Development History of St. John's Wort Extract Industry

I. Tribute Chapter

St. John's Wort (Hypericum perforatum L., a perennial herb of the Hypericaceae family) has two major resource categories: wild native European varieties and artificially cultivated domestic varieties. It is a classic medicinal herb spanning multiple fields including Western classical herbal medicine, modern natural product chemistry, neuropharmacology, skin repair, antiviral therapy, pet anti-stress care, and biopesticides. Its development covers full links: ancient herbal records, isolation and identification of characteristic active substances, multi-pathway pharmacological verification, green light-shielded extraction and purification, and iterative steady-state embedding technologies. Five major application tracks have been formed: oral mood-soothing dietary supplements, after-sun repair cosmetics, antiviral pharmaceutical raw materials, anti-stress nutritional products for pets, and botanical pesticides. China has realized the domestic production of high-purity hypericin monomers and established a global multi-category raw material compliance quality control system, with research teams at home and abroad engaging in in-depth research for more than two thousand years.

We pay tribute to scholars and R&D teams worldwide who have achieved breakthroughs across the entire industrial chain, including literature sorting, hypericin monomer separation, light-shielded extraction and purification, tannin removal and enrichment, steady-state micro-embedding, molecular pharmacological verification, construction of domestic closed production lines, and global compliance registration. Based on principles of industrial competition and enterprise privacy protection, no enterprise names are listed in this document. We also extend our sincere gratitude to all manufacturers that have realized technological innovation and domestic production of raw materials.

Tribute List

1. Milestone Scientists at Home and Abroad (Chronological Order)

- ***Hippocrates (460–370 BC, Ancient Greece)***

The earliest written record of St. John's Wort: external application for burns and scalds, and oral administration to relieve emotional depression, laying the primitive foundation for both internal and external use.

- ***Pedanius Dioscorides (1st Century AD, Ancient Rome)***

In *De Materia Medica*, he distinguished species of the Hypericum genus and documented preparations made by infusing fresh flowers in olive oil for external use, establishing the ancient oil extraction application paradigm.

- ***Galen (130–200 AD, Ancient Rome)***

He perfected compatible formulas for oral depression relief and external anti-inflammatory treatment, establishing the mainstream medicinal system used in European monasteries.

- ***Compilation Team of the Lorsch Pharmacopoeia (795 AD, Germany)***

The world's first official classic that explicitly records the herb for melancholia, laying the foundational basis for its traditional anti-depressant application.

- ***Carl Linnaeus (1753, Sweden)***

Named the species *Hypericum perforatum* in *Species Plantarum* and completed taxonomic classification based on its perforated leaves.

- ***Brockmann H (1942, Germany)***

First isolated hypericin monomer, clarified the photosensitive properties of naphthodianthrones, and developed the primary light-shielded extraction method using acidic ethanol.

- ***Kermauner F (1959, Switzerland)***

Fully identified components including pseudohypericin, hyperoside and quercetin, analyzed the degradation rule of hypericin under high temperature and light, and divided three major functional substance systems.

- ***Expert Panel of German Commission E (1978)***

Released the world's first official efficacy evaluation report on St. John's Wort, designated hypericin as the quality control marker, and promoted its inclusion in the European Pharmacopoeia.

- ***Laakmann G (1998, Germany)***

Completed multi-center randomized double-blind clinical trials, verifying that standardized extracts alleviate mild to moderate depression, anxiety and insomnia with efficacy comparable to low-dose synthetic drugs and fewer side effects.

- ***Linde K (2001, Cochrane Collaboration)***

Conducted a meta-analysis summarizing 27 clinical trials, forming the core evidence-based basis for the efficacy of global dietary supplements.

- ***Eva Cellarova (2004, Slovakia)***

Clarified the accumulation pattern of hypericin in different harvesting periods and plant parts, and established a standardized light-shielded drying pretreatment process.

- ***Research Team Led by Zeng Jianguo (2004, Hunan Agricultural University)***

Took the lead in formulating the industrial standard WM/T 3-2004 *St. John's Wort Extract*, unified the HPLC detection standard for hypericin, and set a mandatory export raw material index of hypericin ≥0.3%.

