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Exuberant Granulation Tissue in Horses: Pathophysiology and Therapeutic Approaches – An Integrative Review


Tecido de Granulação Exuberante em Equinos: Fisiopatologia e Abordagens Terapêuticas – Revisão Integrativa


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Abstract

Exuberant granulation tissue (EGT) in horses constitutes a frequent complication of second-intention wound healing, especially in wounds located on the distal limbs. This integrative review aimed to synthesize the available evidence on the pathophysiology, associated factors, complications, and therapeutic approaches related to EGT in horses. Searches were conducted in the PubMed/MEDLINE, SciELO, and LILACS databases, considering publications from 2013 to 2025. After title and abstract screening, followed by full-text reading, 27 studies were included, comprising experimental studies, case reports, clinical series, reviews, and histological studies. The findings indicated that EGT is related to local and systemic factors, such as low perfusion, hypoxia, edema, mobility of the affected region, persistent infection, and bacterial biofilm formation, which contribute to the maintenance of chronic inflammation, delayed reepithelialization, and reduced wound contraction. The therapeutic approaches described were predominantly combined, involving wound bed preparation, debridement, excision of exuberant tissue when indicated, infection control, and the use of adjuvant therapies. In conclusion, EGT remains a relevant clinical challenge in horses, highlighting the need for controlled studies and standardized protocols to strengthen therapeutic decision-making.

Keywords: Horses. Wound Healing. Skin Wounds. Exuberant Granulation Tissue.

Resumo

O tecido de granulação exuberante (TGE) em equinos constitui uma complicação frequente da cicatrização por segunda intenção, especialmente em feridas localizadas nos membros distais. Esta

revisão integrativa teve como objetivo sintetizar as evidências disponíveis sobre a fisiopatologia, os fatores associados, as complicações e as abordagens terapêuticas relacionadas ao TGE em equinos. Foram realizadas buscas nas bases PubMed/MEDLINE, SciELO e LILACS, considerando publicações entre 2013 e 2025. Após triagem por títulos e resumos, seguida da leitura na íntegra, foram incluídos 27 estudos, abrangendo pesquisas experimentais, relatos de caso, séries clínicas, revisões e estudos histológicos. Os achados indicaram que o TGE está relacionado a fatores locais e sistêmicos, como baixa perfusão, hipóxia, edema, mobilidade da região afetada, infecção persistente e formação de biofilmes bacterianos, os quais contribuem para a manutenção da inflamação crônica, atraso da reepitelização e redução da contração da ferida. As abordagens terapêuticas descritas foram predominantemente combinadas, envolvendo preparo do leito da ferida, desbridamento, excisão do tecido exuberante quando indicada, controle de infecção e uso de terapias adjuvantes. Conclui-se que o TGE permanece como desafio clínico relevante em equinos, sendo necessária a realização de estudos controlados e protocolos padronizados para fortalecer a tomada de decisão terapêutica.

Palavras-chave: Equinos. Cicatrização de Feridas. Feridas Cutâneas. Tecido de Granulação Exuberante.

1 Introduction

Chronic wounds in horses pose a significant challenge both from the perspective of animal welfare and the financial costs involved (Bundgaard *et al.*, 2018). In this context, the healing process in horses is more complex compared to other species, due to anatomical, physiological, and environmental factors that increase susceptibility to complications, with a significant functional, aesthetic, and economic impact, especially in the equine industry (Ribas; Regianini, 2024).

In horses, extensive, contaminated, or inadequately managed wounds in their initial phase heal predominantly by secondary intention, involving the formation of granulation tissue to fill the wound bed, followed by re-epithelialization and, to a lesser extent, tissue contraction. However, in distal limb regions, factors such as low vascularization, reduced skin mobility, local hypoxia, and a greater predisposition to infection make this healing mechanism significantly more complex and prone to dysfunction (Sparks *et al.*, 2021), resulting in slower wound closure, often associated with the formation of extensive scars and the development of exuberant granulation tissue (EGT) (Kamus; Rameau; Théoret, 2019).

Sustained chronic inflammation and the presence of bacterial biofilms also play a central role in the chronicity and complications of the healing process in horses (Jorgensen; Jacobsen; Bundgaard, 2021; Seid; Birhan, 2019; Théoret; Wilmink, 2013). In this context, biofilm formation and the development of microbial resistance increase the complexity of clinical management and hinder the conventional therapeutic response (Marchant; Hendrickson; Pezzanite, 2024). Bacterial biofilms, composed of organized communities of microorganisms adhered to the wound bed and immersed in a self-synthesized extracellular matrix, protect against the host's immune response and reduce the

effectiveness of antimicrobial agents. This organization favors the persistence of infection and the maintenance of local inflammatory stimuli, contributing decisively to the development of chronic wounds in horses (Jorgensen; Jacobsen; Bundgaard, 2021).

