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Marine-Derived Chitosan Biopolymers as Antibacterial Agents: A Review

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Abstract: The growing issue of bacterial resistance to conventional antibiotics has led to an increasing need for alternative antimicrobial agents. Chitosan, a biopolymer derived from marine organisms such as crustaceans (shrimp, crabs) and mollusks (shellfish), has shown significant antibacterial properties. This systematic review aims to evaluate the antibacterial activity of chitosan extracted from various marine sources against Gram-positive (*Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli*) bacteria. A comprehensive search of studies published in the past decade was conducted across multiple databases, using predefined inclusion criteria to identify relevant experimental research that focused on quantitative data, such as inhibition zones. The review analyzes key variables, including chitosan extraction methods, concentrations, and experimental conditions. The results revealed that chitosan exhibited the highest antibacterial activity against *E. coli*, while *S. epidermidis* showed moderate susceptibility. Variations in antibacterial effectiveness were attributed to differences in chitosan extraction methods and experimental conditions. Despite these variations, the overall evidence supports the potential of chitosan as an effective antimicrobial agent, demonstrating significant inhibition against a wide range of bacterial strains. The findings suggest that chitosan may serve as a promising natural alternative to combat bacterial infections, particularly those caused by antibiotic-resistant pathogens. However, further research is needed to standardize extraction techniques, explore the antibacterial mechanisms, and conduct in vivo studies to validate its clinical applications. These findings underscore chitosan's potential as a sustainable and effective solution in addressing the global challenge of bacterial resistance.

Keywords: Antibiotic Resistance; Chitosan; Antibacterial Activity; Marine Animal Sources; Pathogenic Bacteria.

Introduction

Bacterial infections are one of the increasingly serious global health problems, especially with the emergence of various antibiotic-resistant bacterial strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and beta-lactam-resistant *Escherichia coli* [1,2,3]. The impact of this resistance includes increased morbidity and mortality, extended duration of hospitalization, and increased medical costs, making it a public health problem that requires immediate attention [4,5]. The World Health Organization ranks antibiotic resistance as one of the greatest threats to global health and ecosystem sustainability, both for humans and animals [6,7].

The use of antibiotics is still the main approach in overcoming various diseases caused by bacterial infections. Antibiotics work by inhibiting the growth or killing the bacteria that cause infection, thus helping to control the spread of infection [8,9]. In Indonesia, the prevalence of antibiotic use is quite high, which ranges from 40%-60%, it also causes an increased risk of antibiotic resistance if this use is not done appropriately [10,11]. The extensive and uncontrolled use of antibiotics in medical therapy has raised concerns, as it can accelerate the development of bacterial resistance to conventional antibiotics, ultimately reducing the effectiveness of such therapy [12].

Antibiotic resistance arises as a result of bacterial adaptation mechanisms to drugs [13, 14]. One of the common resistance mechanisms is the production of beta-lactamase enzymes, which can hydrolyze the beta-lactam ring on antibiotics so that antibiotics become ineffective [15,16]. The genes that regulate the production of these enzymes are generally found on plasmids, allowing rapid transfer between bacteria through horizontal genetic transfer mechanisms [17]. This process accelerates the spread of resistance across different bacterial populations [18]. As resistance levels increase, effective therapeutic options are increasingly limited, leading to worsening bacterial infection problems worldwide [19,20].

The widespread threat of antibiotic resistance has encouraged researchers to look for alternative solutions that are safer, more effective and environmentally friendly [21]. A natural approach using bioactive ingredients from natural sources is starting to be seen as one of the potential solutions to overcome this resistance [22]. Antimicrobial agents based on natural materials are expected to reduce dependence on conventional antibiotics, offering methods that have the potential to inhibit bacterial growth without triggering resistance to the same [6].

