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TREATMENT OF CHRONIC PURULENT WOUNDS BASED ON PATHOGENETIC MECHANISMS INVOLVING PROTEASES AND PROTEASE INHIBITORS

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Abstract: Chronic purulent wounds represent a major challenge in modern surgery and wound care due to prolonged inflammation, excessive tissue destruction, and impaired healing. Increasing evidence indicates that dysregulation of proteolytic activity is a central pathogenetic mechanism responsible for wound chronicity. Elevated levels of matrix metalloproteinases (MMPs) and serine proteases, combined with insufficient activity of endogenous protease inhibitors, result in degradation of extracellular matrix components and inactivation of growth factors. This review summarizes current evidence from published studies over the last decade focusing on the role of proteases and protease inhibitors in chronic purulent wounds and highlights therapeutic strategies aimed at restoring protease–inhibitor balance.

Keywords: chronic purulent wounds, proteases, matrix metalloproteinases, protease inhibitors, wound healing.

Introduction

Chronic purulent wounds are wounds that fail to heal in an orderly and timely manner and remain trapped in a prolonged inflammatory phase. They are frequently associated with diabetes mellitus, venous insufficiency, pressure injuries, and chronic infection. Despite advances in surgical techniques and wound dressings, treatment outcomes remain unsatisfactory for many patients [1,6].

Recent studies have demonstrated that excessive protease activity plays a critical role in wound chronicity. While proteases are essential for normal wound repair, persistent overexpression leads to extracellular matrix (ECM) destruction, impaired cell migration, and delayed tissue regeneration [2,9]. Understanding these pathogenetic mechanisms provides a rational basis for targeted therapeutic approaches.

Physiological Role of Proteases in Wound Healing

In acute wound healing, proteases contribute to:

- removal of necrotic tissue,

- regulation of inflammatory cell migration,

- release and activation of growth factors,

- remodeling of newly formed ECM [9].

Matrix metalloproteinases, including MMP-2, MMP-8, and MMP-9, are tightly regulated by endogenous inhibitors. Their activity normally decreases during the proliferative phase, allowing fibroblast activity and re-epithelialization to proceed [3,10].

Protease Dysregulation in Chronic Purulent Wounds

Matrix Metalloproteinases

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Numerous clinical and experimental studies have demonstrated significantly elevated levels of MMPs in chronic wound fluid. Increased MMP-9 activity has been consistently associated with delayed healing and poor clinical outcomes, particularly in diabetic foot ulcers [3,6].

Systematic analyses have shown that chronic wounds exhibit a proteolytic environment capable of degrading ECM proteins as well as essential growth factors, thereby preventing progression to the proliferative phase of healing [1,6]. Excessive MMP activity disrupts collagen deposition and destabilizes the wound bed.

Serine Proteases and Chronic Inflammation

Neutrophil-derived serine proteases contribute to sustained inflammation in chronic purulent wounds. These enzymes amplify tissue injury and activate additional proteolytic cascades, creating a self-perpetuating cycle of inflammation and matrix degradation [7,9].

Role of Protease Inhibitors

Protease activity is physiologically regulated by endogenous inhibitors, including tissue inhibitors of matrix metalloproteinases (TIMPs). An appropriate MMP/TIMP balance is essential for effective wound repair.

Several studies indicate that chronic wounds are characterized by reduced TIMP activity and elevated MMP/TIMP ratios, leading to uncontrolled matrix degradation [8,9]. Experimental and clinical data suggest that restoration of this balance correlates with improved healing outcomes [6].

Mathematical modeling studies further support the critical regulatory role of TIMPs in controlling chronic wound progression and emphasize the importance of targeted modulation rather than complete inhibition of protease activity [8].

Therapeutic Strategies Targeting Protease Imbalance

Protease-Modulating Wound Dressings

Protease-modulating dressings have been developed to bind and inactivate excessive proteases within the wound environment. Systematic reviews demonstrate that dressings containing collagen, oxidized regenerated cellulose, or lipid-colloid matrices with nano-oligosaccharide factors significantly reduce MMP activity and promote wound healing [1,10].

