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Review Article

Innovative biosensing technologies for food-medicine homology polysaccharides: Toward precision structural analysis and targeted functional evaluation

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Abstract: The concept of food and medicine homology (FMH), which emphasizes the dual role of natural compounds in both medicinal and nutritional contexts, has seen significant development and presents promising application prospects in various fields. Polysaccharides, as the representative bioactive macromolecules in FMH resources, have demonstrated a wide range of biological activities *in vitro* and *in vivo*, encompassing antioxidant, anti-tumor, anti-aging, immunomodulatory, and metabolic regulatory effects. However, their inherent structural complexity and functional heterogeneity pose significant challenges to their rapid and accurate detection. Traditional analytical methods often lack the requisite sensitivity, specificity, or real-time capability essential for the integrated analysis of functional components. Emerging biosensing technologies, renowned for their high sensitivity and specificity, are revolutionizing the detection of FMH plant polysaccharides (FMHPPs) by correlating structural characteristics with their functional properties. This review comprehensively summarizes recent advances in the extraction, structural characterization, and bioactivities of FMHPPs, with a particular focus on the application and future perspectives of novel biosensing technologies for their detection and functional assessment, aiming to foster their development in functional foods, pharmaceuticals, and related industries.

Keywords: food and medicine homology; polysaccharides; biosensing technologies; structural and bioactivity analysis; detection

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1 Introduction

The concept of food and medicine homology (FMH), denoting the same origin of medicinal and food materials, is a cornerstone of traditional Chinese medicine, with records tracing back to *Huangdi Neijing* (the *Yellow Emperor's Internal Classic*)[1,2]. This philosophy, emphasizing that "fasting food is food, while the patient's food is medicine", reflects the deep-rooted integration of diet and therapy[3]. As of August 2024, the National Health Commission and the National Market Supervision Administration have jointly released four batches of lists, comprising a total of 106 substances that are both food and traditional Chinese medicines. Representative FMH species, such as *Lycium barbarum* (Goji)[4], *Dioscorea polystachya* Turcz. (Chinese Yam)[5], and *Coix lacryma-jobi* L. (Job's tears)[6] have been extensively utilized for their health-promoting properties. In the broader context of plant science, polysaccharides are recognized as essential bioactive macromolecules with sophisticated physiological functions[7,8]. Recent studies have further underscored their critical roles in immunomodulation, gut microbiota homeostasis, and chronic disease management[9-12]. FMH materials are particularly rich in these components[13]. In this review, FMH plant polysaccharides (FMHPPs) are defined as complex polyhydroxy glycans derived from officially recognized FMH species, which can be further categorized into neutral, acidic, and complex polysaccharides based on their structural motifs[14,15]. Owing to their unique structures, low toxicity and minimal side effects, FMHPPs exhibit multiple biological activities both *in vitro* and *in vivo*, including antioxidant[16], anti-tumor[17], anti-aging[18], anti-inflammatory[19], anti-diabetic[20], hypoglycemic and hypolipidemic[21], immunomodulatory[22], and intestinal flora

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regulatory effects[23]. Therefore, they hold significant value in clinical nutrition and pharmaceuticals. However, despite the historical description of FMH, a critical gap remains in validating their modern scientific evidence, as the transition to precise therapy is hindered by their structural complexity[24-26].

Traditional detection technologies, such as ultraviolet-visible (UV-Vis) spectroscopy and high performance liquid chromatography (HPLC), frequently fall short in terms of the resolution for addressing inherent dynamic structural heterogeneity and real-time monitoring requirements[27,28]. To bridge the gap between traditional FMH theory and precision medicine, there is an urgent need for advanced analytical platforms that can resolve structural heterogeneity in real-time. Recent studies have highlighted advancements in polysaccharide detection, including direct and indirect methods, mass spectrometry, and new techniques like the anthrone-sulfuric acid assay with correction factors[29,30]. Currently, progress in analytical technologies—including cutting-edge biosensing, cell imaging, electronic chips, and innovative three-dimensional (3D) printing techniques such as xolography—is transforming the detection of FMHPPs by correlating structural characteristics with functional outcomes[31-34]. Transcending traditional quantification, these platforms enable multidimensional assessments that integrate molecular diagnostics with regenerative medicine, such as monitoring antiplatelet metabolic phenotypes and evaluating tissue-engineered scaffolds[35-38]. Technologies encompassing planar optical waveguide and highly sensitive chemical sensors enable highly sensitive detection while facilitating real-time monitoring and multi-parameter analysis—capabilities crucial for applications in fields such as environmental monitoring[39], medical diagnostics[40-42], and safety surveillance[43]. This article critically examines various biosensor designs (including optical, electrochemical, and piezoelectric sensors) applied to FMHPPs. Biosensors are highlighted for their applications in real-time environmental monitoring for biochemical oxygen demand (BOD) measurement, as well as structural characterization and bioactivity profiling in disease diagnosis and medicinal diagnostics[44-46]. In particular, we explore the application of biosensors in elucidating the interactions between polysaccharides and biological targets, which is crucial for understanding their functional mechanisms.

The complex structures and diverse bioactivities of FMHPPs present significant scientific challenges. While existing reviews often focus on either extraction methods or general pharmacological listings, they lack a critical integration of structural characterization with emerging biosensing feedback loops. This study fills this knowledge gap by explicitly addressing the hypothesis that advanced biosensing platforms can decode the structure-function relationship of FMHPPs more accurately than traditional assays. In this review, we collect relevant literature published since 2020. First, we provide a concise overview of the preparation methods and fundamental bioactivities of FMHPPs. Then, we focus on the pivotal role of emerging biosensing technologies, including a critical evaluation of their experimental performance. Finally, we discuss the current challenges and future prospects, particularly the integration of Artificial Intelligence (AI) to handle multidimensional sensing data[47]. The overarching workflow is visualized in Fig. 1, which serves as a roadmap for leveraging advanced biosensing technologies to unlock the functional potential of FMHPPs.

2 Structure and bioactivities of FMHPPs

2.1 Extraction and purification of FMHPPs

The extraction and purification of FMHPPs are the fundamental processes that significantly impact their structural characteristics and, consequently, their biological activities. The choice of extraction method is critical as it can determine the yield, purity, and integrity of the polysaccharides obtained[48,49].

2.1.1 *Extraction methods*

Currently, numerous extraction methods have been utilized to extract polysaccharides from traditional Chinese medicines. Traditional extraction techniques, such as hot-water extraction (HWE), acid extraction, and alkali extraction, are commonly used due to their simplicity. For instance, HWE involves soaking the plant material in hot water to dissolve the polysaccharides[50]. Acid extraction uses acidic solutions to break down the cell walls and release the polysaccharides, while alkali extraction employs alkaline solutions for the same purpose. However, these traditional methods are usually associated with the drawbacks of low yields. Besides, the harsh conditions of acid and alkali extraction also cause the cleavage of glycosidic bonds and the degradation of polysaccharides, altering their structures and reducing their bioactivities[51,52].

To overcome these limitations, modern extraction methods have been developed[53-55]. Microwave-assisted extraction (MAE) utilizes microwave energy to heat the sample rapidly, increasing the polysaccharide release rate from the plant cells[56]. This method can significantly reduce the extraction time and improve the yield. Ultrasound-assisted extraction (UAE), on the other hand, uses ultrasonic waves to create cavitation bubbles in the extraction medium[57,58]. These bubbles subsequently collapse, generating high-pressure shockwaves that break down the cell walls and enhance the extraction efficiency. Furthermore, enzyme-assisted extraction (EAE) involves the use of specific enzymes[59], such as cellulases, pectinases[60], or proteases, to more effectively degrade the cell wall components and release the polysaccharides.

In recent years, composite extraction methods have gained increasing attention[61]. Among these, ultrasonic-assisted enzymatic extraction has been successfully applied to polysaccharides from *Dendrobium Officinale*[62] and *Gastrodia elata*[63], achieving higher extraction yields compared to single methods. This technique leverages ultrasonic pretreatment to disrupt cell wall structures, thereby facilitating enzyme access to intracellular polysaccharides and improving extraction performance. A comprehensive comparison of these technologies and their critical operational parameters is summarized in Table 1.

