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EFFECT OF CHITOSAN ON BIOCHEMICAL INDICATORS OF IMMUNOGLOBULIN SYNTHESIS AND PHAGOCYTOSIS

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Abstract

This article systematizes current evidence on the immunological effects of chitosan, with special emphasis on immunoglobulin synthesis, phagocytic activity of macrophages and neutrophils, and related biochemical markers. The review demonstrates that molecular weight, degree of deacetylation, solubility, and particulate form are the key determinants of chitosan bioactivity. Chitosan can intensify functional interactions between antigen-presenting cells and B lymphocytes, positively influence IgA, IgG and IgM levels, and modulate phagocytic index, lysosomal enzyme activity, reactive oxygen species generation, and cytokine profiles. The analytical synthesis supports the view that chitosan should be considered not only as a drug-delivery biomaterial, but also as a promising immunomodulator and vaccine adjuvant.

Keywords

chitosan, immunoglobulin, phagocytosis, macrophage, cytokine, immunomodulation, adjuvant, biochemical indicator

Introduction

Chitosan is a natural cationic polysaccharide obtained from chitin and extensively studied because of its biocompatibility, biodegradability, mucoadhesion, and comparatively low toxicity. In contemporary biomedicine, it is no longer regarded merely as a wound dressing component or drug carrier, but increasingly as a material capable of modulating immune function [7–12].

The biological activity of chitosan is not uniform. Its molecular weight, degree of deacetylation, charge density, particle size, solubility, and the possibility of endotoxin contamination may all substantially alter the immune outcome. Therefore, any academically rigorous discussion of chitosan should move beyond generic statements and rely on standardized physicochemical characterization [8, 13–16, 35].

A persistent methodological weakness in the literature is the tendency to describe chitosan as a broad “immune enhancer” without specifying the measurable immunobiochemical endpoints involved. Yet the relevant mechanisms can and should be assessed through concrete markers, including immunoglobulin production, antigen presentation, phagocytic uptake, cytokine secretion, oxidative burst, and lysosomal activation [9–13, 17–20].

Against this background, the present article aims to re-evaluate the effect of chitosan on biochemical indicators associated with immunoglobulin synthesis and phagocytosis, to systematize current evidence, and to formulate analytically grounded conclusions for biochemistry, immunology, and translational medicine.

Main part

Chemically, chitosan is a linear biopolymer composed of D-glucosamine and N-acetyl-D-glucosamine residues linked by β-(1→4) glycosidic bonds. In contrast to chitin, the presence of

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free amino groups gives chitosan a positive charge in acidic media, enabling electrostatic interaction with mucosal surfaces, biomacromolecules, and cellular membranes [21–27].

Among its physicochemical parameters, molecular weight and degree of deacetylation are particularly important. Low-molecular-weight fractions tend to activate macrophage signaling pathways more rapidly and may enhance pinocytosis or phagocytosis, whereas higher-molecular-weight fractions more often display prolonged mucoadhesive and carrier properties [14, 15, 20, 35].

From an immunological perspective, the action of chitosan can be discussed along two interconnected axes. The first concerns innate immune cells, especially macrophages, dendritic cells, and neutrophils. The second concerns humoral immunity, namely the amplification of B-cell differentiation and antibody formation [8–13, 20, 28–33].

The literature repeatedly identifies chitosan as an effective adjuvant in mucosal vaccine systems. Its significance lies in the ability to transiently loosen epithelial tight junctions, facilitate paracellular transport of antigens, prolong antigen residence at the mucosal surface, and increase the duration of contact between antigen and antigen-presenting cells [7, 8, 10–12, 22–25].

For macrophages, chitosan is not merely an inert matrix. It can enter the cell through phagocytosis or clathrin-mediated endocytosis and then engage lysosomal pathways, NF-κB, AP-1, and, in certain settings, the cGAS–STING axis [13–16, 19, 35]. Consequently, its biological action is not limited to an increase in “uptake percentage”; rather, it may reprogram the functional state of the immune cell.

Studies performed by researchers from the CIS scientific space also emphasize the immunomodulatory potential of chitosan. In experimental immunization models, different chitosan formulations have been associated with increased secretory IgA titers, stronger humoral responses, and more stable vaccine-induced immune reactivity [28–34].

Methodology

This paper is an analytical review rather than a report of a new wet-laboratory experiment. A total of 35 sources published between 2001 and 2025 were selected and subjected to structured content analysis. The source base included PubMed, PMC, MDPI, and CIS-oriented scientific resources such as CyberLeninka, eLIBRARY, and regional review materials [7–16, 28–35].

The selected studies met three criteria: (1) they addressed immunomodulatory properties of chitosan; (2) they contained data on immunoglobulins, phagocytosis, or closely related biochemical markers; and (3) they provided at least a partial characterization of the chitosan preparation. Publications lacking immunobiological specificity were not used as core evidence.

A comparative analytical framework was applied. Markers of humoral immunity (IgG, IgA, IgM titers and kinetics of antibody generation), indicators of innate immunity (phagocytic index, phagocytic number, ROS, NO, TNF-α, IL-6, IFN-γ, lysosomal enzymes), and mechanistic data on signaling pathways were separated into distinct analytical clusters [9–18, 28–35].

