



Opinion

The new mission of the central science: Chemistry as the scientific foundation serving food and medicine homology

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1 Introduction

"What we eat becomes who we are". This ancient saying captures the essence of food and medicine homology (FMH), a foundational concept rooted in traditional Chinese medicine (TCM) and dietary therapy^[1]. The *Shennong Bencaojing* (ca. 200 BC) classified upper-grade substances (e.g., ginseng, astragalus, goji berry) as non-toxic and suitable for long-term consumption. This classification is widely regarded as an important early textual foundation for the later concept of FMH. China's 2023 catalog lists over 100 approved FMH substances, underscoring their dual identity: Meeting food safety standards while demonstrating pharmacological activity. This duality defines the core scientific challenge. From the ideal state described in the *Huangdi Neijing*, where "the people of ancient times all lived to over a hundred years and remained active without decline", to modern systematic research on the relationship between diet, nutrition, and health, humanity's pursuit of a healthy life has never ceased. FMH substances are those that fall within the realm of food while also possessing the pharmacological activities characteristic of TCM

ingredients. Their theoretical foundation lies in "holistic nutrition and gentle modulation"—that is, through the daily dietary intake of multiple bioactive molecules, these substances exert systemic, progressive regulation of metabolism, immunity, and gut microbiota. This aligns closely with modern concepts of "precision nutrition" and "metabolic regulation", bridging ancient wisdom with contemporary scientific understanding. Compared with traditional drugs or single chemical components, FMH substances exhibit distinctive characteristics: Their mode of action involves "multi-component, multi-target, network-based" synergistic modulation, rather than "single-target, high-intensity" intervention; they offer high safety and low toxicity, making them suitable for long-term daily dietary intake, whereas chemical drugs, despite their clear efficacy, often carry side effects and risks of drug resistance; their scope of application emphasizes "preventive treatment" and adjunctive management of chronic conditions, rather than definitive treatment of established diseases. However, their chemical complexity, the difficulty in precisely elucidating their mechanisms, and the challenges in quality control represent the very scientific challenges that chemistry, as

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the central science, is uniquely positioned to address. This question essentially seeks to answer how the set of molecules we ingest shapes the quality and length of our lives. Chemistry, as the science that studies matter at the atomic and molecular levels, provides the most direct toolkit for this inquiry.

Chemical knowledge has accompanied human civilization throughout its development, from the use of fire to modern pharmaceuticals. Since the 20th century, chemistry has established its position as "the central science", connecting physics with life sciences, medicine, and engineering^[2]. As Academician Zhang Xi stated, the soul of chemistry lies in creation and its charm in change.

What makes chemistry uniquely suited to advance FMH is its capacity to move this field from empirical tradition to molecular precision. The practice of FMH has long relied on accumulated experience—knowledge of which foods and herbs produce certain effects, passed down through generations. However, experience alone cannot answer the critical questions: Which specific molecules are responsible for the observed effects? How do these molecules interact with each other and with the human body? At what dosage and in what form do they exert optimal benefits? Chemistry addresses these questions directly by identifying the active molecular species, characterizing their interactions, quantifying their concentrations, and elucidating their mechanisms of action. This molecular-level understanding transforms the selection and combination of food and medicinal ingredients from an art guided by tradition into a science guided

by evidence, enabling personalized and predictable health outcomes.

From a philosophical perspective, chemistry's judgment on health can be distilled into the "5R Principle": The right molecule, in the right combination, at the right time, in the right site, and at the right concentration. This principle reveals the essence of health maintenance, which is the precise regulation of molecules in the body (Fig. 1). FMH achieves the systematic maintenance of life homeostasis by ingesting molecular modules for daily needs, representing the quantity dimension of nutrition, while simultaneously performing targeted molecular adjustments that regulate metabolism and repair, representing the quality dimension of therapeutic intervention. Through its analytical, synthetic, and predictive capabilities, chemistry provides the scientific foundation upon which the ancient practice of FMH can be understood, validated, and ultimately advanced.

2 Quantitative interpretation of the 5R Principle

The 5R Principle can be translated into a set of measurable questions. The right molecule refers to the parent compound, metabolite, or structurally defined fraction that contributes to an effect. The right combination concerns component identities, ratios, and interactions. The right time includes administration and the biological response window, whereas the right site refers to the relevant tissue, cell, or intestinal compartment. The right

