names are listed in this article. We also extend our tribute to all manufacturers that have realized technological innovation and full industrial chain localization of ginkgo biloba extract.

Roll of Honored Contributors

1. Milestone Scientists Worldwide (Chronological Order)

- ***Civilian Herbalists and Physicians of the Tang and Song Dynasties (960–1368 AD, ginkgo producing regions in Jiangzhe and Central Plains)***

Locally harvested fresh green ginkgo leaves picked in autumn were shade-dried, honey-fried and decocted for oral administration to treat dizziness, wind headache, cough, chest tightness and limb numbness. This represents the world's earliest recorded medicinal and dietary practice of internal and external ginkgo leaf application, laying the foundation for traditional East Asian applications of activating blood and unblocking collaterals. Distinctions were drawn between the medicinal properties of fresh leaves, dried leaves and honey-fried decoction pieces, and experience was documented that autumn leaves contain higher active ingredients than spring leaves.

- ***Lan Mao, Compiler of Diannan Materia Medica (Ming Dynasty, 1397–1476, China)***

Author of the world's first monograph explicitly recording the medicinal efficacy of ginkgo leaves. The text states: "Harvest leaves, shade-dry them to treat pediatric heat flaming; apply externally to skin sores and swellings". It established the foundational positioning of ginkgo leaves for external anti-inflammatory use and internal collateral-unblocking therapy, marking the earliest written record of ginkgo leaves used independently as medicinal material.

- ***Li Shizhen (1596, Ming Dynasty, China, Compendium of Materia Medica)***

Systematically summarized the core efficacies of ginkgo (seeds and leaves): warming the lung and replenishing qi, suppressing cough and dyspnea, activating blood to resolve stasis, and unblocking collaterals to relieve pain. It clarified that autumn-harvested green leaves possess superior medicinal potency, and standardized traditional processing techniques including shade-drying, honey-frying and mild heat roasting to reduce toxicity and preserve active ingredients, forming the core theoretical basis for later

applications of ginkgo in cardiovascular, cerebrovascular and respiratory health maintenance.

- ***Zhang Bingcheng (Qing Dynasty, Readings of Materia Medica)***

Supplemented records that ginkgo leaves specifically treat phlegmatic cough due to lung deficiency and limb bi pain caused by qi deficiency and blood stasis. It refined classic compound formulas combining ginkgo leaves with Astragalus and Angelica to activate blood and unblock collaterals, and detailed syndrome differentiation criteria for internal and external administration.

- ***Shuji Furukawa (1932, Japan)***

For the first time globally, four ginkgo biflavonoids were isolated from ginkgo leaves and ginkgetin was chemically characterized, launching the era of modern chemical research on flavonoids in ginkgo foliage.

- ***Kaku Nakanishi (1967, Japan)***

First isolated ginkgolide A, B, C and bilobalide from ginkgo tissues, elucidated the characteristic skeletal structure of terpenolides, and identified ginkgolides as exclusive marker compounds of ginkgo responsible for cardiovascular and cerebrovascular protection.

- ***R&D Team of Dr. Willmar Schwabe (1965, Germany)***

Developed and launched the world's first standardized ginkgo biloba extract EGb761 with a classic fixed ratio standard: 24% flavonol glycosides, 6% total terpenolides, and ginkgolic acid ≤5 ppm. Patent filing was completed in 1972, establishing the global benchmark quality standard for ginkgo extracts and ushering in the era of botanical drug industrialization across Europe and America.

- ***European Pharmacology Research Group (1970–1980, Germany / France)***

Multiple rounds of animal trials fully verified that ginkgolides exert potent antagonism against platelet-activating factor (PAF), while flavonol glycosides scavenge free radicals, dilate microvessels and boost cerebral blood supply. Scientific validation was provided for the traditional materia medica efficacy of ginkgo leaves in "activating blood and unblocking vessels", bridging traditional empirical knowledge and modern molecular pharmacology.

- ***Team of E.J. Corey (1990, United States, Nobel Laureate in Chemistry)***

Completed total chemical synthesis of ginkgolide B and clarified the stereochemical structure-activity relationship of terpenolides, laying a chemical foundation for high-purity monomer pharmaceutical R&D and in-depth analysis of action targets.

- ***Ginkgo Preparation Research Team of Beijing Science and Technology Commission (1969, China)***

Initiated research and development of China's first modern ginkgo pharmaceutical preparations (Shuxuening Injection and Shuxuening Tablets), launching independent domestic R&D of ginkgo extract pharmaceutical formulations.

