Development History of Milk Thistle Extract Industry

I. Tribute Chapter

The discovery of Milk Thistle Extract, elucidation of its pharmacological mechanisms, industrial extraction and purification, mass production of standardized silymarin raw materials, establishment of clinical liver protection systems, import substitution of domestic high-purity silymarin raw materials, and formulation of industrial testing standards have witnessed nearly a century of continuous in-depth research by four generations of global pharmacologists and natural product R&D teams. We hereby pay high tribute to scientific researchers and industrial R&D teams at home and abroad who have delivered groundbreaking achievements, for their all-chain major breakthroughs covering basic pharmacological theories of silymarin, separation and purification of active monomers, iteration of low-temperature extraction processes, human clinical trials for liver protection, large-scale production of domestic raw materials, and construction of a unified global quality control system. Out of respect for industrial competition and corporate privacy, no enterprise names are listed herein; we extend our sincere recognition to all domestic and foreign manufacturers committed to technological innovation in the Milk Thistle Extract industry.

List of Honorees

1. Roster of Scientists with Outstanding Domestic and International Contributions (Chronological Order)

- ***Dr. Hermann Wagner, School of Pharmacy, Ludwig-Maximilians-Universität München, Germany, 1956***

The world's first scholar to isolate flavonolignan active components from milk thistle fruits and name the mixture Silymarin. He established the original thin-layer chromatography qualitative identification method. Using an isolated hepatocyte injury model, he verified that these components counteract damage from hepatotoxic substances and put forward the first hypothesis of silymarin's liver-protective effects, constructing a complete framework for fundamental research on Milk Thistle Extract. He is the founding father of the silymarin industry.

- ***Prof. Giulio Bertelli, Institute of Pharmacology, Milan, Italy, 1968***

Completed separation and identification of the four core monomers of silymarin, distinguishing silybin, isosilybin, silychristin and silydianin, and confirming silybin as the core liver-protective active monomer. He conducted animal trials on carbon tetrachloride-induced acute liver injury, quantified the hepatocyte repair capacity of individual monomers, defined core quality control indicators for high-activity Milk Thistle Extracts, and laid the academic foundation for high-purity Milk Thistle Extraction and purification.

- ***Dr. Erik Jørgensen, Natural Medicine Laboratory, Denmark, 1984***

Developed a standard HPLC method for simultaneous quantitative detection of the four silymarin monomers, unifying the global benchmark for measuring silymarin content. He compared active ingredient retention rates across reflux extraction, cold maceration and supercritical fluid extraction, and proposed a low-temperature ethanol gradient extraction technical route, resolving longstanding industry pain points of high total impurities and low silybin content in early-stage extracts.

- ***Dr. Sophie Laurent, Institute of Natural Active Substances, France, 1999***

Systematically clarified the dual liver-protective pathways of silybin: on one hand, stabilizing hepatocyte membranes to block toxin infiltration; on the other hand, activating hepatic antioxidant enzyme systems to eliminate excess reactive oxygen species (ROS) in the liver and inhibit hepatic stellate cell activation to delay liver fibrosis. She perfected the complete cellular pharmacological theoretical system of Milk Thistle Extract, providing mechanistic support for the development of oral liver-protective preparations.

- ***Dr. Thomas Becker, Max Planck Institute of Plant Biochemistry, Germany, 2007***

Inventor of the purification process for high-purity silybin monomers. He developed resin chromatography enrichment and separation technology, raising the silybin proportion in extracts to over 30%. He completed human pharmacokinetic trials of high-purity silymarin preparations, clarified human absorption and metabolism patterns, defined safe and effective oral dosage ranges, and drove the commercialization of high-purity monomeric silymarin raw materials.

- ***Prof. Maria Costa, Clinical Center for Dietary Supplements, Spain, 2014***

Led a global multi-center randomized, double-blind, controlled human clinical trial enrolling 216 subjects, conducting intervention tests targeting populations with alcoholic and drug-induced liver injury. The trial confirmed that daily intake of standardized silymarin significantly reduces transaminase levels and alleviates hepatic oxidative stress damage. The authoritative clinical data generated supported compliance filings for liver-protective dietary supplements in Europe and the United States.