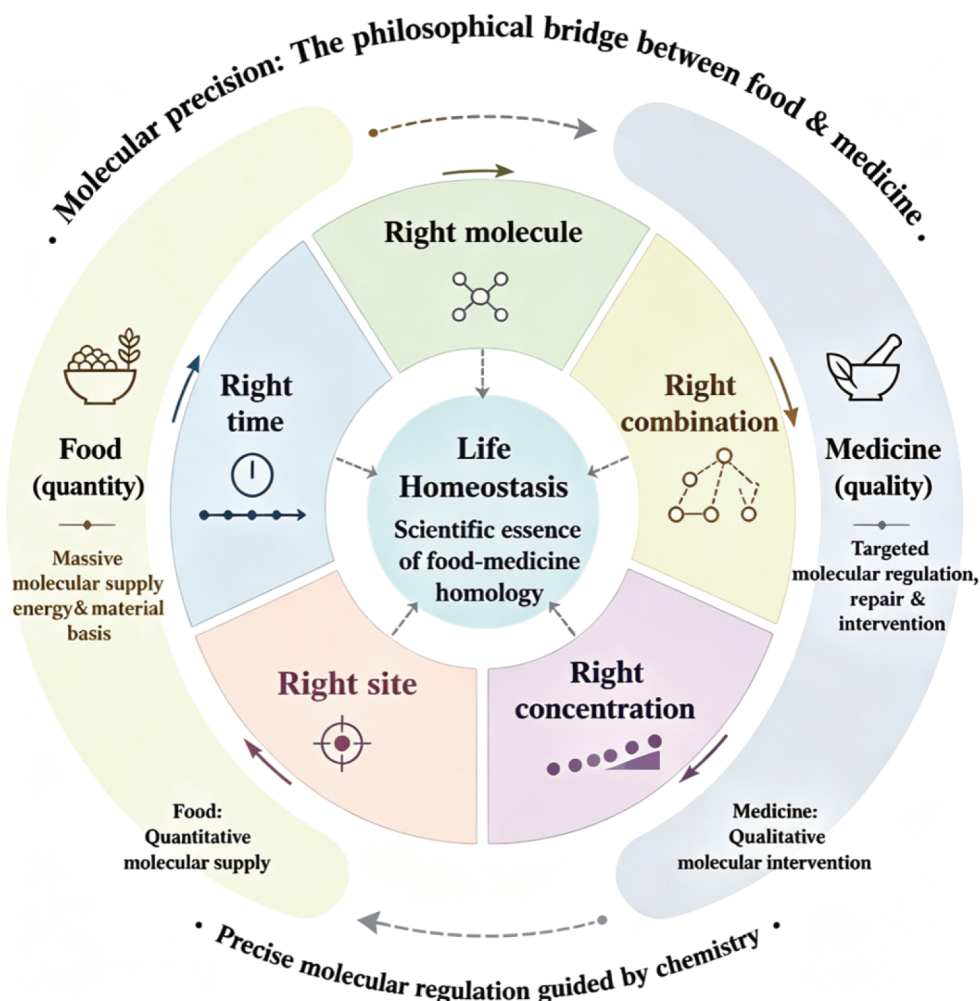


Figure 1 Schematic diagram of the 5R Principle for precise molecular regulation of FMH.

concentration is defined by the exposure range that supports the intended effect within an acceptable safety boundary. For small molecules, this range can be described by maximum plasma concentration, area under the concentration-time curve, time to maximum concentration, half-life, and tissue distribution. For macromolecules represented by polysaccharides, local intestinal exposure, fermentation products, and microbial responses may be more informative than plasma concentration alone.

Published pharmacokinetic studies illustrate why these boundaries must be defined for each substance and formulation. In a 12-participant crossover study, an onion supplement and isolated quercetin-4'-O-glucoside, each equivalent to 100 mg quercetin, produced peak plasma concentrations of 2.3 ± 1.5 and $2.1 \pm 1.6 \mu\text{g mL}^{-1}$ at approximately 0.7 h. A 200 mg quercetin-equivalent dose of rutin produced a lower peak of $0.3 \pm 0.3 \mu\text{g mL}^{-1}$ at 7.0 ± 2.9 h, with a terminal half-life of approximately 11 h.

Natural alkaloids provide a contrasting exposure profile. In healthy volunteers, single oral doses of 100 and 200 mg Sahastara extract produced piperine peak concentrations of 3.77 ± 1.63 and $6.59 \pm 2.86 \text{ ng mL}^{-1}$ at approximately 2 h. Piperine remained detectable for 48 h.

Macromolecular constituents require a different quantitative boundary. In an immunosuppressed mouse model, Astragalus polysaccharides were administered at 200 mg kg^{-1} for seven days, and intestinal butyrate and butyrate-producing bacteria were evaluated on day 8. For polysaccharides, this boundary may therefore be expressed through administered dose, intestinal exposure time, microbial transformation, and fermentation products rather than a universal plasma threshold.

Within TCM theory, these dimensions correspond to the material basis of a formula, compatibility among components, the timing of administration, the location of transformation or action, and the dose boundary. Chemistry does not replace these traditional concepts; it converts them into variables that can be compared across materials, preparations, and intended uses. Dietary therapy generally involves repeated, lower-intensity exposure and long-term safety, whereas medicinal use requires a defined indication, controlled dose and duration, and evidence of efficacy and benefit-risk balance.

3 The evolution of chemical disciplines

The story of chemistry begins with humanity's curiosity about the material world. Before the 1920s, chemistry was traditionally divided into four major branches: Inorganic, organic, analytical, and physical chemistry. This classification effectively organized knowledge accumulation during the discipline's formative stage, allowing researchers to focus on distinct aspects of chemical phenomena.

Chemistry, however, did not remain static. The emergence of quantum mechanics and electronic theory, along with advances in electronic technology and computer science, profoundly changed chemical research^[3]. New branches such as polymer chemistry, biochemistry, and nuclear chemistry emerged as scientists explored increasingly complex molecular systems. Cross-fertilization with materials science, nanotechnology, and life sciences gave rise to interdisciplinary fields like materials chemistry, chemical biology, and environmental chemistry. These new fields grew from the old, breaking down traditional barriers and forming an interconnected network of knowledge that spans multiple scientific domains.

The driving force behind this evolution is interdisciplinary

interaction. Chemistry is called "the central science" because it sits at the core of natural sciences. Upward, it uses physics to explain atomic structure and molecular behavior. Downward, it provides analytical tools for biology and medicine, enabling researchers to understand life at the molecular level. Laterally, it couples with materials science, energy research, and environmental science to address pressing global challenges^[4]. This unique position means chemistry serves as a translator, converting fundamental physical principles into practical tools that biologists, doctors, and engineers can use to solve real-world problems. The branches of chemistry now extend into fields intersecting with astronomy, earth science, and medicine, reflecting the discipline's remarkable openness and adaptability.

Looking toward the coming decade, chemistry is poised for transformative evolution driven by artificial intelligence, automation, and sustainable molecular design. Emerging technologies such as autonomous synthesis platforms, generative AI for molecular discovery, and the shift toward renewable feedstocks will fundamentally redefine the capabilities of chemical research. For the field of FMH, these developments translate into unprecedented opportunities for rational design, sustainable production, and precise quality control of functional food and pharmaceutical ingredients.