- ***Sun Zaoming (1986, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences, China)***

Systematically carried out research on domestic ginkgo leaf extraction processes and oral liquid formulations, established pilot production routes for primary ethanol reflux extraction and resin purification, filling the domestic gap in standardized ginkgo extract preparations.

- ***Expert Panel for Formulating Standards of the Chinese Pharmacopoeia (2002)***

Included quality standards for ginkgo biloba extract in the Chinese Pharmacopoeia for the first time, set minimum content limits for flavonoids and terpenolides, and built the foundational domestic framework for statutory testing.

- ***Domestic Macroporous Resin Purification R&D Team (1995–2010, China)***

Screened special polar adsorption resins to realize synchronous directional enrichment of ginkgo flavonoids and terpenolides while removing sensitizing ginkgolic acid. The purity of active fractions in crude extracts increased by over 10 times, and large-scale industrial purification processes using resins were established, breaking the technological monopoly of European and American manufacturers on resin-based purification.

- ***Supercritical CO_2 Solvent-Free Extraction Research Group (2005–2018, China)***

Realized industrial production of low-temperature solvent-free ginkgolic acid removal and lipophilic terpenolide refining, suitable for high-end pharmaceutical and cosmetic raw materials, drastically reducing residual ethanol organic solvents and sensitizing impurity levels.

- ***Expert Panel of European Pharmacopoeia (EP) (2008)***

Revised and improved the European Pharmacopoeia monograph for ginkgo biloba extract, unified EGb761 ratio specifications, ginkgolic acid limits and simultaneous multi-component HPLC testing methods, establishing the world's stringent safety and quality control system for botanical drugs.

- ***USP Revision Team, United States Pharmacopeia (2009)***

Raised quantitative control standards for ginkgolide monomers, refined grading indicators for dietary supplement-grade ginkgo extracts, and cleared compliance access channels for the North American market.

- ***Drafting Group for Group Standard T/CAFFCI 48 (2021, China)***

Issued the industry standard *Raw Materials for Cosmetics – Ginkgo Biloba Leaf Extract*, regulating limits for flavonoid content, heavy metals, microorganisms and sensitizing impurities in cosmetic-grade raw materials, together with complete supporting testing methods.

- ***Review Panel for Catalogue of Used Cosmetic Raw Materials (2021, China)***

Included GINKGO BILOBA LEAF EXTRACT as an INCI-listed cosmetic raw material, specified safe additive limits for its antioxidant and microcirculation-repairing skincare applications, and opened compliance circulation channels for the cosmetics sector.

- ***Expert Panel Compiling Clinical Consensus on Ginkgo Biloba Extract Injections (2019, Chinese Medical Association)***

Summarized tens of thousands of multi-center global clinical data on cardiovascular and cerebrovascular disorders, formulated standardized clinical application guidelines for ginkgo biloba extract injections, and improved the human evidence chain for pharmaceutical-grade raw materials.

- ***Domestic Natural Product Safety Evaluation Research Institute Team (2026)***

Completed formulation of full sets of safety limit indicators for five categories of ginkgo extract raw materials: pharmaceuticals, health foods, cosmetics, beverages and feeds, and developed supporting national standard HPLC testing methods for simultaneous quantification of six indicators: flavonol glycosides, total terpenolides, ginkgolic acid, heavy metals, pesticide residues and solvent residues.

2. Collective Contributions of Core Scientific Research Teams

- ***Schools of Materia Medica Textual Research in Past Chinese Dynasties:***

  Established a thousand-year traditional processing system covering harvesting, shade-drying, honey-frying and roasting of autumn ginkgo leaves, distinguished efficacy disparities between spring and autumn foliage, preserved classic internal and external compound formulas for dizziness, bi pain, cough and skin sores, and defined core authentic ginkgo producing regions including Jiangsu, Shandong, Zhejiang and Sichuan.

- ***East Asian Traditional Dietary Therapy Research Communities:***

  China and Japan concurrently developed ginkgo leaf substitute tea and blood-activating dietary decoctions, forming daily nutritional regimens targeting cardiovascular, cerebrovascular and cognitive care tailored to middle-aged and elderly Asian populations.

- ***Pioneering Natural Medicinal Chemistry Teams in Japan and Germany:***

  Sequentially isolated, characterized and elucidated the complete fraction system of ginkgo flavonoids and ginkgolides, built foundational lab-scale extraction and purification processes supported by early thin-layer chromatography and ultraviolet detection, and created the globally benchmark standardized EGb761 extract.

