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Effect of the gel based on *Moringa oleifera lam.* as a phytotherapy in wound healing

Efeito do gel a base de *Moringa oleifera lam.* como fitoterapia na cicatrização de feridas

Efecto del gel a base de *Moringa oleifera lam.* como fitoterapia en la cicatrización de heridas

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Abstract

Objective: To evaluate the healing effects of Moringa oleifera in rats (Rattus norvegicus). Methodology: Moringa leaves were collected, dried, crushed, mixed with hexane solvent and filtered. After removing the solvent and moisture, he combined the resulting concentrate with the natrosol gel, reaching concentrations of 5% and 10%. 60 male rats were divided into 4 groups: negative control (without treatment), positive control (treated with AGE), Moringa 5% (treated with Moringa gel at 5%) and Moringa 10% (treated with Moringa gel at 10 %). It was subdivided into three groups of 5 animals according to the evaluation period (7, 14 and 21 days). A longitudinal incision (3.0 cm) was made in the cervical region; in the dorsal region an area of 2 cm² was demarcated and resected with a punch. Result: In the analysis of healing resistance, after 7 days, the 5% and 10% moringa groups showed a significant regression; after 14 and 21 days, the Moringa 10% group showed statistical significance when compared to the other groups. In the microscopic analysis, after 7 days, collagen fibers more evident in the Moringa groups 5% and 10%; after 14 and 21 days, few blood vessels, low intensity inflammatory reaction and more organized and intense collagen deposition in the Moringa 10% group. Conclusion: Moringa, especially at a concentration of 10%, proved to be beneficial in the repair process of surgically induced skin wounds in rats.

Keywords: Rats, Wistar; Wound Healing; Surgical Wound; Moringa oleífera.

Resumo

Objetivo: Avaliar os efeitos de cicatrização da *Moringa oleifera* em ratos Wistar. Metodologia: Folhas da moringa foram coletadas, secas, trituradas, misturadas com solvente hexano e filtrada. Após remoção do solvente e da umidade, combinou concentrado resultante

ao gel natrosol, alcançando concentrações de 5% e 10%. Dividiu-se 60 ratos machos em 4 grupos: controle negativo (sem tratamento), controle positivo (tratados com AGE), Moringa 5% (tratados com gel de Moringa a 5%) e Moringa 10% (tratados com gel de Moringa a 10%). Subdividiu-se em três grupos de 5 animais de acordo com período de avaliação (7, 14 e 21 dias). Realizou-se na região cervical uma incisão longitudinal (3,0 cm); na região dorsal foi demarcada e ressectada uma área de 2 cm² com um *punch*. Resultado: Na análise da resistência cicatricial, após 7 dias, os grupos moringa 5% e 10% mostraram uma regressão significante; após 14 e 21 dias, o grupo Moringa 10% apresentou significância estatística quando comparado aos demais grupos. Na análise microscópica, após 7 dias, fibras colágenas mais evidentes nos grupos Moringa 5% e 10%; após 14 e 21 dias, poucos vasos sanguíneos, reação inflamatória de baixa intensidade e deposição de colágeno mais organizada e intensa no grupo Moringa 10%. Conclusão: A moringa, especialmente na concentração de 10%, mostrou-se benéfica no processo reparativo de feridas cutâneas cirurgicamente induzidas em ratos.

Palavras-chave: Ratos Wistar; Cicatrização; Ferida cirúrgica; Moringa oleífera.

Resumen

Objetivo: Evaluar los efectos curativos de Moringa oleifera en ratas (*Rattus norvegicus*). Metodología: Se recolectaron hojas de moringa, fueron secados, triturados, mezclados con solvente de hexano y filtrado. Luego de remover el solvente y la humedad, combinó el concentrado resultante con el gel natrosol, alcanzando concentraciones de 5% y 10%. Se dividieron 60 ratas macho en 4 grupos: control negativo (sin tratamiento), control positivo (tratado con AGE), Moringa 5% (tratado con gel de Moringa 5%) y Moringa 10% (tratado con gel de Moringa al 10%). Se subdividió en tres grupos de 5 animales según el período de evaluación (7, 14 y 21 días). Se realizó una incisión longitudinal (3 cm) en región cervical; en región dorsal se delimitó un área de 2 cm² y se resecó con un *punch*. Resultado: En el análisis de la resistencia a las cicatrices, después de 7 días, los grupos de 5% y 10% de moringa mostraron una regresión significativa; después de 14 y 21 días, el grupo de moringa al 10% mostró significación estadística en comparación con los otros grupos. En el análisis microscópico, después de 7 días, las fibras de colágeno fueron más evidentes en los grupos de Moringa 5% y 10%; después de 14 y 21 días, pocos vasos sanguíneos, reacción inflamatoria de baja intensidad y deposición de colágeno más organizada y intensa en el grupo de moringa al 10%. Conclusión: La moringa, especialmente concentrado al 10%, demostró ser

beneficiosa en el proceso de reparación de heridas cutáneas inducidas quirúrgicamente en ratas.

Palabras clave: Ratas Wistar; Cicatrización de Heridas; Herida Quirúrgica; Moringa oleífera.

1. Introduction

Wounds are characterized as cutaneous deformities created by electrical, thermal, chemical and mechanical damage that result in an opening or damage the integrity of the skin, or the occurrence of a fundamental therapeutic or physical issue, or can be characterized as a disturbance of anatomical integrity and physiological of living tissue (Abdulah, Atasoy & Omer, 2018).

Skin wounds affect people at any age and, to repair this tissue damage, the body uses intrinsic, dynamic, organized and extremely complex biological processes that can be quick when the clinical situation is favorable and the extent and degree of tissue loss is less (da Cunha, Salomé & Massahud, 2017).

From a pathophysiological point of view, the wound is a lesion that damages the dermal layer of the skin and the natural process, which leads to the restoration of the structural and functional integrity of the injured tissues, represents wound healing (Amri et al., 2017).

Chronic wounds persist for an average of one year, frequently recur in up to 70% of individuals, and can lead to functional impairment and decreased quality of life. In addition, they increase health care costs, the U.S. health care system estimated in a report that it spends about $ 25 billion a year treating just chronic wounds (Kawahara et al., 2019).

