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VIROLA OLEIFERA: A PROMISING ALTERNATIVE TREATMENT FOR FELINE DERMATITIS – A CASE REPORT

VIROLA OLEIFERA: UM TRATAMENTO ALTERNATIVO PROMISSOR PARA DERMATITE FELINA – RELATO DE CASO

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Abstract

Virola oleifera (Schott) A.C. Smith, is commonly used in Brazilian traditional medicine to treat inflammation and heal mucous membranes. Recently, our group has shown the healing capacity of a formulation prepared with its resin through antioxidant mechanisms that contribute to re-epithelialization and reduction of oxidative stress. Other studies conducted by our group with Virola oleifera resin (VO) have also demonstrated an abundance of antioxidant molecules in its chemical composition, as well as various pharmacological activities in several models related to oxidative stress. Therefore, VO holds promise as a natural therapeutic agent for the treatment of wound healing and inflammatory conditions in both veterinary and human fields. Here, we report the case of a 2-year-old Sphynx domestic cat with a three-month history of skin injury on the neck. Our aim was to test the efficacy of VO resin for the treatment of this animal. A cream was prepared from VO (1%) and applied twice a day for 10 days. After 1 week, there was an improvement in tissue coloration and a macroscopic reduction of the lesion, with successful wound healing within 10 days of treatment. This is the first report demonstrating the excellent healing effect of the antioxidant VO in a domestic animal.

Keywords antioxidant, Bicuíba, cats, wound

Resumo

A *Virola oleifera* (Schott) A.C. Smith, é comumente utilizada na medicina tradicional brasileira para tratar inflamações e cicatrizar membranas mucosas. Recentemente, nosso grupo demonstrou a capacidade cicatrizante de uma formulação preparada com sua resina por meio de mecanismos antioxidantes que contribuem para a reepitelização e redução do estresse oxidativo. Outros estudos realizados por nosso grupo com a resina de *Virola oleifera (*VO) também demonstraram abundância de moléculas antioxidantes em sua composição química, bem como diversas atividades farmacológicas em diversos modelos relacionados ao estresse oxidativo. Portanto, a VO é uma promissora agente terapêutica natural para o tratamento de cicatrização de feridas e condições inflamatórias, tanto de uso veterinário como humano. Aqui, relatamos o caso de um gato doméstico Sphynx de 2 anos de idade com história de três meses de lesão de pele no pescoço. Nosso objetivo foi testar a

eficácia da resina VO no tratamento desse animal. O creme foi preparado a partir de VO (1%) e aplicado duas vezes ao dia durante 10 dias. Após 1 semana, houve melhora da coloração dos tecidos e redução macroscópica da lesão, com cicatrização bem-sucedida da ferida em 10 dias de tratamento. Este é o primeiro relato demonstrando o excelente efeito cicatrizante do antioxidante VO em um animal doméstico.

Palavras-chave: antioxidante, bicuíba, felino, ferida

INTRODUÇÃO

The use of medicinal plants is common in traditional practices across various cultures worldwide. Over the past few decades, numerous species have been investigated for their wound-healing, anti-inflammatory, and antioxidant activities (Beling et al., 2014; Hoffmann; Griffiths, 2018). In this context, *Virola oleifera* (Schott) A.C. Smith, a tree belonging to the Myristicaceae family in the Atlantic Forest, has garnered significant attention due to its rich composition of phenolic, flavonoid, and tannin compounds, which exhibit potent antioxidant effects, as well as anti-inflammatory and antiapoptotic properties (BÔA et al., 2015; Pereira et al., 2017).

In Brazil, *Virola oleifera* (VO), commonly known as "Uccuúba," "Bocuva," "Bicuíba," "Bicuíva," or "Candeia-do-caboclo" ´Rodrigues, 1980`, has been widely used to stop bleeding, promote wound healing, alleviate skin diseases, arthritis, and inflammatory conditions (Rodrigues, 1980; Coutinho et al., 2017; Carvalho et al., 2022).

