

## The use of papain gel cream and sunflower oil in promoting healing in a wound in dogs: three case reports

[Uso de gel creme de papaína na cicatrização de feridas em cães: relato de três casos]

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### ABSTRACT

Papain is a proteolytic enzyme removed from the leaves of green papaya and/or latex. This enzyme is widely known as a medicinal fruit used extensively in human medicine for the treatment of wounds of various etiologies. However, studies and reports in veterinary medicine are scarce. Another herbal drug widely used in wound healing is Sunflower oil (*Helianthus annuus*). It has inflammatory and antimicrobial properties which stimulate the local neovascularization, promoting tissue granulation, cell migration, fibroblast proliferation, and differentiation. Three dogs were treated with infected necrosis wounds, considered large, extent, and severe, with varied etiology. All cases were treated with papain gel with the exception of one dog, which was given the sunflower oil at the end of the treatment. Papain gel shows effectiveness in the treatment of wounds especially with wound debridement and removal of necrotic tissue. In addition, the healing time was shorter when compared to the treatment with sunflower oil. Finally, the herbal drugs have a low cost and high accessibility. This study contributes to create a new research regarding the use of this drug in animal wound healing.

Keywords: phytotherapy, Carica papaya L, Helianthus annuus, necrosis

### RESUMO

A papaína é uma enzima proteolítica retirada do mamão-papaia verde e/ou do látex das folhas do mamoeiro, tendo propriedades medicinais conhecidas na medicina humana para tratamento de feridas de diversas etiologias. Estudos e/ou relatos na medicina veterinária são escassos. Nesse sentido, objetivou-se descrever três casos de cães, que foram atendidos no Hospital Veterinário da Universidade Federal de Lavras, Brasil, todos com feridas infectadas, necrosadas, com etiologia variada e consideradas de grande extensão e gravidade, sendo tratados com gel de papaína. O tratamento demonstrou efetividade na recuperação das feridas, com a formação de grande quantidade de tecido de granulação, em um período menor que os tratamentos convencionais. Por se tratar de um fitoterápico, de baixo custo e alta acessibilidade, o gel de papaína pode ser utilizado no tratamento de feridas de grande extensão em cães e, assim como em humanos, parece ter um efeito benéfico no processo de cicatrização. Pesquisas devem ser conduzidas para elucidar a ação desse produto nos tecidos, bem como as diferentes concentrações a serem administradas.

Palavras-chave: fitoterapia, Carica papaya L., reparação tecidual, cães

### INTRODUCTION

Wound healing has been extensively studied in veterinary medicine due to the high incidence of affected animals for different types and kinds of injuries.

In this context, several studies using different therapies have been developed with the aim to speed up the healing process and reduce the risk of secondary infections (Oliveira Jr., 2010; Sanchez Neto *et al.*, 1993). The use of herbal medicines has many advantages, the main being the cost-benefit (Pieri *et al.*, 2009).

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The proteolytic enzyme papain is extracted from green papaya (*Caricapapaya* L.) and/or latex of the leaves and it is widely known as a medicinal fruit with bacteriostatic and anti-inflammatory properties (Moneta, 1987). Several observations of the treatment with papaya preparations facilitated wound-healing responses in different etiologies such as deep burns, ulcers in diabetics, suture dehiscence, and pressure ulcers (Leite *et al.*, 2012).

Through its proteolytic action, papain digests necrotic and infected tissue and facilitates the migration of the viable cells from the wound edge into the interior (Carvalho *et al.*, 2010). This process is responsible for the bacteriostatic action, as it reduces the bacterial load and therefore decreases the production of exudate (Rocha *et al.*, 2005). It has anti-inflammatory properties, leading to the regression of edema (Lima *et al.*, 2011), accelerating tissue repair (granulation tissue and re-epithelialization) (Carvalho *et al.*, 2010), promoting a flatter scar, because of the stimulus in the alignment of collagen fibers (Sanchez Neto *et al.*, 1993).

Therapeutic use may be effective in all phases of wound healing: wound drying, exudation, or infection with or without areas of necrosis (Rocha *et al.*, 2005).

Studies demonstrate the safety and effectiveness of the use of papain in humans (Leite *et al.*, 2012) and rats (Rocha *et al.*, 2005). However, in veterinary medicine, research on papain is scarce and studies need to be conducted to verify the effectiveness of this drug in dogs.

Another herbal drug widely used in wound healing is the sunflower oil (*Helianthus annuus*), (Jr. Oliveira, 2010), a plant with inflammatory and antimicrobial properties which stimulate the local neovascularization, promoting granulation tissue, cell migration, fibroblast proliferation, and differentiation (Wendt, 2005).

Thus, given the importance of herbal medicine, it is necessary to study the therapeutic effects of extracts of plants with medicinal properties. In this sense, the goal of this research is to report three cases of dogs with infected wounds of different etiology and great extension, undergoing treatment with papain gel cream and sunflower oil. Both treatments have been

extensively used for wound healing and have a long history of good efficacy and safety.

