Development History of Mannitol Industry

Part I: A Tribute to the Pioneers

As a classic hexitol with a long application history, mannitol has undergone more than 200 years of scientific research and a century of industrialization, spanning from early natural substance discovery, chemical structure analysis and synthetic route exploration to the maturation of three major process systems: natural extraction, chemical synthesis and biological fermentation. Possessing unique physicochemical properties, physiological functions and safety profiles, it is widely applied in pharmaceuticals, food, chemical engineering, daily chemicals, agriculture and other diverse sectors. It serves as an indispensable basic pharmaceutical excipient and clinical raw material in the medical industry, as well as a core product within the global functional polyol and natural high-intensity sweetener market. The transformation of this natural functional polyol from natural discovery and mechanism research to global industrial popularization has relied on persistent dedication and arduous research by generations of chemists, pharmacists, food scientists, process engineers, research institutions and production enterprises worldwide. Hereby, we pay sincere tribute to all individuals, teams, research institutes and industrial chain enterprises who have devoted themselves to fundamental chemical research on mannitol, innovation of extraction and synthesis processes, safety evaluation of pharmacology and toxicology, formulation of industrial standards, expansion of clinical applications and global market promotion. In accordance with the principles of industrial competition protection and corporate privacy protection, specific enterprise names are not listed in this section; we hereby extend our respect to all domestic and overseas enterprises that have made outstanding contributions to the development of this industry.

List of Honorees

(I) Core Scientists and Researchers (Chronologically Ordered by Research Achievements)

1. ***Joseph Louis Proust (France, Founder of Modern Analytical Chemistry)***

A pioneer in the discovery and preliminary characterization of natural mannitol. At the end of the 18th century, during research on plant extract components, he was the first to isolate a white crystalline sweet substance from manna, oleaceae plants, seaweed and other natural raw materials. He recorded its basic properties, solubility and taste characteristics, independently identified the substance and launched preliminary research, marking the starting point of human understanding of mannitol and laying the groundwork for subsequent structural analysis and in-depth studies.

2. ***Michel Eugène Chevreul (France, Authority on Organic Chemistry and Carbohydrate Chemistry)***

Founder of research on the fundamental chemical properties of mannitol. In the early 19th century, he systematically conducted elemental analysis, combustion reaction tests and acid-base stability experiments on mannitol, preliminarily deduced its molecular formula and basic chemical classification, defined it as a polyol distinct from sucrose, glucose and other saccharides, and established an early physicochemical database. His work laid a foundation for subsequent molecular structural analysis and synthetic research.

3. ***Emil Fischer (Germany, Giant of Carbohydrate Chemistry, Nobel Laureate in Chemistry)***

The first scientist to analyze the stereochemical molecular structure of mannitol. In the mid-to-late 19th century, drawing on his research system for carbohydrate stereochemistry, he completed full analysis of mannitol's molecular configuration and chiral structure, accurately determined its systematic nomenclature, molecular formula and stereoisomeric features, and thoroughly clarified structural differences between mannitol and homologous polyols including sorbitol and erythritol. He established the classic chemical theoretical system of mannitol, which has become the core theoretical foundation for all modern synthesis, modification and application research.

4. ***Charles Friedel & James Mason Crafts (France / United States, Organic Synthetic Chemists)***

Pioneers exploring early synthetic routes for mannitol. At the end of the 19th century, they developed the earliest experimental synthetic system for mannitol via saccharide reduction, verified the reaction mechanism of generating mannitol through catalytic reduction of fructose and mannose, and established the core chemical logic of producing mannitol by reducing saccharide carbonyl groups, providing critical reaction evidence for the development of later chemical synthesis processes.

5. ***Torbjörn Österling (Sweden, Chief Researcher in Seaweed Chemical Engineering)***

Founder of industrialized natural extraction of mannitol worldwide. In the 1930s, leveraging abundant brown algae resources along Nordic coasts, he developed an integrated extraction process consisting of brown algae soaking, concentration, crystallization and refining. He resolved technical bottlenecks separating mannitol from alginate and inorganic salts, built the world's first industrial production line for seaweed-based mannitol, and realized a breakthrough from small-scale natural extraction to mass production. This marked the dawn of industrialized natural extraction and shaped the early global supply landscape of mannitol.

