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PERFORMANCE OF PHYTOTHERAPEUTIC GEL BASED ON LYOPHILIZED DRY EXTRACT OF *anacardium occidentale* L. IN IN VIVO CUTANEOUS SCARRING

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Abstract: The development of new pharmacological therapeutic options based on medicinal plants is a complex process that involves the long PERFORMANCE OF PHYTOTHERAPEUTIC GEL BASED ON FREEZE DRIED EXTRACT OF Anacardium occidentale L. IN SKIN HEALING "IN VIVO" The aim of this research is to evaluate the interference of a gel obtained from the powder of the dried extract of Anacardium occidentale L. through the freeze-drying process on the healing process. In this sense, the aim of this research was to evaluate the interference of a gel obtained from the powder of the dried extract of *Anacardium occidentale L.* through the freeze-drying process on the healing process "*in vivo*". In the "*in vivo*" experimental phase, the sample consisted of 16 adult Wistar albino rats, which were divided into four groups. The standards relating to the macroscopic appearance of the wound and its contraction were assessed daily for 12 days. It was found that the 50% gel had a significant effect on the healing process, since in just eight days all the guinea pigs in Group 4 had recovered from the injury, while those who didn't use the active ingredient or used it at a concentration of 25% took an average of 10 to 12 days to complete this process. Based on the methods and conditions used in this study, the results lead us to conclude that *A. occidentale L.* gel accelerated the skin healing process "in vivo".
Keywords: Wounds. Healing. *A. occidentale L.*

INTRODUCTION

Brazil has a long tradition of the empirical use of medicinal plants linked to popular knowledge passed down from generation to generation, and scientific research to obtain evidence of their action is focused on various biomedical demands.

The current therapeutic agents of synthetic origin have limitations such as adverse effects and high cost, which suggests the prospect of developing an efficient and lower-cost production process, as well as the use of natural products, regionally available and with an adequate therapeutic profile for application in the healing and repair of skin wounds.

The process of wound healing consists of re-establishing tissue continuity in damaged cutaneomucosal tissue through cellular, physiological, molecular and biochemical events that interact to restore the tissue. As a biomedical demand, interference in healing phenomena is of special interest in situations where pathophysiological conditions can negatively interfere with them, which is why research into healing adjuvants is of great relevance.

In the field of bioactive natural products, the promising species *Anacardium occidentale L.,* popularly known as the cashew tree, is a tropical plant native to Brazil and scattered throughout most of its territory. This plant has demonstrated antimicrobial and antioxidant activity in preliminary studies, revealing itself as a promising alternative for the development of herbal medicines.

The process of obtaining products that fit the concept of herbal medicine is a prerequisite for the development of therapeutic options. In the industrial process, the dry extract is used in the preparation of tablets, capsules, granules, ointments and other pharmaceutical forms, as intermediate products, and among other advantages they have greater stability and particle size distribution of the constituents of the preparation.

In view of the above, it can be seen that prospecting for new pharmacological therapeutic options from medicinal plants is a complex process that involves selecting the plant, processing it so that it becomes viable as a raw material, *in vitro* and/or *in vivo* experiments, as well as comparison with other available therapeutic options in terms of productive viability, economic viability and clinical efficiency.

This work is justified by the need to develop or improve production processes used in the prospecting of drugs from medicinal plants, with a view to productivity, quality, efficiency and cost reduction, in order to contribute to the viability of the final product as an innovation. To this end, it makes use of a locally available natural product, with great ethnobotanical recognition as part of popular medicinal gardens, which is widely accepted as a herbal therapeutic option.

The aim of this study was to evaluate the performance of a gel obtained from the powder of the dried extract of *Anacardium occidentale L.* through the freeze-drying process, *in* the healing process "*in vivo*".

MATERIALS AND METHODS

PLACE AND TYPE OF RESEARCH

The research was carried out in three different laboratories: The Freeze-Drying Laboratory of the Food Engineering Course at the CTRN/UFCG, and the Animal Facility at the CFP/UFCG. This is an experimental and descriptive study with a qualitative and quantitative approach.

ETHICAL ASPECTS

This project was submitted to the Ethics Committee for the Use of Animals at the Teacher Training Center of the Federal University of Campina Grande (CEUA- CFP/UFCG), and was based on the ethical and legal precepts contained in Law No. 11.794, of October 8, 2008, and other legislation applicable to the use of animals for teaching and research (Annex I). Only after approval were the *in vivo* trials started. The submission was registered via Process No. 23096.011557/19-32 and was approved according to Certificate No. 04/2019 of the CEUA-CFP-UFCG.