In the last decade, scientific reports from our research group have highlighted the therapeutic potential of crude resin, demonstrating its beneficial effects on atherosclerosis progression, gastroprotection, and protection against renal dysfunction (Bôa et al., 2015; Coutinho et al., 2017; Pereira et al., 2017). Specifically, a recent development involving a 5% VO cream formulation for wound care showed healing effects accompanied by antioxidant properties (Carvalho et al., 2022).

In this context, our case report investigates the possible healing potential of a formulation containing extracts of VO at a lower concentration (1%) for the treatment of resistant wound healing in cats.

CASE REPORT

A 2-year-old female domestic Sphynx cat was presented with a three-month history of a superficial lesion on the right side of the neck. During the clinical history and physical examination, the cat exhibited persistent cutaneous bleeding and pruritus, which were exacerbated by skin itching. These symptoms are indicative of eosinophilic granuloma complex (EGC) (Figure 1A and 1B), a condition characterized by eosinophilic inflammation.

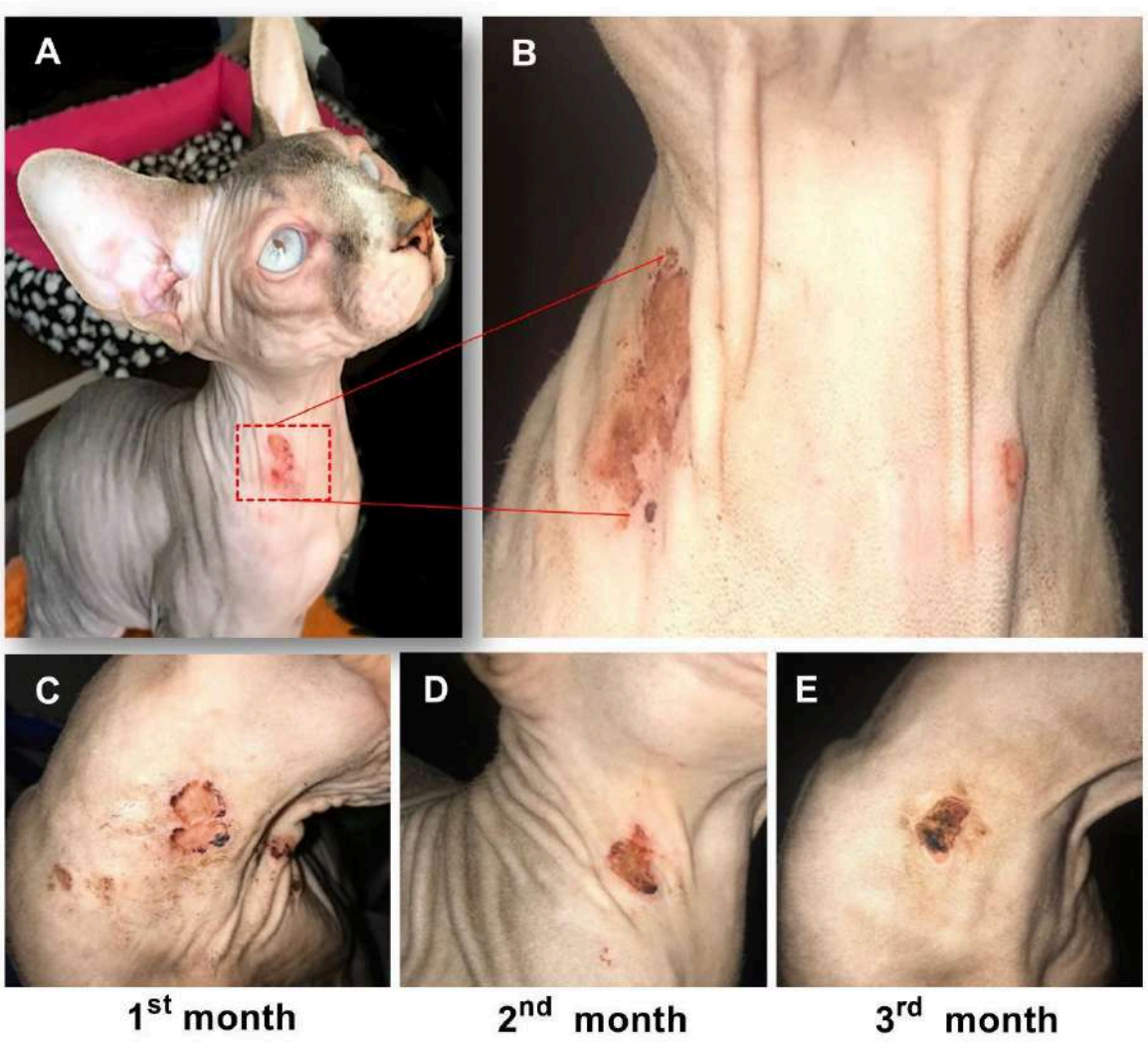

Figure 1. Images of cat skin injury in neck. Skin injury before therapeutic drugs (A - B). Skin injury after 1st (C), 2nd (D) and 3rd (E) months of the classical pharmacotherapy.

The bacterial septic suppurative inflammatory process was confirmed through cytology smear by our group. Additionally, the bacterial culture findings indicated sensitivity and resistance to various microorganisms, including Coagulase-negative *Staphylococcus* and *Acinetobacter baumannii*/*calcoaceticus*. Hematological and serum biochemical inflammatory parameters did not show significant changes. Initially, therapeutic approaches were conducted using the classical Cefalexin (HMC Chemical Technology Co., Ltd., Beijing, China) at a dosage of 100 mg/kg for 10 days, along with Vetaglós® cream (Vitapan, Anápolis-GO, Brazil) containing retinol palmitate (5000 IU/g), vitamin D3 (900 IU/g), and zinc oxide (15%).