According to Muhammad, Arulselvan, Cheah, Abas & Fakurazi (2016) this represents a great burden on the health and well-being of each patient, in addition to a significant financial cost for health systems. For this reason, about 80% of the world population uses natural remedies such as herbs for medicines, mainly because of easy access, economic accessibility and, above all, because of safe therapy (Tshabala et al., 2019). Thus, plant-based strategies have been widely used for wound healing and skin regeneration, and their therapeutic application dates back to ancient times (Amri et al., 2017).

Moringa oleifera is one of the most widely cultivated species in the Moringaceae family, being native to Southeast Asia, Africa and America. This plant contains a profile of important and photochemical nutrients (Fernandes, Pulwale, Patil & Moghe, 2016). In addition to some analgesic, antidiabetic properties, antispasmodic, diuretic, antihypertensive,

cholesterol-lowering, antioxidants, antibacterials and plays beneficial roles in modern medicine (Omadanisi, Aboua & Oguntibeju, 2017).

M. oleifera leaves are rich in beta-carotene, vitamin C, vitamin E and polyphenols and are a good source of natural antioxidants. Due to these reported functions, the bioactivity of *M. oleifera* has gained tremendous attention in the last decade, thus leading to the growing exploration and understanding of its pharmacological functions and underlying mechanisms (Kou, Li, Olayanju, Drake & Chen, 2018). Moringa is known for its multiple uses, among them are the cure of skin infections, anxiety, asthma, wounds, fever, diarrhea and sore throat (Brasil, 1959).

Thus, this work aimed to develop a gel based on *Moringa oleifera* for wound healing.

2. Methods

2.1 Ethical Procedures

The present study followed the guidelines recommended by Law 11.794, of October 8, 2008, of the National Council for Animal Experimentation Control, and was submitted for approval by the Ethics Committee on Animal Use at the State University of Piauí (CEUA / UESPI), with protocol number 0159/2018.

2.2 Research Method

This research is experimental in nature, with a qualitative and explanatory approach from the point of view of its objectives.

2.3 Research location

Held at the Biotechnology and Biodiversity Research Center of the State University of Piauí - Teresina - PI, from March 2018 to November 2019.

2.4 Data Collection

2.4.1 Collection of Plant Material and Hexane Extract from M. oleifera

All leaves of the species were harvested from the Nucleus of Medicinal Plants of the Federal University of Piauí, by a researcher at a fixed time.

These were harvested whole and were dried naturally at room temperature for 2 weeks in the shade. Then, they went through a crushing process, using an industrial shredder model JBM 30, with a capacity of 2L, resulting in greenish colored plant powder with particles of standardized diameter in 20 Mesh.

To obtain the hexanic extract, 100 g of the powder from the crushed leaves were used and added to 1000 mL of hexane solvent, remaining in this state for 5 days, mixing daily. After the end of this period, filtration was carried out using Whatman paper number 1 (Figure 3) and, with that, the first extraction fraction was obtained in closed amber glass, free of any light source in a refrigerator at 8°C . In this solute, 1000 mL of hexane was added, leaving it to stand for another 5 days, repeating the mixing, filtration process and the same time interval two more times. Thus, the volume of 2500 mL of filtrate was reached (Brasil, 1959).

Figure 1. Filtration of fluid extract from leaves.

Source: Personal archive, (2018).

The filtrate was sent to the Interinstitutional Nucleus for the Study and Generation of New Technologies (Geratec) at the State University of Piauí, where it was concentrated in a rotary evaporator coupled to a vacuum (Figure 4), at a temperature of 45 ° C and rotation of 120 rpm in order to remove the solvent. The procedure was completed in a water bath at 45 ° C, until the final volume of 150 mL of concentrated solute was obtained. The remaining moisture was removed in the gas fume hood for 7 days. Finally, the result was a concentrated mass in a pasty form of 7.5 g.

Figure 2. Process for removing the solvent in the Rotary Evaporator Apparatus.

Source: Personal archive, (2018).

2.4.2 Preparation of Moringa oleifera gel

The amount of 100 g of natrosol gel (hydroxyethylcellulose) was obtained by means of a handling pharmacy, which was divided into two equal portions of 50 g. The first half was mixed with 5g of hexane extract concentrate based on *Moringa oleifera*, weighed on an analytical balance, reaching a concentration of 10%. The second half, on the other hand, was mixed with 2.5 g of hexane extract concentrate based on *Moringa oleifera*, weighed in the same way in an analytical balance, reaching a concentration of 5%, and finally stored in a refrigerator at 8 °C.

2.4.3 Wound Induction and Experimental Animal Groups

Sixty male Ratus norvegicus rats, Wistar variety, were used to carry out the study. They were randomly divided into four experimental groups (n = 15 per group) as follows:

• Group I: Negative Control (untreated wound);

• Group II: Positive Control (wound treated with Essential Fatty Acid ointment - AGE);

• Group III: Moringa 5% (wound treated with gel based on hexane extract of Moringa at 5%);

• Group IV: Moringa 10% (wound treated with gel based on 10% Moringa hexane extract).

Each group (I, II, III and IV) was divided into three subgroups of 5 animals according to the evaluation period (7, 14 and 21 days after the operation).

For anesthetic induction, the animals received cutaneous atropine, at a dose of 0.04 mL / 100g, after the time of 20 minutes the anesthetic procedure was started in which the animals were subjected to dissociative anesthesia with ketamine / xylazine in the proportion of 1:1 at a dose of 0.1mL / 100g.

Then, epilation of two areas 24 cm² (6 cm long x 4 cm wide) was performed, located caudally to an imaginary line that passed through the forelimbs: first in the cervical region and then in the dorsal region. Antisepsis was performed with 2% chlorhexidine.

In the cervical region, an incision was made longitudinally (3.0 cm) to the median skin, sparing the underlying muscles. Then the wound edges were sutured, with three simple stitches, using 3-0 monofilament nylon thread. Then, in the dorsal region, in the center of the epilated area, demarcation was performed on the skin of each rat by rotation of the cutting edge of a metallic punch (2 cm in diameter). The resection of the circular skin segment was performed, following the demarcation of the punch, deepening the incision until exposing the dorsal muscle fascia.

