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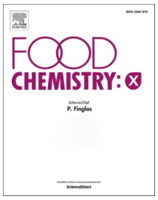

Research progress of edible mushroom polysaccharide-metal trace element complexes

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ABSTRACT

Metal trace elements are crucial for human health, and the complexes of edible mushroom polysaccharides with metal trace elements are currently a research hotspot in the field of food science. This article reviews the preparation methods, structural characterization, and physiological activities of edible mushroom polysaccharide-metal trace element complexes, including iron, selenium, and zinc. Research has shown that iron complexes obtained through Co-thermal synthesis of the $FeCl_3$ method exhibit excellent antioxidant and anti-anemia functions; selenium complexes prepared via selenium-enriched cultivation significantly enhance immunological and anti-cancer properties; zinc complexes improve lipid-lowering, liver protection, and antioxidant capabilities. However, there is an imbalance in research among different metal elements, particularly with a high density of studies on selenium complexes. These studies provide a foundation for the future development of edible mushroom polysaccharide-metal trace element complexes.

1. Introduction

Trace metals, including iron, zinc, iodine, selenium, copper, and approximately 18 other elements, are essential for normal human growth and development. These elements, present in minute quantities in the human body, play crucial physiological roles such as maintaining homeostasis and immune function, regulating enzyme activity and metabolism, facilitating oxygen transport, and promoting bone growth and hormone production (Cannas et al., 2020; Fan et al., 2022; Köhrle, 2023; Seweryn et al., 2021). These trace metals, existing in ionic form or bound to organic molecules, participate in diverse biological processes within the human body. As the body cannot synthesize these elements endogenously, they must be obtained through dietary intake or supplementation. Edible mushrooms, recognized as medicinal foods, are not only rich sources of micronutrients and bioactive compounds but also attract attention for their unique nutritional value and therapeutic potential. These mushrooms are increasingly explored in the development of healthcare products and pharmaceutical preparations, showing promise in addressing various diseases, including cardiovascular disorders, metabolic syndromes, and gastrointestinal cancers (Miao et al., 2011). Polysaccharides, as primary constituents of edible mushrooms, demonstrate a wide range of biological activities, including antitumor, antioxidant, anti-inflammatory, and anti-aging effects (Sun et al., 2022; Yin et al., 2021).

The diverse biological activities of edible mushroom polysaccharides are intrinsically linked to their structural characteristics and conformations. Research has established that these polysaccharides primarily comprise three structural categories: glucans, galactans, and mannans (**Fig. 1**).

Glucans are primarily categorized into homoglucans and heteroglucans (Ruthes et al., 2016). Homoglucans, composed of D-glucose residues, exhibit three main structural configurations: α-D-glucans, β-D-glucans, and mixed α, β-D-glucans (Rostami et al., 2018). β-D-Glucans predominate in edible mushrooms, primarily featuring linear β-(1 → 3)-D-Glc*p* (Glucopyranose) and β-(1 → 6)-D-Glc*p* linkages (Oliveira et al., 2019). Additionally, fungal polysaccharides have been reported to contain glucan structures composed of both α-D-Glc*p* and β-D-Glc*p* (Rostami et al., 2018). Heteroglucans consist of a D-Glc*p* main chain with side chains comprising various monosaccharide residues, such as β-D-Glc*p*, α-D-Gal*p* (α-D-Galactopyranose), α-L-Fuc*p* (α-L-Fucopyranose),

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or α-D-Glc*p* (Le et al., 2022). Wang et al. (2020) isolated β-glucans from *Dictyophora rubrovalvata*, characterizing their structure as a β-(1 → 3)-Glc*p* backbone with β-(1 → 6)-Glc*p* side chains attached at the O-6 position of glucose residues (**Fig. 1a**). Wang, Wang, et al. (2022) isolated β-glucans from *Hypsizygus marmoreus*, revealing a β-(1 → 6)-Glc*p* backbone with O-3 substitutions of non-reducing β-Glc*p* and β-(1 → 3)-Glc*p* side chains in a 1:1 ratio (**Fig. 1b**). Wang et al. (2021) isolated heteroglucans from *Agrocybe cylindracea*, characterizing a main chain composed of β-(1 → 6)-Glc*p*, α-(1 → 6)-Gal*p*, and α-(1 → 2,6)-Glc*p* residues in a 3:1:1 ratio, with side chains terminated by non-reducing α-Fuc*p* residues (**Fig. 1c**).

Heterogalactans, prevalent in basidiomycetes, primarily consist of a α-(1 → 6)-D-Gal*p* main chain with side chains predominantly composed of L-Fuc*p* (L-Fucopyranose), D-Man*p* (D-Mannopyranose), and D-Gal*p* residues (Pires et al., 2017). Based on their side chain composition, these polysaccharides are classified into fucogalactans, fucomannogalactans, and glucogalactans (Wang et al., 2014). Zhang et al. (2006) isolated a fucogalactan from *Hericium erinaceus*, characterizing the structure as an α-(1 → 6)-D-Gal*p* main chain with α-L-Fuc*p* side chains attached at the O-2 position of Gal*p* residues (**Fig. 1d**). Smiderle et al. (2008) isolated a fucomanno galactan from *Flammulina velutipes*, characterized by an α-(1 → 6)-D-Gal*p* main chain with side chains attached at the O-2 position of Gal*p* residues. These side chains consist of terminal α-D-Man*p*,→ 1)-α-L-Fuc*p*-3 → 1-(t-D-Man*p*, and α-L-Fuc*p* units (**Fig. 1e**). Chen,Li, et al. (2023) isolated a glucogalactan from *Termitomyces albuminosus*, characterized by a main chain of α-(1 → 6)-Gal*p* residues with branching points at α-(1 → 2,6)-Gal*p*. The side chains comprise t-β-Glc*p* residues (**Fig. 1f**).

Mannans (heteromannans) in ascomycetous fungi typically feature a main chain of (1 → 3)-, (1 → 6)-, or (1 → 2)-linked α-D-Man*p* residues, with side chains composed of various sugar residues such as α-D-Gal*p* and α-D-Man*p*. Based on their side chain structures, these polysaccharides are classified into galactomannans (Bernabé et al., 2011), glucogalactomannans (Smiderle et al., 2013), and xylomannans (Tu et al., 2021). Cheong et al. (2016) isolated a glucogalactomannan from *Cordyceps sinensis*, characterized by a main chain of α-(1 → 2)-Man*p* residues. The side chains, comprising β-(1 → 2)-Gal*f* (Galactofuranose), β-(1 → 4)-Glc*p*, α-GalA*p* (α-Galacturonic Acid in pyranose form), and α-Man*p* units, are attached to the O-6 position of the mannan core (**Fig. 1g**). Perera et al. (2017) isolated a galactomannan from *Antrodia camphorata*. This polysaccharide primarily comprises α-(1 → 2)- and α-(1 → 6)-linked Man*p* residues, along with α-(1 → 6)-Gal*p* units (**Fig. 1h**). Evsenko et al. (2009) isolated a xylomannanan from *Ganoderma lucidum*. This polysaccharide features an α-(1 → 3)-Man*p* main chain with O-4 substitutions of either single β-Xyl*p* (β-Xylopyranose) residues or disaccharide fragments (**Fig. 1i**). In conclusion, the structural diversity of polysaccharides, characterized by varying combinations of main and side chains, significantly influences their biological functions and properties (Chen, Yang, et al., 2023).

Research on edible mushroom polysaccharide-metal trace element complexes primarily focuses on the preparation and biological activities involving iron, selenium, and zinc et al. (**Table 1**)(Liu et al., 2019; Wang, Chen, Wang, & Xing, 2015; Wang, Huang, et al., 2019; Xu, Ren, et al., 2017; Yi et al., 2012; Yin et al., 2014). While edible mushrooms naturally contain these elements, their low concentrations and extraction difficulties necessitate artificial complexation (Chen et al., 2022; Li et al., 2019; Sarikurkcu et al., 2020). This scientifically sound and efficient process enhances the bioavailability, absorption, stability, and solubility of metal trace elements (Feng et al., 2023). Moreover, the synergistic interaction between edible mushroom polysaccharides and metal trace elements not only improves overall quality but also augments human health benefits through unique bioactive compounds (Fan