REGISTRATION OF RESEARCHERS AND RESEARCH IN SISGEN

As this research includes plant species and living organisms, the applicant has registered with the National System for the Management of Genetic Heritage and Associated Traditional Knowledge - **SisGen, an** electronic system created by Decree No. 8.772, of May 11, 2016, which regulates Law No. 13.123, of May 20, 2015, as an instrument to assist the Genetic Heritage Management Council - CGen - in the management of genetic heritage and associated traditional knowledge. The proof of registration and access on the SisGen platform can be found in Annex II.

COLLECTION, SELECTION OF RAW MATERIALS AND OBTAINING THE POWDERED EXTRACT

In the first stage of this work, the plant material was collected, identified and an exsiccata of the material was deposited, recording the geographical location (latitude coordinates: -6.87214 / S 6º52'19.71707" and longitude: -38.55733 / W 38º33'26.37803"), period of the year and time of day when it was collected. Bark samples were taken from five adult individuals, and 1/3 of the total perimeter of the stem was extracted from the width of the bark and with a height of approximately 3 times the width of the bark collection (FILIZOLA, 2015).

The collected shells were dried in an oven with temperature control using a PT100 sensor up to 200ºC, a chamber and internal door cushion made of 430 stainless steel, with a heating system by natural air convection, using two resistors located at the base, at 50ºC, until the weight stabilized. The dried material was pulverized in a MARCONI MA 680 knife mill, using a 20 mesh (833 μm).

The dried and ground plant material was characterized in terms of its particle size distribution, extractive content, loss on drying, total tannins, total flavonoids, total phenolics, carotenoids and anthocyanins.

To prepare the hydroalcoholic extraction solution, 70% alcohol was added in a ratio of 1:10 (plant: solvent) to the dried and ground bark of *Anacardium occidentale L.*, at an extraction temperature of 50 ºC for 60 minutes, under mechanical agitation, using a jacketed extractor and a temperature-controlled heating bath (FERNANDES et al., 2014). The extracts were then vacuum filtered and kept in amber bottles, protected from light, and stored at 4 ºC for later analysis. The extractive solutions obtained were characterized in terms of solid content, density, alcohol content, pH, total flavonoid, polyphenol and total tannin content and antioxidant activity using the DPPH method.

To prepare the concentrated extract, the solids content obtained in the extraction stage was used as a basis, with the aim of increasing the content to at least 10%, in order to guarantee the effectiveness of the drying process. The desired concentration was obtained in a Fisatom model 802 rotaevaporator, with a temperature not exceeding 50 ºC and a reduced pressure of 600 mmHg. The extract was reduced by 3 times in relation to its initial mass.

The concentrated extract was then dried in a bench-top freeze dryer (*Christ* model ALPHA 1-2 LDplus).

The dry extract of *Anacardium occidentale* L. was packed in plastic molds and subjected to slow freezing by direct contact with the cooled environment in a freezer at -18 °C for 24 hours. The frozen samples were then placed in 500 mL round-bottomed glass flasks and freeze-dried at -40 °C for 48 hours. After freeze-drying, the powder obtained was disintegrated using a mortar and pestle and stored for later analysis. The loss on drying, residual moisture by Karl Fischer, water activity, solubility, flavonoid, polyphenol and total tannin contents were determined, as well as the fluidity properties of the dried extracts, such as apparent and compaction density, Hausner factor and compressibility index, angle of repose and antioxidant activity using the DPPH method.

The configuration of the freeze-dried powder, as well as the size and average diameter of the particles, was determined using scanning electron microscopy (SEM) on the Tescan VEJA 3, summer 2018. The specimens were prepared in a sample holder by gluing them to a suitable tape, without the need for gold metallization. The images were generated using secondary electron radiation and 15 kV acceleration in a chamber with a conventional tungsten cathode in high vacuum. The micrographs were analyzed using imageJ software to determine the diameters of each visible powder particle.

MAKING THE GEL FOR TOPICAL APPLICATION

The herbal gel was produced by a compounding pharmacy (ROVAL® - Campina Grande - PB) using the dry extract obtained in the previous stages of this research (Figure 01).

Figure 1 - Gel herbal medicine

Source: Own collection, 2022.

The Carbopol 940 gel base was determined based on the formulation described by Ferreira (2006). The concentrations of the components of the initial base formula were adjusted in order to obtain a formulation suitable to support the concentrations and relative quantity of the dry extract incorporated, while main-

taining the desired characteristics for the topical gel. Table 01 describes the qualitative and quantitative composition of the final formula defined in the preparation of the base gel.

Components	Concentration/ Volume
EDTA	0,12%
Methylparaben	0,10%
Propylene glycol	3%
Carbopol 940	4%
Optiphen (phenoxyethanol + caprylyl glycol)	0,50%
Sodium hydroxide pH 7.0	Qsp
Purified water	qsp100ml

Table 1 - Qualitative and quantitative composition of the base gel formulation

Source: Ferreira, 2006.