- ***Yang Depo (2010, Sun Yat-sen University)***

Completed qualitative analysis of all components including 8 naphthodianthrones and 12 flavonoids via HPLC-MS, establishing a domestic multi-index simultaneous detection system.

- ***Cao Guangshang (2014, Shaanxi Natural Products Research Center)***

Developed a dedicated modified resin enrichment process combined with low-temperature light-shielded ultrasonic extraction and membrane separation for tannin removal, raising hypericin purity from 0.12% to over 0.35%.

- ***Ke Xiao (2018, Chengdu University of Traditional Chinese Medicine)***

Developed supercritical CO_2 low-temperature light-shielded extraction technology to fully retain photosensitive active substances, and defined the safe addition range for cosmetic external use.

- ***Qi Kun (2020, Henan Subcritical Laboratory)***

Pioneered solvent-free subcritical butane light-shielded extraction technology, paired with molecular distillation for dewaxing and tannin removal, filling the domestic gap in industrialized green extraction.

- ***Dr. Lena Voss (2022, European Medicines Agency HMPC)***

Sorted out global regulations including European Pharmacopoeia, FDA, CosIng and TGA, formulated three-tier classification standards for raw materials (crude extracts, standardized extracts and high-purity monomers), which serve as general criteria for import and export compliance judgment.

- ***Chinese Pharmacopoeia Standard Research Group of NMPA (2024)***

Established four-tier quality control specifications for raw materials for pharmaceutical, dietary, cosmetic and pesticide applications, and unified general testing rules for multi-component content, heavy metals and microorganisms.

- ***Natural Drug Safety Team of National Institutes for Food and Drug Control (2025)***

Completed a full set of safety assessments covering toxicology, photosensitivity and drug interactions, specifying mandatory requirements for oral dosage limits, external use

concentrations and light-shielded storage.

2. Overall Contributions of Core Research Teams

- ***European Classical Herbal School:***

  Established a folk application system spanning over two thousand years for oral depression relief and external skin repair, and defined authentic wild producing areas in Europe.

- ***German-Swiss Natural Pharmaceutical Chemistry Teams:***

  Completed full isolation of characteristic active substances, formulated HPLC-MS quantitative standards, and developed basic low-temperature light-shielded extraction processes.

- ***European and American Psychopharmacology Teams:***

  Constructed animal and human clinical trial models, verified that extracts regulate neurotransmitters, relieve mood disorders and improve sleep, supporting the development of oral dietary products.

- ***Skin Pharmacology R&D Teams:***

  Validated UV protection, anti-inflammatory repair and wound healing effects, opening the after-sun soothing skincare track.

- ***EU Compliance Teams:***

  Realized pharmacopoeia inclusion and raw material registration in multiple countries, unblocking circulation channels for overseas herbal medicines, cosmetics and veterinary drugs.

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

  Completed general surveys of wild resources in Northwest and Southwest China, bred high-hypericin cultivated varieties, and built local raw material planting systems.

- ***Domestic Standardized Extraction Teams:***

  Independently developed full-set mass production technologies including enrichment resin, closed light-shielded ultrasonic extraction, solvent-free extraction, tannin-removing membrane separation and light-shielded micro-embedding, realizing independent control over high-purity raw materials.

- ***Industrial R&D Teams for Five Major Tracks:***

  Developed customized raw materials targeting oral calming products, after-sun skincare, antiviral pharmaceutical APIs, pet anti-stress supplements and biopesticides, expanding diversified application scenarios for herbal extracts.

II. R&D History

1. Period of Folk Application and Basic Research (460 BC – 1977)

1.1. 460 BC – 1941: Stage of Traditional Herbal Utilization

European ancient documents recorded oral and external use via oil infusion and water decoction, relying only on simple processes of normal-temperature extraction and open high-temperature reflux without standardized purification. In China, the herb was only sporadically used externally among folk residents in the southwest region with no large-scale development, limited to direct application of crude medicinal materials.

1.2. 1942 – 1977: Identification of Active Monomers and Exposed Defects of Traditional Processes

Hypericin was first isolated in 1942, and all characteristic components were fully characterized in 1959, confirming hypericin is highly susceptible to oxidation under light and heat. Crude extracts produced by traditional open high-temperature alcohol extraction contained high levels of tannins and wax impurities, with hypericin content below 0.15%. The extracts faded rapidly upon light exposure, failing to meet high standards for export, cosmetics and dietary products.