4 How chemistry serves food and pharmaceutical sciences

Under the holistic concept of food and medicine sharing the same origin, TCM theory, modern functional food intervention strategies, and Western pharmaceutical treatment paradigms do not exist in isolation but instead form a continuous spectrum of health interventions ranging from "health preservation and disease prevention" to "precision therapy". TCM theory emphasizes the "four natures and five flavors" and "meridian affinities", advocating the use of foods with specific properties to regulate the body's yin-yang balance, focusing on constitutional conditioning throughout the life cycle and preventive care before illness occurs. Modern functional food interventions employ advanced processing techniques to extract specific active components—such as polysaccharides and flavonoids—to target subclinical conditions, combining the safety of food with precise physiological modulation. In contrast, Western medical treatment focuses on clearly defined pathological mechanisms, utilizing highly purified compounds for potent therapeutic intervention, particularly during acute or severe phases of disease. The logic behind their synergistic integration lies in chemistry as an interdisciplinary explanatory tool that bridges the gap between traditional experience and modern science. Chemistry not only elucidates the molecular structures and structure-activity relationships of active compounds in herbal medicines and foods but also clarifies their metabolic pathways and molecular targets within the body, thereby bridging TCM traditional functional descriptors (such as 'nature, flavor, and meridian affinity') with measurable chemical and biological profiles. This unified chemical interpretation enables substances derived from food and medicine to seamlessly transition from dietary therapy to pharmacological treatment across different stages of health, supported by a consistent molecular mechanism model.

Each branch of chemistry engages with food and pharmaceutical sciences from different perspectives, collectively building the scientific foundation for modern food and drug research. Together, the five branches follow the natural research

and development pipeline: Understanding molecular behavior (physical chemistry and AI), creating functional molecules and materials (synthetic chemistry and biomanufacturing, polymer chemistry), measuring and validating outcomes (analytical chemistry), and scaling up for industrial application (chemical engineering). The following sections examine the specific contributions of each major branch.

Artificial intelligence is treated here as a cross-cutting methodological layer rather than a subdiscipline owned by physical chemistry. It is introduced in Section 4.1 because physical chemistry supplies the thermodynamic, kinetic, and structural constraints needed to make data-driven predictions chemically meaningful; the subsequent sections then trace how AI acts within synthesis and biomanufacturing, polymer chemistry, analytical chemistry, and chemical engineering. Read through the 5R Principle, these tools connect prediction with action: Molecular and protein design helps identify the right molecule; interaction modeling and formulation optimization address the right combination; spatiotemporal models inform the right time and site; and process and pharmacokinetic models help control the right concentration.

4.1 Physical chemistry and AI: Understanding molecular behavior

Physical chemistry studies thermodynamic and kinetic laws, focusing on molecular interactions and macroscopic properties of chemical systems. In food science, it provides a framework for understanding molecular changes during processing, storage, and consumption. For example, liquid-liquid phase separation can be used to design proteinaceous microdroplets with consistent structure and function, offering new routes for high-protein food systems^[5]. Researchers have also elucidated how novel physical processing technologies such as ultra-high pressure, pulsed electric fields, and cold plasma affect hydrogen bonding networks in water, starch, and proteins, leading to improved food textures and nutritional profiles.

The integration of computational chemistry and artificial intelligence is reshaping this field in fundamental ways. Numerical simulation provides a basis for digital modeling and optimization of food processing operations, while AI promotes data-driven predictive manufacturing. The newest generation of structure and design models extends this role beyond conventional docking. AlphaFold 3 can predict joint structures of complexes that include proteins, nucleic acids, small-molecule ligands, ions, and modified residues, providing testable structural hypotheses about which components may form the right combination and where they may engage at the right site. Rosetta design workflows, now augmented by diffusion models such as RFDiffusion, can generate protein scaffolds, binders, and active-site architectures, shifting computation from selecting among known candidates toward proposing the right molecule. These predictions do not by themselves establish affinity, efficacy, or safety and must be coupled to free-energy calculations, molecular dynamics, and experimental validation. At the food-chemical level, FlavorDiffusion uses a graph-based diffusion framework to reconstruct ingredient relationships and predict chemically informed food pairings, whereas SensoryGAN combines graph convolutional networks with genetic algorithms to design lower-toxicity flavor substitutes. Physical chemistry provides the governing rules of molecular behavior, and AI builds predictive and generative engines constrained by those rules. AI-driven

analysis further promotes the transformation toward data-driven predictive manufacturing. AI frameworks have been developed to predict food-chemical interactions, systematically evaluating physicochemical properties, bioactivity, flavor, and safety of food chemicals^[6,7]. Physical chemistry provides the fundamental physical rules that govern molecular behavior, while AI builds predictive engines on top of those rules to accelerate discovery and optimization.

For TCM, physical chemistry and AI facilitate a transition from empirical formula compatibility to mechanistic molecular interpretation. TCM formulas are complex molecular ensembles whose therapeutic efficacy depends on dissolution, complexation, self-assembly, transmembrane transport, metabolic transformation, and synergistic multi-target effects. Molecular docking and molecular dynamics simulations can predict binding modes and interaction strengths between natural products and protein targets. AI, based on natural product databases, omics data, and disease phenotypes, can predict active constituents, potential targets, biosynthetic pathways, and toxicity risks^[8]. In this way, TCM research is moving beyond compositional identification toward rational design based on molecular-level understanding.

In the context of FMH, physical chemistry and AI equally empower the study of complex homology systems. For example, AI models can predict interactions between FMH active components and human targets; physicochemical principles are used to understand the assembly, release, and delivery behaviors of molecules in complex systems such as medicated diets and fermented functional foods. These approaches move the mechanisms of FMH from a "black box" to a "white box", providing theoretical support for scientific formulation and precise application.

Physical chemistry and AI directly enable the 'Right Time' and 'Right Site' dimensions. By elucidating kinetic profiles of molecular release from complex food matrices, physical chemistry predicts when and where active molecules become bioavailable along the gastrointestinal tract. Molecular dynamics simulations reveal how FMH components competitively or synergistically bind to metabolic enzymes and transporters, enabling rational design of 'Right Combination' formulas where component ratios are optimized to maximize cooperative effects. AI models trained on temporal metabolomics data can predict optimal dosing time, aligning molecular intake with circadian metabolic rhythms.