The diagnosis of biofilms in routine veterinary clinical practice is still considered challenging. Advanced laboratory methods, such as confocal microscopy associated with PNA-FISH and scanning electron microscopy, have high accuracy, but are not easily accessible in clinical practice (Jorgensen; Jacobsen; Bundgaard, 2021). Thus, biofilm identification is often based on indirect clinical criteria, such as wounds refractory to treatment, persistent exudate, frequent recurrences, and the presence of friable or devitalized tissue (Marchant; Hendrickson; Pezzanite, 2024).

Among the most common and clinically challenging complications of secondary intention healing in horses is exuberant granulation tissue (EGT), especially in wounds located on distal limbs. EGT is characterized by the excessive proliferation of granulation tissue that exceeds the level of the adjacent skin, compromising epithelial migration and the normal progress of tissue repair. Clinically, it manifests as a friable, moist, bright red mass with a tendency to bleed (Théoret; Wilmink, 2013).

The etiology of EGT is considered multifactorial, involving local, inflammatory, infectious, and immunological factors, with persistent chronic inflammation being one of the main elements associated with its development. Prolonged maintenance of the inflammatory process favors exacerbated angiogenesis and disorganized deposition of the extracellular matrix, creating a microenvironment conducive to hypergranulation and failure of re-epithelialization (Du Cheyne; Martens; De Spiegelaere, 2021). The management of these lesions remains challenging in clinical practice, requiring careful and individualized therapeutic approaches, and emerging therapies still lack clinical validation in horses (Jorgensen; Jacobsen; Bundgaard, 2021).

Given the above, this integrative review aims to synthesize the available evidence in the literature on the pathophysiology, associated factors, complications, and therapeutic approaches to exuberant granulation tissue in horses, with an emphasis on wounds located in distal limbs and healing by secondary intention.

2 Material and Methods

This is an integrative literature review, designed to gather and synthesize scientific evidence on exuberant granulation tissue (EGT) in horses, considering its pathophysiological aspects, associated factors, clinical complications, and therapeutic approaches. The guiding question was: what pathophysiological characteristics, associated factors, complications, and therapeutic strategies are

described in the scientific literature on EGT in horses?

The process of identifying, screening, eligibility, and inclusion of studies was organized according to the PRISMA 2020 recommendations, with the article selection flow presented in a specific figure. The bibliographic search was conducted in the PubMed/MEDLINE, SciELO, and LILACS databases, including publications available between January 2013 and December 2025.

Controlled descriptors and keywords related to the equine species, wound healing, and exuberant granulation tissue were used. The search strategies combined terms in English and Portuguese, according to the database consulted, including expressions such as: “horse”, “equine”, “wound healing”, “skin wound”, “exuberant granulation tissue”, “proud flesh”, “exuberant granulation tissue”, “equines”, “wound healing” and “cutaneous wounds”, combined by the Boolean operators AND and OR.

The study included original articles, experimental studies, case reports, case series, reviews and clinical guidelines that addressed exuberant granulation tissue, skin wound healing or therapies applicable to the equine context. Studies with full text available and a direct relationship to the theme of the review were considered eligible. Duplicates, publications outside the established period, studies in other species without applicability to the equine context, texts without full access, publications that did not answer the guiding question and studies of a purely contextual nature without a direct contribution to the objectives of the review were excluded.

The selection of studies was carried out in two stages. Initially, the titles and abstracts were read to identify potentially relevant articles. Next, the full texts were evaluated according to the previously defined inclusion and exclusion criteria. The process was conducted by two independent reviewers, and any disagreements were resolved by consensus, with the participation of a third reviewer when necessary.

Data extraction was performed using a standardized spreadsheet, including the following information: author and year of publication, study title, study type, main objective, characteristics of the intervention or approach analyzed, main findings, and methodological limitations. The extracted data were synthesized descriptively and organized into thematic axes: pathophysiological characteristics of the EGT, factors associated with dysfunctional healing, the role of infection and biofilms, conventional therapeutic approaches, and adjuvant or complementary therapies.