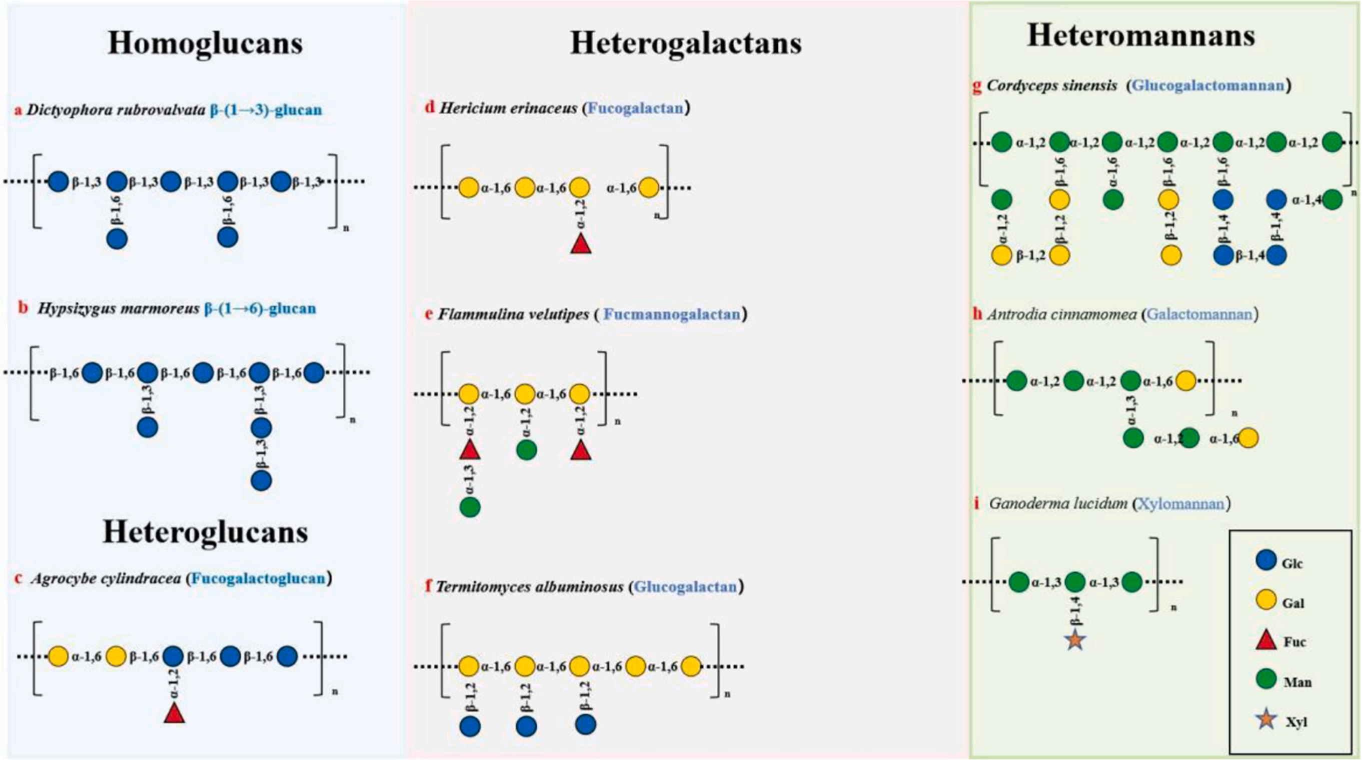

Fig. 1. Representative examples represent the regularity of the relative ordered structure of edible mushroom polysaccharides: (a) β-(1 → 3)-glucan derived from *Dictyophora rubrovalvata* (Wang et al., 2020), (b) β-(1 → 6)-glucan derived from *Hypsizygus marmoreus* (Wang et al., 2022), (c) Fucogalactoglucan derived from *Agrocybe cylindracea* (Wang et al., 2021), (d) Fucogalactan derived from *Hericium erinaceus* (Zhang et al., 2006), (e) Fucmannogalactan derived from *Flammulina velutipes* (Smiderle et al., 2008), (f) Glucogalactan derived from *Termitomyces albuminosus* (Chen et al., 2023), (g) Glucogalactomannan derived from *Cordyceps sinensis* (Cheong et al., 2016), (h) Galactomannan derived from *Antrodia cinnamomea* (Perera et al., 2017), (i) Xylomannan derived from *Ganoderma lucidum* (Evsenko et al., 2009).

Table 1
Types, preparation methods and biological activities of edible mushroom polysaccharide-metal trace element.

Complexes type	Polysaccharide origin	Metal	Preparation method	Biological activity	Ref.
Edible mushroom polysaccharide-iron complexes	*Hypsizygus marmoreus*	Fe	Co-thermal $FeCl_3$ method	Antioxidant activity	(Zhang et al., 2019)
	Flammulina velutipes	Fe	Co-thermal $FeCl_3$ method	Antioxidant activity	(Shi, Cheng, et al., 2023)
	Sparassis latifolia	Fe	Co-thermal $FeCl_3$ method	Antioxidant activity	(He et al., 2022)
	Pleurotus eryngii	Fe	Co-thermal $FeCl_3$ method	Antioxidant activity	(Wu et al., 2023)
	Flammulina velutipes	Fe	Co-thermal $FeCl_3$ method	Antibacterial antifungal Antioxidant activity	(Dong et al., 2017)
	Auricularia auricula	Fe	Co-thermal $FeCl_3$ method	Antioxidant activity	(Liu et al., 2019)
Edible mushroom polysaccharide-selenium complexes	*Auricularia auricular*	Se	Selenium enrichment techniques	Anti-aging activity Immunological activity	(Wang et al., 2019)
	Cordyceps militaris	Se	Chemical synthesis	Antioxidant activity	(Zhu et al., 2016)
	Cordyceps militaris	Se	Chemical synthesis	Anti-tumor activity	(Liu et al., 2017)
	Agrocybe cylindracea	Se	Selenium enrichment techniques	Antioxidant activity Anti-aging activity	(Liu et al., 2016)
	Ganoderma lucidum	Se	Selenium enrichment techniques	Antioxidant activity Immunological activity	(Dong et al., 2021)
	Lentinula edodes	Se	Selenium enrichment techniques	Immunological activity	(Kaleta et al., 2021)
	Cordyceps militaris	Se	Selenium enrichment techniques	Immunological activity	(Yao et al., 2023)
	Morchella sextelata	Se	Chemical synthesis	Anti-tumor activity	(Shi, Deng, et al., 2023)
	Pleurotus ostreatus	Se	Selenium enrichment techniques	Anti-tumor activity Antioxidant activity	(Zhang et al., 2020)
Edible mushroom polysaccharide-zinc complexes	*Auricularia cornea ehrenb*	Zn	Chemical synthesis	Hypoglycemic activity	(Liu et al., 2021)
	Lentinula edodes	Zn	Chemical synthesis	Antioxidant activity	(Du et al., 2023)
	Auricularia polytricha	Zn	Chemical synthesis	Antioxidant activity	(Long et al., 2023)
	Boletus	Zn	Chemical synthesis	–	(Li et al., 2010)
	Flammulina velutipes	Zn	Chemical synthesis	Immunological activity	(Zhao et al., 2017)
	Hericium erinaceus	Zn	Chemical synthesis	Antioxidant activity	(Xue et al., 2021)

et al., 2018).

This review pioneered a comprehensive analysis of edible fungal polysaccharide-metal microelement complexes, elucidating their preparation, structure, and physiological activities. These complexes demonstrate unique advantages in enhancing antioxidant capacity and immunomodulation. The resulting products exhibit high bioactivity, improved absorption, and safety, potentially benefiting public health. However, in vivo metabolic pathways and long-term safety remain understudied. Further in vivo experiments and clinical trials are essential to validate these aspects and fully elucidate the potential of these novel complexes, providing a foundation for future development in functional foods and nutraceuticals.

2. Research progress of edible mushroom polysaccharide-iron complexes

Iron, an essential trace element, plays a crucial role in physiological processes such as oxygen transport, cellular respiration, and DNA synthesis (Blanco-Rojo & Vaquero, 2019; Kazemi-Taskooh & Varidi, 2021). Iron deficiency can lead to anemia, compromised immune function, and pregnancy complications, often necessitating supplementation (Caetano-Silva et al., 2017; Gandhi et al., 2019; Katuwavila et al., 2016). Currently, two types of iron supplements are available: inorganic and organic. Inorganic iron compounds, while high in iron content, exhibit poor bioavailability and may cause gastrointestinal distress and iron toxicity (Liu et al., 2004). In contrast, edible mushroom polysaccharide-iron complexes, as organic iron supplements, demonstrate superior chelating ability, enhanced bioavailability, and improved absorption compared to their inorganic counterparts (Shi et al., 2013; Wang, Li, Liu, et al., 2015). This review comprehensively examines the preparation processes, structural characteristics, and biological activities of these complexes, providing a robust theoretical foundation for future research and development.

2.1. Preparation of edible mushroom polysaccharide-iron complexes

Iron polysaccharide complexes are primarily synthesized via chemical synthesis or composite membrane simulated biomineralization method. While biomimetic mineralization mimics natural processes, yielding structures resembling natural products, its complexity and low yields impede large-scale production (Chan et al., 2009). Conversely, chemical synthesis methods, particularly the Co-thermal $FeCl_3$ approach, offer operational simplicity, controllable conditions, and high yields, making them more suitable for industrial applications (Chi et al., 2018). The *Co*-thermal $FeCl_3$ method involves preparing a polysaccharide-sodium citrate solution, heating to 65–70 °C, adding it dropwise to 2 mol/L $FeCl_3$ under stirring, adjusting pH to 8.0–9.0 with 2 mol/L NaOH, continuing $FeCl_3$ and NaOH addition until reddish-brown precipitate forms, maintaining at 65–80 °C for 1 h, centrifuging at 8000 rad/s for 10 min, and precipitating the supernatant with anhydrous ethanol (Gao, Huang, et al., 2018)(**Fig. 2**). The principle of this method is that under alkaline conditions, ferric iron (Fe^{3+}) is polymerized through oxygen bridge or hydroxyl bridge to form ferric citrate polymer, and a large amount of citric acid is free (Jing et al., 2022). The reaction completes within 1–2 h, demonstrating high efficiency (Chi et al., 2018). After successful complexation, the iron content in the complexes was measured mainly by 1,10-phenanthroline method (Jing et al., 2022). Consequently, it has become the most common approach for synthesizing edible mushroom polysaccharide-iron complexes. **Table 2** summarizes the main reaction conditions and iron content of complexes prepared using this method.