Despite the transformative potential of AI in advancing molecular understanding and predictive design, several critical challenges remain to be addressed. AI-driven predictions in food and drug systems are often constrained by limited training data, insufficient model interpretability, and uncertainties in safety-critical applications, which may hinder the reliability and practical translation of computational outcomes. Developing explainable AI frameworks, integrating high-quality interdisciplinary datasets, and establishing robust experimental validation strategies will be essential to improve model reliability and promote responsible application. Moreover, the complex and dynamic nature of food matrices and herbal decoctions presents additional challenges for accurate modeling, as the enormous diversity and intricate interactions among molecular components often exceed the capabilities of current computational approaches. Looking ahead, integrated digital twins of food and drug systems will combine molecular dynamics, machine learning, and multiscale modeling, and uncertainty-aware experimental feedback. These platforms will enable virtual screening of functional food formulations and

herbal medicine combinations before physical experiments are conducted, followed by active-learning cycles that select the most informative validation experiments. The integration of explainable and physics-informed AI will move the field from retrospective data analysis toward prospective molecular design while retaining mechanistic interpretability and experimentally testable predictions. These platforms will enable virtual screening of functional food formulations and herbal medicine combinations before any physical experiment is conducted. The integration of explainable AI with physical chemistry will transform the field from retrospective data analysis to prospective molecular design, making rational engineering of food and medicine systems a routine practice.

4.2 Synthetic chemistry and biomanufacturing: Creating functional molecules

The core mission of synthetic chemistry is creation: New molecules, new structures, and new substances. In food science, this is reflected in the chemical synthesis of additives such as flavors, colors, and preservatives, as well as the precise creation of functional food components with targeted health benefits.

Chemically synthesized additives are a cornerstone of the modern food industry. Many naturally occurring flavor molecules, pigment molecules, and nutritional fortifiers face constraints such as limited natural extraction sources, high production costs, or poor sustainability. Chemical synthesis provides a reliable and economical route for the production of these essential compounds. Vanillin, one of the most widely used food flavors globally, has natural extraction yields from vanilla beans that fall far below market demand. Chemically synthesized vanillin, with its low cost and stable supply, supports the entire food industry^[9]. Similarly, the large-scale industrial production of citric acid, lactic acid, and ascorbic acid relies on mature chemical synthesis processes that have been optimized over decades.

Another major contribution of synthetic chemistry is structural modification and functional optimization. Through precise chemical modification of natural molecular scaffolds, their stability, solubility, or bioavailability can be significantly improved. For example, natural curcumin has poor water solubility and chemical stability, limiting its application in functional foods. However, chemical synthesis via glycosylation of its phenolic hydroxyl groups or preparation of nano-encapsulates can greatly enhance its bioavailability and therapeutic potential. Synthetic chemistry provides reliable synthetic routes and process development capabilities from milligram scale in the laboratory to ton scale in industry.

Synthetic chemistry and biomanufacturing also constitute a critical pillar for producing TCM active ingredients. Many natural products derived from medicinal plants exhibit well-defined pharmacological activities, yet their low natural abundance, structural complexity, and ecological constraints make stable supply difficult to achieve. Synthetic chemistry, through total synthesis and semi-synthesis, enables access to natural active molecules and their derivatives while also improving solubility, stability, selectivity, and pharmacokinetic properties. A more recent example is the *de novo* biosynthesis of *Pueraria* isoflavonoids in engineered yeast. Reconstruction of the daidzein pathway and introduction of specific glycosyltransferases enabled the production of puerarin and daidzin from glucose, providing controlled access to *Pueraria*-derived molecules relevant to FMH while reducing dependence on variable plant extraction^[10].

Engineered yeast has also been employed to produce noscapine, tropane alkaloids, and the vaccine adjuvant QS-21, illustrating that cell factories can overcome plant resource bottlenecks and enable sustainable manufacturing of scarce natural products.

In the context of FMH, synthetic chemistry and biomanufacturing provide a critical pathway for large-scale acquisition of functional components. Many FMH active substances are present in extremely low concentrations in natural plants, with high extraction costs. Through total synthesis, semi-synthesis, or microbial cell factory biosynthesis, these scarce components can be produced efficiently and at low cost, thereby overcoming natural resource limitations and promoting their large-scale application in functional foods and pharmaceuticals. The yield and productivity of engineered cell factories remain insufficient for many complex natural products, and the high cost of downstream processing often undermines the economic viability of biomanufacturing routes. Additionally, the regulatory landscape for synthetic biology-derived food ingredients and botanical drugs remains unclear in many regions, creating uncertainty for industrial adoption. Potential biosafety concerns associated with engineered microorganisms, including unintended genetic changes and environmental release, highlight the need for genetic safeguard systems, biological containment strategies, and stringent regulatory frameworks. AI strengthens synthetic chemistry and biomanufacturing at three linked levels. Retrosynthetic and reaction-prediction models propose viable routes to the right molecule; protein language and generative models redesign enzymes and metabolic pathways; and self-driving laboratories connect route planning with automated flow synthesis, online analysis, and iterative learning. For FMH ingredients, this closed loop can prioritize candidates by activity, safety, source sustainability, and manufacturability before committing scarce biological material to scale-up.

Synthetic chemistry and biomanufacturing are the primary enablers of the 'Right Molecule' dimension. Many FMH active components (e.g., rare ginsenosides, saffron crocins, cordycepin) exist in natural sources at extremely low concentrations, making dietary intake insufficient for therapeutic effects. Total synthesis, semi-synthesis, and engineered cell factories provide scalable routes to produce these 'right molecules' at concentrations matching their pharmacological potential. Structural modification generates derivatives with improved bioavailability or target selectivity while retaining the safety profile of food sources.

Over the next decade, the convergence of AI-driven retrosynthesis, automated flow chemistry, and multiplexed genome engineering will enable rapid prototyping of biosynthetic pathways for virtually any natural product of interest, allowing on-demand production of rare bioactive molecules.