A meta-analysis was not performed due to the heterogeneity of the designs, interventions, outcomes, and protocols described in the included studies. Similarly, a formal instrument for assessing the risk of bias was not applied, considering the predominance of case reports, clinical

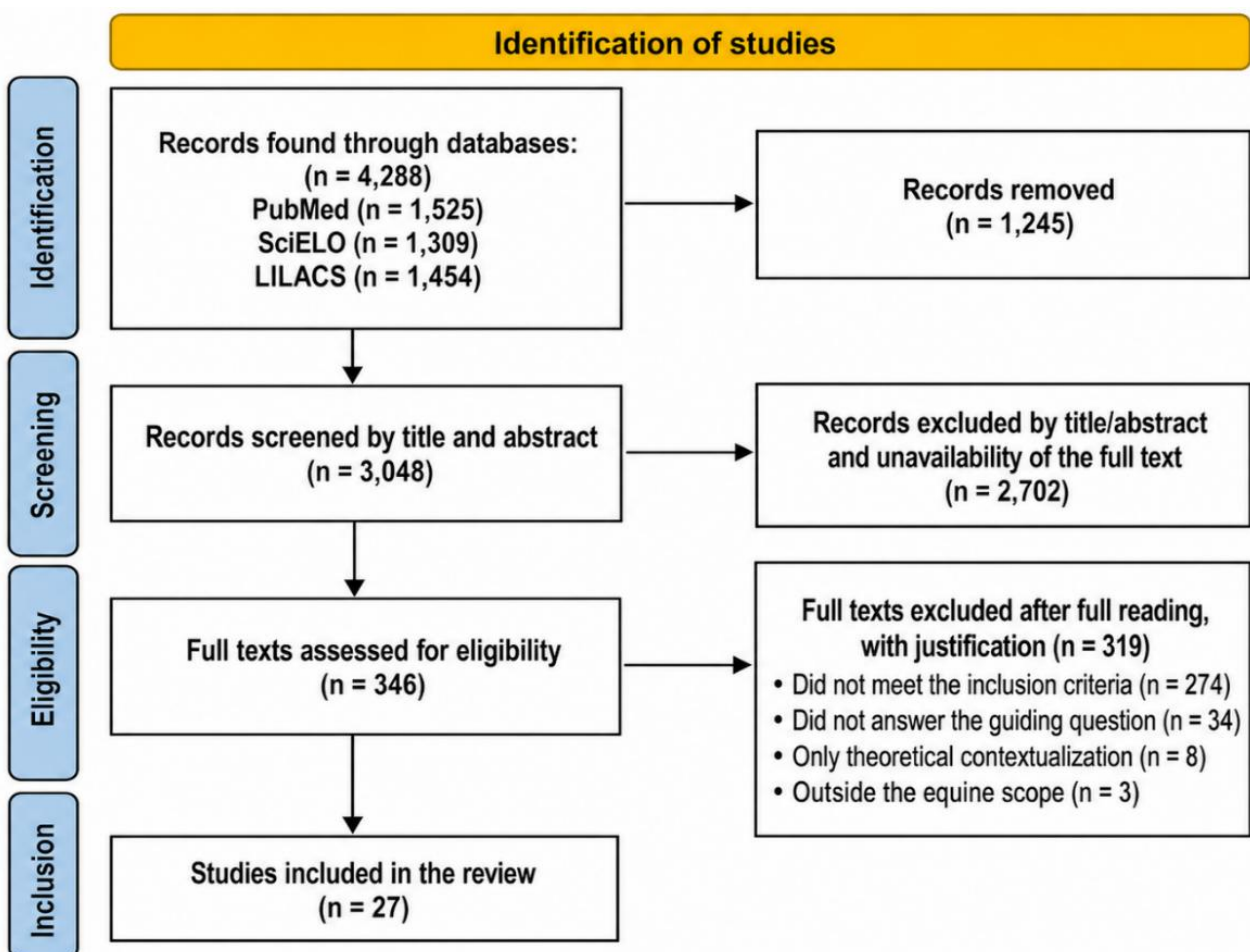
series, and narrative reviews. Even so, the interpretation of the findings considered the type of study, the level of evidence available, and the limitations inherent in each design, avoiding causal inferences or direct comparisons when not supported by the data.

3 Results and Discussion

The results of the procedures adopted for the selection of studies included in this review are presented in Figure 1. Information about the articles included in this review, author and year of publication, article title, type and objective of the study are presented in Tables 1, 2 and 3.