Clinical evidence indicates that these dressings are particularly effective in diabetic foot ulcers and venous leg ulcers, where protease levels are markedly elevated [1,6].

Selective Protease Inhibition

Selective inhibition of specific proteases has emerged as a promising therapeutic strategy. Experimental studies demonstrate that selective inhibition of MMP-9 accelerates wound closure, reduces inflammation, and enhances angiogenesis, while preserving beneficial proteolytic activity required for tissue remodeling [11].

These findings support the concept that targeted protease inhibition is preferable to broad suppression of proteolytic activity.

Biomaterials and Advanced Therapeutic Approaches

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Recent research highlights the potential of biomaterials designed to modulate protease activity locally. Keratin-based matrices and protease-absorbing wound materials have demonstrated the ability to suppress harmful protease activity while supporting cellular migration and ECM stability [4,5].

Nanotherapeutic systems and peptide-based formulations are being explored to protect growth factors from proteolytic degradation and to create a pro-regenerative wound microenvironment [2,12].

Challenges and Future Perspectives

Despite encouraging results, protease-targeted therapies face several challenges, including variability in protease expression among patients and limited availability of point-of-care diagnostics for protease activity assessment. Future research should focus on individualized treatment strategies based on wound protease profiling and combination therapies addressing both inflammation and proteolysis [6,12,15].

Conclusion

Published evidence from the last decade clearly demonstrates that excessive protease activity combined with insufficient protease inhibition is a key pathogenetic mechanism in chronic purulent wounds. Therapeutic strategies aimed at restoring protease–inhibitor balance—particularly through protease-modulating dressings, selective protease inhibition, and advanced biomaterials—represent a rational and promising approach to improving wound healing outcomes. Continued translational research is required to optimize these strategies and integrate them into routine clinical practice.

References

1. Dissemond J. et al. Efficacy of MMP-inhibiting wound dressings in the treatment of chronic wounds. J Wound Care. 2020.

2. An G. et al. Protease-resistant growth factor formulations for the healing of chronic wounds. Adv Wound Care. 2020.

3. Liu Y. et al. Increased matrix metalloproteinase-9 predicts poor wound healing in diabetic foot ulcers. Diabetes Care. 2009.

4. Human keratin matrices suppress matrix metalloproteinase activity to support wound healing. Wound Repair Regen. 2024.

5. Wiegand C. et al. Inhibition of matrix metalloproteinase activity in chronic wounds by wound dressings. Wound Repair Regen. 2008.

6. Smith S.J. et al. Protease activity as a prognostic factor for wound healing in complex wounds. Wound Repair Regen. 2020.

7. Percival S.L., McCarty S.M. Proteases and delayed wound healing. Adv Wound Care. 2013.

8. Smith J. et al. Regulation of chronic wounds by tissue inhibitors of matrix metalloproteinases. J Theor Biol. 2025.

9. Caley M.P., Martins V.L., O'Toole E.A. Metalloproteinases and wound healing. Adv Wound Care. 2015.

pISSN:2349-5707 Volume:12,Issue 12,December-2025 eISSN:2349-5715

10. Cullen B. et al. Mechanism of action of protease-modulating wound dressings. Wound Repair Regen. 2002.

11. Rao N. et al. Selective MMP-9 inhibition in diabetic wound healing. ACS Pharmacol Transl Sci. 2023.

12. Advances in nanotherapeutics for chronic wound healing. Curr Drug Targets. 2024.

13. Protease-absorbing wound dressings and chronic wound fluid degradation. Wound Repair Regen. 2008.

14. Anti-biofilm peptides and protease activity in chronic wounds. Adv Pharm Bull. 2022.

15. Immunomodulatory hydrogels for chronic wound therapy. Bioactive Materials. 2024.