

Original Article

Healing of leprosy-associated chronic plantar wounds with a novel biomembrane containing latex proteins from *Calotropis procera*

Cicatrização de feridas plantares crônicas associadas à hanseníase com uma nova biomembrana contendo proteínas de látex de *Calotropis procera*

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Abstract

Pre-clinical assays demonstrated that a 1% polyvinyl alcohol biomembrane containing latex proteins (10%) from the medicinal plant *Calotropis procera* was biocompatible and stimulated healing of incisional and excisional wounds in murine models, and the mechanistic aspects were established. The efficacy of the biomembrane (BioMemCpLP) to promote healing of chronic ulcers in leprosy patients was investigated. The study started with 28 volunteers. Five were excluded later due to different disconformities. Ulcers from 15 patients were continuously treated with BioMemCpLP for 56 days. Five patients were treated only with silver sulfadiazine and three patients received plain hydrocolloid wound dressings with high absorption capacity. In all cases, wound dressings were renewed three times a week for 56 days and ulcers were evaluated weekly for contraction and healing progress. The extent of the healed area in the ulcers treated with BioMemCpLP was greater than in the control groups. Approximately 88% of ulcers treated with BioMemCpLP were fully healed before day 56, against 6% in both control groups. This result was not correlated with age/gender, duration or location of ulcers, deformity or whether or not the patient was cured of leprosy. The results showed that BioMemCpLP was beneficial for treatment of ulcers suffered by leprosy patients without noticeable side effects.

Keywords: *Calotropis procera*, dressing, Hanseniasis, latex.

Resumo

Ensaíos pré-clínicos demonstraram que uma biomembrana composta de álcool polivinílico a 1%, contendo proteínas de látex (10%) obtidas da planta medicinal *Calotropis procera* (Aiton) era biocompatível e estimulava a cicatrização de feridas incisionais e excisionais em modelos murinos, e aspectos mecanísticos foram estabelecidos. No estudo atual, foi investigada a eficácia da biomembrana (BioMemCpLP) em promover a cicatrização de úlceras crônicas em pacientes acometidos de hanseníase. O estudo foi iniciado com 28 voluntários. Cinco foram excluídos, posteriormente, por diferentes desconformidades. Úlceras de 15 pacientes foram tratadas continuamente com BioMemCpLP durante 56 dias. Outros cinco pacientes foram tratados apenas com sulfadiazina de prata e mais três pacientes receberam curativos simples de hidrocoloide com alta capacidade de absorção. Em todos os casos, os curativos foram renovados três vezes por semana e as úlceras foram avaliadas semanalmente quanto à contração e ao progresso da cicatrização, durante 56 dias. A extensão da área cicatrizada, nas úlceras tratadas com BioMemCpLP, foi maior do que nos dois grupos controles. Aproximadamente 88% das úlceras tratadas com BioMemCpLP foram totalmente curadas, antes do dia 56 de tratamento, contra 6% em ambos os grupos de controle. Esse resultado não foi correlacionado com idade/sexo, tempo de lesão ou localização das úlceras, deformidade ou se o paciente alcançou ou não a cura da hanseníase. Os resultados mostraram que a BioMemCpLP foi benéfica no tratamento de úlceras sofridas por pacientes com hanseníase, sem efeitos colaterais perceptíveis.

Palavras-chave: *Calotropis procera*, curativo, Hanseníase, látex.

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1. Introduction

Leprosy is a chronic infection caused by *Mycobacterium leprae*, and Brazil is among the countries with the highest incidence of the disease (WHO, 2023).

Leprosy patients can develop plantar or trophic skin ulcers due to peripheral nerve damage, which can be infected by opportunistic bacteria (Silva et al., 2015). The pathogenesis of ulcers is mainly related to an abnormal increase of skin pressure in the affected area. In addition to numbness and tingling, in the lower limbs it causes incapacitating deformities, promoting permanent tissue damage (Chan et al., 2019). Treatment of chronic leprosy wounds is an expensive and time-consuming process. Therefore, leprosy causes a heavy economic burden on affected people, besides generating social stigma, impairing the patient's quality of life (Sivasubramanian et al., 2018; Premarathna et al., 2019; Suryawati et al., 2019).

