

## A Comparative Review of Chitinase Enzymes from Microbial and Mammalian Origins and Their Roles in Health Applications

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### Abstract

**Background:** Chitinase is an enzyme crucial in chitin biodegradation, breaking the 1,4-N- $\alpha$ -acetyl-D-glucosamine bonds of its monomers. It is produced by a wide range of organisms, from microorganisms such as bacteria and fungi to macroorganisms including humans. Chitinases have been widely studied for applications in biological control, environmental management, and medical fields, including immune modulation and infection therapy. However, there is still a research gap due to the limited number of systematic comparative studies examining the structural, genetic, and functional differences among chitinases from various biological sources. This limitation hinders optimal and targeted use of chitinases in enzyme-based technologies, particularly for medical applications. Therefore, comprehensive studies are needed not only to describe chitinases by their sources but also to evaluate their practical potential and innovative opportunities for human health. **Methodology:** This study uses a narrative literature review approach. Articles were collected, screened, and systematically organized according to their scope, focusing on chitinase sources, mechanisms of action, and applications in healthcare. **Findings:** The analysis shows fundamental differences in domain structure, gene expression, and catalytic mechanisms of chitinases from bacteria, fungi, and humans. Bacterial chitinases exhibit environmental stability and serve as infection biomarkers, fungal chitinases excel in immunotherapy and bioactive compound production, and human chitinases, though less explored, show potential in precision diagnostics and inflammatory therapy. **Contribution:** This cross-domain comparison maps structural and functional characteristics and opens opportunities for integrating cross-species enzyme functions for innovative enzyme-based biopharmaceuticals and precision therapies addressing modern pathogens

**Keywords:** Chitinase; Types of Chitinase; Sources of Chitinase; Applications of Chitinase; Health



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## INTRODUCTION

Chitin is a structural polysaccharide composed of 1,4-N- $\alpha$ -acetyl-D-glucosamine (NAG) monomer units and exists in three main types:  $\alpha$ ,  $\beta$ , and  $\gamma$ . The difference among the three lies in the arrangement of the bonds between the polymer chains. The  $\alpha$  type has an antiparallel configuration that results in strong hydrogen bonds and high stability, while the  $\beta$  type has a parallel configuration with weaker bonds. In addition,  $\gamma$  type is a combination of  $\alpha$  and  $\beta$ , making it insoluble in common solvents (Islam & Datta, 2015). The use of chitin and its derivatives in biotechnology and health has significantly increased. They have been developed primarily as bioactive compounds in antimicrobial, anti-inflammatory, and wound healing therapy. Chitin can be found in various sources, such as fungal cell walls (Fernando et al., 2021), crustacean exoskeletons (Dahiya et al., 2022), and insects (Kaya et al., 2015).

Chitinase is an enzyme that breaks down chitin polymers into oligomers and NAG monomers through hydrolysis. Based on their mechanism of action, chitinase is classified into three main types: endochitinase, which randomly cleaves the middle of the chitin chain; exochitinase, which acts at the terminal ends of the chain to produce diacetylchitobiose; and  $\beta$ -N-acetylhexosaminidase, which converts diacetylchitobiose to NAG (Islam & Datta, 2015). Chitinases are produced by various organisms, including microorganisms such as bacteria and fungi, as well as macroorganisms such as plants, animals, and humans. A number of chitinase-producing bacteria are among others *Pseudomonas aeruginosa* (Khairah et al., 2023), *Streptomyces coelicolor*, and *Cellulosimicrobium funkei* (Berini et al., 2019; Ali et al., 2020). Among fungi, *Metarhizium anisopliae*, *Penicillium oxalicum*, and *Trichoderma atroviride* have been identified as potential chitinase-producers (Anwar et al., 2019; Xie et al., 2021; Sahu et al., 2024). Chitinase is also found in multicellular organisms such as fish (Watanabe et al., 2018) and humans (Sinelnikov et al., 2021), and has been further developed at the molecular level (Jiménez-Ortega et al., 2021). This enzyme plays an important role in chitin recycling in nature and has great potential in biotechnology and health sectors.