Zhong et al. (2021) synthesized *Agaricus blazei murill* polysaccharide-iron (III) complex (ABMP-Fe (III)) using *Agaricus blazei murill* polysaccharides (ABMP) and $FeCl_3$ as raw materials, the optimum conditions for the synthesis of ABMP-Fe (III) were pH 8, temperature 70 °C, and 1:2 ratio of sodium citrate to ABMP, and the iron content of ABMP-Fe (III) was measured to reach 15.8–16.68%. Dong et al. (2017) synthesized *Flammulina velutipes* polysaccharide-iron (III) complexes (FVP-Fe (III)) by Co-thermal synthesis of the $FeCl_3$ method and orthogonal experiments to determine the optimum experimental conditions for the synthesis of FVP-Fe (III) was for pH 7, temperature 50 °C, and the ratio of sodium citrate to *Flammulina velutipes* polysaccharides (FVP) was 3:4, and the iron content of FVP-Fe (III) was measured to reach 7.19–7.67%. Wu et al. (2023) synthesized *Pleurotus eryngii* polysaccharide-iron (III) complexes (PEP-Fe (III)) using Co-thermal synthesis of the $FeCl_3$ method and determined the experimental reaction conditions as pH 8, temperature 65 °C, the ratio of sodium citrate to *Pleurotus eryngii* polysaccharides (PEP) was 1:4. The iron content of PEP-Fe (III) was measured to reach 5.56%. Yu et al. (2018) prepared *Tremella fuciformis* polysaccharide-iron (III) complexes (TFP-Fe (III)) by Co-thermal synthesis of the $FeCl_3$ method; the optimum conditions for the synthesis of TFP-Fe (III) were pH 8 and temperature 70 °C, the sodium citrate to *Tremella fuciformis* polysaccharides (TFP) ratio was 3:4, and the iron

Table 2
Main reaction conditions for preparation of edible mushroom polysaccharide iron complexes by ferric chloride co-thermal synthesis.

Source of polysaccharides	Factors	Optimum extracting technology	Iron content (%)	Ref.
Agaricus Blazei Murill	Temperature (A); pH (B); the ratio of sodium citrate to ABMP (C)	A = 70°C B = 8.0 C = 1:2 (g/g)	15.8–16.7	(Zhong et al., 2021)
Flammulina velutipes	Temperature (A); pH (B); the ratio of sodium citrate to FVP (C)	A = 50°C B = 7.0 C = 3:4 (g/g)	7.2–7.7	(Dong et al., 2017)
Pleurotus eryngii	Temperature (A); pH (B); the ratio of sodium citrate to PEP (C)	A = 65°C B = 8.0 C = 1:4 (g/g)	5.6	(Wu et al., 2023)
Tremella fuciformis	Temperature (A); pH (B); the ratio of sodium citrate to TFP (C)	A = 70°C B = 8.0 C = 3:4 (g/g)	3.8	(Yu et al., 2018)
Sparassis latifolia	Temperature (A); pH (B); the ratio of sodium citrate to SLP (C)	A = 70°C B = 7.0 C = 1:2 (g/g)	37.5–37.8	(He et al., 2022)
Auricularia auricula	Temperature (A); pH (B); the ratio of sodium citrate to AAP(C)	A = 80°C B = 8.0 C = 1:1 (g/g)	28.4	(Liu et al., 2019)

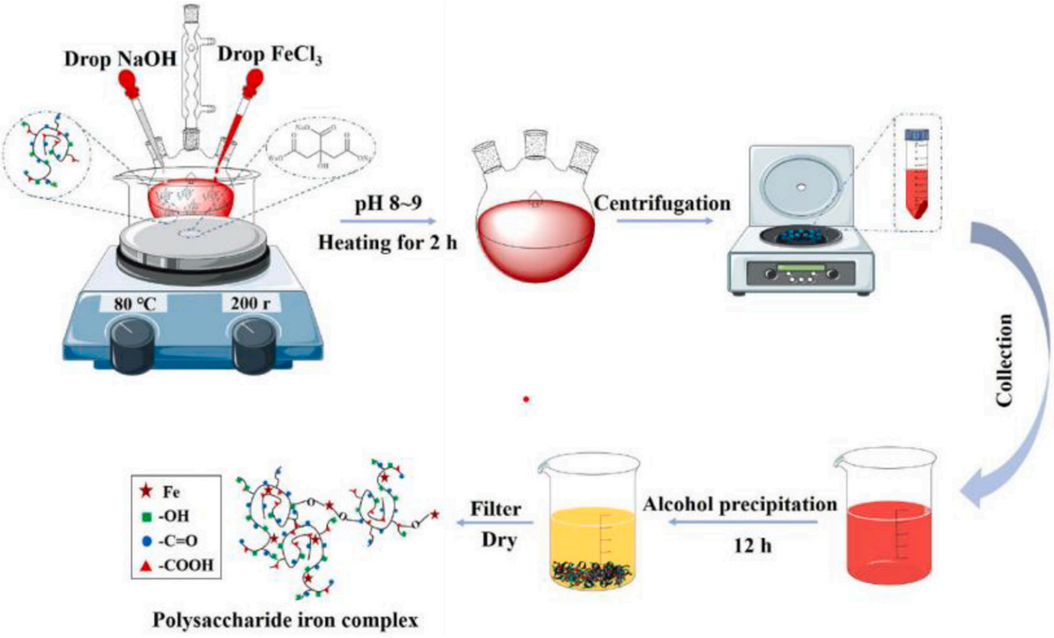

Fig. 2. Flow chart of the Co-thermal $FeCl_3$ method (Jing et al., 2022).

content was measured at 3.75%. He et al. (2022) synthesized *Sparassis latifolia* polysaccharide-iron (III) complexes (SLP-Fe (III)) under the experimental conditions of pH 7, temperature 70 °C, and 1:2 ratio of sodium citrate to *Sparassis latifolia* polysaccharides (SLP) and measured the iron content of SLP-Fe (III) to reach 37.52–37.76%. Liu et al. (2019) synthesized *Auricularia auricula* polysaccharide-iron (III) complexes (AAP-Fe (III)) under the experimental conditions of pH 8, temperature 80 °C, and 1:1 ratio of sodium citrate to *Auricularia auricula* polysaccharides (AAP) and measured the iron content of AAP-Fe (III) up to 28.4%.

The iron content of polysaccharide-iron complexes varies significantly among different edible mushroom species. SLP-Fe(III) and AAP-Fe(III) exhibit relatively high iron content, while FVP-Fe(III), PEP-Fe (III), and TFP-Fe(III) show lower levels. These variations may be attributed to differences in polysaccharide-to-sodium citrate ratios, reaction temperatures, or inherent properties of the raw materials. Based on these observations, optimal reaction conditions for synthesizing edible mushroom polysaccharide-iron complexes can be inferred as pH 7–8, temperature 70–80 °C, and a polysaccharide-to-sodium citrate ratio of 1:1–2.

While the Co-thermal $FeCl_3$ method is predominantly used for synthesizing polysaccharide-iron complexes from edible mushrooms, alternative methods such as fluid-addition $FeCl_3$ synthesis, ammonium ferric sulfate method, and composite membrane simulated biomineralization exist. However, these alternatives have limited practical applications. Further research and development of preparation methods for edible mushroom polysaccharide-iron complexes are necessary to provide a robust foundation for structural characterization and bioactivity studies.

