UNIVERSIDADE FEDERAL DO CEARÁ
PROGRAMA DE PÓS-GRADUAÇÃO EM DESENVOLVIMENTO E INOVAÇÃO TECNOLÓGICA EM MEDICAMENTOS

CINTHIA DE SOUSA BRAGA MENESES

# AVALIAÇÃO DE UMA FORMULAÇÃO CONTENDO ÁGUA DE COCO EM PÓ NO TRATAMENTO DE FERIDAS EXPERIMENTAIS EM EQUINOS

FORTALEZA

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Orientador: Prof. Dr. Edilson Martins Rodrigues Neto (Universidade Federal do Ceará).

Co-Orientadora: Profa. Dra. Lúcia Daniel Machado da Silva (Universidade Estadual do Ceará).

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Aprovada em 29/06/2026.

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Aos meus avós (*in memoriam*), Vô Quim, Vó Lozinha, Vô Ubirajara, pelo amor incondicional. Por terem me ensinado a ter confiança e coragem para buscar os meus sonhos e além de tudo, pelo exemplo de gentileza e bondade. O amor foi a base para tudo.

Ando devagar porque já tive pressa, levo esse sorriso porque já chorei demais. Hoje me sinto mais forte mais feliz quem sabe, só levo a certeza de que muito pouco eu sei, eu nada sei.
Cada um de nós compõe a sua história, cada ser em si carrega o dom de ser capaz, e ser feliz. (Almir Sater)

## AGRADECIMENTOS

Agradeço a Deus pelo dom da vida, a sabedoria, a fé, a força e a coragem para não desistir dos meus sonhos.

A minha família, pelo apoio e incentivo em cada luta, por estarem ao meu lado em todos os momentos. Ao meu esposo Antônio Carlos Meneses, pela paciência e cumplicidade. Aos meus filhos Ana Luiza e Joaquim, desculpa por todas as vezes que mamãe se ausentou, em busca de lutar por dias melhores para vocês, obrigada pelo amor de cada dia que me revigora e renova minhas forças.

A minha mãe Maria Vanúbia de Sousa, que foi a base para que toda minha vida profissional fosse possível. O meu sonho de ser veterinária foi graças a sua garra e determinação em não desistir de mim. A minha avó agradeço por tanto cuidado e zelo.

Ao meu irmão Plácido Júnior, que sonha e vibra comigo em cada conquista. Elas não seriam tão prazerosas sem o seu apoio.

Aos professores, em especial meu orientador professor Dr. Edilson e minha co-orientadora professora Dra. Lúcia Daniel, que acompanharam cada passo, com paciência e empenho. Sempre dispostos a ajudar, mostrando-me o melhor caminho, ensinando-me em cada revisão.

Aos professores Dra. Cristiane Clemente de Mello Salgueiro e Dr. José Ferreira Nunes pelo incentivo à pesquisa que levou a este experimento.

Ao professor Dr. Juscelino Matos pela paciência em cada discussão e todo apoio estatístico, feito com muito zelo.

Ao colega de profissão Dr. João Emanuel e seu pai João Cardoso por ceder sua propriedade e os animais para que pudesse ocorrer o experimento, e por toda ajuda concedida no decorrer de todo processo.

Aos animais, seres iluminados que nos transmitem tanto amor e carinho, vocês são a razão do meu amor pela medicina veterinária.

## RESUMO

A cicatrização de feridas cutâneas em equinos constitui desafio relevante na clínica veterinária, em razão da evolução frequentemente prolongada do reparo tecidual e da demanda por alternativas terapêuticas tópicas eficazes e seguras. Nesse contexto, esta tese teve como objetivo avaliar o desempenho cicatricial de uma formulação tópica à base de água de coco em pó, em comparação com uma pomada antimicrobiana de referência, no tratamento de feridas cutâneas experimentais induzidas em equinos. Trata-se de estudo experimental exploratório, com delineamento pareado intra-animal, realizado com oito equinos clinicamente hígidos, nos quais foram produzidas duas feridas cutâneas circulares padronizadas na região lombar, sendo uma tratada com a pomada de referência e a outra com a formulação experimental, administradas uma vez ao dia durante 14 dias. A avaliação compreendeu análise macroscópica seriada, mensuração morfométrica por planimetria digital nos dias 0, 3, 7, 10 e 14, além de exame histopatológico ao término do período experimental. Os resultados evidenciaram redução progressiva da área das feridas em ambos os grupos ao longo do tempo, com evolução cicatricial satisfatória nas lesões avaliadas. Não foi possível detectar diferença entre os tratamentos quanto aos desfechos macroscópicos, morfométricos e histopatológicos analisados, incluindo edema, exsudato, taxa média de reparação e escores histológicos no 14º dia. Esses achados indicam que, nas condições avaliadas, a formulação tópica à base de água de coco em pó apresentou comportamento cicatricial comparável ao da pomada antimicrobiana de referência, sugerindo evolução cicatricial compatível com o tratamento comparador. De forma complementar, a tese incorporou revisão integrativa sobre tecido de granulação exuberante em equinos, a qual reforçou a relevância clínica do tema e a escassez de protocolos terapêuticos padronizados. Conclui-se que a formulação tópica à base de água de coco em pó constitui alternativa promissora para investigação continuada, recomendando-se a realização de estudos futuros com amostras maiores, maior tempo de seguimento e modelos mais próximos das condições clínicas da rotina veterinária.



**Palavras-chave:** equinos; cicatrização de feridas; água de coco em pó; formulação tópica; tecido de granulação exuberante.

**ABSTRACT**

The healing of cutaneous wounds in horses constitutes a relevant challenge in veterinary practice due to the often prolonged course of tissue repair and the demand for effective and safe topical therapeutic alternatives. In this context, this thesis aimed to evaluate the healing performance of a topical formulation based on powdered coconut water, in comparison with a reference antimicrobial ointment, in the treatment of experimentally induced cutaneous wounds in horses. This was an exploratory experimental study with an intra-animal paired design, carried out with eight clinically healthy horses, in which two standardized circular cutaneous wounds were created in the lumbar region, one treated with the reference ointment and the other with the experimental formulation, administered once daily for 14 days. The evaluation comprised serial macroscopic analysis, morphometric measurement by digital planimetry on days 0, 3, 7, 10 and 14, in addition to histopathological examination at the end of the experimental period. The results showed a progressive reduction in wound area in both groups over time, with satisfactory healing evolution in the lesions evaluated. No difference was detected between the treatments regarding the macroscopic, morphometric and histopathological outcomes analyzed, including edema, exudate, mean repair rate and histological scores on day 14. These findings indicate that, under the evaluated conditions, the topical formulation based on powdered coconut water showed healing behavior comparable to that of the reference antimicrobial ointment, suggesting wound healing progression compatible with the comparator treatment. In a complementary manner, the thesis included an integrative review on exuberant granulation tissue in horses, which reinforced the clinical relevance of the topic and the scarcity of standardized therapeutic protocols. It is concluded that the topical formulation based on powdered coconut water constitutes a promising alternative for further investigation, and future studies with larger samples, longer follow-up and models closer to the clinical conditions of veterinary routine are recommended.

**Keywords:** horses; wound healing; powdered coconut water; topical formulation; exuberant granulation tissue.

## LISTA DE ILUSTRAÇÕES

FIGURAS REFERENTES AO CAPÍTULO 1



FIGURAS REFERENTES AO CAPÍTULO 2

and complete re-epithelialization (HE, 40×). (D) Higher magnification showing neovascularization and organized fibroblasts, interspersed with discrete neutrophils, lymphocytes and macrophages (HE, 400×). 1, granulation tissue; 2, reepithelialization; 3, chronic-active inflammatory infiltrate; 4, reepithelialization; 5, superficial granulation tissue; 6, neovascularization; 7, organized fibroblasts……

## LISTA DE TABELAS

TABELAS REFERENTES AO CAPÍTULO 1



TABELAS REFERENTES AO CAPÍTULO 2

## LISTA DE SÍMBOLOS

± Mais ou menos

% Porcentagem

× Vezes / aumento microscópico

= Igual a

< Menor que

> Maior que

≤ Menor que ou igual a

≥ Maior que ou igual a

## LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| ACP | Água de coco em pó |
| IBGE | Instituto Brasileiro de Geografia e Estatística |
| PNA-FISH | Hibridização fluorescente in situ com ácido nucleico peptídico |
| TGE | Tecido de granulação exuberante |
| VEGF-E | Fator de crescimento endotelial vascular E |

**SUMÁRIO**

## 1 INTRODUÇÃO

Atualmente no Brasil, o rebanho equino é superior a 5 milhões de cabeças, sendo Minas Gerais o estado de maior produção (IBGE, 2023). A equideocultura está presente em todo o território nacional, com animais empregados em atividades agropecuárias, militares, esportivas, terapêuticas e de lazer (PARANÁ, 2017). O segmento do cavalo apresenta relevância econômica e social crescente, impulsionado pela movimentação financeira e pela geração de postos de trabalho associados à atividade. Nesse contexto, a manutenção da saúde e do desempenho desses animais assume importância clínica e produtiva.

Segundo Lesimple (2020), as diferentes condições ambientais em que os cavalos são submetidos podem impactar significativamente o bem-estar animal. Em equinos, a ocorrência de feridas traumáticas relaciona-se tanto a características inerentes à espécie, como comportamento reativo e respostas bruscas a estímulos, quanto a fatores extrínsecos, incluindo uso de equipamentos inadequados, esforço físico excessivo, pastagens contaminadas e instalações mal planejadas. Por essa razão, as lesões cutâneas configuram importante causa de comprometimento da integridade física desses animais e representam desafio frequente na prática clínica. Estudos com equídeos de trabalho indicam que feridas traumáticas estão entre as afecções cutâneas mais frequentes, muitas delas localizadas em membros distais e associadas a tratamento prolongado e maior risco de complicações (Pessoa et al., 2014; Xavier et al., 2022; Kompi et al., 2023; Costa, 2024), o que reforça a complexidade do manejo clínico dessas lesões na espécie equina (HARMAN et al., 2021).

A pele constitui o maior órgão do corpo dos equinos e exerce funções essenciais de proteção, termorregulação e percepção sensorial. Sua organização em epiderme, derme e hipoderme, associada à presença de anexos cutâneos, matriz extracelular e células imunologicamente ativas, é determinante para a resposta ao dano e para a progressão do reparo tecidual (Yousef, 2017; Lopez-Ojeda et al., 2022; Moriello, 2024; Ribas; Regianini, 2024). Do ponto de vista funcional, a pele não atua apenas como barreira física, mas como tecido metabolicamente ativo, capaz de modular inflamação, migração celular, deposição de matriz e remodelação cicatricial.

A cicatrização de feridas constitui um processo biológico dinâmico e multifatorial, didaticamente dividido em fases inflamatória, proliferativa e de

remodelação. Essas etapas envolvem hemostasia, recrutamento celular, deposição e reorganização da matriz extracelular, angiogênese, fibroplasia, contração e reepitelização (Rodrigues et al., 2019; Wilkinson; Hardman, 2020; Pena et al., 2024). Quando há adequada coordenação entre esses eventos, o reparo progride de forma ordenada; quando há desregulação, podem ocorrer atraso cicatricial, cronificação da lesão e formação de tecido patológico (Kolimi et al., 2022; Du Cheyne et al., 2021).

Nos equinos, a cicatrização apresenta particularidades importantes. Feridas localizadas em membros distais tendem a evoluir de forma mais lenta e problemática em razão de fatores como menor perfusão sanguínea, maior exposição à contaminação, mobilidade regional, hipóxia local e ausência de panículo carnoso, o que compromete a contração da ferida e favorece a persistência inflamatória (Seid; Birhan, 2019; Ribas; Regianini, 2024). Além disso, a formação de biofilmes bacterianos pode perpetuar o estímulo inflamatório, degradar a matriz extracelular e dificultar a resposta às terapias convencionais, contribuindo para a cronicidade da lesão (Westgate et al., 2011; Jorgensen et al., 2021; Marchant; Hendrickson; Pezzanite, 2024).

Entre as complicações mais relevantes da cicatrização em equinos, destaca-se o tecido de granulação exuberante (TGE), especialmente em feridas localizadas em membros distais. Essa alteração caracteriza-se pela proliferação excessiva de tecido de granulação acima do plano cutâneo, comprometendo a contração da ferida e a reepitelização (Théoret; Wilmink, 2013; Du Cheyne et al., 2021). Sua ocorrência está associada à persistência de inflamação, angiogênese sustentada, deposição desorganizada de matriz extracelular, hipóxia, edema e mobilidade local, configurando uma das principais causas de cicatrização aberrante na espécie (Wilmink; Van Weeren, 2004; Seid; Birhan, 2019; Jorgensen; Jacobsen; Bundgaard, 2021).

Apesar do uso rotineiro de diferentes abordagens terapêuticas tópicas e sistêmicas, o manejo de feridas em equinos ainda apresenta importante variabilidade quanto às formulações empregadas, frequência de aplicação, protocolos de cobertura e critérios de avaliação de resposta clínica. Além disso, a literatura ainda carece de evidências mais padronizadas e comparáveis sobre a eficácia de diversas intervenções na espécie, o que limita a consolidação de recomendações terapêuticas mais robustas (Freeman et al., 2021). Nesse cenário, cresce o interesse por produtos

naturais, biomateriais e formulações bioativas com potencial de modular o microambiente da ferida e favorecer o reparo tecidual.

Entre esses produtos, a água de coco em pó (ACP) destaca-se como matéria-prima promissora para o desenvolvimento de bioprocessos e bioprodutos na área da saúde, por apresentar potencial farmacotécnico e biológico para aplicação em formulações tópicas (Salgueiro et al., 2019; Salgueiro; Nunes, 2025). Sua composição inclui açúcares, minerais, aminoácidos, vitaminas e compostos fenólicos (DebMandal; Mandal, 2011; Prades et al., 2012), aos quais têm sido atribuídas propriedades antioxidantes e bioativas com possível impacto sobre a modulação do microambiente da ferida e sobre etapas relevantes da cicatrização, como fibroplasia, síntese de colágeno e reepitelização (Magalhães, 2007).

Estudos prévios em outros modelos reforçam esse interesse. Em estudo experimental pré-clínico, Magalhães (2007) investigou os efeitos da ACP em ratos Wistar e observou aceleração do processo de reparação tecidual, com favorecimento do desenvolvimento de fibras colágenas. Santos et al. (2015) estudaram o uso de biofilmes com ACP como adjuvante em afecções bucais de pacientes com câncer de cabeça e pescoço. Moura (2017) demonstrou eficácia de bioemulsão à base de ACP na cicatrização de úlceras de pé diabético em humanos, oferecendo uma abordagem terapêutica inovadora, mais acessível para o cuidado de feridas com melhoria nos indicadores clínicos dos pacientes. Em medicina veterinária, Meneses e Silva (2022) avaliaram o creme de barreira ACP Derma em cães, observando desempenho cicatricial semelhante ao de formulações comparadoras, com vantagem prática relacionada à aderência da formulação à lesão e ao custo.

