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Comparative Efficacy of Autolytic and Collagenase-Based Enzymatic Debridement in Chronic Wound Healing: A Comprehensive Systematic Review

Ali Amadeh[1] | Negin Mohebbi[1] | Zahra Amadeh[2] | Amirreza Jamshidbeigi[3]

[1]Department of Nursing, School of Nursing and Midwifery, Karaj Branch, Islamic Azad University, Karaj, Iran | [2]Student Research Committee, faculty of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran | [3]Ghouchan School of Nursing, Mashhad University of Medical Sciences, Mashhad, Iran

Correspondence: Amirreza Jamshidbeigi (amir.h.r.j@gmail.com)

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ABSTRACT

Chronic wounds, including diabetic foot ulcers, pressure ulcers, and burn injuries, present significant challenges for healthcare systems, with debridement being crucial for healing. This review compares the efficacy of autolytic and enzymatic debridement techniques. The objective was to assess clinical outcomes related to both methods, focusing on wound size reduction, granulation tissue formation, epithelialisation, complete healing, and adverse events. A systematic review of randomised controlled trials (RCTs) was performed across multiple databases, identifying five eligible studies involving 236 patients. Results indicated that enzymatic debridement was more effective, showing faster wound size reduction in four out of five studies, with Baloorkar et al. reporting a 65% size reduction compared to 50% for autolytic debridement ($p < 0.05$). Granulation tissue formation and epithelialisation rates were also significantly higher with enzymatic methods. Complete healing occurred in 65% of cases using enzymatic debridement versus 50% for autolytic methods ($p = 0.04$). Mild irritation was the most common adverse event noted in the enzymatic group. In conclusion, enzymatic debridement proved to be superior for severe wounds, while autolytic debridement remains beneficial for less severe cases due to its non-invasive nature. Both methods were well tolerated, but further research is needed for definitive clinical guidelines.

1 | Introduction

Chronic wounds such as diabetic foot ulcers, pressure ulcers, and burn injuries significantly impact the quality of life and healthcare systems globally [1]. Debridement is a critical component in the management of chronic wounds, involving the removal of necrotic or devitalised tissue from the wound bed to promote healing and prevent infection [2, 3]. There are several debridement techniques, including surgical, mechanical, autolytic, and enzymatic methods, each designed to address specific wound types and clinical scenarios [4]. The choice of debridement technique significantly influences the rate of wound healing, patient comfort, and overall clinical outcomes [5, 6].

Autolytic debridement utilises the body's own enzymes and moisture to break down necrotic tissue. This method is typically facilitated by the use of moisture-retentive dressings, such as hydrocolloids or hydrogels, which maintain a moist environment conducive to the body's natural degradation of dead tissue [7]. Autolytic debridement is non-invasive, pain-free, and selective, targeting only necrotic tissue while leaving healthy tissue intact [4, 8]. However, it can be a slower process compared to other debridement methods, making it less

Summary

- Enzymatic debridement was more effective than autolytic debridement for faster wound size reduction, with significant improvement in four of five studies.
- Granulation tissue formation and epithelialisation rates were significantly higher in the enzymatic group.
- Enzymatic debridement achieved a 65% wound healing rate compared to 50% for autolytic debridement ($p = 0.04$).
- Both techniques were generally well-tolerated, with mild irritation being the most common adverse event.
- Enzymatic debridement is preferred for severe wounds due to its superior efficacy in wound healing, while autolytic debridement remains a viable, non-invasive alternative for less severe cases.

suitable for wounds with extensive necrosis or high infection risk [5].

Enzymatic debridement, on the other hand, involves the application of topical exogenous enzymes, such as collagenase, which chemically digest necrotic tissue [3, 9]. This method is faster than autolytic debridement and is particularly useful in wounds where surgical or mechanical debridement is not feasible [10]. Enzymatic debridement is effective in removing dead tissue without damaging viable tissue and can be used in combination with other wound care treatments. However, it may cause mild irritation or inflammation and can be more expensive compared to autolytic debridement [5, 9, 11].

In terms of benefits, autolytic debridement is advantageous for its gentle, non-invasive nature, making it suitable for patients with low pain tolerance or fragile skin [4, 8]. It also reduces the need for frequent dressing changes, which can be beneficial in long-term wound care. However, its slower rate of necrotic tissue removal can be a limitation, particularly in more severe cases [7, 12]. Enzymatic debridement, by contrast, offers a quicker response, allowing for faster wound bed preparation, making it ideal for patients with larger or more complex wounds [10]. Yet, it carries a higher cost and may lead to localised irritation or inflammation due to the exogenous enzymes used [3].