The immunophysiology of wound healing requires recruitment steps of different specialized cells, such as innate immune cells, endothelial cells, keratinocytes and fibroblasts (Souza et al., 2023). These cells promote defense and tissue remodeling, so healing is achieved when newly synthesized collagen is added, and the inflammatory process ceases. However, in plantar ulcers, healing does not progress adequately due to repeated impacts on the injured area, which increases the size of lesions and promotes chronic inflammation. Due to opportunistic bacterial colonization, prophylaxis of these chronic ulcers involves the use of broad-spectrum antibiotics to prevent infections while healing is in progress. However, leprosy ulcers can remain even after the disease is controlled.

Treatments of plantar ulcers include dressings, ointments and creams containing various medications to aid healing, regardless of etiology. Leprosy especially affects people living in poor regions of India, Africa and Brazil, where it is recognized as a neglected disease (WHO, <https://www.who.int/news-room/fact-sheets/detail/leprosy#Scope%20of%20The%20Problem>). To access modern pharmaceutical products can be a challenge. In these countries, herbal medicines are usually the first or the only option for the treatment of all clinical adversities resulting from leprosy.

Phytomedicines have been found to be safe alternatives to expensive pharmaceutical products, as well as composing a storehouse for bioprospecting to find new drugs (Hmood et al., 2022). In this regard, many reliable studies have reported pharmacological activities of secondary metabolites and proteins contained in the latex of the medicinal plant *Calotropis procera* (Awaad et al., 2018; Wadhwani et al., 2021; Tavares et al., 2021; Tavares et al., 2022). Furthermore, this plant's latex proteins were shown to be biocompatible (Nunes et al., 2021) and able to improve healing of incisional and excisional wounds (Figueiredo et al., 2014; Ramos et al., 2016; Vasconcelos et al., 2018). A polyvinyl alcohol biomembrane containing these laticifer proteins prompted mast cell degranulation, macrophage activation, neutrophil recruitment, and release of inflammatory mediators such as nitric oxide, TNF- α and IL1- β in a mouse model of wound healing. These inflammatory stimuli accelerated the healing

process by increasing fibroplasia and collagenosis, leading to complete closure of the wounds (Figueiredo et al., 2014). This study aimed to evaluate whether a novel biomembrane containing *C. procera* latex proteins could promote healing of chronic ulcers in clinical leprosy patients.

2. Materials and Methods

2.1. Plant material

Calotropis procera (Aiton) specimens used to obtain latex were located in the city of Fortaleza, capital of the state of Ceará, Brazil. The geographic coordinates of the field of wild plants are 3°43'6" South; 38°32'36" West (Silveira et al., 2021). A voucher prepared with vegetative and reproductive parts of a specimen of *C. procera* (English common name: sodom apple) was deposited in the Prisco Bezerra Herbarium of Federal University of Ceará (no. 32663). To access the plant material and perform the study, the concerning data was fulfilled at the SisGen online platform (<https://sisgen.gov.br/paginas/login.aspx>) and registered with the number A689147.

2.2. Latex extraction protein isolation

The latex was drained after cutting branches and storing the volume released in plastic tubes (50 ml) and mixing with an equal volume of distilled water and preserved in sealed tubes. The samples were centrifuged at 10,000 x g (4 °C, 20 min). The precipitated material was discarded and the remaining latex solution was dialyzed in distilled water (10 °C) until release of small molecules (< 8 KDa) and total precipitation of residual water-insoluble matter, which was further removed by a similar centrifugation step (Silveira et al., 2021). The latex protein fraction recovered (CpLP) was freeze dried and stored at 25 °C until use.