The synthesis of evidence was organized into thematic axes that reflect factors associated with the chronicity of wounds in horses, complications of repair by secondary intention, with emphasis on exuberant granulation tissue (EGT), and the main therapeutic approaches reported in the literature.

Figure 1 - Flowchart for selecting studies included in the integrative review, according to PRISMA recommendations



Source: the authors.

Table 1 - Experimental studies included in the integrative review. Fortaleza, CE, 2013 to 2025

Author (Year)	Title	Objective (Synthesis)
Sparks, H.D. <i>et al.</i> (2021)	Biomechanics of wound healing in an equine limb model	To develop a biomechanical assay method to evaluate functional wound outcomes in an equine distal limb model, characterize differences by location, and investigate the effect of a peptide-modified collagen-chitosan hydrogel on wound healing.
Lucas, F.A. <i>et al.</i> (2017)	Copaiba oil in experimental wound healing in horses	To evaluate the effects of 10% copaiba oil on experimentally induced wounds in horses.
Kauer, D.P. <i>et al.</i> (2020)	Experimental treatment of cutaneous wounds with <i>Copaifera langsdorffii</i> extract and oleoresin in horses	To evaluate the healing potential of hydroalcoholic extract and oleoresin creams of <i>Copaifera langsdorffii</i> in equine cutaneous wounds.
Di Filippo, P.A. <i>et al.</i> (2020)	Effects of pure and ozonated sunflower seed oil (<i>Helianthus annuus</i>) on hypergranulation tissue formation, infection and healing of equine lower limb wounds	To evaluate the therapeutic effects of topical application of pure and ozonized sunflower seed oil on the healing of acute cutaneous wounds in horses, comparing exuberant granulation tissue formation, infection, contraction, and re-epithelialization.

Source: research data.

Table 2 - Clinical reports and case series included in the integrative review. Fortaleza, CE, 2013 to 2025)

Author (Year)	Title	Objective (Synthesis)
Viana, L.F.S. <i>et al.</i> (2014)	Complementary treatments for wound with exuberant granulation tissue in one horse - Case report.	To report the complementary treatments used in the postoperative period of exuberant granulation tissue in a horse, highlighting the positive points and limitations of each approach.
Varasano, V.; Marruchella, G.; Petrizzi, L. (2018)	Exuberant granulation tissue in a horse: successful treatment by the intralesional injection of 4% formaldehyde solution	To describe the treatment of exuberant granulation tissue in a horse by means of intralesional injection of a 4% formaldehyde solution, evaluating the clinical outcome and highlighting the need for further studies to better determine efficacy and possible adverse reactions.
Andrade, C.F.O. <i>et al.</i> (2022)	Use of copper sulfate for debridement of exuberant granulation tissue in traumatic equine wounds	To report two cases of horses with lacerating wounds in pelvic limbs with exuberant granulation tissue, treated topically with 20% copper sulfate, describing clinical evolution and feasibility of the technique.
Bandeira, AL. <i>et al.</i> (2020)	Use of lasertherapy in tissue repair in equine	To report a clinical case of a wound/laceration in a horse limb submitted to low-power laser therapy, describing the evolution of healing throughout the sessions.
Costa, B.O. <i>et al.</i> (2020)	Treatment of a Traumatic Equine Wound Using Nile Tilapia (<i>Oreochromis niloticus</i>) Skin as a Xenograft	To report a case of a traumatic wound in a horse treated with tilapia skin as a xenograft, evaluating the potential of the biomaterial as an effective, practical and low-cost therapy.
Boscarato, A.G. <i>et al.</i> (2020)	Use of Calender Extract Cream in Equine Lacerate Wound	To evaluate the effectiveness of a 2% non-ionic <i>Calendula officinalis</i> cream in the treatment of an extensive lacerating wound in a horse.
Ribeiro, R.M. <i>et al.</i> (2019)	Use of sacarose in second intention healing in 3rd degree wound in equine: Case report	To describe the evolution of the treatment of a 3rd-degree wound in a horse with sucrose, evaluating its evolution and recovery.
Almeida, P.N.M.; Giovanoni, H.F.; Giovanoni, R.F. (2020)	Open wound treatment in equine using <i>Stryphnodendron adstringens</i> infusion associated with crystal sugar – case report	To present a case report on the topical application of <i>Stryphnodendron adstringens</i> associated with granulated sugar in an open wound in a horse, monitoring the healing process until complete closure of the lesion and describing the characteristics of the final scar tissue.