Then the animals were photographed and the treatment prescribed for each group started. After anesthetic recovery, the animals were transferred to their specific cages, where 5 rats were housed in each cage and identified as to the belonging group demarcated on their tails with blue ink, in order of one to five. The treatment of groups G II, G III and G IV were performed daily, in the same shift.

2.4.4 Herbal Treatment

Group I, aged 7, 14 and 21 days, did not receive any treatment, being, therefore, the negative control. Group II, of 7, 14 and 21 days, was applied topically essential fatty acid ointment (AGE), daily. In groups III and IV, of 7, 14 and 21 days, topical gel formulation based on *Moringa oleifera* hexane extract was applied daily in concentrations of 5% and 10%, respectively.

2.5 Resistance Analysis

The resistance of the cutaneous scar was measured by removing the skin flap from the cervical region of 4x2 cm across the scar, and in its middle part of one of the incisions

after the treatment period. Then, the samples submitted to the stress resistance test by means of the Dynamometer Test Machine, with manually adjustable pressure claws and electronic data acquisition system using the software. The skin was clamped by means of a stainless steel device with gradual pressure, observing the rupture force (FR). The FR corresponds to the highest value of force necessary during the traction of the sample, that is, the highest value of resistance of the sample to reach the rupture (de Castro Carvalho et al., 2010).

2.6 Macroscopic Analysis

For macroscopic analysis, regression of the wound was observed. The lesion was photographed by a digital camera Model Iphone7plus, Apple Inc, United States, held on a tripod at a constant distance of 34 cm, with an approximation of 1.3x and a resolution of 1280 x 960 points, immediately after the induction of the surgical wound and in 7th, 14th and 21st day after surgical wound induction.

After obtaining the images, the image analysis program (Imaje J) was used to determine the wound area. After determining the wound area, the following calculation was applied: initial area (day 1) - final area (day 7, day 14 or day 21) / initial area * 100 to determine the percentage of regression.

2.7 Microscopic Analysis

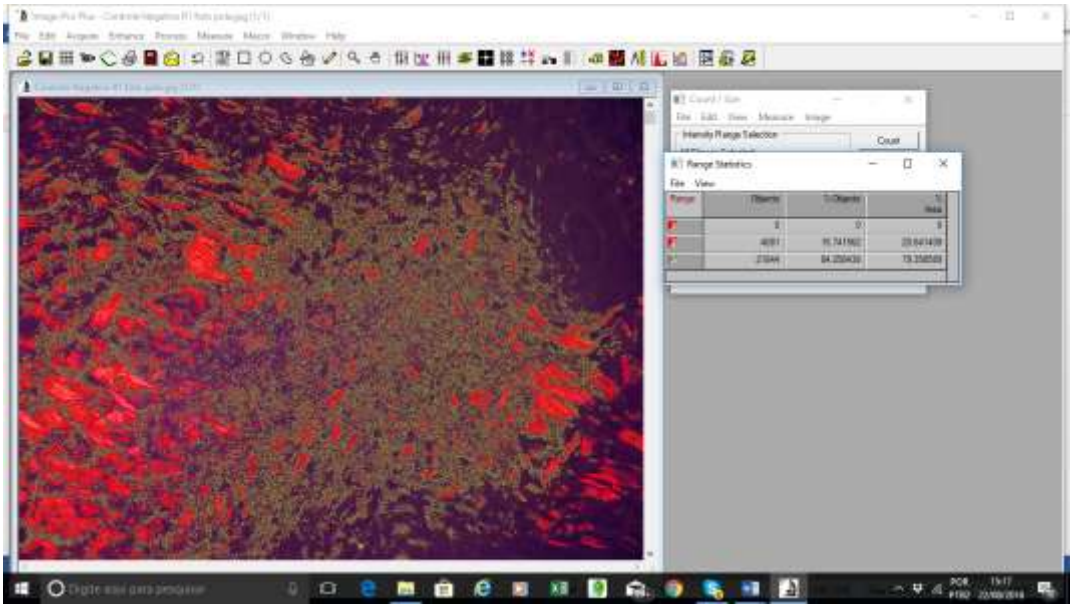
The wounds were removed with an intact skin margin and fixed in 10% formalin buffered solution for 24 hours. Two to three cross-sectional samples centered on the wound were subjected to routine histological processing and included in paraffin, obtaining histological sections 5μm thick, which were stained with hematoxylin-eosin. (H.E.) and Picrossirius Red (PSR). Histological preparations were examined using a trinolucular optical microscope (Olympus ® CX31, Japan), equipped with a digital camera (Bell & Howell, EU 16.0 Plus, U.S.A.) coupled to a microcomputer. As the wound healing process occurs from the periphery to the center, photographic documentation, for comparative purposes, was made at the center of the injuries.

In optical microscopy observations, histological differences were evaluated regarding fibroblastic proliferation, collagen fibers and reepitalization

After microtomy, the histological sections were stained by picrosiriusred - F3BA. To identify mature (type I) and immature (type III) collagen, histological sections were analyzed

using an optical microscope, at 400 times magnification, with a polarized light source. The images were captured by a camera and transmitted to a color monitor, frozen and digitized by means of plates. Finally, image analysis was performed using the Image Pro-Plus version 4.5 for Windows (Cybernetic Media, São Paulo, SP). In the RGB system (Red, Blue, Green) values were considered for red, yellow and orange tones (type I collagen) and for green tones (type III collagen), as seen in Figure 3.

Figure 3. Digitized histological findings for analysis of collagen deposition in the wound. Teresina-PI.



Source: Personal archive, (2018).

Figure 3 shows a slide containing histological tissue being analyzed by the Image Pro-Plus program, in which it is possible to observe the different colors represented by collagens according to their maturation.