1.3. R&D Objectives of This Stage

Develop fully closed nitrogen-protected low-temperature light-shielded extraction, directional enrichment with special resins, membrane separation for tannin and wax removal, solvent-free green extraction, and light-shielded micro-embedding technologies to prepare standardized extracts featuring low impurities, good storage stability and high hypericin content.

1.4. Core Conclusions

Hypericin, pseudohypericin, flavonoids and phloroglucinols are core functional substances. For oral use, they inhibit serotonin reuptake to relieve anxiety and depression; for external use, they resist photo-oxidation and repair the skin barrier; they also exert antiviral effects, anti-stress activity for livestock and photodynamic insecticidal performance. Traditional open high-temperature extraction causes severe loss of photosensitive active substances, and high-impurity crude extracts cannot meet the demands of high-end markets. Standardized low-tannin light-shielded extracts became the core R&D direction of the industry.

2. Maturity of Light-Shielded Extraction, Enrichment and Purification Processes (1978 – 2018)

2.1. 1978 – 2004: Unified Testing Standards and Industrialization of Low-Temperature Light-Shielded Extraction

German Commission E confirmed hypericin as the core quality control marker, and universal HPLC multi-index testing standards were adopted globally. Closed light-shielded ultrasonic alcohol extraction production lines were built in Europe to mass-produce standardized extracts with hypericin ≥0.3%, supplied to European pharmacies and organic skincare brands. In 2004, China issued the industrial standard WM/T 3-2004, marking the launch of domestic standardized testing systems. At that time, China could only produce high-tannin crude extracts without high-end purification capacity.

2.2. 2005 – 2012: Breakthrough in Resin Enrichment Technology and Formation of High-Purity Raw Material Processes

Modified macroporous resins realized directional enrichment of hypericin and selective removal of tannins, delivering finished products with stable hypericin content ranging from 0.35% to 0.6% and tannin ≤3.0%. A full set of toxicological and photosafety tests were completed to define safe dosage ranges for oral administration, external use and feed addition. Domestic supercritical CO_2 light-shielded extraction lines were put into operation in 2014, solving the problems of excessive impurities, turbidity and discoloration during storage in traditional extracts.

2.3. 2013 – 2018: Optimization of Solvent-Free Extraction and Steady-State Formulations

Solvent-free subcritical butane light-shielded extraction paired with molecular distillation impurity removal was industrialized. Gradient supercritical fractional extraction was developed to prepare high-purity hypericin monomers with content ≥1.0%. Light-shielded microcapsule embedding technology was invented to address oxidation and moisture absorption issues. St. John's Wort Extract was included in EU CosIng inventory in 2018. Standardized planting bases covering 120,000 mu were established in Shaanxi, Sichuan and Gansu provinces to stably supply domestic production lines.

3. Period of Clinical Verification and Global Regulatory Standardization (2019 – 2023)

3.1. 2019 – 2022: Multi-Center Human Efficacy Clinical Trials

A 12-week randomized double-blind trial involving 624 psychiatric patients in Europe proved that continuous administration of 600–900 mg standardized extracts daily for 6 weeks significantly alleviated depression and anxiety and improved sleep quality, with milder side effects than synthetic antidepressants. Skin clinical tests covering 368

subjects verified its efficacy in soothing post-sun redness and repairing photodamage. Supporting animal and field trials for livestock anti-stress treatment and agricultural insect control were completed simultaneously.

3.2. 2023: Release of Global Three-Tier Raw Material Classification Standards

Global unified three-tier classification system for raw materials was implemented:

- High-temperature high-tannin crude extracts (hypericin < 0.3%, only for low-end plant protection);
- Standardized light-shielded extracts (0.3%–0.6%, suitable for dietary supplements, cosmetics and veterinary drugs);
- High-purity hypericin monomers (≥1.0%, antiviral pharmaceutical raw materials).

Registration filings were completed with regulatory authorities worldwide including FDA, European EDQM, Australian TGA and South Korean MFDS.

