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Case Report

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Topical ternary copper (II) complex (DRI-12) for management of an infected cutaneous wound in a dog: a case report

Abstract

The ternary copper (II) complex with 4-fluorophenoxyacetic acid hydrazide (DRI-12) may promote healing by combining antimicrobial activity, immunomodulatory effects, and antioxidant action, contributing to the reduction of microbial load, modulation of oxidative stress, and improvement of re-epithelialization and collagen deposition. This case report describes the use of DRI-12 in the treatment of a wound resulting from an encounter with a giant anteater in a dog. The lesion underwent surgical debridement. Postoperatively, systemic treatment with meloxicam and amoxicillin with clavulanate was instituted, along with topical treatment using chlorhexidine for the first 10 days. A sample from the wound bed was collected for bacterial culture and antimicrobial susceptibility testing (AST), isolating Klebsiella sp. In the absence of systemic signs, local management was adjusted to include daily topical application (once daily) of the DRI-12 solution over the entire wound area, using a spray device, followed by a dressing for 50 days. Wound areas were measured every 10 days until complete healing (D0, D10, D20, D30, D40, and D50), yielding measurements of 3,520.047 mm², 2,787.205 mm², 1,503.325 mm², 297.134 mm², 102.182 mm², and 0.00 mm², respectively. The contraction potential was calculated for the intervals of 0–10, 10–20, 20–30, 30–40, and 40–50 days, corresponding to −20.82%, −46.06%, −80.23%, −65.61%, and −100.00%, respectively. Complete healing was observed by day 50, suggesting that DRI-12 may serve as a promising adjunct in the process of cutaneous wound repair in dogs.

Keywords: wound contraction, re-epithelialization, collagen deposition, debridement, antimicrobial susceptibility testing

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Abbreviations: DRI-12, the ternary copper (II) complex with 4-fluorophenoxyacetic acid hydrazide; VEGF, vascular endothelial growth factor; HIF-1α, hypoxia inducible factor 1-alpha; AST, antimicrobial susceptibility testing; CP, wound contraction potential; THP 1, human monocytic cell line; TGF-β, transforming growth factor beta

Introduction

The skin is the largest organ of the body and performs essential functions, acting as a physical barrier, regulating body temperature, and protecting against external agents.[1,2] Cutaneous wounds are a frequent challenge in veterinary practice, arising from external or internal trauma, and they involve a complex healing process comprising inflammatory, proliferative, and remodeling phases.[3,4] However, bacterial infection, persistent inflammation, and oxidative stress often delay wound repair, prolong treatment, and increase the risk of complications in animals.[1,2]

Given the high incidence of infected wounds in dogs and the need for effective and accessible topical therapies, innovations such as the ternary copper (II) complex with 4-fluorophenoxyacetic acid hydrazide (DRI-12) have emerged as promising alternatives. DRI-12 combines antimicrobial activity against pathogens commonly associated with cutaneous lesions, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*,[5] with immunomodulatory and antioxidant effects that modulate inflammation and oxidative stress.[6,7] Its ability to coordinate transition metals such as copper may potentiate these properties and support angiogenesis via VEGF and HIF-1α upregulation,[8,9] as well as re-epithelialization and collagen deposition.[10] Reviews on advanced wound therapies highlight nanomaterials and metal complexes as effective adjuvants for contaminated lesions, with potential to control biofilms and reduce reliance on systemic antibiotics.[11,12]

Recent clinical reports in dogs and other species demonstrate the value of bioactive topical adjuvants, such as grape seed oil[11] and ozone therapy,[12] in accelerating closure of extensive wounds, although tissue repair quality may depend on ultrastructural methods to assess collagen maturation.[13] This clinical case contributes to the literature by documenting the use of DRI-12 in a real-world setting of an infected wound, with quantitative monitoring of wound area and contraction potential over time.

Case report

A mixed-breed female dog, 2 years old and weighing 24.7 kg, from a rural area (Patrocínio, Minas Gerais, Brazil), was presented for evaluation of an extensive cutaneous wound on the lateral aspect of the right thigh, adjacent to the coxofemoral joint. The lesion resulted from traumatic injury during an encounter with a giant anteater (*Myrmecophaga tridactyla*) three days prior to presentation. On physical examination, the patient was mildly hyperthermic (rectal temperature 39.4°C), with cardiorespiratory parameters within normal limits and adequate hydration. The wound exhibited marked signs of infection, including devitalized tissue, purulent exudate, and fetid odor. Complete blood count revealed leukocytosis (19.71 ×10³/µL) with neutrophilia (14.46 ×10³/µL) and monocytosis (3.32 ×10³/µL), as well as platelet anisocytosis (7.5 fL).

