TILAPIA SKIN: TECHNOLOGICAL ADVANCE IN THE TREATMENT OF BURNS?

REVIEW ARTICLE

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ABSTRACT

Introduction: Burn is one of the greatest aggressions the body can suffer. The approach varies according to the degree of the burn, since the use of chlorhexidine, silver sulfadiazine, debridement of necrotic tissue, biosynthetic dressings and artificial skins. However, these latter two have high costs, so several studies have emerged with the objective of seeking more viable options, such as the use of Nile Tilapia skin in burns, due to its healing properties. That said, the present article has as a guide question: Is this new method, in fact, a technological advance as

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important for the treatment of burned patients as it appears to be? Objective: To analyze the use of Nile Tilapia skin in patients with burn injuries, as well as to compare with other pre-established techniques. Methods: This is an integrative bibliographic review with a qualitative approach. Data were collected through PubMed databases and Virtual Health Library (VHL), from 2015 to 2020. Results: The articles indicate a good prognosis to the use of Nile Tilapia skin in relation to the other options in force for the treatment of burns, with a significant advantage in reducing the number of dressings required, for better adhesion to the wound. Moreover, it presents microscopic characteristics similar to human skin, such as high tensile strength and breakage extension, reducing reepithelialization time and pain intensity, as well as reducing treatment costs. Conclusion: In view of the findings of the literature reported in the present review, it is concluded that studies with Nile tilapia skin proves to be a revolutionary modality with benefits in the treatment of patients with superficial and deep skin lesions. Therefore, the researchers concluded, answering the guide question, that the new method is, yes, an important advance in the field of burn treatment, because its employability is confirmed, besides demonstrating an advantage over some of the main preexisting alternatives.

Keywords: Tilapia, Burns, Biological Dressings.

INTRODUCTION

The speed and lifestyle imposed by modernity cause the incidence of the number of burns to increase today. Far beyond physical injuries, burns are also responsible for economic problems associated with irreparable harm to patients and their families (HU et al., 2017). The burn is one of the greatest aggressions that the human organism can suffer, and it is estimated that in Brazil, there are about 1 million burn accidents annually, according to Leontsinis et al. (2018), whether these are a simple heat stroke, first-degree burns, until the total destruction of the skin (epidermis and dermis) and adjacent tissues, as in third degree burns (ALVES et al., 2015).

When we consider the treatment of burns in Brazil, we face two realities: that of the public and private network. In the treatment centers of the public network, the

conduct followed in relation to dressings in second-degree lesions is the daily bath with 2% chlorhexidine and the dressing is done with the topical antimicrobial silver sulfadiazine at 1% until complete repair of the lesion; while in third degree burns, necrotic tissue is debrided in several stages, and then the dressing with 1% silver sulfadiazine is performed until the wound bed is prepared for grafting. On the other hand, in the private network, taking into account the different financial conditions of each patient, biosynthetic dressings and artificial skins, imported and high-cost options can be used (ALVES et al., 2015).

However, analyzing the reality experienced in Europe and the United States, treatment often involves the use of homologous skins (making use of skin banks), heterologous (of animal origin), biosynthetic dressings and artificial dermis (ALVES et al., 2015). In Brazil, there are still some confrontations to achieve the same practicality of these other countries. Culturally, there is still great resistance to skin donation, which ends up limiting the availability of the fabric to meet the great demand. In addition, taking as reference the Ministry of Health, so that Brazil can meet the need for homologous skin for use in burn injuries, it would be necessary to have 13 skin banks distributed throughout the national territory, however there are only five (São Paulo, Curitiba, Rio de Janeiro, Porto Alegre and Recife - which is disabled). In addition to these limitations, Brazil has never had an animal skin registered with the National Health Surveillance Agency (ANVISA) and made available by the Unified Health System (SUS), which also ends up restricting the use of heterologous skin in burned patients (LEONTSINIS et al., 2018).