2.2. *Structural characterization of edible mushroom polysaccharide-iron complexes*

Fourier transform infrared spectroscopy (FT-IR), Differential scanning calorimetry (DSC), Thermogravimetric analysis (TGA), and Scanning electron microscopy (SEM) are commonly employed to investigate the structure of polysaccharide-iron complexes. He et al. (2022) utilized FT-IR to analyze SLP-Fe(III), revealing similar characteristic absorption peaks between SLP and SLP-Fe(III). Notably, the complex exhibited peaks at 582.74 cm^{-1} and 684.93 cm^{-1}, consistent with β-FeOOH (Lu et al., 2016), indicating SLP-Fe(III) interaction. Similarly, Cheng et al. (2019) observed that the FT-IR spectra of FVP-Fe(III) complex displayed characteristic absorptions at 860–900 cm^{-1} and 630–680 cm^{-1}, aligning with β-FeOOH (Yang et al., 2011). Zhong et al. (2021) corroborated β-FeOOH formation in ABMP-Fe(III) through FT-IR and XRD analyses, while maintaining the polysaccharide backbone structure. Zhang, Zhang, Gu, et al. (2021) conducted methylation analysis on synthesized *Cordyceps militaris mycelia* polysaccharide-iron (III) complexes (CMP-Fe (III)), revealing a highly branched structure composed of → 2)-β-D-Glcp-(1 → and → 2,4)-α-D-Glcp-(1 → units. Additionally, Congo red assay demonstrated the flocculation effect of CMP-Fe(III) on Congo red solution. Zhang, Khan, et al. (2019) utilized SEM to examine *Hypsizygus marmoreus* polysaccharides (HMP) and *Hypsizygus marmoreus* polysaccharide-iron (III) compexes (HMP-Fe (III)). HMP exhibited a smooth, compact surface with flake-like or crumb-like morphology, while HMP-Fe (III) chelates displayed irregular, bumpy surfaces, suggesting increased molecular repulsion and weakened attraction. Similarly, Liu et al. (2019) employed SEM to analyze morphological changes in AAP upon iron complexation. Uncomplexed AAP showed a rough, blocky structure with an inhomogeneous surface, whereas AAP-Fe (III) complexes formed relatively smooth, flaky structures. DSC and TGA further revealed high thermal stability of AAP-Fe (III) within the temperature range of 50–256 °C.

In summary, the complexation reaction affects polysaccharides' molecular chain conformation, size, dimension, and apparent morphology. The complexation of edible mushroom polysaccharides with iron results in the formation of β-FeOOH peaks at 582.74 cm^{-1} and 684.93 cm^{-1} or 860–900 cm^{-1}, 630–680 cm^{-1}, and possibly γ-FeOOH peaks, but there are fewer reports on the formation of γ-FeOOH peaks by edible mushroom polysaccharide-iron complexes. Molecular and morphological changes and enhanced thermal stability are also observed, which is essential for further understanding polysaccharide-iron complexes' nature and potential applications.

2.3. *Bioactivity of edible mushroom polysaccharide-iron complexes*

Edible mushroom polysaccharide-iron complexes not only preserve but also augment the inherent bioactivities of the precursor polysaccharides, notably their antioxidant and anti-anemic efficacies. Cheng et al. (2019) found that the FVP-Fe (III) complex exhibits superior cellular uptake and lower intestinal cytotoxicity compared to traditional iron supplements. This advantageous profile potentially reduces adverse effects associated with oral administration. Enhanced bioavailability and improved safety characteristics position FVP-Fe (III) as a promising candidate for novel iron supplementation. Zhang, Wang, et al. (2019) demonstrated that HMP-Fe (III) exhibited superior 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging ability compared to pure HMP, providing a theoretical foundation for HMP-Fe (III) as a potential novel iron supplement with antioxidant properties. He et al. (2022) demonstrated that SLP-Fe(III) complexes exhibited significantly enhanced scavenging capacities for superoxide anion ($O2•^{-}$) and hydroxyl radical (•OH) compared to uncomplexed SLP. Dong et al. (2017) employed a $FeCl_3$ *Co*-thermal synthesis method to generate two *Flammulina velutipes* polysaccharide-iron complexes (FVP-Fe and FVP2-Fe). These complexes exhibited potent bacteriostatic activity against *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis*. Additionally, they demonstrated superior antioxidant properties, evidenced by their capacity to scavenge diverse free radicals, augment reducing power, and attenuate Fe^{2+}/H_2O_2-mediated lipid peroxidation in murine hepatic homogenates. The results suggested that FVP was a significantly strong and natural antioxidant. In addition, FVP-Fe and FVP2-Fe might be used as effective antibacterial agents. Shi, Cheng, et al. (2023) investigated a novel FVP-Fe(III), for treating iron-deficiency anemia (IDA). In vitro studies revealed sodium-dependent glucose transporter-1 (SGLT1) and glucose transporter-2 (GLUT2)-mediated uptake, with multidrug resistance-associated protein-2 (MRP-2) facilitating efflux. FVP-Fe(III) outperformed ferrous sulfate in vivo, improving hematological parameters through hepcidin downregulation and microbiota restoration. Vitamin C enhanced its efficacy, suggesting FVP-Fe(III)'s potential as an innovative iron supplement.

The preparation, structural characterization, and biological activity assessment of edible mushroom polysaccharide-iron complexes (**Fig. 3**) reveal that the iron content in these complexes varies depending on the ratio of polysaccharide to trisodium citrate, reaction temperature, and raw material differences. FT-IR, DSC, TGA, and SEM analyses demonstrate that iron coordination with edible mushroom polysaccharides induces changes in molecular chain conformation, size, and apparent morphology, including the formation of distinct β-FeOOH peaks. These structural modifications enhance thermal stability and improve antioxidant and anti-anemia activities (Liu et al., 2019). While reports on γ-FeOOH peaks are limited, understanding these alterations is crucial for elucidating the properties and applications of polysaccharide-iron complexes.

3. Research progress of edible mushroom polysaccharide-selenium complexes

Selenium, a critical trace element, modulates enzymatic functions, enhances immune efficiency, regulates thyroid hormone metabolism, and exhibits anti-cancer properties (Oropeza-Moe et al., 2015; Rostami et al., 2020; Wrobel et al., 2016; Yang et al., 2017). While supplementation is crucial, selenium's narrow safety margin necessitates careful

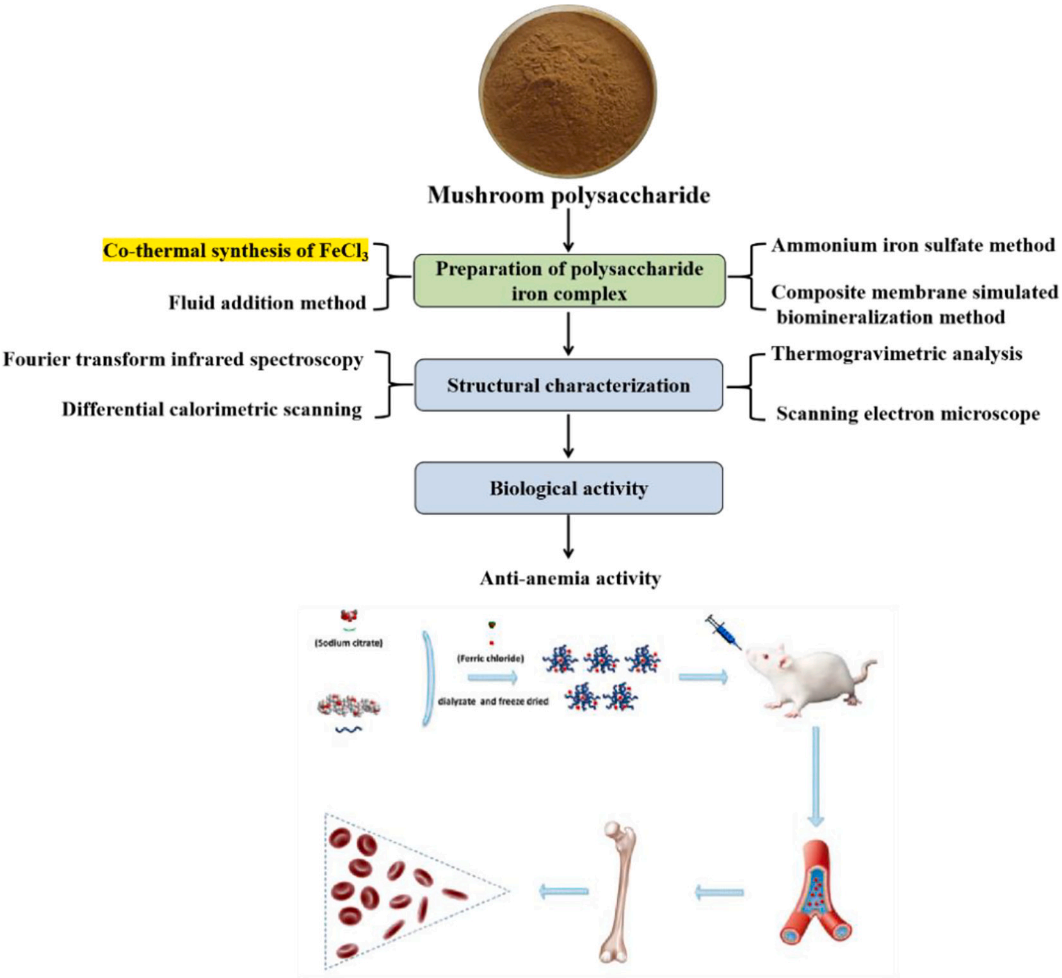

Fig. 3. Preparation and research roadmap of edible mushroom polysaccharide-iron complexes. Schematic diagram of iron deficiency anemia supplementation in vivo (Jia et al., 2019).

intake management (Lenz & Lens, 2009). Organic selenium supplements (e.g., selenium polysaccharides, selenoproteins) are preferred over inorganic forms (e.g., sodium selenite, selenate) due to higher bioavailability and lower toxicity (Xu et al., 2021). Notably, edible mushrooms like *Ganoderma lucidum*, *Lentinula edodes* valuable selenium sources, capable of biotransforming inorganic selenium into organic forms (Hadrup & Ravn-Haren, 2020; Kiełczykowska et al., 2018).