Author (Year)	Title	Objective (Synthesis)
Mazzo, H.C. <i>et al.</i> (2014)	<i>Topical use of coconut oil in equine wound healing</i>	To demonstrate the effectiveness of the topical use of extra virgin coconut oil, in association with copper sulfate, in the treatment of a traumatic lacerative wound in a horse healing by secondary intention.
Basha, K.M.A. <i>et al.</i> (2019)	Surgical Management of Proud Flesh – A Report of Two Equines	To report two horses with exuberant granulation tissue (proud flesh) in different regions of the limb, describing the therapeutic approaches employed (surgical resection in one case and topical use of astringents in the other) and the clinical evolution without recurrence.

Source: research data.

Table 3 - Clinical reviews and guidelines included in the integrative review. Fortaleza, CE, 2013 to 2025

Author (Year)	Type	Objective (Synthesis)
Théoret, C.L.; Wilmlink, J.M. (2013)	Review	To discuss the use of the horse as a model for wound healing, highlighting similarities with human wound healing and the spontaneous occurrence of fibroproliferative disorders, such as exuberant granulation tissue.
Seid, A.M.; Birhan, M. (2019)	Review	To review wound management in horses and the healing process, including classification, treatment principles, and factors influencing evolution.
Jorgensen, E.; Jacobsen, S.; Bundgaard, L (2021)	Review	To raise awareness of the presence of biofilms in equine wounds and discuss how to suspect, detect, and treat biofilms in the clinical context.
Marchant, K.; Hendrickson, D.A.; Pezzanite, L.M. (2024)	Review	To summarize evidence on biofilms in equine wounds, highlighting clinical signs, diagnostic methods, and biofilm-oriented management strategies to support practice.
Anantama, N.A. <i>et al.</i> (2022)	Review (narrative + scoping review)	To consolidate and describe the basic and clinical literature on exuberant granulation tissue (EGT) in horses, identify knowledge gaps, and synthesize evidence on prevention and treatment methods, highlighting opportunities for future research.
Lux, C.M. (2022)	Review	To review the phases of wound healing in animals, discuss intrinsic and extrinsic factors associated with delayed or aberrant healing, and present the TIME principle as a framework for systematic clinical assessment of wounds.
Paiva, B.J.D. <i>et al.</i> (2023)	Review	To demonstrate the efficiency and benefits of using laser therapy in the treatment of cutaneous wounds in horses, based on a literature review.
Castro, B.C. <i>et al.</i> (2024)	Narrative review	To conduct a literature review on the use of ozone therapy in the treatment of different wounds in horses, gathering information on the advantages and applications of the technique.
Liang <i>et al.</i> (2021)	Review	To describe the process of skin injury and healing and analyze the role of Aloe vera in tissue repair, discussing types of dressings and applications of Aloe vera in wound coverings.
Xavier, J.C.; Barroso, M.I.R.; Araripe, M.G.A. (2022)	Integrative review	To understand the clinical and therapeutic aspects of the use of natural products in wound healing in horses, focusing on sugar, Aloe vera, barbatimão, and calendula.
Ribeiro G. <i>et al.</i> (2024)	Review	To identify and synthesize protocols for the treatment of cutaneous wounds in horses healing by secondary intention (scoping review). Develop evidence-based clinical guidelines for wound management in horses, using a systematic review of veterinary and human literature with the application of the GRADE framework, in order to support decision-making in clinical practice.

Author (Year)	Type	Objective (Synthesis)
Freeman, S.L. <i>et al.</i> (2021)	Review of clinical evidence/guidelines (GRADE)	To develop evidence-based clinical guidelines for wound management in horses, using a systematic review of veterinary and human literature with the application of the GRADE framework, in order to support decision-making in clinical practice.
Steiner, S.; Smith, J.; Brown, P. (2019)	Review	To review factors associated with wound healing in horses and related challenges.

Source: research data.

3.1 Exuberant granulation tissue: characteristics and pathophysiological aspects

In this review, exuberant granulation tissue (EGT) is presented as one of the most frequent complications of secondary intention healing in horses, especially in wounds located in distal limbs (Anantama *et al.*, 2022). Studies have indicated that EGT is associated with the presence of persistent inflammation, marked fibroblastic proliferation, exacerbated angiogenesis, and inadequate remodeling of the extracellular matrix, resulting in the maintenance of a persistent inflammatory microenvironment (Lux, 2022; Théoret; Wilmlink, 2013). Alterations in keratinocyte differentiation and deficiency in contraction mechanisms have also been identified as relevant factors for wound chronicity (Anantama *et al.*, 2022).