- ***Modern Molecular Pharmacology Verification Schools:***

  Gradually validated antioxidant vasodilatory effects of flavonoids and anti-thrombotic neuroprotective pathways of terpenolides via in vitro PAF enzyme activity assays, animal ischemia models and global multi-center human clinical trials, pioneering the core botanical drug sector for natural cardiovascular care and cognitive improvement.

- ***Domestic Forest Chemical Extraction R&D Teams:***

  Independently developed full mass-production processes including hermetic low-temperature countercurrent ethanol gradient extraction, ultrafiltration membrane removal of ginkgolic acid and macromolecular colloidal impurities, simultaneous enrichment of flavonoids and terpenolides via macroporous resins, supercritical solvent-free refining, vacuum low-temperature freeze-drying and cyclodextrin stable encapsulation. Three major industry pain points were resolved: terpenolide degradation from traditional high-temperature extraction, excessive ginkgolic acid impurities, and easy oxidative browning of extracts.

- ***Global Pharmacopoeia and Regulatory Standardization Teams:***

  Promoted the inclusion of ginkgo biloba leaves in the Chinese Pharmacopoeia, European Pharmacopoeia (EP), United States Pharmacopoeia (USP), health food raw material catalogs, EU traditional botanical drug registers, Japanese functional food raw material directories and cosmetic raw material inventories, enabling unimpeded cross-border circulation worldwide.

- ***Domestic Ginkgo Resource Domestication Research Groups:***

  Relying on millions of mu of standardized leaf-harvesting ginkgo orchards in Pizhou (Jiangsu) and Tancheng (Shandong), bred superior leaf cultivars with high flavonoid and terpenolide content, and built a full cold-chain system for harvesting and transporting autumn green leaves under low temperature and light shielding within 4 hours to lock in active ingredients.

- ***National Standard Testing System R&D Teams:***

  Formulated statutory HPLC simultaneous multi-component quantitative testing standards for pharmacopoeia and group standards for cosmetic raw materials, unifying grading, quality control and judgment criteria for ginkgo extracts globally.

- ***Industrial R&D Teams Covering Six Major Sectors:***

  Developed graded customized raw materials targeting prescription cardiovascular drugs, cognitive health foods for seniors, soothing anti-aging cosmetics, eye-protecting functional beverages, bulk TCM blood-activating APIs and natural antioxidant food additives, expanding diversified industrial application scenarios for ginkgo biloba extract.

II. R&D History

1. Period of Primitive Folk Application and Basic Exploration (960 AD – 1964)

1.1 960 AD – 1964: Crude Processing and Self-Made Decoction Stage of Ginkgo Leaves

Domestic civilians only harvested natural green ginkgo leaves in autumn, prepared decoctions for oral administration after shade-drying, honey-frying and roasting, and crushed fresh leaves for external application on skin sores and swellings. Processing relied on manual air-drying, open-pot boiling and simple natural sedimentation filtration, without technologies for active component separation, impurity removal or activity stabilization. The core marker ginkgolides decomposed and were lost rapidly under prolonged high-temperature decoction, while flavonoids oxidized and browned during open storage. Highly sensitizing ginkgolic acid, plant colloids, polysaccharide macromolecules and other impurities could not be eliminated at all. Only homemade folk decoctions and bulk crude ginkgo leaf decoction pieces circulated; no standardized industrial extracts existed, and there was no concept of quantitative quality control for flavonoid and terpenolide activity. Physicians of successive dynasties accumulated basic safety knowledge: autumn leaves deliver superior efficacy, honey-frying reduces toxicity, and prolonged boiling causes terpenolide loss.

In Europe and America, ginkgo trees were merely cultivated as ornamental landscape plants with no medicinal development research. In Japan, only lab-scale isolation of ginkgo flavonoid monomers was carried out without forming industrial extraction processes.

1.2 R&D Objectives of This Period

Develop fully hermetic low-temperature countercurrent controllable ethanol gradient extraction, ultrafiltration membrane directional removal of ginkgolic acid and colloidal macromolecular impurities, special macroporous resin synchronous fractional enrichment of flavonoid and terpenolide dual components, supercritical solvent-free elimination of sensitizing phenolic acid impurities and cyclodextrin stable encapsulation processes. The goal was to produce standardized ginkgo extracts with high flavonoid and terpenolide content, low ginkgolic acid, good storage resistance and low browning tendency, realizing complete removal of sensitizing impurities while fully retaining heat-

sensitive terpenolide and flavonoid activity. Supporting upstream raw material processes were established for standardized autumn leaf harvesting and hermetic low-temperature transport within 4 hours to lock active ingredients.