Despite one month of treatment, the lesion did not show any improvement. Therefore, Ketoconazole cream (HMC Chemical Technology Co., Ltd., Beijing, China) at a dosage of 10 mg/kg was added (Figure 1C). Subsequently, the medication was switched to Alcort® (CEPAV Pharma, São Paulo-SP, Brazil), a prednisolone formulation, at a dosage of 2.5 mg/kg for 5 days. In the second month, Doxycycline (HMC Chemical Technology Co., Ltd., Beijing, China) at a dosage of 20 mg/kg for 10 days and Trok-N® cream (Eurofarma, Itapevi-SP, Brazil) containing ketoconazole (2%), betamethasone dipropionate (6.4%), and neomycin sulfate (0.25%) were used (Figure 1D). Despite one month of ineffective therapy, prednisolone (4.5 mg/kg for 12 days) in combination with Quadriderm® cream (Schering-Plough, Kenilworth, New Jersey, USA) containing betamethasone (6.1%), clioquinol (1%), tolnaftate (1%), and gentamicin (0.16%) was administered. However, at the end of the treatment, there was no improvement in the magnitude and quality of the lesion, and bleeding and itching persisted (Figure 1E).

Considering the need for alternative or complementary treatments to the traditional therapeutic approach, the use of VO cream was suggested based on previous data by Carvalho et al. (2022) in rats. Interestingly, this study from our lab demonstrated enhanced wound contraction and reduced levels of protein oxidation and lipid peroxidation. Thus, the healing capacity of VO may be attributed, at least in part, to its antioxidant properties, which can contribute to reepithelialization, supporting our hypothesis that VO is a promising approach for the treatment of superficial lesions.