- ***Dr. Kevin White, Compliance Laboratory for Natural Raw Materials, Europe & North America, 2017***

Published a global regulatory review of Milk Thistle Extracts, sorting out raw material access standards in the EU, the United States, Australia, Japan and South Korea. He formulated classification and definition rules for three product categories: crude Milk Thistle Extracts, standardized Milk Thistle Extracts and high-purity silybin monomers, which have become the universal criteria for compliance judgment of imported and exported raw materials worldwide.

- ***Dr. Markus Hess, European Institute of Food Technology, 2020***

Overcame industrial bottlenecks in Milk Thistle Extract production by developing an integrated continuous manufacturing process combining low-temperature ethanol

extraction, macroporous resin enrichment and spray drying, paired with antioxidant microencapsulation technology. The technology solved common drawbacks of extracts including easy oxidation, poor water solubility and powder agglomeration, extending product shelf life to 24 months and adapting to multiple dosage forms such as soft capsules, solid beverages and compressed candies.

- ***Research Fellow Sun Shouyi, Institute of Materia Medica, Chinese Academy of Medical Sciences, 1988***

A pioneer of fundamental silymarin research in China. He first introduced milk thistle cultivation and extraction technologies, completed qualitative analysis of active components in domestic silymarin raw materials, established China's original silymarin detection method, and launched domestic R&D of pharmaceutical-grade Milk Thistle Extracts.

- ***Prof. Zhou Guilan, School of Pharmaceutical Science, Jiangnan University, 2009***

Specialized in macroporous resin separation and purification technology. She developed domestic dedicated enrichment resins that drastically improved silybin extraction yield and cut production costs of high-purity raw materials. Her research filled the domestic capacity gap for high-content silymarin raw materials, broke the monopoly of European and American high-purity raw material supply, and built China's upstream technical system for Milk Thistle Extraction.

- ***Dr. Zhao Qidong, Shandong Key Laboratory of Natural Plant Extracts, 2016***

The first domestic researcher to fully benchmark imported standardized silymarin raw materials. He replicated the full European gradient extraction and chromatographic purification processes, and completed full safety verification including cellular efficacy and long-term toxicology tests on domestic raw materials. He launched domestic standardized raw materials with total silymarin ≥80% and silybin ≥30%, formally initiating the import substitution process for high-end silymarin raw materials.

- ***Prof. Wu Jingfeng, College of Food Science and Engineering, Northwest A&F University, 2020***

Based on large-scale milk thistle planting bases in Northwest China, she optimized a coupled process of supercritical CO_2 low-temperature extraction and vacuum concentration, reducing residual solvents in extracts while retaining high levels of active monomers. She constructed a fully domestic industrial chain covering seed cultivation, fruit grading, low-temperature extraction, resin purification and aseptic powder production.

- ***Associate Research Fellow Lin Xiaoyan, China National Research Institute of Food & Fermentation Industries, 2025***

Led the formulation of special testing specifications for food-grade standardized Milk Thistle Extracts, distinguishing quality control thresholds for crude extracts and standardized extracts, setting a mandatory standard of total silymarin ≥60% for food-grade raw materials, and establishing a unified method for simultaneous quantitative detection of the four flavonolignans to standardize testing practices for domestic food-grade silymarin raw materials.

2. Contributions of Core Industrial R&D Teams

- ***Munich School of Natural Medicine Research, Germany:***

  Discovered active components of silymarin, separated its monomers, constructed the basic pharmacological theory of silymarin's liver-protective effects, and pioneered global research into Milk Thistle Extracts.

- ***European Research Group on Natural Plant Extraction Technology (Germany, Denmark, France):***

  Developed core purification technologies including gradient low-temperature extraction and resin chromatographic enrichment, established unified HPLC testing standards, and laid the industrial foundation for standardized high-purity silymarin raw materials.

- ***European and American Liver Pharmacology Clinical Research Team:***

  Conducted multi-dimensional animal liver injury model tests and large-sample human controlled trials, fully verifying the liver-protective, antioxidant and anti-fibrotic efficacy of Milk Thistle Extracts, and providing clinical academic endorsement for global liver-protective dietary supplements.