To prepare the base gel, the general procedures for preparing gels as described by Ferreira (2006) were followed. The mixture of EDTA (M. Cassab®) and methylparaben (M. Cassab®) was levigated in propylene glycol (DEG-Brasil®) and added to deionized water, previously heated to 60ºC. After homogenization, Carbopol 940 (M. Cassab®) was added little by little and stirred vigorously until the polymer swelled completely. After swelling, Optiphen (DEG) was added. The mixture was homogenized and the pH was adjusted using sodium hydroxide (All Chemistry®) in a 25% solution. After adjusting the pH, the active ingredient was added, in the form of a dry extract, and the final viscosity and pH adjustment was made.

APPLICATION OF *A. occidentale L.* GEL TO GUINEA PIGS

In the "*in vivo*" experimental phase, the sample consisted of 16 adult male Wistar albino rats, weighing around 350g, from the animal house of the UFCG Teacher Training Center - Cajazeiras Campus.

The animals were kept in open polypropylene cages measuring 41x34x16cm, holding a maximum of 3 animals and in an environment with a temperature of 21°C with a variation of ± 2°C and controlled lighting with a 12-hour light/dark cycle, with free access to balanced commercial pelleted feed (Purina® São Paulo - SP) and drinking water (Figure 02). The acclimatization period of seven days before the start of the experiment was respected.

As a way of separating the treatments applied, the animals were randomly divided into four different groups, each comprising four animals. The animals in Group 1 were the control group (spontaneous healing); Group 2 consisted of the use of the gel free of the active ingredient; in Group 3, 25% *A. occidentale L.* gel was applied; and in Group 4, 50% *A. occidentale L.* gel.

For the surgical procedure, the animals were weighed and then anaesthetized with 10% ketamine hydrochloride (dose of 80 mg/kg), combined with 2% xylazine hydrochloride (dose of 10 mg/ kg), both via the intraperitoneal (IP) route. The area was then trichotomized, 4cm long and 4cm wide, using the dorsal midline as a reference. The animal was placed in a prone position and after asepsis of the skin with 2% chlorhexidine, the surgical wound was made by excising the layer that includes the epidermis, dermis and dorsal fascia using a 12mm surgical punch[2] to standardize the size of the wound. The depth of the wound was standardized according to the visualization of the muscular plane. Each animal was identified on the tail using a dermographic pen.

In order to relieve post-operative pain, dipyrone monohydrate was administered at a dose of 10 mg/kg in the water of each container in the cages before recovery from anesthesia and for a period of at least 12 - 24 hours after recovery. After the procedures, the animals were housed in polypropylene cages and kept throughout the experiment in ideal conditions of hygiene, lighting and temperature, and fed food and water *ad libitum*.

Figure 2 - Group formation, surgical procedure and identification of the rats

Source: Own collection, 2022.