Entretanto, até onde foi possível verificar, na literatura consultada no escopo desta tese, não foram identificados estudos experimentais ou clínicos que avaliem a aplicação tópica de formulações à base de água de coco em pó na cicatrização de feridas cutâneas em equinos. Também não foram encontrados trabalhos comparando esse tipo de formulação com pomadas antimicrobianas tópicas de uso corrente na rotina veterinária equina. Essa ausência de evidências específicas para a espécie caracteriza uma lacuna científica relevante e fundamenta a realização da presente tese.

Dessa forma, esta tese foi delineada para integrar dois eixos complementares de investigação: um primeiro eixo voltado à análise crítica da literatura sobre tecido

de granulação exuberante em equinos, suas características, fatores associados e abordagens terapêuticas; e um segundo eixo direcionado à avaliação experimental de uma formulação tópica à contendo água de coco em pó em feridas cutâneas induzidas em equinos. Com isso, busca-se contribuir tanto para a compreensão do contexto clínico e biológico do reparo cutâneo na espécie quanto para a prospecção de alternativas terapêuticas inovadoras acessíveis e cientificamente fundamentadas, podendo ser potencialmente aplicáveis à medicina veterinária.

## 2 OBJETIVOS

### 2.1 OBJETIVO GERAL

Analisar, de forma integrada, o contexto científico e terapêutico da cicatrização de feridas cutâneas em equinos, por meio da síntese das evidências disponíveis sobre tecido de granulação exuberante, seus fatores associados, complicações e abordagens terapêuticas, bem como avaliar o desempenho cicatricial do creme de barreira ACP Derma, contendo água de coco em pó, em comparação com uma pomada antimicrobiana de referência, no tratamento de feridas cutâneas experimentais induzidas em equinos.

### 2.2 OBJETIVOS ESPECÍFICOS

• Sintetizar as evidências disponíveis na literatura sobre as características, fatores associados, complicações e abordagens terapêuticas relacionadas ao tecido de granulação exuberante em equinos.

• Avaliar a evolução macroscópica das feridas cutâneas experimentais tratadas com ACP Derma e com a pomada antimicrobiana de referência.

• Mensurar parâmetros morfométricos das lesões, incluindo comprimento, largura e área, ao longo do período de acompanhamento.

• Comparar o grau de reparação, a presença de edema, exsudato e a taxa média de reparação entre os tratamentos instituídos.

• Analisar os achados histopatológicos das feridas ao final do período experimental, comparando os grupos tratados.

• Investigar o potencial do ACP Derma como alternativa terapêutica tópica aplicável ao manejo de feridas cutâneas em equinos.

## 3 CAPÍTULO 1

### TITLE PAGE

Artigo aprovado na Revista Ensaios e Ciência

**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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**Received:** February 2026
**Accepted:** June 2026

### 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 (Théoret; Wilmink, 2013; Seid; Birhan, 2019; Jorgensen; Jacobsen; Bundgaard, 2021). 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.

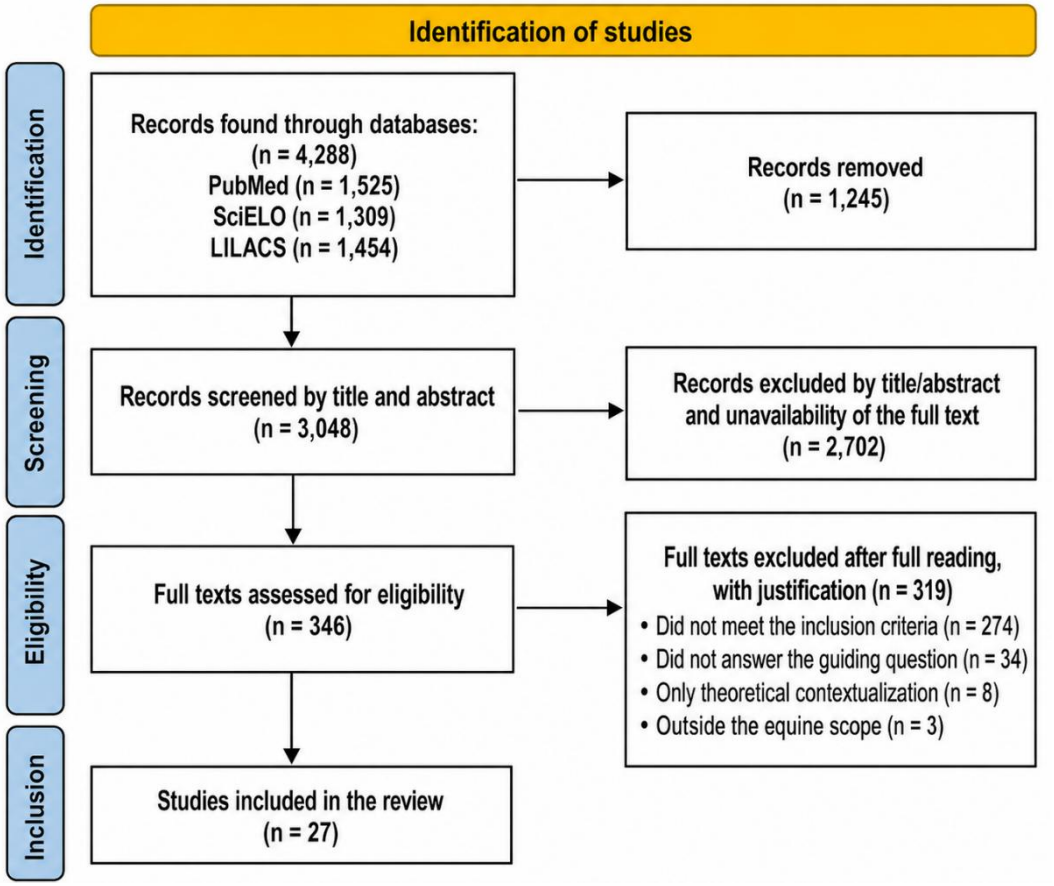


Figure 1 - Flowchart for selecting studies included in the integrative review, according to PRISMA recommendations.

Source: Created by the authors (2026).

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

| AUTHOR (year) | TITLE | OBJECTIVE (SYNTHESIS) |
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| Sparks HD, Sigaeva T, Tarraf S, et al. (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 FA; Kandrotas AL; Nardin Neto E, et al. (2017) | Copaiba oil in experimental wound healing in horses | To evaluate the effects of 10% copaiba oil on experimentally induced wounds in horses. |
| Kauer DP; Alonso JM; Gushiken LFS, et al. (2020) | Experimental treatment of cutaneous wounds with Copaifera langsdorffii extract and oleoresin in horses | To evaluate the healing potential of hydroalcoholic extract and oleoresin creams of Copaifera langsdorffii in equine cutaneous wounds. |
| Di Filippo PA; Ribeiro LMF; Gobbi FP, et al. (2020) | Effects of pure and ozonated sunflower seed oil (Helianthus annuus) 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: Created by the authors (2026).

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

| AUTHOR (year) | TITLE | OBJECTIVE (SYNTHESIS |
|---|---|---|
| Viana LFS; Wenceslau AA; Costa SCL, et al. (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 |

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| | | solution, evaluating the clinical outcome and highlighting the need for further studies to better determine efficacy and possible adverse reactions. |
| Andrade CFO; Silva AJM; Pereira FA, et al. (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; Pinheiro M; Rocha MV; Vago PB (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 BO; Lima Júnior EM; Fechine FV, et al. (2020) | Treatment of a Traumatic Equine Wound Using Nile Tilapia (Oreochromis niloticus) 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 AG; Orlandini CF; Laginestra BFA, et al. (2020) | Use of Calender Extract Cream in Equine Lacerate Wound | To evaluate the effectiveness of a 2% non-ionic Calendula officinalis cream in the treatment of an extensive lacerating wound in a horse. |
| Ribeiro RM; Ribeiro DSF; Predoza HP; Vasconcelos PHM (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 PNM; Giovanoni HF; Giovanoni RF (2020) | Open wound treatment in equine using Stryphnodendron adstringens infusion associated with crystal sugar – case report | To present a case report on the topical application of Stryphnodendron adstringens associated with granulated sugar in an open wound in a horse, monitoring the healing process until complete closure of the lesion and |

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| | | describing the characteristics of the final scar tissue. |
| Mazzo HC, et al. (2014) | Topical use of coconut oil in equine wound healing | 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 KMA; Shah MA; Khan S; Amarpal (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: Created by the authors (2026).

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

| AUTHOR (year) | TYPE | OBJECTIVE (SYNTHESIS) |
|---|---|---|
| Théoret CL, Wilmink JM (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 AM, 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. |

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| Marchant K; Hendrickson DA; Pezzanite LM (2024) | Review | To summarize evidence on biofilms in equine wounds, highlighting clinical signs, diagnostic methods, and biofilm-oriented management strategies to support practice. |
| Anantama NA et al. (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 CM (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 BJD; Mendanha MG; Silva Junior VP; Campos SBS (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 BC; Agostinho ACB; Santos AM, et al. (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 et al. (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 JC; Barroso MIR; Araripe MGA (2022) | Integrative review | To understand the clinical and therapeutic aspects of the use of natural products in wound healing in |

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| | | horses, focusing on sugar, Aloe vera, barbatimão, and calendula. |
| Ribeiro G; Carvalho L; Borges J, Prazeres J (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. |
| Freeman SL; Wilmink JM; Ashton NM, et al. (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: Created by the authors (2026).

### 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 (Théoret; Wilmink, 2013; Lux, 2022). 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 EGTas 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; Wilmink, 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 (Théoret; Wilmink, 2013; Marchant; Hendrickson; Pezzanite, 2024).

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 (Théoret; Wilmink, 2013; Seid; Birhan, 2019; 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, 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 (Théoret; Wilmink, 2013; Lux, 2022).

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 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 (Basha et al., 2019; Anantama et al., 2022). 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 (Viana et al., 2014; Anantama et al., 2022). 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 (Lucas et al., 2017; Kauer et al., 2020). 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 (Seid; Birhan, 2019; Ribeiro et al., 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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## 4 CAPÍTULO 2

### TITLE PAGE

Artigo submetido no periódico Journal of Equine Veterinary Science

# Wound healing of experimental cutaneous wounds in horses: comparison between a topical formulation containing coconut water powder and an antimicrobial ointment

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## Abstract

Context: Skin wounds in horses often present prolonged healing, stimulating the search for alternative topical therapies. To date, there are no experimental studies in horses evaluating topical formulations containing powdered coconut water.

Objective: To compare the macroscopic, morphometric, and histopathological evolution of experimental skin wounds in horses treated with a topical formulation containing powdered coconut water compared to a reference antimicrobial ointment.
Methods: Eight clinically healthy horses received two standardized circular skin wounds in the lumbar region, in an intra-animal paired design. The cranial lesion received the reference antimicrobial ointment and the caudal lesion received the experimental formulation, once a day for 14 days. Length, width, and area were measured by planimetry on days 0, 3, 7, 10, and 14. Edema, exudate, degree of repair, mean repair rate, and histopathological findings were evaluated.
Results: There was a progressive reduction in wound area in both groups, with a time effect, but no overall treatment effect or treatment × time interaction. Edema, exudate, mean repair rate, and histopathological scores on day 14 did not differ between the groups.
Conclusion: Under the conditions evaluated, no difference was detected between the treatments. The results are exploratory and do not demonstrate superiority, therapeutic equivalence, or an isolated effect of coconut water powder, justifying further investigations of the formulation in larger samples and in more clinically challenging models.

*Keywords:* equine; wound healing; topical administration; coconut water powder; natural products; antimicrobial resistance.

## 1. Introduction

Skin wounds represent a significant challenge in equine medicine, both due to their high incidence and the frequency of complications and tendency towards chronicity. Many lesions become refractory to available therapies and exhibit great variability in location, extent, and severity, which makes clinical management difficult [1-2]. In addition to compromising performance, chronic lesions prolong recovery time and increase therapeutic costs [3-5].

Wound healing in mammals is a dynamic and coordinated process involving the inflammatory, proliferative, and remodeling phases, with the integrated participation of inflammatory cells, fibroblasts, extracellular matrix deposition, and angiogenesis [6]. In horses, however, healing by secondary intention presents relevant particularities, with a tendency towards an exacerbated fibroproliferative response, especially in certain anatomical locations, such as the distal limbs, where factors such as lower skin mobility, local hypoxia, and a higher risk of contamination make the process more complex [7].

In horses, persistent granulation tissue formation, and in some cases exuberant granulation tissue (EGT), can hinder re-epithelialization and prolong tissue repair [8]. Although granulation tissue formation is essential for healing by secondary intention, its persistence and excessive proliferation reflect an imbalance in the transition between the proliferative and remodeling phases, with maintenance of fibroblastic activity, sustained angiogenesis, and prolonged inflammatory signaling [9-10]. EGT remains a relevant clinical problem, with multifactorial mechanisms and still limited therapeutic options, and may favor secondary complications and prolong healing time [4, 10-11].

Conventional wound management includes debridement, reduction of microbial load, and the use of topical therapies and antiseptics for decontamination of the wound bed and support for healing [12-13]. However, some antiseptics can induce local cytotoxicity and compromise tissue repair, which is why their use should be judicious in the management of equine wounds [14]. In cases of persistent infection, antimicrobials may be necessary, but their use should be carefully monitored to reduce the risk of bacterial resistance, especially in wounds with biofilm [15,16]. In this context, non-antimicrobial topical alternatives become clinically relevant when they are able to sustain satisfactory scar progression compared to reference therapies, especially in scenarios where it is desirable to minimize exposure to antimicrobials [17-19].

In this scenario, natural products have been investigated as adjuvants, provided they have standardized concentration and vehicle and are used in association with debridement, adequate dressing, infection control and regular clinical monitoring [20]. Many bioproducts contain compounds related to key events in the healing cascade in mammals, which justifies their investigation in controlled designs [21]. In horses, understanding the mechanisms associated with prolonged inflammation, exacerbated fibroplasia, and disordered angiogenesis remains relevant to reducing convalescence time and therapeutic costs, particularly in chronic wounds complicated by EGT [22-24].

Coconut water has received scientific attention due to its nutritional value and the presence of sugars, minerals, vitamins, and bioactive metabolites. However, it has high perishability and is susceptible to rapid physicochemical and microbiological deterioration, which makes its preservation and processing difficult [25]. Stabilization technologies have allowed its conversion into powdered coconut water (PCW), expanding the viability of storage and standardization [26-27]. In the context of tissue

repair, coconut water has been associated with components related to cell growth induction, phytohormones, vitamins, and sugars [28-30]. Moreover, powdered coconut water has polymers with glycosidic residues, with piezoelectric properties comparable to those of collagen, a characteristic that can contribute to maintaining moisture in the wound bed and potentially promote healing [27].