2.1.2 *Purification methods*

After extraction, the crude polysaccharide extracts often contain impurities including proteins, pigments, and small molecules[64]. Therefore, purification is an essential process to obtain homogeneous polysaccharide fractions for accurate structural and functional characterization. Typically, the purification of polysaccharides relies on strategies exploiting differences in (1) molecular size (e.g., membrane separation), (2) solubility (e.g., precipitation), and (3) specific intermolecular interactions (e.g., column chromatography), which are often used in combination to achieve a high purity.

Dialysis is a membrane separation technique that removes small molecules and salts using a semi-permeable membrane

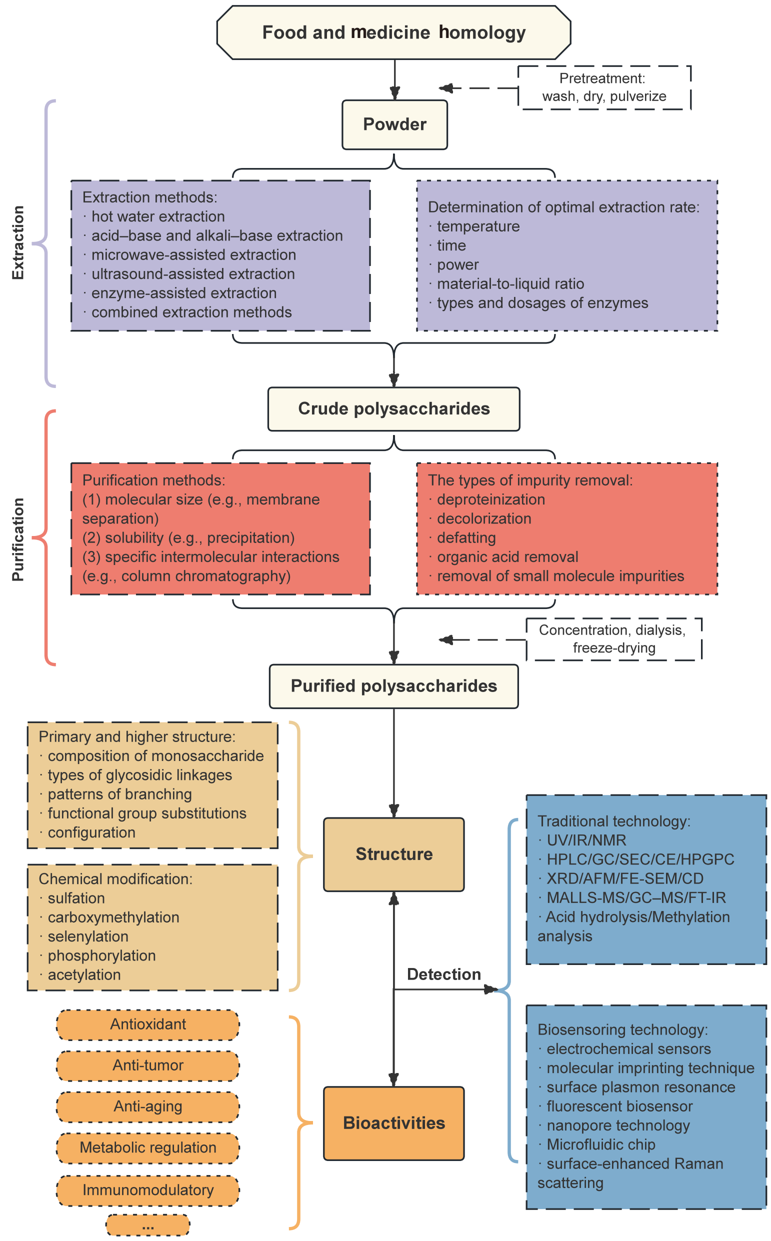

Figure 1 Schematic workflow illustrating the analysis of FMHPPs from preparation to functional application.

Table 1 Comparison of traditional and modern extraction methods for FMHPPs

Extraction Method	Mechanism	Key Parameters	Advantages	Disadvantages	Ref.
Hot-water (HWE)	Thermal diffusion and solvent penetration	Temp: 80–100 °C; Time: 2–6 h; Solid-liquid ratio: 1:10-1:30	Simple, low cost, equipment-accessible	Low yield, long time, high energy	[19, 50]
Microwave-assisted (MAE)	Dipole rotation and ionic conduction causing rapid heating	Power: 400–800 W; Time: 5–20 min; Temp: 50–90 °C	Rapid heating, high extraction efficiency	Risk of polysaccharide chain cleavage	[56, 107]
Ultrasound-assisted (UAE)	Acoustic cavitation and mechanical shear effects	Freq: 20–60 kHz; Time: 20–40 min; Power: 100–500 W	Low temp, high yield, simple operation	High noise, potential free radical generation	[57, 58]
Enzyme-assisted (EAE)	Targeted degradation of cell wall components	Enzyme: Cellulase、pectinase; pH: 4.5–6.0; Temp: 40–55 °C	Mild conditions, high specificity, eco-friendly	High enzyme cost, strict pH/Temp control	[59, 60]
Composite Methods	Synergistic integration (e.g., Ultrasound-enzyme extraction)	Combined parameters of individual methods	Superior yields, shorter time, structural preservation	Complex process optimization	[62, 63]

based on different molecular sizes, serving as an effective desalting and preliminary purification step[65]. Ethanol precipitation, a widely adopted method, leverages the insolubility of polysaccharides in high-concentration ethanol[66]. Adding ethanol induces polysaccharide precipitation, allowing for their concentration and separation from soluble impurities *via* centrifugation. Among column chromatographic techniques, affinity chromatography is particularly powerful for its high specificity. It purifies polysaccharides based on selective biological interactions, such as binding to an immobilized lectin or antibody. The target polysaccharide is specifically captured and then eluted under controlled conditions, yielding a highly pure product. Other chromatographic methods like size-exclusion and ion-exchange chromatography are also frequently employed for fractionation[67,68].

These purification methods are usually used in combination to yield high-purity polysaccharide fractions[69,70]. For example, the crude extract may first be dialyzed to remove small molecules, followed by ethanol precipitation to concentrate the polysaccharides. Thereafter, affinity chromatography or other chromatographic techniques can be further applied to obtain high-purity polysaccharides for detailed studies.

The extracted and purified FMHPPs provide well-defined samples for subsequent structural and functional analysis. Their physicochemical properties, such as molecular weight and monosaccharide composition, directly influence the design and interpretation of biosensing assays.

2.2 Structure characteristics of FMHPPs

2.2.1 *Hierarchical structural organization*

FMHPPs possess a complex and hierarchical structural makeup. At the most fundamental level, their primary structures are determined by several key elements: the composition of monosaccharides, the types of glycosidic linkages (such as β-(1→3) or α-(1→4)), the patterns of branching, and the presence of functional group substitutions[2]. For instance, the *Eucommia ulmoides* leaf polysaccharides (EUP) have been shown to consist of a specific monosaccharide ratio, namely glucose, fructose, mannose, fucose, galactose, and arabinose in a molar ratio of 36.6:16.6:14.2:15.7:9.5:7.4[71]. This specific monosaccharide composition endows EUP with unique properties. In addition, the *Astragali Radix* polysaccharides with high molecular weights (APS-I, ~2.0×10^6 Da) often exhibit an enhanced anti-inflammatory activity[72], indicating that molecular weight within the primary structure can be a crucial factor for determining bioactivity. Besides, glycosidic linkages play a particularly important role, as they directly affect the solubility of the polysaccharide in various solvents and its ability to bind to specific receptors, which in turn impacts its biological functions.

Moving beyond the primary structure, FMHPPs also adopt higher-order structures, including random coil conformations (where the polysaccharide chains are in a relatively disordered arrangement), helical conformations (which can provide stability and specific binding sites), and supramolecular aggregates or network formations[73]. These higher-order structures are vital for the solubility of polysaccharides in physiological environments and for their proper biological functioning. Branched structures, as seen in the *Ziziphus jujuba* Mill. (jujube) polysaccharides, have been shown to significantly restore immune organ indices and promote the production of immune-related cytokines like IFN-γ in immunosuppressed mice[74]. Moreover, such branched structures also play a role in regulating the gut microbiota, contributing to the overall gut health.

2.2.2 *Chemical modification of FMHPPs*

Despite the valuable properties of natural polysaccharides, their bioactivity levels may sometimes be insufficient for certain applications. To overcome this limitation, chemical modification strategies including sulfation, carboxymethylation, selenylation, and acetylation, have been developed to expand the structural diversity of polysaccharides and enhance their functionality[75].