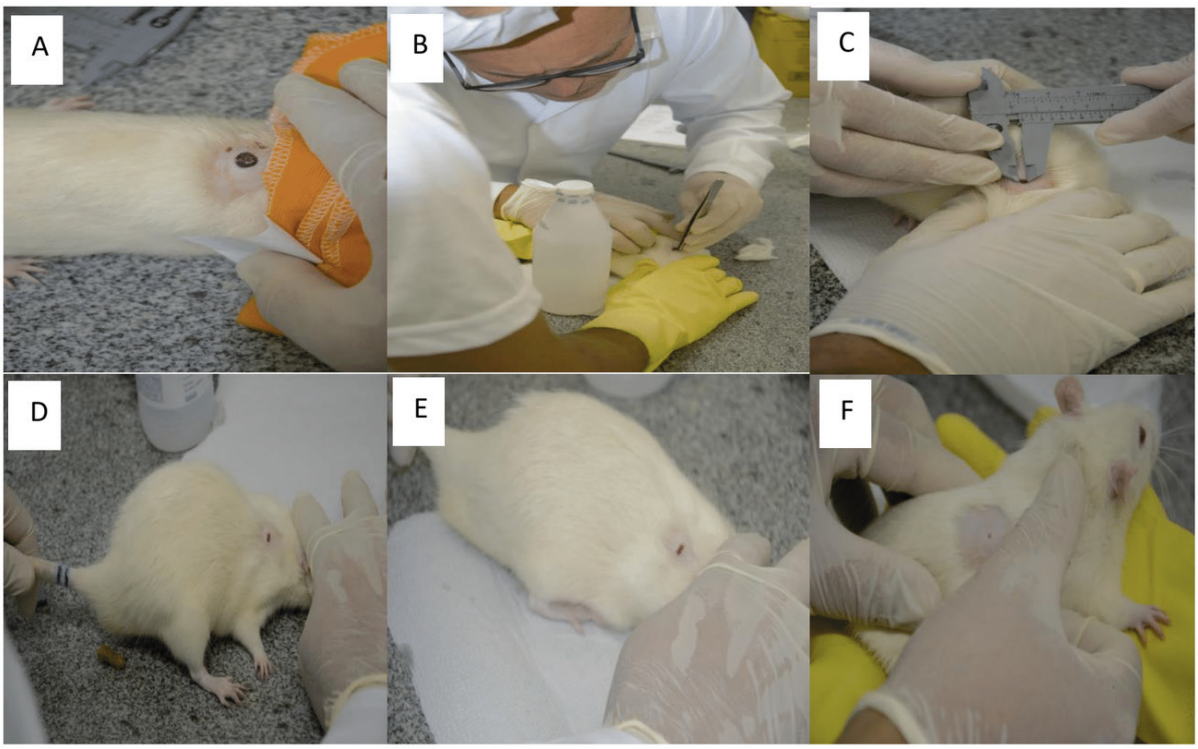

Figure 3 - Macroscopic healing progress and wound measurement

Source: Own collection, 2022. *A: start of healing; B: removal of dirt; C: measurement of the area; D: macroscopic analysis; E: phlogistic signs; F: tissue reconstitution.

For data analysis, absolute and percentage distributions were obtained (descriptive statistics techniques) and the F-test (ANOVA) with LSD (Least Significant Differences) paired comparisons, with a significance level (alpha) of 0.05.

The data was entered into spreadsheets and analyzed using Microsoft Excel analysis tools.

RESULTS AND DISCUSSION

The standards relating to the macroscopic appearance of the wound and its contraction were assessed daily, after the first 24 hours of the surgical procedure, and until the wounds had completely healed, a process that lasted up to 12 days.

The dressings on the four groups of guinea pigs were done daily, and the bench used throughout the procedure was first antiseptically cleaned. The rats were placed one at a time and the lesion was irrigated with 0.9% saline solution to remove any dirt. After the initial cleaning, the gel was applied to the entire length of the lesion, using an individual spatula per sample unit, in order to avoid possible contamination. Macroscopic evaluations of the lesions were carried out while the dressings were being applied. The area was measured daily using a caliper.

The wounds were assessed from a clinical point of view, showing the following phlogistic signs: edema, hyperemia, crust, exudate, bleeding bottom, necrotic edge, contraction, as well as measuring the area using a caliper.

At the end of the "in vivo" experiment, the animals were euthanized in accordance with CONCEA Resolution No. 37 of February 15, 2018, using an overdose of the combination of dissociative anesthetics (ketamine 3x the anesthetic dose of 100mg/kg corresponding to 300mg/kg) and Alpha-2 adrenoreceptor agonists (xylazine 3x the anesthetic dose of 10mg/kg corresponding to 30mg/kg), both intraperitoneally.

In group 1 (spontaneous healing) it was found that the wound healed completely on the 7th day for R1 and on the 11th day for R2, R3 and R4, as shown in Table 02 and Figure 04.

GROUP 1: spontaneous healing SAMPLES (measured in square mm)					
Interval in days	**R1**	**R2**	**R3**	**R4**	**Average**
Day 0 (surgery)	36	42	42	42	40,5
Day 1	36	42	42	42	40,5
Day 2	36	42	42	42	40,5
Day 3	30	35	36	36	34,25
Day 4	25	35	36	36	33
Day 5	18	25	25	20	22
Day 6	9	15	20	16	15
Day 7	0	12	16	12	10
Day 8	0	12	12	9	8,25
Day 9	0	9	12	6	6,75
Day 10	0	4	6	4	3,5
Day 11	0	0	0	0	0
Day 12	0	0	0	0	0

Table 2 - Evaluation of spontaneous healing in group 1

Source: survey data, 2022.

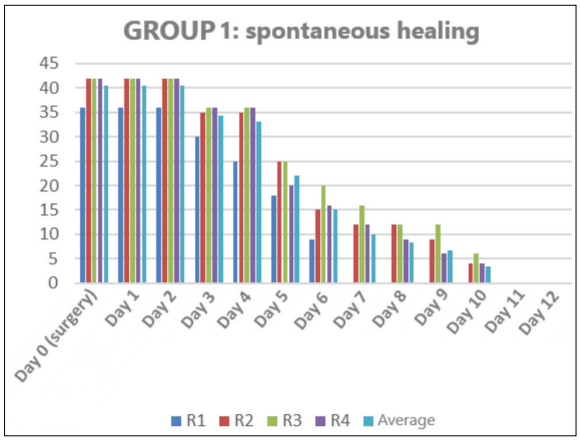

Figure 4 - Evaluation of spontaneous healing in group 1**Source:** survey data, 2022.