3.1. Preparation of edible mushroom polysaccharide-selenium complexes

Currently, the main methods for preparing selenium polysaccharides include selenium-enriched cultivation and chemical synthesis (Cheng et al., 2018). Selenium-enriched cultivation involves adding Na_2SeO_3 or selenium-containing fertilizers to microbial media, resulting in bio-transformed, organic selenium polysaccharides with enhanced bioavailability but lower yields due to biological and environmental factors (Zhou et al., 2020). Conversely, chemical synthesis utilizes reactions between polysaccharides and selenium compounds (e.g., HNO_3-selenate, HNO_3-Na_2SeO_3, or Se_2Cl_2), based on selenium ester formation with semi-acetylated C_6-OH groups (Cheng et al., 2018; Yang et al., 2020). While offering a more stable production process, chemically synthesized selenium polysaccharides may have reduced bioavailability. Consequently, selenium-enriched cultivation remains the primary approach for producing selenium polysaccharides from edible mushroom polysaccharides (Zhou et al., 2020). After successful complexation, the selenium content in the complexes was measured by flame atomic absorption spectrometry (FAAS), graphite furnace atomic absorption spectrometry (GFAAS), atomic fluorescence spectrometry

Table 3
Main reaction conditions for preparation of polysaccharide selenium complexes from edible mushrooms by selenium-enriched culture and chemical synthesis.

Source of polysaccharides	Factors	Optimum extracting technology	Selenium content	Ref.
Agrocybe cylindracea	Na_2SeO_3 -concentration (A);Temperature (B); Incubation time (C)	A = 6 μg/mL B = 25°C C = 10 d	1.76 ± 0.10 mg/g	(Liu et al., 2016)
Cordyceps militaris	Temperature (A); Time (B); HNO_3 -concentration (C); Na_2SeO_3 addition (D)	A = 60°C B = 6 h C = 0.6%, v/v D = 1.0 g	16.30–576.40 μg/g	(Zhu et al., 2016)
Cordyceps militaris	Temperature (A); Time (B); HNO_3 -concentration (C); Na_2SeO_3 addition (D)	A = 60°C B = 6 h C = 0.6%, v/v D = 1.0 g	541.30 g/g 863.70 g/g 623.30 g/g	(Liu et al., 2017)
Ganoderma lucidum mycelia	Na_2SeO_3 -concentration (A); pH (B); Incubation time (C)	A = 10 mg/L B = 7 C = 14 d	18.91 ± 1.80 μg/g	(Dong et al., 2021)

(AFS), inductively coupled plasma mass spectrometry (ICP-MS). **Table 3** summarizes the key reaction conditions, analytical methods, and selenium contents of complexes prepared via selenium-enriched cultivation and chemical synthesis.

Liu et al. (2016) cultivated selenium-enriched *Agrocybe cylindracea* mycelia and extracted selenium-enriched *Agrocybe cylindracea* polysaccharides complexes (Se-ACP) under optimized conditions (extraction temperature: 94.99°C, pH 9.0, precipitation temperature: 12°C). The purified selenium-polysaccharide complex was analyzed using FAAS, revealing a selenium content of 1.76 ± 0.10 mg/g. Zhu et al. (2016) synthesized *Cordyceps militaris* polysaccharide-selenium complexes (Se-CMP) using 40 mL of 0.6% (*v*/*v*) HNO_3, 1.0 g Na_2SeO_3, and 1.0 g $BaCl_2$ as catalysts. The selenium content of the complexes, determined by GFAAS, ranged from 16.3 to 576.4 μg/g. Liu et al. (2017) made three *Cordyceps militaris* polysaccharide-selenium complexes (Se-CMP-I、Se-CMP-II and Se-CMP-III), and the selenium contents were measured as 541.3, 863.7, and 623.3 g/g by GFAAS. Dong et al. (2021) enriched *Ganoderma lucidum mycelium* with selenium to produce selenium-polysaccharide complexes (Se-GLP). AFS analysis revealed that the selenium content in Se-GLP was 18.91 ± 1.8 μg/g. Wang, Zhang, et al. (2019) extracted selenium polysaccharides from cultured selenium-enriched *Auricularia auricular* polysaccharide complexes (Se-AAP). The extraction process involved soaking in 6-fold volumes of distilled water for 1 h, followed by double decoction at boiling temperature for 1.5 h each, centrifugation at 4500 rpm for 5 min, concentration of the supernatant, and freeze-drying. ICP-MS analysis determined the selenium content to be 31.79 mg/kg.

In summary, selenium-enriched culture is currently the primary approach for producing selenium complexes from edible mushroom polysaccharides. However, the efficiency of selenium biotransformation is influenced by multiple factors, leading to inconsistent selenium content in the final selenium polysaccharide products. Consequently, further research and development are necessary to optimize the preparation methods for selenium complexes derived from edible mushroom polysaccharides.

3.2. *Structural characterization of edible mushroom polysaccharide-selenium complexes*

Currently, the methods commonly used for the structural study of polysaccharide selenium complexes include fourier transform infrared spectroscopy (FT-IR), methylated analysis, scanning electron microscope (SEM), and so on. Liu et al. (2018) performed FT-IR analysis of selenium-enriched *lentinula edodes* polysaccharide complexes and found that two characteristic absorption peaks appeared at 600–750 cm^{-1}, caused by S=O and S-O-C stretching vibrations after selenidation. In addition, selenium-enriched *lentinula edodes* polysaccharide complexes of the ultraviolet and visible spectrum showed a strong absorption peak at 356 nm, indicating the presence of selenium. Zhu et al. (2016) analyzed the surface morphology of Se-CPM by SEM. The results showed that the surface of Se-CMP was rougher than that of *Cordyceps militaris* polysaccharides (CMP), with several regular circular pores, and that the spherical and short stick-like surface of the leaf-like structure of CMP structures became separated parts with distinct cut edges in Se-CMP. These changes may be due to the modification process that changes the interaction, linking mode, and Van der Waals force among polysaccharide molecules. And determined that Se-CMP and CMP have similar primary compositions and chemical structures based on monosaccharide analysis, FT-IR, and ^{13}C NMR results. The ^{13}C NMR spectra revealed that C-6 substitution predominates in Se-CMP, as indicated by signals from O-substituted carbons. Qian et al. (2023) found that *Morchella esculenta (L.) Pers* polysaccharide-selenium complexes (Se-MEP) had a similar spectral profile to *Morchella esculenta (L.) Pers* polysaccharides (MEP) by FT-IR spectroscopy. The low-intensity absorption peaks at 927 cm^{-1} and 854 cm^{-1} indicated the presence of α-glycosidic bonds. Absorption peak at 1025 cm^{-1} suggests that organic selenium may bind to MEP through O-Se-O bonding, which tentatively confirms the presence of organic selenium in Se-MEP without alteration of the structure of the functional group. Zhang, Zhang, Liu, et al. (2021) elucidated the chain structure of selenium polysaccharides in selenium-enriched *Pleurotus ostreatus* (Se-POP) using methylation analysis and 2D NMR. The main chain comprises →[3)-β-D-Glc*p*-(1 → 2)-β-D-Glc*p*-(1 → 3,6)-β-D-Glc*p*-(1 → 3)-β-D-Glc*p*-(1→] → α-D-Glc*p*-(1 → 6)-α-D-Glc*p*-(1→), with α-D-Glc*p*-(1 → [4)-α-D-Glc*p*-(1→)]4 → branches attached to the O-3 of →3,6)-β-D-Glc*p*-(1→) linkages. Yao et al. (2023) conducted methylation analysis on selenium-enriched *Cordyceps militaris* polysaccharides compexes, revealing multiple sugar residues. Three predominant residues were identified: T-Gal*p*-(1→, → 2)-Gal*p*-(1→, and → 6)-Man*p*-(1→, comprising both α and β configurations, with α configurations predominating. These findings suggest that galactose and mannose, linked by specific glycosidic bonds, form the backbone of selenium-enriched *Cordyceps militaris* polysaccharide compexes (Se-CMP). Zhang et al. (2020) compared the mixed solution with pure Congo red solution and observed a negligible shift in λ_{max} from 480 nm to 500 nm, suggesting that selenium-enriched *Pleurotus ostreatus* polysaccharide compexes (Se-POP) likely exists in a random coil conformation rather than a triple-helix structure. Ma et al. (2022) found that *Pleurotus ostreatus* polysaccharide-selenium complexes (Se-POP) has a sizeable lamellar structure with tiny irregular pores on its surface similar to Se-enriched tea polysaccharides (Wang, Li, & Yang, 2015) by SEM analysis, and the regularity of its structure is fragmented, intertwined, and somewhat rough.

In summary, the structure of the selenide polysaccharide complexes from edible mushrooms could be characterized in detail by different analytical methods such as FT-IR, SEM, UV, and methylated analysis. These analyses showed that the selenidation treatment may affect the functional groups, intermolecular interactions, surface morphology, and molecular backbone of the polysaccharides. Since the structural features of polysaccharides are closely related to the biological functions, the structural changes after selenidation modification may alter the functional and biological properties of selenium polysaccharides (Yang et al., 2021).