Critically, different modification strategies yield distinct functional shifts. For instance, while natural *Astragalus* polysaccharides (APS) possess baseline bioactivity, their sulfated derivatives (sAPS) with an appropriate degree of substitution significantly enhance antiviral activity[76,77]. In contrast, phosphorylated APS (pAPS) demonstrate superior antioxidant capacities, increasing the hydroxyl radical scavenging rate from 35.2% in the native form up to 78.4%[78,79]. Furthermore, while modifications like carboxymethylation improve water solubility, evidence suggests that a degree of substitution exceeding 0.85 can decrease immunomodulatory effects due to steric hindrance. These comparisons indicate that sulfation is more effective for antitumor enhancements, while phosphorylation specializes in boosting antioxidant defense[80,81].

Notably, chemical modifications can address the bottlenecks associated with natural polysaccharides, such as low solubility, poor stability, and weak bioactivity[82]. By tailoring the polysaccharide structures through these modification methods, it becomes possible to develop novel polysaccharide-based materials with enhanced properties for a wide range of applications, including functional foods, pharmaceuticals[83], and biomedical materials.

Ultimately, the bioactivities of FMHPPs are a direct consequence of their complex structures. The relationship between key structural elements—such as glycosidic linkage, chain conformation, and chemical modifications—and their resulting biological functions, particularly the antioxidant activity, is systematically elucidated in Fig. 2. This structure-activity relationship provides a fundamental basis for the targeted enhancement of FMHPPs efficacy through structural modifications.

2.3 Bioactivities of FMHPPs

2.3.1 *Disease prevention and cellular protection activities*

FMHPPs exhibit remarkable properties in disease prevention and cell protection. Their antioxidant capabilities are primarily manifested in scavenging free radicals, for instance, *Ganoderma lucidum* polysaccharides exhibit a dose-dependent scavenging effect on DPPH radicals *in vitro*, with a measured IC50 value of approximately 1.2–1.5 mg/mL[85,86]. *In vivo* experiments show that *Panax notoginseng* polysaccharides demonstrate a strong antioxidant capacity by activating the nuclear factor erythroid 2-related factor 2 (Nrf2)/antioxidant response element pathway[87]. This antioxidant activity is crucial since excessive free radicals can accelerate oxidative processes, leading to cell damage and various aging-related disorders[84].

Furthermore, FMHPPs have shown great potential in anti-tumor activity by regulating immune checkpoints, such as the programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) pathway[88], thereby enhancing tumor cell recognition. They also induce apoptosis, a natural defense mechanism against cancer. *In vitro*, APS at concentrations of 50–200 μg/mL significantly enhance the phagocytic activity of RAW 264.7 macrophages and stimulates the release of NO and TNF-α[77]. This effect translates effectively to animal models. *In vivo* anti-tumor assays, administration of APS (400 mg/kg) in mice inhibited tumor growth by approximately 45.2% compared to the control group, primarily by increasing the spleen and thymus indices[89-91]. Moreover, chemical modifications like sulfation of polysaccharides have been found to further enhance these activities[92,93].

Moreover, FMHPPs exert notable anti-aging effects. *Gastrodia elata* Blume polysaccharides can delay skeletal muscle aging *in vivo* by reducing the mRNA expression and protein levels of caspase-3, muscle RING-finger protein-1 (MURF-1), and muscle

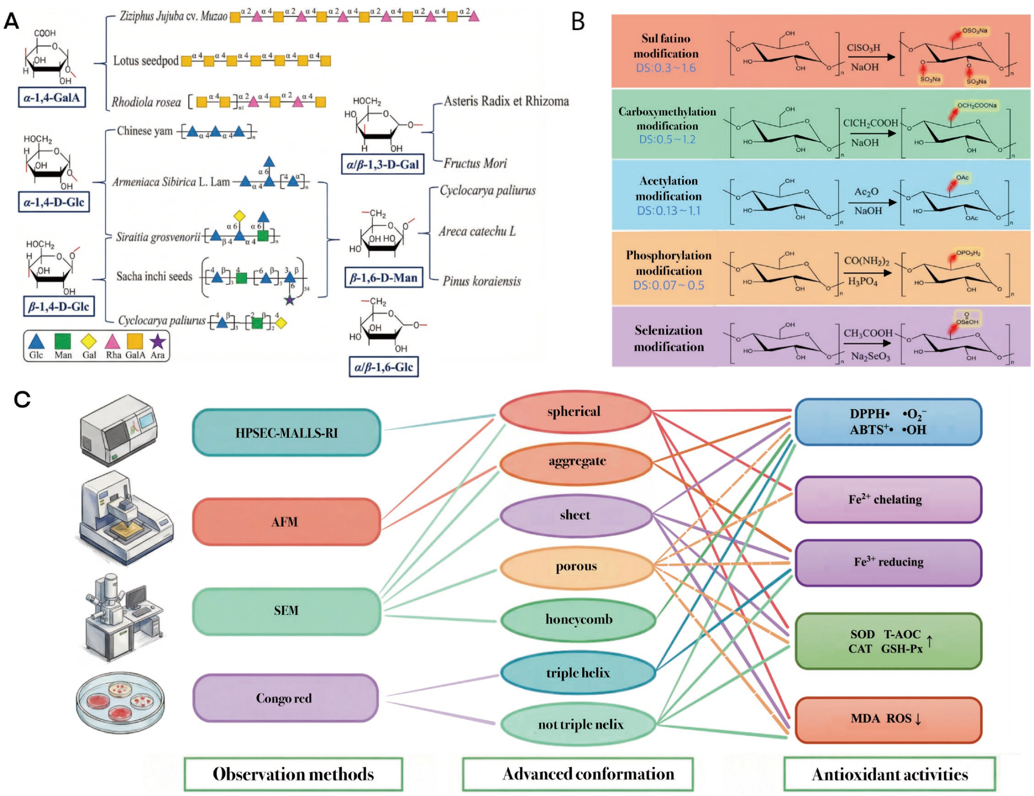

Figure 2 Elucidating the structure-activity relationship of polysaccharides in antioxidant function. (A) Schematic diagram of the main glycosidic linkage connections contained in antioxidant polysaccharides. (B) Illustration of different chemical modification reactions of polysaccharides to enhance their bioactivity. (C) Characterization of different chain conformations of antioxidant polysaccharides using various observation methods and their corresponding antioxidant activities. Reproduced with permission from ref. [84]. Copyright 2024, Elsevier.

atrophy F-box (MAFbX)[94]. *Astragalus* polysaccharides, on the other hand, mitigate cellular aging by enhancing telomerase activity and reducing oxidative stress[95, 96].

2.3.2 Systemic regulation and health maintenance activities

FMHPPs play crucial roles in maintaining overall health by regulating metabolism and the immune system. In terms of metabolic regulation, *Cynomorium songaricum* polysaccharides (200 mg/kg) in mice (*in vivo*) led to a 25% reduction in fasting blood glucose levels after 4 weeks[11]. Specifically, *Mulberry* leaf polysaccharides enhance insulin sensitivity *via* the AMP-activated protein kinase (AMPK)/glucose transporter type 4 (GLUT4) pathways, facilitating the uptake of glucose by cells and thus helping regulate the blood glucose levels[97]. Jujube polysaccharides can lower blood glucose by inhibiting α-glucosidase, an enzyme involved in carbohydrate digestion[98].

FMHPPs also have a significant impact on the gut microbiota. They can repair the intestinal mucosa, inhibit the production of intestinal inflammatory factors, and maintain the balance of the intestinal flora. This is important for gut health because an imbalanced gut microbiota has been linked to various diseases, including metabolic disorders and immune-related diseases. By analyzing the jujube polysaccharide-gut microbiota-potential disease network, Li *et al.*[99] found that jujube polysaccharides could improve the homeostasis of the bacterial community and play a potential role in treating blood diseases and nervous system diseases.

In the immune system, FMHPPs act as the immunomodulators. They activate macrophages and dendritic cells *via* the Toll-like receptor 4 (TLR4)/myeloid differentiation factor 2 (MD2)/nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, promoting the secretion of cytokines, which are the important messengers in immune responses. The typical examples are *Perilla frutescens* polysaccharides[100] and *Poria cocos* polysaccharides[101], which enhance immunoglobulin A (IgA) secretion to protect the intestinal mucosa from pathogens, exerting a crucial effect on gut immunity. In aquatic species, *Poria cocos* polysaccharides promote antibody production, highlighting the diverse immunomodulatory effects of FMHPPs[102].