All slides were evaluated under the same regulation conditions, within the parameters required by that application. In the histological sections, 4 microscopic fields were acquired over the lesion area where measurements of the different areas were obtained. In each of them, the software calculated the percentage of the area occupied by the fibers that contained types I and III collagen in relation to the total area examined. From the measure of the percentage of collagen fibers, the collagen maturation index (IMaC) was calculated as described by Biondo-Simões, Sichciopi, Ioshii, Robes & Biondo-Simões (2018), being obtained through the percentage ratio of type I collagen to the percentage of type III collagen,

where values greater than 1 indicate that the percentage of type I collagen is greater than the percentage of type III collagen.

2.8 Euthanasia and Disposal of Animals

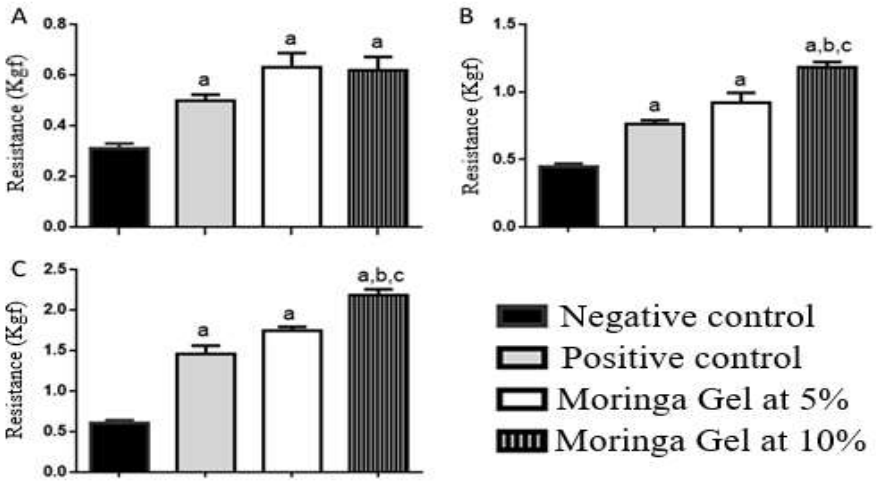
After the period of 7, 14 and 21 days of treatment, the animals were euthanized according to the ethical principles established by the Brazilian College of Animal Experimentation (COBEA) for the dissection of the samples that were submitted to the analysis. Euthanasia was performed by injection of Tiopental 100mg. After removing the healing wounds, the corpses were frozen in a freezer and later discarded by the technician responsible for the institution's vivarium.

3. Results

3.1 Assessment of healing resistance

In the analysis of the healing tension of the skin flaps, superior rupture strength was observed in the groups using the Moringa oleifera gel throughout the experimental time 7,14 and 21 days.

Graph 1. Analysis of skin tensiometric resistance after 7.14 and 21 days of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%.

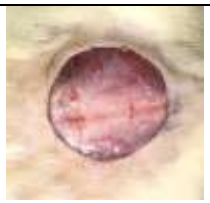
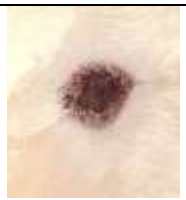
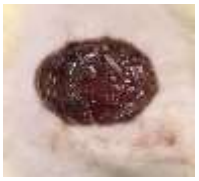
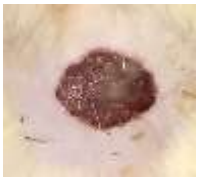
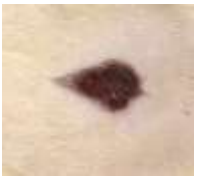
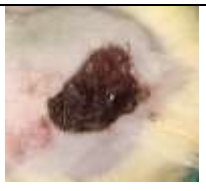


Source: Personal archive, (2018).

3.2 Macroscopic Analysis

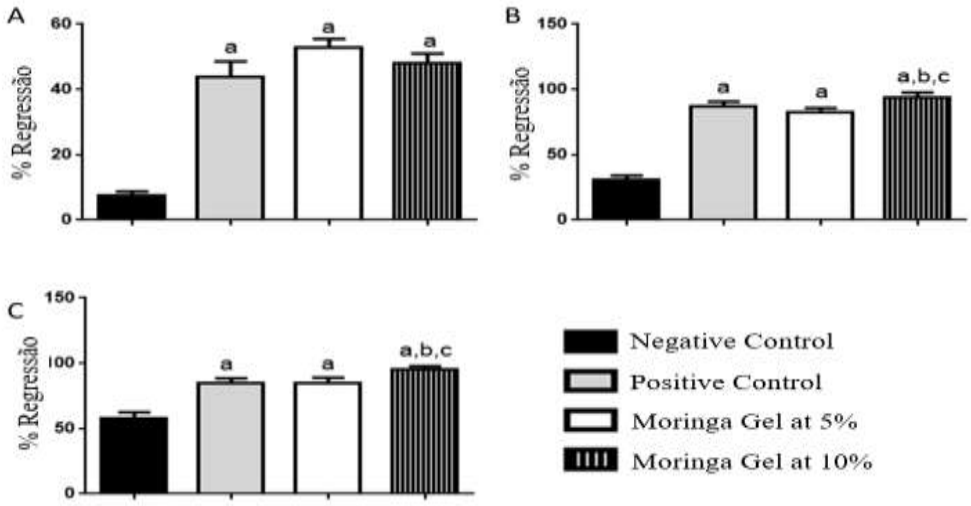
In the analysis of scar regression, it was observed that at the end of seven days of treatment, the groups treated with 5% and 10% moringa showed a significant increase in regression ($p < 0.05$) when compared to the negative control group and did not observe difference with positive control group.

Figure 4. Macroscopic images of the surgical wound area of the animals in the groups Negative control, Positive control, Moringa 5% and Moringa 10% at 0, 7, 14 and 21 days after surgery.

	Dia 0	**Dia 7**	**Dia 14**	**Dia 21**
Controle negativo				
Controle positivo (AGE)				
Moringa 5%				
Moringa 10%				

Source: Personal archive, (2018).

Graph 2. Analysis of skin scar regression after 7, 14, 21 days of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%.