## CASE REPORT

Three animals were presented to the small animal service clinic in the Veterinary Hospital of the Federal University of Lavras, in Lavras, Minas Gerais, Brazil.

In all cases, the treatment consisted of wound cleaning with 0.9% saline twice a day. Soon after, the substance containing papain in gel-cream presentation was applied in concentrations of 3 or 5%. The product was made by combining 50% gel (Natrosol 2%, 3% propylene glycol, 0.5% nipagin and distilled water qs 100ml) and 50% cream (15% self-emulsifying wax, lanolin 0.4%, propylene glycol 5%, 0.15% nipagin, 0.05% nipazol and distilled water qs 100g). Bandages were used in all treatments.

In case 1 a 6 years old female, mixed breed dog, castrated, weighing 15Kg was attended on March 18, 2011. Dehydration, pale mucous, poor physical condition, with a score of 2/9, as described by the interpretation system Laflamme (1997) were noted. The wound was observed in the left flank region, probably originated from a ruptured abscess. This patient has not had clinically relevant abnormalities on a blood chemistry panel and complete blood count. Meloxicam (0.1mg / kg once a daily for five days) was prescribed. The wound was observed and characterized by a deep ulcer with involvement of muscle layers, intense areas of necrosis and fibrin, irregular edges and presence of mucopurulent secretions. The length was about 10cm wide by 5.0cm in diameter.

The therapy started with the 5% concentration of papain cream-gel throughout the injured area. Twenty-four hours after the first application, the therapy showed significant improvement, as it was no longer possible to observe the presence of fibrin and purulent secretion (Figure 1). On the second day, reepithelialization was noted early on the edges. On the fourth day, the acceleration in the healing process was noted.

Later during the fifth day, a gradual appearance of an erythematous area next to the bottom edge of the lesion was noticed, indicating an

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accelerated scar evolution, with exuberant granulation tissue formation.

From the ninth day, the erythematous area on the edge of the lesion presented itself with the formation of small amounts of exudate serous. At this time, after nine days of treatment with the 5% concentration papain gel, the therapy was changed and sunflower oil was initiated.

After the first application, there was a significant decrease in perimarginal erythematous area and tissue retraction, granulation tissue formation, and early tissue repair. This therapy was continued for 22 days, occurring with complete occlusion of continuity with melanin hyperpigmentation and marginal perimarginal.



Figure 1. Dog. Wound evolution during treatment with gel-cream containing 5% papain and sunflower oil in case 1. 1 In the retreatment picture of the lesions, note that there are intense areas of necrosis and fibrin, irregular edges and the presence of mucopurulent secretion. 2 The picture taken on the second day shows improvement in the wound and fibrin and purulent secretion were removed with the papain solution. 5 Five days after the start of the treatment, the presence of erythematous area on the edge of the wound was evident. 10 The picture shows the start of the therapy with sunflower oil. 16-2-24 and 31 Days of treatment with sunflower oil demonstrated a significant decrease in the perimarginal erythematous area and tissue retraction, granulation tissue formation and early tissue repair.

In case 2 (Figure 2), a canine, female, Dalmatian, intact, three years old, weighing 15.2kg was examined on March 19, 2012. The patient had a poor physical condition, a score of 2/9, infestation Ixodes, 7% dehydration status and pale mucous. The right auditory meatus canal had stenosis, suggesting the presence of chronic otitis. Hematologic abnormalities revealed normocytic normochromic anemia and leukocytosis with a left shift, suggesting presumptive and concomitant diagnosis of babesiosis, subnutrition and infection probably caused by skin lesions. The following therapy was prescribed: enrofloxacin (10mg/kg once a daily for 10 days), meloxican (0.1mg / kg once a daily for 5 days), nitenpyram (57mg/animal, once a daily for 3 days), metronidazole (30mg / kg twice a day for 10 days) and imidocarb (5.0mg/kg, two applications with an interval of 15 days between each dose). The right auditory meatus canal had stenosis, suggesting the

presence of chronic otitis. In the temporal peri-auricular bone it was possible to view a wide area of skin lesions approximately 12cm long and 7cm wide, characterized by a deep ulcer with the involvement of muscle layers, with areas of necrosis and fibrin, as well as jagged edges, which were heavily infested with myiasis. The wound treatment started with the therapy including the papain gel with 5% cream for three days. On the fourth day the papain concentration was reduced to 3% due to the fact that the wound did not show areas of necrosis and there was an exuberant formation of granulation tissue. This concentration was administered for 25 days. After the introduction of the new concentration of papain, the gradual appearance of an erythematous area was noticed, indicating an accelerated scar evolution, with exuberant granulation tissue formation.

After eight days from the start of the treatment, the erythematous area on the edge of the lesion had become more evident. On the twelfth day there was a formation of a low amount of serous

exudate, erythema perimarginal large decrease in area as well as tissue retraction with the new tissue formation consequently healing the skin.