Due to severe contamination and the presence of necrotic tissue and debris, surgical debridement was indicated. Premedication consisted of midazolam (0.5 mg/kg, IM) and methadone (0.5 mg/kg, IM). After cephalic venous catheterization, lactated Ringer's solution was administered (3 mL/kg/h). Anesthetic induction was performed with propofol (5 mg/kg, IV) combined with ketamine (1 mg/kg, IV), followed by maintenance with a continuous propofol infusion (0.2 mg/kg/h, IV). The surgical field was prepared using 2% chlorhexidine scrub and 0.5% chlorhexidine in alcohol on intact surrounding skin, whereas the wound bed was cleansed with 0.2% aqueous chlorhexidine. Radical debridement of necrotic tissues was performed using Metzenbaum scissors and a No. 24 scalpel blade, followed by copious irrigation with sterile 0.9% sodium chloride solution. Immediately thereafter, a wound-bed sample was collected using a sterile swab, placed in Stuart transport medium, and submitted for bacterial culture and antimicrobial susceptibility testing (AST).

During the immediate postoperative period (first 7 days), the patient received meloxicam (0.2 mg/kg, once daily, for 3 days), amoxicillin–clavulanate (20 mg/kg, twice daily, for 7 days), and topical wound care with 0.2% aqueous chlorhexidine. Culture yielded *Klebsiella* sp., which was susceptible to multiple antimicrobials (including amikacin, ciprofloxacin, and imipenem) but resistant to amoxicillin alone, ampicillin, and cephalexin.

Following systemic stabilization and in the absence of persistent fever or other systemic signs, systemic antimicrobial therapy was discontinued and a topical protocol with the ternary copper (II) complex [Cu(4-fh)(phen)(ClO_4)$_2$] (4-fh = 4-fluorophenoxyacetic acid hydrazide; phen = 1,10-phenanthroline), designated DRI-12,[5] was initiated at a concentration of 50 mmol/L. The first day of DRI-12 application was defined as D0. Daily wound management consisted of cleansing with sterile 0.9% sodium chloride solution followed by once-daily topical application of the DRI-12 solution using a spray device, and placement of a three-layer dressing (gauze, bandage roll, and elastic wrap).

The wound healing progression was documented photographically every 10 days until complete closure (D50). Digital images were processed using ImageJ® software, and the wound area (mm²) was measured using the polygon selection tool. The wound contraction potential (CP) was calculated for each 10-day interval using the following formula: CP = [(AF - AI) × 100] / AI, where (AI) is the initial area and (AF) is the final area.

Measured wound areas were 3520.05 mm² (D0), 2787.21 mm² (D10), 1503.33 mm² (D20), 297.13 mm² (D30), 102.18 mm² (D40), and 0.00 mm² (D50) (Figures 1&2). Corresponding contraction percentages by interval were −20.82% (D0–10), −46.06% (D10–20), −80.23% (D20–30), −65.61% (D30–40), and −100.00% (D40–50) (Figure 3). Complete wound healing was achieved by day 50 under topical management with DRI-12.

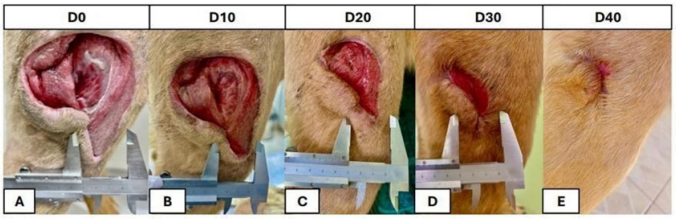

Figure 1 Serial photographs showing wound healing progression in a dog treated with topical ternary copper(II) complex (DRI-12). (A) Day 0 (D0): wound bed appearance prior to DRI-12 application. (B–E) Clinical evolution at days 10, 20, 30, and 40 (D10, D20, D30, and D40), respectively, demonstrating progressive centripetal contraction and re-epithelialization.

Figure 2 Serial reduction in wound area (mm²) in a dog treated topically with a ternary copper (II) complex (DRI-12). Wound area was measured every 10 days from treatment initiation (D0–D50), showing a progressive decrease, with the greatest reduction occurring between D10 and D30.