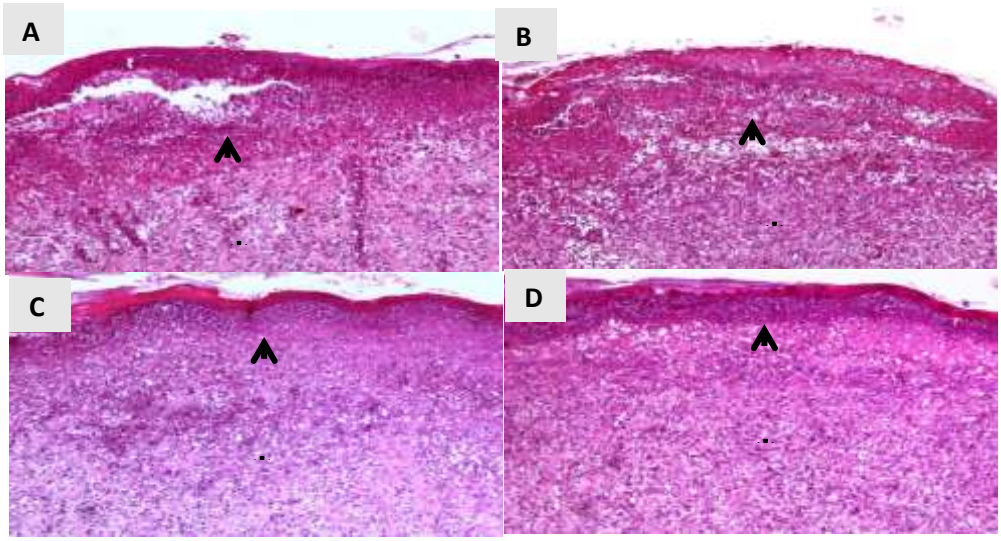


Source: Personal archive, (2018).

3.3 Microscopic Analysis

After seven days of evolution, the wounds were covered by a thick crust formed by fibrinous material and a high number of neutrophils and pyocytes. In the wound bed, young granulation tissue with loose extracellular matrix (ECM) was present, with numerous newly formed blood capillaries and a large number of inflammatory cells, especially neutrophils.

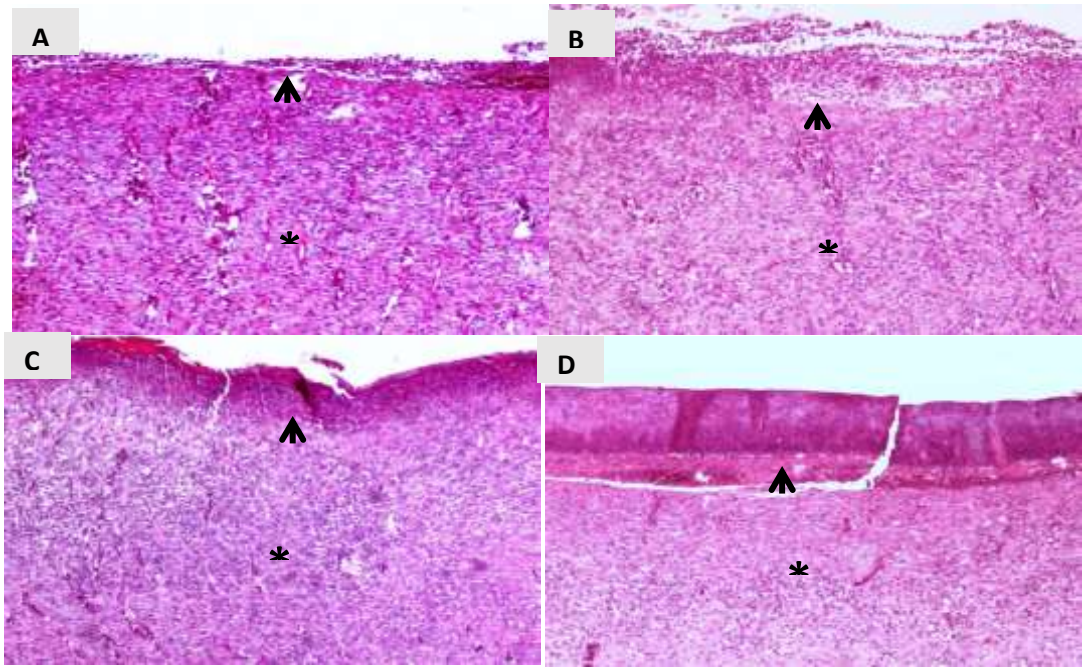
Figure 5. Microscopy showing wound healing on the 7th day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%. Hematoxylin Eosin 40x. Teresina-PI.



Caption: Fibrinoneutrophilic crust (arrows) deposited on the surface of the wounds. In the wound bed, young granulation tissue (asterisks) with loose extracellular matrix containing numerous inflammatory cells and newly formed blood capillaries. A: Negative Control; B: AGE; C: Moringa 5%. D: Moringa 10%. H.E., 40x
Source: Personal archive, (2018).

After fourteen days of evolution, none of the groups had re-epithelialized the wounds at this stage, the wounds being still with residual scab. The granulation tissue contained predominantly macrophages and lymphocytes, the inflammation being less pronounced in the G4 group (Figure 6).