In group 2 (placebo), complete wound healing occurred on the 8th day for R1, on the 12th day for R2, and on the 10th day for R3 and R4, as shown in Table 03 and Figure 05.

GROUP 2: placebo					
SAMPLES (measured in square mm)					
Interval in days	**R1**	**R2**	**R3**	**R4**	**Average**
Day 0 (surgery)	42	42	40	48	43
Day 1	42	42	40	48	43
Day 2	42	35	35	35	36,75
Day 3	40	35	35	30	35
Day 4	36	35	24	20	28,75
Day 5	20	20	20	16	19
Day 6	12	16	12	12	13
Day 7	12	16	9	9	11,5
Day 8	0	12	6	6	6
Day 9	0	9	4	4	4,25
Day 10	0	6	0	0	1,5
Day 11	0	4	0	0	1
Day 12	0	0	0	0	0

Table 3 - Evaluation of healing in group 2.

Source: survey data, 2022.

GROUP 3: 25% gel					
SAMPLES (measured in square mm)					
Interval in days	**R1**	**R2**	**R3**	**R4**	**Average**
Day 0 (surgery)	48	42	42	45	44,25
Day 1	48	42	42	45	44,25
Day 2	40	36	36	35	36,75
Day 3	36	30	28	25	29,75
Day 4	30	30	20	20	25
Day 5	30	20	16	12	19,5
Day 6	25	16	12	9	15,5
Day 7	16	9	6	6	9,25
Day 8	6	6	0	0	3
Day 9	0	0	0	0	0
Day 10	0	0	0	0	0
Day 11	0	0	0	0	0
Day 12	0	0	0	0	0

Table 4 - Evaluation of healing in group 3.

Source: survey data, 2022.

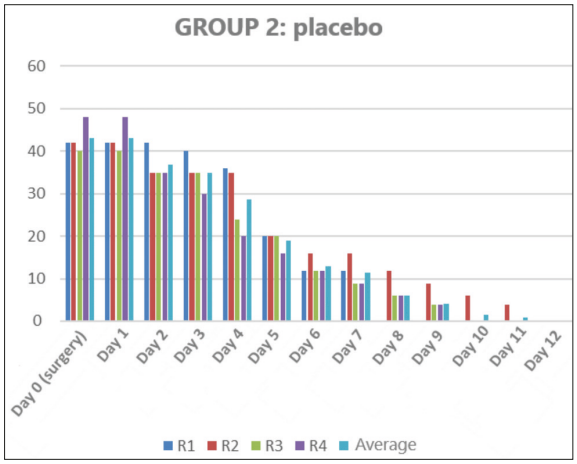

Figure 5 - Evaluation of healing in group 2.

Source: survey data, 2022.

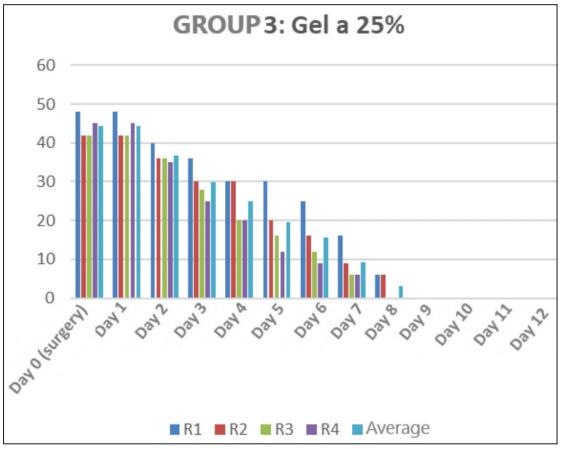

Figure 6 - Evaluation of healing in group 3.

Source: survey data, 2022.

In group 3, the 25% gel was used. In this group, complete wound healing occurred on the 9th day for R1 and R2, and on the 8th day for R3 and R4, as shown in Table 04 and Figure 06.

In group 4, the 50% gel was used. In this group, complete wound healing occurred on the 8th day for R1 and on the 7th day for R2, R3 and R4, as shown in Table 05 and Figure 07.

GROUP 4: 50% gel SAMPLES (measured in square mm)					
Interval in days	**R1**	**R2**	**R3**	**R4**	**Average**
Day 0 (surgery)	48	42	42	42	43,5
Day 1	42	35	40	40	39,25
Day 2	35	30	25	36	31,5
Day 3	35	20	20	20	23,75
Day 4	30	16	16	16	19,5
Day 5	25	12	12	9	14,5
Day 6	16	6	6	4	8
Day 7	8	0	0	0	2
Day 8	0	0	0	0	0
Day 9	0	0	0	0	0
Day 10	0	0	0	0	0
Day 11	0	0	0	0	0
Day 12	0	0	0	0	0

Table 5 - Evaluation of healing in group 4.