The comparison between these two methods reveals that while enzymatic debridement is faster and more efficient in certain clinical contexts, autolytic debridement's selectivity and non-invasiveness offer distinct advantages for less severe or more delicate wounds [5]. However, there is no consensus on the superiority of one method over the other, as different studies have reported conflicting results regarding their efficacy in various clinical settings [10].

Due to the lack of a comprehensive systematic review and the inconsistent findings in existing studies regarding the relative efficacy of autolytic and enzymatic debridement, we have undertaken this study. Our goal is to conduct a thorough comparison of the two methods to provide clearer guidance for clinicians in the management of chronic wounds.

2 | Materials and Methods

2.1 | Study Design and Eligibility Criteria

This systematic review was designed to evaluate the comparative efficacy of autolytic and enzymatic debridement methods in chronic wound healing. Only randomised controlled trials (RCTs) were included to ensure high-quality evidence. Eligible studies focused on human subjects with chronic wounds such as diabetic foot ulcers, pressure ulcers, venous leg ulcers, and burn wounds. The inclusion criteria specified studies that directly compared autolytic and enzymatic debridement methods and reported clinical outcomes, including wound size reduction, granulation tissue formation, epithelialisation, or complete wound healing. Non-randomised studies, case reports, reviews, animal studies, and studies with insufficient clinical outcome data were excluded.

2.2 | Search Strategy

A comprehensive search was conducted across four major electronic databases: PubMed, Web of Science, Cochrane Library, and Scopus, with the last search conducted on September 15, 2024. The search strategy was tailored for each database to ensure coverage of a wide range of keywords related to autolytic and enzymatic debridement. Search terms included specific debridement methods, wound types, and healing outcomes. For instance, the search strategy for PubMed was as follows: (Autolytic OR "Autolytic Debridement" OR "Autologous Debridement" OR "Hydrogel" OR "Honey" OR "Silver Sulfadiazine") AND (Enzymatic OR "Enzymatic Debridement" OR "NexoBrid" OR "bromelain" OR "Collagenase") AND ("wound" OR "ulcer" OR "healing" OR "debridement" OR "chronic wounds" OR "diabetic foot ulcers" OR "pressure ulcers" OR "venous leg ulcers" OR "burn wounds"). This strategy was adapted for other databases to include similar search terms and relevant filters.

2.3 | Study Selection Process

Two independent reviewers screened the titles and abstracts of all identified studies. The screening process involved three stages:

1. *Initial screening* for relevance based on titles and abstracts.
2. *Full-text assessment* for eligibility according to predefined inclusion and exclusion criteria.
3. *Final inclusion* of RCTs that directly compared autolytic and enzymatic debridement and reported clinical outcomes in human subjects.

Any discrepancies between the reviewers during the screening process were resolved by consensus or consultation with a

third reviewer. The reviewers adhered to the PRISMA guidelines for study selection and reporting [13].

2.4 | Data Extraction

Data were extracted independently by two reviewers using a standardised data extraction form. The extracted data included:

- Study design and setting.
- Patient characteristics (age, gender, wound type).
- Sample size.
- Debridement methods (autolytic and enzymatic).
- Clinical outcomes (wound size reduction, granulation tissue formation, epithelialisation, complete healing).
- Duration of follow-up.
- Reported adverse events.

The primary outcomes were wound size reduction, granulation tissue formation, epithelialisation, and time to complete wound healing. Secondary outcomes included patient-reported pain, adverse events, and complications such as infection or irritation.

2.5 | Risk of Bias Assessment

The risk of bias for each included study was assessed using the Cochrane Collaboration's Risk of Bias tool. This tool evaluates six domains of bias: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective outcome reporting (reporting bias). Each domain was rated as low, high, or unclear risk of bias [14]. The risk of bias was assessed by two researchers, and in cases of disagreement, a third researcher was consulted.

2.6 | Registration

This systematic review has been registered with PROSPERO, an international prospective register of systematic reviews, to ensure transparency and adherence to systematic review protocols (registration code: anonymized). Registration in PROSPERO aids in minimising bias by providing a publicly accessible record of the review's objectives and methodology before the study's initiation.