1.3 Core Conclusions

The core functional substance system of ginkgo is a dual active complex: ginkgo flavonol glycosides (markers for antioxidant activity, microvascular dilation and eye repair) and ginkgo terpenolides (core markers for PAF antagonism, anti-thrombosis and neurocognitive protection). It exerts multiple effects including improving cerebral and peripheral microcirculation, antioxidant anti-inflammation, vascular endothelial protection, memory enhancement and skin soothing. Ginkgolic acid is a strongly sensitizing impurity that must be strictly controlled at ≤5 ppm. High temperatures, prolonged open extraction and long-term room-temperature storage lead to ginkgolide degradation, flavonoid oxidative browning, excessive sensitizing impurities in crude products, poor storage stability and weak oral efficacy. Standardized ginkgo extracts produced via low-temperature hermetic fractional purification, synchronous resin dual-component enrichment, inert gas light-shielded stable encapsulation and supercritical acid removal refining became the core global R&D direction of the industry.

2. Period of Isolation of Characteristic Ginkgo Fractions and Formation of Primary Standardized Extracts (1965–1999)

2.1 1965–1972: Birth of the World's First Standardized EGb761 and Complete Elucidation of Terpenolides

In 1965, the German Willmar Schwabe team developed EGb761 standardized ginkgo extract with the classic fixed ratio of 24% flavonol glycosides plus 6% total terpenolides, with a global patent granted in 1972 to establish unified international standards. In 1967, Kaku Nakanishi of Japan fully isolated four categories of ginkgolides and elucidated their molecular skeletons. During the same period, Germany adopted ethanol reflux crude extraction and silica gel column chromatography lab purification to mass-produce pharmaceutical-grade extracts for European cardiovascular preparations. In 1969, China launched R&D of Shuxuening Injection relying solely on traditional crude water decoction without supporting processes for terpenolide enrichment and ginkgolic acid removal, resulting in product purity far below European and American standards.

2.2 1973–1999: Complete Verification of Pharmacological Pathways and Initial Domestic Breakthroughs in Extraction Technology

Multi-center animal trials in Germany and France confirmed that ginkgolides specifically antagonize platelet-activating factor (PAF), while flavonoids scavenge free radicals and dilate cardiovascular and cerebrovascular vessels, fully explaining the modern pharmacological mechanism of ginkgo's blood-activating and collateral-unblocking effects.

Ethanol gradient extraction replaced single water decoction, boosting flavonoid extraction efficiency by over 40%. Full acute toxicity, skin sensitization and long-term cumulative safety tests were completed to define safe dosage ranges for oral and external use. Europe and America launched ginkgo tablets, drops and injections, forming an initial global botanical drug market. China completed pilot primary purification using macroporous resins but could not simultaneously remove ginkgolic acid and enrich terpenolides; high-purity pharmaceutical-grade standardized extracts and terpenolide monomers relied entirely on imports. China boasted the world's largest ginkgo leaf harvesting resources yet lacked supporting systems for intensive purification and multi-indicator activity testing, only exporting low-value bulk dried ginkgo leaves.

3. Period of Global Multi-Center Clinical Evidence and Multi-National Regulatory Standardization (2000–2014)

3.1 2000–2010: Full-Scale Launch of Human Evidence-Based Clinical Trials for Cardiovascular Care and Cognitive Improvement

Summary data from tens of thousands of randomized double-blind controlled clinical trials across Europe, North America, Japan and South Korea confirmed that long-term oral administration of standardized low-ginkgolic-acid ginkgo extracts improves cerebral blood supply, alleviates memory decline, relieves intermittent claudication, stabilizes angina pectoris and mitigates oxidative stress damage. Parallel verification confirmed external applications of flavonoids deliver antioxidant soothing effects and improve periocular microcirculation. Supporting in vitro and animal safety tests were completed for food antioxidant, skin repair and senior dietary supplement applications. Driven by global population aging, high prevalence of chronic cardiovascular diseases and rising demand for natural anti-aging skincare, ginkgo biloba extract became an essential multi-functional natural botanical raw material worldwide.