Furthermore, FMHPPs demonstrate other beneficial activities such as anti-inflammatory, liver protection, and memory improvement effects[49], making them valuable candidates for functional foods and nutraceuticals, eventually contributing to overall health and well-being.

As summarized in Fig. 3, the diverse biological activities of FMHPPs are intrinsically linked to their unique chemical structures.

3 Biosensing technologies for the detection of FMHPPs

3.1 Overview of biosensing technologies and structural characterization of FMHPPs

3.1.1 Overview of biosensing technologies

As depicted in Fig. 1, the therapeutic potential of FMHPPs originates from their diverse biological activities. Nevertheless, it is

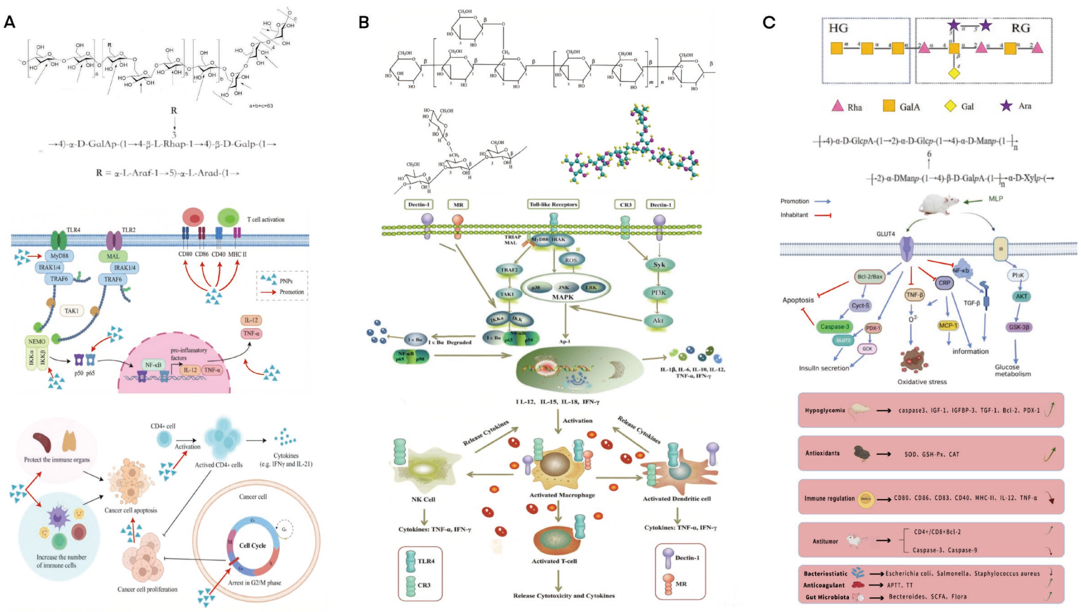

Figure 3 Interplay between structural features and core biological mechanisms of representative FMHPPs. (A) *Panax notoginseng* polysaccharides (PNPs): Representative chemical structure of PNPs; schematic of its anticancer and anti-inflammatory mechanisms. Reproduced with permission from ref. [87]. Copyright 2024, Elsevier. (B) *Ganoderma lucidum* polysaccharides: Representative chemical structure of *Ganoderma lucidum* polysaccharides; schematic of its immunomodulatory and antitumor mechanisms *via* receptor binding and immune pathway activation. Reproduced with permission from ref. [86]. Copyright 2023, Elsevier. (C) *Mulberry* leaf polysaccharides (MLPs): Representative chemical structure of MLPs; schematic of its hypoglycemic mechanism, particularly through the AMPK/GLUT4 signaling pathway. Reproduced with permission from ref. [97]. Copyright 2024, Elsevier.

challenging to conduct a comprehensive analysis owing to their structural complexity, heterogeneity, and the intricate nature of their biological interactions. Traditional analytical methods, including colorimetric assays, chromatography, spectrophotometry and mass spectrometry, while foundational, often suffer from limitations like prolonged analysis time, insufficient sensitivity for trace components, and inability to monitor dynamic biological processes in a real-time manner[27,73]. Typically, the selection of a method is influenced by the particular requirements of the analysis, including the type of sample, the amount of polysaccharides present, and the obtainable resources[103]. Compared to these approaches, the emerging biosensing technologies, such as nanomaterial-based electrochemical sensors[103], surface plasmon resonance (SPR) sensors[104], and molecular imprinting technology (MIT), have provided new analytical strategies for the detection and application of FMHPPs[105]. These advanced technologies, which convert biological recognition events into quantifiable physical signals, not only enhance the detection sensitivity and specificity but also enable the potential applications of FMHPPs in food safety, clinical diagnosis, and environmental monitoring[105,106].

3.1.2 *Structural characterization of FMHPPs*

Biosensing technologies offer powerful, complementary tools to traditional chromatographic and spectroscopic methods for the structural analysis of polysaccharides. In Fig. 4, these advanced platforms, including electrochemical sensors, optical biosensors, and nanopore technology, enable the multidimensional analysis of FMHPPs by converting structural information into measurable signals, thereby facilitating the real-time, label-free, and highly sensitive investigations.

(1) Electrochemical platforms: Composition, content, and biosynthesis dynamics

Electrochemical sensing serves as a high-throughput alternative for profiling FMHPPs composition without the need for prior hydrolysis. Instead of isolated studies, the field is moving toward electrochemical fingerprinting as a diagnostic tool. For instance, the diagnostic peaks at +0.31 V and +0.52 V for *Hedysarum polybotys* polysaccharides (HPS) provide a calculated correlation (r = 0.92) with total sugar and uronic acid content, respectively[107]. Compared to the phenol-sulfuric acid method, these platforms achieve significantly lower detection limits, enabling the differentiation of FMHPPs from different geographical origins based on their unique redox-active motifs. Furthermore, Liu and Yan[108] employed differential pulse voltammetry (DPV) to establish a series of electrochemical fingerprints of *Astragalus membranaceus* from different geographical locations, reflecting the proportional contents of various components.

Beyond compositional insights, electrochemical platforms are also adept at monitoring biosynthesis dynamics. On one hand, by tracking the evolution of interfacial electrical properties during microbial cultivation, sensing strategies based on 3D porous electrodes and electrochemical impedance spectroscopy (EIS) enable real-time, label-free monitoring of the exopolysaccharide (EPS) secretion kinetics, thereby identifying critical time points for optimizing fermentation processes[109]. On the other hand, it is further extended to high-precision recognition detection centered on polysaccharide-specific interactions. For instance, an impedimetric biosensor for the rapid and ultrasensitive detection of *Pseudomonas aeruginosa* was successfully developed by immobilizing Lectin B (LecB), which specifically recognizes mannose-containing polysaccharides, onto a nanoporous gold electrode interface[110].

(2) Optical biosensors: Chemical group identification and spatial imaging

Complementarily, optical biosensors contribute to structural characterizations by enabling the non-destructive identification of chemical motifs and molecular conformations. While conventional spectroscopic methods like Fourier transform infrared spectroscopy (FT-IR) and standard Raman spectroscopy