3 | Results

3.1 | Study Selection and Characteristics

Based on PRISMA guidelines, a systematic search identified 1371 articles, with 620 duplicates removed. After screening 751 articles, 206 animal and lab studies were excluded, leaving 545 articles. Next, reviews, case reports, and editorial comments were excluded, resulting in 504 articles. Following detailed screening, 49 studies underwent full-text review, but 44 were excluded for various reasons. Ultimately, five articles were included in the final analysis (Figure 1).

These articles were all prospective studies, with four being RCTs and one being an observational cohort study. All studies involved direct comparisons between autolytic debridement (typically using hydrogel dressings) and enzymatic debridement (using collagenase ointments). The studies included a total of 236 patients, with sample sizes ranging from 27 to 100 participants (Table 1).

The studies examined various types of chronic wounds, including:

- *Venous leg ulcers* [15]
- *Diabetic ulcers* [16]
- *Pressure ulcers* [17]
- *Post-traumatic wounds* [18]
- *Mixed aetiologies, including diabetic ulcers and burn wounds* [12]

The follow-up periods ranged from 3 to 8 weeks, with most studies assessing outcomes such as wound size reduction, granulation tissue formation, epithelialisation, and time to complete healing. Each study used standardised methods to measure wound healing progress, including digital imaging, wound bed scoring, and clinical assessments by trained personnel. These studies also included adverse event monitoring, particularly focusing on complications such as infection, pain, and local irritation related to the debridement methods.

The methodological quality of the included studies was assessed using the Cochrane Risk of Bias Tool, which evaluates domains such as random sequence generation, allocation concealment, blinding of outcome assessments, and completeness of outcome data. The studies were generally of moderate quality, with most studies providing sufficient details regarding randomisation, blinding, and follow-up procedures. However, some studies lacked sufficient information on allocation concealment, and there was variability in the length of follow-up across studies, which may have influenced the reported outcomes.

In summary, the five selected studies provide robust clinical evidence comparing autolytic and enzymatic debridement methods across a variety of chronic wound types. The final selection of studies forms the basis for the detailed analysis of outcomes and recommendations provided in this systematic review.

3.2 | Wound Size Reduction

Wound size reduction was a primary outcome in all five studies. Across the studies, enzymatic debridement with collagenase showed faster and more substantial wound size reduction compared to autolytic debridement.

