LUMEN ET VIRTUS

Advances in veterinary ophthalmology: Acellular protein matrix from tilapia skin (Oreochromis niloticus) in the recovery of corneal ulcers in dogs and cats

https://doi.org/10.56238/levv15n39-035

Mirza de Souza Melo[1], Sofphia Martins da Silva[2], Antonio Eufrásio Vieira Neto[3], Natália Chaves Gondim Vieira[4], Maria Elisabete Amaral de Moraes[5], Edmar Maciel Lima Júnior[6], Felipe Augusto Rocha Rodrigues[7], Carlos Roberto Koscky Paier[8] and Manoel Odorico de Moraes Filho[9]

ABSTRACT

The acellular protein matrix from tilapia skin has excellent biomechanical properties, lack of immunogenicity and high biocompatibility in vitro and in vivo. Therefore, it provides an environment conducive to cell regeneration, specifically in more invasive and delicate applications, such as the recovery of corneal ulcers in dogs and cats. The objective of this literature review is to present the use of the scaffold as a new approach in veterinary ophthalmology in the treatment of corneal injuries in relation to conventional methods. When applied to corneal ulcers, the biomaterial acts as a tissue scaffold, facilitating cell migration, promoting angiogenesis and minimizing the inflammatory response; thus, significantly accelerating the healing process. It also improves corneal transparency, reduces recovery time and reduces post-treatment complications. Clinical trials involving dogs and cats have had significant success, demonstrating the applicability and effectiveness of this innovation in the context of veterinary ophthalmology. This study highlights both the effectiveness of the tilapia skin scaffold and emphasizes its potential to transform clinical practice by providing a sustainable, affordable and pioneering approach to treating corneal ulcers in small animals.

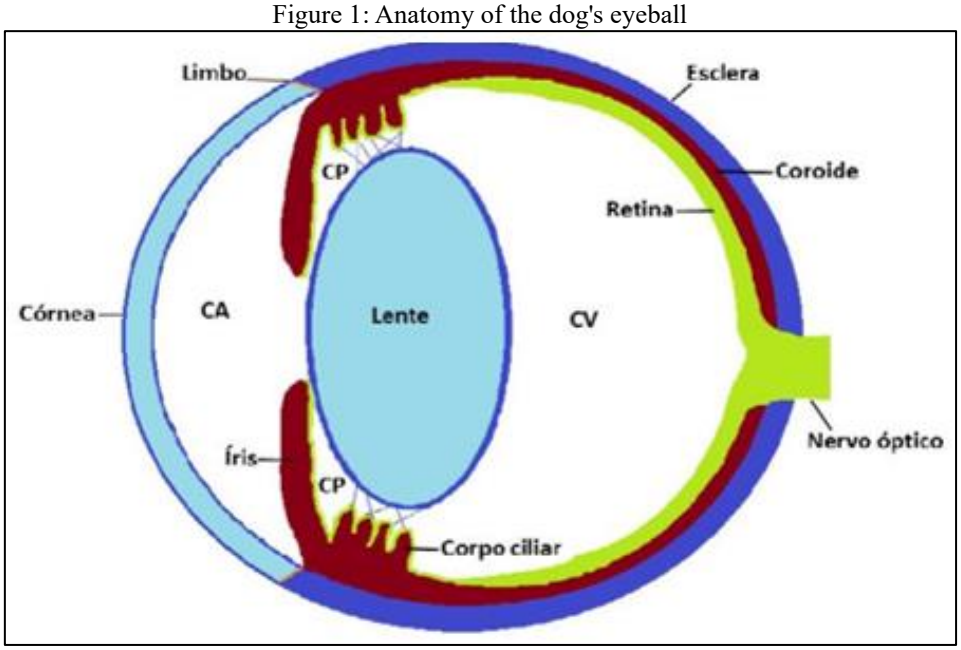
[1] Medicines Research and Development Center of the Federal University of Ceará, Fortaleza, Ceará, Brazil, mirzamelo@centrodeolhosveterinario.com.br
Orcid ID (https://orcid.org/0000-0002-5413-4755)
[2] Medicines Research and Development Center of the Federal University of Ceará, Fortaleza, Ceará, Brazil, sofphia.jg@gmail.com
Orcid ID (https://orcid.org/0000-0002-5555-8680)
[3] Experimental Biology Center at the University of Fortaleza, Fortaleza, Ceará, Brazil, aevneto@gmail.com
Orcid ID (https://orcid.org/0000-0001-7003-6461)
[4] Experimental Biology Center at the University of Fortaleza, Fortaleza, Ceará, Brazil, natyvieira@alu.ufc.br
Orcid ID: (https://orcid.org/0000-0002-0038-2745)
[5] Medicines Research and Development Center of the Federal University of Ceará, Fortaleza, Ceará, Brazil, betemora@ufc.br
Orcid ID (https://orcid.org/0000-0002-6826-8930)
[6] Burn Support Institute, Fortaleza, Ceará, Brazil, edmarmaciel@gmail.com
Orcid ID (https://orcid.org/0000-0003-3158-7994)
[7] Federal Institute of Education, Science and Technology of Ceará, Ceará, Brazil, felipe.rocha@ifce.edu.br
Orcid ID (https://orcid.org/0000-0002-8241-3903)
[8] Medicines Research and Development Center of the Federal University of Ceará, Fortaleza, Ceará, Brazil, carlos.paier@ufc.br
Orcid ID (https://orcid.org/0000-0001-5255-4644)
[9] Medicines Research and Development Center of the Federal University of Ceará, Fortaleza, Ceará, Brazil, odorico@ufc.br
Orcid ID (https://orcid.org/0000-0003-3378-8722)