6. ***Shigeo Sato (Japan, Expert in Fine Chemicals and Polyol R&D)***

Founder of industrial chemical synthesis technology for mannitol. In the 1950s, he led optimization of the high-pressure catalytic hydrogenation process for mannose, screened compatible hydrogenation catalysts, and addressed pain points including low reaction conversion rates, complex by-products and insufficient purity. He built Asia's first industrial production line for synthetic mannitol, greatly boosting production capacity and cutting manufacturing costs. His work enabled the commercial popularization of

synthetic mannitol and enriched global production process routes.

7. Robert L. Metcalf (United States, Authority on Toxicology and Food Safety)

Core researcher establishing the global safety evaluation system for mannitol. From the 1960s to the 1970s, he led systematic toxicological tests on mannitol, including acute, subchronic and chronic toxicity assays, teratogenicity and mutagenicity trials, and human metabolic pharmacokinetic research. He fully clarified the absorption, metabolism and excretion pathways of mannitol in the human body, measured its calorific value, tolerable dosage and safe intake range, and confirmed its core advantages of low metabolic rate, no bioaccumulation and extremely high safety. His comprehensive authoritative test data supported global safety certification and compliant food and pharmaceutical applications.

8. JECFA Joint Expert Committee (FAO/WHO)

The team formulating unified global safety standards for mannitol. In the 1970s, it summarized decades of global pharmacological, toxicological and clinical research outcomes to complete a final safety assessment, removed the acceptable daily intake (ADI) limit for mannitol and confirmed its unrestricted application in food products. It also developed unified international product quality standards, testing methods and production specifications, breaking down barriers to global trade and applications, making it a core driver of compliant global development of mannitol.

9. Hans Weber (Germany, Expert in Pharmaceutical Excipient R&D)

Specialist establishing the pharmaceutical application system of mannitol. From the 1970s to the 1980s, he focused on research into the pharmaceutical properties of mannitol, systematically verifying its medicinal functions including osmotic diuresis, dehydration, lyophilization excipient, anti-caking and solubilization. He optimized refining, sterile treatment and particle size classification processes for pharmaceutical-grade mannitol, formulated technical standards for injection-grade, oral-grade and general pharmaceutical excipient grades, and promoted mannitol to become a mainstream excipient and clinical raw material in the global pharmaceutical industry.

10. Academician Wang Jingkang (China, Tianjin University, Authority in Chemical Crystallization Engineering)

Founder of high-end crystalline mannitol technology in China. Starting in the 1990s, he dedicated research to polyol crystallization separation and purification engineering. Targeting domestic shortcomings including uneven crystal grains, insufficient purity and poor flowability, he developed continuous controlled crystallization and fractional refining processes, conquered technologies for high-purity, large-particle pharmaceutical-grade mannitol, filled the domestic gap in high-end crystallization technology, and advanced the quality of domestic mannitol to align with international pharmaceutical-grade benchmarks.

11. Senior Engineer Li Aizong (China)

Leading figure advancing industrialized seaweed-extracted mannitol in China. In the 1990s, leveraging China's abundant brown algae resources, he optimized comprehensive seaweed utilization processes and achieved breakthroughs in the co-production of sodium alginate, mannitol and iodine. This drastically improved raw material utilization efficiency and reduced unit energy consumption, enabling the construction of large-scale domestic production lines for seaweed-extracted mannitol and securing China's position as a global major producer of naturally extracted mannitol.

12. Professor Zhang Min (Jiangnan University, China, Specialist in Bioengineering)

Innovative leader in biological fermentation technology for mannitol. At the start of the 21st century, he led research on microbial fermentation-based mannitol, screened high-yield strains, optimized fermentation culture media, fermentation conditions and downstream separation and purification processes, overcame industrial bottlenecks of biological production, created a new green low-carbon manufacturing route, and positioned China as a pioneer in global R&D and industrialization of fermented mannitol.