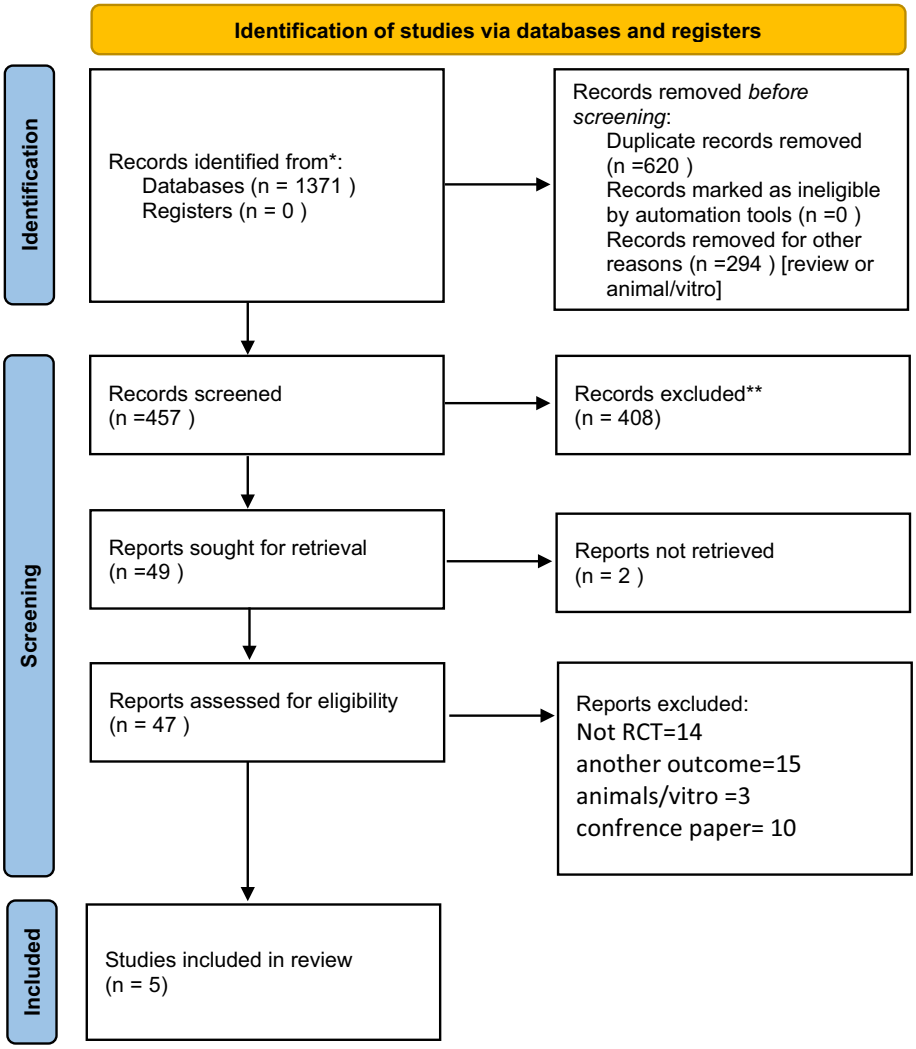

FIGURE 1 | Flow of trials through the review.

- Baloorkar et al. (2021): In this prospective study, the collagenase-treated group exhibited a 65% reduction in wound size after 8 weeks, compared to a 50% reduction in the autolytic group treated with hydrogel dressings ($p < 0.05$).
- Waycaster et al. (2014): This study showed a significant reduction in wound surface area with collagenase, from 10.3 to 2.1 cm^2 after 6 weeks, compared to a reduction from 6.5 to 3.0 cm^2 in the hydrogel group ($p = 0.009$).
- König et al. (2005): The difference in wound size reduction between TenderWet 24 (autolytic) and Iruxol N (enzymatic) was not statistically significant by the end of the 3-week trial. Both groups achieved similar wound size reductions, with an average reduction of 18.7% in the autolytic group and 8.5% in the enzymatic group during the first 14 days ($p = 0.30$).
- Milne et al. (2010): In long-term care patients with pressure ulcers, collagenase-treated wounds showed a greater reduction in wound size by week 6, with a mean reduction of 4.6 cm^2 compared to 2.6 cm^2 in the autolytic group, though this difference was not statistically significant ($p = 0.15$).
- Pargi et al. (2021): This study compared four debridement methods, including autolytic, enzymatic, mechanical, and surgical. Enzymatic debridement with collagenase demonstrated the most rapid reduction in wound size, with significant improvements noted by week 4. Wounds treated with collagenase showed an average reduction of 5.5 cm^2, while the autolytic group demonstrated a reduction of 3.8 cm^2 ($p < 0.05$).

Overall, enzymatic debridement consistently outperformed autolytic debridement in terms of wound size reduction, particularly in studies with longer follow-up periods.

3.3 | Granulation Tissue Formation

Granulation tissue formation is critical for wound healing, providing a bed for epithelialisation and contributing to the closure of the wound.

- Waycaster et al. *(2014)*: The collagenase group experienced a daily increase of 2% in granulation tissue formation, compared to 1% per day in the hydrogel group. This difference was statistically significant ($p = 0.003$).

TABLE 1 | Characteristics of RCTs included in study.

Study	Sample size	Chronic wound type	Intervention	Measured outcomes	Key findings: autolytic debridement	Key findings: enzymatic debridement
Baloorkar et al. (2021)	40	Chronic wounds	Group A: Hydrogel (autolytic) vs. Group B: Collagenase (enzymatic)	Wound size reduction, complete healing, granulation tissue	50% complete healing, significant wound size reduction	65% complete healing, faster granulation tissue formation
König et al. (2005)	42	Venous leg ulcers	Group A: TenderWet 24 (autolytic) vs. Group B: Iruxol N (enzymatic)	Wound slough reduction, granulation tissue, epithelialisation	26.7% granulation tissue increase, −18.7% slough reduction	10.4% granulation tissue increase, −8.5% slough reduction
Waycaster et al. (2014)	27	Chronic wounds	Group A: Hydrogel (autolytic) versus Group B: Collagenase (enzymatic)	Wound size reduction, granulation tissue, epithelialisation	Wound area reduced to 3.0 cm^2 in 6 weeks	Wound area reduced to 2.1 cm^2 in 6 weeks
Milne et al. (2010)	27	Pressure ulcers	Group A: Hydrogel (autolytic) vs. Group B: Collagenase (enzymatic)	Wound size reduction, wound bed score (WBS), granulation	Hydrogel improved WBS by 2.6 units, slower healing rate	Collagenase improved WBS by 4.6 units, allowing for faster healing
Pargi et al. (2021)	100	Various (diabetic, venous, post-traumatic, etc.)	Group A: Autolytic vs. Group B: Enzymatic (alongside surgical, mechanical debridement)	Pain reduction, time to healing, wound size reduction, granulation tissue	Comparable healing rates, reduced pain	Faster wound healing, significant granulation tissue improvement