Preclinical and clinical studies have explored PCW-based formulations. In an experimental model with rodents, treatment with PWC favored tissue repair and the development of collagen fibers [29]. PWC was used in the formulation of bioactive biofilms (PWC-501), being evaluated as an adjuvant in the treatment of oral conditions in patients treated for head and neck cancer [27], and an PWC-based bioemulsion (PWC-502) was evaluated in diabetic foot ulcers, with favorable clinical indicators and reduced healing time [31]. In veterinary medicine, Meneses and Silva [32] observed similar healing performance with PWC-based barrier cream in dogs, with good adherence and potential economic advantage when compared to conventional topical treatments.

Considering these findings and the absence of experimental or clinical studies on the use of commercial topical formulations containing coconut water powder in equine skin wounds, this study was designed as an exploratory experimental investigation. The main hypothesis was not to test a direct antimicrobial action of coconut water powder, nor to isolate the effect of this ingredient in relation to the other components of the formulation, but to evaluate whether a non-antimicrobial topical formulation containing coconut water powder could sustain satisfactory scar progression when pragmatically compared to a reference antimicrobial ointment used in veterinary practice. Thus, this study aimed to compare, in a paired intra-animal design, the macroscopic and morphometric evolution of wounds, as well as the histopathological findings on the 14th day of standardized cutaneous wounds in horses treated with a commercial topical formulation containing coconut water powder, compared to wounds treated with a commercial reference ointment containing antimicrobials. The results should be interpreted as a comparison between two topical approaches to wound management, and not as a demonstration of superiority, therapeutic equivalence, or isolated activity of coconut water powder.

## 2. Materials and methods

*2.1 Ethical approval*

The study was approved by the Ethics Committee on the Use of Animals (CEUA) of the State University of Ceará (UECE), under protocol no. 31032.002962/2025-16, approved on August 11, 2025. All procedures complied with ARRIVE guidelines and institutional norms applicable to the use of animals in research [33].

*2.2 Animals and experimntal design*

Eight horses (Equus caballus), of undefined breed, seven females and one male, weighing between 250 and 460 kg and aged between 2 and 14 years, were used. The experiment was conducted at Fazenda Santa Luzia, located in the rural area of Pentecoste, Ceará. The animals were considered clinically healthy based on a prior physical examination. All were kept in a semi-intensive system, preserving their usual management routine, and remained under the same feeding and environmental conditions throughout the experimental period. A paired intra-animal design was adopted, in which each horse received two standardized skin wounds, one for each treatment. The allocation of lesions was not randomized. The cranial lesion received the control treatment and the caudal lesion received the experimental treatment, with the aim of standardizing the application of the products, facilitating serial monitoring of the lesions, and minimizing operational variations during the experiment. The number of animals was determined based on the ethical and operational feasibility of the experimental model, in line with previous studies of cutaneous wound healing in horses. Therefore, this is an exploratory experimental study with an intra-animal paired design and fixed lesion allocation.

*2.3 Wound making*

After trichotomy and antisepsis with 5% povidone-iodine, two circular wounds were created in the lumbar region, approximately 5 cm apart, using a 1 cm diameter disposable punch. The depth was standardized by the total height of the punch blade, including skin and subcutaneous tissue removal. Sedation was not considered necessary, as the animals were previously accustomed to handling, allowed adequate physical restraint, and did not present behavioral signs that compromised the safety of

the procedure or indicated a clinical need for sedation. Local anesthesia was performed with 2% lidocaine without vasoconstrictor, using an inverted U-block, providing adequate local analgesia for wound creation. Hemostasis was achieved by manual compression with sterile gauze. As post-procedure analgesia, dipyrone (50 mg/kg) was administered intravenously every 12 hours for 2 days. Throughout the procedure, safe conditions of physical restraint and behavioral monitoring of the animals were maintained. After the wounds were created, the animals remained under clinical monitoring throughout the experimental period, including general clinical observation and daily assessments of the lesions regarding macroscopic evolution, presence of edema, exudate, scabs, and any local or systemic complications.

*2.4 Treatments*

The experimental treatment consisted of applying ACP Derma cream (Biomatika, Brazil), a topical formulation containing powdered coconut water (PWC), osmonized water, and vegetable oils (coconut oil, moringa oil, and linseed oil), according to the manufacturer's information. The product was described in the study as a compound topical formulation. The control treatment consisted of applying the reference antimicrobial ointment Vetaglós (Vetnil, Brazil), whose composition, per 100 g, includes gentamicin sulfate (0.5 g), sulfanilamide (5.0 g), sulfadiazine (5.0 g), urea (5.0 g), and vitamin A palmitate (120,000 IU), plus excipients q.s.p. Vetaglós ointment was used as a pragmatic clinical comparator because it is a commercially available topical antimicrobial product used in routine veterinary practice, and not because it represents a validated gold standard for wound healing or a pharmacologically equivalent formulation to the experimental product. Applications were made once a day for 14 consecutive days. The wounds remained open, without the use of occlusive dressings, to reproduce conditions frequently observed in a field environment and to avoid external interference in the dynamics of contraction and epithelialization. No prior cleaning of the lesions was performed before photography or reapplication, in order to preserve the local microenvironment of the wound and to reproduce conditions frequently observed in field management.

*2.5. Macroscopic evaluation*

The wounds were clinically assessed daily for the presence of edema, exudate intensity, general appearance of the wound bed, and occurrence of scabs. Daily clinical assessments were performed by the same researcher throughout the experimental period. Due to the topical nature of the products and the visual differences between the formulations, blinding during treatment application and routine clinical inspection was not feasible.

Edema and exudate were classified using ordinal scores (0 = absent, 1 = slight, 2 = moderate, and 3 = marked). The presence of scabs was recorded as present or absent, and described qualitatively in terms of size and color, when applicable. Clinical assessments were performed daily. For statistical analysis and presentation of results, edema and exudate scores were consolidated at predefined times. Edema and exudate records were consolidated on days D1, D3, and D7, and exudate was also recorded on days D10 and D14. On day 21 (D21), photographic documentation of the lesions was performed to supplement the macroscopic closure, without including this time point in the main inferential analysis. The wound was considered healed when superficial epithelialization was visible in the images obtained at this time.

*2.6. Photographic record and planimetric measurement*

The lesions were photographed with a smartphone with a maximum resolution of 8064 × 6048 pixels. The device was positioned approximately 30 cm from the wound surface, perpendicular to the skin plane, maintaining a standardized distance and angle between assessments. The images were obtained under natural lighting, avoiding shadows cast directly on the lesion bed. For dimensional calibration, a marker with a QR code provided by the Imito Wound application (Imito B.V., Netherlands) was used, positioned in the same plane as the wound in all photographs. The delimitation of the lesion area was performed manually, with digital enlargement of the image, by a single previously trained evaluator, using coded images to mask the allocation of treatments during the planimetric analysis. The same device was used throughout the experiment in order to reduce measurement variability. Length, width and area (primary outcome) were recorded on days D0, D3, D7, D10 and D14, with day 0 (D0) considered a baseline measurement for calculating the derived variables. The use of a calibrated

digital system allowed objective and reproducible planimetric measurements throughout longitudinal monitoring.

*2.7. Derived variables*

The degree of repair (GRt, %) was calculated using the expression:

GRt = [(Area0 − Areat) / Area0] × 100

where Area0 corresponds to the wound area on day 0 (D0) and Areat corresponds to the wound area at time t.

The average rate of repair (TRm, cm²/day) was calculated for each interval as:

TRm = (Areat1 − Areat2) / (t2 − t1)

where Areat1 and Areat2 correspond to the wound areas at times t1 and t2, respectively, and (t2 − t1) corresponds to the number of days between assessments. Positive TRm values indicate a reduction in wound area, while negative values indicate an increase in area during the assessed interval. TRm was estimated for the intervals of 0–3, 3–7, 7–10, and 10–14 days.

The relative efficiency on day 14 (E, %) was calculated descriptively using the following expression:

E = [(GR14(T) − GR14(C)) / GR14(C)] × 100

where GR14(T) corresponds to the average degree of repair on day 14 in the experimental group, and GR14(C) corresponds to the average degree of repair on day 14 in the control group. This measure was used exclusively to describe the relative difference between treatments at the end of the follow-up, without inferential purpose.

*2.8. Histopathological evaluation*

On day 14 after wound creation, an incisional biopsy was performed with a 5 mm diameter punch, including the wound margin and adjacent intact tissue. This time point was selected because it corresponds to a proliferative phase of skin repair, in which granulation tissue, fibroplasia, angiogenesis, and initial deposition of extracellular matrix can be histologically evaluated. Histopathological evaluation was performed at a single time point, on day 14, in order to minimize additional injury to the wound bed and preserve the longitudinal analysis of the primary outcome. It is recognized, however, that histological evaluation at a single time point does not allow

for a full characterization of the temporal dynamics of healing, especially early inflammatory events or late remodeling changes.

The samples were immediately fixed in 10% buffered formalin for 24–48 h. After fixation, the fragments were processed using conventional histopathological techniques: dehydration in increasing series of alcohol, clearing in xylene, and paraffin embedding. Histological sections 4–5 µm thick were obtained using a rotary microtome and mounted on glass slides. The sections were stained with hematoxylin-eosin for general morphological evaluation. The presence of bacterial structures compatible with coccoid morphology was recorded upon histological examination, assessing intensity and location. For bacteria, intensity was classified as not observed = 0, discrete = 1, moderate = 2, and marked = 3. For standardization, location was categorized as epidermal crust/superficial exudate, viable epidermis, and dermis (superficial and/or deep). The evaluation was performed by a single experienced pathologist, blinded to the treatment, using an optical microscope (Nexcope NE620, Nexcope, China) at magnifications of 100× and 400×. The following histological parameters were evaluated using a semi-quantitative ordinal scoring system: fibroblasts, mononuclear inflammation, polymorphonuclear inflammation, presence of bacteria, and collagenization. For fibroblasts, the following coding was adopted: + = 1 and ++ = 2. For mononuclear inflammation and polymorphonuclear inflammation: mild = 1, moderate = 2, and marked = 3. For collagenization: disorganized = 0, partially organized = 1, and organized = 2.

### *2.9. Data evaluation and statistical analysis*

The analyses were conducted using a paired intra-animal design with repeated measures over time, since each horse presented two experimental wounds (one per treatment), evaluated on days D0, D3, D7, D10, and D14. The animal was considered a grouping factor in the analyses, as each individual contributed two wounds monitored longitudinally. Area ($cm^2$) was defined as the primary outcome; length (cm) and width (cm) as secondary outcomes. The results of the continuous outcomes are presented as mean ± standard deviation (SD). Area, length, width, degree of repair, and mean repair rate (MRRm) were analyzed using linear mixed-effects models, including treatment, time (categorical factor), and the treatment × time interaction as fixed

effects, with a random intercept per animal. Due to the typical asymmetry of area measurements, this variable was analyzed using the natural logarithm [ln(area)], with the results presented on the original scale. Length, width, degree of repair, and MRRm were analyzed on the original scale. Perilesional edema, exudate intensity, and histopathological variables, due to their ordinal nature, were analyzed using a paired non-parametric approach. Edema and exudate were coded on a semi-quantitative scale from 0 to 3 (0 = absent, 1 = mild, 2 = moderate, and 3 = marked) and presented descriptively by time and treatment as n (%). For the overall comparison between treatments, scores were summed longitudinally per animal throughout the follow-up and compared using the paired Wilcoxon test. For the degree of repair, paired exploratory comparisons between treatments at each post-baseline time point (D3, D7, D10, and D14) were performed using the paired Wilcoxon test, with p-value adjustment using Holm's method. Semi-quantitative histopathological variables were compared between treatments at D14 using the paired Wilcoxon test (n = 8 pairs), with results presented as median and interquartile range (IQR). The significance of fixed effects was assessed using likelihood ratio tests between nested models, and the adequacy of the models was verified by graphical inspection of the residuals. In all analyses, $\alpha = 0.05$ was adopted. The analyses were performed using R software (R Core Team), version 4.5.2. The effect of sex was not inferentially evaluated due to the small sample size and the unequal distribution between sexes. No formal calculation of statistical power was performed a priori. The sample size was defined based on ethical and operational criteria and the feasibility of the experimental model in horses, with the study being interpreted as exploratory. Thus, the absence of statistically significant differences between treatments should be understood as the absence of a detectable difference in the evaluated conditions, and not as a demonstration of therapeutic equivalence or a definitive absence of effect.

## 3. Results

### *3.1 Macroscopic evaluation*

The horses did not present systemic clinical alterations throughout the experimental period. Macroscopic alterations were more evident in the first days of the inflammatory period. All wounds healed by secondary intention, without complications

requiring additional therapeutic intervention. Perilesional edema was concentrated in the first days of follow-up, with a predominance of low scores and progressive reduction throughout the evaluations (Table 1). On day 1 (D1), the absence of edema was recorded in 87.5% (7/8) of the lesions in both treatments. On day 3 (D3), a predominance of absent scores was observed in both groups, with occasional records of moderate and marked edema in the control group. On day 7 (D7), edema was absent in most lesions, being completely absent in the experimental group. In general, a reduction in edema was observed over time in both treatments. In the overall analysis of longitudinal edema scores per animal, no statistically significant difference was observed between treatments (paired Wilcoxon test, P = 0.75), indicating similar behavior of the groups throughout the follow-up period.

Table 1. Percentage distribution of perilesional edema scores in horses in the control and experimental groups on days 1, 3, and 7 (n = 8 pairs).

| Day | Treatment | 0 (Absent) | 1 (Discreet) | 2 (Moderate) | 3 (Marked) |
|---|---|---|---|---|---|
| D1 | Control group | 87.5 | 0.0 | 0.0 | 12.5 |
| | Experimental group | 87.5 | 12.5 | 0.0 | 0.0 |
| D3 | Control group | 75.0 | 0.0 | 12.5 | 12.5 |
| | Experimental group | 87.5 | 12.5 | 0.0 | 0.0 |
| D7 | Control group | 87.5 | 12.5 | 0.0 | 0.0 |
| | Experimental group | 100.0 | 0.0 | 0.0 | 0.0 |

Note: Data presented as a percentage (%). Ordinal scale: 0 = absent; 1 = slight; 2 = moderate; 3 = marked. The overall inferential comparison between treatments was performed using the paired Wilcoxon test, based on the longitudinal sum of scores per animal.

*3.2 Exudate and crust formation*

Exudate was most evident in the first few days and progressively reduced throughout the follow-up period in both treatments (Table 2). No purulent secretion was observed in any of the lesions. In the overall analysis of longitudinal exudate scores per animal, based on the sum of scores at times D1, D3, D7, D10, and D14, no statistically significant difference was observed between treatments (paired Wilcoxon test, P = 0.19). Crust formation became more noticeable from D7 onwards,

accompanying the gradual drying of the lesions. On D3, the beginning of granulation tissue formation was observed at the wound edge in isolated cases, recorded in one lesion from the experimental group and in one lesion from the control group. Lesions with persistent exudate presented absent or less evident crusts. On D10 and D14, with the exception of one animal, most lesions were dry, with crusts varying in size and color. On day 21, the images obtained indicated macroscopic closure of the lesions in all animals.