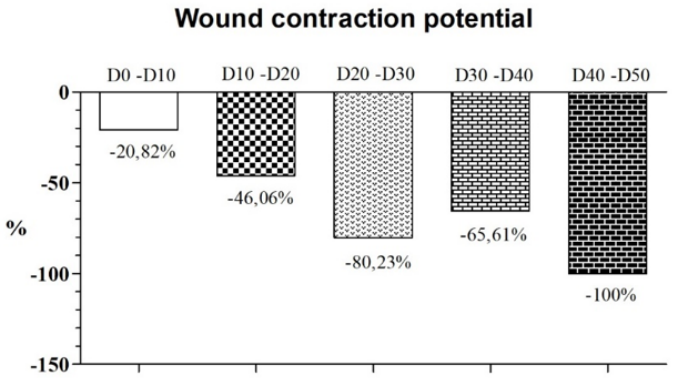

Figure 3 Wound contraction potential (CP, %) in a dog treated topically with a ternary copper (II) complex (DRI-12). The graph illustrates the variation in contraction rates across serial 10-day intervals (D0–D50), demonstrating the dynamics of wound closure throughout the treatment.

Discussion

Wound healing in extensive and contaminated cutaneous lesions remains a significant clinical challenge in veterinary medicine and often requires strategies combining standard wound-bed management with adjuvant therapies. Advanced modalities such as nanomaterials and metal complexes have gained increasing attention due to their ability to modulate the inflammatory microenvironment and promote key steps of repair, including re-epithelialization and angiogenesis.[4,10] In the present case, topical application of the ternary copper (II) complex DRI-12 [Cu(4-fh)(phen)(ClO_4)$_2$] resulted in complete wound closure without the need for prolonged systemic antibiotic therapy.

The rationale for using DRI-12 is supported by robust *in vitro* evidence of antimicrobial and anti-biofilm activity. Paixão et al.[5] demonstrated inhibitory effects of this complex against common pathogens involved in cutaneous infections, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. In addition, Monteiro et al.[7] showed that DRI-12 can control both planktonic and sessile (biofilm) forms of multidrug-resistant bacteria and may exhibit synergistic effects when combined with conventional antibiotics. These findings are consistent with the absence of macroscopic signs of infection (purulent exudate, fetid odor, or progressive necrosis) observed throughout the follow-up period, suggesting that

the compound contributed to maintaining a healthy wound bed and controlling the local microbial burden.

Quantitative assessment of healing revealed distinct dynamics across the phases of repair. During the initial interval (D0–D10), the wound contraction potential (CP) of −20.82% is compatible with the latency/inflammatory phase. At this stage, copper-mediated immunomodulation may be particularly relevant. Díez-Tercero et al.[6] demonstrated in THP-1-derived macrophages that bioactive copper ions, within an appropriate concentration range, can favor polarization toward an M2-like (pro-regenerative) phenotype, supporting inflammation control and preparing the tissue for an earlier transition to the proliferative phase. Adequate resolution of inflammation is critical to prevent wound chronicity, a concept also highlighted in case reports using oxidative-based therapies such as ozone therapy, which aim to optimize the redox microenvironment to accelerate repair.[12]

The most evident acceleration in healing occurred between D10 and D20, with a CP of −46.06%, which corresponds to the peak of the proliferative phase. This improvement may be related to the pro-angiogenic effects of copper. Experimental evidence indicates that copper can stimulate cellular proliferation and neovascularization through upregulation of vascular endothelial growth factor (VEGF) and hypoxia-inducible factor 1-alpha (HIF-1α).[8,9] Such angiogenic stimulation, together with immunomodulatory effects favoring fibroblast migration, is essential for robust granulation tissue formation and centripetal wound contraction.

During later stages (D20–D50), contraction indices (80.23% to 100%) indicate efficient tissue remodeling. The literature suggests that copper may enhance transforming growth factor beta (TGF-β) signaling, facilitating the replacement of type III collagen with type I collagen.[6] Although the present report relied on macroscopic outcomes, the quality of cutaneous repair also depends on collagen organization and maturation within the extracellular matrix. Rezende et al.[13] demonstrated that ultrastructural approaches, such as transmission electron microscopy, may be more sensitive to detect fibrillar collagen maturation than conventional histology, suggesting that the favorable clinical evolution observed herein may reflect improved collagen architecture and increased tensile strength of the repaired tissue.