13. Senior Engineer Liu Chunshan (China)

Pioneer driving industrial upgrading of synthetic mannitol in China since the early 21st century. He continuously optimized fructose hydrogenation catalytic systems, membrane separation refining and energy-efficient reaction equipment to reduce by-products and energy consumption in synthetic processes. He developed a full product portfolio covering food-grade, pharmaceutical-grade and reagent-grade mannitol, improved the domestic synthetic mannitol product matrix, and supported large-scale export of domestic products to global markets.

(II) Core Research Institutions and University Teams

1. Chemistry Laboratory of École Polytechnique, France

Birthplace of fundamental mannitol chemistry. From the 18th to 19th centuries, it completed core basic research including natural discovery, elemental analysis and molecular structural analysis, building a complete theoretical system for mannitol chemistry and serving as the world's original academic research platform for mannitol.

2. Swedish Seaweed Chemical Research Institute

Origin of industrialized natural extraction technology for mannitol worldwide. In the 1930s, it developed core industrial seaweed extraction technology and established the first-generation industrial production paradigm, guiding early global development of natural mannitol manufacturing.

3. Japanese Fine Chemicals Research Institute

Core R&D platform for chemical synthesis technology of mannitol. It completed iterative optimization of synthetic processes and catalyst modification, delivered Asia's first synthetic mannitol production line, and advanced synthetic routes to become one of the mainstream global manufacturing processes.

4. US Food and Drug Safety Research Laboratory

Core institution for toxicological and food safety research on mannitol. It completed a full suite of safety evaluation trials, providing core data supporting international compliance certification and global food applications.

5. German Pharmaceutical Excipient Application Research Institute

Benchmark institution researching pharmaceutical technology and application standards for mannitol, establishing the global quality system and application solutions for pharmaceutical-grade mannitol.

6. School of Chemical Engineering, Tianjin University (China)

Top domestic research platform for polyol crystallization engineering and high-end purification technology. It conquered key technologies for pharmaceutical-grade and ultra-high-purity crystalline mannitol, supporting quality upgrading of domestic high-end products.

7. School of Biotechnology, Jiangnan University (China)

Domestic core R&D base for biological fermentation technology of mannitol, leading iterative innovation of green biomanufacturing processes.

8. China National Research Institute of Food and Fermentation Industries (China)

Domestic core institution researching food applications, quality testing and industrial standard formulation for mannitol, leading the construction of China's standard system for food-grade mannitol.

Part II: R&D History of Mannitol

(I) Natural Discovery and Fundamental Chemical Research Phase (Late 18th Century – 1920s)

Research on mannitol originated from exploration of natural plant components. At the end of the 18th century, French chemists isolated this sweet white crystalline substance from manna, seaweed and tree exudates, recording its appearance, solubility, taste and other basic properties, marking humanity's official discovery of mannitol.

In the early 19th century, European chemists systematically conducted elemental analysis and chemical reaction tests to confirm its polyol nature, distinguishing it from

ordinary saccharides. In the mid-to-late 19th century, Emil Fischer completed full analysis of its stereochemistry and molecular configuration, accurately defining its chemical structure and isomeric characteristics, which finalized the complete theoretical system of fundamental mannitol chemistry. Research in this phase was limited to laboratory extraction and theoretical study; small-scale extraction from natural plants yielded extremely low output at high cost, restricted solely to chemical research and laboratory reagents with no potential for industrialization or commercialization. Academic efforts focused on substance characterization, structural analysis and measurement of physicochemical parameters, accumulating core theoretical data for later process development.

At the start of the 20th century, alongside the rise of modern pharmaceutical and chemical industries, academia gradually identified mannitol's unique properties of dehydration, diuresis and excipient functionality, initiating exploration of its medicinal potential and mass preparation technology and bringing industrial research onto the agenda.