Table 2. Percentage distribution of exudate intensity in horses in the control and experimental groups on days 1, 3, 7, 10, and 14 (n = 8 pairs).

| Day | Treatment | 0 (Absent) | 1 (Discreet) | 2 (Moderate) | 3 (Marked) |
|---|---|---|---|---|---|
| D1 | Control group | 0.0 | 75.0 | 25.0 | 0.0 |
| | Experimental group | 37.5 | 62.5 | 0.0 | 0.0 |
| D3 | Control group | 25.0 | 25.0 | 25.0 | 25.0 |
| | Experimental group | 25.0 | 12.5 | 50.0 | 12.5 |
| D7 | Control group | 75.0 | 0.0 | 12.5 | 12.5 |
| | Experimental group | 75.0 | 0.0 | 12.5 | 12.5 |
| D10 | Control group | 87.5 | 12.5 | 0.0 | 0.0 |
| | Experimental group | 87.5 | 12.5 | 0.0 | 0.0 |
| D14 | Control group | 87.5 | 12.5 | 0.0 | 0.0 |
| | Experimental group | 87.5 | 12.5 | 0.0 | 0.0 |

Note: Data presented as a percentage (%). Ordinal scale: 0 = absent; 1 = slight; 2 = moderate; 3 = marked. The overall inferential comparison between treatments was performed using the paired Wilcoxon test, based on the longitudinal sum of scores per animal.

Representative macroscopic images of the wounds are shown in Figure 1.

Figure 1. Representative macroscopic evolution of paired cutaneous wounds in equines over 14 days of follow-up. Images were obtained on days 0, 3, 7, 10, and 14. The upper line corresponds to the cranial wound (control group), and the lower line to the caudal wound (experimental group). The panels were arranged in temporal sequence, from left to right.

*3.3 Evolution of length, width, wound area and derived variables*

Progressive reduction in area, length, and width was observed over the 14 days in both treatments (Table 3). The reduction in area throughout the follow-up is illustrated in Figure 2. In the linear mixed-effects model, there was a significant effect of time for all three variables (all $P < 0.001$), with no evidence of an overall treatment effect or a treatment × time interaction. This pattern indicates a lack of evidence of a differential effect between treatments on the healing process under the evaluated conditions. The mean areas decreased from 0.89 ± 0.12 cm² to 0.15 ± 0.05 cm² in the experimental group and from 0.86 ± 0.13 cm² to 0.16 ± 0.07 cm² in the control group between D0 and D14, with no evidence of a detectable difference between treatments throughout the follow-up. Length showed a significant reduction over time ($P < 0.001$), with no overall treatment effect ($P = 0.459$) and no treatment × time interaction ($P = 0.983$). Width also decreased significantly over time ($P < 0.001$), with no overall treatment effect ($P = 0.112$) and no significant interaction between treatment and time ($P = 0.558$).

Table 3. Morphometric evolution of cutaneous wounds in the control and experimental groups throughout the follow-up period (days 0 to 14). Values presented as mean ± standard deviation (SD), n = 8 pairs.

| Variable | Time | Experimental group | Control group |
|---|---|---|---|
| Area (cm²) | D0 | 0.89 ± 0.12 | 0.86 ± 0.13 |
| | D3 | 0.54 ± 0.21 | 0.61 ± 0.19 |
| | D7 | 0.45 ± 0.11 | 0.47 ± 0.09 |
| | D10 | 0.45 ± 0.05 | 0.53 ± 0.13 |
| | D14 | 0.15 ± 0.05 | 0.16 ± 0.07 |
| | | Global effects (P)<br>Treatment: 0.236 \| Time: <0.001 \| Interaction: 0.870 | |
| Length (cm) | D0 | 1.18 ± 0.09 | 1.18 ± 0.09 |
| | D3 | 0.94 ± 0.21 | 0.95 ± 0.21 |
| | D7 | 0.84 ± 0.07 | 0.85 ± 0.12 |
| | D10 | 0.86 ± 0.07 | 0.91 ± 0.11 |
| | D14 | 0.49 ± 0.11 | 0.51 ± 0.12 |
| | | Global effects (P)<br>Treatment: 0.459 \| Time: <0.001 \| Interaction: 0.983 | |
| Width (cm) | D0 | 1.00 ± 0.11 | 1.01 ± 0.10 |
| | D3 | 0.70 ± 0.19 | 0.83 ± 0.19 |
| | D7 | 0.70 ± 0.11 | 0.74 ± 0.09 |
| | D10 | 0.70 ± 0.05 | 0.78 ± 0.10 |
| | D14 | 0.42 ± 0.09 | 0.45 ± 0.13 |

| Variable | Time | Experimental group | Control group |
|---|---|---|---|
| | | Global effects (P)<br>Treatment: 0.112 \| Time: <0.001 \| Interaction: 0.558 | |

Note: Linear mixed-effects model with treatment, time, and interaction as fixed effects and random intercept per animal. The area variable was analyzed as ln(area); values presented on the original scale. Overall effects assessed by likelihood ratio test.

Figure 2. Temporal evolution of the area of cutaneous wounds in the control and experimental groups on days 0, 3, 7, 10, and 14. Values presented as mean ± standard deviation (SD), n = 8 pairs.

The degree of wound repair over time is presented in Table 4 and Figure 3. There was a significant effect of time in the mixed model ($P < 0.001$), with no overall treatment effect ($P = 0.284$) and no treatment × time interaction ($P = 0.618$). Descriptively, the mean degrees of repair were numerically higher in the experimental group throughout the follow-up. In exploratory paired comparisons by time, a difference between treatments was observed only on day 3 (D3), with a higher degree of repair in the experimental group (crude $P = 0.0078$; Holm's adjusted $P = 0.0313$). At the other evaluated times (D7, D10, and D14), no statistically significant differences were observed after adjustment for multiple comparisons. On D14, the mean degree of repair was 82.61% in the experimental group and 80.70% in the control group, corresponding to an absolute difference of approximately 2 percentage points. The relative efficiency on day 14, calculated from the average repair scores, was approximately 2.4% in favor of the experimental group, taking the control group as a reference.

Figure 3. Temporal evolution of the degree of wound repair in the experimental group and the control group on days 0, 3, 7, 10, and 14. Values presented as mean ± standard deviation (SD), n = 8 pairs. * Significant difference between treatments on day 3 after Holm adjustment (adjusted $P = 0.0313$).

Table 4. Degree of repair (%) of skin wounds in the control and experimental groups over time. Values presented as mean ± standard deviation (SD), n = 8 pairs.

| Day | Experimental group (%) | Control group (%) | Crude P | Adjusted P (Holm) |
|---|---|---|---|---|
| 3 | 39.35 ± 23.99 | 28.71 ± 21.00 | 0.0078 | 0.0313 |
| 7 | 48.27 ± 15.44 | 43.18 ± 16.24 | 0.2969 | 0.6563 |
| 10 | 47.95 ± 11.82 | 38.07 ± 16.89 | 0.2188 | 0.6563 |
| 14 | 82.61 ± 7.09 | 80.70 ± 10.48 | 0.7344 | 0.7344 |

Note: The degree of repair was calculated from the basal area (D0). The global analysis was performed using a linear mixed-effects model (α = 0.05). Comparisons between treatments at each time were carried out in an exploratory manner using the paired Wilcoxon test, with adjustment of p-values using the Holm method.

The average rate of repair per interval (TRm) is presented in Table 5. In the overall model, no statistically significant difference was observed between the treatments (P = 0.341). Descriptively, both groups showed greater area reduction in the 0–3 and 10–14 day intervals, while the intermediate intervals remained close to each other. Taken together, the TRm values indicate similar behavior of wound area reduction between the groups throughout the initial inflammatory and proliferative phases.

Table 5. Mean repair rate (TRm) per interval (cm²/day) of cutaneous wounds in the control and experimental groups. Values presented as mean ± standard deviation (SD), n = 8 pairs.

| Range (days) | Experimental group (cm²/day) | Control group (cm²/day) |
|---|---|---|
| 0–3 | 0.12 ± 0.07 | 0.08 ± 0.06 |
| 3–7 | 0.02 ± 0.05 | 0.03 ± 0.05 |
| 7–10 | 0.00 ± 0.04 | -0.02 ± 0.07 |
| 10–14 | 0.08 ± 0.02 | 0.09 ± 0.04 |

Note: TRm was calculated as the change in wound area between two consecutive time points, divided by the number of days in the interval. Positive values indicate a reduction in wound area, while negative values indicate an increase in area during the evaluated interval. The overall analysis was performed using a linear mixed-effects model (α = 0.05).

*3.4. Histopathological evaluation*

The semi-quantitative histopathological findings on day 14 (D14) are presented in Table 6. In the paired comparison between treatments, no statistically significant differences were observed regarding the scores for fibroblasts (P = 0.98), mononuclear inflammation (P = 0.08), polymorphonuclear inflammation (P = 0.58), bacteria (P = 0.52), and collagenization (P = 0.27). Descriptively, the experimental group presented a higher median for mononuclear inflammation, while the control group presented a slightly higher median for collagenization. For fibroblasts, polymorphonuclear inflammation, and bacteria, the medians were similar between treatments. Taken together, the findings on D14 did not indicate a detectable histopathological difference between treatments in the variables evaluated (Table 6). Representative histopathological photomicrographs of the control and experimental groups on D14 are presented in Figure 4.

Table 6. Semiquantitative histopathological findings on day 14 in cutaneous wounds from the control and experimental groups.

| Variable | Median control (IQR) | Experimental median (IQR) | P-value |
|---|---|---|---|
| Fibroblasts | 2.0 (1.0–2.0) | 2.0 (1.0–2.0) | 0.98 |
| Mononuclear inflammation | 1.0 (1.0–2.0) | 2.0 (1.75–2.25) | 0.08 |
| Polymorphonuclear inflammation | 2.0 (1.0–2.0) | 2.0 (1.0–3.0) | 0.58 |
| Bacteria | 1.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.52 |
| Collagenization | 2.0 (1.75–2.0) | 1.5 (1.0–2.0) | 0.27 |

Note: Data presented as median (interquartile range, IQR). Comparisons between treatments were performed using the paired Wilcoxon test. Score coding: fibroblasts, + = 1 and ++ = 2; mononuclear and polymorphonuclear inflammation, mild = 1, moderate = 2 and severe = 3; bacteria, not observed = 0, mild = 1, moderate = 2 and severe = 3; collagenization, disorganized = 0, partially organized = 1 and organized = 2.

Figure 4. Representative histopathological photomicrographs of cutaneous wounds in horses on day 14. (A, B) Control group. (A) Healing skin, with evident

granulation tissue, complete re-epithelialization, discrete chronic-active inflammatory infiltrate and edema (HE, 40×). (B) Higher magnification of the same lesion (HE, 200×). (C, D) Experimental group. (C) Healing skin, with superficial granulation tissue, discrete chronic-active inflammatory infiltrate and complete re-epithelialization (HE, 40×). (D) Higher magnification showing neovascularization and organized fibroblasts, interspersed with discrete neutrophils, lymphocytes and macrophages (HE, 400×). 1, granulation tissue; 2, reepithelialization; 3, chronic-active inflammatory infiltrate; 4, reepithelialization; 5, superficial granulation tissue; 6, neovascularization; 7, organized fibroblasts.

## 4. Discussion

As far as could be verified in the consulted literature, no published clinical or experimental studies were identified evaluating the topical application of liquid coconut water or commercial topical formulations containing coconut water powder on equine skin wounds. Nor were any studies found comparing this type of formulation with topical antimicrobial therapies widely used in routine veterinary practice. In this context, the present study represents, to our knowledge, an initial experimental evaluation of this approach in the equine species. However, the findings should be interpreted as referring to the evaluated composite topical formulation, and not to coconut water powder in isolation.

In the present study, it was not possible to detect a difference between the topical formulation containing coconut water powder and the reference ointment regarding the healing evolution of experimental skin wounds in equines, considering the macroscopic, morphometric, and histopathological outcomes evaluated. Although descriptive trends of greater contraction and a higher degree of repair were observed in the experimental group at some points, especially on D3, these differences did not reach statistical significance and should be interpreted with caution. Taken together, the findings indicate that, under the conditions evaluated, the experimental formulation, free of topical antimicrobials, sustained scar progression compatible with that observed with the commercial reference ointment. Still, the results do not demonstrate therapeutic equivalence or superiority of the experimental formulation, they only indicate the absence of a detectable difference under the conditions tested.

The absence of an overall treatment effect and treatment × time interaction indicates that the scar response evolved similarly between the groups throughout the follow-up. Although the superiority of the experimental formulation was not demonstrated, the results suggest that its use did not compromise the tissue repair process during the evaluated period. Discreet numerical differences observed at specific times should be interpreted with caution, considering the biological variability inherent in healing and the exploratory nature of the study, associated with the small sample size. In the statistical model, a significant effect of time was observed, with no effect of treatment or treatment × time interaction, with a difference between the groups detected only on D3 for the degree of repair.

The literature on coconut water powder applied to wound healing is still limited and consists mostly of experimental studies and reports in other species. In this context, the findings of the present study contribute in an unprecedented way to equine medicine by providing initial evidence on the behavior of a topical formulation containing coconut water powder in experimental cutaneous wounds. The investigation of the formulation was based on previous evidence describing the bioactive properties of coconut water associated with inflammatory modulation and tissue repair in different models. In humans, formulations derived from coconut water powder have already been investigated in chronic wounds, such as diabetic foot ulcers, with favorable clinical outcomes [31].

In rodents, formulations containing lyophilized coconut water have been associated with improved repair parameters, especially collagen deposition [29]. In dogs, Meneses and Silva [32] observed similar scarring performance with a barrier cream based on PWC in dogs, with good scar evolution, good adherence, and potential economic advantage when compared to conventional topical treatments. In the present study, the macroscopic and morphometric evolution observed in horses was consistent with this preliminary scenario, with no indication of worse performance of the experimental formulation compared to the comparator used. However, it is important to highlight that the evaluated formulation is composed of powdered coconut water, vegetable oils, and excipients. Therefore, the observed results should be interpreted as an effect of the commercial topical formulation as a whole, and it is not possible to determine the isolated contribution of each component to the scarring process. Furthermore, the comparator used differs from the experimental formulation in terms

of composition, presence of antimicrobials, vehicle, oil content, viscosity, hydration, and possible occlusive effect. Therefore, the comparison carried out had a clinical-pragmatic character, and not a pharmacological or mechanistic one. The absence of a negative control group, without treatment and a group subjected only to cleaning with water or saline solution, or a group treated only with the vehicle, also prevents determining whether the observed evolution resulted from a specific effect of the coconut water powder, the vegetable oils, the vehicle, the natural physiological evolution of the wounds, or a combination of these factors, or discriminating the relative contribution of the oils, the vehicle, and the other components of the formulation. Therefore, the findings should be interpreted as a comparison between two topical approaches to wound management, and not as a demonstration of superiority, therapeutic equivalence, or intrinsic activity of coconut water powder.