2.3. Biomembrane preparation

CpLP fraction was solubilized in a 1% w/v aqueous polyvinyl alcohol (PVA) solution to yield a final concentration of 10% CpLP. This mixture was added to sterile 90x15 mm Petri dishes. The dishes were placed in an oven at 50 °C for 24 hours. The membranes formed at the bottom of the dishes were called BioMemCpLP. These biomembranes were placed in packs of surgical grade and exposed to UV light for 15 minutes for sterilization. Then they were stored at 25 °C until use. The flowchart in Figure 1 depicts the BioMemCpLP preparation.

2.4. Study design

This clinical study was a randomized controlled trial. Patients with one or more plantar ulcers were recruited at specialized health care units for the treatment of leprosy located in Fortaleza, capital of the state of Ceará, Brazil. Patients who agreed to participate in the study signed a consent form which contained the entire established protocol and complementary information. These forms are available on reasonable request. This trial was conducted in compliance with applicable regulatory requirements of the Declaration of Helsinki and good clinical practices.

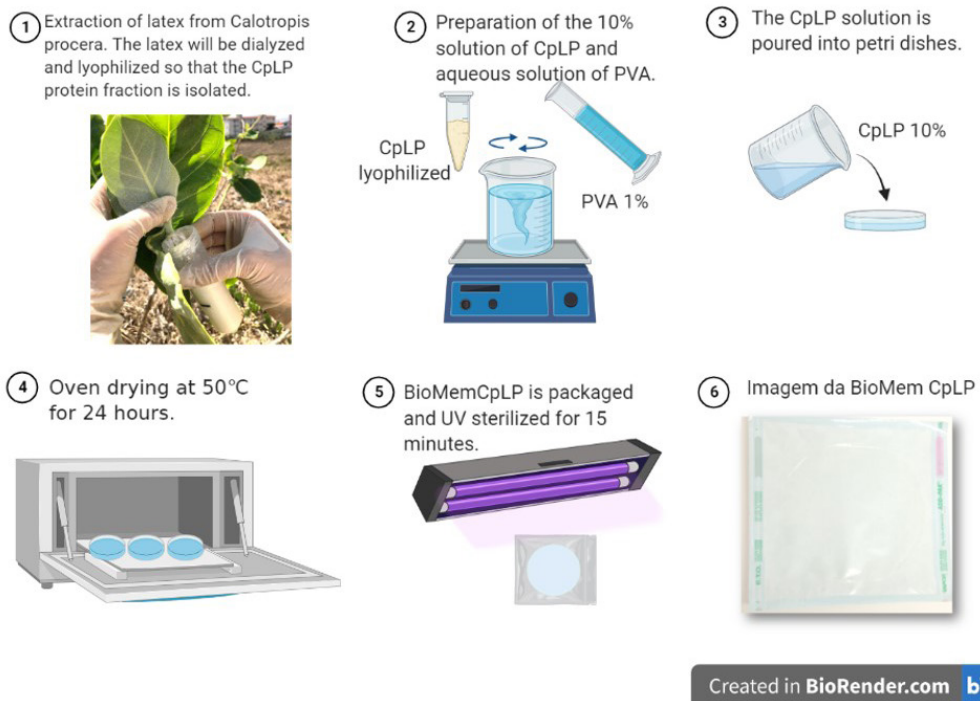


Figure 1. Latex extraction, processing and biomembrane preparation. Biomembrane was prepared, sterilized and stored at 25 °C until use.

The study was authorized by the Research Ethics Committee of Federal University of Ceará –CEP/UFC/PROPESQ (License number: 2.072.752.) and registered with “Plataforma Brasil” of the Ministry of Health.