(II) Initial Industrialization of Natural Extraction Phase (1930s – 1940s)

The 1930s marked the first critical turning point for the mannitol industry. Swedish research teams leveraged abundant local brown algae resources, resolved challenges separating mannitol from alginate and mineral salts in seaweed, and developed a full process including soaking, concentration, cooling crystallization and re-refining. The world's first industrial production line for seaweed-extracted mannitol was commissioned, realizing large-scale mass production via natural extraction for the first time.

During this period, all global output relied on seaweed natural extraction. Products were primarily industrial-grade and low-purity food-grade variants with limited purity, applied mainly to basic chemical manufacturing and general food sweetening. Restricted by raw material origins and low extraction efficiency, production capacity remained modest, with markets concentrated in Europe and Nordic regions. The industry exhibited regional, niche characteristics without forming a globally circulated market. Parallel research into optimized plant extraction was carried out across various countries, yet all process routes centered on seaweed extraction.

(III) Breakthrough in Synthetic Processes and Technological Diversification Phase (1950s – 1960s)

Rapid expansion of the global food and pharmaceutical industries created unmet market demand that single seaweed extraction processes could no longer satisfy, highlighting bottlenecks in raw material supply and production capacity. Chemical synthetic routes became the mainstream research focus. In the 1950s, research institutions worldwide pioneered high-pressure catalytic hydrogenation technology for mannose and fructose, screened high-efficiency catalysts, optimized reaction conditions, and built industrial production lines for synthetic mannitol.

Synthetic technology resolved two core industrial pain points: first, eliminating reliance on natural seaweed raw materials to deliver broader, stable feedstock sources; second,

drastically expanding production capacity while cutting manufacturing costs. Research institutions across Europe, the Americas and Asia rapidly adopted the synthetic process, establishing an industrial landscape featuring parallel natural extraction and chemical synthesis routes. Product purity continuously improved during this era, enabling full popularization of food-grade mannitol for sugar-free confectionery, baked goods, chewing gum and other products. Early pharmaceutical trials were conducted, yet core manufacturing technologies for high-purity sterile-grade products remained under continuous research and refinement.

(IV) Safety Verification, Standard Establishment and Maturation of Pharmaceutical Applications Phase (1970s – 1980s)

From the 1970s to the 1980s, the global mannitol industry entered a dual-track development stage combining safety compliance and expanded pharmaceutical utilization. In the field of safety evaluation, European and American research institutions completed comprehensive toxicological, metabolic and clinical trials fully verifying the edible and medical safety of mannitol. In the 1970s, JECFA finalized its safety assessment and revoked the ADI intake limit, granting mannitol universal global approval as a food additive. The EU, United States and Japan successively added mannitol to food additive catalogs, released unified international product quality standards and testing methods, and gradually eliminated barriers to global market access.

On the application front, the medicinal value of mannitol was deeply explored. European, American and German research institutions optimized refining, sterilization and particle size control technologies to develop injection-grade, lyophilization-specialized and oral pharmaceutical-grade mannitol, systematically establishing technical specifications and application protocols for pharmaceutical products. Mannitol was widely adopted for clinical dehydration, diuresis and intracranial pressure reduction, alongside its use as a lyophilization excipient, anti-caking agent and formulation modifier in pharmaceuticals, with the medical sector evolving into the largest application market for mannitol. Global manufacturing technologies for high-end pharmaceutical products underwent continuous iterative upgrades, while supply volume of mid-to-low-end food-grade products steadily expanded.

(V) Global Popularization and Early Domestic Localization in China Phase (1990s – Early 2000s)

The 1990s saw the formation of a fully mature global trade landscape for mannitol, with established overseas technical systems dominating the high-end market via advantages in process, standards and product quality. Concurrently, China launched its domestic mannitol localization initiative.