3.2 2011–2014: Formation of the Global Five-Tier Classification Framework for Ginkgo Raw Material Standards

A unified five-tier classification system for global ginkgo raw materials was initially established:

① Crude processed dried ginkgo leaves / coarse powder (flavonoids <5%: low-grade decoction pieces, feed fillers, bulk herbal tea, no ginkgolic acid control);

② Low-temperature water-extracted concentrated paste (flavonoids 5%–15%: ordinary functional beverages, basic food antioxidant additives, ginkgolic acid ≤100 ppm);

③ Lyophilized powder via basic resin purification (flavonoids 15%–22%: dietary supplements for seniors, basic cosmetic raw materials, ginkgolic acid ≤10 ppm);

④ Standardized EGb761-type extract (flavonoids 24%±2%, total terpenolides 6%±1%: pharmaceutical preparations, high-end eye-protecting beverages, clinical skincare repair products, ginkgolic acid ≤5 ppm);

⑤ High-purity ginkgolide / flavonoid monomers (terpenolides ≥98%, flavonoids ≥95%: innovative drugs, high-activity medical beauty essences, clinical nutritional

intervention).

The EU finalized full registration of ginkgo as a traditional botanical drug; the United States Pharmacopeia (USP) tightened limits for terpenolide monomers. In 2002, the Chinese Pharmacopoeia formally incorporated ginkgo biloba extract, and domestic R&D of simultaneous multi-component HPLC testing methods began to fill the gap in statutory multi-indicator quality control.

4. Period of Domestic Independent Replacement via Green Technology and Maturity of the Full Industrial Chain (2015–2026)

4.1 2015–2022: Comprehensive Breakthroughs in Domestic Full-Set Purification Technologies, Local Production Lines Matching Imported European Materials

China independently constructed complete production lines for hermetic low-temperature countercurrent ethanol gradient extraction, resolving four core bottlenecks: terpenolide degradation under high temperature, incomplete removal of sensitizing ginkgolic acid impurities, easy browning of extracts and poor powder storage stability. Supporting full green processes were deployed: supercritical CO_2 solvent-free ginkgolic acid refining, low-temperature ultrafiltration membrane removal of colloidal macromolecules, synchronous fractional enrichment of flavonoids and terpenolides via special macroporous resins, and vacuum low-temperature freeze-drying. Product indicators including flavonoid and terpenolide content, ginkgolic acid limits, solvent residues, browning degree and microbial standards fully matched imported European EGb761 raw materials, while comprehensive production costs decreased significantly. Full domestic replacement of mid-to-low grade standardized extracts was realized, and breakthroughs were made to break overseas import monopolies on high-purity terpenolide monomers.

China built over 1.3 million mu of contiguous standardized ginkgo leaf-harvesting plantations, forming a closed-loop full industrial chain: manual harvesting during the autumn green leaf window → hermetic low-temperature light-shielded transport within 4 hours → temperature-controlled fixation, activity locking, crushing and grading → hermetic low-temperature ethanol gradient extraction → ultrafiltration membrane removal of ginkgolic acid, polysaccharide and colloidal macromolecular impurities → directional fractional enrichment of flavonoids and terpenolides via macroporous resins → supercritical CO_2 solvent-free elimination of residual phenolic acid impurities → vacuum low-temperature concentration / freeze-drying → cyclodextrin inert gas stable encapsulation → light-shielded low-temperature sterile warehousing.

Domestic supporting statutory HPLC simultaneous quantitative testing methods were launched, enabling enterprises to independently conduct full-item testing of flavonoids, terpenolides and ginkgolic acid. The group standard T/CAFFCI 48 for cosmetic-grade ginkgo extracts was implemented in 2021, forming a compliance system for graded raw materials in the cosmetics sector.

4.2 2023–2026: Comprehensive Iteration and Upgrade of Customized Products for Six Segmented Sectors

A fully mature graded customized product system took shape across the industry: crude ginkgo leaf powder, low-acid concentrated paste, standardized pharmaceutical-grade EGb761 lyophilized powder, high-purity terpenolide monomers, antioxidant cosmetic extraction liquid and pre-blended nutritional mixes for seniors. Low-temperature hermetic extraction and supercritical solvent-free green refining processes were universally adopted across the industry, drastically cutting organic solvent consumption and three-waste discharge.

Cyclodextrin encapsulation technology elevates oral bioavailability of ginkgolides and resolves oxidative browning of flavonoid powders, compatible with full dosage forms: oral tablets, oral liquids, functional eye-protecting drinks, anti-aging facial masks, essences, TCM blood-activating compound formulas and cardiovascular injections. Driven by three factors – population aging, clean-label natural ingredient policies and consumption upgrading for anti-aging cosmetics – the global ginkgo biloba extract market continues to expand, with domestic raw materials dominating global supply.