The potential of chitinases from various sources has been applied across a fairly wide range of areas, including environmental and health sectors. Chitinases from bacteria have been used as insecticides, fungicides, and bioremediation (Ali et al., 2020; Dikbaş et al., 2021), while chitinases from fungi, in addition to having a high fungicidal effect, are also promising as a candidate for antifungal therapy. Chitinases from plants, animals, and humans also demonstrate potential in the health sector (Anwar et al., 2019; Kurç et al., 2025). A number of studies have also proved that hydrolysis products of chitinases, such as chitooligosaccharides (COS) and N-acetylglucosamine (NAG), play a role in the health sector as they exhibit immunomodulatory and antitumor effects as well as can be used in tissue engineering and drug delivery systems (Mamache et al., 2025). Furthermore, the increasing incidence of resistance to conventional antifungals makes chitin and its degrading enzyme, chitinase, a potential research target for the development of enzyme-based alternative therapies. A comparative study between bacterial and fungal chitinases demonstrated that chitinase from the fungus *Trichoderma harzianum* can inhibit the

growth of *Candida albicans* by up to 92%, higher than 75% inhibition shown by chitinase at the same concentration from the bacterium *Bacillus subtilis* (Ghurye et al., 2025). One early clinical trial also demonstrated the effectiveness of chitinase as an adjuvant therapy for oropharyngeal candidiasis, with a 1.5 log<sub>10</sub> CFU/mL reduction in *Candida* colonies after 7 days of administration (Inácio et al., 2023).

Although extensive data on chitinase are available, there has been no study conducted to systematically compare the characteristics, effectiveness, and clinical applications of chitinases from various biological sources, particularly within the context of their application in the human health sector. Previous studies have generally been fragmented and focused on a single producing organism, without any cross-species and cross-domain exploration. Therefore, this article aims to comprehensively examine the characteristics, activities, and potential health applications of chitinases from three main groups: bacteria, fungi, and humans.

This article provides a scientific contribution by delivering an integrative, comparative perspective on the sources, mechanisms of action, and medical applications of chitinases across biological domains. This article also highlights its novelties: the opportunity to explore human chitinases, which have been relatively under-explored, and new directions for further research in the development of chitinase-based biopharmaceuticals. This study is expected to serve as a foundation for further experimental research and the development of enzyme-based therapies in the human health sector.

## METHOD

This study was non-experimental and employed literature review approach, in particular narrative review. The approach allowed for the descriptive and comprehensive search and compilation of scientific information from various sources without any limitation due to strict systematic protocols (Ferrari, 2015). This method was suitable for developing a narrative synthesis comparing the characteristics and potential applications of chitinases from various sources. The processes were: developing inclusion and exclusion criteria through a five-component framework (Population, Intervention, Comparator, Outcome, and Study Design–PICOS), followed by literature data selection and management by their respective topic, thereby forming a comprehensive and systematic information.

### PICOS Structure for Developing Inclusion and Exclusion Criteria

The following are the components and descriptions in accordance with the PICOS structure for developing the inclusion and exclusion criteria.

**Table 1.** Component description of the PICOS structure

| No | Component  | Description  |
|----|------------|--|
| 1  | Population | Chitinases derived from bacteria, fungi, and humans and applied in the health sector |

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|   |                     |  |
|---|---------------------|--|
| 2 | <b>Intervention</b> | Studies evaluating the production, characterization, or application of chitinases in a medical context (antifungal therapy, immunomodulation, wound healing) |
| 3 | <b>Comparator</b>   | Studies comparing the activities of chitinases from various sources or comparing them with conventional therapies  |
| 4 | <b>Outcome</b>      | Biological effectiveness (antifungal, antibacterial, immunomodulation), potential medical applications, preclinical or clinical outcomes                     |
| 5 | <b>Study design</b> | Original research articles (in vitro/in vivo experiments, clinical trials), narrative studies, or non-systematic literature reviews                          |

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The inclusion criteria were:

1. studies evaluating chitinases from bacteria, fungi, or humans in a medical or health biotechnology context;
2. experimental studies (in vitro/in vivo), clinical trials, or narrative scientific reviews;
3. publications in English or Indonesian; and
4. publication period from 2015 to 2025.