Figure 2. Dog. Evolution of the patient's wound in Case 2, during the treatment with papain gel-cream containing 5% and 3%. 1 Pretreatment picture of the lesion's presence of deep ulcer with involvement of muscle layers, with areas of necrosis and fibrin, as well as jagged edges. 5 After 5 days of treatment showed the presence of exuberant formation of granulation tissue. 18-30. Use of papain 3% during days 18, 21, 25 and 30 of the start of treatment. The picture showed an exuberant formation of granulation tissue, new tissue formation and healing of the skin.

In case 3 (Figure 3). a male dog, 5 years old, mixed breed, weighing 21.7kg was attended on July 10, 2012. According to the owner's description, the animal was fighting with another dog and it hurt the left limb. On the initial presentation, the dog showed ideal body score (5/9) (Laflamme, 1997), adequate hydration, presence of moderate amounts of Ixodes and increased direct popliteal lymph node. A blood sample showed normocytic normochromic anemia, mild thrombocytopenia, suggesting the presumptive and concomitant diagnosis of ehrlichiosis. The therapy was instituted with meloxicam (0.1mg/kg once a daily for five days) and doxycycline (10mg/kg, once a daily for 28 days).

The large extended wound in a large left limb was approximately 7.0cm long by 5.0 wide, and had crusts and a large amount of necrotic tissue throughout the injured area.

The therapy involved applying the papain gel cream 5% in a single application, during which the wound was debrided by removing some crust lesions. On the second day, the concentration of papain cream gel was reduced to 3%. During treatment there was a decrease of wound granulation tissue formation.





Figure 3. Dog. Evolution of the patient's wound in Case 3, during the treatment with papain gel-cream containing 5% and 3%. 1 Pretreatment picture of the lesions. The picture shows a large amount of necrotic tissue throughout injured area 3 Third day of wound treatment with presence of fewer necrotic material and site erythema. 5, 7, 10 and 13 Evolution of the wound with the presence of granulation tissue and healing of tissue. 22 and 23 The last days of treatment with the presence of new skin in the area around the wound.

## DISCUSSION

Several studies in human patients showed the action of papain in debridement, liquefaction of necrotic tissue, and restoration of devitalized tissue (Sanchez Neto *et al.*, 1993; Carvalho *et al.*, 2010; Lima *et al.*, 2011).

All cases in the present study showed a chemical debridement in the wound with decrease of fibrin and necrotic material following the application of 5% papain gel from the first day of the therapy. Furthermore, an intense regeneration of the injured area, reduction in the extent of the wound, granulated tissue formation and re-epithelialization of the edges were found.

Papain can be inactivated by reacting with oxidizing agents such as iron, oxygen, iodine derivatives, hydrogen peroxide and silver nitrate (Sanchez Neto *et al.*, 1993). Hence, all the above cases with the lesions were cleaned with 0.9% saline solution.

The papain is a proteolytic enzyme. Therefore, it is very important to determine the concentration of its presentation. Thus, the determination of these values should be in accordance with the macroscopic characteristics of each wound (Monetta, 1987; Rocha *et al.*, 2005).

In the presented cases the initial concentration of papain gel cream was determined in accordance

with the macroscopic characteristics of the lesions. In cases 2 and 3 the change in concentration occurred in different phases, because the extension of the injury was different in both cases. This reduction in the concentration of papain gel is required in wounds that do not have necrotic material and do not require the formation of a large amount of granulation tissue. A high concentration may cause irritation to the intact skin and result in erythema and scaling (Rocha *et al.*, 2005; Leite *et al.*, 2012). In agreement with a study conducted by Rocha *et al.* (2005), which stated that the determination of the concentration of papain depends on the characteristic of the lesion, the concentrations used in the present study varied from 2 to 4% depending on the wounds or dry granulation tissue. In the presence of lesions with purulent exudate and / or infections, concentrations can vary from 4 to 6%.

Unfortunately, the changes were not made regarding the concentrations of papain. In case 1, the changes were made for sunflower oil. The papain 5% was used for nine days, when it was possible to observe the wound edges with a fabric appearance and exudative erythema edge. Therefore, a new treatment was used.

The sunflower oil has been studied in healing wounds in animals (Oliveira, 2010). This oil is composed by fatty acids and linoleic oil, which may promote improvement in the healing of skin

with reduction of the wound, retraction of tissue edges and development of granulation tissue in a short time (Wendt, 2005)

In case 1, after the use sunflower oil, the macroscopic improvement in the wound was noted, with the formation of regular edges, erythema and the absence of the complete healing of the lesion. However, it had a higher treatment time when compared with papain therapy alone.

Consequently, it appears that the use of the papain gel cream at different concentrations (cases 2 and 3) has a reduced total time of reepithelialization of lesions. The case 1, including the cream therapy based on papain gel and sunflower oil has shown satisfactory results, although longer periods are needed for the total wound healing.

The findings provide supporting evidence that a papain gel cream showed effectiveness in the treatment of infected wounds, especially regarding the healing time, debridement and granulation process. It showed efficacy as a chemical debriding, when applied in high concentrations, and facilitated the healing and granulation tissue in less concentrations process.

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