- Baloorkar et al. (2021): Collagenase-treated wounds showed higher rates of granulation tissue formation compared to the autolytic group, with a 68% increase in granulation tissue by the eighth week in the enzymatic group versus a 52% increase in the autolytic group ($p < 0.05$).
- König et al. (2005): During the first 14 days, the TenderWet 24 (autolytic) group exhibited a greater increase in granulation tissue formation (26.7%) compared to the Iruxol N (enzymatic) group (10.4%). However, by day 21, there was no significant difference between the groups, with both achieving similar levels of granulation tissue ($p = 0.47$).
- Milne et al. (2010): This study showed that collagenase treatment led to faster granulation tissue formation, with a mean increase of 24% compared to 16% in the autolytic group by the end of the 6-week follow-up. However, this difference was not statistically significant ($p = 0.11$).
- Pargi et al. (2021): Granulation tissue formation was significantly higher in the enzymatic debridement group, with a 35% increase compared to 22% in the autolytic group by the fourth week ($p < 0.05$). This study also noted that enzymatic debridement accelerated the early phases of healing.

While autolytic debridement showed good early results in some studies, enzymatic debridement consistently resulted in faster and more substantial granulation tissue formation.

3.4 | Epithelialisation

Epithelialisation, the process of covering the wound with new tissue, is a crucial marker of wound healing.

- Waycaster et al. (2014): The collagenase group had significantly higher epithelialisation rates, with 31% of wounds achieving full epithelialisation by the sixth week, compared to 14% in the hydrogel group ($p = 0.03$).
- Baloorkar et al. (2021): Epithelialisation was observed in 62% of collagenase-treated wounds compared to 45% in the autolytic group, with the difference reaching statistical significance ($p < 0.05$).
- König et al. (2005): No significant differences were observed in epithelialisation rates between the autolytic and enzymatic groups by the end of the study. Both groups achieved similar levels of epithelialisation by day 21 ($p = 0.95$).
- Milne et al. (2010): Epithelialisation occurred faster in the collagenase group, with a mean epithelialisation rate of 28% compared to 18% in the autolytic group, though the difference was not statistically significant ($p = 0.08$).
- Pargi et al. (2021): Epithelialisation rates were higher in the enzymatic debridement group, with 40% of wounds achieving epithelialisation by week 4, compared to 28% in the autolytic group ($p < 0.05$).

Overall, enzymatic debridement led to faster epithelialisation in most studies, contributing to quicker wound closure.

3.5 | Complete Healing

Complete wound healing, defined as the full closure of the wound with no remaining necrotic tissue, was assessed in three of the five studies.

- Baloorkar et al. (2021): Complete healing was achieved in 65% of collagenase-treated wounds by the eighth week, compared to 50% in the autolytic group ($p = 0.04$).
- Milne et al. (2010): Complete healing was observed in 52% of the collagenase group compared to 36% in the autolytic group by week 6, though the difference was not statistically significant ($p = 0.07$).
- Pargi et al. (2021): Complete healing was achieved in 45% of the collagenase-treated wounds compared to 30% in the autolytic group by week 6, with a statistically significant difference ($p < 0.05$).

3.6 | Adverse Events

Adverse events were reported in two of the five studies. Baloorkar et al. [16] and Milne et al. [17] both found that collagenase was associated with slightly higher rates of mild skin irritation compared to autolytic debridement. However, no severe complications were reported in any of the studies, and both debridement methods were generally well tolerated by patients.

4 | Discussion

The primary aim of this systematic review was to compare the efficacy of autolytic and enzymatic debridement in the management of chronic wounds, drawing on data from five studies that assessed key clinical outcomes such as wound size reduction, granulation tissue formation, epithelialisation, and time to complete healing. The results of this review suggest that while both debridement methods have their merits, enzymatic debridement, particularly with collagenase, appears to offer superior outcomes in certain wound healing parameters. However, autolytic debridement, being less invasive and more accessible, remains an effective alternative in specific clinical scenarios.