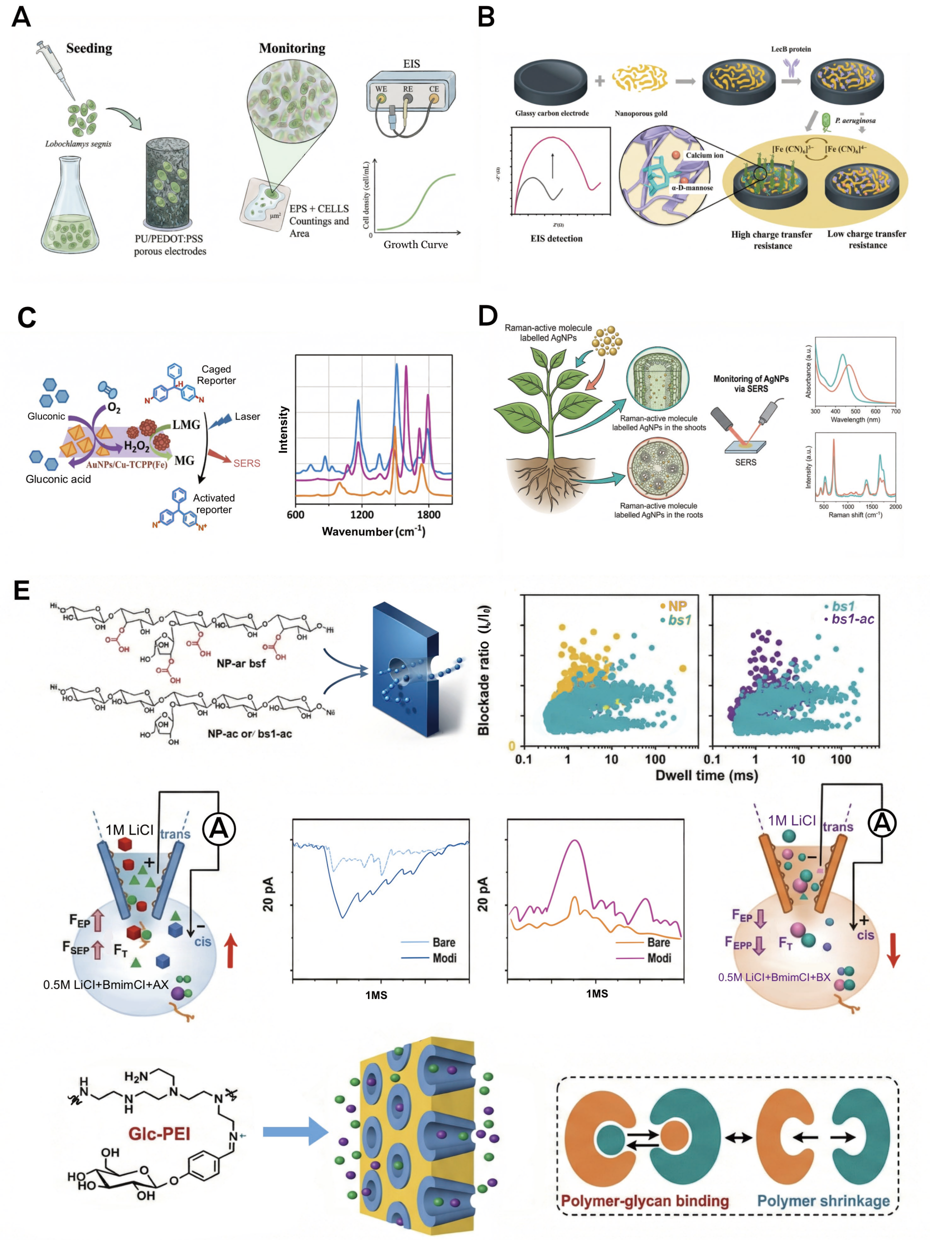

Figure 4 Advancing FMHPPs analysis with integrated biosensing platforms. (A) Real-time monitoring of microbial exopolysaccharide (EPS) secretion kinetics using a 3D porous electrode and electrochemical impedance spectroscopy. Reproduced from ref. [109] under a Creative Commons Attribution (CC BY) license. (B) Ultrasensitive pathogen detection *via* a lectin (LecB)-functionalized nanoporous gold impedimetric biosensor for *Pseudomonas aeruginosa* recognition. Reproduced with permission from ref. [110]. Copyright 2025, Elsevier. (C) Continuous metabolic monitoring through SERS-based strategies for in-situ glucose detection. Reproduced with permission from ref. [114]. Copyright 2022, Elsevier. (D) In-situ tracking of nanomaterial transport by monitoring chemically and green-synthesized silver nanoparticles (AgNPs) in maize seedlings *via* surface-enhanced Raman spectroscopy (SERS). Reproduced with permission from ref. [116]. Copyright 2021, Elsevier. (E) Single-molecule structural analysis of polysaccharides using solid-state nanopore technology, enabling the differentiation of polysaccharides with varying degrees of acetylation. Reproduced from ref. [121] under a CC BY license.

can non-destructively identify characteristic chemical bond vibrations of cell wall polysaccharides (e.g., cellulose and pectin), they are not sensitive or specific enough in complex matrices[111, 112]. To bridge the sensitivity gap, surface-enhanced Raman scattering (SERS) biosensors are developed, which combine the high sensitivity of plasmonics with the high specificity of biological recognition elements, allowing for label-free and highly specific detection of target macromolecules[113, 114].

Typically, the application of SERS is expanding from *in vitro* detection to complex living systems. It has been extensively developed for the continuous, quantitative glucose monitoring in body fluids using strategies like partition layers or boronic acid probes[114, 115]. Moreover, its capability extends to plant systems, where the pioneering visualization of functionalized silver nanoparticles in maize seedlings demonstrates its potential for tracking the transport of exogenous molecules, including polysaccharides, in plants[116]. Furthermore, its successful deployment in detecting pesticide residues on fruits and vegetables[117] also confirms its exceptional robustness in complex plant-derived matrices.

(3) Nanopore technology: Towards glycan sequencing

Nanopore technology represents the frontier of single-molecule structural resolution. By measuring the ionic current blockade and dwell time as a single polysaccharide chain transits a nanoscale pore, researchers can identify the degree of polymerization and specific modifications like acetylation[118]. For example, biological nanopores can sensitively detect monosaccharides such as glucose by utilizing specific binding proteins or pore modifications. In contrast, solid-state nanopores can specifically recognize and quantitatively analyze polysaccharides (such as heparin and hyaluronic acid) through surface functionalization and pH-gating mechanisms[119]. For plant polysaccharides, solid-state nanopores can distinguish xylans with different degrees of acetylation and directly detect water-insoluble starch molecules dissolved in ionic liquids[120, 121].

In summary, the advent of biosensing technologies is profoundly revolutionizing the field of polysaccharide structural analysis. These technologies contribute to the rapid macroscopic composition profiling, in-situ imaging, and single-molecule resolution of fine structures, and are transforming analytical capabilities toward real-time, label-free and highly sensitive detection. Future research should focus on expanding the validation scope of these methods, enhancing their anti-interference performance in complex real samples, and actively exploring their integration with artificial intelligence and miniaturized devices to develop the intelligent, on-site characterization systems[122-124].

3.2 Bioactivity evaluation of FMHPPs: Functional assessments and technology selection

Biosensing technologies, particularly electrochemical sensing platforms and chip-based bioassays, have emerged as powerful tools for the rapid, sensitive, and quantitative analysis of FMHPPs bioactivities. These techniques enable indirect yet efficient evaluation by detecting key active molecules produced upon polysaccharide intervention, monitoring the induced physiological changes, or quantifying the regulatory effects on specific biological processes. They offer significant advantages in assessing diverse bioactivities, including fundamental functional properties and targeted physiological regulatory effects.

3.2.1 Assessment of fundamental functional activities

Traditionally, antioxidant and antimicrobial assessments of FMHPPs relied on endpoint colorimetry, which lacks kinetic depth. Advanced biosensors now prioritize mechanism-driven quantification.

For antioxidant activity evaluation, biosensing technologies quantify the overall functional activity of polysaccharide-containing products, making them ideal for application in functional foods and beverages. The sensing mechanism of nanostructured electrochemical platforms is based on monitoring electron transfer during radical scavenging[125]. Specifically, in the superoxide radical ($O_2^{\bullet-}$) assay, a nanoparticle-modified electrode records the reduction current of $O_2^{\bullet-}$ generated in situ by the xanthine oxidase-hypoxanthine system. Upon addition of antioxidant FMHPPs, these molecules donate electrons to neutralize the radicals, causing a proportional decrease in cathodic current that reflects scavenging efficiency[84, 126]. Through constructing a carbon black-gold nanoparticle (CB-AuNP) modified electrode, Zhao *et al.*[126] successfully applied this principle to determine the antioxidant capacity of *Ganoderma*-infused white tea, expressing results as Trolox equivalent antioxidant capacity (Fig. 5A). Strong positive correlations between electrochemically measured antioxidant capacity and polysaccharide content have been confirmed in products such as