Keywords: Occlusive Dressing, Scaffold, Tilapia Skin, Crystalline, Corneal Ulcer.

INTRODUCTION

The eye has structures that have the ability to capture light stimuli from the environment, recognize them, and transform them into electrical signals; and then convert them into images with the help of the nervous system (Forrester *et al.,* 2020; Mannis *et al.*, 2016). The main process responsible for vision is the eyeball, while adjacent structures have the function of protecting the eye (Silva, 2017; Queiroz & Reis, 2023). The eyeball is made up of three layers: outer, middle and central. The outer layer encompasses the cornea and sclera; the middle layer comprises the iris, ciliary body and choroid; and the central layer is composed of the retina and the optic nerve. The sclera is opaque and connects to the cornea. The cornea, in addition to being transparent, is avascular, except in its periphery, where it has a well-developed nervous system (Queiroz & Reis, 2023). It is composed of four histological tissues: epithelium, stroma, Descemet's membrane and endothelium (Ross *et al*., 2016; Gervasio *et al*., 2022) (Figure 1).

Figure 1: Anatomy of the dog's eyeball



Source: Lobo et al., 2021.

The cornea is a convex, thin and transparent structure (Meekins, 2021). Due to its external location, the cornea is constantly subject to aggression and can be seriously injured in chemical burns, abnormal adhesions of the conjunctiva, persistent defects in the superficial layer of the epithelium, neoplasms on the ocular surface, corneal ulcers that are difficult to heal, protrusions, total loss or partial limbar region, bullous keratopathy, corneal infections or ocular perforation (Queiroz & Reis, 2023). Specifically, corneal ulcers, also known as ulcerative keratitis, are the most common ophthalmopathies in small animals (dogs and cats), being very present in clinical routine (Lobo *et al*., 2021). When left untreated, they can cause impairment or loss of vision, or severely, loss of the eyeball. Even with drug treatment, some ulcers do not respond to conventional therapy, these are

called refractory ulcers, which range from persistent epithelial defects to stromal involvement (Schuerch *et al*., 2020). Furthermore, they can affect the sensory nerves, presenting challenging dysfunctions for the healing process (Bremond *et al.*, 2019).

The diagnosis of ulcers is generally carried out through a clinical examination and the use of eye drops with fluorescein (De Miranda *et al*., 2023). Speedy diagnosis and treatment are essential so that the injury does not progress to eye perforation; therefore, enabling the preservation of vision. These injuries are common in domesticated animals and other species can also be affected by this pathology, and, consequently, the demand for clinical management is increased. Pet owners are increasingly aware of the importance of taking care of their animals eye health, as treatment aims to eliminate the underlying cause and avoid complications (Machado, 2019). The main therapeutic alternatives include antibiotic therapy, ophthalmic ointments and non-steroidal anti-inflammatory medications (Afonso, 2017; Borges *et al*., 2021). In the case of deep ulcers, surgical intervention becomes necessary when more than half of the cornea is compromised or when a satisfactory response to medical treatment is not obtained.