2.5. Sample size

Participants aged over 18 years and with a previous diagnosis of leprosy with at least one plantar ulcer smaller than 24 cm² were included in the study. Volunteers with severe comorbidities as well as patients with hypersensitivity to the components of the formula (as proven by the patch test) were excluded. After screening, 28 patients were included in the study. However, five patients were excluded afterwards due to different disconformities such as clinical worsening (one patient using hydrocolloid dressing and four that did not return to conclude the treatment). The remaining 23 participants, with a total of 32 ulcers, were evaluated for 56 days.

Plantar ulcers were treated with the BioMemCpLP or silver sulfadiazine (positive control), standardized antibiotic treatment in Brazilian health care units for eight weeks or until complete wound healing. A commercial hydrocolloid product without bioactive substances was used as positive control. Patients of all groups with worsening of clinical symptoms were withdrawn from the study (Ulcers with necrosis, fibrin, intense exudate, foul odor). The overall scheme describing the groups is depicted in Figure 2.

Wound dressings were renewed three times a week on alternating days and ulcers were evaluated weekly. Contraction and healing progress were recorded by photographic images. A caliper was used to measure

the diameter of skin lesions and calculate the ulcer area (mm²). The rate of ulcer healing (RUH) corresponded to the difference between the initial area (IA) and the final area (FA) divided by the initial area, multiplied by 100:

$$RUH = \frac{(IA - FA)}{IA} \times 100 \quad (1)$$

At each dressing-change, wounds were clinically evaluated according to the following criteria: appearance of the wound bed: () healthy granulation () friable granulation () fibrin () necrosis () slough () epithelialization; Wound bed staining: () whitish () straw yellow () citrine yellow () pinkish () reddish () greenish () grayish () blackish/black; Exudate: () absent () present: () serous () bloody () sero-sanguinous () purulent () sero-purulent () fibrinous.

2.6. Statistics and outcomes

The RUH was measured in all groups after eight weeks and compared to measurements recorded on the first day of the trial. The mean time for complete ulcer healing was also recorded. The results were expressed as absolute and relative percentage frequencies and compared using Fisher's exact test or Pearson's chi-square test. Wound areas and percentages of ulcer healing were expressed as mean and standard error, submitted to the Kolmogorov-Smirnov normality test, and analyzed using the Friedman/Dunn test (nonparametric data). Kaplan-Meier curves were plotted to estimate the average time for total healing of the wounds, which were analyzed using the Mantel-Cox log-rank test. Additionally, the chi-square test and multinomial logistic

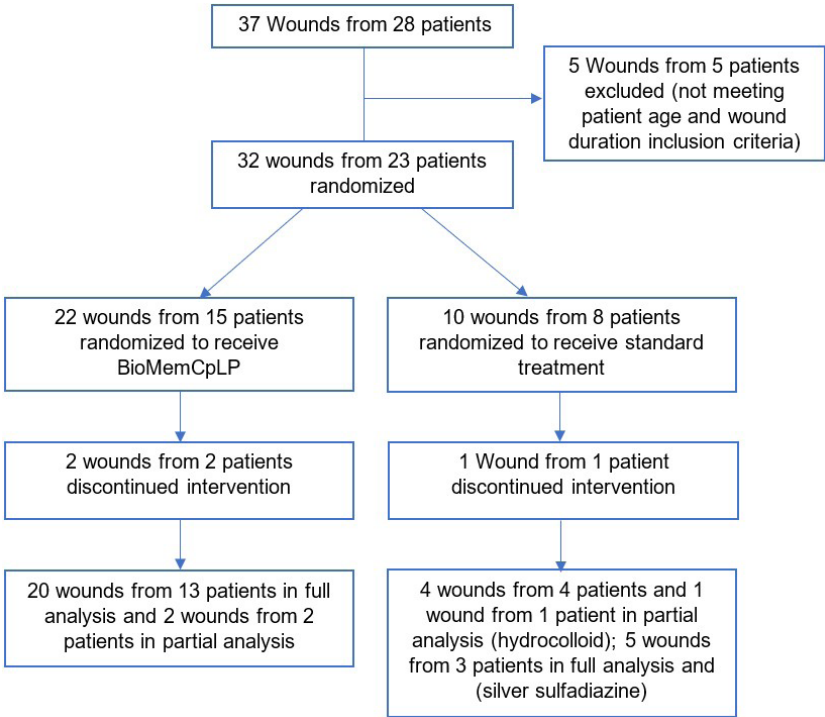


Figure 2. Study flowchart.

regression model were used to analyze unforeseen external factors that may have influenced the wound healing. A confidence interval of 95% was set.