Source: survey data, 2022.

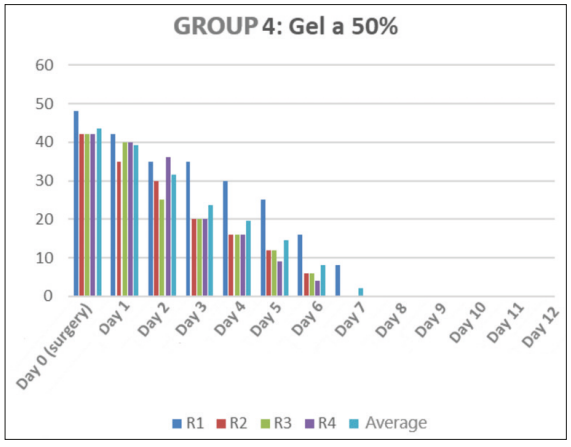

Figure 7 - Evaluation of healing in group 4.

Source: survey data, 2022.

The data recorded was subjected to statistical treatment, an absolute mean was obtained and the F-test (ANOVA) was carried out with LSD (Least Significant Differences) paired comparisons, with a significance level (alpha) of 0.05, as shown in Table 06.

Comparison between the means (mm) of the wounds				
	Control	Placebo	Gel 25%	Gel 50%
Day 0	40,5	43	44,25	43,5
Day 1	40,5	43	44,25	39,25
Day 2	40,5	36,75	36,75	31,5
Day 3	34,25	35	29,75	23,75
Day 4	33	28,75	25	19,5
Day 5	22	19	19,5	14,5
Day 6	15	13	15,5	8
Day 7	10	11,5	9,25	2
Day 8	8,25	6	3	0
Day 9	6,75	4,25	0	0
Day 10	3,5	1,5	0	0
Day 11	0	1	0	0
Day 12	0	0	0	0

Table 6 - Comparison between the means (mm) of the wounds.

Source: survey data, 2022.

The F-test (ANOVA) showed no statistically significant difference between the treatments applied (Tables 07, 08 and 09), although it was possible to observe "in vivo" that the experimental wounds healed more quickly.

F-test: two samples for variances		
	Control	*Placebo*
Average	19,5576923	18,67308
Variance	262,095353	273,8998
Observations	13	13
gl	12	12
F	0,95690218	
P(F<=f) one-tailed	0,47021494	
One-tailed critical F	0,37221253	

Table 7 - F-test (ANOVA) for the control and placebo groups

Source: survey data, 2022.

F-test: two samples for variances		
	Control	Gel 25%
Average	19,5576923	17,48077
Variance	262,095353	293,2756
Observations	13	13
gl	12	12
F	0,89368265	
P(F<=f) one-tailed	0,42440705	
One-tailed critical F	0,37221253	

Table 8 - F-test (ANOVA) for the 25% gel control groups

Source: survey data, 2022.

F-test: two samples for variances		
	Control	Gel 50%
Average	19,55769231	14
Variance	262,0953526	258,3020833
Observations	13	13
gl	12	12
F	1,014685399	
P(F<=f) one-tailed	0,490134858	
One-tailed critical F	2,686637112	

Table 9 - F-test (ANOVA) for the 50% gel control groups

Source: survey data, 2022.

From the p-values obtained between the control and placebo groups, it can be inferred that the presence of the gel without an active ingredient does not cause a significant change in the healing pattern, and that the smaller difference in days until healing shown in the 25% gel and 50% gel groups is not due to the gel film without an active ingredient.

The macroscopic evaluation used is of fundamental importance in monitoring the scarring and healing process, since in clinical practice it is the most common means available, given that in human trials it is not possible to obtain the histological specimen in order to verify the different scarring phenomena at a histological level, although the possible use of techniques to analyze collagenization, quantify and identify cellular scarring alterations is relevant.

A reduction in the lesions could be seen in the 50% gel group from the third day onwards, starting from the edges of the lesion towards the bed. The evolution of the healing process can be seen in Figure 08.