The biological plausibility of the coconut water powder-based formulation is supported by its composition, which includes sugars, minerals, amino acids, vitamins, and phenolic compounds, which have antioxidant and anti-inflammatory properties. These components, especially phenolic compounds, can contribute to the modulation of local oxidative stress, an important factor in the dynamics of tissue healing. Vitamin C, present in coconut water, plays a crucial role in the hydroxylation of proline and lysine during collagen synthesis, a process essential for the integrity and repair of the extracellular matrix. In vitro studies in human dermal fibroblasts have shown that coconut water reduces reactive oxygen species, suggesting a cytoprotective effect under oxidative stress conditions [38]. Furthermore, experimental models in rodents indicate that coconut water may exert a positive effect on tissue repair, reducing inflammation and promoting healing [39]. Coconut water also contains phytohormones, such as auxins and cytokinins, known to promote cell division and influence tissue growth and development in plants, which raises hypotheses about a possible contribution to regenerative events [30, 40].

The equine species was selected due to the particularities of the cutaneous scarring process in these animals, characterized by a greater predisposition to prolonged inflammatory responses and the formation of exuberant granulation tissue, factors that frequently hinder the adequate resolution of wounds by secondary intention [8], as well as by the tendency to form exuberant granulation tissue in contexts of aberrant healing [9]. Although exuberant granulation tissue is more frequently

observed in distal limbs of horses, lesions were induced in the lumbar region in order to evaluate the effects of the formulations in a more controlled experimental environment, prioritizing the internal validity of the study. This strategy is common in experimental models of wound healing in horses, as it allows multiple replicates in the same animal and reduces mechanical and environmental interferences [34-36]. Furthermore, healing in the lumbar region tends to occur more rapidly than in distal limbs, favoring experimental control [34, 37].

The intra-animal paired design and serial measurement of wound area by digital planimetry reinforce the methodological robustness of the study, by reducing interindividual variability and providing an objective quantitative outcome. However, from a clinical point of view, the lumbar model has limited external validity for direct extrapolation to wounds in distal limbs, which constitute the main challenge in equine practice. In this location, factors such as greater contamination, less skin mobility, greater local tension, and predisposition to the formation of exuberant granulation tissue make repair more complex. Thus, the present model may underestimate healing difficulties in distal limbs. This limitation is particularly relevant because traumatic limb wounds in horses are more subject to chronicity and infectious complications, including bacterial biofilms, which can hinder healing and clinical management [16]. Therefore, the choice of the lumbar region favored internal validity and experimental control, but reduces the direct extrapolation of results to wounds in distal limbs, which represent a more challenging clinical scenario in the equine species.

The sample size was small, although consistent with experimental studies in horses, in which samples of four to eight animals with multiple wounds per individual are frequently used due to the ethical and logistical limitations inherent to the species [7, 35, 41]. Even so, the number of animals limits the statistical power of the study and increases the possibility of type II error, especially for subtle or moderate differences between treatments. Furthermore, the standardized wound size of 1 cm in diameter may have reduced the model's sensitivity to detect small therapeutic differences. Small wounds in the lumbar region tend to exhibit relatively rapid contraction and epithelialization, which can generate a roof effect and limit morphometric discrimination between topical treatments. The fixed allocation of lesions may have introduced systematic spatial bias, since local differences in vascularization, lymphatic drainage, and skin tension can influence the scarring response independently of the treatment.

Although the intra-animal paired design reduces individual variability, it does not completely exclude the possibility of indirect biological interactions between lesions or minimal cross-absorption between topical formulations applied to the same animal. Additionally, daily clinical assessments were not blinded, which may introduce observer bias, even though the planimetric analysis was performed in a treatment-blind manner. The absence of standardized prior cleaning before photography and reapplication, in order to preserve the natural dynamics of the wound microenvironment, may have contributed to greater local microbiological variability between lesions. These limitations do not invalidate the model used, but they limit its inferential scope.

From a clinical standpoint, all wounds healed by secondary intention without infectious or systemic complications. Perilesional edema was predominantly absent or mild, with progressive reduction throughout the follow-up, and the exudation pattern was consistent with the physiological evolution of the inflammatory and proliferative phases of healing. On day 1 (D1), the experimental group presented a higher proportion of lesions without exudate compared to the control group. However, the overall intensity of exudate did not differ between treatments, and there was progressive resolution until day 14 (D14), suggesting maintenance of a local environment favorable to tissue repair. Taken together, these findings indicate that the formulation containing PWC did not promote evident exacerbation of the local inflammatory response. Furthermore, although it is a formulation without topical antimicrobials, no clinical evidence of worse local evolution was observed compared to the reference ointment. This finding is relevant in the context of the rational use of antimicrobials in veterinary medicine, but it should be interpreted with caution, since the design does not allow us to conclude therapeutic equivalence or specific intrinsic activity of PWC.

The histopathological evaluation was performed at a single time point (D14), without the use of special stains or immunohistochemical markers, which limits the mechanistic characterization of tissue repair. D14 was selected because it corresponds to the peak of the proliferative phase of equine cutaneous healing, a period in which granulation tissue is established, characterized by intense fibroplasia, active angiogenesis, and the deposition of extracellular matrix is more easily recognizable [1, 9]. Evaluations performed at earlier times tend to reflect inflammatory predominance

and immature matrix, while later evaluations predominantly capture events associated with collagen remodeling. Thus, D14 represents an appropriate time window to characterize the quality of the newly formed tissue. Performing a single biopsy aimed to avoid additional injury that could interfere with the dynamics of lesion closure and compromise the longitudinal analysis of the primary outcome. However, the absence of serial evaluations limits the dynamic analysis of the different phases of tissue repair.

In the histopathological evaluation of D14, it was not possible to detect differences between the groups regarding the semi-quantitative scores evaluated. Descriptively, the experimental group showed a tendency towards greater mononuclear inflammation, while the control group showed slightly higher collagenization, without statistical significance. Under physiological conditions, the mononuclear infiltrate, especially with the participation of macrophages, plays a central role in the transition to the proliferative phase and in the coordination of extracellular matrix deposition. Taken together, this profile suggests that both treatments sustained similar tissue evolution in the period corresponding to the proliferative phase of equine cutaneous healing and that, at the time point analyzed, the experimental formulation was not associated with a marked morphological alteration of tissue repair compared to the reference treatment.

Although the observed findings suggest a consistent pattern of tissue response, this interpretation should be considered essentially exploratory. The absence of immunohistochemical markers limits the precise characterization of the cell populations involved in the wound bed, restricting the understanding of the mechanisms underlying the repair process. Additionally, the histological analysis was conducted at a single time point and without the use of special stains or complementary techniques, which imposes important limitations on the robustness of the inferences. In this context, interpretations related to angiogenesis, collagen organization, and the cellular inflammatory profile necessarily remain indirect and should be considered with caution.

The presence of structures with morphology compatible with cocci was observed in both groups, with no statistically significant difference between treatments on day 14. These structures, associated with the wound bed, are compatible with secondary bacterial colonization, frequently observed in open skin lesions with discontinuity. As the microbiological evaluation did not include special stains, culture,

or molecular methods, these findings should be interpreted in a strictly morphological and semi-quantitative manner. Furthermore, the absence of purulent exudate and exuberant neutrophilic infiltrate suggests that, under the conditions evaluated, there was no histological evidence of infectious aggravation associated with the experimental formulation. These findings are particularly relevant because they indicate that, even without incorporating topical antimicrobials, the experimental formulation was able to maintain a microenvironment compatible with the physiological progression of healing, possibly due to favorable physicochemical characteristics, such as maintaining moisture and covering the wound bed.

The absence of evident clinical or histological signs of adverse effects, such as hypersensitivity or inflammatory exacerbation, suggests good local tolerability of the formulation in the evaluated model. Although the formulation containing PWC does not contain compounds described as repellents, no evident attraction of insects to the exposed wounds was observed during clinical follow-up. This finding suggests adequate maintenance of the local wound environment under the evaluated conditions, without evidence of secondary complications related to this aspect. In addition, the observed results are consistent with previous findings by Meneses and Silva [32], who describe good adherence of the formulation to the wound surface. This aspect is relevant because the good adherence of the formulation can favor the permanence of the product on the wound bed, with a positive impact on ease of use and therapeutic efficacy. Considering these aspects, the formulation also presents potential practical interest from the point of view of clinical management.

The joint interpretation of the morphometric and histopathological findings should, therefore, consider the exploratory nature of the study and the limited statistical power to detect differences of small or moderate magnitude. The absence of statistical significance does not constitute evidence of therapeutic equivalence, but of the absence of a detectable difference in the conditions evaluated. Even so, these findings have translational relevance in the context of the rational use of antimicrobials in veterinary medicine, as they indicate that the formulation containing PWC was not associated with detectable impairment of wound healing. Taken together, the results justify the continuation of the investigation in future studies with larger samples, randomized allocation of lesions, additional controls, and evaluation in more

challenging clinical conditions of equine veterinary medicine, especially in distal limb wounds.

## 5. Conclusion

Under the evaluated conditions, it was not possible to detect a difference between the commercial topical formulation containing coconut water powder and the reference antimicrobial ointment in the macroscopic, morphometric, and histopathological outcomes analyzed in experimental cutaneous wounds in horses. The results should be interpreted as exploratory and do not demonstrate superiority, therapeutic equivalence, or an isolated effect of coconut water powder. Future studies with more robust designs are needed to better clarify the potential of the evaluated non-antimicrobial formulation as an alternative in the management of equine wounds.

## Funding

This research did not receive specific funding from public, commercial, or non-profit funding agencies. The Article Processing Fee for the publication of this research was covered by the Coordination for the Improvement of Higher Education Personnel - CAPES - identifier ROR: 00x0ma614). For open access purposes, the authors have assigned a Creative Commons CC BY license to any accepted version of the article.

## Declaration of conflicts of interest

The authors declare no conflicts of interest.

## Authors' contributions (CRediT)

Cinthia de Sousa Braga Meneses: Conceptualization, Methodology, Research, Data curation, Writing – original draft.

Lúcia Daniel Machado da Silva: Supervision, Writing – review and editing.

João Emanuel Campelo Cardoso: Resources, Research, Support in conducting the experiment.

Fábio Ranyeri Nunes Rodrigues: Resources, Formal analysis, Research.

Edilson Martins Rodrigues Neto: Supervision, Methodology, Writing – review and editing.

## Data availability

The data supporting the findings of this study may be made available by the corresponding author upon reasonable request.

## Declaration of the use of generative AI and AI-assisted technologies in the manuscript preparation process.

During the preparation of this work, the authors used ChatGPT (OpenAI) to improve the language and readability of the manuscript. After using this tool, the authors reviewed and edited the content as necessary and take full responsibility for the content of the publication.

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**Legends figures:**

**Figure 1.** Representative macroscopic evolution of paired cutaneous wounds in a horse over a 14-day follow-up period. Images were obtained on days 0, 3, 7, 10, and 14. The upper row corresponds to the cranial wound (control group), and the lower row to the caudal wound (experimental group). The panels were arranged in chronological order from left to right.

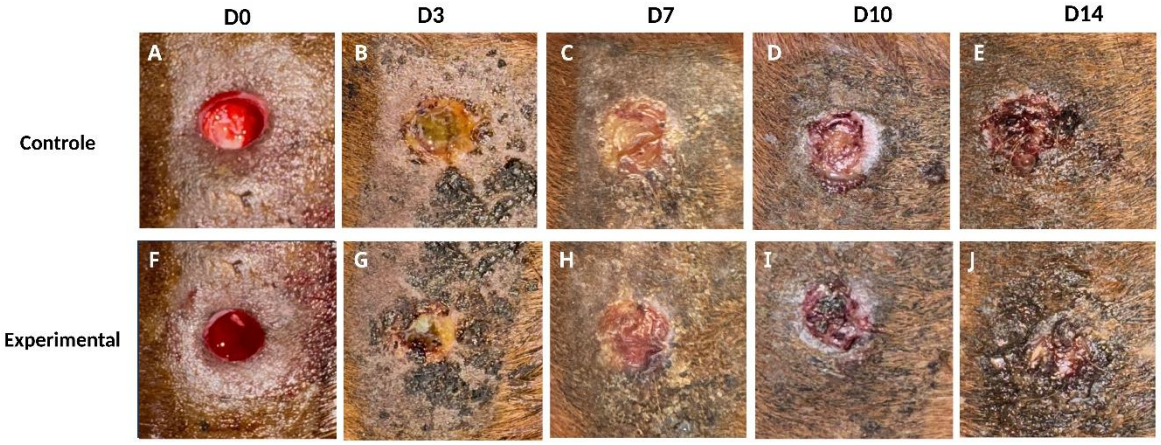



**Figure 2.** Temporal evolution of cutaneous wound area in the control and experimental groups on days 0, 3, 7, 10, and 14. Values are presented as mean ± standard deviation (SD), n = 8 pairs.

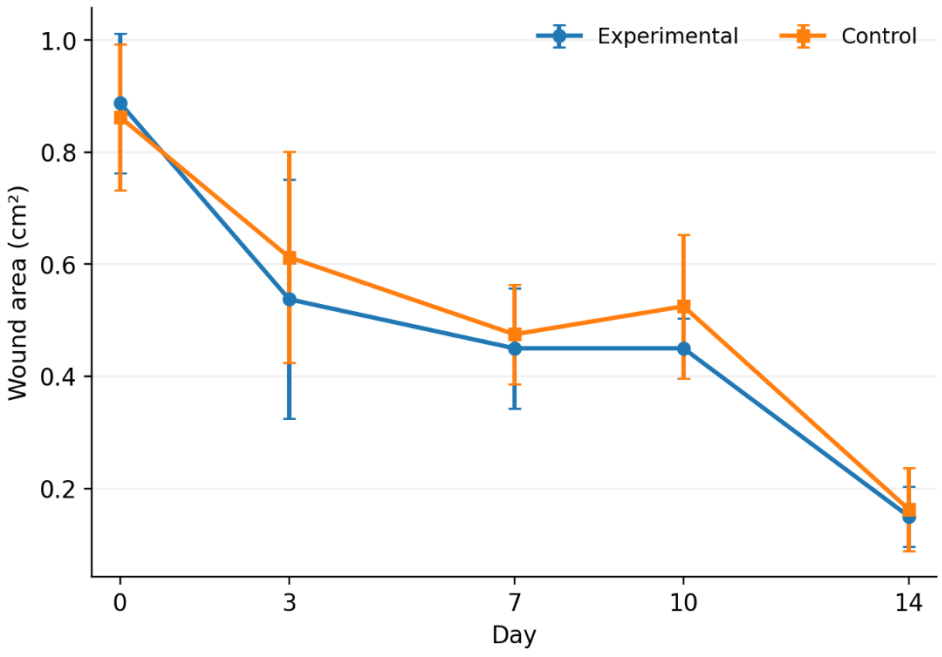


**Figure 3.** Temporal evolution of the degree of wound repair in the experimental and control groups on days 3, 7, 10, and 14. Values are presented as mean ± standard deviation (SD), n = 8 pairs. * Significant difference between treatments on day 3 after Holm adjustment (adjusted P = 0.0313).