3. Results

Table 1 shows the descriptive characteristics of participants included in the study. The sociodemographic characteristics such as gender and age were similar among all groups. The number of participants still infected (patients still receiving oral antibiotics against *Mycobacterium leprae*) and cured (patients that had completed the oral antibiotics protocol) of leprosy per group was statistically different ($p=0.036$). However, data analysis was not impaired. The statistical evaluation suggested the beneficial effect of the wound treatments were not associated with cured or still treated leprosy.

Figures 3-5 show ulcers of leprosy patients treated with different agents. The absorbent dressing containing a hydrocolloid product, without antibiotics, successfully helped achieve complete healing of smaller ulcers but did not repeat this performance in the large ones (Figure 3). This commercial product served as reference control to evaluate the efficiency of BioMemCpLP and did not produce any adverse effect on wounds. In all cases, the ulcers treated with the hydrocolloid product were clean, without exudate or signs of infection (ulcers with necrosis, fibrin, intense exudate, foul odor) (Figure 3). In the second group, patients that had ulcers treated with silver sulfadiazine (standard antibiotic) showed healing progress, and smaller ulcers reached 100% healing (Figure 4). However, the antibiotic

alone did not modify the status of bigger wounds at the end of the treatment.

Figure 5 shows the performance BioMemCpLP for treatment of ulcers. The biomembrane promoted complete healing of smaller ulcers and reduced the size of larger ones without any adverse effect recorded during the study. It should be mentioned that these patients were not treated with antibiotics. In addition, the clinical aspects of the wounds resembled those of patients treated with the hydrocolloid product.

A comparison of the clinical progression of wound healing was performed among the groups (Figure 6). It was clear that the BioMemCpLP-treated group had a significant reduction in the mean ulcer area from the second week onwards ($p<0.001$), with an earlier healing process than the treatments with hydrocolloid ($p=0.072$) or silver sulfadiazine ($p=0.077$).

We confirmed through analysis of Kaplan-Meier curves that clinical evolution of leprosy wounds was greater in patients treated with BioMemCpLP (Figure 7). Conversely, patients treated with the hydrocolloid product or silver sulfadiazine exhibited similar healing progress ($p=0.048$) each other and worse compared to the BioMemCpLP.

There was no correlation between specific participant characteristics such as gender, age, location or duration of ulcers, deformities, and general clinical status of patients with overall healing performance per treatment. However, the number of ulcers treated with BioMemCpLP that reached complete healing was greater than in patients treated with the hydrocolloid product or silver sulfadiazine ($p < 0.05$) (Table 2).

Table 1. Demographic characterization of the sample of patients with leprosy lesions treated with BioMemCpLP, hydrocolloid (Curatec) and silver sulfadiazine.