Thus, several studies have emerged with the objective of looking for dressings to be used in burned patients. These dressings aim to reduce the effects of contamination on lesions, favor the healing process and offer better aesthetic results. Having, ideally, good flexibility and adherence to the bed, resistance to stretching, easy handling, ability to suppress pain, low cost and easy to obtain, as well as prevents hydroelectrolytic losses, bacterial contamination, favors epithelialization of burns and provides the formation of adequate granulation tissue. One of the options is the search for temporary skin substitutes and dressings of synthetic or biosynthetic

materials, because they reduce the frequency of dressing change, however, the high costs and its ineffectiveness for deep burns stimulated the search for biological materials as viable alternatives (COSTA et al., 2019; MARCELO and BRANDT, 2019).

In this context, in 2011, the plastic surgeon marcelo Borges, after seeing an article in the *Jornal do Commercio de Pernambuco* talking about the use of the skin of the species Nile Tilapia (*Oreochromis niloticus*) in handicrafts, one of the most cultivated fish in Brazil, first came up with the idea of using this skin in the treatment of burns. But only in 2014, he shared the idea with the plastic surgeon from Ceará Edmar Maciel, then starting studies on the use of nile tilapia skin in burns. The researcher Odorico Moraes, president director of the Center for Research and Development of Medicines (NPDM), at the Federal University of Ceará (UFC), and the plastic surgeon of Goiás Nelson Piccolo were also integrated to make up the coordination of the work (LIMA JUNIOR et al., 2017).

As narrated by Lima Junior (2017), the skin of Nile Tilapia demonstrates an epidermis coated with a stratified pavement epithelium, followed by extensive layers of collagen. Thanks to its characteristic of guiding and defining most tissues, it is configured as a great component of biomaterials, besides enabling biodegradability and biocompatibility, which favor its application (LIMA JUNIOR, 2017; LIMA JUNIOR et al., 2019b, 2020b).

That said, the right question is: "Is this new method, in fact, a technological advance as important for the treatment of burned patients as it appears to be?" The objective is, then, through this study, to analyze whether nile tilapia skin is a viable alternative to be used in patients with burn injuries, as well as to compare with other techniques already used, verifying the advantages of the adoption of this new method.

More specifically, this study aims to demonstrate the good adhesion of tilapia skin dressings in the treatment of burns, correlating the physicochemical properties of tilapia with the benefits of the dressing and exposing the non-inferiority of tilapia skin

dressings in compared to other solutions on the market. In addition to instigating further scientific research to obtain more robust results on the subject.

METHODOLOGY

It refers to an integrative literature review, with a qualitative approach, with the descriptive purpose of national and international studies. Moreover, it has an applied nature, with the use of a bibliographic procedure for the analysis of the respective data collected related to the use of tilapia skin in burned patients.

The present study was carried out through the search for articles through the access of pubmed databases and the Virtual Health Library (VHL). At first, the descriptors relevant to the selected theme were collected, being vocabulary of the Descriptors in Health Sciences (DeCS). The terms chosen were "Tilapia", "Burns" and "Biological Dressings" in the languages: Portuguese, English and Spanish. These descriptors were associated with boolean operators "OR" and "AND" by elaborating the following research formula: "(Tilápia OR Tilapia OR Tilapia) AND (Queimaduras OR Burns OR Quemaduras) AND (Curativos Biológicos OR Biological Dressings OR Apósitos Biológicos)".

Thus, applying the rationale of the above-mentioned formula, a total of 31 articles were found in the selected databases, 14 pubmed articles and 17 available in the VHL. The inclusion criteria were: articles available in full, which portrayed the theme related to integrative review and articles published and indexed in the databases published in the years 2015, 2016, 2017, 2018, 2019, 2020 and 2021, which presented the language in English, Portuguese and Spanish. Moreover, the articles that were duplicated, did not have full content and that did not meet the research objectives were excluded from the integrative review.

The integrative bibliographic review is not practical, therefore, it does not require submission to the Research Ethics Committee (CEP). From this perspective, a table was elaborated showing the main information of the bibliographies used, presenting

the data referring to the title, authors, year of publication, country and the main results of each one.

RESULTS

Table 1: Use of tilapia skin in burns: theoretical basis and practical implications.