3.3. *Bioactivity of edible mushroom polysaccharide-selenium complexes*

Polysaccharide-selenium complexes derived from edible mushrooms significantly enhance selenium's bioavailability and biological effects while mitigating potential side effects, thus improving safety profiles (Gao, Zhang, et al., 2018; Yang et al., 2020; Zhang et al., 2020). These complexes exhibit diverse physiological activities, including antioxidant, anti-tumor, immunomodulatory, hypoglycemic, and hepatoprotective effects. By optimizing selenium absorption and utilization, they offer comprehensive health support through multiple mechanisms, underscoring their potential as an efficacious and safe form of selenium supplementation (Malinowska et al., 2009). This review synthesizes current knowledge on the beneficial physiological activities of these complexes, highlighting their promising role in enhancing human health.

3.3.1. *Immunological activity*

More and more pharmacological and clinical studies have shown that edible mushroom polysaccharide-selenium complexes could effectively regulate and enhance the body's immune function by promoting cytokine production and regulating cell signaling pathways (Li et al., 2018). Kaleta et al. (2021) found that selenium-enriched *Lentinus edodes* polysaccharide (Se-LEP) was effective in inhibiting the proliferation of human peripheral blood mononuclear cells, decreasing the production of tumor necrosis factor (TNF)-α by CD^{3+} T-cells, and reduce the cytotoxicity of natural killer (NK) cells. These findings suggest that Se-LEP exhibits specific immunosuppressive properties, indicating its potential as a novel immunosuppressive agent. Qin et al. (2017) found that selenated *Hericium erinaceus* polysaccharide (Se-HEP) significantly reduced endocytosis and enhanced cytokine (IL-12 and IFN-γ) production in dendritic cells and activated TLR4 signaling by increasing ERK, p38, and JNK phosphorylation as well as by promoting the intranuclear translocation of p-c-Jun, p-CREB, and c-Fos. TLR4 signaling is activated by increasing ERK and p38 and JNK phosphorylation and promoting intranuclear translocation of p-c-Jun, p-CREB, and c-Fos. In addition, sHEP activates NF-κB signaling, as shown by the degradation of IκBα and nuclear translocation of p65 and p50. Therefore, Se-HEP is considered to be a potent immunostimulant. Wang, Zhang, et al. (2022) demonstrated that Se-POP significantly enhances RAW264.7 cell proliferation and phagocytosis in vitro. It upregulates cluster of differentiation 80 or cluster of differentiation 86 (CD80/CD86) co-stimulatory molecules and promotes NO, ROS, TNF-α, IL-1β, and IL-6 secretion via NF-κB activation. These findings indicate effective RAW264.7 cell activation by Se-POP, suggesting its potential application in immunomodulatory therapeutics or functional foods. Qian et al. (2023) found that Se-MEP activate the TLR4-TRAF6-MAPKs-NF-κB cascade signaling pathway, thereby enhancing macrophage activity and phagocytic ability, promoting the secretion of pro-inflammatory cytokines, and exerting immunomodulatory functions. The results indicate that Se-MEP are potential natural immune system enhancers that can be used as food or medicine to boost human immunity.

3.3.2. *Anti-tumor activity*

While conventional cancer therapies like chemotherapy and radiotherapy effectively target malignant cells, they often cause severe side effects and have limited efficacy. Edible mushroom polysaccharide-selenium complexes offer a promising alternative, demonstrating lower toxicity, broad-spectrum inhibition of various cancer cells (including hepatocellular carcinoma and lung cancer), and minimal effects on normal cells (**Fig. 4a**)(Li et al., 2019).

Zhang et al. (2020) found that Se-POP could be effective anti-tumor by promoting apoptosis, which could reduce the cell viability of human lung (A549), ovarian (SKOV3), hepatocellular carcinoma (HepG2), and breast cells (MCF-7) and did not have a significant effect on normal cells. These findings provide a theoretical foundation for the potential application of Se-POP as antitumor agents or functional foods, particularly against gastrointestinal malignancies. Liu et al. (2017) employed the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay to investigate the in vitro anti-tumor effects of Se-CMP on HepG-2 and A549 cells. Their findings revealed a positive correlation between the selenium content in these polysaccharides and their anti-tumor activity. Dong et al. (2021) used Se-GLP to act on mouse hepatocellular carcinoma cells, and the results showed a direct inhibitory effect on cancer cells when the dose was in the range of 12.5–200 μg/mL. The result suggests that Se-GLP can be used as a potential functional selenium supplement. Zhang, Zhang, Liu, et al. (2021) demonstrated that Se-POP reduces Mucosal gastric cancer-803 (MGC-803) and Human colon tumor-116 (HCT-116) cell viability, induces apoptosis, and inhibits migration and invasion in vitro. The mechanism likely involves

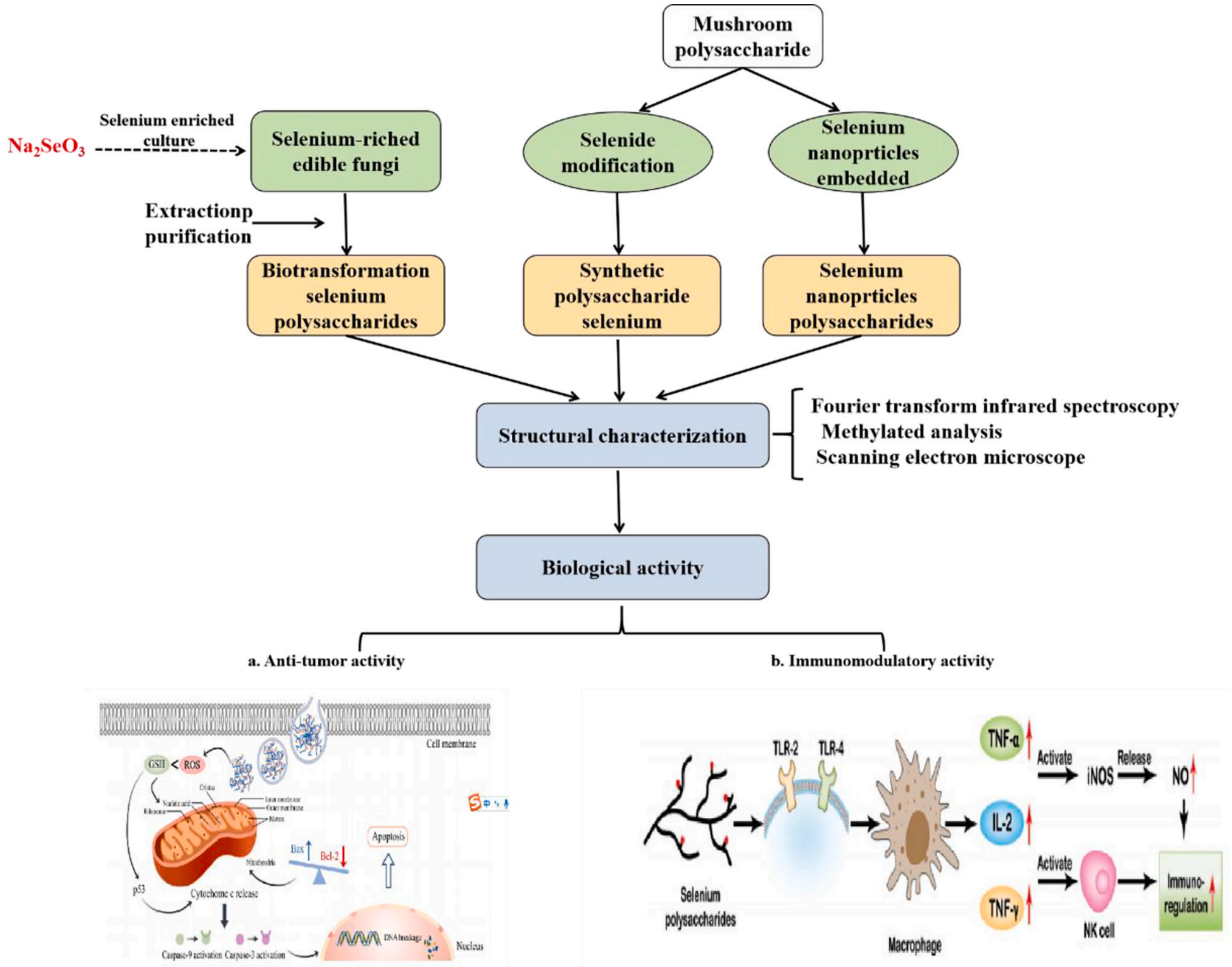

Fig. 4. Preparation and research roadmap of edible mushroom polysaccharide-selenium complexes. (a) Schematic diagram of mitochondrial apoptosis pathway (Shi, Cheng, et al., 2023). (b) Schematic diagram of selenopolysaccharide enhancement of immune activity (Zhou et al., 2020).

disruption of the Bax/Bcl-2 protein ratio, suggesting mitochondria-mediated apoptosis, and inhibition of epithelial-mesenchymal transition. Cell counting kit-8 (CCK-8) assays revealed dose-dependent cytotoxicity against cancer cells without affecting normal cell growth. These findings provide a foundation for further structure-activity relationship studies and potential applications of Se-POP as an anti-gastrointestinal tumor agent or functional food ingredient.