One such material that has attracted widespread attention is chitosan, a biopolymer extracted from chitin found in marine sources such as crustaceans (shrimps, crabs) and mollusks (shellfish) [23]. Chitosan is a biopolymer produced through deacetylation of chitin, which is the main component of the exoskeleton of crustacean animals such as shrimp, crabs, and mollusks [24, 25]. Chemically, chitosan consists of glucosamine units connected through glycosidic bonds, giving it distinctive properties such as solubility in acids and the ability to form films [27]. In addition, chitosan can also be found in terrestrial sources, such as insect shells,

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silkworms and fungi [28]. The advantage of chitosan derived from marine animals lies in its molecular structure that has a higher degree of deacetylation, which increases the concentration of active amino groups [10]. This contributes to its effectiveness as an antimicrobial agent. In addition, chitosan from marine animals is often more accessible and cheaper to extract on a large scale compared to terrestrial animal sources making it a more efficient and environmentally friendly option for various medical and industrial applications [28].

The objective of this study is to review and assess the effectiveness of chitosan extracted from different marine animal sources, including crustaceans (shrimps, crabs), mollusks (scallops), and other marine animals, in inhibiting the growth of gram-positive and gram-negative pathogenic bacteria. This literature review aims to deeply understand the biological activities of chitosan from various marine sources and assess its potential as an antibacterial agent. The results of this study are expected to provide valuable insights into the application of chitosan from different marine animal sources in the healthcare field, particularly in addressing antibiotic-resistant bacterial infections. Given the rising global concern over the spread of antibiotic resistance, this research is urgent as it explores alternative antimicrobial agents that could help mitigate the impact of resistant pathogens. By evaluating the effectiveness of chitosan, this study aims to contribute to developing sustainable, natural solutions for combating bacterial infections, which have become a major public health challenge.

Research Methods

PICO

PICO	
Population **(P)**	Gram-positive and negative pathogenic bacteria
Intervention **(I)**	The use of chitosan from marine animal sources
Comparison **(C)**	Positive control and negative control
Outcome **(O)**	Antibacterial activity of chitosan measured

Inclusion-Exclusion Criteria

Inclusion	Exclusion
Experimental studies on antibacterial activity of chitosan	Studies that did not discuss experimental on antibacterial activity of chitosan
Published in the last 10 years (2014-2024)	Published more than the last 10 years
Journal in English or Indonesian	Journal in addition to English and Indonesian languages
Studies that do not include quantitative results on the zone of inhibition against bacteria	Studies that do not include quantitative results on the zone of inhibition against bacteria
Studies that discuss the source of chitosan from marine animals	Studies that discuss chitosan other than marine animals

The literature review process in this study involved searching for articles from three main sources, namely PubMed, Google Scholar, and Science Direct. The article/journal search used keywords such as “Chitosan” AND “Biopolymer” AND “Marine Animals” AND “Antibacterial Activity” with a total of 263 articles identified. After the initial screening stage, 222 articles were eliminated as they were not relevant to the topic. Of the remaining 41 articles, further selection was made based on the predefined inclusion criteria, which resulted in the removal of 31 additional articles. Ultimately, 10 articles were selected for analysis in this review that matched the relevance and validity according to the research objectives.