MATERIALS E METHODS

Resin Material, Cream Preparation and Administration

The VO was collected in November 2019 from the Fazenda Guandu district (Afonso Claudio-ES, Brazil; coordinates: S20°13490'W041°06692') under proper official authorization (IEMA 629/09 and Resolution29-12/06/2007). A voucher specimen (VIES 19648) was deposited at the Department of Botany, Federal University of Espirito Santo. The fluid exudate was obtained from 0.5 cm incisions made in the tree trunk. The fluid (90 ml) was collected in an aseptic amber glass container and stored at 4°C until complete drying. Subsequently, the exudate was dried at 40°C for 75 hours, resulting in 36.5g of dried granulated resin (Bôa et al., 2015; Pereira et al., 2017). For the cream preparation, 10 mg of the granulated resin was incorporated into 1g of the base cream. The cream was applied twice daily for 10 days.

RESULTS

On the 3rd day of treatment, we observed that VO was able to reduce the wound size, bleeding, and itching. By the 7th day, there was an improvement in tissue coloration and a noticeable reduction in the size of the lesion, indicating successful wound healing within the 10th day treatment period (Figure 2). It is important to highlight that no adverse effects were reported by the owner. Interestingly, this feline did not experience a recurrence of EGC even 6 months after the treatment, demonstrating only the presence of a discrete scar (Figure 3).

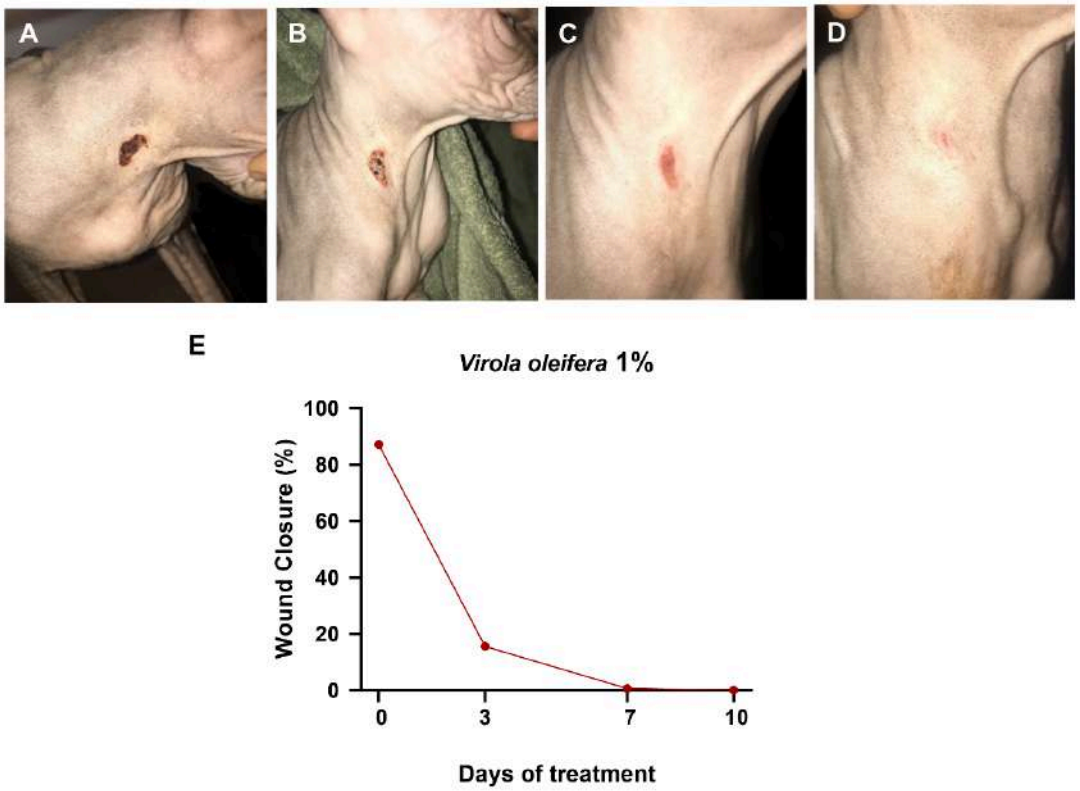

Figure 2. Images of cat skin injury in neck under treatment of VO cream (1%). Start (A), 3rd (B), 7th (C) and 10th (D) days of treatment. Quantitative analysis of wound contraction (E).