4.3 Polymer chemistry: Creating macromolecular architectures and delivery systems

Starch, protein, dietary fiber, and other core components in food are essentially natural polymers. Polymer chemistry provides theoretical tools for understanding their conformational changes, chain dynamics, and assembly behavior, which directly influence food texture, digestibility, and nutritional value.

The work of Academician Wu Qi's team is particularly illustrative of how polymer chemistry can revolutionize food processing. They systematically applied macromolecular physics and polymer processing theories to food processing, focusing on the whole food processing of natural macromolecules such as

starch and plant proteins. Starting from the conformational transition of protein molecules from coiled to extended states, they elucidated the differences in relaxation times of macromolecular chains in dilute solutions, concentrated solutions, and solids. Based on this theoretical framework, they achieved multiple breakthroughs: A whole-bean tofu process that produces no wastewater, plant-based meat from soybean meal with appearance and taste comparable to beef, and "potato rice" made from fresh potatoes processed into a low-cost, long-storable staple food. These achievements represent philosophical innovations that physically alter starch macromolecules, remodeling polymer chains and turning coarse grains into staple foods.

Supramolecular self-assembly is another important direction in polymer chemistry with broad application prospects. Self-assembled systems can form ordered nanostructures through intermolecular non-covalent interactions such as hydrogen bonds, hydrophobic interactions, and π - π stacking. These systems can be used for targeted delivery of nutrients, sensory quality regulation, and construction of novel food matrices. Research in this area has been recognized by the Nobel Prize in Chemistry, and its deeper application in food science is highly anticipated.

For TCM, polymer chemistry provides a molecular framework to understand the structure–property–function relationships of macromolecular active substances, including polysaccharides, proteins, peptides, and tannins. These natural polymers are not merely inactive excipients but bioactive molecules capable of regulating immune responses, gut microbiota, barrier integrity, and inflammation. Their biological functions are closely associated with macromolecular features, including molecular weight, monosaccharide composition, glycosidic linkages, branching architecture, charge distribution, and higher-order conformation. Through molecular weight fractionation, structural characterization, conformational analysis, and rheological studies, polymer chemistry enables the rational interpretation and optimization of these complex natural polymers. Representative examples illustrating how polymer structural features regulate the biological and pharmaceutical functions of TCM-derived natural polymers are summarized in Table 1.

Lycium barbarum polysaccharides (LBP), a representative FMH polymer, provide an illustrative example of how polymer

chemistry advances TCM modernization. Our recent studies demonstrated that distinct LBP fractions with different molecular architectures exhibit diverse biological activities. A specific molecular weight fraction of LBP showed enhanced antitumor immunity by promoting tumor-associated macrophage repolarization, highlighting molecular weight as an important structural determinant of immunomodulatory activity. Furthermore, structural elucidation of an arabinogalactan-rich LBP revealed that specific arabinose-containing glycosidic architectures contributed to its TLR4-mediated dendritic cell activation and adjuvant activity for nanovaccine-based cancer immunotherapy. These findings demonstrate that the therapeutic potential of TCM polysaccharides can be rationally optimized through precise understanding of their polymer structures.

Beyond their roles as bioactive molecules, natural polymers also serve as functional materials for pharmaceutical engineering. The abundant hydroxyl groups, hydration properties, and network-forming capabilities of polysaccharides enable the construction of nanoparticles, hydrogels, microspheres, and colon-targeted delivery systems for TCM compounds. For example, an LBP-based hydrogel was developed as an oral colon-targeted drug delivery platform, in which LBP functioned simultaneously as the structural matrix and immunoregulatory component. The engineered hydrogel improved intestinal retention and controlled drug release while enhancing antitumor efficacy through macrophage lipid reprogramming. Therefore, polymer chemistry provides a powerful strategy to transform TCM polysaccharides from empirically used herbal components into programmable macromolecular systems with defined structures and functions.

In the context of FMH, starches, dietary fibers, fungal polysaccharides, and plant proteins are themselves the most important macromolecular homology substances. Polymer chemistry, by modulating the chain conformation, aggregation state, and self-assembly behavior of these macromolecules, can significantly improve the texture, digestibility, and bioactivity of FMH products. For example, molecular modification of polysaccharides can modulate chain conformation to enhance immunomodulatory activity; regulation of protein fibrillar aggregation enables the design of plant-based homology products with mouthfeel mimicking animal tissues.

Table 1 Structural features of TCM-derived natural polymers and their biological and pharmaceutical functions.

Polymer structural feature	Chemical basis	Functional consequence	Representative examples
Molecular weight	Determines chain length, hydrodynamic volume, solubility, and molecular mobility	Regulates immune activity, bioavailability, and biological potency	Astragalus polysaccharides: Fractionation of APS into different molecular-weight populations revealed that Mw significantly affected polysaccharide structure and immunomodulatory activity, with approximately 10 kDa APS showing stronger immune-enhancing activity
Monosaccharide composition and glycosidic linkage	Defines polymer backbone structure and conformational characteristics	Determines interaction with biological receptors and downstream signaling responses	Poria cocos polysaccharides: A purified polysaccharide (PCP-2) containing 1,3- β -D-Glc, 1,6- β -D-Glc and 1,6- α -D-Gal linkages exhibited immunomodulatory and gut barrier-protective effects, demonstrating the importance of linkage-defined structures
sBranching architecture and higher-order conformation	Controls three-dimensional organization and accessibility of functional domains	Influences receptor recognition, immune activation, and biological activity	Ganoderma lucidum polysaccharides: Structural features of fungal polysaccharides, including β -glucan architecture, contribute to their interaction with immune cells and immunomodulatory effects
Charge distribution and functional groups	Determines electrostatic interaction, hydration behavior, and biological interface compatibility	Enables mucoadhesion, permeability enhancement, and improved delivery performance	Chitosan-based delivery systems: Protonated amino groups promote mucosal adhesion and epithelial interaction, facilitating oral and mucosal delivery of bioactive compounds
Network-forming capability	Enables formation of hydrated polymer networks through ionic or physical crosslinking	Provides sustained release, protection of unstable compounds, and site-specific delivery	Pectin and alginate-based systems: Polysaccharide hydrogels and microspheres provide controlled release and colon-targeted delivery platforms for natural products

Polymer chemistry governs the 'Right Combination' and 'Right Concentration' dimensions by controlling how FMH molecules are assembled into deliverable matrices. Through modulation of macromolecular chain conformation and intermolecular interactions, polymer chemistry enables co-assembly of multiple FMH components into unified nanostructures, ensuring designed stoichiometry is maintained during processing, storage, and digestion. Controlled-release matrices (e.g., pH-responsive chitosan-based hydrogels for intestinal targeting) sustain therapeutic levels of active molecules at absorption sites, preventing burst release.