The effectiveness of topical adjuvants for severe wounds in dogs has also been described in other case reports, such as topical grape seed oil, which achieved complete closure of extensive infected lesions, possibly due to antioxidant and anti-inflammatory properties.[11] However, comparing different therapies also reinforces that clinical success depends on both appropriate wound-bed preparation (debridement and irrigation) and the selection of agents within a safe and effective therapeutic window. As highlighted by Díez-Tercero et al.,[6] copper effects are concentration-dependent, and excessive levels may induce cytotoxicity. Therefore, although the outcomes obtained with DRI-12 are promising, controlled studies and dose–response experiments are needed to standardize application protocols and to further assess safety and long-term effects.

It is important to note that the observation of the most pronounced contraction gain between days 20 and 30 (80.23%) is descriptive in nature. No statistical inference was performed, as this would require a larger sample size and a control group for valid comparative analysis. Future studies including more than five animals and a control group are necessary to confirm and quantitatively compare the contraction potential of DRI-12 and its impact on the need for systemic antibiotics.

Conclusion

It can be concluded that the topical treatment with the ternary copper (II) complex DRI-12 was associated with favorable healing progression, showing a progressive reduction in wound area and an increase in contraction potential until complete closure, without macroscopic evidence of active infection during follow-up. In light of the literature on copper-based compounds, the findings are consistent with a possible contribution of DRI-12 to local microbial control and modulation of the inflammatory response, favoring tissue repair during the proliferative and remodeling phases. However, since this is a case report, causality cannot be inferred, and controlled studies are recommended, including microbiological and histological/biomechanical assessments, to confirm efficacy, safety, and to standardize the usage protocol.

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Conflicts of interest

The Authors declares that there are no conflicts of interest.

References

1. Bizinoto LB, Soares FO, Rosado IR, et al. Wound treatment principles—part one. *Int J Health Sci.* 2022;2(18):1–13.
2. Bizinoto LB, Soares FO, Rosado IR, et al. Wound treatment principles—part two. *Int J Health Sci.* 2022;2(18):1–14.
3. Quadros EA, Soares FO, Bertassoli BM, et al. Advances in wound treatment: part 1**.** *Peer Rev.* 2024;6(4):209–224.
4. Quadros EA, Soares FO, Bizinoto LB, et al. Advances in wound treatment: part 2. *Peer Rev.* 2024;6(4):225-239.
5. Paixão DA, Marzano IM, Jaimes EHL, et al. Novel copper(II) complexes with hydrazides and heterocyclic bases: synthesis, structure, and biological studies. *J Inorg Biochem*. 2017;172:138–146.
6. Díez-Tercero L, Delgado LM, Bosch-Rué E, et al. Evaluation of the immunomodulatory effects of cobalt, copper, and magnesium ions in a proinflammatory environment. *Sci Rep*. 2021;11:11707.
7. Montero DA, Arellano C, Pardo M, et al. Antimicrobial properties of a novel copper-based composite coating with potential for use in healthcare facilities. *Antimicrob Resist Infect Control.* 2019;8:3.
8. Tao B, Lin C, Deng Y, et al. Copper-nanoparticle-embedded hydrogel for killing bacteria and promoting wound healing with photothermal therapy. *J Mater Chem* B. 2019;7(15):2534–2548.
9. Li S, Wang X, Chen J, et al. Calcium ion cross-linked sodium alginate hydrogels containing deferoxamine and copper nanoparticles for diabetic wound healing. *Int J Biol Macromol*. 2022;202:657–670.

10. Salvo J, Sandoval C. Role of copper nanoparticles in wound healing for chronic wounds: a literature review. *Burns Trauma*. 2022;10:tkab047.

11. Quadros EA, Chaban NM, Bizinoto LB, et al. Grape seed oil in the treatment of severe wound in a dog: case report. *Acta Vet Bras.* 2024;18(1):25–28.

12. Teodoro AN, Quadros EA, Rosado IR, et al. Severe facial injury in a white-eared opossum (Didelphis albiventris): treatment with ozone therapy. *Acta Sci Vet*. 2023;51(suppl 1):875.

13. Rezende RS, Eurides D, Alves GLA, et al. Ultrastructural analysis of collagen in cutaneous wounds of rabbits treated with equine platelet-rich plasma. *Arq Bras Med Vet Zootec*. 2020;72(3):827–835.

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