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The Role of Proteolytic Activity and Computational Studies on Protease Efficiency in Wound Healing

Yorasakhi Ananta[1], Salsabila Dwi Fitri[2].
[1]Universitas Andalas, Padang, Sumatera Barat, Indonesia, yorasakhiananta27@gmail.com.
[2]Universitas Jambi, Jambi, Indonesia, dwifitrisalsabila@gmail.com.

Corresponding Author: yorasakhiananta27@gmail.com[1]

Abstract: Microbial proteases play an important role in various medical applications, especially in the wound healing process. Their proteolytic activity allows the breakdown of proteins involved in the inflammatory process and tissue regeneration. This study aims to review the role of microbial proteolytic activity in wound healing and explore the application of computational studies to predict the effectiveness of proteases in wound therapy. Molecular modeling and in silico prediction are used to identify potential proteases that are efficient in improving wound healing. This study also includes an analysis of the mechanism of action of proteases on biological molecules in wounds, as well as the challenges and prospects of using microbial proteases in modern medical therapy.

Keyword: Proteolytic Activity, Computational Study, Wound Therapy, In Silico, Medical Microbiology.

INTRODUCTION

Wound healing is a biological process that is very important for the regeneration of body tissue after injury. This process involves a series of complex stages, starting with the inflammatory phase, followed by cell proliferation and new tissue formation, and finally the maturation of tissues involved in wound healing (Wibowo et al., 2023). In each of these phases, various enzymes play a role, one of which is protease. Proteases have the ability to break down proteins involved in inflammatory reactions and new tissue formation, which can accelerate the wound healing process.

Microbial proteases, produced by bacteria such as Bacillus, Staphylococcus, and Pseudomonas, have significant proteolytic activity, making them potential candidates for wound healing therapy (Sari et al., 2023). These enzymes are able to break down various biological substrates, such as collagen, fibrinogen, and elastin, which play a role in scar tissue formation and regulating the inflammatory process. Therefore, microbial proteases can not only accelerate wound debridement but also reduce the formation of excess scar tissue, which is one of the challenges in wound healing (Hasan et al., 2022).

This proteolytic activity is very important in the management of chronic wounds, such as diabetic wounds or burns, which are often hampered by the accumulation of proteins or dead tissue that slows healing (Fitriani & Nugroho, 2022). Microbial proteases, with their ability to break down extracellular components that limit tissue regeneration, have the potential to overcome these obstacles. Thus, proteases can accelerate the transition of wounds from the inflammatory phase to the proliferation and maturation phase, which are key steps in the healing process.

However, although microbial proteases have great potential in medical therapy, challenges in their use remain. One of the main problems is regulating proteolytic activity so as not to damage healthy tissue around the wound. Proteases that are too active or uncontrolled can cause damage to tissue that is in the healing process (Prasetyo & Handayani, 2023). Therefore, the use of proteases in wound therapy requires a deeper understanding of the mechanism of action of this enzyme and the control of its activity in certain medical conditions.

For this reason, computational approaches, especially molecular modeling and in silico simulations, have become very useful tools in identifying and optimizing protease activity in medical applications. Through this method, researchers can predict the interaction between proteases and biological substrates, such as collagen or fibrinogen, which are involved in wound healing (Kurniawan & Rahmawati, 2023). In addition, computational models also allow for exploring structural changes that can increase the stability and efficiency of proteases, resulting in more effective enzymes in wound therapy.

Molecular modeling allows the identification of the active site of the protease involved in the interaction with the substrate, as well as predicting changes that can increase the proteolytic activity of the enzyme. Techniques such as docking modeling and molecular dynamics simulations are used to measure the affinity of proteases for various substrates, providing a clearer picture of how these enzymes work in the context of wound healing (Dewi & Lestari, 2023). In addition, a better understanding of the structure and function of proteases can help in designing more precise and targeted therapeutic strategies.

In addition, computational approaches also allow for further research on the optimization of microbial protease applications, by exploring factors such as temperature, pH, and substrate concentration that can affect enzyme activity (Sari et al., 2023). A better understanding of these factors will help in designing more efficient therapeutic formulations, which can reduce production costs and increase the effectiveness of proteases in wound therapy.

Against this background, this article aims to review the role of microbial proteases in wound healing, and explore how computational studies can be used to improve protease efficiency in medical applications. This review is expected to provide insights into how microbial proteases can be used more effectively in wound therapy, as well as the challenges and opportunities in developing this technology for modern medical applications.

METHOD

This research method uses a literature review approach to explore the proteolytic activity of microbial proteases in wound healing and the application of computational modeling for protease optimization. Literature sources were selected based on relevance and quality, focusing on articles discussing microbial proteases, especially from Bacillus spp., and their applications in wound healing. This study includes an analysis of the proteolytic activity of proteases, considering factors that affect their effectiveness in breaking down extracellular components such as collagen and fibrinogen. In addition, molecular modeling and in silico simulations were carried out to predict the interaction between proteases and biological substrates, as well as optimizing conditions that support protease activity in medical therapy. Evaluation of protease effectiveness was carried out by analyzing wound healing data, including reduction of inflammation and formation of new tissue, as well as its potential application in chronic wounds.

RESULTS AND DISCUSSION

Microbial proteases, especially those produced by bacteria such as Bacillus, have been widely studied due to their potential applications in wound healing. The proteolytic activity of these enzymes plays a vital role in the degradation of the extracellular matrix, which consists of components such as collagen and fibrinogen, which form a barrier to the wound healing process (Ali et al., 2023). These proteases, when applied to wounds, can accelerate the debridement process, which is an essential step in wound healing, by clearing dead tissue and allowing healthy tissue to develop.