Nevertheless, the translation of polymer chemistry innovations from laboratory research to food and pharmaceutical applications faces substantial challenges. The lack of standardized characterization methods for food-grade macromolecules and the high batch-to-batch variability of natural polymers remain major obstacles to reproducible manufacturing and quality control. Furthermore, the long-term safety, biodegradation behavior, and potential immunological responses associated with engineered polymer materials and polymeric nanocarriers require systematic evaluation before broad application. Future efforts should focus on developing highly biocompatible, biodegradable, and structurally controllable polymer systems to minimize potential biological risks and facilitate their safe translation into food and biomedical applications. In polymer chemistry, emerging AI methods learn sequence-conformation-assembly-property relationships that are difficult to resolve by experiment or simulation alone. Polymer-specific string representations can improve data-efficient prediction of polymer properties. Combined with graph models, generative design, and active learning, this approach can support multi-objective optimization of digestibility, texture, mechanical behavior, degradation, and cargo-release profiles. Coupled with coarse-grained simulation and experimental rheology, these tools create a route to inverse design of food macromolecules and delivery matrices that place the right molecular cargo at the right site and release it at the right time and concentration.

In the coming decade, precision polymer synthesis and characterization will enable *de novo* design of food macromolecules with programmable structures and functionalities, such as starch-like polymers with tailored digestibility profiles or protein assemblies that mimic animal tissues.

4.4 Analytical chemistry: Measuring and validating molecular outcomes

The fundamental mission of analytical chemistry is to "visualise molecules", which intrinsically corresponds to the five dimensions of the 5R principle for assessing molecular homeostasis in complex food and herbal matrices: Distinguishing the presence of the right molecule, disentangling synergistic right combination of multi-component systems, tracing dynamic molecular evolution across the right time window, mapping spatial distribution to identify the right site of biological action, and calibrating safe and efficacious right concentration thresholds. Modern high-throughput green analytical workflows integrating chromatography, spectroscopy and microfluidics enable efficient simultaneous quantification of all 5R metrics while minimising resource consumption and environmental footprint.

Deep integration of AI and advanced spectroscopic techniques substantially improves the precision of 5R validation. Novel spectroscopic techniques have been developed that significantly

increase detection sensitivity for contaminants in food products. Mass spectrometry imaging achieves precise spatial distribution visualization of food components and contaminants with high spatial resolution. Machine learning models have been applied to adulterant identification, enabling rapid and reliable food authenticity testing with high accuracy. Collectively, this analytical toolkit establishes full-chain molecular visibility, enabling early identification and control of undesirable molecular species, rational optimization of component combinations and processing parameters, and precise regulation of molecular concentrations within safe ranges during consumption. These capabilities collectively advance health-oriented applications by providing analytical support for the 5R Principle.

For TCM, analytical chemistry transforms empirical knowledge embedded in complex systems into identifiable, quantifiable, and traceable molecular evidence. Chinese medicinal materials, decoction pieces, extracts, and compound formulations often contain hundreds to thousands of chemical constituents, and their chemical profiles are altered by factors such as geographical origin, harvest time, processing methods, and preparation techniques. Modern TCM research relies on techniques including UHPLC-HRMS, GC-MS, NMR, mass spectrometry imaging, metabolomics, chemical proteomics, and multidimensional fingerprinting to achieve the transition from compositional elucidation to the discovery of quality markers. Analytical chemistry not only authenticates materials, controls impurities, and establishes quality standards, but also enables tracking of absorption, distribution, metabolism, and excretion of TCM components *in vivo*. This elucidates the links between blood-absorbed components, parent compounds, metabolites, and their targets. Target discovery technologies such as chemical proteomics, thermal stability analysis, affinity-based probes, and activity-based probes have advanced TCM research from observing pharmacological effects to confirming targets and explaining mechanisms. Astragali Radix provides a more recent food-and-medicine homology case. A pharmacokinetic study compared the *in vivo* conversion and systemic exposure of the principal astragalosides after oral administration and proposed astragalosides I, II, III, and IV as multi-component quality markers on the basis of their abundance, metabolic conversion, and exposure characteristics. An exploratory study enrolled 20 healthy adults and administered Astragali Radix for 14 consecutive days. It integrated serum, urine, and fecal metabolomics and lipidomics with gut microbiome and immune indicator measurements. The observed associations generate hypotheses about immunomodulation, but they do not establish clinical immunological efficacy or causal mechanisms. In this analytical workflow, chemical fingerprints define the material under study, serum pharmacochimistry and pharmacokinetics identify absorbed constituents and their time course, and metabolomic, lipidomic, and microbiome data characterize downstream responses. Meaningful integration requires matched materials, doses, biological samples, and collection times.

In the context of FMH, analytical chemistry establishes full-chain molecular evidence for homology products. The complexity of FMH products far exceeds that of single foods or herbs. By constructing high-resolution chemical fingerprints, analytical chemistry enables authentication, geographical traceability, batch-to-batch consistency evaluation, and quality monitoring during processing. Meanwhile, through *in vivo* metabolomic analysis, the absorption, distribution, metabolism, and excretion trajectories of homology active components can be traced, revealing their multi-

component, multi-target mechanisms of action. These capabilities are fundamental to advancing the modernization, standardization, and internationalization of FMH products.