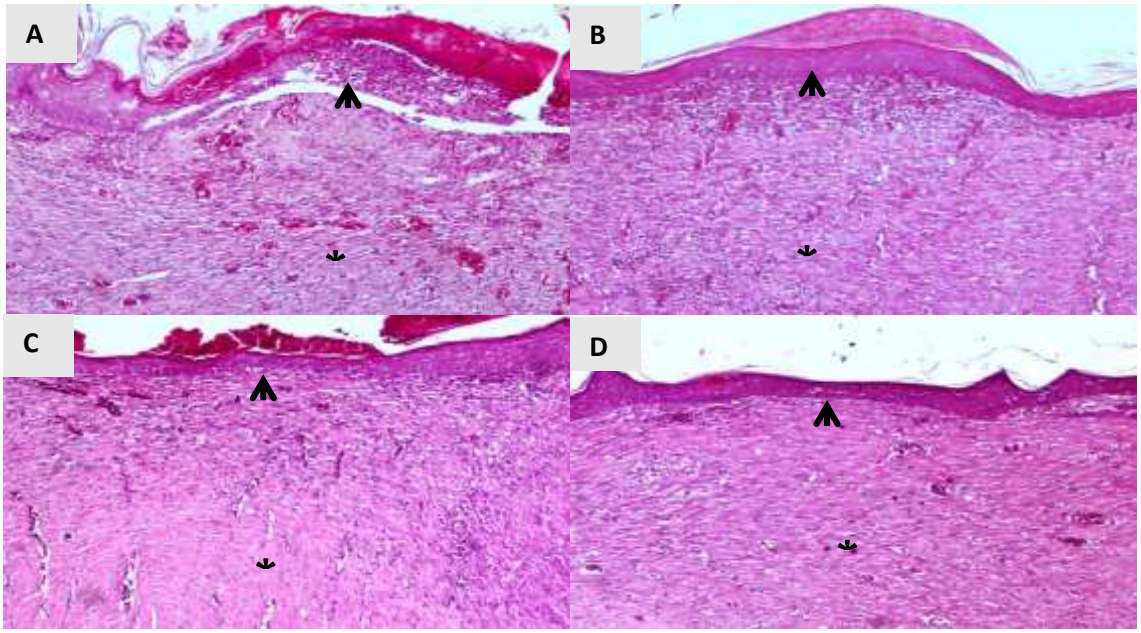
Figure 6. Microscopy showing wound healing on the 14th day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10% Hematoxylin Eosin 40x. Teresina-PI.



Legend: Fibrinoneutrophilic material (arrows) still present in the center of the wound. At the base, granulation tissue (asterisks) containing inflammatory cells and fibroblasts. The inflammatory activity is lower in Group G4. A: Negative Control; B: AGE; C: Moringa 5 ;. D: Moringa 10%. H.E., 40x
Source: Personal archive, (2018).

Twenty-one days later, the wound was completely re-epithelized, with the exception of the Negative Control group. MEC was more dense and with less inflammatory activity in the Moringa 5% and Moringa 10% groups. In the latter, mature fibroblasts were arranged bundles parallel to the epidermal surface (Figure 7).

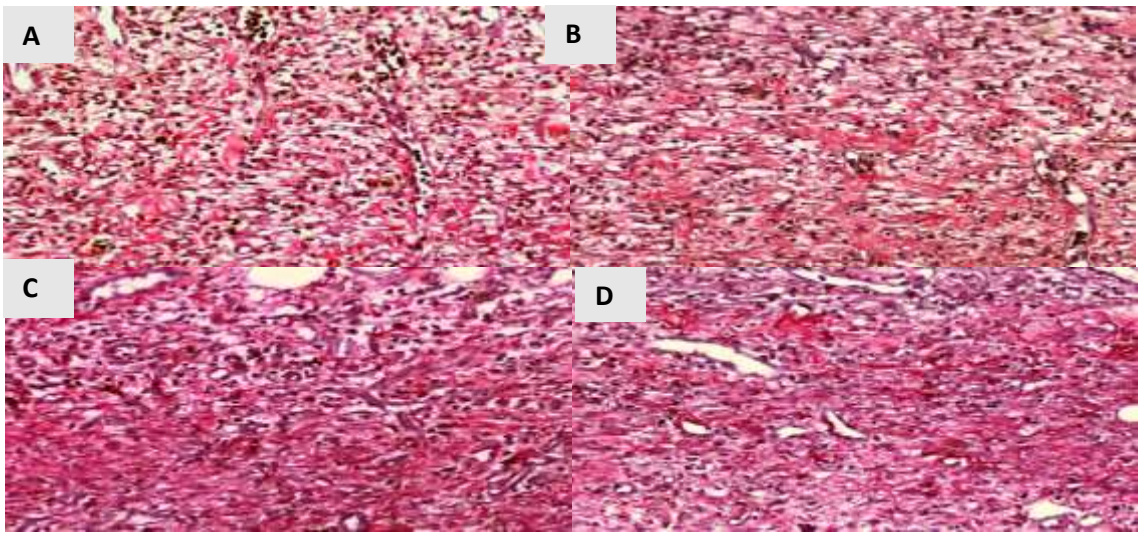
Figure 7. Microscopy showing wound healing on the 21st day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%. Hematoxylin Eosin 40x. Teresina-PI.



Legend: Incomplete reepithelization (arrows), with the presence of fibrinoneutrophilic crust in the G1 group. Granulation tissue (asterisks) shows scarce inflammatory cells and fibroblasts aligned in bundles parallel to the surface in the G4 group. A: Negative Control; B: AGE; C: Moringa 5%; D: Moringa 10%. H.E., 40x.
Source: Personal archive, (2018).

Samples stained with Pricrosirius Red (PSR) also show collagen deposition according to groups and throughout the experiment. After seven days of evolution, delicate collagen fibers were more evident in the Moringa 5% and Moringa 10% groups (Figure 8).