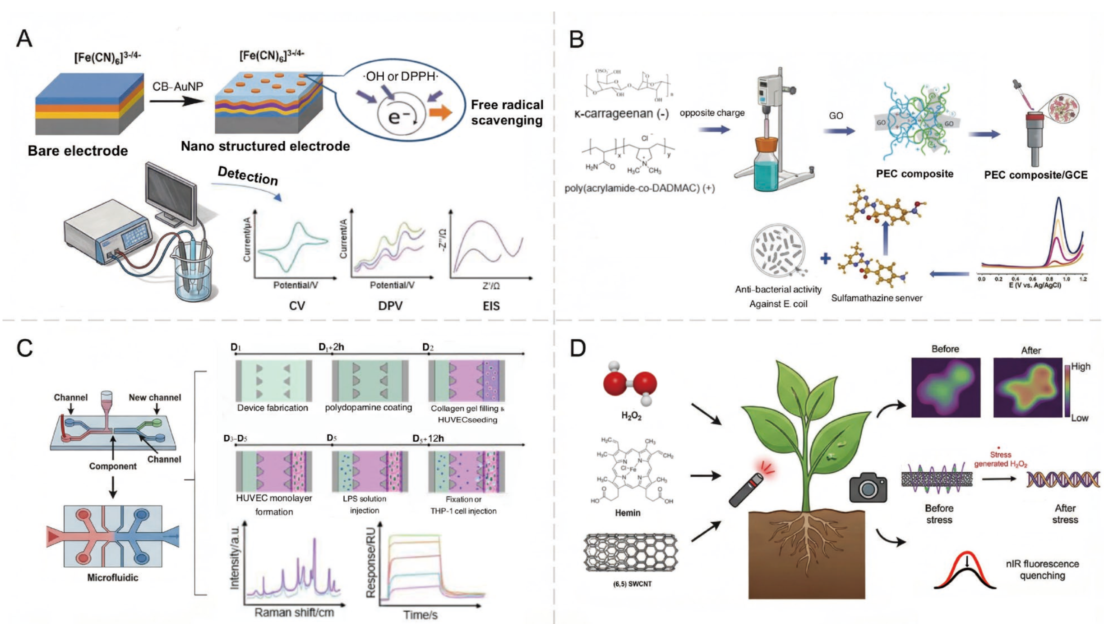

Figure 5 Biosensing platforms for FMHPPs bioactivity evaluation (such as antioxidant, antibacterial, anti-inflammatory, and immunomodulatory activities). (A) Electrochemical sensing platform for antioxidant activity assessment using a nanostructured electrode to monitor free radical scavenging. Applicable for: Rapid quality control of antioxidant functional foods and beverages. Reproduced from ref. [126] under a CC BY license. (B) Polysaccharide-based composite integrating electrochemical sensing and antibacterial activity against *E. coli*. Reproduced with permission from ref. [130]. Applicable for: Simultaneous detection of antibiotic residues and bacterial inhibition in food safety monitoring. Copyright 2025, Elsevier. (C) Microfluidic chip platform for anti-inflammatory evaluation by monitoring endothelial barrier integrity and immune cell migration. Applicable for: real-time evaluation of anti-inflammatory compounds and immune cell dynamics. Reproduced from ref. [133] under a CC BY license. (D) Near-infrared fluorescent nanosensor for immunomodulatory activity monitoring through real-time H_2O_2 detection in living plants. Applicable for: Non-invasive monitoring of plant immune responses and immunomodulatory activity of FMHPPs. Reproduced with permission from ref. [144]. Copyright 2020, American Chemical Society.

radix hedysari and *Cistanche deserticola* Ma[126-128], directly linking the electrochemical signal to functional ingredient concentration. Additionally, the well-characterized electrochemical behaviors of small-molecule antioxidants (e.g., curcumin[129]) have revealed links between electron-transfer mechanisms and radical-scavenging activity, facilitating the development of nanostructured electrodes with enhanced signal responses for robust polysaccharide antioxidant evaluation.

Regarding antimicrobial activity profiling, electrochemical and material-integrated biosensors provide efficient characterization approaches for polysaccharide-based composites. A typical example is the sensing platform developed by Hsiao *et al.* using a κ-carrageenan (κ-CGN)-based polyelectrolyte complex, which not only served as an electrode modifier for sulfamethazine detection but also exhibited a significant antibacterial activity against *Escherichia coli* (*E. coli*), as validated by colony counting and agar diffusion methods[130,131]. The dual functionality arises from the polyelectrolyte complex formed *via* electrostatic interactions between anionic κ-CGN and cationic poly(acrylamide-co-DADMAC). Electrochemical detection relies on oxidation of the analyte's amine group, while antibacterial activity is attributed to disruption of negatively charged bacterial cell membranes by the polycationic complex[130]. Fig. 5B exemplifies the potential of polysaccharide-functionalized sensors for simultaneous detection and antimicrobial action. Similarly, Shivaswamy *et al.*[132] synthesized graphene oxide (GO)-dispersed Bi_2CuSe_5 nanoflakes with potent antibacterial effects against *E. coli* and *Staphylococcus aureus*, indicating that FMHPPs employed as modifying layers hold potential for dual sensing and bacterial inhibition capabilities.

3.2.2 *Evaluation of targeted physiological regulatory activities*

This section focuses on assessing the anti-inflammatory, hypoglycemic and immunomodulatory activities of FMHPPs, reflecting their sophisticated regulatory effects on specific physiological processes. The transition from *in vitro* assays to *in vivo* efficacy is guided by sensors that profile signaling cascades.

For anti-inflammatory activity, microfluidic chip-based biosensors and bioassays enable real-time quantitative monitoring. For instance, Nam *et al.*[133] established a microfluidic vascular inflammation model to evaluate the protective effects of bioactive polysaccharides. The chip mimics the vascular endothelium by culturing human umbilical vein endothelial cells (HUVES) in a microchannel. Inflammation is induced by lipopolysaccharide (LPS), leading to upregulation of intercellular adhesion molecule 1 (ICAM-1) and disruption of tight junctions (VE-cadherin), which are visualized by immunofluorescence staining. The anti-inflammatory effect of FMHPPs is assessed by the reduction of these markers and the decreased migration of fluorescently labeled THP-1 monocytes across the endothelial layer. This platform enables real-time, quantitative evaluation of barrier integrity and immune cell recruitment (Fig. 5C). Alternatively, electrochemical strategies for detecting pro-inflammatory bacterial metabolites enable monitoring of polysaccharide treatment efficacy by quantifying reductions in inflammatory mediator production from pathogenic biofilms, thereby offering an indirect yet quantitative assessment of anti-inflammatory properties[134].

For the indirect assessment of hypoglycemic activity, polysaccharide-based optical sensing technologies show great potential. These sensors typically detect glucose *via* enzymatic generation of H_2O_2, which subsequently quenches the fluorescence of incorporated quantum dots or other fluorophores. Through developing a superabsorbent nanohydrogel biosensor based on carob polysaccharide, Qasemi and Ghaemy[135] achieved highly sensitive optical glucose detection *via* co-immobilized cadmium telluride (CdTe) quantum dots and glucose oxidase. The sensor, relying on hydrogen peroxide (H_2O_2)-induced fluorescence quenching, demonstrates excellent stability and reproducibility. This technology can be adapted to evaluate the hypoglycemic activity of FMHPPs (e.g., *Mulberry* leaf polysaccharide[136,137]) by measuring residual glucose production after α-glucosidase inhibition, indirectly reflecting the inhibitory potential of polysaccharides.

For immunomodulatory activity monitoring, fluorescent biosensing displays unparalleled capabilities in tracing polysaccharides and sensing immune responses[138]. A key strategy involves using fluorescently labeled polysaccharides (e.g., *Lycium barbarum*[139], *Polygonatum sibiricum*[140] and *Mulberry* fruit[141] polysaccharides) to map them *in vivo* distribution, consistently revealing their accumulation in immune-rich tissues like the intestines and liver. In addition to distribution, advanced nanosensors also enable the real-time monitoring of immune signaling[142,143]. Wu *et al.*[144] developed near-infrared fluorescent nanosensors based on DNA-functionalized single-walled carbon nanotubes (SWCNTs) that emit fluorescence in the near-infrared region. In the presence of H_2O_2—a key signaling molecule in plant immunity—the fluorescence is quenched due to charge or energy transfer mechanisms[145,146]. By embedding these nanosensors in living plants, real-time monitoring of H_2O_2 dynamics during immune responses becomes possible, offering direct insight into the immunomodulatory activity of FMHPPs (Fig. 5D). The integration of nanocomposite materials allows for the synergistic combination of different components like precious metal alloys, semiconductor nanomaterials, and carbon cloth, leading to improved sensor stability and sensitivity in H_2O_2 detection[147]. These direct and dynamic insights into the immunomodulatory mechanisms significantly enrich the functional profiling of FMHPPs.

3.2.3 *Technology comparison and strategy selection*

As illustrated in Fig. 5, a range of representative biosensing technologies have been developed to quantitatively assess the core bioactivities of FMHPPs. These platforms provide critical tools for rapidly profiling antioxidant, antibacterial, anti-inflammatory, and immunomodulatory activities, laying the basis for rational technology selection.