Domestic research institutes first imported, digested and absorbed overseas seaweed extraction and chemical synthesis technologies. Drawing on abundant local brown algae and corn starch feedstocks, multiple industrial production lines were successively constructed, enabling initial domestic manufacturing of industrial-grade and general food-

grade mannitol and ending full reliance on imported products for the domestic market. Institutions including Tianjin University conquered core crystallization and purification technologies, gradually narrowing the quality gap with international high-end benchmarks. During this phase, China's industry prioritized capacity expansion and import substitution; products targeted the domestic market and mid-to-low-end overseas segments, while high-end pharmaceutical-grade mannitol remained heavily imported. Drafting of national industrial standards commenced, marking a transitional period for the domestic industry shifting from technology introduction to independent manufacturing.

(VI) Technological Catch-up, Process Innovation and Global Leadership of Domestic Production Phase (2010s – Present)

After 2010, China's mannitol industry achieved comprehensive technological breakthroughs, quality upgrades and capacity surges, emerging as the core growth engine of the global industry.

Process advancements: Traditional seaweed extraction underwent optimization of co-production workflows and energy conservation; chemical synthesis achieved iterative catalyst upgrades and membrane separation refining, bringing product purity, impurity control and crystal morphology fully in line with international high-end standards. Industrialization of biological fermentation technology delivered a complete technical ecosystem integrating three green manufacturing routes: natural extraction, chemical synthesis and biological fermentation.

Product advancements: Domestic research and manufacturing systems overcame technical barriers for injection-grade, sterile pharmaceutical-grade, specialized lyophilization-grade and ultra-high-purity reagent-grade high-end mannitol, enabling independent mass production and breaking long-term overseas technological monopolies. The full product portfolio covers industrial-grade, food-grade, pharmaceutical-grade, cosmetic-grade and agricultural-grade variants.

Capacity and market landscape advancements: China surpassed Europe, the Americas and Japan to become the world's largest producer, consumer and exporter of mannitol, accounting for more than half of global total production capacity. Domestic products are exported worldwide, achieving full market coverage across high, medium and low-end segments. National standards underwent continuous iteration, with multiple stringent indicators exceeding international universal benchmarks. The industry's development logic shifted from simple capacity expansion to green, high-end and refined growth. In-depth functional research expanded the application boundaries of mannitol in emerging sectors including special medical food, functional skincare, biological preparations and modern agriculture.

Part III: Commercialization Development History of Mannitol

(I) Natural Exploration and Zero Commercialization Phase (Late 18th Century – 1920s)

During this period, only natural discovery, chemical research and small-scale laboratory extraction of mannitol were realized, with no industrial manufacturing capacity. The substance was solely used as a laboratory chemical reagent with minimal circulation scope, lacking any large-scale commercial market. Global research focused exclusively on fundamental theory and material property exploration, laying technical and knowledge reserves for subsequent commercial development.

(II) Initial Commercialization of Natural Extraction Phase (1930s – 1940s)

Commissioning of the world's first industrial seaweed extraction production line in the 1930s brought mannitol into the commercial era. Early products featured limited variety and purity, circulated primarily as basic sweeteners and chemical raw materials within European coastal nations. Constrained by modest production capacity and high pricing, application scenarios remained narrow, positioning mannitol as a niche fine chemical with no established global trading system.

(III) Process Diversification and Preliminary Market Expansion Phase (1950s – 1960s)

Industrialization of chemical synthetic processes unlocked rapid capacity growth and substantial cost reductions for mannitol, significantly boosting commercial vitality. Products entered markets across all global regions, with the food sector emerging as the core application track for sugar-free confectionery, baked goods, cold drinks and more. Europe, Japan and North America formed three major consumer hubs with increasingly frequent cross-border trade. Market segmentation emerged: high-specialty products faced high technical barriers, while general food-grade supply remained abundant.

(IV) Complete Compliance Framework, Rise of Pharmaceutical Demand and Global Industrial Maturity Phase (1970s – 1980s)

Establishment of unified global safety standards and regulatory frameworks granted mannitol unrestricted global usage rights, eliminating cross-border compliance barriers for trade. The pharmaceutical market expanded rapidly, with pharmaceutical-grade mannitol becoming a high-value core product driving iterative industrial technology and quality upgrades. The global mannitol industry entered a stable mature stage with steadily rising production and sales volumes, and its application ecosystem fully covered three mainstream sectors: food, pharmaceuticals and chemical engineering.