	Total	Group			
	Ulcers	BioMemCpLP	Hydrocolloid	Silver sulfadiazine	<i>p-value</i>
Gender					
Female (n,%)	6 (18.8%)	4 (18.2%)	2 (40.0%)	0 (0.0%)	0.267
Male	26 (81.3%)	18 (81.8%)	3 (60.0%)	5 (100.0%)	
Age					
≤ 60	19 (59.4%)	13 (59.1%)	2 (40.0%)	4 (80.0%)	0.436
> 60	13 (40.6%)	9 (40.9%)	3 (60.0%)	1 (20.0%)	
Cured of leprosy					
No	3 (9.4%)	1 (4.5%)	2 (40.0%)*	0 (0.0%)	0.036
Yes	29 (90.6%)	21 (95.5%)*	3 (60.0%)	5 (100.0%)*	
Ulcer age					
≤ 2 years	17 (53.1%)	13 (59.1%)	2 (40.0%)	2 (40.0%)	0.605
>2 years	15 (46.9%)	9 (40.9%)	3 (60.0%)	3 (60.0%)	
Ulcer location					
Forefoot	17 (53.1%)	13 (59.1%)	2 (40.0%)	2 (40.0%)	0.601
Plant surface	10 (31.3%)	6 (27.3%)	1 (20.0%)	3 (60.0%)	
Instep	2 (6.3%)	1 (4.5%)	1 (20.0%)	0 (0.0%)	
Heel	2 (6.3%)	1 (4.5%)	1 (20.0%)	0 (0.0%)	
Malleolus	1 (3.1%)	1 (4.5%)	0 (.0%)	0 (0.0%)	
Deformity					
Yes	10 (31.3%)	5 (22.7%)	2 (40.0%)	3 (60.0%)	0.241
No	22 (68.8%)	17 (77.3%)	3 (60.0%)	2 (40.0%)	

*p<0,05, Fisher's exact test or Pearson's chi-square (n, %).

The multivariate analysis confirmed that leprosy wounds in patients treated with BioMemCpLP healed faster than in patients treated with hydrocolloid and silver sulfadiazine ($p=0.015$). This effect was also observed in more recent ulcers ($p=0.028$), which healed completely with use of BioMemCpLP (Table 3). The healing performance of this biomembrane was associated with *C. procera* latex proteins (CpLP).

4. Discussion

Leprosy is a neglected disease with high incidence in Brazil and India, where occurrence is strongly associated with poverty. Long-term treatment of the disease causes large economic impacts on affected families, due to income loss and unemployment. Patients with plantar ulcers face additional treatment challenges since these wounds are continuously exposed to impacts from locomotion and contact with unclean surfaces.

Leprosy wounds are commonly infected by opportunistic bacteria, and chronic ulcers can develop and persist even after the infection is cured by antibiotics. The wound

healing process is slow and pharmaceuticals available to treat wounds are expensive for poor people affected.

Calotropis procera is a shrub native to India and the Middle East used in local folk medicine (Pompelli et al., 2019). This plant is well adapted to tropical regions of the globe and is widely distributed in Brazil's Northeast region, where it is classified as an invasive species. *C. procera* is known to produce and store cardenolides that can be lethal to mammals after ingestion (Ramos et al., 2022). Nevertheless, therapeutic properties, such as anti-inflammatory and anti-diabetic ones, have been attributed to *C. procera* latex.

C. procera latex has a milky appearance and can be easily extracted after cutting/breaking leaf petioles. It is rich in bioactive secondary metabolites and macromolecules. The therapeutic potential of *C. procera* latex proteins has been demonstrated for treatment of various human ailments (Rangel et al., 2022). Previously, it was shown that the whole set of soluble latex proteins from *C. procera* was capable of protecting Swiss mice from lethal bacterial infection (Sousa et al., 2020) and of restoring the normal architecture of erythrocytes (Silva et al., 2019). These



Figure 3. Illustrative images of healing performance of patients that had plantar ulcers treated with hydrocolloid product. Area informed as (mm²); healing performance calculated as total reduced area at the end of the treatment and day zero, expressed in percent of healing contraction.

same proteins were incorporated in the biomembrane used in this study.

The healing potential of *C. procera* proteins was previously assayed in animal models and different aspects of its action mechanisms were discovered (Ramos et al., 2016). Similarly, the polyvinyl alcohol biomembrane used in the present study was chemically characterized and validated for efficacy and safety for testing in humans (Figueiredo et al., 2014).