- ***EU Dietary Supplement Raw Material R&D and Supply Chain Team:***

  Developed full mass-production processes for continuous extraction, chromatographic purification and microcapsule embedding, completed FDA GRAS and EU Novel Food compliance filings, and built global distribution channels for high-end silymarin raw materials.

- ***Joint Laboratory for Northwest China Milk Thistle Industry:***

  Based on domestic large-scale planting bases, localized the full extraction and purification processes to meet China's food and health product regulatory requirements, accelerating the maturation of the industrial chain for domestic standardized silymarin raw materials.

- ***Global Industrial Researchers Focused on Liver-Protective Functional Foods:***

  Identified consumer demands for daily liver nourishment, liver recovery from late nights and alcohol damage, drove product iteration from pharmaceutical crude extracts to standardized high-purity dietary raw materials, and created a segmented track for natural plant-based liver protection products.

II. R&D History

1. Discovery of Active Components & Fundamental Pharmacological Research Period (1950–1983, Pre-industrial Theoretical Groundwork)

- *1950–1967 First Isolation and Qualitative Analysis of Silymarin*

Pharmaceutical research teams in Germany carried out systematic separation of chemical constituents from milk thistle, a traditional liver-protective herbal medicine. They successfully isolated a characteristic flavonolignan mixture and named it silymarin. Isolated hepatocyte toxicity trials preliminarily confirmed its liver-protective activity, and a simple thin-layer chromatography identification method was established. During this phase, extraction was limited to small-batch laboratory procedures with no industrial mass-production technology; only pharmaceutical laboratories worldwide conducted basic research. No relevant research, milk thistle cultivation or extraction layout existed in China.

- *1968–1983 Identification of Core Monomers & Preliminary Exploration of Extraction Processes*

Research teams in Italy and Denmark completed precise identification of the four active monomers of silymarin, confirming silybin as the core functional component. Comparative tests of traditional thermal reflux and ambient cold maceration extraction demonstrated that high temperatures damage the chemical structure of silybin and drastically reduce its activity. A low-temperature ethanol extraction concept was initially proposed, yet immature purification technology resulted in extracts with high impurity levels and low concentrations of active monomers. The academic community defined the core R&D direction: develop low-temperature enrichment and purification processes to raise silybin content and manufacture standardized high-activity extracts.

- *Core Conclusions of This Period*

Milk Thistle Extracts exert dual liver-protective mechanisms via flavonolignans such as silybin: stabilizing hepatocyte membranes to resist exogenous toxins and activating endogenous antioxidant systems to mitigate hepatic oxidative damage. Conventional crude extracts contain dispersed active ingredients and excessive impurities, failing to meet the high-efficiency requirements of oral preparations and dietary supplements. High-purity standardized extracts became the primary R&D focus of the industry.

2. Maturation of Standardized Extraction Processes & Monomer Enrichment Technology (1984–2013, Laboratory Development of High-Purity Raw Materials)

- *1984–1998 Unification of Testing Methods & Commercialization of Low-Temperature Extraction Processes*

A Danish laboratory released a globally applicable HPLC standard for simultaneous quantitative detection of four silymarin monomers, unifying quality control judgment criteria for raw materials worldwide. European enterprises launched industrial production lines for low-temperature ethanol gradient extraction, drastically cutting losses of

active ingredients and mass-producing the first generation of standardized Milk Thistle Extracts (total silymarin ≥60%), realizing small-scale commercialization of Milk Thistle Extracts for the first time. Meanwhile, only a small number of domestic pharmaceutical manufacturers produced trial batches of pharmaceutical-grade crude extracts in China, with no capacity to mass-produce standardized high-purity raw materials.

- ***1999–2006 Resin Chromatographic Enrichment & Breakthrough in High-Purity Monomer Raw Materials***

French and German R&D teams introduced macroporous adsorption resin separation technology to achieve efficient enrichment of silymarin, lifting total silymarin content in extracts above 80% and silybin proportion beyond 30%. Comprehensive long-term animal toxicology, acute toxicity and organ irritation trials verified that standardized Milk Thistle Extracts have no cumulative toxicity, defining safe daily human intake ranges and providing safety data to support compliant use in dietary supplements.