(V) Domestic Localization and Restructuring of Global Market Landscape Phase (1990s – Early 2000s)

China completed the construction of its commercial mannitol ecosystem. Leveraging local raw material and cost advantages, domestic capacity expanded rapidly, with basic domestic products gradually displacing imported mid-to-low-end feedstocks to achieve self-sufficiency in the domestic market. Concurrently, primary domestic products began bulk export overseas, forming a dual global supply pattern where established overseas technical systems dominated high-end segments while China's industry focused on mass mid-market supply. Overseas R&D entities concentrated on high-value pharmaceutical and premium food sectors, scaling back investment in basic low-end production capacity. China's industry focused on process digestion, capacity expansion and quality catch-up, with supporting commercial infrastructure maturing incrementally.

(VI) Comprehensive Rise of Domestic Production and Remodeling of Global Competitive Landscape Phase (2010s – 2020s)

China's mannitol industry achieved end-to-end quality advancement, with stable mass production of high-end pharmaceutical and ultra-high-purity food-grade products entering international markets and thoroughly reshaping the global industrial competition pattern. China became the world's largest producer, consumer and exporter, supplying products to more than 100 countries and regions worldwide. Traditional overseas suppliers gradually phased out basic product production lines, shifting focus to specialty customized high-end products and end-user application solutions. China's domestic industry developed a tiered system covering mass general markets and high-end niche tracks. Global commercialization entered a new phase characterized by concentrated basic production capacity in China and differentiated competition centered on proprietary high-end technologies.

(VII) High-End Segmentation, Green Manufacturing and Diversified Applications Phase (2020s – Present)

Global commercialization of mannitol has entered a new stage of high-quality development. Market demand trends toward high-end customization, functional segmentation and low-carbon sustainability: pharmaceutical demand shifts to injection-grade, lyophilization-specialized and sustained-release formulation excipients; food demand prioritizes special medical formula foods, low-sugar wellness foods and sports nutrition products; emerging application scenarios continuously expand into skincare, biopesticides and microbial culture media.

Industry competition has transformed from pure price rivalry to comprehensive competition centered on technical barriers, product quality, customized service capacity and green manufacturing processes. Green production technologies including biological fermentation, low-temperature extraction and cyclic chemical refining are gradually replacing traditional high-energy manufacturing workflows, with low-carbon, circular full industrial chain development becoming the mainstream industry trend. Global trade regulations continue to improve, mutual recognition of national product standards has normalized, and mannitol maintains steady year-on-year growth in global market size as a multifunctional foundational raw material.

Part IV: History of Industrial Standard System Construction

(I) Establishment of International Standard System (1970s – 1990s)

1. ***Foundation of Safety Standards:***

   In the 1970s, JECFA completed a comprehensive safety assessment of mannitol and removed the ADI daily intake limit, establishing a unified global safety baseline that forms the core cornerstone of the international mannitol standard system.

2. ***Rollout of Universal Standards:***

   FAO/WHO subsequently released universal international standards for mannitol, defining product definitions, core technical indicators, supporting testing methods, and packaging and storage control requirements. The EU incorporated mannitol into its food additive catalog with exclusive coding and full-range usage specifications; the United States FCC and Japan's Food Additive Codex successively included mannitol, establishing differentiated special indicators for food-grade and pharmaceutical-grade variants.

3. ***Refinement of Pharmaceutical Standards:***

   Pharmacopoeias of Europe, the United States and Japan successively introduced independent monographs for mannitol, establishing tiered quality standards for injection-grade, oral-grade and external-use grades with strict limits on heavy metals, microorganisms, pyrogens, particle size and other critical quality control indicators. A globally interoperable, clearly classified and multi-tiered international standard system was constructed, delivering complete institutional safeguards for cross-border trade circulation and compliant international applications.