III. Commercialization Development History

1. Stage of Bulk Ginkgo Leaf Decoction Pieces and Lab Microscale Extraction (960 AD – 1964)

Civilians in China and Japan only harvested autumn ginkgo leaves, shade-dried them to prepare homemade decoctions and external formulations for personal use. Laboratories in Germany and Japan only isolated trace amounts of flavonoid and terpenolide monomers for pharmacological research, with no standardized commercial extract raw materials. Only bulk crude dried ginkgo leaves circulated for export domestically; no industrial purification factories existed, and no compliant standardized ginkgo extract products were traded on the market.

Industrial Characteristics: No technologies for hermetic low-temperature countercurrent extraction, membrane separation of sensitizing ginkgolic acid, resin dual-component enrichment or stable encapsulation refining; no unified global grading and quality control standards covering flavonoids, terpenolides and ginkgolic acid; the industrial sector for standardized ginkgo biloba extracts was entirely non-existent.

2. Stage of Early German Industrialization and Full Dependence on Imports for Domestic High-End Pharmaceutical Raw Materials (1965–1999)

2.1 1965–1989: World's First Mass Production of Standardized EGb761 in Germany

Ethanol reflux and silica gel chromatography purification processes matured, and Germany launched ginkgo tablets and injections for European and American pharmaceutical

markets. Global annual consumption of standardized ginkgo extracts reached approximately 1,200 tons in 1999, concentrated in European pharmacies and premium dietary supplement brands in North America. China only exported low-value small volumes of dried ginkgo leaves and coarse powder, lacking production capacity for low-acid standardized enriched extracts. All EGb761-type extracts and high-purity terpenolide monomers required for pharmaceutical preparations were imported exclusively from Germany and France.

2.2 1990–1999: Low-End Domestic Industry with Prohibitive Prices for Imported High-End Raw Materials

Overseas enterprises held monopolies over core purification technologies for ginkgolide separation, ginkgolic acid removal and low-temperature activity locking. Unit prices for imported pharmaceutical-grade EGb761 lyophilized powder and high-purity terpenolide monomers remained extremely high, supplied solely to European and American cardiovascular drugs and premium medical beauty repair products. Domestic manufacturers lacked compliant production qualifications for low-sensitizing pharmaceutical-grade raw materials, only exporting bulk leaves and coarse powder with excessive ginkgolic acid impurities and solvent residues that barred entry to pharmaceutical and high-end health food sectors.

Industrial Characteristics: Leading overseas enterprises held full sets of core patented technologies for active ingredient purification, impurity removal and stabilization. China possessed the world's largest ginkgo leaf harvesting cultivation resources yet lacked supporting systems for industrial intensive extraction and simultaneous multi-indicator testing. Domestic pharmaceutical and cosmetic markets had extremely low awareness of graded standardized low-acid ginkgo extracts.

3. Stage of Domestic Production Capacity Maturity and Rapid Expansion of Six Application Sectors (2000–2022)

Global demand simultaneously surged across senior cardiovascular dietary supplements, anti-aging antioxidant skincare, clean-label natural food preservatives, TCM blood-activating APIs, eye-protecting functional beverages and senior nutritional supplements, making ginkgo biloba extract the world's highest-volume botanical drug raw material. Global annual consumption of all categories of raw materials exceeded 12,500 tons in 2022.

China fully deployed six application sectors: cardiovascular prescription drugs and injections, cognitive-improving health foods for seniors, natural antioxidant food additives, soothing anti-aging cosmetics, eye-protecting functional beverages and bulk APIs for blood-activating TCM compound formulas. In 2022, stable large-scale domestic production was realized for standardized concentrated paste, medium-low acid resin-purified lyophilized powder and pharmaceutical-grade extracts matching EGb761 standards, breaking the long-term technological monopoly of Germany and France over high-end raw materials. Domestic annual market consumption reached 3,800 tons,

with 5,600 tons of standardized ginkgo extracts exported yearly to over 60 countries worldwide.

A complete localized full industrial chain supporting system took shape, delivering integrated technical services covering full-item raw material testing, terminal formula compounding and multi-dosage form development, fully covering all application scenarios: pharmaceuticals, cosmetics, health foods, beverages and feeds.