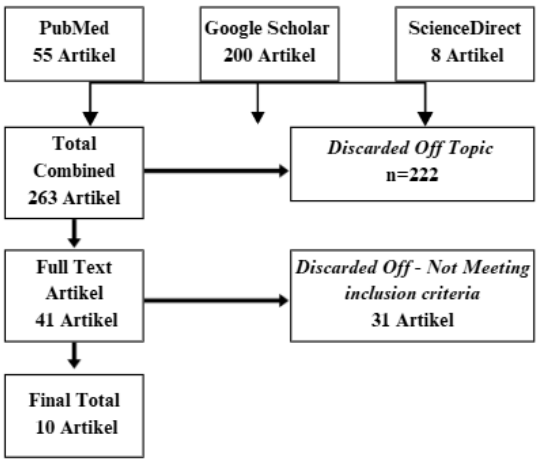

Figure 1. Reference Data Collection Phase

Results and Discussion

Chitosan is a biopolymer derived from chitin, a compound found in the exoskeleton of marine organisms such as shrimp, crabs, and shellfish [23]. It has attracted attention as an effective natural antibacterial agent due to its ability to inhibit and kill pathogenic bacteria. The antibacterial mechanism of chitosan involves interaction with the negatively charged bacterial cell wall, causing damage to the cell wall structure until lysis and bacterial cell death occur [29]. In addition, chitosan contains lysozyme enzymes and aminopolysaccharide groups that can damage bacterial cell walls, causing lysis and death of bacterial cells [30]. The primary advantage of chitosan as an antimicrobial agent is that it is non-toxic and easily biodegradable in the environment, making it safe and suitable for various medical applications [31].

Table 1. Antibacterial Activity of Chitosan from Various Animal Sources

Animal Sources	Method	Types and Antibacterial Activity	Source
Kerang Hijau *(Perna viridis* L.)	Agar Diffusion Method	The results showed the inhibition zone of chitosan at a concentration of 0.8%, 12.5 mm (*S. aureus*), 16.5 mm (*E. coli*).	[32]
Cangkang rajungan (*Portunus pelagicus*)	Agar Diffusion Method	The results showed that chitosan at a concentration of 0.4% produced a zone of inhibition of 10.27 mm, and at 0.8% produced a zone of inhibition of 11.60 mm, with KHTM in the range of 0.05-0.1%.	[35]
Tulang Rawan Cumi-Cumi *(Loligo sp.*)	Agar Diffusion Method	The results showed that 0.8% chitosan produced a zone of inhibition of 11.1 mm against Staphylococcus aureus and 12.8 mm against *Escherichia coli*, indicating an increasing antibacterial effectiveness as the concentration increased.	[38]
Cangkang Kerang Bulu (*Anadara inflata)*	Disc Diffusion Method	The results showed that chitosan from feather clam shells (*Anadara inflata*) effectively inhibited *Staphylococcus epidermidis* and *Escherichia coli*. At a concentration of 7%, the inhibition against S. epidermidis was 12.5 mm and increased significantly, while for *E. coli*, a concentration of 1% showed a significant inhibition against S. epidermidis. significantly, while for *E. coli*, the 1% concentration showed a stable inhibition of 7.5 mm.	[42]
Kulit Udang Vannemei (*Litopenaeus vannamei*)	Paper Disk Diffusion Method	The results showed that chitosan from *Vannemei shrimp* skin (*Litopenaeus vannamei*) has significant antibacterial potential against *Staphylococcus epidermidis* 14.10 mm, *Pseudomonas aeruginosa* 15.30 mm, *Propionibacterium agnes* 17.26 mm, and *Escherichia coli* 17.26 mm. The most effective concentration to inhibit the growth of these bacteria is at a concentration of 7% b/v, with analysis of variance (ANOVA) showing significant differences between treatments and positive control (tetracycline) at a significant level of P = 0.000 (<0.05).	[44]
Kulit Udang Vannemei (*Litopenaeus vannamei*)	Paper Disk Diffusion Method	The results showed that chitosan from *Vannemei shrimp* shell at 1% concentration had weak antibacterial activity against Staphylococcus aureus with an inhibition zone of 2.49 mm and against *Escherichia coli* with an inhibition zone of 4.57 mm. The zone of inhibition was smaller than the positive control (Dettol), which showed higher effectiveness.	[45]
Cangkang kepiting lunak (*Scylla olivaceae*)	Agar Diffusion Method	The results showed zones of inhibition at concentrations of 0.2% (8.3 mm), 0.5% (11.16 mm), and 1% (13.33 mm). There was no zone of inhibition in the negative control.	[46]
Kulit udang vannamei (*Litopenaeus vannamei*)	Agar Diffusion Method	Results showed the largest zone of inhibition at 0.3% micro-chitosan concentration: 20.1 mm for *E. coli* (very strong) and 16.3 mm for *S. aureus* (strong). This zone of inhibition was greater than that of 70% alcohol.	[38]
Cangkang lobster (*Cherax quadricarinatus*)	Agar Diffusion Method	The results showed the largest zone of inhibition at 0.9% chitosan concentration: 17.2 mm, while the 0.3% concentration produced a zone of inhibition of 13.5 mm. Antibacterial activity increased as the concentration increased, with the 0.9% inhibition zone categorized as strong inhibition.	[47]
Cangkang lobster (*Cherax quadricarinatus*)	Agar Diffusion Method	The results showed the best zone of inhibition at a concentration of 4.5%: 8.8 mm for *E. coli* and 10 mm for *S. aureus*, categorized as moderate inhibition.	[49]