While the exclusion criteria were:

1. studies discussing chitin only without any focus on chitinase;
2. non-medical applications, such as agriculture, waste, or non-pharmaceutical industries;
3. studies not available in full-text form; and
4. editorials, opinion pieces, or conference abstracts without any experimental data.

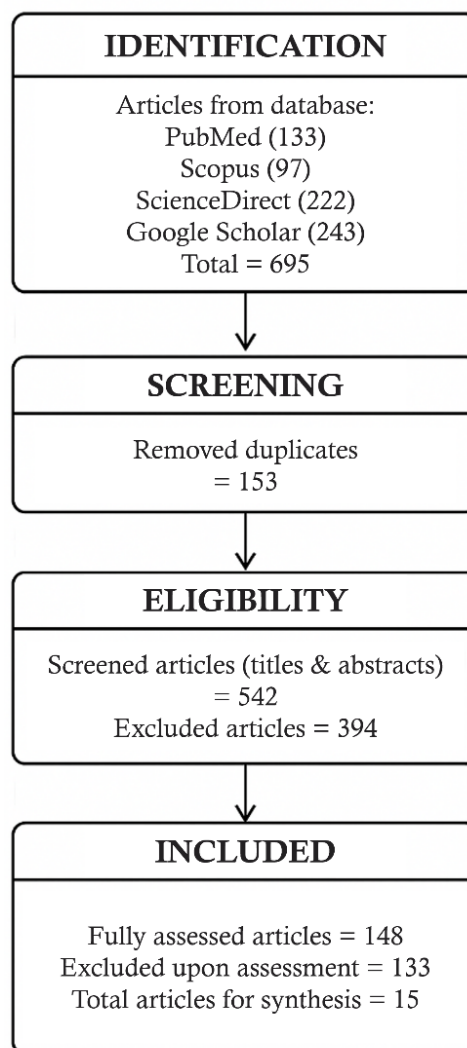
### **Literature Data Selection Procedure**

The data consisted of articles published over the last 10 years (2015–2025). They were sourced from various databases, including PubMed, Scopus, Google Scholar, and ScienceDirect. Keywords for database search were selected based on the materials relevant to this study's topics of discussion, including: the biological diversity of chitinase-producing organisms (micro- or macro-organisms), the types of chitinases well as their mechanisms of action, and the use of chitinase in the health sector from each source.

This study employed a combination of Boolean search terms as the search strategy: > (“chitinase” OR “chitinases”) AND (“bacteria” OR “fungi” OR “humans”) AND (“therapeutic” OR “medical application”). During the initial selection, duplicates between databases were removed. Titles and abstracts were then screened based on the inclusion criteria. Full-text evaluation was conducted to assess eligibility based on content completion criteria. Articles that were irrelevant, lacking biological data, or inaccessible were then excluded. The study was finalized by narratively analyzing articles that met all criteria.

### Data Management

The searching process obtained a total of 695 articles from various sources. All were screened and assessed for eligibility, resulting in 15 selected articles (Figure 1). The collected data were then organized according to the writing order, forming a coherent idea. The resulting information was therefore comprehensive and met the state-of-the-art flow.



**Figure 1.** PRISMA Flow

## RESULT

Chitinases from bacteria, fungi, and humans differ in terms of GH family characteristics, coding gene types, and activity types, leading to variations in their applications in the health sector (Table 2).