Analytical chemistry is the guardian of all five Rs. 'Right Molecule' is validated through HRMS-based identification and quantification; 'Right Combination' is confirmed through multi-analyte fingerprinting; 'Right Concentration' is ensured by validated quantitative methods; 'Right Time' and 'Right Site' are tracked through pharmacokinetic studies and mass spectrometry imaging. Without analytical chemistry, the 5R principle remains conceptual rather than implementable.

However, analytical chemistry faces persistent challenges in food and pharmaceutical applications. Complex food matrices and herbal preparations cause severe matrix effects that compromise detection accuracy, and the vast chemical diversity of TCM formulas makes comprehensive characterization practically impossible with current technologies. The lack of reference standards for most natural products further limits quantitative analysis, and the high cost and complexity of advanced instrumentation restrict their accessibility for routine quality control in developing regions. In the next decade, the convergence of nanotechnology, microfluidics, and portable mass spectrometry will bring laboratory-grade analytical capabilities to the point of use, enabling real-time quality control across the food supply chain. Multifunctional molecular probes will allow simultaneous detection of multiple analytes with high sensitivity. Emerging multimodal and self-supervised AI models can align spectra, chromatograms, images, omics profiles, and process metadata, transferring knowledge from large unlabeled datasets to tasks with few reference samples. With uncertainty estimation and explainable feature attribution, these models can distinguish a confident molecular assignment from a hypothesis requiring confirmation. AI-powered data fusion will thus generate comprehensive molecular portraits of food and drug systems, shifting analytical chemistry from reactive quality control toward predictive risk assessment and personalized nutrition guidance.

4.5 Chemical engineering: Scaling up from laboratory to industry

Where analytical chemistry addresses whether existing substances satisfy the 5R criteria, chemical engineering resolves how to economically, sustainably and scalably manufacture molecular products that consistently adhere to the 5R principle. Its core mandate is to upscale laboratory-scale 5R-optimised synthetic routes into industrially viable workflows, encompassing reaction engineering, separation intensification, synthetic biological biomanufacturing and AI-enabled intelligent process control. Every process optimisation strategy is designed to lock in the five dimensions of the 5R standard throughout production.

Artificial synthesis of starch is a landmark achievement in this field. In 2021, a team at the Tianjin Institute of Industrial Biotechnology achieved complete synthesis of starch molecules from carbon dioxide in the laboratory, designing an 11-step non-natural carbon fixation and starch synthesis pathway. The synthesis rate and energy conversion efficiency both far exceed those of natural photosynthesis, and the natural synthesis cycle of months was shortened to days. This breakthrough signifies that workshop manufacturing of starch independent of land and fresh water is now possible. One cubic meter of bioreactor produces starch equivalent to five acres of maize harvest. The process achieves deep coupling of chemical catalysis, which reduces CO₂ to methanol, with biocatalysis, which converts methanol into

triose sugars that are further polymerized into starch. A similar technical route for photoelectrochemical-coupled microbial synthesis of optically pure lactic acid from CO₂ has achieved energy conversion efficiency substantially higher than natural photosynthesis.

The integration of synthetic biology and biomanufacturing has greatly expanded the boundaries of chemical engineering. Traditional chemical engineering primarily deals with non-biological systems, whereas modern biomanufacturing incorporates engineered microorganisms and enzyme catalysis into the framework of process engineering. Using precise gene editing, AI-assisted enzyme engineering, and intelligent fermentation, researchers can efficiently synthesize complex functional products such as terpenoids, flavonoids, artificial proteins, and human milk oligosaccharides from simple carbon sources in microbial cell factories. Chemical engineering plays the roles of scale-bridger and system integrator, extending molecular-level design to the reactor level and optimizing trade-offs between economy and sustainability.

For TCM, chemical engineering determines whether research findings can translate into stable, controllable, and scalable pharmaceutical products. The core challenges facing industrialization include high variability in raw materials, low extraction efficiency, difficulties in impurity control, insufficient batch-to-batch consistency, and the difficulty of standardizing complex formulation processes. Chemical engineering can systematically optimize production through extraction and separation engineering, membrane separation, continuous flow preparation, process analytical technology, smart manufacturing, and quality by design. In extraction processes, engineering studies can enhance performance by optimizing solvent systems, mass transfer efficiency, temperature, pressure, and extraction time. In formulation stages, techniques such as spray drying, microencapsulation, nano-delivery, solid dispersions, and controlled-release technologies can improve stability and bioavailability. The integration of synthetic biology provides new industrialization pathways for scarce TCM ingredients from artemisinic acid to complex alkaloids and saponins.

In the context of FMH, chemical engineering is crucial for translating homology products from laboratory to market. The large-scale production of FMH functional components faces engineering challenges such as unstable bioactivity, low extraction yields, and high batch-to-batch variability. Chemical engineering addresses these through optimization of fermentation processes, separation and purification workflows, formulation technologies, and continuous production schemes, enabling efficient, stable, and standardized manufacturing of homology active ingredients. These engineering solutions are typical examples of chemical engineering empowering the industrialization of FMH.

Chemical engineering transforms laboratory-validated 'Right Molecule' into industrially viable products while preserving all 5R Principle. Process intensification maintains 'Right Concentration' across scales; PAT guarantees 'Right Combination' consistency batch-to-batch; formulation engineering protects 'Right Time' release profiles during storage; smart packaging prevents premature degradation. Chemical engineering is the scale-bridging discipline that prevents 5R collapse during industrial translation.

Despite these advances, the gap between laboratory breakthroughs and industrial implementation remains wide. The scale-up of biomanufacturing processes often suffers from unpredictable losses in yield and productivity, and the economic feasibility of many novel production routes has yet to be

demonstrated at commercial scale. Regulatory approval for food and drug products derived from novel biomanufacturing processes is slow and costly, and the integration of new production platforms with existing manufacturing infrastructure presents significant technical and financial challenges. In the coming decade, AI-autonomous continuous manufacturing lines will establish closed-loop dynamic 5R regulation for functional food and herbal medicine production. Multi-objective AI optimisation dynamically tunes feedstock ratios, reactor residence durations, internal flow field distributions, and substrate feeding rates. Real-time PAT feedback corrects process parameters autonomously upon detecting deviations from 5R metrics, drastically reducing inter-batch variability. Powered by AI-driven sustainable manufacturing, these platforms deliver long-term, consistent production of health-oriented molecular products fully compliant with the 5R precision regulation principle.