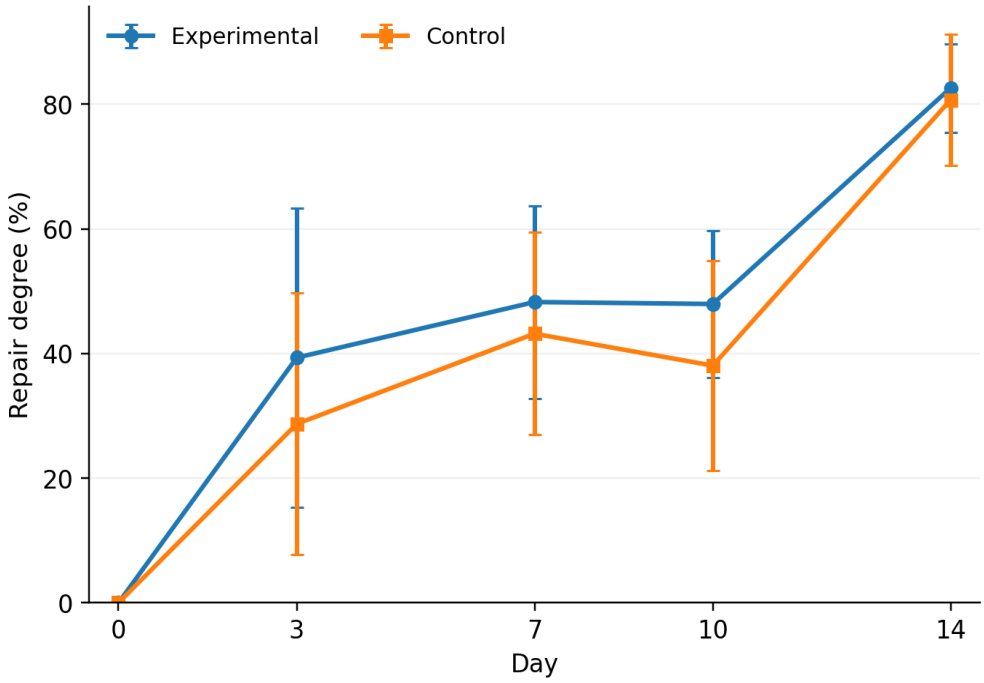
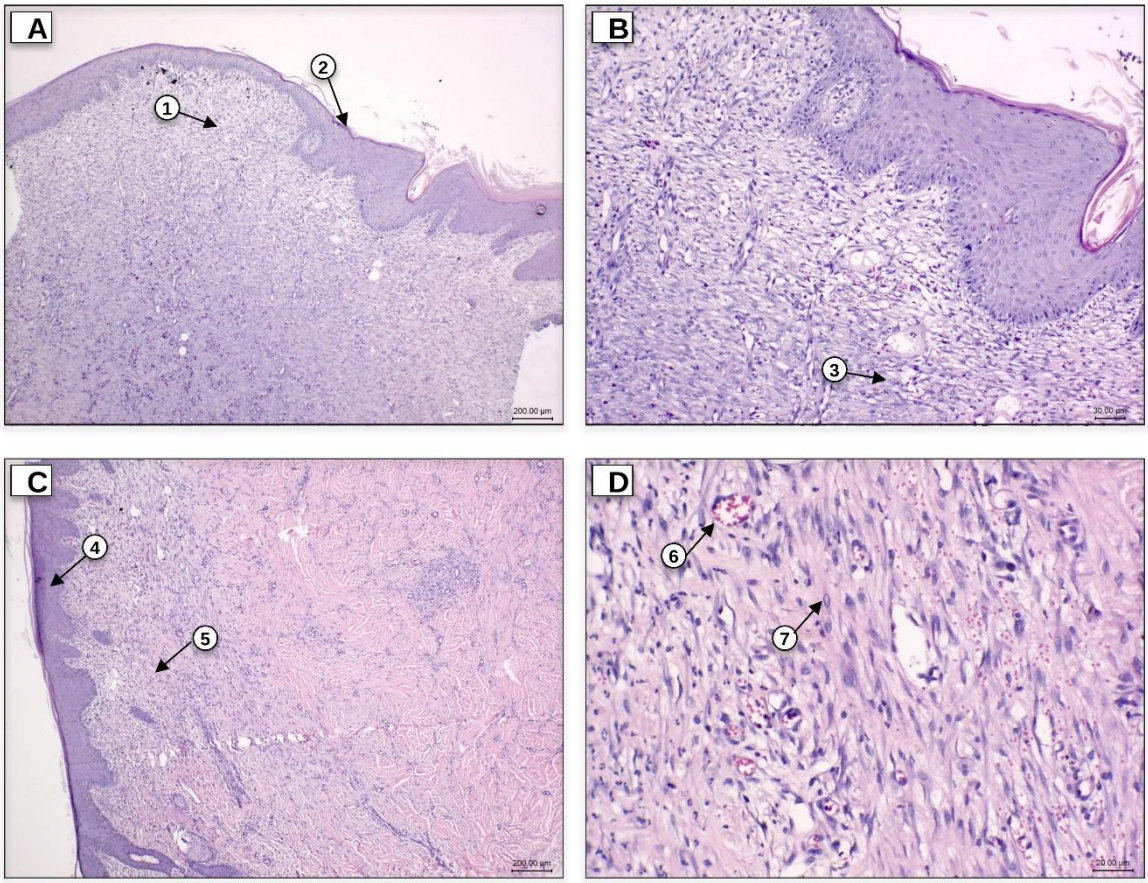



**Figure 4.** Representative histopathological photomicrographs of equine cutaneous wounds on day 14. (A, B) Control group. (A) Healing skin with evident granulation tissue, complete re-epithelialization, mild chronic-active inflammatory infiltrate, and edema (H&E, 40×). (B) Higher magnification of the same lesion (H&E, 200×). (C, D) Experimental group. (C) Healing skin with superficial granulation tissue, mild chronic-active inflammatory infiltrate, and complete re-epithelialization (H&E, 40×). (D) Higher magnification showing neovascularization and organized fibroblasts interspersed with scattered neutrophils, lymphocytes, and macrophages (H&E, 400×). 1, granulation tissue; 2, re-epithelialization; 3, chronic-active inflammatory infiltrate; 4, re-epithelialization; 5, superficial granulation tissue; 6, neovascularization; 7, organized fibroblasts




## 5 DISCUSSÃO GERAL

As feridas cutâneas em equinos constituem condição clínica de elevada relevância, não apenas por sua frequência, mas também pela tendência à evolução prolongada e ao desenvolvimento de complicações que dificultam o reparo tecidual. Ao longo desta tese, esse problema foi abordado sob duas perspectivas complementares. No primeiro artigo, buscou-se compreender, por meio de revisão integrativa, os principais fatores associados à cicatrização aberrante, com ênfase no tecido de granulação exuberante (TGE). No segundo, investigou-se experimentalmente o desempenho de uma formulação tópica à base de água de coco em pó em feridas cutâneas induzidas em equinos. Em conjunto, os achados permitem discutir o reparo cutâneo equino não apenas como um fenômeno biológico complexo, mas também como um campo em que persistem limitações terapêuticas e lacunas

importantes de evidência.

A síntese obtida no capítulo de revisão reafirma que o TGE não deve ser compreendido como evento isolado, mas como manifestação de um microambiente cicatricial persistentemente desfavorável. Os estudos incluídos associaram o TGE à baixa tensão de oxigênio, à persistência inflamatória, à angiogênese sustentada, à mobilidade tecidual e, em alguns casos, à presença de biofilmes bacterianos, fatores que comprometem a progressão ordenada do reparo e favorecem cicatrização aberrante. Esse conjunto de achados é coerente com a própria fundamentação teórica da tese, segundo a qual feridas em membros distais de equinos apresentam maior dificuldade de resolução em razão de características anatômicas e fisiológicas que favorecem a cronicidade. Assim, o TGE emerge menos como uma complicação ocasional e mais como expressão clínica de desequilíbrios locais prolongados no processo reparativo.

Além disso, a revisão integrativa evidenciou heterogeneidade metodológica entre os estudos, tanto no delineamento quanto nas intervenções e nos desfechos avaliados, o que limita comparações diretas e dificulta a consolidação de protocolos terapêuticos mais robustos. As abordagens terapêuticas descritas para o TGE foram predominantemente combinadas, envolvendo manejo do leito da ferida, desbridamento, excisão do tecido quando indicada e controle das complicações infecciosas, com grande variabilidade de protocolos e desfechos. Esse dado tem implicação importante para a leitura do estudo experimental da tese: na ausência de protocolos amplamente padronizados e comparáveis, o desenvolvimento e a avaliação de novas formulações tópicas tornam-se especialmente relevantes. Assim, a revisão não apenas contextualizou a complexidade do problema, mas também justificou a necessidade de ensaios controlados que testem estratégias terapêuticas em condições mais bem delimitadas.

Nesse contexto, o estudo experimental com a formulação tópica à base de água de coco em pó assume relevância como tentativa de produzir evidência inicial em um campo ainda pouco explorado. Até onde foi possível verificar, não havia estudos prévios em equinos avaliando essa formulação no reparo cutâneo, tampouco comparações com terapias antimicrobianas tópicas amplamente utilizadas na rotina veterinária. Os resultados indicaram que não foi possível detectar diferença entre a formulação contendo água de coco em pó e a pomada de referência quanto à

evolução cicatricial das feridas cutâneas experimentais, considerando os desfechos macroscópicos, morfométricos e histopatológicos avaliados. Houve progressão do reparo ao longo do tempo em ambos os tratamentos, sem evidência de superioridade terapêutica da formulação experimental nas condições testadas. A despeito dos resultados, o estudo já representa contribuição original ao inserir a ACP no debate sobre reparo cutâneo equino em modelo experimental padronizado.

Os resultados obtidos indicaram que não foi possível detectar diferença entre a formulação contendo água de coco em pó e a pomada de referência quanto à evolução cicatricial das feridas cutâneas experimentais em equinos, considerando os desfechos macroscópicos, morfométricos e histopatológicos avaliados. Esse achado deve ser interpretado com cautela e, ao mesmo tempo, com maturidade analítica. A ausência de diferença estatisticamente detectável não significa ausência de relevância terapêutica. Nas condições avaliadas, a formulação experimental, mesmo isenta de antimicrobianos tópicos, sustentou progressão cicatricial compatível com a observada com a pomada comercial de referência. Esse ponto é particularmente importante porque sugere viabilidade biológica da formulação estudada como alternativa tópica, ainda que sem superioridade demonstrada no delineamento empregado.

Do ponto de vista histopatológico, os achados do D14 reforçam essa interpretação. As medianas foram semelhantes entre os tratamentos para fibroblastos, inflamação polimorfonuclear e bactérias, sem diferença histopatológica detectável nas variáveis avaliadas. Além disso, as fotomicrografias mostraram reepitelização completa em ambos os grupos; no grupo experimental, observou-se tecido de granulação superficial, neovascularização e fibroblastos organizados, enquanto no grupo controle também se verificou pele em cicatrização com tecido de granulação evidente, reepitelização completa e discreto infiltrado inflamatório crônico-ativo. Em termos integrativos, isso indica que a formulação à base de ACP foi capaz de sustentar um microambiente compatível com reparo tecidual organizado, sem sinalizar prejuízo ao curso cicatricial.

A articulação entre os dois artigos permite extrair uma inferência mais robusta: se a cicatrização equina é particularmente vulnerável à manutenção de inflamação, biofilmes, hipóxia e fibroplasia desregulada, então uma formulação tópica candidata ao uso clínico deve, no mínimo, não agravar esse cenário e idealmente favorecer um

ambiente reparativo estável. Nessa tese, a formulação à base de água de coco em pó não demonstrou superioridade estatística em relação ao comparador, mas tampouco mostrou desempenho inferior detectável no conjunto de variáveis analisadas. Isso a posiciona, preliminarmente, como formulação com potencial de uso e merecedora de investigação adicional, sobretudo quando se considera o racional biológico previamente descrito para a ACP e os resultados promissores obtidos em outros modelos experimentais e clínicos.

Outro aspecto relevante diz respeito à natureza do próprio modelo avaliado. O artigo experimental analisou feridas cutâneas padronizadas em delineamento pareado intra-animal, com foco em evolução morfométrica e histopatológica no 14º dia. Esse desenho é adequado para gerar evidência inicial em condições controladas, mas não reproduz integralmente a complexidade observada em feridas clínicas complicadas, crônicas ou associadas a tecido de granulação exuberante estabelecido. Assim, o desenho fortalece a comparabilidade entre tratamentos, mas também delimita o alcance das conclusões. Dessa forma, não se deve extrapolar automaticamente os achados para cenários clínicos mais desafiadores, embora eles sustentem a continuidade da investigação da formulação em estudos futuros com maior poder estatístico, seguimento mais prolongado e modelos mais próximos da rotina veterinária. Essa limitação dialoga diretamente com a revisão integrativa, que mostrou que boa parte da complexidade clínica do TGE decorre justamente da interação prolongada entre múltiplos fatores locais e sistêmicos, cenário mais heterogêneo do que aquele reproduzido em lesões experimentais padronizadas.

Nesse sentido, a principal contribuição científica desta tese talvez não esteja em demonstrar superioridade terapêutica imediata da formulação, mas em estabelecer um elo consistente entre plausibilidade biológica, necessidade clínica e evidência experimental inicial. A revisão mostrou que o campo ainda sofre com heterogeneidade metodológica e ausência de protocolos padronizados; o estudo experimental, por sua vez, ofereceu um primeiro passo controlado para avaliar uma formulação derivada da água de coco em pó na espécie equina. Assim, a tese contribui ampliando a compreensão do TGE e das condições que perpetuam a cicatrização aberrante em equinos, e lança a avaliação comparativa da ACP tópica nesse contexto.

A partir desses achados, torna-se possível delinear implicações práticas e perspectivas futuras. Em termos clínicos, os resultados sugerem que formulações à

base de água de coco em pó podem ser consideradas candidatas promissoras para investigação continuada em medicina veterinária, especialmente pela compatibilidade cicatricial observada em comparação com uma pomada de referência. Em termos científicos, os dados reforçam a necessidade de estudos subsequentes com amostras maiores, acompanhamento por períodos mais longos, avaliação microbiológica mais aprofundada, inclusão de feridas com diferentes graus de complexidade e eventual investigação em cenários naturalmente complicados por infecção, biofilme ou predisposição ao TGE. Essa agenda futura é coerente com a lacuna já apontada pela revisão integrativa e com a necessidade de ensaios clínicos controlados e protocolos mais padronizados no campo.

Em síntese, a presente tese sustenta que a cicatrização de feridas em equinos permanece um desafio multifatorial, particularmente em condições que favorecem persistência inflamatória, biofilmes e desenvolvimento de tecido de granulação exuberante. Ao mesmo tempo, demonstra que a formulação tópica à base de água de coco em pó merece investigação continuada, por ter apresentado comportamento cicatricial semelhante ao da pomada de referência no modelo experimental empregado, sem que isso implique, neste estágio, comprovação de superioridade, equivalência terapêutica formal ou aplicabilidade clínica ampliada. Desse modo, o conjunto dos resultados não encerra a discussão sobre o uso da ACP no reparo cutâneo equino; ao contrário, inaugura uma linha de pesquisa com potencial translacional e relevância tanto para a medicina veterinária quanto para o desenvolvimento de formulações inovadoras aplicadas ao tratamento de feridas.