Infection has been described as one of the main factors associated with delayed healing of cutaneous wounds in horses, especially in traumatic wounds, and is aggravated by the formation of bacterial biofilms (Jorgensen; Jacobsen; Bundgaard, 2021). The presence of subclinical infection and biofilms has been identified as a potential enhancer of local inflammation, contributing to the formation and maintenance of EGT, although this association is not always easily identifiable in routine clinical practice (Anantama *et al.*, 2022).

The literature converges in interpreting EGT as a marker of dysfunctional healing, in which fibroblastic hyperplasia and immature angiogenesis mechanically interfere with epithelial migration and contraction, prolonging treatment time and increasing costs (Théoret; Wilmlink, 2013; Seid; Birhan, 2019). In addition to the aesthetic impact, the persistence of exuberant tissue can compromise locomotor function, especially when it involves regions of greater mobility, and favor secondary colonization and recurrent bleeding, perpetuating the inflammatory cycle (Varasano; Marruchella; Petrizzi, 2018). Clinically, these findings indicate that controlling the microenvironment (exudate, edema, mobility, and bacterial load) is as important as removing exuberant tissue when it blocks re-epithelialization.

Although the studies analyzed converge in recognizing EGT as a result of a persistent and disorganized inflammatory response, there are still divergences regarding the relative weight of each factor involved in its formation. While pathophysiological studies emphasize cellular alterations, exacerbated angiogenesis, and inadequate remodeling of the extracellular matrix, clinical reports tend

to highlight practical factors such as wound location, infection, regional mobility, and failures in initial management. This difference between experimental and clinical approaches limits the definition of a single explanatory model for EGT in horses.

3.2 Factors associated with complications in wound healing in horses

The unfavorable evolution of cutaneous wounds in horses results from the combination of local and systemic factors that favor the persistence of an inflammatory microenvironment, impairing re-epithelialization and contraction. Among the local factors, the location of the injury, the presence of infection, constant movement of the affected region, hypoxia and edema stand out. These factors are especially relevant in wounds on the distal limbs, which heal slower due to limited blood perfusion, compromising oxygenation and the transport of repair cells to the wound bed (Seid; Birhan, 2019).

Furthermore, the absence of a fleshy panniculus and the mobility of joints and tendons make wound contraction difficult, favoring micro-ruptures of immature collagen and prolonging the inflammatory phase. Even in the absence of evident clinical signs of infection, bacterial contamination and biofilm formation have been described as capable of sustaining local inflammation and delaying wound closure (Marchant; Hendrickson; Pezzanite, 2024; Théoret; Wilmink, 2013).

Among the systemic factors, age, nutritional status, presence of metabolic diseases and use of drugs are mentioned. Young animals tend to present a more intense fibroblastic response, while weakened animals have slower healing. Nutritional deficiencies, especially of proteins, zinc, copper and vitamins A and C, compromise collagen synthesis and the immune response, negatively impacting tissue repair (Viana *et al.*, 2014). Prolonged use of systemic corticosteroids and the presence of equine metabolic syndrome have also been associated as unfavorable modulators of the inflammatory response and angiogenesis (Théoret; Wilmink, 2013).

The set of findings supports that the combination “distal limb + limited perfusion + mobility + edema and hypoxia” creates a microenvironment predisposing to inflammatory persistence and delayed re-epithelialization and contraction, favoring complications. The practical implication is that management must be simultaneously local and systemic: control edema and movement, reduce microbial load and review nutritional and metabolic conditions and use of drugs potentially harmful to repair (Seid; Birhan, 2019; Théoret; Wilmink, 2013; Viana *et al.*, 2014).

3.3 Bacterial biofilms and infection as factors in chronicity

The studies analyzed indicate that infection is one of the main factors associated with delayed healing of cutaneous wounds in horses, especially traumatic wounds, and is aggravated by the formation of bacterial biofilms (Jorgensen; Jacobsen; Bundgaard, 2021).

In wounds located on distal limbs, conditions such as low vascularization, local hypoxia,

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persistent exudation, and the presence of devitalized tissue were frequently related to the establishment and maintenance of these biofilms, being associated, in the studies analyzed, with the maintenance of continuous inflammatory stimulus and the delay of the stages of wound closure, including re-epithelialization and contraction (Marchant; Hendrickson; Pezzanite, 2024).