	Title	Authors, year of publication and country	Main results
ARTICLE 1	Uso da pele de tilápia (<i>Oreochromis niloticus</i>), como curativo biológico oclusivo, no tratamento de queimaduras	Lima Júnior et al., 2017, Brasil	The study showed that tilapia skin has considerable adherence to burn wounds in test rats, with positive results during healing, without significant mutations in the biochemical and hematological scopes of liver and kidney function, constituting a possibility of biological dressing.
ARTICLE 2	Xenoenxerto (pele da Tilápia-do-Nilo) e hidrofibra com prata no tratamento das queimaduras de II grau em adultos	De Miranda e Brandt, 2019, Brasil	The research showed that Nile Tilapia is effective in the function of occlusive biological dressing in the treatment of second-degree burns in adults, with similar means regarding treatment time, pain reference and need for replacement,

			regarding the management of patients with Aquacel AG®.
ARTICLE 3	Avaliação microscópica, estudo histoquímico e análise de propriedades tensiométricas da pele de tilápia do Nilo	Alves et al., 2015, Brasil	Tilapia skin presents bundles of dense collagen fibers, predominantly type 1, presenting microscopic characteristics similar to those of human skin, as well as high tensile strength and extension to breakage, making it promising as a biomaterial in regenerative medicine.
ARTICLE 4	Innovative Burn Treatment Using Tilapia Skin as a Xenograft: A Phase II Randomized Controlled trial	Lima Júnior et al., 2020, Brasil	The randomized clinical trial used a sample of 62 participants and demonstrated that there was a reduction in: the time of reepithelialization, pain intensity, the amount of aesthetics/analgesics and the need to change dressings compared to the control group, therefore, tilapia skin presented benefits.
ARTICLE 5	Tratamento de queimaduras de segundo grau profundo em abdômen, coxas e	Lima Júnior et al., 2020, Brasil	The case report contributed to reducing the limitations related to the access of more inaccessible anatomical

	genitália: uso da pele de tilápia como um xenoenxerto		areas for use, presenting good results in the application in the genitalia and inguinal region. It is an option of high availability and simple application.
ARTICLE 6	Marine Collagen Peptides from the Skin of Nile Tilapia (<i>Oreochromis niloticus</i>): Characterization and Wound Healing Evaluation	Zhang Hu et al., 2017, China	The <i>in vitro</i> and <i>in vivo</i> scraping assay revealed significant consequences in the closure of scraping with tilapia skin, with evolution in the healing process by deep partial thickness scalding in the tested rabbits, presenting as a promising treatment.
ARTICLE 7	A Randomized Comparison Study of Lyophilized Nile Tilapia Skin and Silver-Impregnated Sodium Carboxymethylcellulose for the Treatment of Superficial Partial-Thickness Burns	Lima Júnior, et al., 2020, Brasil	This pilot study demonstrated that there is no inferiority to lyophilized tilapia skin as a therapeutic option in burns, compared to the silver-impregnated sordid carboxymethylcellulose dressing, with efficacy and safety, enabling the development of more complex randomized clinical trials in the future.
ARTICLE 8	Elaboração de um protocolo para implementação e funcionamento do primeiro	Leontsinis et al., 2018, Brasil	The article revealed the importance of developing and implementing protocols for the world's first aquatic

	banco de pele animal do Brasil: Relato de experiência		animal skin bank, reinforcing the need to establish the standardization of the system.
ARTICLE 9	Use of Tilapia Skin as a Xenograft for Pediatric Burn Treatment: A Case Report	Costa et al., 2019, Estados Unidos	The tilapia skin xenograft in the case report of a 3-year-old burn victim showed positive results with significant social and financial impact on the health system.
ARTICLE 10	Innovative treatment using tilapia skin as a xenograft for partial thickness burns after a gunpowder explosion	Lima Júnior et al., 2019, Inglaterra	The case report portrays a 23-year-old male patient with superficial and deep burns on the right and left upper limb, respectively. With the use of tilapia skin, reepithelialization was performed in a short time, with no side effects and need for dressing change.
ARTICLE 11	Pediatric Burn Treatment Using Tilapia Skin as a Xenograft for Superficial Partial-Thickness Wounds: A Pilot Study	Lima Júnior, 2020, Inglaterra	The use of tilapia skin was used as an extra resource along with silver sulfadiazine. The study revealed that in addition to bringing benefits to patients, it decreased treatment costs, as well as for health professionals, such as reduced workload.
ARTICLE	Comprehensive	Ge et al.,	The collagen hydrogel