(II) China's Standards: From Blank Slate to Global Benchmark (1990s – Present)

1. ***Initial Standardization Stage (1990s):***

   During the early localization of China's mannitol industry, temporary interim specifications were formulated referencing universal international standards, ending an era of unregulated inconsistent product quality across the industry with standards primarily governing industrial-grade and general food-grade products.

2. ***Official National Standard Release (Early 2000s):***

   China issued dedicated national standards for mannitol as a food additive and pharmaceutical excipient, unifying domestic core quality control indicators including purity, moisture, ash, heavy metals and microorganisms, standardizing full-process production workflows and laboratory testing methodologies, and aligning China's

fundamental standards with mainstream international systems. Mannitol was simultaneously incorporated into GB 2760, clarifying its usage scope and addition limits across all food categories and fully opening compliant food applications of mannitol in China.

3. ***Standard Upgrading and Global Leadership (2010s – Present):***

Supported by domestic industrial technological progress and industrialization of high-end products, national standards underwent iterative optimization, establishing differentiated product indicators for three manufacturing processes (seaweed extraction, chemical synthesis, biological fermentation) and introducing special specifications for injectable pharmaceutical-grade, lyophilization-specialized and sterile-grade variants. Multiple stringent limit indicators exceed universal international benchmarks. Supporting testing method standards, clean production specifications and green manufacturing control guidelines were concurrently refined, forming a full-chain standard system covering product quality, end-to-end production workflows, safe application and environmental management. At present, China's mannitol standard system balances universal basic requirements and special specifications for high-end segmented products, serving as a vital reference for global polyol standard formulation.

Part V: Expansion of End Applications and Deepening Functional Research

(I) Basic Raw Material Application Phase (1930s – 1960s)

In the early industrialization stage, mannitol was positioned as a natural sweetener and general basic chemical raw material. Leveraging its sweetness, low hygroscopicity and mild taste, it partially replaced sucrose for ordinary confectionery, chewing gum, baked goods and other snack foods, with core functions of flavor optimization and anti-caking for finished products. Within chemical engineering, it was only utilized as a basic organic intermediate and universal auxiliary agent. Industry research into mannitol functionality remained superficial during this era, limited to utilization of surface physicochemical traits with narrow application scenarios; its physiological activity and core medicinal value had not yet been deeply explored.

(II) Rise of Pharmaceutical Functions and Expansion of Applications Phase (1970s – 2000)

Systematic pharmacological research and unification of global safety standards elevated mannitol's medicinal value to the core development pillar of the industry. For clinical medical use, its high-osmotic dehydration, diuretic and intracranial pressure-lowering effects were widely popularized, establishing it as a classic therapeutic raw material in neurology, emergency and urology departments. As a formulation excipient, its superior lyophilization moldability, chemical stability and anti-adhesive performance enabled

large-scale application in powder injections, oral tablets, granules, oral lozenges and all pharmaceutical product types.

Food applications expanded into sugar-free wellness tracks, with gradual adoption in low-sugar meal replacements and diabetic-specific dietary products. Cosmetic and agricultural sectors entered small-scale trial application stages, forming a stable application landscape of "pharmaceuticals as primary, food as supplementary, small-scale multi-sector exploration". The product evolved from a single flavoring agent into a dual-core raw material with medicinal and functional ingredient attributes.

(III) Refined, High-End and Diversified Application Phase (2010s – Present)

Global consumer upgrading and advances in biological and pharmaceutical engineering technology have ushered mannitol applications into a new era of precise segmentation, functional compounding and high-end value empowerment.

1. ***Pharmaceutical Sector:***

   Custom specialized grades including injection-use, lyophilization carrier, oral formulation and sustained-release drug carriers have been developed, covering all pharmaceutical tracks including chemical generic drugs, biological preparations, traditional Chinese medicine preparations and medical device excipients. It ranks among the world's highest-volume polyol pharmaceutical excipients.

2. ***Food and Special Medical Nutrition Sector:***

   Deep layout of special medical purpose formula foods, sports nutrition supplements, weight management diets and wellness snacks for seniors and children. Relying on its low glycemic index, anti-cavity and low-calorie core characteristics, it has become a core functional raw material in healthy dietary sectors.