Regarding diagnosis, studies highlight limitations in the routine application of advanced laboratory methods, such as confocal microscopy associated with PNA-FISH and scanning electron microscopy, which means that the identification of biofilms in clinical practice often depends on indirect signs, such as refractory wounds, persistent exudate, recurrences, and the presence of friable or devitalized tissue (Jorgensen; Jacobsen; Bundgaard, 2021; Marchant; Hendrickson; Pezzanite, 2024).

The evidence reinforces that biofilm acts as a factor in maintaining inflammation, reducing the effectiveness of the immune response and antimicrobials, which contributes to the chronicity of lesions and the failure of orderly progression of the repair phases (Jorgensen; Jacobsen; Bundgaard, 2021; Marchant; Hendrickson; Pezzanite, 2024). Clinically, this implies adopting combined and repeated management strategies, with emphasis on debridement, wound bed optimization, and culture- and sensitivity-guided antimicrobial therapies when available, in addition to antibiofilm agents such as iodocadexomer, nanocrystalline silver, and organic acids (Jorgensen; Jacobsen; Bundgaard, 2021).

3.4 Treatments and therapeutic approaches (conventional, adjuvant and complementary)

The included studies describe that the treatment of cutaneous wounds and EGT in horses is multifactorial and based on a combination of different therapeutic approaches. The initial strategies reported involve rigorous wound cleaning and the use of antiseptic solutions, such as povidone-iodine, chlorhexidine, sodium hypochlorite, and hydrogen peroxide, with the aim of reducing the bacterial load. However, cytotoxic effects associated with the continuous use of these agents have been described, especially on fibroblasts (Lux, 2022; Théoret; Wilmlink, 2013).

Among the adjuvant approaches, satisfactory results have been described with the intralesional injection of 4% formaldehyde in cases of EGT (Varasano; Marruchella; Petrizzi, 2018). The topical use of 20% copper sulfate has also been reported as an effective, low-cost, and easy-to-apply method of chemical debridement, especially in situations where surgical resection is not feasible (Andrade *et al.*, 2022).

Low-level laser therapy has been associated with reduced healing time, with anti-inflammatory and analgesic effects, and stimulation of cell proliferation and fibroblast synthesis (Bandeira *et al.*, 2020; Paiva *et al.*, 2023). The use of hydrogels has been described as safe and effective in the biomechanical modulation of the wound bed and in promoting closure in wounds with delayed

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healing (Sparks *et al.*, 2021). Approaches such as tilapia skin as a biological dressing have also been reported in a clinical report, with positive results in complete re-epithelialization and absence of adverse effects (Costa *et al.*, 2020). Additionally, ozone therapy was described in a narrative review as an approach with anti-inflammatory, antimicrobial, and analgesic effects (Castro *et al.*, 2024).

Convergently, studies indicate that effective management of the external gastrointestinal tract (EGT) depends on correcting perpetuating factors (infection/biofilm, exudate, edema, and mobility), combined with removal and debridement of the tissue when it prevents re-epithelialization and normal progression of repair (Anantama *et al.*, 2022; Basha *et al.*, 2019). Surgical excision is frequently cited as the approach of choice because it removes hyperplastic tissue and preserves the epithelial margin, in addition to allowing histopathological evaluation when indicated. However, it may require repetition until the underlying inflammatory stimulus is controlled (Anantama *et al.*, 2022; Viana *et al.*, 2014). Surgical removal of the EGT can promote faster healing when compared to wounds not subjected to resection (Ribeiro *et al.*, 2024). Complementary therapies described in the literature should be interpreted as adjuvant strategies to conventional management, and not as substitutes for fundamental measures such as adequate debridement, infection control, and wound bed stabilization (Viana *et al.*, 2014). The treatment of cutaneous wounds in horses represents a significant clinical challenge due to the wide variability in the type, location, and severity of lesions, as well as the scarcity of primary evidence to support the definition of ideal therapeutic protocols. The British Equine Veterinary Association (BEVA) guidelines highlight this limitation, pointing to the general lack of robust studies and evidence-based medicine in the management of wound healing in horses (Freeman *et al.*, 2021).

Recent reviews indicate that the methodological heterogeneity of studies, coupled with the predominance of case reports and case series, still limits direct comparisons between therapeutic approaches and the extrapolation of results to clinical practice (Ribeiro *et al.*, 2024). In this context, conducting controlled clinical trials with objective criteria for evaluating and monitoring the total healing time is essential to improve clinical decision-making and reduce the incidence of complications such as exuberant granulation tissue (Steiner *et al.*, 2019).