**Table 2.** Comparative summary of chitinases from bacteria, fungi, and humans

| Source   | GH Family         | Coding Gene Type  | Activity Type  | Application in the Health Sector   | Reference   |
|----------|-------------------|---|--|--|---|
| Bacteria | GH18 (main), GH19 | Chi A, Chi B, Chi C, Chi D; Chit62  | <ul style="list-style-type: none"> <li>Chi A, B, D: Exochitinase</li> <li>Chi C: Endochitinase</li> <li>Chit62: Acid resistance</li> </ul> | <ul style="list-style-type: none"> <li>Infection and colonization marker (<i>C. violaceum</i>, <i>V. cholerae</i>)</li> <li>Virulence factor (biofilm, QS)</li> <li>Antifungal therapy in combination with antibiotics</li> <li>Detection of gastrointestinal infection (<i>C. paraputificum</i>)</li> </ul> | Orikoshi et al., (2005); Danişmazoğlu et al., (2015); Devlin & Behnsen, (2023); Dade et al., (2022); Bai et al., (2016)                               |
| Fungi    | GH18, GH19        | Chi1 ( <i>M. anisopliae</i> ), Chi28 ( <i>A. fumigatus</i> ), Chi33 ( <i>T. harzianum</i> ) | <ul style="list-style-type: none"> <li>Endochitinase (Chi1, Chi33)</li> <li>Endo &amp; Exo Combination (Chi28)</li> </ul>                  | <ul style="list-style-type: none"> <li>DNA vaccine (gen Chi3 <i>C. albicans</i>)</li> <li>Th1/Th17 &amp; Th2 immune induction (<i>C. neoformans</i>)</li> <li>Antioxidant from chitooligosaccharides</li> </ul>  | Anwar et al., (2019); Wu et al., (2022); Jiménez-Ortega et al., (2021); Wiesner et al., (2015); Costa-Barbosa et al., (2023); Kidibule et al., (2020) |
| Humans   | GH18              | CHIT1 (Chitotriosidase) AMCase  | Endoexochitinase (CHIT1, AMCase)   | <ul style="list-style-type: none"> <li>Pulmonary infection marker (<i>K. pneumoniae</i>)</li> <li>Infection biomarker (<i>C. albicans</i>, CF)</li> <li>Pulmonary fibrosis therapy (engineered AMCase)</li> </ul>  | Fadel et al., (2016); Sharma et al., (2018); Hector et al., (2016); Okawa et al., (2025)  |



Bacterial chitinases, particularly those belonging to GH18, exhibit high structural complexity with additional domains such as Carbohydrate-Binding Modules (CBM) and Fibronectin type III, as well as a diverse gene expression such as ChiA–ChiD that distinguish their endochitinase function from the exochitinase (Bai et al., 2016; Orikoshi et al., 2005). *Alteromonas* sp. has all four genes, while *Serratia marcescens* only has three (Orikoshi et al., 2005; Danişmazoğlu et al., 2015). Meanwhile, fungal chitinases such as Chi33 and Chi28 exhibit high catalytic efficiency through expansive active domains and complex enzymatic action combinations (Jiménez-Ortega et al., 2021; Wu et al., 2022). On the other hand, human chitinases, CHIT1 and AMCase, exhibit specialization in immunological functions and are involved in the body's response to infection through their activities as biomarkers and immunomodulatory agents (Fadel et al., 2016; Hector et al., 2016).

In practical application, bacterial chitinases are highly effective in infection management, serving as colonization marker, virulence factor, and defense agent against pathogens. For example, *Francisella tularensis* expresses Chi A and B, both involved in biofilm formation during pulmonary infections (Devlin & Behnsen, 2023), while *Vibrio cholerae* produces Chi A which plays a role in nutrient utilization from intestinal mucin (Wong et al., 2012; Fennell et al., 2021). Furthermore, *Clostridium paraputificum* produces acid-resistant Chit62, enabling continuous chitin-hydrolyzing activity in the gastrointestinal tract and making it a candidate biomarker for gastrointestinal infection (Dade et al., 2022; Shinha & Hadi, 2015). Moreover, chitinases from terrestrial bacteria rich in polyketide genes can even be combined with antibiotics to enhance antifungal efficacy (Bai et al., 2016).