This methodological approach made it possible to evaluate chitosan not through isolated single endpoints, but as part of an integrated immunobiochemical model. The findings were subsequently interpreted from the perspective of translational medicine, biochemistry, and vaccinology.

Table 1. Key biochemical markers associated with the immunological effects of chitosan

Direction	Main markers	Expected change	Comment
Humoral immunity	IgA, IgG, IgM	Often increased	Secretory IgA tends to rise most consistently in mucosal formulations.

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Direction	Main markers	Expected change	Comment
Innate immunity	Phagocytic index, phagocytic number	Activated	Macrophage and monocyte uptake capacity may improve.
Cytokine profile	TNF-α, IL-6, IFN-γ, IL-10	Context-dependent	Pro- or anti-inflammatory responses depend on dose, MW and cell model.
Effector mechanisms	ROS, NO, iNOS, lysosomal enzymes	Modulated	Oxidative burst and antimicrobial potential may be enhanced.
Signaling pathways	NF-κB, AP-1, cGAS–STING	May be activated	Closely related to adjuvanticity and antigen presentation.

Analysis

At the level of humoral immunity, the most reproducible observation is that chitosan enhances IgA and IgG responses when administered together with antigens. In mucosal formulations, increased secretory IgA appears especially consistent, which is highly relevant for strengthening barrier immunity at the portal of pathogen entry [7, 9, 11, 12, 20, 23, 24, 30, 32].

Some experimental studies also indicate beneficial effects on IgM and the early phase of humoral reactivity. In a leukemia mouse model, chitosan administration improved IgG and IgM values as well as monocyte phagocytic activity [17]. Such findings support the notion that chitosan may serve as a functional bridge between innate and adaptive immunity.

At the level of dendritic cells and macrophages, chitosan may enhance antigen presentation, amplify costimulatory signaling, and influence T-helper polarization. Data implicating cGAS–STING signaling and type I interferons suggest that the adjuvant effect of chitosan is mechanistically much more complex than simple physical carriage of antigen [13, 19].

Evidence on phagocytosis shows that chitosan is closely associated with intracellular uptake, transport, and degradation in macrophages. Chitosan nanoparticles can enter macrophages via clathrin-mediated endocytosis and phagocytosis, followed by partial intracellular degradation [16]. This supports the interpretation of chitosan as a biologically active particulate signal rather than a passive scaffold.

Regarding macrophage effector responses, chitosan may increase TNF-α, IL-6, IFN-γ, NO, and iNOS in a dose- and molecular-weight-dependent manner. Low-molecular-weight fractions appear particularly capable of activating NF-κB and AP-1 pathways and strengthening macrophage functional activity [14, 15]. At the same time, recent reviews stress that chitosan can also contribute to anti-inflammatory effects under specific cellular and physicochemical conditions, which means that context is decisive [35].

CIS authors likewise report increased immunogenicity of vaccine formulations, higher secretory IgA titers, and differences in adjuvant potency depending on the form of chitosan used [28–33]. These observations are broadly consistent with the international literature and indicate a noteworthy convergence of evidence across scientific schools.

Analysis of biochemical indicators linked to phagocytosis further suggests that chitosan can modulate the phagocytic index, phagocytic number, reactive oxygen species, lysosomal enzyme systems, and inflammatory mediators. However, not all studies show identical directions of change; therefore, molecular characterization of the preparation, endotoxin control, and dose specification should be treated as essential standards in future research [8, 15, 16, 35].

From a translational perspective, the combined influence of chitosan on immunoglobulin synthesis and phagocytosis makes it a promising platform for intranasal vaccines, mucosal

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immunoprophylaxis, antitumor nanovaccines, and immunoregenerative biomaterials [7, 9, 11–13, 18, 19].

Results

The analytical synthesis of the reviewed literature demonstrates that the immunological action of chitosan is multi-level and depends on both biological context and material design. First, chitosan shows a consistent tendency to intensify humoral immune markers, particularly IgA and IgG. Second, it can activate macrophage and monocyte phagocytic function, thereby strengthening innate immune responsiveness.

Third, the biological efficacy of chitosan is tightly linked to its molecular weight, degree of deacetylation, solubility, particle size, and method of preparation. Fourth, chitosan represents a rare platform that combines biomaterial, carrier, and immunomodulatory functions, which is especially valuable for mucosal vaccination and nanovaccine design.

Conclusion

In summary, chitosan should be regarded as a natural biopolymer capable of significantly influencing biochemical indicators related to immunoglobulin synthesis and phagocytosis. On the one hand, it can enhance antigen presentation and B-cell-associated antibody responses; on the other, it can modulate macrophage uptake and effector functions.

The principal scientific and practical implication is that the model “one substance — one effect” is insufficient for chitosan research. Reliable comparison of studies requires a clear physicochemical passport of each preparation, endotoxin control, and explicit biological modeling. Standardized chitosan formulations therefore constitute a promising basis for future immunobiological products, vaccine adjuvants, and regenerative medical technologies.

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