3.3.3. Anti-aging activity

Wang et al. (2019) demonstrated that Se-AAP mitigated D-galactose-induced memory impairment, oxidative stress, and inflammation via the RAGE/MAPK/NF-κB pathway. This finding offers novel insights into the protective mechanisms of selenocompounds against aging processes, suggesting Se-AAP as a potential therapeutic agent for age-related neurological disorders.

3.3.4. Hypoglycemic activity

Edible mushroom polysaccharide-selenium complexes exhibit hypolipidemic and hypoglycemic activities. Yu et al. (2009) found that selenium-enriched *Coprinus comatus* mycelial polysaccharide complexes significantly reduced blood glucose levels and enhanced antioxidant enzymatic and non-enzymatic activities, particularly in the liver and kidneys, contributing to their hypoglycemic and hypolipidemic properties. Additionally, Yu et al. (2021) demonstrated that Se-CMP ameliorated fat accumulation, dyslipidemia, inflammation, and gut microbiota dysregulation in obese mice, suggesting its therapeutic potential for lipid metabolism disorders.

The preparation, structural characterization, and biological activity of edible mushroom polysaccharide-selenium complexes (**Fig. 4**) reveal that selenium-enriched culture is the primary production method. However, variable factors affect the method's efficiency, resulting in inconsistent selenium content. Biological methods, generally less efficient than chemical processes, may hinder large-scale production, emphasizing the need for improved preparation techniques. Analytical methods such as FT-IR, SEM, UV, and methylation analysis can elucidate the structural modifications induced by selenidation, including changes in functional groups, intermolecular interactions, surface morphology, and polysaccharide backbone. These modifications potentially alter the complexes' biological functions and properties. Notably, selenidation significantly enhances the immunomodulatory, anti-tumor, and hypoglycemic activities of these complexes, offering promising avenues for future therapeutic applications.

4. Research progress of edible mushroom polysaccharide-zinc complexes

Zinc, an essential micronutrient for various physiological functions, zinc deficiency can lead to health issues such as stunted growth and cognitive decline (Ueda et al., 2006; Zhang et al., 2017). As a result, research on zinc supplements has become a hot topic in recent years. While zinc supplements are available in both inorganic and organic forms, the latter are preferred due to higher bioavailability (Dong et al., 2018). Edible mushroom polysaccharide-zinc complexes, an emerging organic zinc supplement, are gaining scientific attention for their nutritional value, bioactivity, and potential to enhance zinc bioavailability and confer health benefits (Buff et al., 2005; Eshak et al., 2018).

4.1. Preparation of edible mushroom polysaccharide-zinc complexes

Current methods for the preparation of zinc polysaccharides include zinc-rich cultures and chemical synthesis. Zinc-enriched culture, a technique for preparing zinc-enriched edible mushroom polysaccharides, involves supplementing the culture medium with zinc sources (e.g., $ZnSO_4$) to enhance zinc content in edible mushrooms (Lee et al., 2020). However, this approach is time-consuming and yields inconsistent results. Chemical synthesis, the most prevalent method, typically uses $ZnCl_2$ or $ZnSO_4$ to form stable -O-Zn bonds with polysaccharide functional groups (Li et al., 2016). This approach enables precise control over zinc content and complex structure, facilitating large-scale production and reproducibility (Bai et al., 2022). After successful complexation, the selenium content in the complexes was measured by flame atomic absorption spectrometry (FAAS), graphite furnace atomic absorption spectrometry (GFAAS). **Table 4** summarizes the main reaction conditions and zinc contents of the complexes prepared by chemical synthesis.

Li (2010) synthesized *Boletus* polysaccharide-znic complexes (BP-Zn) by reacting $ZnSO_4$ (0.45 mol/L) with *Boletus* polysaccharides (0.9 g/mL) at 90 °C for 4 h. The zinc content of the complexes, determined by FAAS, was 2.64 μg/g. Long (2023) prepared *Auricularia polytricha* polysaccharide-znic complexes (APP-Zn) by reacting $ZnSO_4$ with *Auricularia polytricha* polysaccharides (APP) under the experimental conditions of time 2 h, temperature 70 °C, pH 4.5, and $ZnSO_4$ (0.1 mol/L) addition 15 mL, and the binding rate of AAP-Zn was (64.64 ± 0.67) %. Liu et al. (2021) synthesized *Auricularia cornea ehrenb* polysaccharide-zinc (ACEP-Zn) complexes under conditions of a 10:8 (*w*/w) ratio of *Auricularia cornea Ehrenb* polysaccharides (ACEP) to $ZnSO_4$ (0.60 mol/L), pH of 6, reaction temperature of 50 °C, and reaction time of 2 h. The zinc content was measured as 5.41 ± 0.01 mg/g using a GFAAS. Zhao et al. (2017) prepared *Flammulina velutipes* polysaccharide-Znic complexes (FVP-Zn) at a $ZnSO_4$ concentration of 6 mg/mL, a temperature of 30 °C, a chelation time of 8 h, and a pH of 5. The Zn content in FVP-Zn was determined to be 0.18 mg/mg by FAAS.

In conclusion, synthesis routes and conditions significantly influence the zinc content and binding rate of the complexes. Further optimization of preparation methods is therefore necessary to enhance efficiency and yield.

4.2. Structural characterization of edible mushroom polysaccharide-zinc complexes

The zinc structure of edible mushroom polysaccharides is typically characterized using UV–Vis spectroscopy, FT-IR, and SEM. Long (2023) demonstrated through UV analysis that neither APP nor APP-Zn

Table 4
Main reaction conditions for preparation of edible mushroom polysaccharides-zinc complexes by chemical synthesis.

Source of polysaccharides	Factors	Optimum extracting technology	Selenium content	Ref.
Boletus	$ZnSO_4$ concentration (A); Boletus polysaccharide concentration (B); temperature (C),; Time (D)	A = 0.45 mol/L B = 0.90 g/mL C = 90°C D = 4 h	2.64 μg/g	(Li et al., 2010)
Auricularia polytricha	$ZnSO_4$ concentration (A); Temperature (B); pH (C); Time (D)	A = 0.10 mol/L B = 70°C C = 4.5 D = 2 h	16.30–576.40 μg/g	(Long et al., 2023)
Auricularia cornea ehrenb	$ZnSO_4$ (A); Temperature (B); pH (C); Time (D)	A = 0.60 mol/L B = 50°C C = 6 D = 2 h	5.41 ± 0.01 mg/g	(Liu et al., 2021)
Flammulina velutipes	$ZnSO_4$ (A); Temperature (B); pH (C); Time (D)	A = 6.00 mg/mL B = 30°C C = 5 D = 8 h	0.18 mg/mg	(Zhao et al., 2017)

exhibited absorption peaks between 260 and 280 nm, indicating the absence of nucleic acids and proteins. Furthermore, the zinc complex showed enhanced absorption intensity compared to the polysaccharide alone, likely due to the binding of Zn^{2+} to reactive functional groups such as -OH in the APP. Xue et al. (2021) utilized FT-IR analysis to characterize the *Hericium erinaceus* polysaccharide-zinc complexes (HEP—Zn), identifying absorption peaks at 3450, 1634, 1376, 1081, and 1039 cm^{-1}. These results suggest the formation of coordination bonds between zinc and carboxylic acid or carboxyl groups in *Hericium erinaceus* polysaccharides (HEP). Du et al. (2023) employed SEM to observe morphological differences between *lentinula edodes* polysaccharides and *lentinula edodes* polysaccharide-zinc complexes. Unchelated polysaccharides exhibited spherical or ellipsoidal structures with smooth surfaces, whereas the zinc complexes displayed irregular, lamellar surfaces, compact structures, and clustered particle formation. These morphological changes suggest that chelation with Zn^{2+} altered the sugar chain arrangement in *lentinula edodes* polysaccharides, indicative of ligand bond formation via interactions between functional groups and Zn^{2+} (Du et al., 2023).

In conclusion, the complexation of edible mushroom polysaccharides with zinc alters the structure and morphology of edible mushroom polysaccharides, probably because the chelation reaction alters the arrangement of the polysaccharide chains, and the formation of ligand bonds after chelation indicates the interaction of functional groups in edible mushroom polysaccharides with Zn^{2+} (Du et al., 2023).

4.3. Bioactivity of edible mushroom polysaccharide zinc complexes

4.3.1. Antioxidant activity

Studies have demonstrated that edible mushroom polysaccharide-zinc complexes exhibit enhanced antioxidant properties compared to their precursor polysaccharides. These complexes effectively mitigate oxidative stress-induced damage to hepatic and renal tissues, as well as atherosclerosis and cardiovascular diseases (Wang et al., 2019; Shi et al., 2024). Gu et al. (2019) found that *Pleurotus eryngii* polysaccharide-zinc complexes (PEP—Zn) exhibited weakened DPPH radical scavenging and enhanced scavenging of hydroxyl radicals and superoxide anion compared to *Pleurotus eryngii* polysaccharides. The result provide a theoretical foundation for the development of PEP-Zn as a novel zinc supplement with potential antioxidant activity. Xue et al. (2021) found that in comparison to HEP, HEP-Zn exhibited good DPPH radiolytic scavenging activity, strong superoxide anion scavenging activity, and slightly weaker hydroxyl radical scavenging activity (**Fig. 5a**). The results indicate that HEP-Zn demonstrates significant potential as a novel zinc supplement or antioxidant for applications in the food industry.