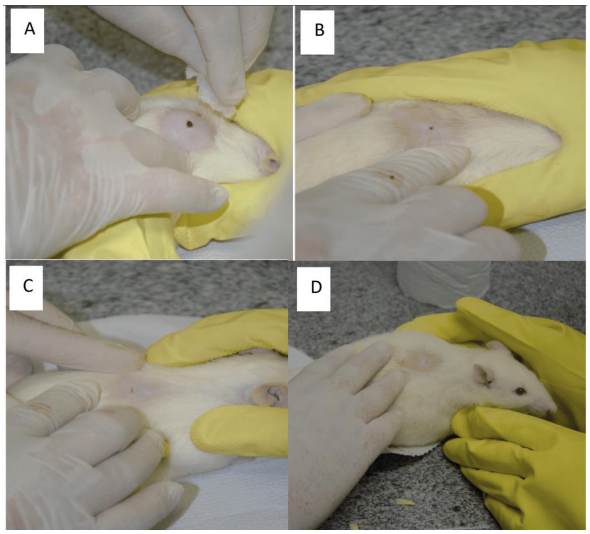

Figure 8 - Healing progress with the use of 50% gel.

Source: Own collection, 2022. *A: hygienization of the wound; B: absence of a necrotic edge; C: absence of a bleeding bottom; D: healing.

The healing process involves a series of complex and dynamic cellular and biochemical events. With regard to the pathophysiology of tissue repair, skin wounds heal in four phases or periods: hemostasis, inflammation, proliferation and remodeling. In cases of chronic wounds, this natural progression is affected and the repair process is absent or slowed down (WILLIAMSON; HARDING, 2014; SILVA; SILVA, 2021).

During the initial phases of the healing process there is an increase in the local concentration of growth factors, where cytokines rise, the processes of vascular regeneration and fibroplasia intensify through angiogenesis, migration and fibroblast proliferation, forming a tissue rich in vascular and cellular elements and the production of granulation tissue, which gradually spreads and fills the void resulting from the eliminated tissues. In

the early stages of the scarring process, fibronectin and hyaluronic acid are deposited, providing a favorable atmosphere for cell movement. The progress of the process modifies the locally synthesized substrates, which become composed of proteoglycans that anchor the cells, benefiting the change in cell phenotype, not to mention that as new layers of granulation tissue are formed, the older, deeply situated layers lose their richness in vessels, and fibroblasts and collagen bundles begin to predominate (BALBINO et al., 2015).

Wound contraction is mediated by cytokines and in particular by Transforming Growth Factor (TGF). Through contraction, the size of the wound decreases substantially, this is primarily caused by the fibroblasts found in the granulation tissue and many of them differentiate into a phenotype, which are referred to as myofibroblasts (O' LEARY, 2002). The occurrence of slower wound contraction in the control group should be considered and may provide macroscopic evidence of the accelerating action of *A. Occidentale L*, possibly due to the stimulation of myofibroblasts (RESENDE; PEREIRA; CASTRO, 2005).

In view of the data presented, it can be seen that the 50% gel had a significant effect on the healing process, since in just eight days all the guinea pigs in group 4 had recovered from the injury, while those who didn't use the active ingredient, or used it at a concentration of 25%, took an average of 10 to 12 days to complete this process.

Despite the fact that wound contraction was accelerated and the wounds healed in less time when *A. Occidentale L-based* products were applied, the small difference in the performance of the 25% Gel and 50% Gel groups leads us to believe that increasing the amount of freeze-dried product to increase the concentration of the active ingredient in the gel product would not lead to better therapeutic performance and could cause inconveniences in the presentation of the product and its rheological properties, negatively interfering with its application on the wound.

During the course of the study, it was possible to verify the absence of infection in all the sample units, which proves that all the antisepsis precautions were carried out properly. In order to assess the performance of the product tested against infectious episodes, it would be necessary to carry out "in vitro" antimicrobial activity experiments and a subsequent "in vivo" study with prior induction of an infectious condition in the surgical wound to be treated.

The plant species *Anacardium occidentale L.* has been used in scientific studies and has shown satisfactory therapeutic results, potentiating the healing process in preliminary studies (MELO-CAVALCANTE, 2018). Several compounds in this plant have been shown to have anti-inflammatory potential, such as the presence of phenolics, tannins and flavonoids (SERAFINI, 2019).

Vasconcelos et al., 2015, emphasized that flavonoids have the ability to act on the immune system, making them a promising therapeutic alternative for the treatment of inflammatory processes, since the healing process is a complex event involving various vascular, cellular and biochemical mechanisms, which are obviously dependent on the available nutritional substrates, such as vitamin C, which is directly related to collagen synthesis.

The results found in this study corroborate Vasconcelos et al. (2018), Vanderlinde et al. (2019), Melo-Cavalcante et al. (2018), who concluded in their research that the extract based on the bark of *A.* occidentale L. has pro-inflammatory mediators, which favor tissue restoration (granulation tissue and re-epithelialization), due to its anti-inflammatory effects. *occidentale L bark extract* has pro-inflammatory mediators, which favour tissue restoration (granulation tissue and re-epithelialization),

due to its anti-inflammatory, healing and antibacterial effects, promoting positive results in tissue healing and, when associated with electrophysical resources, it is able to stimulate fibrinolytic activity, accelerating the formation of granulation tissue and the biosynthesis of collagen and elastin, achieving a more effective repair (OLIVEIRA, 2015).