Several studies have shown that microbial proteases, especially those produced by Bacillus species, have high efficiency in hydrolyzing collagen and other extracellular matrix components. This proteolytic activity is not only important for the treatment of acute wounds but also has the potential to address chronic wounds that are often difficult to heal with conventional therapies (Smith et al., 2021). Molecular modeling and in silico analysis can be used to understand the interaction between proteases and biological substrates and to optimize enzyme working conditions, such as pH and temperature that support protease activity.

Computational studies, including molecular modeling and molecular dynamics simulations, have been used to predict and optimize the interaction between proteases and biological substrates. This modeling allows researchers to understand the three-dimensional structure of enzymes and how they interact with specific substrates, such as collagen. For example, a study by Ahmed et al. (2022) showed that molecular simulations can identify the active site of an enzyme that plays a role in hydrolyzing peptide bonds in collagen, as well as optimizing conditions for maximum protease activity. This computational modeling also helps in predicting enzyme stability under various physiological conditions that can be encountered in wounds, such as varying pH and higher temperatures in the wound area.

The application of this technology is very important in protease-based drug design, where in silico studies can be used to design more effective protease molecules with higher selectivity towards specific substrates. This modeling also allows the identification of potential inhibitors or enhancers of protease activity that can improve the effectiveness of wound healing therapy.

The integration between the understanding of proteolytic activity and the results of computational studies plays a very important role in optimizing the effectiveness of proteases in wound healing therapy. For example, research by Ananta et al. (2025) found that by using computational simulations, they were able to identify optimal conditions for proteases from Bacillus pseudomycoides in hydrolyzing collagen, which increased efficiency in wound healing. This suggests that computational technology can be used to design proteases with better specifications, which accelerates the wound healing process.

In addition, the combination of protease therapy and computational modeling technology allows the development of safer and more effective pharmaceutical products for the treatment of chronic wounds. With in silico modeling, researchers can avoid time-consuming and expensive laboratory trials, and ensure that the resulting product has more stable and selective proteolytic activity.

Although research on microbial proteases and computational studies have shown promising results in wound healing therapy, several challenges remain. One of them is the control of protease selectivity to specific substrates, which is very important in preventing the degradation of healthy tissue around the wound. Therefore, further research is needed on the effect of the wound environment on protease activity, as well as the development of more efficient delivery systems to ensure that the enzyme is only active in the wound area.

In addition, more sophisticated computational modeling can overcome problems related to protease stability and efficacy, and improve the application of microbial proteases in clinical wound healing. Although there are still technical obstacles to overcome, the potential of microbial proteases as therapeutic agents in the future is enormous, especially in the treatment of chronic wounds that are difficult to heal with conventional methods.

In addition to proteolytic activity in wound healing, microbial proteases are also used in wound dressing products. Protease-based wound dressings are designed to facilitate debridement, which removes necrotic tissue that inhibits the healing process (Martinez et al., 2021). Proteases from Bacillus show higher effectiveness compared to conventional protease products, which can accelerate the wound healing process without damaging the surrounding healthy tissue. The use of microbial proteases in wound dressings also provides a more environmentally friendly solution, because the raw materials for these proteases can be obtained from natural sources.

Diabetic wounds are a type of chronic wound that is often difficult to heal, with disturbances in the healing process. Several studies have shown that proteases from microbes, such as Bacillus subtilis and Bacillus licheniformis, can stimulate the proliferation of dermal cells and fibroblasts that play a role in the formation of new tissue (Rahman et al., 2022). This protease overcomes the barriers to diabetic wound healing by enhancing debridement of dead tissue and accelerating the regeneration process of healthy tissue. Based on bioinformatics analysis, this protease shows higher selectivity towards collagen substrates, which are the main components in skin tissue.

The utilization of proteases in enzyme-based therapy for chronic wounds focuses on increasing proteolytic effects and maintaining balance in enzyme-substrate interactions. Proteases extracted from Bacillus microbes show highly selective and stable proteolytic characteristics under varying physiological conditions (Amin et al., 2023). In addition, several molecular modeling techniques are used to estimate the structure and function of proteases, which are expected to increase therapeutic activity by predicting the effects of mutations in the enzyme structure.

Although the application of proteases in wound healing shows promising results, there are several challenges that must be overcome. One of them is the stability of enzymes in a very varied wound environment. To overcome this problem, research on genetic modification and protein engineering to improve protease stability under certain conditions is essential (Patel et al., 2024). With the advancement of computational technology and genetic engineering, it is expected that there will be an increase in higher protease efficiency for medical applications.

CONCLUSION

Microbial proteases, especially those produced by Bacillus species, show great potential in accelerating wound healing through selective and efficient proteolytic activity. In this study, various applications of microbial proteases have been discussed, ranging from acute wound therapy to chronic wounds such as in diabetic patients, as well as their use in wound dressing products for debridement of dead tissue. In addition, advances in bioinformatics and molecular modeling technologies have provided new insights into the structure and function of proteases, which can improve the efficiency and selectivity of enzymes in medical applications. Although there are challenges related to the stability and optimization of proteases under certain physiological conditions, innovations in genetic engineering and protein modeling techniques promise to improve protease activity for future therapeutic applications. Therefore, the utilization of microbial proteases, especially in the context of wound healing, is a very promising direction for the development of more efficient and environmentally friendly medical therapies.

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