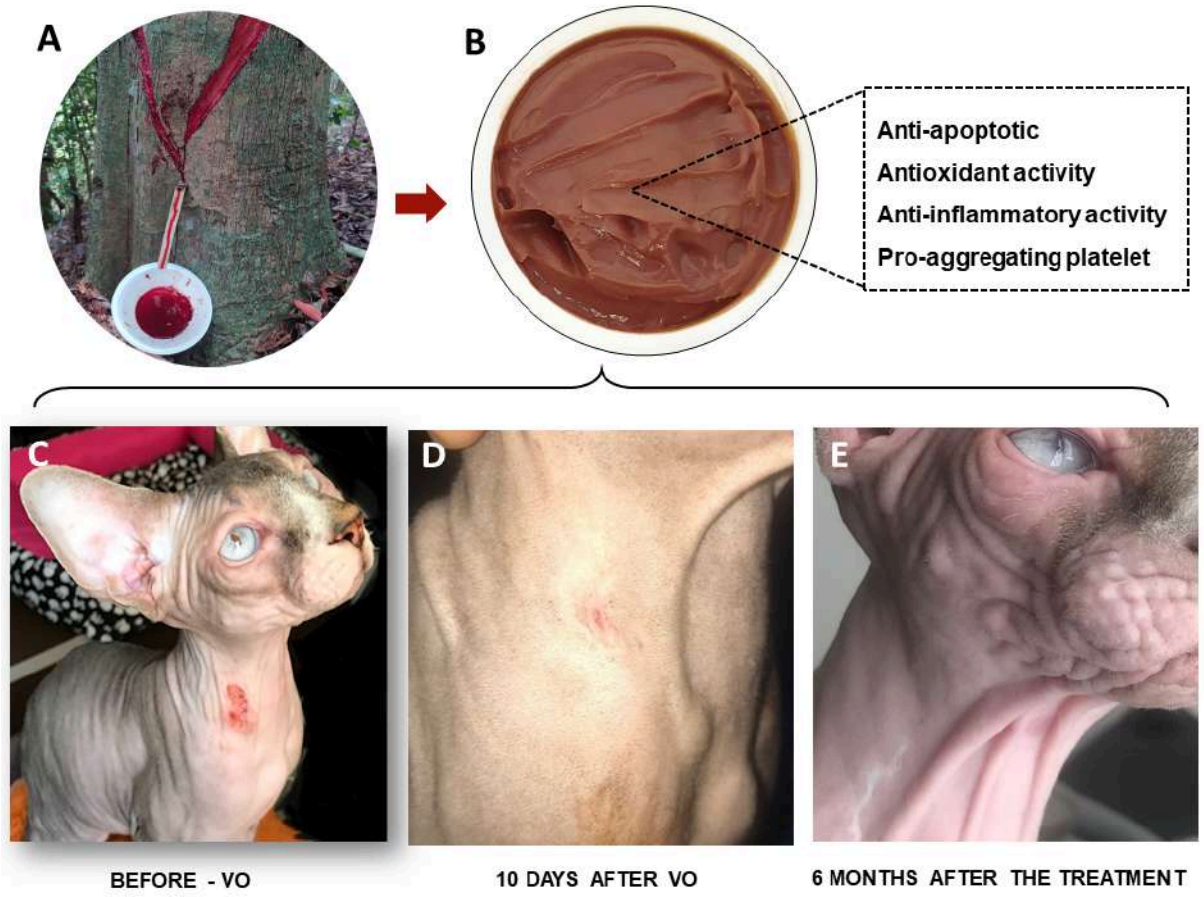

Figure 3. (A) Collection of resin from the *Virola* tree. (B) VO cream and its properties. (C-D) Skin scar before and 10 days after treatment with 1% VO cream. (E) Skin scar observed six months after treatment with VO cream.