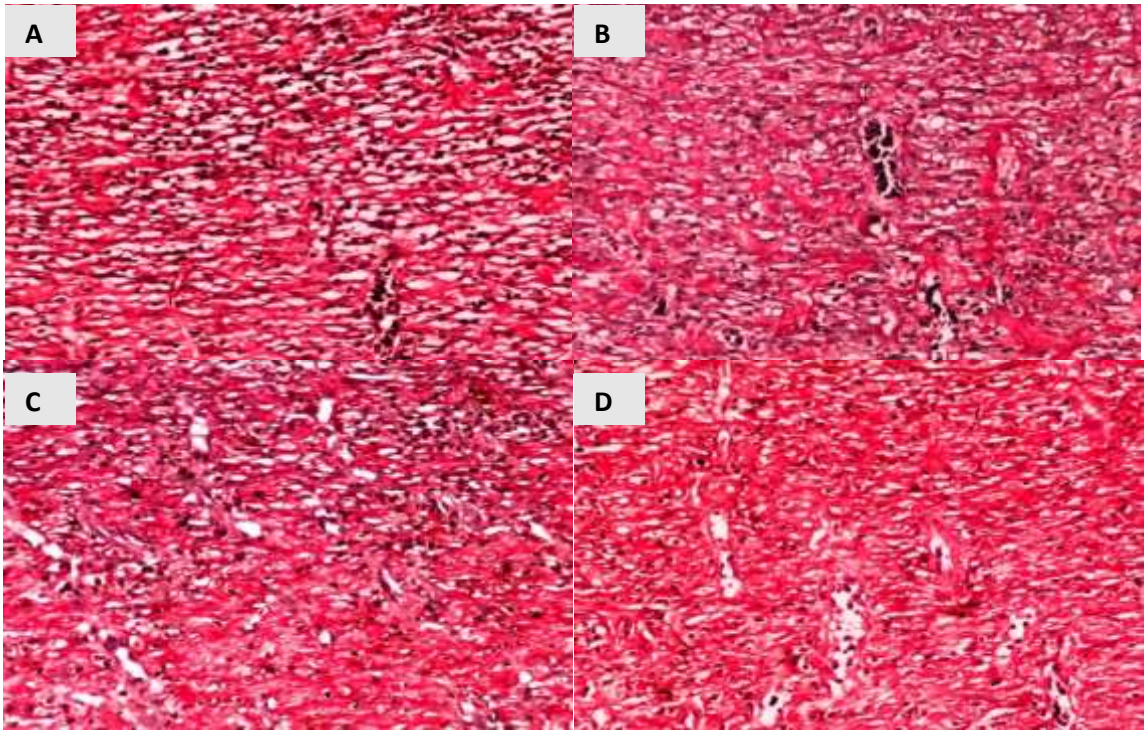
Figure 8. Microscopy showing wound healing on the 7th day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%. Pricrosirius Red 100x. Teresina-PI.



Legend: Collagen fibers (colored red) dispersed in a loose MEC and with intense inflammatory infiltrate. The fibers appear more condensed in groups G3 and G4. A: Negative Control; B: AGE; C: Moringa 5%. D: Moringa 10%. PSR, 100x.
Source: Personal archive, (2018).

With fourteen days of evolution, collagen deposition is accentuated especially in the Moringa 10% group, in which there are few blood vessels and less intense inflammatory reaction (Figure 9).

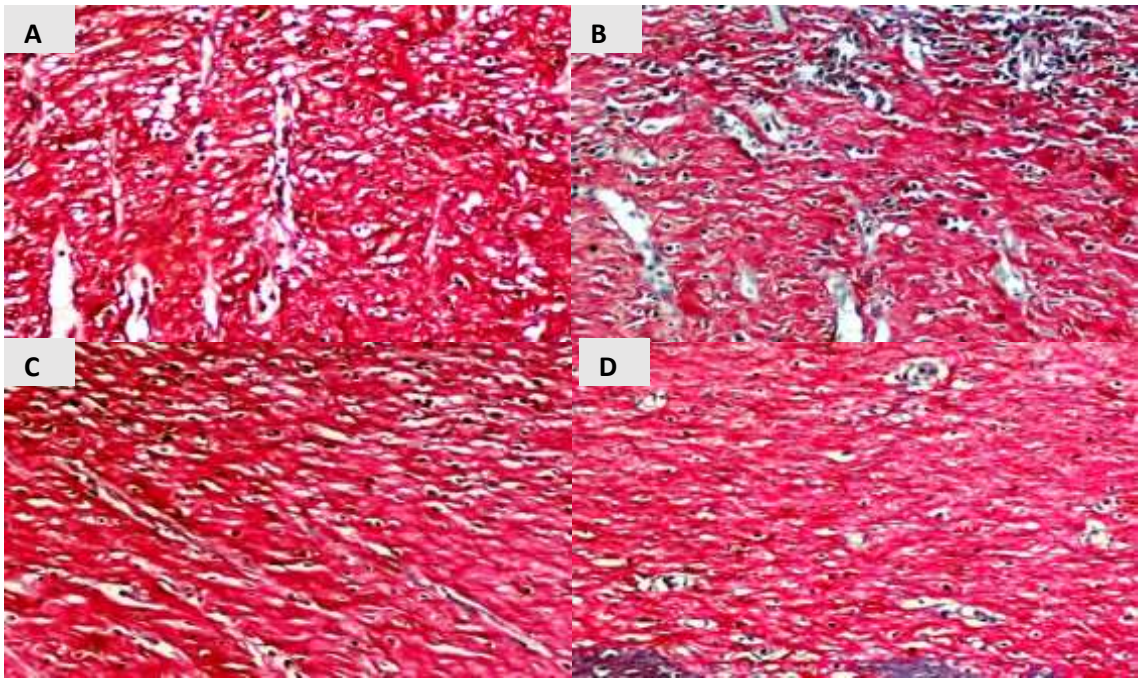
Figure 9. Microscopy showing wound healing on the 14th day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%.



Caption: Deposition of collagen fibers (colored red) more evident in the Moringa groups 5% and 10%. Note foci of inflammatory infiltrate in the groups Negative control, Positive control and Moringa 5%. A: Negative Control; B: AGE; C: Moringa 5%. D: Moringa 10%. PSR, 100x.
Source: Personal archive, (2018).