This biomembrane was impregnated with *C. procera* latex proteins and called BioMemCpLP, and was used to promote healing, causing significant amelioration of leprosy ulcers that varied from total healing of small ulcers

to faster healing of the larger ones. In particular, a chronic ulcer existing longer than six years was totally healed after treatment with BioMemCpLP. None of participants treated with BioMemCpLP had worse clinical status during or after treatment.

The potential of latex fluids as sources of pro-healing compounds was also reported by Tonaco et al. (2018). They demonstrated the capacity of a proteolytic fraction obtained from the latex of *Vasconcellea cundinamarcensis* to promote better healing of diabetic foot ulcers. The active sample was presented as a 0.1% dressing formulated with Polivax. It was capable of healing ulcers after 16 weeks of treatment. Therefore, laticifer plants should be more

Day – 0
area – 6.28
Healing performance – 100%



Day – 30
area – 0.71



Day – 56
area – 0.0



Day – 0
area – 54.95
Healing performance – 89.28%



Day – 30
area – 56.91



Day – 56
area – 5.89



Figure 4. Illustrative images of healing performance of patients that had plantar ulcers treated with silver sulfadiazine (antibiotics). Area informed as (mm²); healing performance calculated as total reduced area at the end of the treatment and day zero, expressed in percent of healing contraction.

extensively investigated for the presence of healing compounds.

In Brazilian healthcare units, after the cleaning and disinfection protocol, leprosy ulcers are topically treated with silver sulfadiazine to prevent infection. However, retrospective data suggest that this antibiotic is not indicated for the treatment of larger ulcers due to lack of influence on the healing process. On the other hand, the benefits of hydrocolloid dressings are related to their great capacity to absorb the exudate fluids commonly leaked

from deep wounds, avoiding infections. The combined use of BioMemCpLP (or the hydrocolloid product) with silver sulfadiazine was not evaluated in this study, but could potentially improve wound healing performance in leprosy patients. This will be further investigated.

Although the mechanisms underlying the effect of BioMemCpLP on wound healing are not fully clear, previous studies have shown strong anti-inflammatory activity of *C. procera* latex proteins. These proteins do not have direct antibacterial activity, suggesting that an



Figure 5. Illustrative images of healing performance of patients that had plantar ulcers treated with BioMemCpLP (latex proteins as active agents). Area informed as (mm²); healing performance calculated as total reduced area at the end of the treatment and day zero, expressed in percent of healing contraction.

Table 2. Influence of clinical characteristics and treatment with biomembrane, hydrocolloid and silver sulfadiazine in patients with leprosy lesions.

	Complete wound healing		<i>p-Value</i>
	No	Yes	
Group			
BioMemCpLP	7 (46.7%)	15 (88.2%)*	0.041
Hydrocolloid	4 (26.7%)*	1 (5.9%)	
Silver sulfadiazine	4 (26.7%)*	1 (5.9%)	
Gender			
Female	2 (13.3%)	4 (23.5%)	0.659
Male	13 (86.7%)	13 (76.5%)	
Age			
≤ 60	7 (46.7%)	12 (70.6%)	0.280
>60	8 (53.3%)	5 (29.4%)	
Cured of leprosy			
No	1 (6.7%)	2 (11.8%)	1.000
Yes	14 (93.3%)	15 (88.2%)	
Ulcer age			
≤ 2 years	5 (33.3%)	12 (70.6%)	0.074
>2 years	10 (66.7%)	5 (29.4%)	
Ulcer location			
Forefoot	6 (40.0%)	11 (64.7%)	0.201
Plant surface	7 (46.7%)	3 (17.6%)	
Instep	1 (6.7%)	1 (5.9%)	
Heel	0 (.0%)	2 (11.8%)	
Malleolus	1 (6.7%)	0 (0.0%)	
Deformity			
Yes	4 (26.7%)	6 (35.3%)	0.712
No	11 (73.3%)	11 (64.7%)	

* $p < 0.05$, Fisher's exact test or Pearson's chi-square (n, %).