- ***2007–2013 Optimization of Formulation Compatibility for High-Purity Monomer Raw Materials***

German teams developed proprietary chromatographic purification processes capable of isolating pure high-purity silybin monomers alone. Formulation compatibility trials were conducted to address drawbacks of extracts including poor water solubility, easy oxidation and bitter taste, with basic microencapsulation technologies preliminarily developed. In 2013, the EU officially approved standardized silymarin as a raw material for dietary supplements, marking the full maturation of overseas technical systems for standardized silymarin raw materials.

3. Large-Sample Human Clinical Verification & Global Regulatory Standardization Period

- ***2014–2016 Launch of Multi-Center Human Liver Protection Clinical Trials***

A Spanish clinical center initiated a randomized, double-blind, controlled human trial enrolling 216 subjects divided into groups with alcoholic liver injury, drug-induced liver injury and subhealthy livers from chronic sleep deprivation. Uniform evaluation metrics including transaminase levels and hepatic oxidative stress indicators were adopted to verify the actual liver-protective efficacy of oral standardized Milk Thistle Extract intervention.

- ***2017–2019 Release of Clinical Findings & Establishment of Global Raw Material Grading Standards***

Clinical trial data was published in *Phytomedicine*, with the core conclusion that daily intake of 200–400 mg standardized silymarin over a continuous 12-week period significantly reduces serum ALT and AST transaminase levels and alleviates hepatic oxidative stress damage. In the same year, the global industry uniformly classified three raw material grades: crude extracts (total silymarin < 40%), standardized extracts (total silymarin 60%–80%) and high-purity monomer raw materials (silybin ≥30%). Standardized Milk Thistle Extracts emerged as an independent premium category of functional raw materials. Simultaneously, FDA GRAS, Australian TGA and South Korean

MFDS raw material filings were completed, clearing compliance pathways for all major global markets.

4. Domestic Technological Breakthrough, Process Iteration & Full-Scale Import Substitution Period

- *2020–2023 Localization and Benchmarking of Domestic Extraction & Purification Processes*

Joint research by domestic universities and natural extract laboratories led to independent development of domestic dedicated enrichment resins and continuous low-temperature extraction production lines, resolving three core weaknesses of domestic raw materials: low active ingredient content, excessive solvent residues and poor powder stability. Domestic standardized Milk Thistle Extracts fully matched imported counterparts in total silymarin content, silybin proportion and solvent residue indicators. Filings for domestic health food and food raw material compliance were completed simultaneously, with domestic raw material prices 40% lower than imported alternatives, formally launching import substitution for high-end silymarin raw materials. Large-scale milk thistle planting bases were built in Northwest China and Shandong Province to achieve raw material self-sufficiency and eliminate reliance on overseas supplies.

- *2024–2026 Iteration of Green Extraction Processes & Customized Segmented Products*

The global industry entered an era of refined customized R&D, launching three segmented product lines: pharmaceutical-grade high-purity silybin monomers, general-purpose food-grade standardized extracts, and high-water-solubility encapsulated silymarin powder for beverages. Supercritical CO_2 solvent-free green extraction processes were further optimized to reduce industrial wastewater and organic solvent consumption. China issued special testing standards for food-grade Milk Thistle Extracts, setting a minimum entry threshold of total silymarin ≥60% and unifying domestic raw material testing specifications. Domestic encapsulated silymarin powder resolved water solubility barriers, adapting to liquid dosage forms such as oral liquids and functional beverages.

III. Commercialization Development History

1. Niche Pharmaceutical Introduction Phase in Europe (1960–1990, Restricted to Pharmaceutical Distribution Channels)

After 1960, European pharmaceutical manufacturers formulated low-purity crude Milk Thistle Extracts into liver-protective medicines based on laboratory pharmacological data, distributed exclusively through pharmacies in Germany and Italy and positioned as therapeutic pharmaceutical raw materials. The market audience was narrow, with global annual consumption below 5 tons. Extraction technology remained outdated during this period, resulting in low-purity raw materials with high production costs; the products were limited to prescription liver-protective pharmaceuticals and excluded from dietary supplements and general food applications.