Fungal chitinases also belong to the GH18 and GH19 families. Their functional structures display unique features, such as the expanded catalytic domain of Chi33 from *Trichoderma harzianum*, which has six polar binding sites (Jiménez-Ortega et al., 2021), and the combined exo- and endochitinase activities of Chi28 encoded by *Aspergillus fumigatus* (Wu et al., 2022). Fungal chitinases play a significant role in immunology and vaccine development, such as a recombinant DNA vaccine, developed based on the Chi3 gene from *Candida albicans*, which successfully induced a Th1/Th17-adaptive immune response (Wiesner et al., 2015). In *Cryptococcus neoformans* infection, however, chitin cleaved by chitotriosidase triggers Th2 cell formation, with CD11b<sup>+</sup> dendritic cells playing a key role (Costa-Barbosa et al., 2023). Furthermore, fungal chitinases are also used to produce bioactive compounds such as chitooligosaccharides that exhibit a strong antioxidant activity. Their highest activity was found within the molecular size ranges of 0.5–2 and 2–10 kDa (Kidibule et al., 2020).

In the human body, active enzymes classified as chitinases are CHIT1 (chitotriosidase) and AMCase (Acidic Mammalian Chitinase), both belonging to the GH18 family (Fadel et al., 2016). These enzymes are synthesized by macrophages and neutrophils and have a chitin-binding domain (CBM14). Both play a role in maintaining innate immune system homeostasis, particularly during infection. During which, CHIT1 functions as an immunological biomarker, as observed in lung infections caused by *Klebsiella pneumoniae* where CHIT1 activity decreases as neutrophil activity increases to eliminate the bacteria (Sharma et al., 2018). In patients

with Cystic Fibrosis (CF) colonized by *Candida albicans*, increased CHIT1 levels were detected, indicating its potential as a fungal infection biomarker (Hector et al., 2016).

The limited exploration of the role of human chitinases in therapy and diagnostics has been addressed in this study. Based on the studies have shown that CHIT1 and AMCase not only function in innate immune regulation but also have potential as precision indicators for specific infections. For example, increased CHIT1 levels in patients with cystic fibrosis and altered AMCase expression in chronic inflammation provide preliminary evidence for their use in personalized diagnosis and therapy (Sharma et al., 2018; Okawa et al., 2025). In addition, while AMCase has low physiological activity, it can be molecularly engineered using amino acid derivatives from *Macaca fascicularis*. This engineering successfully increased AMCase activity and demonstrated its potential as an alternative therapy for pulmonary fibrosis caused by chitin accumulation (Okawa et al., 2025).

The barriers to integration across biological domains for clinical applications have also been successfully bridged through the comparative synthesis approach in this study. Not only highlights the unique characteristics of each source, this study also opens up the possibility of synergy among enzymes. For example, the high antifungal activity of fungal chitinases (up to 92% inhibition against *Candida albicans*) can be combined with the extreme environmental stability of bacterial chitinases (such as Chit62 from *Clostridium paraputificum*) and the immunological compatibility of human chitinases to create a multifunctional and effective adjuvant therapy approach for resistant fungal infections (Dade et al., 2022; Wiesner et al., 2015).

Therefore, this discussion not only fills the gaps in information elaborated in the introduction but also provides a systematic conceptual framework to promote the transition from basic biological understanding of chitinases toward developing more targeted clinical applications. This study provides a scientific basis for enzyme-based intervention strategies in infection treatment, immunotherapy, and biomarker development, in line with the need for more specific and responsive medical approaches to contemporary pathogens.

## CONCLUSION

This study provides a comprehensive analysis and in-depth comparison of the characteristics, activities, and potential medical applications of chitinases from bacteria, fungi, and humans. Each source exhibits unique structural, genetic, and functional characteristics that influence their applicability in the health sector, ranging from antifungal therapy and immunomodulation to disease biomarker. Bacterial chitinases excel in extreme environmental stability and infectious applications. Fungal chitinases exhibit high potential in immunotherapy and bioactive compound production. Meanwhile, human chitinases offer innovative opportunities in the development of precision therapies and immune-based diagnostics. The comparative synthesis approach in this study not only bridges existing research gaps but also opens up prospects for synergies across biological domains aiming at the development of enzyme-based biopharmaceuticals. Therefore, this study provides a strong scientific foundation for further research and clinical innovation in chitinase-based therapy.



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