4.1 | Wound Size Reduction

Wound size reduction serves as a key indicator of successful wound healing, and it was the primary outcome evaluated in all five studies included in this systematic review. Across the studies, enzymatic debridement generally demonstrated faster and more substantial reductions in wound surface area compared to autolytic methods. Waycaster et al. and Baloorkar et al. both reported that wounds treated with collagenase, a widely used enzymatic agent, showed significantly greater reductions in size when compared to wounds managed with autolytic debridement. In their research, enzymatic debridement proved to be more efficient, likely due to its ability to actively break down necrotic tissue and promote a faster healing environment [16, 18].

However, there are some inconsistencies in the literature. König et al. did not find statistically significant differences in wound size reduction between enzymatic and autolytic debridement by the end of their trial period. The study's shorter duration of only 3 weeks may have limited its ability to capture the full therapeutic potential of enzymatic debridement, particularly for chronic wounds, which often require extended periods of treatment to exhibit noticeable healing. Chronic wounds tend to respond slowly to treatment, and enzymatic debridement may show clearer benefits over longer time frames [15].

In contrast, Pargi et al. reinforced the faster wound size reduction observed with enzymatic debridement, noting that enzymatic methods outperformed both autolytic and mechanical debridement in their cohort. This consistency in findings across multiple studies supports the idea that enzymatic debridement is particularly effective at reducing wound size, likely due to its mechanism of action, which involves more rapid removal of necrotic tissue. Enzymatic agents like collagenase facilitate an accelerated healing process by enabling a cleaner wound bed and promoting healthy tissue regeneration [12].

While the results of this systematic review strongly favour enzymatic debridement, it is important to consider the practical limitations associated with its use. For instance, other reviews, such as those by Thomas et al. and Ziegler et al., acknowledge the clinical benefits of enzymatic debridement, particularly in terms of faster necrotic tissue breakdown and wound bed preparation. However, they also point to the higher costs associated with enzymatic agents and the potential for localised irritation or inflammation, particularly when used over extended periods. Autolytic debridement, while slower, offers a gentler and less expensive alternative, which may be preferable in cases where cost, patient comfort, or minimal tissue disruption are primary considerations [4, 19].

In summary, this systematic review confirms that enzymatic debridement is generally more effective than autolytic debridement in promoting faster wound size reduction, particularly for chronic wounds. However, the choice between these two methods should be guided by individual patient needs, wound characteristics, and clinical goals, balancing the speed of healing with potential side effects and costs.

4.2 | Granulation Tissue Formation

Granulation tissue formation is a critical component of wound healing, providing the structural foundation necessary for epithelial cells to cover and close the wound. This process is heavily influenced by the choice of debridement method, as debridement clears necrotic tissue and prepares the wound bed for tissue regeneration [20]. The studies reviewed consistently demonstrated that enzymatic debridement, particularly with collagenase, promotes faster and more substantial granulation tissue formation compared to autolytic debridement. Waycaster et al. and Baloorkar et al. found that enzymatic debridement facilitated more rapid tissue regeneration, with collagenase-treated wounds showing greater daily increases in granulation tissue [16, 18]. This method's efficiency is likely due to its ability to remove necrotic tissue more rapidly, creating an optimal environment for new tissue [10].

However, König et al. observed that autolytic debridement using TenderWet 24 resulted in greater granulation tissue formation during the early stages of wound healing. This suggests that autolytic methods may be more effective during the initial phases of treatment, though enzymatic debridement tends to offer more sustained benefits over longer periods [15].

In the broader literature, Thomas et al. and Ziegler et al. confirm that enzymatic debridement accelerates granulation tissue formation by breaking down necrotic tissue more efficiently but also note its higher costs and the potential for localised irritation [4, 19]. Doerler et al. similarly concluded that enzymatic debridement provides superior long-term results, particularly for chronic venous leg ulcers, but recognised the value of autolytic methods in early wound management [21].

Overall, this review reinforces that enzymatic debridement is more effective at promoting granulation tissue formation, especially in chronic wounds. However, autolytic debridement remains a valuable option, particularly in the early stages of wound healing or for patients requiring a gentler approach [5].