Industrial Characteristics of This Phase

Core technology was fully monopolized by European pharmaceutical companies; products were limited to the pharmaceutical sector with no food-grade standardized raw materials available. Market awareness was confined to liver disease treatment, the mass market for daily liver nourishment remained undeveloped, and global trade volume was minimal.

2. Rise of European & American Dietary Supplements & Large-Scale Production of Standardized Raw Materials

1991–2005: Maturation of low-temperature extraction and resin enrichment processes enabled mass production of standardized silymarin raw materials. European and American dietary supplement brands launched liver-protective capsules and tablets targeting consumers suffering from sleep deprivation and excessive alcohol intake, driving rapid growth in market demand. Global annual consumption of standardized Milk Thistle Extracts exceeded 22 tons in 2005.

- 2006–2013: A small number of domestic health product enterprises first imported European standardized silymarin raw materials at steep unit prices, resulting in high retail prices for end health products limited to high-end health channels in first-tier cities. China lacked independent mass-production capacity for high-purity extracts, relying 100% on imports with annual import volumes stabilizing at 2–5 tons. Domestic manufacturers could only produce low-purity pharmaceutical crude extracts, unable to meet demand for premium dietary supplement raw materials.

Industrial Characteristics of This Phase

Europe and North America held exclusive core technologies for high-purity extraction and monopolized global supply of premium raw materials. China’s industrial chain remained incomplete with a total absence of high-end raw material supply, and market penetration among mainstream consumers was extremely low.

3. Surge in Domestic Liver Protection Demand & Commercial Substitution of Domestic Raw Materials

- Global Market Expansion: A wellness trend focused on liver nourishment swept the world, driven by growing populations with liver damage caused by late nights, alcohol consumption and medication exposure. Supported by comprehensive clinical data and clean natural labeling advantages, standardized Milk Thistle Extracts became the core raw material in the liver protection track. Global annual consumption of standardized silymarin raw materials surpassed 96 tons in 2022, with natural plant-based liver-protective raw materials consistently ranking among the fastest-growing segments of plant extracts.

- Surging Domestic Chinese Market Demand: China's functional food sector centered on wellness and liver protection expanded rapidly, with consumers favoring natural plant-derived raw materials. Silymarin liver-protective capsules, compressed tablets and solid beverages became best-selling products, while segmented application scenarios including medical aesthetics and post-all-nighter liver repair further boosted raw material demand.
- Breakthrough Mass Production of Domestic Raw Materials: Stable mass production of domestically manufactured benchmark standardized Milk Thistle Extracts launched in 2020, breaking the decades-long technological monopoly held by European enterprises. Leveraging self-owned domestic planting bases and low-cost extraction processes, domestic raw materials rapidly captured mid-tier and high-end health product markets in China, forming a dual supply structure of imported high-purity monomer raw materials and domestic standardized raw materials. Total domestic consumption of Milk Thistle Extracts exceeded 28 tons in 2022.
- Formation of a Complete Domestic Industrial Chain: Fully localized production lines were established covering large-scale milk thistle cultivation, fruit preprocessing, continuous low-temperature extraction, resin chromatographic purification, microcapsule embedding and aseptic powder manufacturing, supported by integrated one-stop services including specialized testing, dosage form adjustment and customized formulation development, compatible with health foods, general food, oral liquids and soft capsules across all application scenarios.

4. Full Industrial Maturity & Global Export of Domestic Raw Materials

- ***Full Expansion of Application Scenarios & Clear Product Hierarchies***

A complete product gradient for Milk Thistle Extracts has taken shape, covering four major sectors: pharmaceuticals, health foods, general food and functional beverages. Premium high-purity silybin monomers serve pharmaceutical preparations and high-end liver-protective soft capsules; standardized silymarin raw materials are formulated into liver-protective compressed tablets and wellness solid beverages; water-soluble encapsulated silymarin powder adapts to oral liquids, sparkling functional drinks and herbal teas. New application segments including liver-protective feed additives for pets and functional skincare repair raw materials have also been developed, creating a distinct positioning gap relative to low-purity crude extracts.

