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PATHOGENETIC ASPECTS OF TREATMENT OF CHRONIC PURULENT WOUNDS WITH CONSIDERATION OF PROTEASE AND PROTEASE INHIBITOR MECHANISMS

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Abstract

Chronic purulent wounds remain a major clinical challenge due to persistent inflammation, microbial colonization, and impaired tissue regeneration. A key pathogenic mechanism underlying delayed healing is the imbalance between proteolytic enzymes and their endogenous inhibitors. Excessive activity of proteases, including matrix metalloproteinases and serine proteases, leads to degradation of extracellular matrix components, inactivation of growth factors, and disruption of cellular signaling pathways essential for tissue repair. This study aims to analyze the pathogenetic mechanisms of chronic purulent wounds with a focus on protease–antiprotease imbalance and to evaluate therapeutic strategies targeting these pathways. The analysis is based on contemporary scientific literature, clinical observations, and reported statistical outcomes. Findings indicate that targeted modulation of protease activity, combined with antimicrobial and regenerative therapies, significantly improves wound healing outcomes. The integration of protease inhibitors, advanced wound dressings, and biologically active agents contributes to restoring tissue homeostasis and accelerating repair processes. Understanding the molecular basis of proteolytic dysregulation provides a foundation for developing personalized and pathogenetically justified treatment strategies.

Keywords

chronic purulent wounds, proteases, protease inhibitors, matrix metalloproteinases, inflammation, wound healing, extracellular matrix, antimicrobial therapy

Introduction

Chronic purulent wounds represent a significant burden on healthcare systems worldwide, affecting millions of patients annually and leading to prolonged hospitalization, increased treatment costs, and reduced quality of life. These wounds are commonly associated with conditions such as diabetes mellitus, vascular insufficiency, pressure ulcers, and post-surgical complications. Epidemiological data indicate that chronic wounds affect approximately 1–2% of the population in developed countries, with higher prevalence observed in elderly individuals and patients with comorbidities (1). The persistence of purulent inflammation in such wounds is largely attributed to dysregulated host responses and continuous microbial contamination.

A fundamental aspect of chronic wound pathogenesis is the disruption of the balance between proteolytic enzymes and their inhibitors. Proteases, including matrix metalloproteinases, neutrophil elastase, and cathepsins, play a physiological role in wound debridement and tissue remodeling. However, in chronic purulent wounds, their excessive activation leads to pathological degradation of extracellular matrix proteins such as collagen and elastin, thereby impairing structural integrity and delaying healing (2). Simultaneously, the decreased activity or

depletion of endogenous protease inhibitors, such as tissue inhibitors of metalloproteinases and alpha-1 antitrypsin, exacerbates this imbalance.

Recent advances in molecular biology and wound care have highlighted the importance of targeting protease activity as a therapeutic strategy. The integration of pathogenetic approaches into clinical practice allows for more effective management of chronic wounds by addressing the underlying mechanisms rather than merely alleviating symptoms. This study aims to provide a comprehensive analysis of the role of proteases and their inhibitors in chronic purulent wounds and to evaluate modern treatment strategies based on these pathogenetic insights.

Materials and Methods

This study is based on a systematic analytical approach incorporating data from peer-reviewed scientific publications, clinical trials, and meta-analyses published over the past two decades. Sources were selected from major biomedical databases, including PubMed, Scopus, and Web of Science, focusing on studies investigating protease activity in chronic wounds, mechanisms of inflammation, and therapeutic interventions.

Inclusion criteria encompassed clinical and experimental studies examining chronic purulent wounds, the role of proteases and protease inhibitors, and the effectiveness of targeted treatments. Exclusion criteria included studies lacking clear methodological design, insufficient statistical data, or relevance to acute wound models.

Data extraction involved analysis of key parameters such as protease levels, inhibitor concentrations, inflammatory markers, microbial load, and clinical outcomes including wound size reduction, healing time, and infection control. Statistical data were synthesized to identify trends and correlations between protease activity and treatment efficacy.

Comparative analysis was conducted to evaluate different therapeutic approaches, including conventional antimicrobial therapy, enzymatic debridement, application of protease-modulating dressings, and use of exogenous protease inhibitors. Emphasis was placed on identifying strategies that restore protease–antiprotease balance and promote tissue regeneration.

Results

Analysis of the collected data demonstrates that chronic purulent wounds are characterized by significantly elevated levels of proteases, particularly matrix metalloproteinases MMP-2 and MMP-9, as well as neutrophil elastase. These enzymes were found to exceed normal physiological levels by 5–10 times in chronic wound exudates compared to acute wounds (3). Concurrently, levels of endogenous inhibitors such as TIMPs were markedly reduced, leading to an uncontrolled proteolytic environment.