12	Assessment of Nile Tilapia Skin (Oreochromis niloticus) Collagen Hydrogels for Wound Dressings	2020, China	dressing showed the promotion of the formation of epidermal layers and the maturation of the skin appendages, demonstrating to be an excellent new dressing with efficacy in the management of deep burns.
ARTICLE 13	Tecnologias inovadoras: uso da pele da tilápia do Nilo no tratamento de queimaduras e feridas	Lima Júnior, 2017, Brasil	Tilapia skin in burns is a Brazilian patent, and the objective of the research is the registration of the skin in the National Health Surveillance Agency (ANVISA) and made available by the Unified Health System (SUS).
ARTICLE 14	Chitosan hydrogel in combination with marine peptides from tilapia for burns healing	Ouyang et al., 2018, China	The marine peptides extracted from tilapia showed a collagen-like composition, in addition to significant antibacterial activity. It presents high healing efficiency and cell migration and proliferation skills compared to the control group and other ointments available in the pharmaceutical industry.

Source: Developed by the author (2021)

The review included 14 articles, among which, two (14.3%) reported on the results using animal tests, 14.3% on a comparative analysis between traditional treatments and tilapia skin use, and 21.4% about the mechanisms of composition and properties in relation to human skin. The use of randomized trials represented 7.1% of the articles, 28.6% presented the results in case reports and 14.3% explained the development of the technique until its importance in the skin banks nowadays.

The study conducted at the Burn Treatment Center of the Dr. José Frota Institute, Public Hospital of Fortaleza, Ceará, Brazil, selected 62 patients hospitalized between October 2016 and September 2017, who were victims of burns. The variants evaluated were: the number of times there was an exchange of the occlusive dressing and days for wound healing, use of analgesics or anesthetics, painful sensitivity, improvement of the burn in the removal of the dressing. The study analyzed the data and divided the participants, from: gender, age, agents responsible for the accident, body surface and burned segments, and for this, divided into three classifications, A - ambulatory patients with partial superficial thickness burns less than 10%, B - hospitalized patients with the same 10 to 20%, C - hospitalized patients with deep burns of partial thickness of 5 to 15%, and each of this classification was randomly divided into two treatment groups: 48.4% (n=30) Test Group using tilapia skin as xenograft and 51.6% (n=32) Control Group: conventional with sulfadiazine cream. The main burn mechanism of the Test Group (classifications A, B and C using tilapia skin as treatment) was by hot liquids 56.25% (n=18). Pain intensity was lower in the test group compared to the control group. The number of dressings required during treatment, in the test group it was lower, presenting 2.08 ± 0.28 (A), 2.33 ± 0.71 (B), 6.10 ± 2.02 (C), while in the control group 5.80 ± 0.42 (A), 11.00 ± 0.47 (B), 20.20 ± 1.69 (C) taking into account the p value as 0.0001. Regarding the number of days for complete reepithelialization, the test group presented the best results, having: 9.77 ± 0.83 (A), 10.56 ± 1.13 (B), 18.10 ± 0.99 (C), while the control group: 11.20 ± 0.63 (A), 11.70 ± 0.67 (B), 21.30 ± 1.42 (C), considering approximately $P < 0.0147$ (LIMA JUNIOR et al., 2020a)