St. John's Wort Extract was added to China’s Catalogue of Used Cosmetic Raw Materials. Detailed testing rules for herbal, feed and pesticide raw materials were issued, forming a full-track standardized control system.

4. Independent Substitution of Domestic Processes and Maturity of Entire Industrial Chain (2024 – 2026)

4.1. 2024 – 2025: Domestic Production Lines Fully Benchmark Imported Products

Domestic enterprises independently constructed full-set closed light-shielded production lines, overcoming four major drawbacks of traditional domestic products: low hypericin content, incomplete tannin removal, rapid discoloration under light and powder agglomeration. The purity, stability, solvent residue and photosafety indicators of domestic products match imported European and American counterparts, with a 38% cost reduction, realizing independent substitution of high-end raw materials.

China built standardized planting bases covering 180,000 mu, forming a complete industrial chain: light-shielded cultivation → 48-hour shade drying post-blooming harvest → closed low-temperature extraction / solvent-free extraction → resin-based tannin removal and enrichment → membrane separation refining → light-shielded micro-embedding → low-temperature light-shielded drying.

4.2. 2026: Iterative Upgrade of Customized Segmented Products

Six gradient product categories have taken shape in the industry: pharmacopoeia-grade high-purity hypericin monomers, low-irritation repair extracts for professional beauty salons, daily anti-photoaging skincare stock solutions, oral calming composite powders, pet anti-stress premixes, and crude botanical pesticide extracts. Solvent-free green extraction has been widely adopted to reduce three-waste emissions. China has unified quantitative detection methods for multi-component analysis, and light-shielded acid-base resistant embedding technology solves poor water solubility and easy degradation of active substances, compatible with all dosage forms including oral liquids, facial masks, tablets, feed additives and pesticides.

III. Commercial Development History

1. Stage of Direct Medicinal Material Utilization and Microscale Laboratory Extraction (460 BC – 1977)

In Europe, only dried herbs were processed via oil infusion or water decoction. In China, the herb was merely used sporadically by folk residents for external care. Laboratories in Europe and America only separated trace amounts of hypericin for scientific research, with no standardized commercial raw materials available. Domestic small workshops only produced high-tannin crude extracts for self-use, and no formal extracted raw materials circulated on the market.

Industrial Characteristics: No closed light-shielded purification or tannin-removing steady-state processes; unified quality control standards absent; the market lacked awareness of standardized extracts; the industry was largely undeveloped.

2. Stage of Early European Industrialization and Domestic Reliance on Imported Raw Materials (1978 – 2013)

- *1978 – 2004: Small-Scale Mass Production of Standardized Raw Materials in Europe*

Light-shielded ultrasonic extraction and resin purification processes matured, and Europe launched anti-depressant capsules and after-sun repair skincare products. Global annual consumption of standardized raw materials reached 26 tons in 2004, limited to European and American local markets. China could only export low-end crude extracts, relying on imports for 95% of high-end raw materials.

- *2005 – 2013: Full Dependence on Imports for Domestic High-End Markets*

Imported extracts carried high prices and were only available in high-end supermarkets and overseas pharmacies. Domestic crude extracts exceeded impurity limits and could not enter the dietary supplement, cosmetic and pharmaceutical API tracks, only supplied to low-end pesticide markets at low prices.

Industrial Characteristics: German and Swiss enterprises monopolized core technologies for high-purity light-shielded extraction; supporting systems for domestic planting, extraction and testing were incomplete; public awareness of standardized extracts remained insufficient.

3. Formation of Domestic Production Capacity and Rapid Market Expansion Across Multiple Tracks (2014 – 2023)

Global demand for anxiety and sleep relief, after-sun skin repair, green pesticides and pet care grew simultaneously, making St. John's Wort Extract an essential raw material. Global annual consumption hit 168 tons in 2023.

Five major application tracks took shape in the domestic market: calming dietary supplements, soothing skincare products, exported herbal pharmaceutical APIs, anti-stress feed additives for pets, and botanical pesticides. Domestic standardized low-tannin light-shielded extracts achieved stable mass production in 2023, breaking European technological monopoly. Domestic annual consumption reached 56 tons, with total export volume of 126.7 tons.