## 6 CONSIDERAÇÕES FINAIS

Conclui-se que a cicatrização de feridas cutâneas em equinos permanece como desafio clínico multifatorial, especialmente diante da persistência inflamatória, da formação de biofilme bacteriano e do desenvolvimento de tecido de granulação exuberante. A revisão integrativa demonstrou que a literatura ainda apresenta heterogeneidade metodológica e limitação de evidências padronizadas sobre o manejo dessas complicações, o que dificulta a definição de estratégias terapêuticas mais consistentes para a espécie.

No modelo experimental adotado, a formulação tópica à base de água de coco

em pó apresentou desempenho cicatricial semelhante ao da pomada de referência, sem diferença detectável entre os tratamentos nos parâmetros avaliados. Esse resultado sustenta a relevância da formulação como objeto de investigação e amplia o campo de estudo de alternativas terapêuticas aplicáveis à medicina veterinária.

A presente tese contribui para o avanço do conhecimento sobre o reparo cutâneo em equinos e inicia, nessa espécie, a avaliação experimental de formulação tópica derivada da água de coco em pó. Assim, amplia o campo de estudo de alternativas terapêuticas aplicáveis à medicina veterinária e fornece base para investigações futuras com maior número de animais, seguimento mais prolongado e inclusão de modelos clinicamente mais desafiadores.

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# ANEXO A — RELATÓRIO DE FERIDA IMITO WOUND

Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

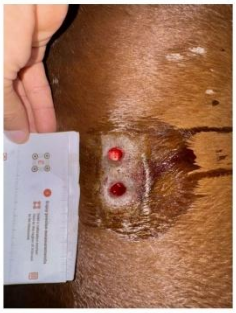
ID do paciente

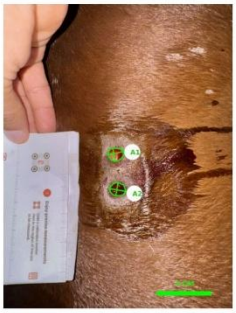
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)







Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 2.0 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 1.0 cm² |
| Circunferência | 3.7 cm | Comprimento | 1.3 cm |
| Largura | 1.1 cm | Profundidade | N/A |
| A2 | | Área | 1.0 cm² |
| Circunferência | 3.6 cm | Comprimento | 1.3 cm |
| Largura | 1.0 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

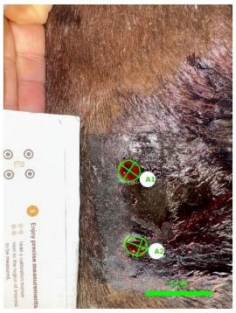
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)





Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

ID do paciente

## Medição

Área geral 1.6 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.8 cm² |
| Circunferência | 3.3 cm | Comprimento | 1.1 cm |
| Largura | 1.0 cm | Profundidade | N/A |
| A2 | | Área | 0.8 cm² |
| Circunferência | 3.2 cm | Comprimento | 1.2 cm |
| Largura | 0.9 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

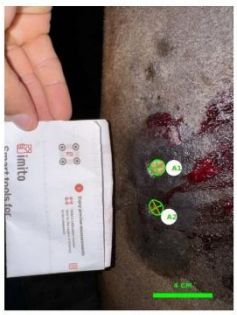
Data de nascimento (idade) -
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

## Medição

Área geral 1.7 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.9 cm² |
| **Circunferência** | 3.5 cm | **Comprimento** | 1.1 cm |
| **Largura** | 1.1 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.8 cm² |
| **Circunferência** | 3.3 cm | **Comprimento** | 1.2 cm |
| **Largura** | 0.9 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |



Relatório de ferida

imito

UFC

Ledy **Santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

Ledy **Santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

## Medição

Área geral 1.5 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.7 cm² |
| **Circunferência** | 3.1 cm | **Comprimento** | 1.2 cm |
| **Largura** | 0.9 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.8 cm² |
| **Circunferência** | 3.2 cm | **Comprimento** | 1.3 cm |
| **Largura** | 1.0 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |

Relatório de ferida

imito

UFC

morena **santa Luzia** ♀

Data de nascimento (idade) -

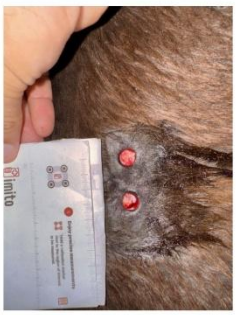
ID do paciente

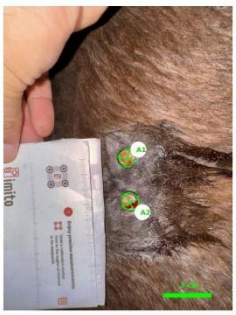
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

morena **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 2.1 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 1.0 cm² |
| Circunferência | 3.6 cm | Comprimento | 1.3 cm |
| Largura | 1.1 cm | Profundidade | N/A |
| A2 | | Área | 1.1 cm² |
| Circunferência | 3.7 cm | Comprimento | 1.2 cm |
| Largura | 1.2 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -

ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 2.1 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 1.0 cm² |
| Circunferência | 3.6 cm | Comprimento | 1.2 cm |
| Largura | 1.1 cm | Profundidade | N/A |
| A2 | | Área | 1.0 cm² |
| Circunferência | 3.7 cm | Comprimento | 1.2 cm |
| Largura | 1.1 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

Paloma **santa Luzia** ♀

Data de nascimento (idade) -

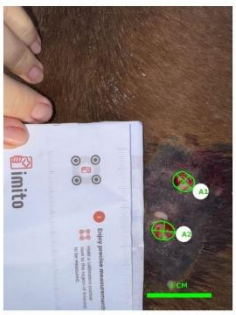
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

Paloma **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 1.6 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.8 cm² |
| Circunferência | 3.2 cm | Comprimento | 1.1 cm |
| Largura | 0.9 cm | Profundidade | N/A |
| A2 | | Área | 0.8 cm² |
| Circunferência | 3.3 cm | Comprimento | 1.2 cm |
| Largura | 0.9 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -

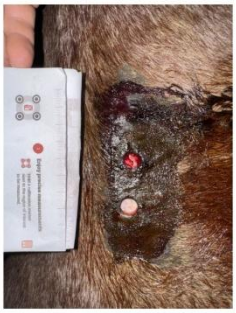
ID do paciente

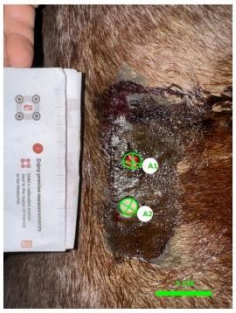
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 1.5 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.7 cm² |
| Circunferência | 3.1 cm | Comprimento | 1.1 cm |
| Largura | 0.9 cm | Profundidade | N/A |
| A2 | | Área | 0.8 cm² |
| Circunferência | 3.1 cm | Comprimento | 1.0 cm |
| Largura | 1.0 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

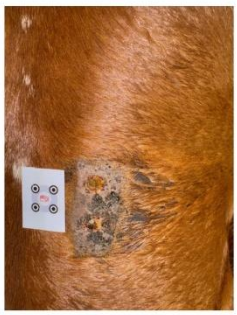
ID do paciente

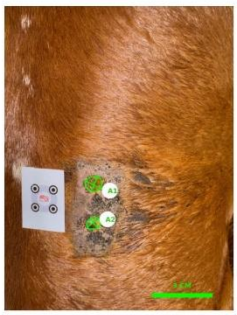
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 0.9 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.7 cm | Área | 0.6 cm² |
| Largura | 0.8 cm | Comprimento | 0.9 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.2 cm | Área | 0.4 cm² |
| Largura | 0.6 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

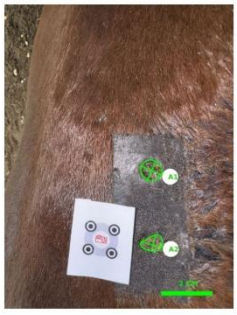
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

ID do paciente

## Medição

Área geral 1.1 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.8 cm | Área | 0.6 cm² |
| Largura | 0.9 cm | Comprimento | 0.9 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.6 cm | Área | 0.5 cm² |
| Largura | 0.7 cm | Comprimento | 0.9 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 1.5 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.8 cm² |
| **Circunferência** | 3.2 cm | **Comprimento** | 1.1 cm |
| **Largura** | 1.0 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.7 cm² |
| **Circunferência** | 3.2 cm | **Comprimento** | 1.2 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |



Relatório de ferida

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Ledy **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

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Ledy **Santa Luzia** ♀

Data de nascimento (idade) -

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## Medição

Área geral 1.2 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.8 cm | **Comprimento** | 0.9 cm |
| **Largura** | 0.9 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.9 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.7 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |

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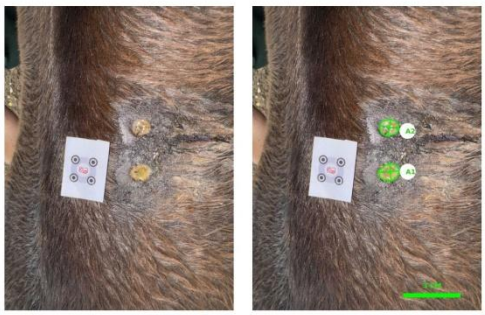
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)





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## Medição

Área geral 1.6 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 3.3 cm | Área | 0.8 cm² |
| Largura | 1.0 cm | Comprimento | 1.2 cm |
| | | Profundidade | N/A |
| A2 | | Área | 0.8 cm² |
| Circunferência | 3.2 cm | Comprimento | 1.1 cm |
| Largura | 0.9 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



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## Mecânico / Traumático

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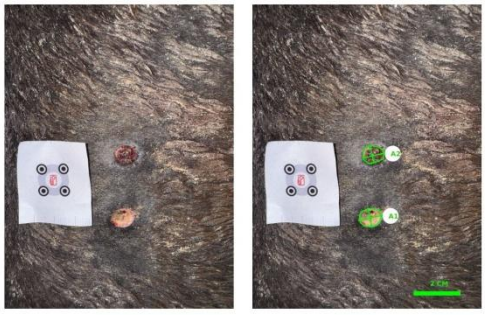
Influenciando o fator de cura de feridas

Avaliação (1 de 1)





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## Medição

Área geral 1.3 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 3.0 cm | Área | 0.7 cm² |
| Largura | 0.8 cm | Comprimento | 1.1 cm |
| | | Profundidade | N/A |
| A2 | | Área | 0.6 cm² |
| Circunferência | 2.9 cm | Comprimento | 1.0 cm |
| Largura | 0.8 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

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## Paloma **santa Luzia** ♀

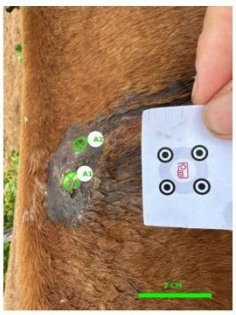
Data de nascimento (idade) -
ID do paciente

### Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)



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## Paloma **santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

### Medição

Área geral 0.3 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.2 cm² |
| **Circunferência** | 1.4 cm | **Comprimento** | 0.5 cm |
| **Largura** | 0.4 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.1 cm² |
| **Circunferência** | 1.3 cm | **Comprimento** | 0.5 cm |
| **Largura** | 0.3 cm | **Profundidade** | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |



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Data de nascimento (idade) -
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### Mecânico / Traumático

Região do corpo

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## Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

### Medição

Área geral 1.2 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.8 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.8 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |

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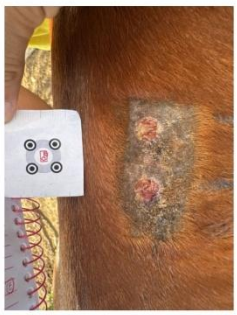
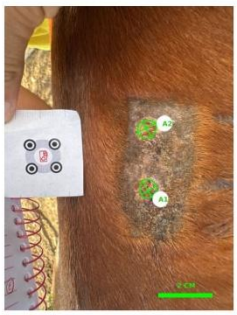
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)





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ID do paciente

## Medição

Área geral 0.8 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 2.2 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.7 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.4 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |



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Data de nascimento (idade) 06/05/2025 (0)

ID do paciente

## Medição

Área geral 0.8 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 2.8 cm | Área | 0.5 cm² |
| Largura | 0.8 cm | Comprimento | 0.9 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.0 cm | Área | 0.3 cm² |
| Largura | 0.5 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |

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## Medição

Área geral 1.2 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.9 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.8 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |



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## Medição

Área geral 1.2 cm²

| | | | |
|---|---|---|---|
| **A1** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.9 cm | **Comprimento** | 1.0 cm |
| **Largura** | 0.9 cm | **Profundidade** | N/A |
| **A2** | | **Área** | 0.6 cm² |
| **Circunferência** | 2.7 cm | **Comprimento** | 0.9 cm |
| **Largura** | 0.8 cm | **Profundidade** | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| **Nome** | Pecel Meneses | **Email** | antoniocarlos.2501@icloud.com |
| **Número de telefone** | | | |

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## Mecânico / Traumático

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Data de nascimento (idade) -

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## Medição

Área geral 0.7 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.2 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.7 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.2 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



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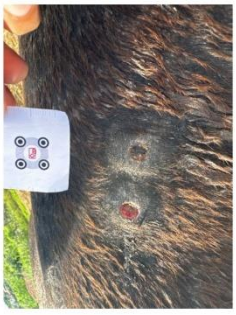
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)



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Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 0.9 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.3 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.6 cm | Área | 0.5 cm² |
| Largura | 0.8 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

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Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




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Paloma **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

### Medição

Área geral 0.9 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.5 cm² |
| Circunferência | 2.5 cm | Comprimento | 0.9 cm |
| Largura | 0.7 cm | Profundidade | N/A |
| A2 | | Área | 0.4 cm² |
| Circunferência | 2.4 cm | Comprimento | 0.8 cm |
| Largura | 0.7 cm | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



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Data de nascimento (idade) -

ID do paciente

### Mecânico / Traumático

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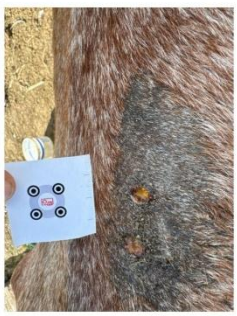
Influenciando o fator de cura de feridas

Avaliação (1 de 1)



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Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

### Medição

Área geral 0.8 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.4 cm² |
| Circunferência | 2.2 cm | Comprimento | 0.8 cm |
| Largura | 0.6 cm | Profundidade | N/A |
| A2 | | Área | 0.4 cm² |
| Circunferência | 2.3 cm | Comprimento | 0.8 cm |
| Largura | 0.6 cm | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