Given the complexity of the cellular and biochemical events that involve the healing process and the factors that can interfere with it, the choice of treatment and the type of covering to be applied must be made taking into account all the characteristics of the wound. In this way, the application of the dressing, which in this case was the gel incorporating the active ingredient based on *A. occidentale L.*, proved to be an effective therapeutic tool, promoting an increase in the speed of healing of the injured tissue.

CONCLUSION

Based on the methods and conditions used in this study, the results lead us to conclude that the *A. occidentale L.* gel accelerated the skin healing process "in vivo". It promoted rapid recovery of the lesion, so it is speculated that its extract and its possible isolated pro-angiogenic components have potential value for pharmaceutical application in the treatment of wounds in humans.

In order to elucidate the plant's inflammatory, antimicrobial, antioxidant and healing role as an active ingredient in the form of a lyophilized extract, it is necessary to expand scientific research in order to confirm it as a potential and promising alternative for wound treatments.

REFERENCES

BALBINO, C.A.; PEDREIRA, L.M.; CURI, R. Mecanismos envolvidos na cicatrização: uma revisão. **Revista Brasileira de Ciências Farmacêuticas**, v. 41, p. 27-51, 2015.

FERNANDES, M. R. V.; DIAS, A. L. T.; CARVALHO, R. R.; SOUZA, C. R. F.; OLIVEIRA, W. P. Antioxidant and antimicrobial activities of Psidium guajava L. spray dried extracts. **Industrial Crops and Products**, v. 60, p. 39-44, 2014.

FERREIRA, A. O. **Formas farmacêuticas semi-sólidas**. São Paulo: ANFARMAG, 2006. p. 2-3.

FILIZOLA, B. C. S.; BONESSO, M. **Boas Práticas de Manejo para o Extrativismo Sustentável de Cascas**. Brasília: Instituto Sociedade, População e Natureza. 2015. 108 p.

FNFB. **Formulário Nacional Da Farmacopeia Brasileira**. 2ª edição - Revisão, 2012. . Disponível em: <FNFB%202_Revisao_2_COFAR_setembro_2012_atual.pdf>. Acesso em: 13 de setembro, 2020.

MELO-CAVALCANTE, A.A.A.; PICADA J. N.; RUBENSAM G.; HENRIQUES. J .A .P. Antimutagenic activity of cashew apple (Anacardium occidentale Sapindales, Anacardiaceae) fresh juice and processed juice (cajuína) against methyl methanesulfonate, 4-nitroquinoline N-oxide and benzo[a]pyrene. **Genetics and Molecular Biology**. n. 31, v. 3, p. 759-766, 2018.

O' LEARY, R; WOOD, E.J; GUILLOU, P.J. Pathological Scarring: Strategic Interventions. **Eur J Surg**. v. 168, p. 523-534, 2002.

OLIVEIRA P.D.D. et al. Effect of low-inten-sity pulsed ultrasound therapy on a fibroblasts cell culture. **Fisioterapia e Pesquisa**. n. 22, v. 2, p. 112-118, 2015.

RESENDE, M.A.; PEREIRA, L.S; CASTRO, M.S.A. Proposta de um modelo teórico de intervenção fitoterapêutica no controle da dor e inflamação. **Fitoterapia Brasil**. v. 6, n. 5, p. 368-371, set./out. 2005.

SERAFINI, M.; PELUSO, I.; RAGUZZINI, A. **Flavonoids as anti-inflammatory agents. Proceedings of the Nutrition Society**. n . 69, p. 273–8, 2019.

SILVA, S. A. S.; SILVA, E. C. Tratamento de feridas complexas e o uso de coberturas antimicrobianas. **Revista Feridas**, n. 46, p. 1663-1663, 2021.

VASCONCELOS, M. S. et al., Anti-inflammatory and wound healing potential of cashew apple juice (Anacardium occidentale L.) in mice. **Experimental Biology And Medicine**. 2015; 240(12): 1648-1655.

VANDERLINDE, F. A.; LANDIM H. F.; COSTA, E. A.; GALDINO, P. M.; MACIEL, M. A. M.; ANJOS, G. C.; MALVAR, D.C.; CÔRTES W. S.; ROCHA F. F. Evaluation of the antinociceptive and anti-inflammatory effects of the acetone extract from Anacardium occi-dentale L. Brazilian. **Brazilian Journal of Pharmaceutical Sciences**. 2019; 45: 437–42.

WILLIAMSON, D.; HARDING. K. **Wound Healing**. Medicine, v. 32, p. 12, 2014.