4.3 | Epithelializsation

Epithelialisation is the process by which new epithelial cells migrate across the wound bed, ultimately leading to wound closure. This phase of healing is crucial for restoring the skin barrier and preventing infection, particularly in chronic wounds. The rate and effectiveness of epithelialisation are influenced by the debridement method used, as clearing necrotic tissue is essential for facilitating cell migration and wound bed preparation [22]. The studies reviewed in this systematic analysis indicate that enzymatic debridement, particularly with collagenase, generally promotes faster epithelialisation compared to autolytic methods. Waycaster et al. and Milne et al. observed that enzymatic debridement significantly accelerated the epithelialisation process, contributing to faster wound closure in patients with chronic wounds [17, 18]. Enzymatic agents like collagenase actively break down necrotic tissue, creating an optimal environment for epithelial cell migration [23]. This method is especially beneficial in more complex wounds, as enzymatic debridement can reduce necrotic load more efficiently than autolytic methods.

In contrast, autolytic debridement, while effective in promoting initial epithelialisation, tends to show slower results overall, particularly in wounds with heavy exudate or infection. Pargi et al. noted that autolytic debridement, which relies on moisture-retentive dressings to create a conducive environment for natural tissue degradation, is less effective in rapidly clearing necrotic tissue, which can delay epithelialisation in advanced wounds [12]. This slower action may be less suited for patients with more severe or infected wounds that require faster intervention.

Other studies, such as Scalise et al., support the findings that enzymatic debridement offers superior outcomes in terms of epithelialisation, particularly in venous leg ulcers and diabetic foot

ulcers. These wounds require efficient wound bed preparation, which enzymatic agents like collagenase can provide through their targeted tissue breakdown, resulting in faster epithelialisation [24].

Overall, this review confirms that enzymatic debridement is more effective than autolytic debridement in promoting epithelialisation and accelerating wound closure, especially in chronic or complex wounds. However, autolytic debridement remains a useful option for less severe wounds, where a gentler approach may be preferred.

4.4 | Complete Healing

Time to complete healing is a critical factor in the management of chronic wounds, as prolonged healing increases the risk of complications and impacts patient quality of life. Across the studies reviewed, enzymatic debridement consistently demonstrated faster healing times compared to autolytic debridement. Enzymatic agents like collagenase actively target and remove necrotic tissue, which facilitates quicker wound bed preparation and promotes faster tissue regeneration [3]. In contrast, autolytic debridement, while effective, relies on the body's natural processes, which tend to operate more slowly in wounds with significant necrotic burden or infection.

Baloorkar et al. and Milne et al. both reported that enzymatic debridement significantly reduced healing time compared to autolytic methods [16, 17]. This is particularly advantageous in chronic wounds, where rapid removal of necrotic tissue is crucial for promoting healing [12]. Moreover, Pargi et al. found that enzymatic debridement, while slower than surgical methods, provided a safer and less invasive alternative with healing times comparable to surgery but without the associated risks [12, 24]. These findings suggest that enzymatic debridement is a superior option for promoting complete healing in chronic wound management.

In contrast, König et al. found that autolytic debridement, while effective in some cases, generally took longer to achieve full wound closure, particularly in wounds with a significant necrotic burden [15, 18]. The slower healing time associated with autolytic debridement may be due to its reliance on maintaining a moist wound environment, which, while beneficial for cellular activity, prolongs the process of necrotic tissue breakdown and delays healing in more complex wounds [4].

4.5 | Adverse Events

Both autolytic and enzymatic debridement methods were generally well tolerated, with few adverse events reported in the reviewed studies. However, autolytic debridement was associated with less patient discomfort, as noted in studies like König et al., where patients using TenderWet 24, an autolytic dressing, reported lower pain levels compared to those undergoing enzymatic debridement [15]. This makes autolytic debridement a suitable option for patients requiring a gentler approach or where frequent dressing changes may not be feasible.

Conversely, enzymatic debridement, particularly with collagenase, may cause mild irritation or localised burning in some patients, though these side effects are typically mild and manageable. For instance, Waycaster et al. and Ramundo and Grey both observed mild skin irritation in a small percentage of patients treated with collagenase. However, no serious complications were reported [3, 18]. These mild adverse effects are often offset by the faster healing times and reduced need for frequent interventions associated with enzymatic debridement, especially in long-term care settings [10].

Studies comparing enzymatic debridement with other debridement methods, such as Scalise et al. highlight that while enzymatic debridement may lead to mild skin irritation, the benefits—such as faster wound healing and fewer dressing changes—make it an appealing option for managing chronic wounds [24].