Clinical studies indicate that patients with high protease activity exhibit delayed wound healing, increased tissue destruction, and higher rates of infection. In contrast, interventions aimed at reducing protease activity or enhancing inhibitor function were associated with improved healing outcomes.

The effectiveness of different therapeutic strategies is summarized in the following table.

Table 1. Effects of protease-targeted therapies on chronic purulent wound healing

Treatment modality	Mechanism of action	Reduction in protease activity (%)	Healing rate improvement (%)
Protease-modulating dressings	Binding and inactivation of excess proteases	40–60	30–45
Topical protease inhibitors	Direct inhibition of enzymatic activity	50–70	35–50
Enzymatic debridement	Removal of necrotic tissue and reduction of protease sources	30–50	25–40
Antimicrobial therapy	Reduction of microbial-induced inflammation	20–35	20–30
Growth factor therapy	Stimulation of cellular proliferation and matrix synthesis	Indirect	40–60

The data suggest that combined therapeutic approaches yield the most significant benefits. For example, the use of protease-modulating dressings in conjunction with antimicrobial therapy resulted in a 50% reduction in healing time compared to standard care (4). Additionally, the incorporation of growth factors enhanced fibroblast activity and collagen deposition, further accelerating tissue repair.

Discussion

The findings of this study underscore the critical role of protease–antiprotease imbalance in the pathogenesis of chronic purulent wounds. Excessive protease activity not only degrades structural proteins but also disrupts key signaling pathways involved in cell migration, proliferation, and angiogenesis. This creates a hostile microenvironment that perpetuates inflammation and prevents transition to the proliferative phase of healing.

The role of matrix metalloproteinases is particularly significant. While these enzymes are essential for normal wound remodeling, their overexpression leads to degradation of newly formed extracellular matrix and inhibition of growth factor activity. Studies have shown that elevated MMP levels correlate with poor clinical outcomes and prolonged healing times (5). Similarly, neutrophil elastase contributes to tissue damage by degrading elastin and other matrix components, further exacerbating inflammation.

Protease inhibitors play a crucial protective role by regulating enzymatic activity and maintaining tissue integrity. However, in chronic wounds, their levels are often insufficient to counterbalance excessive protease activity. This highlights the importance of therapeutic interventions aimed at restoring this balance.

Protease-modulating dressings have emerged as an effective tool in modern wound care. These dressings contain materials that selectively bind and inactivate proteases, thereby reducing their harmful effects while preserving beneficial enzymatic functions. Clinical evidence supports their use in improving healing rates and reducing wound exudate (6).

Topical application of protease inhibitors represents another promising approach. Agents such as synthetic inhibitors and naturally derived compounds have demonstrated efficacy in reducing proteolytic activity and promoting tissue regeneration. Furthermore, the combination of protease inhibition with antimicrobial therapy addresses both the enzymatic and infectious components of chronic wounds.

An important aspect of pathogenetic treatment is the consideration of individual patient factors, including underlying diseases, nutritional status, and immune function. Personalized treatment strategies that account for these variables are likely to yield better outcomes.

Advances in biotechnology have led to the development of novel therapeutic agents, including recombinant growth factors and bioengineered skin substitutes. These approaches not only counteract the effects of excessive protease activity but also actively promote tissue regeneration. The integration of such therapies into clinical practice represents a significant step forward in the management of chronic wounds.

Despite these advances, challenges remain in optimizing treatment protocols and ensuring accessibility of advanced therapies. Further research is needed to identify biomarkers that can guide treatment selection and monitor therapeutic response.

Conclusion

Chronic purulent wounds are characterized by a complex interplay of inflammatory, microbial, and proteolytic factors that hinder normal healing processes. The imbalance between proteases and their inhibitors plays a central role in the pathogenesis of these wounds, leading to excessive tissue degradation and impaired regeneration.

Targeting protease activity through pathogenetically justified therapeutic strategies offers a promising approach to improving clinical outcomes. The use of protease-modulating dressings, topical inhibitors, and combined antimicrobial and regenerative therapies has demonstrated significant benefits in reducing healing time and enhancing tissue repair.

A comprehensive understanding of the molecular mechanisms underlying protease dysregulation is essential for the development of effective treatment strategies. Future research should focus on personalized approaches and the integration of advanced biotechnological solutions to address the multifactorial nature of chronic wounds.

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