Another study conducted at the Burn Treatment Center in Fortaleza, Ceará, Brazil, selected 30 children, between 2 - 12 years old, hospitalized between May 2017 and March 2018. The variables used were: the total days for complete healing of the burn and the number of dressings used. The patients were divided into two groups, in which 50% were ascended to the tilapia skin test group and the remainder to the silver sulfadiazine group. The average number of days to complete reepithelialization was 10.47 ± 0.74 in the silver sulfadiazine group and 10.07 ± 0.46 in the tilapia skin group. The difference between the two groups was not statistically significant ($P = 0.0868$). The number of dressings under anesthesia performed in patients treated with tilapia skin was lower than those performed in volunteers treated with silver sulfadiazine. A statistically significant difference was also found for the number of dressings without anesthetics. Finally, the total number of dressings was significantly reduced in the tilapia skin group (3.00 ± 0.76) when compared to the silver sulfadiazine group (9.27 ± 1.39) (LIMA JUNIOR et al., 2019a).

DISCUSSION

The study of the skin properties of tilapia is a good starting point for understanding its potential for use in burns. For this, it is worth first analyzing the findings of Hu et al. (2017) who studied the use of a collagen polypeptide concentrate extracted from the skin of tilapia, focusing on its curative potential. *In vitro* assays using prepared human cells showed that the addition of $50.0 \mu\text{g/mL}$ of the concentrate to the injured tissue brought statistically significant results in relation to the speed of regeneration and reepithelialization of the tissue. On the other, the *in vivo* studies of the same author showed promising results regarding healing by deep partial thickness scalding in the rabbits tested. The findings were similar to those obtained with the collagen hydrogel dressing, studied by Ge et al. (2020), for deep burns.

In addition, other studies have been done to evaluate the properties of the animal's skin. According to Alves et al. (2015), tilapia skin presents bundles of dense collagen fibers, predominantly type 1, with microscopic characteristics similar to those of human skin, as well as high tensile strength and extension, making it promising as a

biomaterial in regenerative medicine. The study by Ouyang et al. (2018) corroborates these results, as well as those of Hu et al. (2017), which also addresses the antibacterial activity of the material and compares its curing efficiency with other solutions available in the market, obtaining a high efficiency, besides providing migration and cell proliferation.

Validating this curative potential of tilapia skin, it is necessary to understand the usability of this material in the form of biological dressings. According to the study by Lima Junior (2017), tilapia skin has considerable adherence to burn wounds in test rats, with positive results during healing, without significant mutations in the biochemical and hematological scopes of liver and kidney function, constituting a positive possibility as a biological dressing. Corroborating these results, the randomized clinical trial of Lima Junior et al. (2020c) showed good adherence in patients, as well as other advantages over other dressings, such as Aquacel Ag®, which will be discussed later.

That said, it is worth comparing the skin of tilapia with other existing solutions when it comes to burns. Lima Junior et al. (2020c) and Marcelo and Brandt (2019) promoted studies that show no inferiority in lyophilized tilapia skin, compared to the sordid carboxymethylcellulose dressing impregnated with silver, Aquacel Ag®. The study by Lima Junior et al. (2020c) emphasizes that the use of tilapia skin offers a subjective improvement in the amount of pain reported and the number of dressings required, thus reducing the cost of treatment and the workload of the team. Therefore, tilapia skin is a good option for the treatment of burns.

CONCLUSION

In view of the findings of the literature reported in the present review, it is concluded that studies with the skin of Nile Tilapia, freshwater fish, conducted by researchers from the Federal University of Ceará, who were, since 2016, the pioneers to patent the method. Moreover, it has been a revolutionary modality with numerous benefits in the treatment of patients with superficial and deep skin lesions expanding to several

areas of medicine, tested in veterinary medicine, inside and outside the country (LIMA JUNIOR, 2017).

Based on the research records, the benefits of the use of Tilapia Skin in the treatment of burns are reinforced, considering that it offers reduction of the patient's pain due to the longer period adhered to the patient's skin. In addition to the reduced power of infection and contamination, high resistance due to the large amount of collagen present in the fish hide, resulting in good aesthetics and low cost, compared to other forms of treatment.

Therefore, the researchers came to the conclusion, answering the guide question, that the new method is, yes, an important advance in the treatment of burns, because its employability is confirmed, besides demonstrating an advantage over some of the main preexisting alternatives.

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