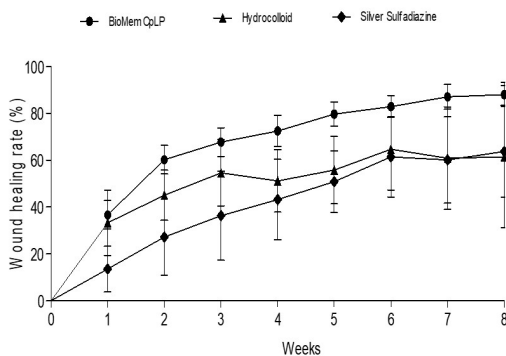


Figure 6. Clinical progression of leprosy lesions after treatment with biomembrane, hydrocolloid and silver sulfadiazine. * $p < 0.05$ versus week 0, Friedman/Dunn Test. The biomembrane-treated group showed a significant reduction in the mean ulcer area from the second week onwards ($p < 0.001$) and the groups treated with hydrocolloid ($p = 0.072$) and silver sulfadiazine ($p = 0.077$) showed no significant variation in this parameter.

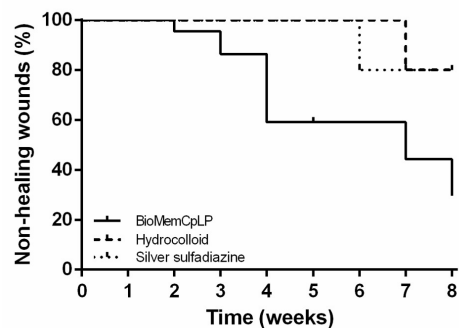


Figure 7. Kaplan Meier curves with clinical evolution of leprosy lesions after treatment with biomembrane, hydrocolloid and silver sulfadiazine. There was a significant reduction in the meantime of open wound in the biomembrane treated group (6.0 ± 0.4 days) compared to the hydrocolloid (7.8 ± 0.2) and silver sulfadiazine (7.6 ± 0.2) treated groups, with a higher incidence of closed wounds in the biomembrane group (68.2%) when compared to the others (20.0%) ($p = 0.048$, Log-Rank Mantel-Cox test) at the end of eight weeks of evaluation.

Table 3. Multivariate analysis of determining factors in the healing of leprosy wounds in patients treated with biomembrane, hydrocolloid and silver sulfadiazine.

Complete wound healing	p-Value	Adjusted OR (CI95%)
Group		
BioMemCpLP	*0.015	67.52 (2.28-2000.07)
Hydrocolloid / Silver sulfadiazine		1
Gender		
Female	0.073	24.57 (0.75-809.02)
Male		1
Age		
≤ 60	0.067	22.88 (0.80-655.02)
>60		1
Cured of leprosy		
No	0.332	9.48 (0.10-894.56)
Yes		1
Ulcer age		
≤ 2 years	*0.028	31.51 (1.46-681.36)
>2 years		1
Local		
Forefoot	0.169	10.19 (0.37-279.56)
Other sites		1
Deformity		
Yes	0.639	2.65 (0.05-155.77)
No		1

*p<0.05, multinomial logistic regression.

immunomodulatory effect underpins the efficiency of BioMemCpLP in treating leprosy ulcers. Since *C. procera* is abundantly found in countries with high incidence of leprosy and the production of BioMemCpLP does not require sophisticated technologies, it can be a low-cost alternative for patients. The mechanisms underlying pro-healing activity of CpLP on ulcers are currently under evaluation.

5. Conclusion

It was demonstrated that a biomembrane composed of 1% polyvinyl alcohol and latex proteins (10%) from the medicinal plant *Calotropis procera* promoted healing of plantar ulcers in patients affected by leprosy. The healing performance of wounds belonging patients using the

membrane was better than those following only antibiotic prophylaxis or commercial hydrocolloid product.

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