Antibacterial Activity of Chitosan from Green Shells (*Perna viridis* L.)

Research has highlighted the potential of chitosan synthesized from green mussel shells (Perna viridis L.) as an antibacterial agent. In a study, chitosan was obtained through deproteination, demineralization, and deacetylation processes, with the concentration of chitosan tested varying from 0.2% to 0.8% (b/v). The results showed that chitosan with a concentration of 0.8% effectively provided an inhibition zone of 12.5 mm against *Staphylococcus aureus* and 16.5 mm against

Escherichia coli. This data indicates that chitosan has better antibacterial activity against *Escherichia coli* than *Staphylococcus aureus*, likely due to the different cell wall structures of the two bacteria [32, 33].

This finding is further supported by a study which also tested the antibacterial activity of a substance derived from green mussel shells, but in the form of calcium oxide (CaO). The study demonstrated that the CaO powder produced by calcining green mussel shells at 1000°C for 6 hours exhibited inhibition zones of 13.7 ± 0.26 mm against *Staphylococcus aureus* and 12.5 ± 0.3 mm against *Escherichia coli*. Although these results are lower than those obtained from chitosan, the findings provide additional insights into the antibacterial potential of green mussel shells when processed into different forms, such as CaO [50].

According to another study, *Escherichia coli*, as a gram-negative bacterium, has a cell wall structure with a thin peptidoglycan layer (about 2-7 nm) coated by an outer membrane measuring 7-8 nm, containing lipopolysaccharides and porins. This structure allows chitosan to more easily penetrate the *E. coli* cell wall through the pores of the outer membrane. In contrast, *Staphylococcus aureus*, which belongs to gram-positive bacteria, has a thick peptidoglycan layer (about 20-80 nm) without an outer membrane. The thickness of peptidoglycan in *S. aureus* becomes a stronger barrier to chitosan penetration, so the antibacterial activity of chitosan against *S. aureus* tends to be lower than that of *E. coli* [34].

Antibacterial Activity of Chitosan from Crab Shell (*Portunus pelagicus)*

The inhibition of chitosan from crab shells against *Staphylococcus aureus* was tested using the agar diffusion method, where the formation of a clear zone around the hole filled with chitosan solution indicates the presence of antibacterial activity. At a chitosan concentration of 0.4%, the diameter of the inhibition zone formed reached an average of 10.27 mm, while at a concentration of 0.8%, the inhibition zone reached an average of 11.60 mm. This indicates that the higher the concentration of chitosan used, the larger the inhibition zone produced, reflecting the increased antibacterial effectiveness of chitosan [35].

From these results, chitosan shows fairly strong antibacterial activity against *S. aureus* at concentrations of 0.4% and 0.8%. In addition, at lower concentrations (0.1% and 0.2%), no zone of inhibition was observed, indicating that these concentrations were insufficient to inhibit bacterial growth. The determination of the Minimum Growth Inhibition Concentration (KHTM) was carried out by the graded dilution method, and the KHTM value for chitosan was found to be in the range of 0.05-0.1%. In comparison, the Minimum Kill Concentration (KBM) was reached at 0.1%, when no further bacterial growth was observed [35].