4. Stage of Highly Mature Industry and Large-Scale Global Exports of Domestic Raw Materials (2023–2026)

4.1 Clear Product Tiering with Precise Coverage of All Application Scenarios

The five-tier raw material classification delivers clear positioning and differentiated competition: crude ginkgo leaf powder serves low-grade decoction pieces, livestock feed fillers and bulk herbal tea; low-temperature water-extracted concentrated paste targets mass-market beverages and natural food antioxidant preservation; resin-purified lyophilized powder caters to senior dietary supplements and daily basic skincare; standardized low-acid EGb761 lyophilized powder supplies cardiovascular pharmaceutical preparations, high-end eye-protecting beverages and clinical repair cosmetics; high-purity terpenolide / flavonoid monomers are provided for innovative drugs, high-activity medical beauty essences and clinical nutritional intervention, fully covering both high-end and mass global markets.

4.2 Mass Overseas Exports of Domestic Raw Materials with Rising Global Market Share

Domestic ginkgo extracts match top-tier German EGb761 raw materials across indicators including flavonoid and terpenolide stability, low-acid impurity removal performance, anti-browning powder storage capacity and residual organic solvent limits. Leveraging the world’s largest domestic standardized ginkgo leaf supply chain, proprietary customized low-temperature fractional purification, supercritical solvent-free acid removal and inert gas stable encapsulation technologies alongside cost advantages, domestic extracts are exported in bulk to the EU, North America, Southeast Asia, Japan, South Korea and Australia, continuously eroding the global supply share of traditional German and French raw material manufacturers. Standardized pharmaceutical-grade ginkgo lyophilized powder dominates mainstream overseas markets for cardiovascular dietary supplements with high cost performance and full global compliance certifications.

4.3 Formation of Standardized, Healthy Industry Competition Landscape

Regulatory governance of the industry centers on six core standards: ginkgo extract specifications in the Chinese Pharmacopoeia, European Pharmacopoeia (EP), United States Pharmacopoeia (USP), EU traditional botanical drug regulations, group standard T/CAFFCI 48 for cosmetic raw materials and the Catalogue of Used Cosmetic Raw Materials.

Clear access thresholds are defined for safe limits of flavonoids, terpenolides, ginkgolic acid, solvent residues and heavy metals across pharmaceutical, food and cosmetic grades. Imported high-purity terpenolide monomers are only supplied in small volumes to global innovative pharmaceutical enterprises and premium medical beauty brands, while domestic graded low-acid standardized raw materials hold dominant market share in China's mass market and emerging overseas markets. Industry competition has shifted from the earlier low-price scramble for dried leaves and coarse powder to comprehensive strength competition centered on flavonoid and terpenolide purity, customized deep removal of ginkgolic acid, long-term powder storage stability and complete sets of multi-country global compliance certifications.

4.4 Medium and Long-Term Industrial Development Trends (Post-2026)

- ***Full-Scale Popularization of Fully Hermetic Green Low-Temperature Production***

Large-scale promotion of controllable low-temperature countercurrent ethanol gradient extraction, supercritical CO_2 solvent-free ginkgolic acid refining, low-temperature ultrafiltration membrane removal of colloidal macromolecular impurities and biological enzymatic degradation of plant proteins. Full-process light shielding and inert gas protection eliminate oxidative degradation of heat-sensitive ginkgolides and flavonoids. Ginkgo branches, leaf-pruning byproducts and extraction residues are fermented for resource recycling to produce composite feed raw materials, realizing full-plant circular low-carbon green production of ginkgo.

- ***Customized Graded Specialized Raw Materials for Segmented Sectors***

Develop specialized graded raw materials with customized flavonoid-terpenolide ratios, water solubility, acid-alkali stability and ultra-low ginkgolic acid content for six core sectors: cardiovascular prescription drugs, oral cognitive-improving beverages for seniors, clean-label natural antioxidants, sensitive-skin anti-aging repair cosmetics, eye-protecting functional drinks and innovative TCM APIs.

- ***Development of Pre-Blended Integrated Composite Functional Raw Materials***

Formulate pre-blended raw materials for cardiovascular care and ocular microcirculation repair by combining ginkgo with Salvia miltiorrhiza, hawthorn, lutein, phospholipids and probiotics, reducing secondary compounding procedures for terminal manufacturers and delivering one-stop finished formula solutions.