To select an appropriate biosensing strategy for evaluating FMHPPs bioactivities, several factors should be considered, including target function, required sensitivity, real-time capability, and cost. Table 2 summarizes the recommended technologies for profiling key bioactivities, highlighting their respective advantages and critical experimental considerations.

3.3 Bridging detection-bioactivity-application and FMH-based functional biosensors

3.3.1 *Bridging detection, bioactivity, and practical applications*

Apart from content quantification and bioactivity profiling, a paramount goal in FMHPPs analysis is to directly bridge the gap between their presence and their biological functions. Advanced biosensing technologies like MIT and SPR sensors are no longer just detection tools but structure-activity probes.

As an emerging molecular recognition technique, MIT creates synthetic receptors with "lock-and-key" recognition capabilities,

Table 2 Comparison of biosensing technologies for FMHPPs bioactivities analysis

Target Activity	Recommended Technologies	Advantages	Considerations	Key Parameters	Ref.
Antioxidant	Electrochemical sensors (nanostructured electrodes); genetically encoded probes	High sensitivity; real-time detection; limited matrix interference	Requires calibration with standard; purity critical; low intrinsic electroactivity	LOD: 0.01 mmol/L Trolox equivalent; Linear range: 0.1–1.0% w/v extract; Sensitivity: current change proportional to radical scavenging	[126, 129]
Antimicrobial	Electrochemical sensors; agar diffusion and colony count	Enables real-time, quantitative analysis; polysaccharides as active sensor components	Material integration; sample preparation	LOD: 3.0 nmol/L for sulfamethazine; Linear range: 0.008–496.5 μmol/L; Inhibition zone: 12.2 mm against *E. coli*	[130-132]
Anti-inflammatory	Microfluidic organ-on-a-chip models; electrochemical sensors	Real-time; mechanistic insight; high sensitivity	Model complexity; equipment cost	ICAM-1 upregulation: 9.3% → 61.8% at 12 h LPS; VE-cadherin disruption: 25.8% → 14.7% at 4 h LPS; THP-1 migration distance: 16.8–32.8 μm	[133, 134]
Hypoglycemic	Enzyme-based optical biosensor; electrochemical biosensors	High sensitivity, real-time monitoring	Requires enzyme immobilization, affected by sample opacity	LOD: 0.5 μmol/L glucose; Linear range: 0.5–100 μmol/L; Mechanism: H_2O_2-induced fluorescence quenching	[135, 147]
Immunomodulatory	Fluorescent biosensor; nanomaterial-based electrochemical biosensors	High specificity; visual; dynamic; non-invasive	Fluorescence quenching; require specialized equipment	H_2O_2 sensitivity: 10–100 μmol/L (quenching: −9.4% at 10 μmol/L); Selectivity: ΔF <10% for 10 interferents; Spatial resolution: subcellular	[139-141, 144]

offering a powerful platform for such selective detection[105] (see Fig. 6). By employing glucose as a dummy template, the molecularly imprinted electrochemical sensor (MIES) enables highly selective indirect quantification of *Polygonatum sibiricum* polysaccharides (PSP) through the detection of glucose released after acid hydrolysis[148]. The MIES platform achieves a limit of detection (LOD) of 0.766 ng/mL with excellent green analytical performance, making it ideal for on-site rapid quality control of traditional Chinese medicine[149, 150]. Furthermore, by designing molecularly imprinted polymers (MIP) with templates mirroring specific bioactivities, the sensing platform can be tailored to evaluate functional properties like antioxidant and hypoglycemic capacities, thereby linking molecular detection with functional bioactivity assessment[151]. The utility of MIP also extends to precisely detecting other active components (e.g., alkaloids and flavonoids[105]) and selectively monitoring hazardous substances (e.g., pesticide residues and endogenous toxins[152]) within complex herbal matrices, ensuring efficacy and safety. Notably, a significant innovation for clinical monitoring is the construction of MIP-bioreceptor (e.g., antibody and aptamer) hybrid systems[153, 154]. These systems synergize the superior stability of synthetic polymers with the exquisite affinity of biological elements, paving

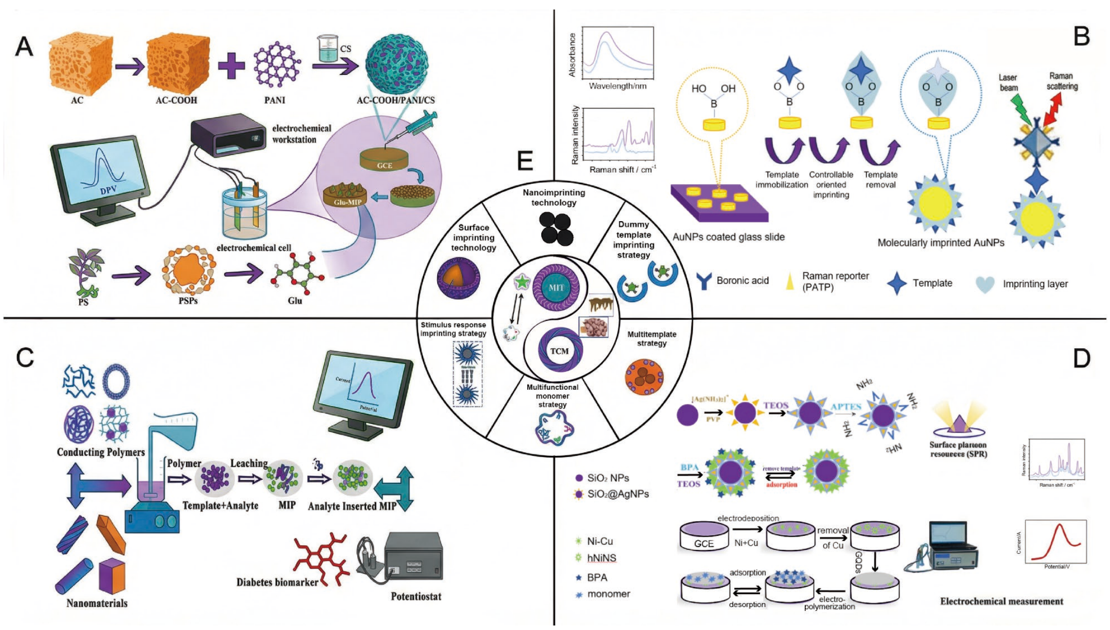

Figure 6 Advanced molecular imprinting platforms for bioanalysis. (A) Molecularly imprinted electrochemical sensor for selective detection of *Polygonatum sibiricum* polysaccharides. Reproduced with permission from ref. [148]. Copyright 2025, Elsevier. (B) Plasmonic immuno-sandwich assay for ginsenoside analysis in ginseng samples. Reproduced with permission from ref. [155]. Copyright 2020, Elsevier. (C) MIP-based electrochemical sensor for diabetes biomarkers monitoring. Reproduced with permission from ref. [151]. Copyright 2025, Taylor & Francis. (D) MIP-integrated SERS and electrochemical sensor for bisphenol A detection. Reproduced with permission from ref. [152]. Copyright 2019, Elsevier. (E) Emerging imprinting technologies for TCM-related MIPs preparation. Reproduced from ref. [105] under a CC BY license.

the way for a new generation of robust biosensors for disease diagnostics.

Additionally, by monitoring the binding process of polysaccharides to specific receptors, SPR sensors serve as a powerful tool to elucidate the relationship between polysaccharide structure and biological function. For example, Liu *et al.*[104] quantitatively compared the binding affinity of polysaccharides with varying structures through immobilizing α-glucosidase, and demonstrated the exceptional sensor sensitivity to structural-activity relationship. Currently, the field is advancing towards integrated and multi-parametric sensing platforms, such as dual-mode sensors. Electrochemical-fiber optic SPR (EC-FO-SPR), which combines the real-time monitoring capability of SPR with the high sensitivity of electrochemical detection, provides a more comprehensive analytical dimension for investigating polysaccharide-receptor interactions[156].

Looking forward, the field is moving towards multi-mode cross-validation to enhance reliability, while integrating with technologies such as microfluidics and portable devices to extend detection capabilities[157-159]. In conclusion, these sophisticated strategies successfully transform polysaccharide detection from a static "content analysis" to a dynamic "functional interaction analysis". This evolution not only directly illustrates their biological activities but also seamlessly translates the findings into practical applications, including quality control, safety monitoring, and clinical diagnostics[160], thereby effectively closing the loop between detection, bioactivity, and practical application.