DISCUSSION

This is the first case report describing an innovative and effective therapeutic approach for dermatitis disorders using a low-concentration cream obtained from the resin of the VO tree found in the Atlantic Forest. Our findings corroborate previous research from our team, which demonstrated a significant healing effect of VO cream in rats (Carvalho et al., 2022). These results further support our hypothesis that VO holds great promise as an approach for treating superficial lesions.

Virola oleifera is commonly used in traditional medicine due to its notable responses to inflammatory conditions (Ebeling et al., 2014). Within the tree trunk, a reddish exudate is produced, which possesses antioxidant and anti-inflammatory properties. Its composition comprises a combination of antioxidants such as polyphenols, flavonoids, ferulic acid, and

gallic acid, which contribute to its reparative effects, partly through antioxidant pathways (Bôa et al., 2015; Pereira et al., 2017; Carvalho et al., 2022). In parallel, the eosinophilic granuloma complex is characterized by an exaggerated inflammatory response, oxidative stress, hypersensitivity, cutaneous manifestations on the skin, pruritus, and pain (Rocha et al., 2019; Ravens et al., 2014; Buckley, 2012; Ramirez et al., 2018). These clinical manifestations align with the diagnosis of EGC in the present case, wherein a Sphynx domestic cat experienced an intense inflammatory process persisting for three months, accompanied by challenges in healing, bleeding, and itching.

The classical therapeutic options for EGC include topical and systemic approaches with antimicrobials and anti-inflammatory drugs (Hopke et al., 2019; Forsythe, 2011). However, in the current case, these treatments failed to heal the lesion or alleviate the symptoms of itching. In light of the unsuccessful therapeutic outcomes, we decided to test the VO cream as a new therapy for this condition. Surprisingly, the 10-day treatment with VO ´at low dose) resulted in effective wound healing without any adverse effects. This finding can be supported by in vivo and in vitro studies that have demonstrated the potential of antioxidants to promote wound healing and regulate local oxidative stress (Guidoni et al., 2019; Baek, Min-Geol, 2015; Fitzmaurice et al., 2011).

Numerous studies have provided strong evidence of the involvement of oxidative stress in the pathogenesis of various skin diseases (Baek, Min-Geol, 2015; Fitzmaurice et al., 2011). Furthermore, phenolic compounds such as ferulic and gallic acid have been shown to act as scavengers and/or inhibit enzymes involved in the production of oxidant factors. They also exhibit potential antioxidant, anti-inflammatory, and antibacterial activities, supporting pro-collagen synthesis (Guidoni et al., 2019; Baek, Min-Geol, 2016; Carvalho et al., 2022). Interestingly, previous *in vitro* (Pereira et al., 2017` and *in vivo* ´BÔA et al., 2015; Coutinho et al., 2017; Pereira et al., 2017) experiments have demonstrated the potential antioxidant effects of VO resin.

Therefore, our hypothesis regarding the healing effect of VO can be justified, at least in part, by its antioxidant properties. An additional mechanism of action of VO could be its proaggregating effect, which activates the GPIIb/IIIa pathway (data not yet published). This property may explain the observed reduction in bleeding in the wound of cat treated with VO. Furthermore, the low cytotoxicity of VO, as previously demonstrated in *in vitro* studies on fibroblasts (Coutinho et al., 2017), may also justify the favorable reepithelialization.

In conclusion, this report provides the first evidence of a notable healing effect achieved with a cream containing VO resin with antioxidant properties. These findings warrant further research in veterinary clinical practice.

Author contributions

Carvalho GR, Braz DS and Gonçalves TCO collected the resin *Virola oleifera* and prepared the cream.
Mendes RMA treated the animal and performed hematological and cytologic analysis.
Carvalho GR, Aires R and Pereira TMC performed data analysis.
Carvalho GR, Aires R, Campagnaro BP, Pereira TMC performed writing and critical revision of manuscript.
Pereira TMC and Campagnaro BP performed conception, study's design and supervision of the study.

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