- ***Integrated Global Multi-Regional Compliance Layout***

Complete synchronized registration and certification for pharmaceutical raw materials under the Chinese Pharmacopoeia, EU traditional botanical drugs, U.S. dietary supplements, Japanese functional foods, Korean health functional foods and cosmetics. Unify global testing judgment criteria and safety limits for flavonoids, terpenolides and ginkgolic acid to enable unimpeded cross-border circulation of ginkgo raw materials worldwide.

- ***Continuous Iteration of High-Stability Targeted Delivery Technologies***

Nanoliposome and cyclodextrin composite microcapsule encapsulation technologies boost oral bioavailability of ginkgolides and transdermal skin absorption of flavonoids. Develop premium dosage forms including sterile single-dose eye-protecting oral liquids, sustained-release memory chewable tablets, cardiovascular sustained-release soft candies, medical soothing repair essences and aquaculture micro-pellets for microcirculation regulation. Advance suspended cell culture of ginkgo to enrich high-activity terpenolides and flavonoids, breaking supply limitations imposed by seasonal field harvesting and land resources. Continuous iteration of ultra-low ginkgolic acid, non-browning and high-stability ginkgo extracts will unlock blue ocean segmented markets for vascular-sensitive populations and sensitive-skin anti-aging.

Conclusion

The ginkgo biloba extract industry originates from over a thousand years of Tang and Song folk dietary therapy practice using ginkgo leaf decoctions to activate blood and unblock collaterals. Its complete development cycle spans systematic efficacy documentation in officially compiled Ming and Qing materia medicas, modern separation of fractions via natural medicinal chemistry in Japan and Germany, industrialization of standardized EGb761 botanical drugs in Europe and America, tens of thousands of global human evidence-based clinical trials for cardiovascular disorders, and independent catch-up of full domestic green extraction and purification technologies. It has evolved into a globally benchmarked functional botanical raw material sector based on terpenolide-flavonoid complexes covering six major fields: cardiovascular and cerebrovascular prescription drugs, cognitive health foods for seniors, natural antioxidant food additives, eye microcirculation beverages, anti-aging repair cosmetics and bulk APIs for blood-activating TCM compound formulas.

The full industrial development chain includes textual research on blood-activating collateral-unblocking efficacy of ginkgo leaves in ancient materia medica classics; isolation and characterization of dual characteristic markers (ginkgo flavonol glycosides and ginkgo terpenolides); multi-center human evidence-based clinical verification of PAF antagonism and microcirculation protection; hermetic low-temperature countercurrent ethanol gradient extraction; ultrafiltration membrane removal of sensitizing ginkgolic acid and colloidal macromolecular impurities; simultaneous directional enrichment of flavonoid and terpenolide dual components via macroporous resins; supercritical CO_2 solvent-free acid removal refining; cyclodextrin inert gas stable encapsulation; and independent breakthrough of full domestic purification technologies. A full-chain industrial upgrade has been achieved, ranging from natural fresh autumn ginkgo leaves and crude dried leaf decoction pieces to globally graded low-sensitizing high-end standardized ginkgo extract raw materials.

Compared with crude ginkgo leaf products processed via traditional high-temperature open-pot water decoction without ginkgolic acid impurity removal, standardized low-temperature graded low-acid ginkgo extracts rely on five core technologies: hermetic controllable low-temperature countercurrent extraction, ultrafiltration membrane removal of phenolic acid and colloidal impurities, macroporous resin dual-active-component fractional enrichment, in-depth supercritical solvent-free acid removal and cyclodextrin inert gas stable encapsulation. Their core competitive advantages include complete retention of heat-sensitive active ginkgolides and flavonoids, thorough elimination of strongly sensitizing ginkgolic acid impurities, strong powder resistance to light, high temperatures and long-term browning, ultra-low organic solvent residues, compatibility with all dosage forms for pharmaceuticals, cosmetics and health foods/beverages, and compliance registration with pharmacopoeias worldwide. It perfectly aligns with long-term global market trends: intervention for chronic cardiovascular diseases amid population aging, mild natural anti-aging skincare, clean-label food preservation and cognitive nutritional supplementation for the elderly.

With continuous commercialization of new technologies including solvent-free green refining, customized graded raw materials for segmented sectors, nano-targeted stable delivery, ginkgo suspended cell culture and ultra-low ginkgolic acid high-stability purification, ginkgo biloba extract will permanently maintain its position as a core botanical raw material for global cardiovascular care and natural anti-aging skincare, becoming an indispensable classic relict medicinal and edible functional raw material of the Ginkgoaceae family for the pharmaceutical, health food, cosmetic and traditional Chinese medicine industries.