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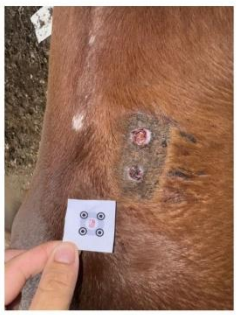
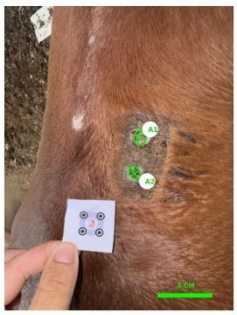
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)





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ID do paciente

## Medição

Área geral 1.0 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.7 cm | Área | 0.5 cm² |
| Largura | 0.7 cm | Comprimento | 1.0 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.4 cm | Área | 0.4 cm² |
| Largura | 0.6 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



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Data de nascimento (idade) 06/05/2025 (0)

ID do paciente

## Medição

Área geral 1.1 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.8 cm | Área | 0.6 cm² |
| Largura | 0.8 cm | Comprimento | 1.0 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.7 cm | Área | 0.5 cm² |
| Largura | 0.7 cm | Comprimento | 0.9 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

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Data de nascimento (idade) -
ID do paciente

## Medição

Área geral 0.8 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.3 cm² |
| Circunferência | 2.1 cm | Comprimento | 0.7 cm |
| Largura | 0.6 cm | Profundidade | N/A |
| A2 | | Área | 0.5 cm² |
| Circunferência | 2.6 cm | Comprimento | 0.9 cm |
| Largura | 0.7 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
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Data de nascimento (idade) -
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## Medição

Área geral 1.0 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.5 cm² |
| Circunferência | 2.8 cm | Comprimento | 0.9 cm |
| Largura | 0.8 cm | Profundidade | N/A |
| A2 | | Área | 0.5 cm² |
| Circunferência | 2.5 cm | Comprimento | 0.9 cm |
| Largura | 0.8 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
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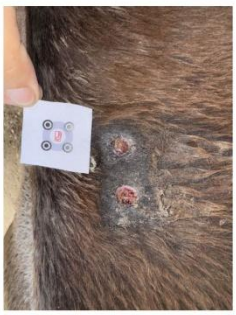
Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

morena **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 1.0 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.8 cm | Área | 0.6 cm² |
| Largura | 0.9 cm | Comprimento | 0.9 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.3 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -

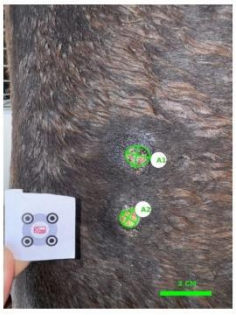
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 1.1 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.9 cm | Área | 0.7 cm² |
| Largura | 0.9 cm | Comprimento | 1.0 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.4 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

## Paloma **santa Luzia** ♀

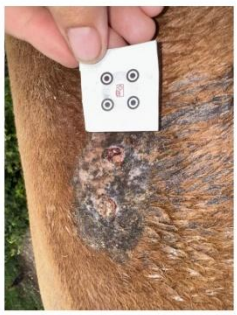
Data de nascimento (idade) -
ID do paciente

### Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)






Relatório de ferida

imito

UFC

## Paloma **santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

### Medição

Área geral 0.8 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.4 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.2 cm | Área | 0.4 cm² |
| Largura | 0.7 cm | Comprimento | 0.8 cm |
| | | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

## Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

### Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

## Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

### Medição

Área geral 1.1 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.8 cm | Área | 0.6 cm² |
| Largura | 0.8 cm | Comprimento | 1.0 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 2.7 cm | Área | 0.5 cm² |
| Largura | 0.7 cm | Comprimento | 1.0 cm |
| | | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

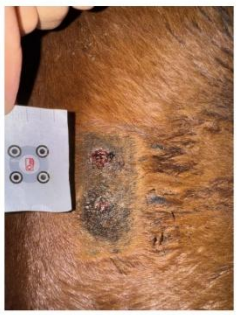
ID do paciente

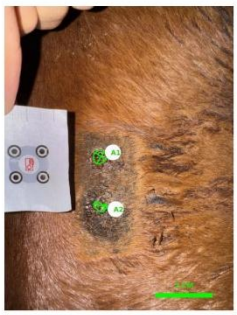
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

carrapeta **santa Luzia**

♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 0.3 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 1.6 cm | Área | 0.2 cm² |
| Largura | 0.5 cm | Comprimento | 0.5 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.4 cm | Área | 0.1 cm² |
| Largura | 0.3 cm | Comprimento | 0.5 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |



Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

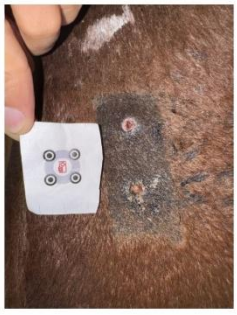
ID do paciente

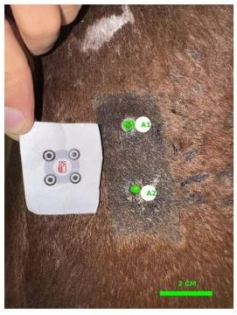
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

castanha **Santa Luzia**

♀

Data de nascimento (idade) 06/05/2025 (0)

ID do paciente

## Medição

Área geral 0.2 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 1.3 cm | Área | 0.1 cm² |
| Largura | 0.4 cm | Comprimento | 0.4 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.0 cm | Área | 0.1 cm² |
| Largura | 0.3 cm | Comprimento | 0.3 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |

Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

gigante **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 0.4 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 1.7 cm | Área | 0.2 cm² |
| Largura | 0.5 cm | Comprimento | 0.6 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.5 cm | Área | 0.2 cm² |
| Largura | 0.5 cm | Comprimento | 0.5 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |



Relatório de ferida

imito

UFC

Ledy **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

Ledy **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

## Medição

Área geral 0.2 cm²

| A1 | | | |
|---|---|---|---|
| Circunferência | 0.9 cm | Área | 0.1 cm² |
| Largura | 0.3 cm | Comprimento | 0.3 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.3 cm | Área | 0.1 cm² |
| Largura | 0.4 cm | Comprimento | 0.4 cm |
| | | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
|---|---|---|---|
| Número de telefone | | | |

Relatório de ferida

imito

UFC

morena **santa Luzia** ♀

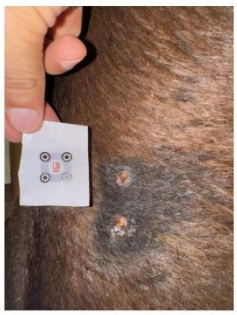
Data de nascimento (idade) -
ID do paciente

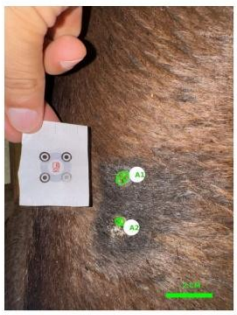
## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

morena **santa Luzia** ♀

Data de nascimento (idade) -
ID do paciente

## Medição

Área geral 0.3 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.2 cm² |
| Circunferência | 1.8 cm | Comprimento | 0.6 cm |
| Largura | 0.5 cm | Profundidade | N/A |
| A2 | | Área | 0.1 cm² |
| Circunferência | 1.2 cm | Comprimento | 0.4 cm |
| Largura | 0.4 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -
ID do paciente

## Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

negona **santa Luiza** ♀

Data de nascimento (idade) -
ID do paciente

## Medição

Área geral 0.3 cm²

| | | | |
|---|---|---|---|
| A1 | | Área | 0.1 cm² |
| Circunferência | 1.4 cm | Comprimento | 0.5 cm |
| Largura | 0.4 cm | Profundidade | N/A |
| A2 | | Área | 0.2 cm² |
| Circunferência | 1.8 cm | Comprimento | 0.6 cm |
| Largura | 0.5 cm | Profundidade | N/A |

## Estado

## Terapia

Terapia de pressão negativa para feridas Não

## Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

Relatório de ferida

imito

UFC

## Paloma **santa Luzia** ♀

Data de nascimento (idade) -

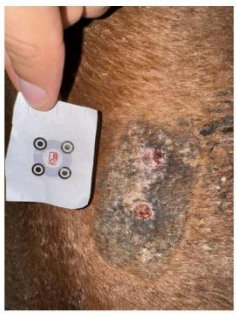
ID do paciente

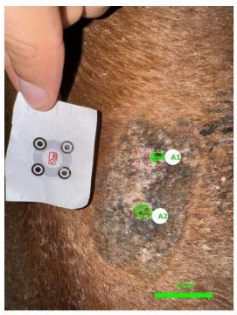
### Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)








Relatório de ferida

imito

UFC

## Paloma **santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

### Medição

Área geral 0.3 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 1.3 cm | Área | 0.1 cm² |
| Largura | 0.3 cm | Comprimento | 0.5 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.7 cm | Área | 0.2 cm² |
| Largura | 0.5 cm | Comprimento | 0.6 cm |
| | | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |



Relatório de ferida

imito

UFC

## Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

### Mecânico / Traumático

Região do corpo

Influenciando o fator de cura de feridas

Avaliação (1 de 1)




Relatório de ferida

imito

UFC

## Rosilha **Santa Luzia** ♀

Data de nascimento (idade) -

ID do paciente

### Medição

Área geral 0.6 cm²

| | | | |
|---|---|---|---|
| A1 | | | |
| Circunferência | 2.1 cm | Área | 0.3 cm² |
| Largura | 0.7 cm | Comprimento | 0.7 cm |
| A2 | | Profundidade | N/A |
| Circunferência | 1.7 cm | Área | 0.2 cm² |
| Largura | 0.5 cm | Comprimento | 0.6 cm |
| | | Profundidade | N/A |

### Estado

### Terapia

Terapia de pressão negativa para feridas Não

### Assessor

| | | | |
|---|---|---|---|
| Nome | Pecel Meneses | Email | antoniocarlos.2501@icloud.com |
| Número de telefone | | | |

# ANEXO B — PARECER DO COMITÊ DE ÉTICA

UNIVERSIDADE ESTADUAL DO CEARÁ

**Comissão de Ética para o Uso de Animais**
**Av. Dr. Silas Munguba, 1700 – Itaperi**
**CEP 60740-903 – fone 3101-9890**
**ceua.uece@uece.br – www.uece.br/ceua**

GOVERNO DO ESTADO DO CEARÁ
Secretaria da Ciência, Tecnologia e Educação Superior

## CERTIFICADO

Certificamos que o Projeto intitulado: **" Avaliação do creme de barreira ACP Derma no processo de cicatrização de ferida induzida em equinos"**, registrado sob o número **NUP 31032.002962/2025-16**, tendo como pesquisador principal **Lúcia Daniel Machado da Silva**, está de acordo com os Princípios Éticos de Experimentação Animal adotados pela **Comissão de Ética para o Uso de Animais da Universidade Estadual do Ceará** (CEUA – UECE). Este certificado expira-se em #####.

## CERTIFICATE

We hereby certify that the Project entitled " Evaluation of ACP derma barrier cream in the process of induced wound healing in horses**",** registered with the protocol **NUP 31032.002962/2025-16**, under the supervision of **Lúcia Daniel Machado da Silva**, is in agreement with Ethical Principles in Animal Experimentation, adopted by the **Ethics Committee in Animal Experimentation of Ceará State University** (CEUA – UECE). This certificate will expire on #####.

**RESUMO**

| | | | | | |
|---|---|---|---|---|---|
| **Vigência do projeto** | Início | 07/2025 | Fim | 01/2028 | |
| **Espécie/Linhagem** | Equídeos | | | | |
| **Número de animais** | 10 | Peso | 300-400Kg | Idade | 2,3 a 16 anos |
| **Sexo** | X | Feminino | X | Masculino | |
| **Origem** | Fazenda Santa Luzia, (propriedade particular) localizada em Pentecoste, Ceará | | | | |
| **Normativa CONCEA 49/2021: Atende** | | | | | |
| **SISGEN** | | | | | |
| **Metodologia** | X | Adequada | | Não adequada | |
| **Cronograma** | X | Adequado | | Ausente/ Não adequado | |
| **Ofício de encaminhamento** | X | Presente | | Ausente/ Não adequado | |
| **Orçamento** | X | Adequado | | Ausente/ Não adequado | |
| **Financiamento** | Órgão de fomento | Recursos próprios | | | |
| | Edital ou N. processo | | | | |

Fortaleza, .11/08/2025

gov.br Documento assinado digitalmente
ARICLECIO CUNHA DE OLIVEIRA
Data: 11/08/2025 16:03:40-0300
Verifique em https://validar.iti.gov.br

Prof. Dr. Ariclecio Cunha de Oliveira
Presidente CEUA-UECE

## ANEXO C — TERMO DE ACEITE DO PROPRIETÁRIO

### TERMO DE ACEITE

Eu, João Emanuel Campelo Cardoso, RG 20073456837, CPF 06544058327, proprietário da Fazenda Santa Luzia, localizada na zona rural, município de Pentecoste- CE. Declaro, para os devidos fins, que estou ciente e concordo com desenvolvimento das atividades referentes ao Projeto de Pesquisa, intitulado: **AVALIAÇÃO DO CREME DE BARREIRA ACP DERMA NO PROCESSO DE CICATRIZAÇÃO DE FERIDAS INDUZIDA EM EQUINOS**. Bem como em disponibilizar aos pesquisadores, os animais (equinos) da minha propriedade para participarem do projeto de pesquisa.

Pentecoste, 11 março 2025.

gov.br
Documento assinado digitalmente
JOAO EMANUEL CAMPELO CARDOSO
Data: 11/03/2025 22:17:15-0300
Verifique em https://validar.iti.gov.br

João Emanuel Campelo Cardoso – Fazenda Santa Luzia

## ANEXO D — COMPROVANTE DE ACEITE - ARTIGO DO CAPÍTULO I


**Selma Ellwein via Open Journal Systems**
Para: eu · seg., 8 de jun. às 13:10

Dear Cinthia de Sousa Braga Meneses:

Following the completion of the peer review process, we are pleased to inform you that your manuscript entitled Ensaios e Ciência: Ciências Biológicas, Agrárias e da Saúde, "Exuberant Granulation Tissue in Horses: Characteristics, Associated Factors and Therapeutic Approaches - An Integrative Review "has been **accepted for publication** in *Ensaios e Ciência: Ciências Biológicas, Agrárias e da Saúde*.

We congratulate all authors on the quality of the work and thank you for your valuable scientific contribution to our journal. Further instructions regarding the next steps in the editorial process will be sent shortly.

Sincerely,

## ANEXO E — COMPROVANTE DE ENVIO - ARTIGO DO CAPÍTULO II

Aries systems
Para: eu · qua., 10 de jun. às 18:09

Acessar o site

Manuscript Number: **JEVS-D-26-00161R1**

Wound healing of experimental cutaneous wounds in horses: comparison between a topical formulation containing coconut water powder and an antimicrobial ointment

Dear Mrs. Meneses,

The above referenced manuscript will be handled by Professor Catherine McGowan Editor-in-Chief.

To track the status of your manuscript, please log into Editorial Manager at https://www.editorialmanager.com/jevs/.

Thank you for submitting your work to this journal.

Kind regards,

Journal of Equine Veterinary Science