INPLASY

Immunomodulatory Effects and Mechanisms of Plant and Edible Fungal Polysaccharides: A Scoping Review Protocol

Corresponding author:
Huijuan Cao

huijuancao327@hotmail.com

Author Affiliation:
Beijing University of Chinese Medicine.

Wang, CL; Liu, WT; Xue, QY; Zhang, WT; Cao, HJ..

ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 January 2026 and was last updated on 31 January 2026.

INTRODUCTION

*R*eview question / Objective This scoping review will be conducted in accordance with the internationally recognized five-stage framework proposed by Arksey and O'Malley, which includes: (1) identifying the research question; (2) identifying relevant studies; (3) study selection; (4) data charting; and (5) collating, summarizing, and reporting the results. The reporting of this review will follow the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines to ensure methodological rigor and transparent reporting.

The objective of this scoping review is to systematically map and synthesize the existing evidence on polysaccharides derived from medicinal plants and edible fungi in the context of immunomodulation. Specifically, this review aims to summarize the current research landscape, explore reported immunomodulatory mechanisms and biological activities, and examine their potential applications. In addition, this review seeks to identify key limitations and research gaps within the existing literature, thereby providing an evidence-informed foundation for future basic research, translational studies, and the development of polysaccharide-based immunomodulatory products.

Background The global prevalence and disease burden of immune-related conditions—including autoimmune diseases, chronic inflammatory disorders, and immune dysregulation syndromes—have continued to increase in recent decades, placing growing pressure on public health systems worldwide. Epidemiological evidence suggests an overall upward trend in both the incidence and prevalence of various autoimmune and immune-mediated diseases. Some studies have estimated that autoimmune diseases may affect approximately 10% of the global population, with certain conditions showing a sustained increase in incidence over time. In particular, age-standardized incidence and prevalence rates of inflammatory diseases such as psoriasis and inflammatory bowel disease have risen steadily in recent years,

contributing substantially to impaired quality of life and increased healthcare resource utilization.

Conventional pharmacological management of immune-related diseases primarily relies on immunosuppressive agents, glucocorticoids, and small-molecule targeted therapies. In clinical settings, immune function may be further compromised by factors such as surgical stress and poor nutritional status, often necessitating additional immunonutritional support. However, existing therapeutic strategies are associated with notable limitations, including systemic adverse effects related to long-term use, elevated risks of infection due to immunosuppression, and the development of drug tolerance in some patients. These challenges can adversely affect long-term treatment effectiveness and patient adherence, highlighting the need for complementary or alternative immunomodulatory approaches.

In this context, naturally derived immunomodulators have attracted increasing research interest, particularly owing to their structural diversity and generally favorable safety profiles. Polysaccharides, a class of high-molecular-weight natural compounds widely distributed in medicinal plants, edible fungi, and other biological sources, exhibit considerable structural heterogeneity and functional versatility. Accumulating evidence indicates that polysaccharides are capable of modulating immune function and are involved in a range of immune-related activities, including anti-inflammatory, antitumor, and anti-infective effects. Their low toxicity and multi-target regulatory characteristics suggest potential applications in immunotherapy, immune adjuvant strategies, and functional food development.

At the mechanistic level, polysaccharides have been reported to modulate immune responses through multiple pathways. Experimental studies have shown that certain polysaccharides can interact with pattern recognition receptors (PRRs) expressed on immune cells, such as Toll-like receptors (TLR2 and TLR4) and Dectin-1, thereby influencing the activation of innate immune cells including macrophages and dendritic cells. This interaction may promote the production of cytokines and chemokines, such as TNF-α and IL-6, and contribute to downstream immune regulation. Further mechanistic evidence suggests that polysaccharides are involved in the modulation of intracellular signaling pathways, including MAPK and NF-κB pathways, which are associated with immune cell activation and phagocytic function.

Rationale   Although a growing number of studies have investigated the immunomodulatory effects of polysaccharides from diverse sources, several challenges remain in synthesizing the existing evidence. Polysaccharides derived from different plants and edible fungi have been reported to exhibit immunomodulatory activity; however, their proposed mechanisms of action show considerable variability, alongside certain overlapping features. To date, findings in this field have not been comprehensively mapped or systematically integrated, resulting in a fragmented understanding of immunomodulatory patterns across different polysaccharide types.

In addition, the core immunomodulatory targets and key signaling pathways associated with specific polysaccharides remain incompletely characterized, and in-depth mechanistic evidence at the molecular level is unevenly reported. Existing studies also demonstrate a degree of redundancy in experimental design, with results that are sometimes convergent and at other times inconsistent, making it difficult to derive an overarching conceptual framework or research consensus. Together, these factors underscore the need for a scoping review to systematically map the breadth of available evidence, clarify research trends, and identify knowledge gaps, thereby supporting future mechanistic investigations and facilitating the translational application of polysaccharide-based immunomodulatory strategies.

METHODS

Strategy of data synthesis   Strategy of data synthesis：

Data extraction will be conducted using a dual-reviewer independent approach. Two reviewers will independently extract data from all included studies using a predesigned and standardized data extraction form developed in Microsoft Excel, in order to ensure comprehensive and accurate capture of relevant information.