A fully localized industrial chain was established, supported by integrated technical services covering raw material testing, dosage form formulation and compound development, covering all application scenarios of cosmetics, health food, veterinary drugs and pesticides.

4. Industrial Maturity and Global Export of Domestic Raw Materials (2024 – 2026)

4.1 Clear Product Hierarchy and Full Coverage of Application Scenarios

Five gradient product lines with clear high-end and low-end positioning for differentiated competition: plant protection crude extracts, low-tannin light-shielded extracts for beauty salons, daily skincare stock solutions, oral embedded powders, and composite premixes for pets.

4.2 Mass Overseas Export of Domestic Raw Materials

All indicators of domestic products match European and American standards. Leveraging complete local supply chains, customized purification steady-state technologies and cost advantages, domestic raw materials are exported to the EU, North America, Southeast Asia and other regions, breaking the long-term supply monopoly of overseas enterprises.

4.3 Standardized and Healthy Industrial Competition

Centered on WM/T 3-2004 and the Catalogue of Used Cosmetic Raw Materials, a market access threshold of hypericin ≥0.3% for cosmetic raw materials has been established. Imported high-purity monomers are exclusively supplied to high-end pharmaceutical manufacturers, while domestic standardized extracts cover domestic mass markets and emerging overseas markets. Industrial competition has shifted from cutthroat price wars over low-quality crude extracts to comprehensive competition covering purity, customized tannin removal, light-shielded stability and full global compliance support.

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

- ***Full-Process Green Closed Light-Shielded Production***

Supercritical and subcritical solvent-free extraction, low-temperature membrane enrichment and biological enzymatic hydrolysis technologies will be widely adopted to reduce organic solvent consumption. Herb residues will be recycled for resource utilization to realize whole-plant circular production, eliminating photosensitive active substance loss through full-process light shielding.

- ***Scenario-Oriented Customized Raw Materials***

Specialized raw materials with tailored hypericin content, tannin grades and water solubility will be developed for six segmented tracks: mood regulation, after-sun repair, pet anti-stress care, agricultural insect control and others.

- ***Integrated Composite Raw Materials***

Compound raw materials blended with other soothing, calming and insecticidal extracts will be developed to reduce compounding procedures for end manufacturers and provide one-stop application solutions.

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

Synchronized raw material registration filings in China, EU, the US, Australia, Japan and South Korea, unified cross-border testing standards to achieve unobstructed global circulation.

- ***Iteration of High-Absorption Steady-State Technologies***

Nanoliposome light-shielded encapsulation will enhance transdermal and oral absorption rates. High-end dosage forms such as freeze-dried essences and single-dose oral liquids will be developed. Plant cell suspension culture technology for hypericin enrichment will be promoted to reduce reliance on wild medicinal material supply.

Conclusion

The St. John's Wort Extract industry originates from over two thousand years of Western classical herbal applications and has evolved into a standardized herbal raw material track covering five core sectors: oral calming products, after-sun skincare, antiviral pharmaceutical APIs, pet nutrition and biopesticides. It has completed a full development cycle including ancient herbal literature research, active substance isolation and identification, multi-pathway clinical verification, green closed light-shielded extraction, tannin removal enrichment, iterative light-shielded micro-embedding processes, and independent technological catch-up by domestic manufacturers, realizing full-chain upgrading from wild medicinal herbs to global functional raw materials.

Compared with traditional high-temperature open high-tannin crude extracts, standardized light-shielded St. John's Wort Extract adopts four core technologies: closed low-temperature ultrasonic extraction, solvent-free gradient separation, resin-based tannin removal enrichment and light-shielded microcapsule modification. They feature stable hypericin content, low tannin impurities, light-resistant storage, low solvent residues, compatibility with all dosage forms and global cross-track compliance, aligning with market trends of natural mood regulation, skin repair, green agriculture and pet care. With the commercialization of new technologies including green extraction, segmented customization, nano-delivery and cell culture, St. John's Wort Extract will remain a core raw material in herbal calming, anti-inflammatory repair and botanical pesticide sectors, becoming a mainstream functional plant raw material for cosmetics, big health, veterinary and agricultural industries.