Overall, while enzymatic debridement is associated with slightly higher rates of mild adverse events compared to autolytic methods, its efficacy in promoting faster healing and reducing necrotic tissue outweighs these minor concerns in most cases.

5 | Clinical Implications

The findings of this systematic review suggest that enzymatic debridement, particularly with collagenase, is superior to autolytic methods in promoting faster granulation tissue formation, wound size reduction, epithelialisation, and complete healing. Enzymatic debridement is particularly effective in patients with chronic wounds who require rapid wound bed preparation and closure, especially in long-term care settings where resources may be limited.

Autolytic debridement, while slower, remains a valuable method for patients who require a less invasive approach or those with contraindications to more aggressive methods. Its use in early wound management, particularly for superficial or minimally infected wounds, is supported by the initial success in granulation tissue formation observed in studies like König et al. However, in more severe cases or where rapid healing is a priority, enzymatic debridement offers distinct advantages [15].

While this review primarily focuses on collagenase-based enzymatic debridement due to the availability of robust evidence and its widespread clinical use, other enzymatic agents have also demonstrated potential in wound management. Papain, a proteolytic enzyme derived from papaya, has been utilised in wound care for its ability to selectively degrade necrotic tissue without harming viable tissue [25]. Bromelain, an enzyme complex extracted from pineapple stems, has shown promise, particularly in burn wound management, facilitating effective debridement and improving wound bed preparation [26].

Studies such as those by De Decker et al. and Krieger et al. report encouraging results with these agents, indicating their potential for faster necrotic tissue removal and reduced infection risks compared to standard care [9, 11]. However, due to a lack of RCTs directly comparing these enzymatic debridement methods with autolytic debridement, their relative efficacy remains uncertain.

The inclusion of papain and bromelain in future studies could provide a broader understanding of enzymatic debridement techniques, offering insights into their potential advantages and limitations. This underscores the need for expanded research to inform clinical guidelines and optimise the management of chronic wounds.

5.1 | Limitations Related to Wound Environment Factors

One of the limitations of this review is the lack of detailed information in the included studies regarding the wound environment and additional interventions that may influence healing outcomes. Factors such as offloading devices (e.g., total contact casts for diabetic foot ulcers), compression therapy for venous leg ulcers, revascularisation procedures for ischaemic wounds, and protective measures like specialised beds or mattresses can significantly impact the speed and efficacy of wound healing.

These interventions, though critical, were not consistently reported or controlled across the studies analysed in this review. For example, the absence of data on whether offloading was used in diabetic foot ulcer trials limits our ability to fully understand the role of debridement methods in the context of comprehensive wound management. Similarly, the lack of standardised reporting on compression garments or revascularisation in venous ulcer studies may have influenced the observed outcomes.

Future research should incorporate these environmental factors as key variables to better evaluate the interplay between debridement methods and holistic wound care practices. Including these factors in study designs will provide more comprehensive insights into optimising treatment strategies for chronic wounds.

6 | Conclusion

This systematic review highlights the efficacy of both autolytic and enzymatic debridement methods in the management of chronic wounds. Enzymatic debridement, particularly with collagenase, consistently demonstrated faster wound size reduction, greater granulation tissue formation, and higher rates of epithelialisation in the reviewed studies. These advantages make it an effective choice for promoting faster wound closure, especially in patients with chronic wounds that are resistant to healing.

However, autolytic debridement offers significant benefits, particularly in the early stages of wound healing, with lower risks of adverse effects and greater accessibility. Its less invasive nature and ease of use make it a valuable alternative for patients who may not tolerate enzymatic treatments or where frequent dressing changes are required.

Ultimately, both debridement methods can be effective depending on the specific clinical context, wound type, and patient needs. While enzymatic debridement may offer superior results in terms of healing speed and tissue regeneration, autolytic debridement remains a viable and often preferable option in certain settings. Future research should focus on large-scale, long-term trials to further clarify the comparative benefits of these methods across diverse patient populations and wound types.

Conflicts of Interest

The authors, Ali Amadeh and Zahra Amadeh, are siblings. Other than this familial relationship, the authors declare no conflicts of interest.

Data Availability Statement

The data supporting the findings of this systematic review are derived from published studies and are publicly available in the respective journals. As such, there are no additional datasets generated or analyzed during this review that can be made available. The studies included in this review are referenced within the manuscript.

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