Extracted data will include basic bibliographic information (such as document identification number, year of publication, and country or region of origin) to facilitate analyses of geographical distribution and research context. Study characteristics will be charted according to study content, including polysaccharide source and type, and study design. Particular attention will be given to study type (e.g., in vitro experiments, animal studies, or clinical studies), population or experimental model characteristics (such as age, sex, and immune status), and reported immunomodulatory effects.

With respect to immune regulation, data will be charted on reported immune targets, signaling pathways, and functional outcomes, including

immune enhancement, suppression, or immune balance. Where applicable, effects on immune organs (such as changes in spleen or thymus indices) and disease-related outcomes (e.g., tumor inhibition rates or symptom improvement) will be recorded as reported in the original studies. Safety-related information, including adverse events, toxicity assessments, and safety evaluations, will also be extracted when available. In addition, authors' reported study limitations and proposed future research directions will be documented.

Data analysis

Descriptive analytical methods will be used to summarize and map the extracted data. Both quantitative summaries and qualitative narrative synthesis will be applied to present the characteristics of the included literature, distribution of polysaccharide types, proportions of different study designs, reported immune regulatory mechanisms, targets and pathways, and the range of diseases or conditions investigated. No statistical inference or meta-analysis will be performed.Data extraction will be conducted using a dual-reviewer independent approach. Two reviewers will independently extract data from all included studies using a predesigned and standardized data extraction form developed in Microsoft Excel, in order to ensure comprehensive and accurate capture of relevant information.

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Eligibility criteria

Inclusion criteria

(1)Study types

Eligible studies will include clinical studies (such as randomized controlled trials, non-randomized controlled trials, cohort studies, case–control studies, cross-sectional studies, single-arm trials, crossover trials, and case reports), animal experiments, and in vitro studies.

(2)Research content

Studies must report immunomodulatory-related outcomes or indicators, including but not limited to: Humoral immunity (e.g., serum IgA or IgG levels); Cellular immunity (e.g., lymphocyte proliferation, macrophage phagocytic activity); Inflammatory mediators or cytokines (e.g., IL-6, TNF-α); Immune-related molecules or cell subsets (e.g., CD4, CD8, T-cell subsets); Immune regulatory targets or signaling pathways describing the mechanisms through which polysaccharides modulate immune responses.

(3)Special inclusion considerations

Studies involving traditional Chinese medicine (TCM)–derived polysaccharides or compound polysaccharide preparations with reported immunomodulatory effects will be eligible, provided that immune regulation outcomes are clearly described.

Exclusion criteria

(1)Studies lacking sufficient immunomodulatory outcome data, containing incomplete datasets that prevent valid extraction, or with inaccessible full texts.

(2)Duplicate publications, including conference abstracts or preprints that have already been formally published, or studies reporting redundant data without additional information.

(3)Studies published in languages other than Chinese or English.

(4)Patent literature and experimental studies serving solely as positive controls.

(5)Studies involving adjuvant or combination therapies in which the independent immunomodulatory effects of polysaccharides cannot be clearly distinguished.

(6)Studies focusing on newly synthesized polysaccharide materials, polysaccharide complexes, chemical structure analyses, pharmaceutical formulations, vaccines, or adjuvant development where extractable immunomodulatory outcome data are unavailable.

(7)Studies on bacterial polysaccharides or polysaccharides derived from non-edible fungal sources.

(8)Studies in which polysaccharides function only as auxiliary components and do not directly participate in immunomodulation.

Source of evidence screening and selection

Search strategy

The search strategy will be developed using the PCC (Population, Concept, Context) framework to ensure comprehensive identification of relevant evidence.

Population: Studies related to immunomodulation.

Concept: Polysaccharides, including plant-derived polysaccharides and edible fungal polysaccharides, with particular attention to medicinal and edible sources commonly used for health promotion.

Context: Human medicine and related biomedical research settings.

Information sources

Electronic searches will be conducted in four Chinese databases (China National Knowledge Infrastructure [CNKI], Wanfang Database, VIP Database, and SinoMed) and three English-language databases (PubMed, Embase, and Web of Science). The search will cover studies published between January 1, 2020 and December 1, 2025. This time frame was selected to capture recent advances and emerging trends in polysaccharide-related immunomodulatory research.

Data management All retrieved records will be imported into NoteExpress reference management software for data management. Automatic duplicate detection will be applied, followed by manual verification using customized duplication fields to ensure complete removal of duplicate records.

Two trained reviewers will independently screen titles and abstracts according to the predefined inclusion and exclusion criteria. Screening results will be cross-checked, and any discrepancies will be resolved through discussion, with consultation of a third reviewer if consensus cannot be reached. Full-text articles of potentially eligible studies will be retrieved and independently assessed by the two reviewers. Disagreements arising at the full-text screening stage will be resolved by a third reviewer to ensure accuracy and consistency in study selection.

Language restriction English and Chinese.

Country(ies) involved China.

Keywords immunomodulatory effects; immunomodulatory mechanisms; plant polysaccharides; edible fungal polysaccharides.

Contributions of each author

Author 1 - Chenlu Wang.
Email: shanelle7718@163.com

Author 2 - Wanting Liu.
Author 3 - Wanting Zhang.
Author 4 - Qingyuan Xue.
Author 5 - Huijuan Cao.