4.3.2. Immunological activity

Zhao et al. (2017) examined the anti-inflammatory effects of FVP-Zn on LPS-stimulated RAW 264.7 macrophages. At 5–50 μg/mL, FVP-Zn exhibited minimal cytotoxicity while effectively suppressing inflammatory cytokine (IL-6, TNF-α, INF-γ) and NO production. Safety was confirmed by OD_{570} values comparable to control groups. Consequently, low concentrations (5–50 μg/mL) were used in LPS-induced inflammation studies, suggesting FVP-Zn's potential as a therapeutic agent.

4.3.3. Hypoglycemic lipid activity and hepatoprotective effects

Both edible mushroom polysaccharides and the metal trace element zinc have hypoglycemic properties, and the complexation enhances the efficacy. Xu, Gao, et al., 2017; Xu, Ren, et al., 2017 investigated the hepatoprotective and antioxidant effects of enzymatic-extractable mycelia polysaccharide-zinc (En-MZPS) from *Pleurotus eryngii* var. *tuoliensis* on hyperlipidemic mice induced by high-fat-high-cholesterol emulsion (HFHCM). Optical microscope observations showed that the liver structure of the control group mice was normal, while the HFHCM group exhibited pathological changes such as swollen hepatocytes, fat vacuole accumulation, and nuclear disappearance. However, following En-MZPS intervention, especially in the high-dose group, there was a significant reduction in fat vacuoles and hepatocyte degeneration, with

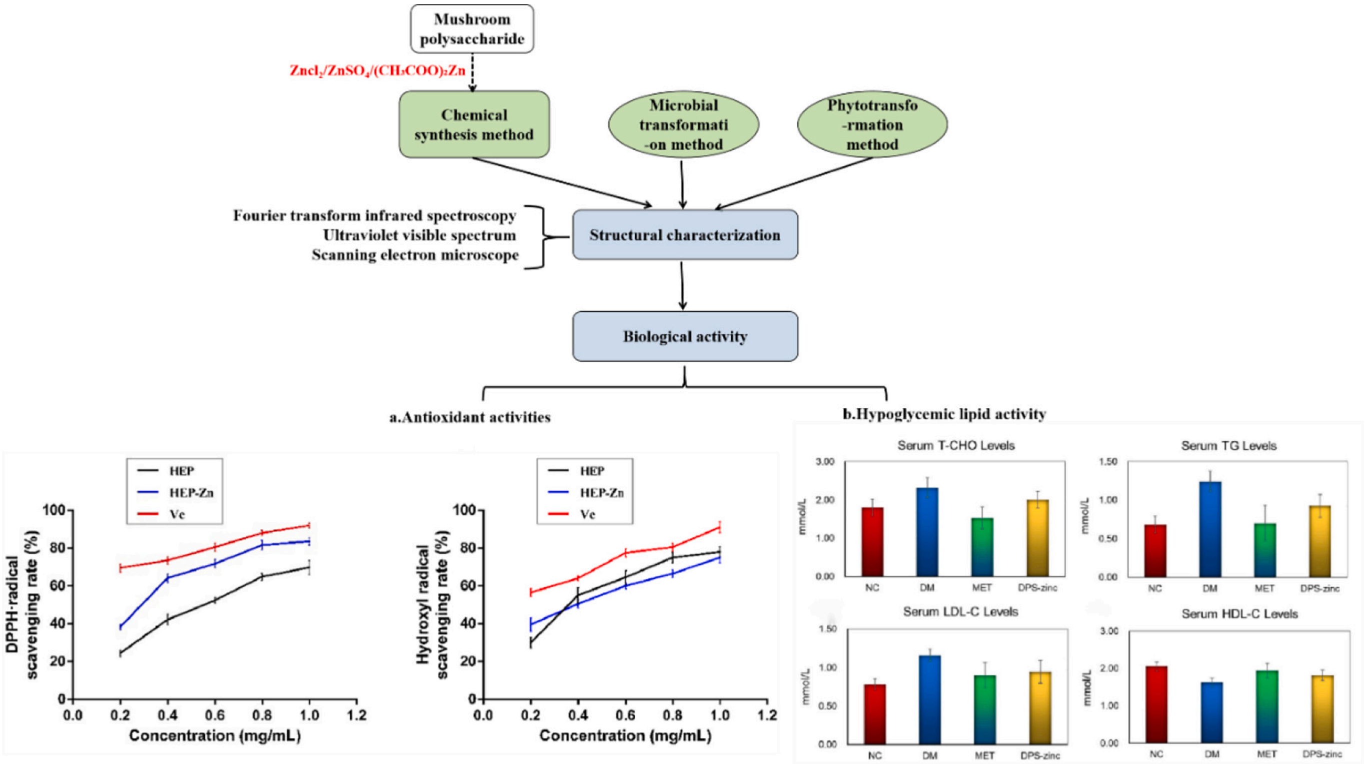

Fig. 5. Preparation and research roadmap of edible mushroom polysaccharide-zinc complexes. (a) The scavenging effect of HEP and HEP–Zn on DPPH radical, hydroxyl radical (Xue et al., 2021). (b) Antihyperlipidemic effects of DPS-zinc in diabetic rats (Zhang et al., 2019).

liver structure approaching normal. These results indicate that En-MZPS significantly inhibits HFHCM-induced morphological changes. Additionally, in vivo experiments showed that En-MZPS reduced adverse lipid and liver enzyme levels, increased beneficial liver function and antioxidant indices, and exhibited a hepatoprotective effect. Liu et al. (2021) demonstrated that ACEP-Zn complexes exhibit enhanced inhibition of α-glucosidase and α-amylase, with structural modifications improving in vitro hypoglycemic activity. At specific concentrations, these complexes increased glucose consumption and enzyme activities in insulin-resistant HepG2 hepatocytes. The complexes' hypoglycemic effects are attributed to mitigation of oxidative stress in hepatocytes and enhanced glucose metabolism. These findings provide a theoretical foundation for applying polysaccharide-zinc complexes in hypoglycemic functional foods, offering potential new avenues for diabetes management and prevention.

Comprehensive analysis indicates that synthesis methods and conditions significantly influence zinc content and binding performance of edible mushroom polysaccharide-zinc complexes. UV, FT-IR, and SEM analyses reveal structural and morphological changes in polysaccharides post-complexation, likely due to chelation-induced rearrangement of polysaccharide chains and Zn^{2+} ligand bond formation (Du et al., 2023). These complexes demonstrate enhanced lipid-lowering, hepatoprotective, and antioxidant activities, underscoring their research and application potential (**Fig. 5**).

5. Research progress of edible mushroom polysaccharide-other metal trace elements complexes

Recent research has expanded beyond the three primary types of edible mushroom polysaccharide-metal trace element complexes to include other trace elements such as Cr, Mn, and Ge. Yin et al. (2014) synthesized *Auricularia auricula* polysaccharide-Cr complexes, achieving a 41.56% chelation rate with Cr^{3+}. Yi et al. (2012) found that Mn ions enhanced antioxidant enzyme activity in *Cordyceps militaris* mycelium, with cordycepin content peaking at 2.32 mg/g at 80 g/L Mn concentration, although higher concentrations inhibited adenosine synthesis. Wang et al. (2015) reported that *Cordyceps militaris* effectively enriched Ge, with organic Ge conversion rate in mycelium reaching a maximum of 85.10% at 200 mg/L Ge concentration in the culture medium.

6. Summary and outlook

Research on edible mushroom polysaccharide-metal trace element complexes, although in its early stages, has shown promising results, particularly in anticancer and antimicrobial properties. Laboratory and animal studies demonstrate benefits in immune enhancement, wound healing, antioxidant capacity, and anti-tumor activity. These findings suggest potential applications in enhancing human health by improving trace element bioavailability and overall well-being. Food and pharmaceutical industries are exploring their use in functional foods, supplements, and biomedical materials.

Despite the progress in research on edible mushroom polysaccharide-metal trace element complexes, several challenges hinder their widespread application in healthcare and disease prevention. These include imbalanced research focus, incomplete preparation methods, lack of standardization and quality control, safety verification concerns, and the need for long-term clinical efficacy studies. Future research should address these issues to facilitate the broader utilization of these complexes in promoting health and preventing diseases.

CRediT authorship contribution statement

Yanbo Hu: Writing – review & editing, Funding acquisition. **Yi Cao:** Writing – original draft. **Yuzhu Shen:** Methodology, Investigation. **Yakun Shan:** Methodology, Investigation. **Jiaxin Liu:** Validation, Methodology. **Yudi Song:** Supervision, Methodology. **Yue Yang:** Supervision. **Jun Zhao:** Writing – review & editing, Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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