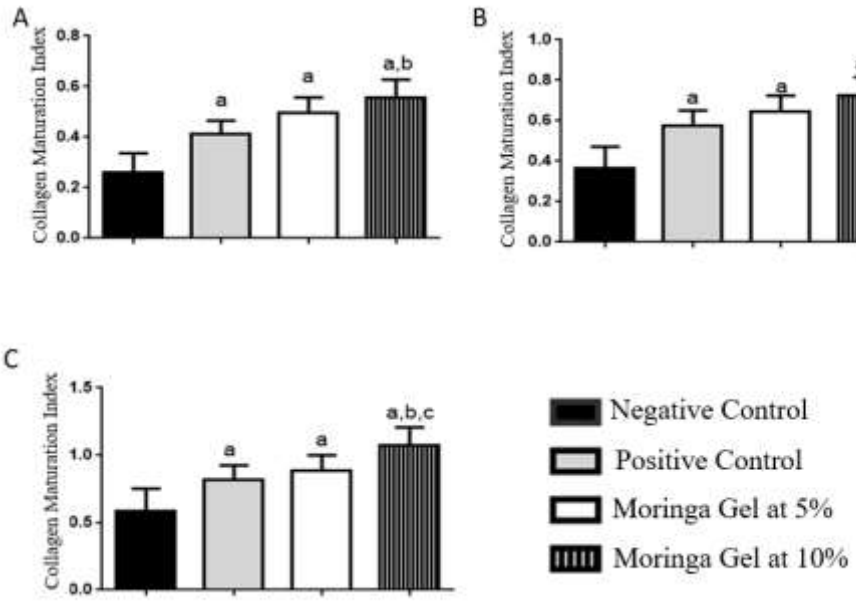
And with twenty-one days, MEC presented itself diffusely collagenized in all groups; however, the Negative Control and Positive Control groups contained foci of inflammatory infiltrate and blood vessels more numerous and arranged vertically in relation to the surface. In the Moringa 10% group, blood vessels were scarce and collagen deposition was more organized and intense, with the fibers arranged in parallel to the skin surface (Figure 10).

Figure 10. Microscopy showing wound healing on the 21st day of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%. Pricrosirius Red 100x. Teresina-PI.



Legend: Diffuse deposition of collagen fibers (in red). In the Moringa 10% group, blood vessels are scarce and the fibers are arranged parallel to the skin surface. A: Negative Control; B: AGE; C: Moringa 5%. D: Moringa 10%. PSR, 100x
Source: Personal archive, (2018).

Graph 3. Analysis of the collagen maturation index in the lesions after 7, 14 and 21 days of treatment with AGE, Moringa Gel at 5% and Moringa Gel at 10%. Teresina-PI, 2020.



Source: Personal archive, (2018).

4. Discussion

Moringa oleifera is a medicinal plant widely used in human nutrition because it is a relevant source of proteins, vitamins and minerals. M. oleifera leaf extract has been used in folk medicine as an anti-inflammatory, analgesic, hepatoprotective, hypotensive, anti-anemic, detoxifying, hypocholesterolemic, memory activator, among others. Regarding bioactive compounds, M. oleifera leaves contain 33.9 µg.g-1 of carotenoids (Falowo, Muchenje, Hugo, Aiyegoro & Fayemi, 2017).

In this study, the animals presented post-operative without complications, remaining alive until the end of the experiment. The evaluation of the external surface of the surgical wound did not demonstrate the presence of abscess or dehiscence in any of the animals.

In the analysis of the tensiometric resistance of this study, it was evidenced that the Moringa gel showed an increase as the experimental time progressed, this factor is attributed by the presence of hydroxyproline which is the factor responsible for the increase in the tensiometric resistance due to its affinity with the fibers collagen that aid in the healing process (Bhattacharya, Tiwari, Sahu & Kumar, 2018). It was also observed that the Moringa

gel in higher concentration statistically demonstrates high levels of significance in relation to other treatments.

M.oleifera is rich in fatty acids, amino acids, vitamins C and D and which have biological importance as a source of energy for cells and as fundamental elements in the construction of their membrane and their permeability (Gothai et al., 2017). In the tissue repair process, fatty acids promote chemotaxis and angiogenesis, keep the environment moist, accelerate the process of granulation tissue formation, facilitate the entry of growth factors into cells, promote mitosis and cell proliferation (Carvalho et al., 2016).

In the present study, the degree of wound contraction in the groups evolved over the experimental time. It was also observed that the groups treated with M. oleifera at 10%, were shown to be significant in relation to other treatments, which showed the effectiveness in healing using M.oleifera (Monteiro, Pavanelli, Valentini & Biazon, 2015).

Healing is a complex phenomenon characterized by a sequence of biological events that involve the organization of cells, chemical signals and extracellular matrix in a dynamic and harmonic process in order to ensure tissue restoration. Three consecutive phases of the process are identified, which occur in a progressive manner, overlapping at certain times, called exudative (or inflammatory), proliferative and scarring (or remodeling) (Souza, 2013). In this experiment, it was evidenced that the inflammatory phase in the seven-day histological cut occurs chemotaxis where the inflammatory cells migrate to the wound site.

In the same analysis, at the end of 14 days of treatment, according to the histological cuts, there was a greater reduction in the inflammatory process in the groups treated with Moringa, compared to the control group, with this reduction being even more pronounced in the Moringa group, 10%, it is suggested. this fact is due to its anti-inflammatory property (Jwa, 2019). It was also observed that in the 14-day treatment there was no complete re-epithelialization of the wound and the presence of a tissue crust was also observed. Complete reepithelialization of the wounds was only observed at 21 days.

Carotenoids are precursors of vitamin A and play an important role in the skin repair process, stimulating the formation of fibroblasts and collagen deposition (Amaliya, Muhaimina, Susanto & Sutjiatmo, 2019).

Fibroblasts, in turn, move in the wound along the extracellular matrix produced by them and, after entering this matrix, can assume three phenotypes: migratory, collagen-producing or contractile. Not only collagen, but the fibroblast also produces elastin, fibronectin, glycosaminoglycan and proteases, which are responsible for debridement and physiological remodeling. The extracellular matrix of connective tissue plays a fundamental

role in this phase of repair, forming a complex of macromolecules that not only provides structural support for tissues, but also modulates various functions of cellular components, such as: proliferation, differentiation, movement and cellular junction (Souza, 2013; Amaliya, Muhaimina, Susanto & Sutjiatmo, 2019).

5. Conclusion

The study made it possible to produce Moringa Oleifera gel at 5 and 10% and after analyzing its effectiveness in the healing process of skin lesions surgically induced in rats, it found a significant difference between the regression of wounds with the use of moringa gel and that the 10% presentation was able to present a satisfactory effect when compared to the AGE.

The results indicate that the moringa, especially at the concentration of 10%, has a beneficial effect on the repair process of surgically induced skin wounds in rats. These effects were characterized by accelerated closure and re-epithelialization of treated wounds, as well as more organized collagen deposition.

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