3.3.2 *Other biosensors employing FMHPPs as functional components*

Apart from serving as detection targets, FMHPPs can also function as materials in biosensors designed to enhance stability and biocompatibility[161-164]. A notable example is the dual-mode biosensor developed by Zhao Han *et al.*[159], which used *Aloe vera* polysaccharides to stabilize core-shell nanoflowers and red carbon dots. This biosensor enabled colorimetric and fluorescent detection of organophosphorus pesticides, highlighting the capability of FMHPPs to enhance sensor performance and pioneer green and degradable sensing platforms. Furthermore, Wang Hao *et al.*[165] constructed a hybrid-modified biosensor by doping the conductive polymer PEDOT with *Glycyrrhiza* polysaccharides, achieving ultrasensitive electrochemical detection of microRNA, and demonstrating the material potential of FMHPPs in electrochemical sensing.

3.4 Current challenges and future perspectives

The quantitative comparison in Table 3 underscores the paradigm shift driven by biosensing technologies. The quantifiable performance metrics of biosensing technologies in terms of sensitivity, speed, and versatility position them as powerful tools for the comprehensive analysis of FMHPPs. Despite this progress, significant technical hurdles remain. A primary challenge is the structural complexity of polysaccharides, which often necessitates indirect detection strategies that may not fully capture their native bioactivities[126,148]—and such traditional indirect methods typically rely on manual parameter optimization, leading to inefficiencies in adapting to diverse polysaccharide subtypes. Furthermore, signal interference from co-extracted compounds, like phenolics in crude plant matrices, poses a challenge to both optical and electrochemical sensors[129,166], as distinguishing target signals from noise often requires labor-intensive data post-processing with limited real-time adaptability.

To address these limitations, future research should AI technologies into biosensing frameworks alongside existing directions: first, developing advanced direct sensing technologies for real-time monitoring of polysaccharide-receptor interactions, where nanomaterials with highly conjugated structures and high electron mobility have been demonstrated to enable stable signal transduction[167], and machine learning models can preprocess raw sensor data to eliminate interference signals autonomously and

Table 3 Performance comparison of analytical methods for bioactive compounds

Method	Principle	Target Analyte	Linear Range	LOD	Ref.
Phenol-Sulfuric Acid	Acid hydrolysis, colorimetric reaction	Total Polysaccharides	Depends on calibration curve	~1 μg/mL (typical)	[51]
HPLC with RID	Chromatographic separation	Polysaccharide fractions	Wide (depends on column)	0.1–1 μg/mL (typical)	[18, 28]
Near-Infrared Spectroscopy (NIRS)	Molecular overtone and combination vibrations	Polysaccharides in *Ganoderma* mycelia	-	(Used with multivariate calibration)	[122]
Mid-Infrared Spectroscopy (MIRS)	Molecular fundamental vibrations	Polysaccharides in *Lycium barbarum*	1800–400 cm^{-1}	(Provides structural fingerprint)	[111]
Raman Spectroscopy	Inelastic light scattering	Pectin in onion cell wall	-	(Spatial resolution for imaging)	[112]
Molecularly Imprinted Electrochemical Sensor (MIES)	Specific cavity recognition, electrochemical transduction	*Polygonatum sibiricum* Polysaccharides	100–1000 ng/mL	0.766 ng/mL	[148]
Electrochemical Sensor (e.g., CB-AuNP/GCE)	In-situ superoxide radical scavenging, amperometric detection	Antioxidant Capacity (*Ganoderma* Tea)	0.1–1.0% w/v extract	High sensitivity (expressed as TEAC)	[126]
Surface-Enhanced Raman Scattering (SERS)	Plasmonic enhancement of Raman signals	Pesticide (Thiram) on fruit	Not explicitly stated	0.24 nmol/L (on grape peel)	[117]
Molecular Imprinting Technology (MIT)	"Lock-and-key" specific recognition	Ginsenosides	Various (pM-μM range reported)	As low as pM-nM	[105]
MIP-based SERS & Electrochemical Sensor	Combined MIP pre-concentration & SERS detection	Bisphenol A (BPA)	Not explicitly stated	High selectivity & sensitivity demonstrated	[152]
Colorimetric/Fluorescent Dual-mode Biosensor	*Aloe vera* polysaccharide-stabilized nanoflowers & red carbon dots	Organophosphorus Pesticides	0.01–100 μmol/L	3.4 nmol/L	[159]

(Note: NIRS, MIRS, and Raman spectroscopy are often employed for qualitative structural analysis or require multivariate calibration models for quantification; therefore, conventional linear ranges and detection limits are not directly applicable. For detailed performance parameters of these spectral methods (e.g., R^2, RPD, RMSECV), readers are referred to the original studies cited and the comprehensive review by[112]) predict binding affinity with higher accuracy; second, integrating advanced materials to enhance sensor performance[168], with AI-driven high-throughput screening accelerating the design of novel nanocomposite sensing layers tailored to specific polysaccharide structures; third, creating multi-modal sensing platforms, where deep learning algorithms can fuse data from optical, electrochemical, and mass spectrometric modules to construct holistic FMHPPs analysis models, reducing reliance on single-modal data biases. Additionally, AI-enabled real-time feedback loops could dynamically adjust sensor operating parameters based on in-situ data, analogous to the pH-based dynamic calibration mechanism recently established for correcting glucose measurements in complex wound exudates[169], further improving the adaptability of biosensors to complex sample matrices.

4 Conclusions

Taken together, this review systematically synthesizes advances in FMHPPs, linking their complex structural features to diverse bioactivities and critically evaluating the pivotal role of advanced biosensing technologies in their detection. Our analysis reveals a notable paradigm shift in FMHPPs analysis: From a primary focus on chemical composition and molecular conformation toward a functional assessment of bioactivities. Crucially, biosensors, particularly electrochemical and optical platforms integrated with nanomaterials and molecular imprinting technology, are revolutionizing FMHPPs profiling. Their precision and specific recognition capabilities enable real-time, sensitive, and specific analysis. The implications extend beyond traditional analytical chemistry: Endowed with robust quality control and bioactivity validation capabilities, biosensors are instrumental in translating FMHPPs from laboratory research to clinical applications. Their high sensitivity and real-time monitoring ensure detection efficacy and safety, which is critical for accurate diagnosis and treatment monitoring.

Amid the rapid advancement of AI technology and wearable devices—a defining trend of future development—future research should prioritize: (1) developing multiplexed, AI-powered sensing platforms that integrate machine learning algorithms for simultaneous monitoring of multiple bioactive targets and real-time data interpretation; (2) managing real-sample complexity *via* anti-fouling interface design, such as hydrophilic polymer brushes or zwitterionic coatings, to enable wearable-compatible detection in complex biological matrices; (3) promoting cross-disciplinary collaborations to elucidate FMHPPs-related metabolic pathways, leveraging techniques such as metabolomics, gut microbiome profiling, and organ-on-a-chip models; and (4) establishing standardized protocols for sensor fabrication and validation to facilitate clinical translation and commercialization. With the advancement of such novel analytical technologies coupled with AI and wearable innovations, progress in this field will not only deepen our understanding of FMHPPs but also accelerate their development into next-generation, standardized, high-value functional foods and portable health monitoring tools, thereby advancing proactive healthcare and public well-being.

Data availability

All data needed to support the conclusions in the paper are presented in the manuscript and the Electronic Supplementary Material. 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 work. Axin Liang is an Editorial Board Member of Food & Medicine Homology, but was not involved in the processing, peer review or decision making of this article.

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Author contribution statement

Chen-Xi Xiong: Conceptualization, investigation, visualization, writing – original draft. Yao Xie: Data curation, investigation, validation. Zi-Yu Zhu: Data curation, investigation. Tian-Jian Lv: Data curation, formal analysis, visualization. Yuan Gao: Investigation, visualization. Peng-Yu Wang: Data curation, investigation. He-Ao Zhang: Supervision, validation, writing – review & editing. Rui Wang: Funding acquisition, project administration, supervision, writing – review & editing. A-Xin Liang: Conceptualization, funding acquisition, project administration, supervision, validation, writing – review & editing. All the authors have read and approved the final manuscript.

Informed consent

Not applicable.

Ethics statement

Not applicable.

Use of AI statement

None.

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