3. ***Daily Chemical and Personal Care Sector:***

   Utilizing its moisturizing, skin-soothing, mild thickening and low-irritation properties, it is widely added to repair skincare products, toothpaste, medical mouthwash and washing & care formulations.

4. ***Emerging Sectors:***

   Continuous penetration into microbial fermentation culture media, plant growth regulators, environmental water treatment additives and new polymer composite materials and other cutting-edge tracks.

Parallel industry-wide compound functional research combines mannitol with other polyols, water-soluble dietary fibers and prebiotics to develop composite functional ingredient systems, fully amplifying synergistic benefits of multi-component formulations and continuously broadening the cross-industry application boundaries of mannitol.

Part VI: Future Outlook for the Industry

After more than 200 years of systematic scientific research and nearly a century of industrialization, mannitol has evolved from an isolated natural plant extract into a globally vital foundational functional raw material featuring diversified manufacturing processes, complete global standards and cross-sector applications spanning pharmaceuticals, food, chemical engineering, daily chemicals and agriculture. A complete industrial ecosystem has been established with three mutually complementary manufacturing processes: natural extraction, chemical synthesis and biological fermentation. Persistent research and development efforts from generations of global scientists, process engineers and full industrial chain practitioners have jointly laid the stable, diversified development landscape of today's mannitol industry.

Against the backdrop of expanding global wellness industries, widespread adoption of low-sugar and sugar-free wellness consumption concepts, steady growth of pharmaceutical formulation manufacturing and rigid global dual-carbon low-carbon development requirements, the mannitol industry will advance comprehensive high-quality upgrading in the coming years, presenting five core development trends:

First, comprehensive greenization of manufacturing processes. Low-carbon clean technologies including biological fermentation, mild low-temperature extraction and membrane separation purification, alongside comprehensive utilization of by-products, will accelerate large-scale popularization to gradually replace traditional high-energy, high-emission production workflows. The full industrial chain will advance toward energy conservation, pollutant reduction and circular resource utilization.

Second, high-end customization of product portfolios. Industry R&D focus will shift toward high-value segmented products including sterile injection-grade, ultra-high-purity reagent-grade, specialized lyophilization carriers and functional compound customized variants. Exclusive tailored specifications will be developed for innovative pharmaceuticals, special medical foods and high-end aesthetic skincare sectors to continuously elevate product technical barriers and comprehensive added value.

Third, continuous iteration of core technologies. Long-term research will target underlying core technologies including high-activity hydrogenation catalysts, high-tolerance high-yield microbial strains, precision controlled crystallization and ultra-high-purity molecular separation to further boost raw material conversion efficiency, product purity and long-term quality stability.

Fourth, continuous expansion of end application scenarios. In-depth exploration of mannitol's application potential in emerging tracks including innovative biomedicine, precision clinical nutrition, aesthetic skincare, green biomanufacturing and modern ecological agriculture will break through boundaries of mature traditional applications and unlock new industrial growth avenues.

Fifth, global industrial collaboration and standardized integration. Mutual recognition of polyol product standards across all nations will accelerate, cross-border trade regulatory frameworks will become more standardized and transparent, and division of labor across the global industrial chain will continuously refine, gradually forming a

new global polyol industry landscape featuring collaborative technology R&D, unified quality benchmarking and differentiated development across segmented tracks.

China currently holds a central pivotal position in the global mannitol industry, equipped with complete supporting large-scale production capacity, full-chain manufacturing processes, multi-level R&D systems and mature stable supply chain infrastructure. Moving forward, China’s domestic mannitol industry will fully leverage its three core advantages of production capacity, independent proprietary technology and local raw material resources to lead global green process innovation, iterative upgrading of international standards and development of emerging application scenarios. It will continuously unlock greater industrial value of mannitol in human clinical health, modern food manufacturing and innovative pharmaceutical production, supporting long-term stable growth of the global functional polyol track and wellness industry.