These results align with other studies showing that chitosan from king crab (*Portunus pelagicus*) exhibits strong antibacterial activity against *Porphyromonas gingivalis* biofilm. In these studies, the biofilm test method was used with chitosan concentrations of 0.25%, 0.5%, and 1%, and the results indicated that chitosan at a concentration of 1% exhibited the highest antibacterial power. This supports the finding that increasing chitosan concentration is directly proportional to increased bacterial inhibition [36]. Further research has shown that an increase in chitosan concentration from crab shells (*Portunus pelagicus*) also led to increased inhibition against bacteria. At a chitosan concentration of 9%, a zone of inhibition of 1.205 cm was formed against *Propionibacterium acnes*, indicating that higher concentrations provide a more significant bacterial inhibitory effect [37].

Antibacterial Activity of Chitosan from Squid Cartilage (*Loligo sp.*)

Research has shown that chitosan from squid cartilage effectively inhibited *Staphylococcus aureus* with an inhibition zone of 11.1 mm and *Escherichia coli* with an inhibition zone of 12.8 mm using the agar diffusion method [38]. Chitosan demonstrated higher antibacterial effectiveness against Gram-negative bacteria such as *E. coli*, which is explained by the electrostatic interaction between the positively charged amine groups on chitosan and the negatively charged bacterial cell wall. This interaction is particularly effective against Gram-negative bacteria, which have thinner and more permeable cell walls. As a result, the cell membrane is damaged, and intracellular components leak, thereby inhibiting bacterial growth [39].

Further research supported these findings, with a study showing that chitosan extracted from squid spine (*Loligo sp.*) had significant antibacterial activity against *Porphyromonas gingivalis*. At chitosan concentrations of 10.75% and 12.5%, bacterial growth was completely inhibited (100% inhibition), with no detectable bacterial colonies. This confirms the effectiveness of chitosan as a potential antibacterial agent, especially at higher concentrations, in inhibiting pathogens associated with oral infections [40].

Antibacterial Activity of Chitosan from Feather Clam Shell (*Anadara inflata*)

Research has shown that chitosan from feather clam shells (*Anadara inflata*) exhibits strong antibacterial effectiveness. In activity tests against *Staphylococcus epidermidis* and *Escherichia coli*, the results indicated that the higher the chitosan concentration, the larger the inhibition zone formed. At a 7% chitosan concentration, the inhibition zone reached 12 mm for *S. epidermidis* and 14 mm for *E. coli*. This supports the view that chitosan, particularly from feather clam shells, effectively inhibits bacterial growth, especially at higher concentrations [41].

These findings align with research showing that a 5% chitosan-based anti-acne cream formulation produced significant inhibition against *Propionibacterium acnes*. However, adding up to 15% of chitosan concentrations resulted in decreased diffusion power, reducing its effectiveness [42].

Further research strengthened the antibacterial potential of chitosan in a study by Tuti Aulia et al. (2022), where a 7% chitosan concentration produced an inhibition zone of 6.85 mm against *Aeromonas hydrophila*,

classified as medium. While not as large as the positive control using chloramphenicol, this study confirms that chitosan still has notable inhibitory effects against pathogenic bacteria. Collectively, these studies affirm that chitosan from feather clam and crab shells demonstrates significant antibacterial activity, particularly at higher concentrations, making it a promising material for antimicrobial applications [43].

Antibacterial Activity of Chitosan from Vannamei Shrimp Skin (*Litopenaeus vannamei*)

Chitosan extracted from shrimp shells has demonstrated significant antibacterial potential against various pathogenic bacteria, making it a promising agent for medical and hygienic applications [33]. Microcitosan obtained from Vannamei shrimp skin (*Litopenaeus vannamei*) was effective in inhibiting the growth of *Staphylococcus aureus* and *Escherichia coli* through the agar diffusion method. At a microcitosan concentration of 0.3%, the resulting inhibition zone reached 20.1 mm for *E. coli* and 16.3 mm for *S. aureus*, showing strong antibacterial activity, particularly against Gram-negative bacteria [38].