Despite the variety of therapies described, most studies have a low level of evidence, especially since they are case reports, clinical series, or studies with small samples. Thus, although approaches such as surgical excision, chemical debridement, laser therapy, ozone therapy, hydrogels, and biological dressings show promising results, it is not yet possible to establish therapeutic superiority among them. The choice of treatment should consider the location of the wound, the presence of infection or biofilm, the extent of exuberant tissue, the availability of resources, and the individual response of the animal.

3.5 Natural products in the treatment of wounds and EGT

The studies evaluated describe natural substances and herbal remedies as adjuvant strategies in the management of equine wounds, including situations associated with EGT. The evidence is heterogeneous regarding design, type of lesion, formulation, and outcomes. Products with bioactive compounds (flavonoids, tannins, triterpenes, and polysaccharides) associated with anti-inflammatory, antimicrobial, antioxidant, and extracellular matrix modulating effects were cited.

Among the examples, *Calendula officinalis* was associated with the absence of infection and the progressive filling of the wound bed by granulation tissue, with a possible contribution to the inflammatory phase of the healing process (Boscorato *et al.*, 2020). Similar results are described for *Aloe vera*, with reports of stimulation of collagen synthesis, fibroblast proliferation, and angiogenesis in the initial phases of tissue repair, in addition to rapid granulation and absence of EGT (Liang *et al.*, 2021).

Copaiba oil, in experimental studies, has shown benefits in the healing of equine wounds, with improvement in macroscopic and microscopic parameters (Kauer *et al.*, 2020; Lucas *et al.*, 2017). Barbatimão (*Stryphnodendron adstringens*), rich in tannins, has been associated with reduced exudation, inflammatory modulation, and antimicrobial activity, being described as an effective topical alternative in the management of equine wounds (Xavier; Barroso; Araripe, 2022).

Other reported products include the use of granulated sugar, associated with a reduction in bacterial load and acceleration of healing (Ribeiro *et al.*, 2019; Seid; Birhan, 2019), as well as the association between *Stryphnodendron* spp. and sugar, with positive results in accelerating repair and absence of EGT formation (Almeida; Giovanon; Giovanoni, 2020).

The topical use of extra virgin coconut oil combined with copper sulfate has been described in a case with favorable outcomes, in addition to ease of application and low cost (Mazzo *et al.*, 2014). Finally, ozonized sunflower seed oil (*Helianthus annuus*) demonstrated greater wound contraction, early re-epithelialization, and absence of infection in a controlled experimental study, with EGT formation observed only in the control group (Di Filippo *et al.*, 2020).

Although several natural products have a plausible biological rationale, the literature emphasizes that such therapies should be interpreted as adjuvants, since designs with lower levels of evidence predominate and there is a lack of standardization of concentrations, vehicles, frequency, and duration of treatment. Reviews and guidelines reinforce that methodological heterogeneity limits direct comparisons and extrapolations to clinical practice, emphasizing the need for controlled clinical trials and standardized protocols (Freeman *et al.*, 2021; Ribeiro *et al.*, 2024; Steiner *et al.*, 2019).

3.6 Study limitations

Although there is relevant evidence on EGT in horses, some of the interventions described in the literature have limitations regarding clinical applicability, due to the heterogeneity of protocols used. Furthermore, the paucity of equine-specific clinical validation for emerging therapies restricts direct comparisons between approaches and reduces the strength of recommendations.

4 Conclusion

The synthesis of the included studies indicates that EGT remains a frequent and clinically challenging complication of secondary intention healing in horses, especially in wounds located on distal limbs. Local factors, such as low perfusion, hypoxia, edema, and movement, associated with infectious complications, particularly the formation of bacterial biofilms, are strongly related to the maintenance of chronic inflammation and the disorganization of tissue repair, hindering re-epithelialization and wound contraction.

The management of EGT requires an integrated and individualized approach, involving adequate wound bed preparation, debridement/excision when indicated, optimization of the local microenvironment, and surveillance of infectious complications, especially those related to biofilms. Although complementary therapies and natural products show potential as adjuvants, their application remains limited by the heterogeneity of protocols and the scarcity of controlled clinical trials, reinforcing the need for future studies that allow for the standardization and consolidation of more effective and safe therapeutic strategies for equine clinical practice.

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