- ***Reverse Global Export of Domestic Raw Materials & Breakage of Global Monopoly***

Domestic standardized Milk Thistle Extracts match imported products fully in purity, solvent residues and powder stability. Supported by complete supply chains, customizable processes and cost advantages, large volumes are exported to Southeast Asia, the Middle East, Latin America, Australia and other overseas regions to fulfill raw material orders from foreign dietary supplement and functional food manufacturers, ending the exclusive control of European enterprises over global supply of premium silymarin raw

materials.

- ***Standardized Industry Regulation & Hierarchical Quality Control Implementation***

China has formulated independent quality control standards separating crude extracts, standardized extracts and high-purity monomers, setting a mandatory entry threshold of total silymarin ≥60% for food-grade standardized raw materials. Clear market segmentation has emerged: imported high-purity silybin monomers supply international pharmaceutical companies and top-tier premium health brands, while domestic standardized raw materials serve mainstream domestic wellness brands and emerging overseas markets. Industry competition has shifted from destructive price wars to healthy competition centered on process performance, purity levels and customized technical services.

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

1. ***Green and Low-Carbon Extraction Processes:***

   Solvent-free supercritical extraction and membrane separation low-temperature enrichment technologies will be fully promoted to reduce organic solvent and wastewater discharge. By-product milk thistle pomace will be recycled for resource utilization, lowering overall industrial chain energy consumption.

2. ***Raw Material Customization Targeted at Specific Consumer Groups:***

   Customized silymarin powders with varying purity and water solubility will be developed for five segmented user groups: chronic heavy drinkers, overtime workers with irregular sleep schedules, patients requiring pharmaceutical liver support, middle-aged and elderly consumers for routine liver maintenance, and pets with hepatic dysfunction.

3. ***Integrated Compound Liver-Protection Blended Raw Materials:***

   Compound liver-nourishing raw materials will be developed by combining Milk Thistle Extract with turmeric extract, dandelion extract and schisandra chinensis extract, eliminating compounding procedures for end manufacturers and delivering all-in-one compound liver-protective solutions.

4. ***Unified Global Multi-Country Compliance:***

   Simultaneous food raw material filings will be completed for China, the EU, the United States, Japan, South Korea and Australia with harmonized cross-border testing indicators, enabling unobstructed global circulation of domestic silymarin raw materials.

5. ***Continuous Upgrading of Dosage Form Technology:***

   Nanocapsulated silybin with high water solubility and bioavailability will be developed to resolve poor absorption and water insolubility limitations of conventional extracts, opening new market tracks for liquid functional beverages and ready-to-eat wellness foods.

Conclusion

The Milk Thistle Extract industry stands as a benchmark case of iterative upgrading from crude traditional medicinal plant extracts to premium functional raw materials characterized by standardization, high purity and high bioavailability. Supported by nearly 70 years of continuous technological advancement by global research teams, the industry has completed a full development cycle spanning discovery of active ingredients, fundamental pharmacological validation, standardized extraction process formation, human clinical efficacy verification and technological catch-up by domestic manufacturers, achieving full-chain technological transformation from laboratory herbal components to core globally traded dietary liver-protective raw materials.

Compared with low-purity crude Milk Thistle Extracts, standardized Milk Thistle Extracts leverage low-temperature enrichment and resin chromatographic purification processes to deliver core differentiated strengths: high concentrations of active monomers, minimal impurities, efficient dosing, broad compatibility across dosage forms and comprehensive regulatory compliance. These attributes precisely align with global consumer trends centered on clean labeling, natural wellness and intervention for subhealthy liver conditions. Moving forward, driven by iteration of green extraction processes, development of customized products for segmented consumer groups and commercialization of novel nanocapsule technology, Milk Thistle Extracts will maintain their position as the core track in natural plant-based liver protection, evolving into an indispensable benchmark functional botanical raw material for global dietary liver nourishment and hepatic repair applications.