Further research showed that chitosan from Vannamei shrimp skin at a concentration of 7% (b/v) produced inhibition zones of 14.10 mm against *Staphylococcus epidermidis*, 15.30 mm against *Pseudomonas aeruginosa*, and 17.26 mm against *Propionibacterium acnes* and *Escherichia coli*. Analysis of variance (ANOVA) revealed significant differences between the treatments and the positive control (tetracycline), with a significance level of P = 0.000 (<0.05), indicating high antibacterial effectiveness at this concentration, which is comparable to the antibacterial activity of tetracycline [44].

These findings were further supported by research, which found that chitosan in hand sanitizer gel formulations at 1% concentration exhibited inhibition against *Staphylococcus aureus* and *Escherichia coli*, although the inhibition zones were relatively low, measuring 2.49 mm and 0.705 mm, respectively. These results suggest that while chitosan exhibits antibacterial activity at low concentrations, increasing its concentration significantly enhances its effectiveness. Overall, these studies demonstrate that chitosan extracted from shrimp shells, especially at higher concentrations or in specialized forms such as microparticles, has great potential as a natural antibacterial agent and is highly promising for use in the formulation of health and hygiene products [45].

Antibacterial Activity of Chitosan from Soft Crab (*Scylla olivacea*)

Chitosan extracted from soft crab (*Scylla olivacea*) shells showed significant antibacterial activity against *Vibrio harveyi*, a common pathogenic bacterium in aquatic environments. Research showed that this chitosan was able to produce an inhibition zone that increased with concentration, measuring 8.3 mm at 0.2%, 11.16 mm at 0.5%, and reaching 13.33 mm at 1%. The absence of an inhibition zone in the negative control confirmed that the observed antibacterial activity was derived from chitosan [46]. The antibacterial mechanism of chitosan involves electrostatic interaction between the positively charged amino groups on chitosan and the negatively charged surface of the bacterial cell wall. This interaction causes structural disruption of the bacterial cell membrane, leading to leakage of important intracellular components, thereby inhibiting bacterial growth and proliferation [39].

Antibacterial Activity of Chitosan from lobster shell (*Cherax quadricarinatus*)

Chitosan produced from lobster shells (*Cherax quadricarinatus*) has been shown to exhibit antibacterial activity against various pathogenic bacteria. Research demonstrated that chitosan at a concentration of 0.9% produced an inhibition zone of 17.2 mm against *Escherichia coli*, while a concentration of 0.3% produced an inhibition zone of 13.5 mm [47]. These results confirm that increasing chitosan concentration is positively correlated with antibacterial effectiveness, highlighting the strong antibacterial potential of chitosan against Gram-negative bacteria such as *E. coli* [48].

These findings are reinforced by research examining the effectiveness of chitosan-based hand sanitizer gel from lobster shells against *Escherichia coli* and *Staphylococcus aureus*. At a concentration of 4.5%, the chitosan gel produced inhibition zones of 8.8 mm for *E. coli* and 10 mm for *S. aureus*, which were categorized as moderate inhibition. These results suggest that chitosan from crayfish shells can be used as an antibacterial active ingredient in antiseptic formulations, although further optimization may be needed to improve its inhibitory properties [49].

Conclusion

This literature review concludes that chitosan extracted from various marine animal sources has antibacterial effectiveness against gram-positive and gram-negative pathogenic bacteria. Differences influence this effectiveness in the origin of chitosan sources as well as variations in bacterial cell wall structure, where chitosan shows higher penetration in gram-negative bacteria that have thinner cell walls. In addition, this review supports the potential of chitosan as an alternative to conventional antibiotics, especially in treating infections caused by resistant bacteria. This review provides a scientific basis for the clinical application of chitosan from marine sources as a potential, effective, safe, and environmentally friendly antibacterial agent, supporting its use in medical product development as well as sustainable antimicrobial therapy.

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