5 Conclusion

From the discussion of five branches, it is clear that chemistry, as the central science, is systematically serving the scientific advancement of FMH. Physical chemistry provides the theoretical foundation for molecular interactions. AI endows it with predictive and design capabilities. Synthetic chemistry and biomanufacturing create new functional components. Polymer chemistry opens new paradigms in texture regulation, processing optimization, and drug delivery. Analytical chemistry ensures full-chain control of safety and quality. Chemical engineering translates scientific breakthroughs into large-scale production practice. Each branch works in synergy with the others, and this intrinsic collaboration is chemistry's unique advantage in addressing the complex challenges of FMH.

The five branches of chemistry establish an iterative and interconnected framework for realizing the 5R Principle. Analytical chemistry and AI enable the discovery and identification of the right molecules, while physical chemistry and AI provide mechanistic insights into their optimal sites, combinations, and temporal behaviors. Synthetic chemistry facilitates the creation and scalable production of functional molecules, whereas polymer chemistry enables the rational assembly of molecular components into optimized formulations with appropriate concentrations and delivery properties. Chemical engineering further ensures the industrial translation of these principles by maintaining molecular precision throughout large-scale manufacturing. Continuous analytical feedback reinforces this closed-loop process, enabling adaptive optimization across different stages. Looking ahead, the integration of these chemical disciplines with digital twin platforms will facilitate virtual screening and rational design of FMH formulations. Ultimately, the convergence of AI-guided molecular design, synthetic biology-based production, and intelligent manufacturing may enable autonomous development of personalized food and health products. In this emerging paradigm, chemistry serves as the molecular language that connects molecular understanding with precision health regulation.

Within the expansive domain of "medicine and food homology", chemistry is undergoing a profound paradigm shift from a supportive service role to a proactive leadership position. Historically, chemistry functioned primarily as an auxiliary tool, providing compositional analysis and quality assessment for traditional empirical knowledge. Today, however, it is spearheading the modernization of this ancient wisdom with unprecedented momentum. By precisely elucidating the molecular

structures of phytochemicals, chemists have not only unveiled the multi-target synergistic mechanisms of active constituents—such as polyphenols and flavonoids—found in homology substances, but have also innovatively proposed molecular assembly and intelligent delivery strategies. These advancements effectively address the longstanding challenges of poor stability and low bioavailability associated with natural products. Such comprehensive breakthroughs, spanning from fundamental mechanisms to applied technologies, have transformed chemistry from a mere instrument for validating tradition into the core engine driving the industry toward precision nutrition, personalized health management, and high value-added functional foods, thereby truly realizing a remarkable transition from supportive service to innovative leadership. Looking ahead, chemistry's role in this field will evolve from service to leadership. With continuous breakthroughs in synthetic biology, AI-assisted design, supramolecular assembly, and green catalysis, we will more precisely understand the interaction network among the tens of thousands of chemical molecules in food and their effects on human health. Chemistry's "5R" judgment, which concerns selecting the right molecules in the right combination at the right concentration, time, and site, is moving from concept to practice. This is the ultimate goal of the scientific pursuit of FMH. The history of chemistry is essentially a continuous approach toward this goal, and as the central science, chemistry's new mission lies herein.

Data availability

All data needed to support the conclusions in the paper are presented in the manuscript. Additional data related to this paper may be requested from the corresponding author upon request.

Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

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None.

References

- [1] Hou, Y., Jiang, J. G. Protective effects of natural products against oxidative stress and inflammation. *Food & Function*, **2013**, 4: 1727–1741. <https://doi.org/10.1039/c3fo60398a>
- [2] Brown, T. E., LeMay, H. E., Bursten, B. E. *Chemistry: The Central Science*, 10th ed. Upper Saddle River, NJ: Prentice Hall, 2006.
- [3] Prabhu, G. R. D., Urban, P. L. The dawn of the chemistry of the central science: A review. *Chemical Reviews*, **2020**, 120: 7587–7611. <https://doi.org/10.1021/acs.chemrev.0c00312>
- [4] Mehta, G., Yam, V. W. W., Krief, A., et al. Chemistry as the central science: A new mission for the chemical sciences. *Angewandte Chemie International Edition*, **2018**, 57: 14690–14698. <https://doi.org/10.1002/anie.201808765>
- [5] Doshi, N., Reddy, S. K. K., Pouvreau, L., et al. Structural and functional characterization of polysaccharides from onion and their effects on gut microbiota. *Food Research International*, **2026**, 223: 117710. <https://doi.org/10.1016/j.foodres.2026.117710>
- [6] Seo, J., Kim, D., Jeong, J., et al. *Proceedings of the ACL 2025*. Albuquerque, NM, 2025: 70–77.
- [7] Yang, J. Q., Zhang, J. Z., Xu, J. W., et al. Polysaccharides from Goji berry and their immunomodulatory effects. *Food Research International*, **2025**, 218: 116785. <https://doi.org/10.1016/j.foodres.2025.116785>
- [8] Mullowney, M. W., Duncan, K. R., Elsayed, S. S. Natural products as a source of new drugs: Challenges and opportunities. *Nature Reviews Drug Discovery*, **2023**, 22: 895–916. <https://doi.org/10.1038/s41573-023-00767-4>
- [9] Xu, L., Liaqat, F., Sun, J., et al. Microalgae polysaccharides: Bioactivities and industrial applications. *Renewable and Sustainable Energy Reviews*, **2024**, 189: 113905. <https://doi.org/10.1016/j.rser.2024.113905>
- [10] Ro, D. K., Paradise, E. M., Ouellet, M. Production of the antimalarial drug precursor artemisinic acid in engineered yeast. *Nature*, **2006**, 440: 940–943. <https://doi.org/10.1038/nature04640>