Currently, there are not many accessible options with optimized cost/benefit ratio for surgical intervention in ophthalmological medicine, proving to be an urgent demand in the clinic (Schuerch *et al*., 2020; Gonçalves, 2022). On the market, amniotic membrane of commercial bovine origin is the most used due to its effectiveness. The results are satisfactory, however, some limitations must be considered, such as its use in severe eye burns and large corneal perforations (Rock *et al*., 2018). Furthermore, the majority of animals are excluded from the benefits received, as the biomaterial is expensive and imported, making access difficult for owners. Another option is autografting, used alone or combined with platelet-based biomaterials (suspensions, glue, buffers and membranes) and specific surgical techniques), increasing the cost of the surgical procedure (Arnalich et al., 2016; Can et al., 2016; Sanchez-avila et al., 2018; Gonçalves, 2022). Recent research demonstrates the efficiency in the healing process of deep ulcers using fibrin membranes rich in platelets and leukocytes (L-PRF) xenologous and/or associated with an autologous plug, presenting itself as a viable alternative in the ophthalmological clinic (Gonçalves, 2022; Sousa, 2023).

However, there is a great difficulty in relation to the development of any biomaterial, as the most promising ones may be prematurely discarded for therapeutic use if they are not developed with a view to reducing their immunogenic, inflammatory and cytotoxic potential (Silva, 2023). Such problems make it necessary to make efforts to develop devices that meet all the criteria of a good biomaterial, are easy to produce and have a good cost/benefit ratio. It is desirable to have a surface with a structure and chemical composition that allows access, penetration, proliferation and cell differentiation, in addition to having a size and shape conducive to regeneration and repair of the receptor region (Wagner *et al*., 2020; Moerbeck-Filho *et al*., 2019). They must be biocompatible,

biodegradable and their degradation rates must match the rate of growth and cell repopulation of the tissues to be regenerated (Lau *et al*., 2019). Because of this, product developers seek to present new collagen-based therapeutic approaches for applicability in these ophthalmological pathologies.

One of the advantages associated with the administration of collagen products is the short healing period, neovascularization and the organization of skin cells in the formation of scar tissue (Jacob *et al*., 2018; Park *et al*., 2017; Salgado *et al*., 2016). Specifically, decellularized biological scaffolds or matrices (*scaffolds*) developed from the extracellular matrix (ECM) of animal tissues, have the necessary components to promote the tissue regeneration process. However, the scaffolds available on the market are expensive, imported and come from land animals, creating a greater risk of rejection and some religious restrictions. When the raw material is derived from tissues of aquatic animals, it becomes more promising, as in the case of tilapia skin, extensively used in clinical trials for the treatment of burns (Park & Lakes, 2007; Lima-Junior *et al*., 2017; 2019).

The studies carried out by researchers from the Medicines Development Research Center (NPDM) at the Federal University of Ceará (UFC), made it possible to decellularize tilapia skin and produce a protein matrix with potential for therapeutic use in different areas of medicine, being standardized for use in internal, more invasive and complex surgeries (Mendoza, 2020; Silva, 2023) (Figure 2). The *scaffold* has fibrous connective tissue made up of bundles of compacted and well-structured collagen fibers (Silva, 2023). It is known that to enhance the tissue healing process, collagen is essential to enhance the cascade of molecular signaling in the inflammatory process. Therefore, the excellent disposition of type III collagen makes the *scaffold* a strong alternative as an efficient biotechnological graft in the repair of corneal ulcers in animals (Lima-Júnior *et al*., 2017). Furthermore, polymers are the most produced biomaterials in Brazil, ranking third in the tissue engineering segment (RCR, 2022). Thus, presenting itself as a promising and profitable alternative for the coming years, specifically for use in reconstructive and delicate surgeries.

Figure 2: Acellular protein matrix (scaffold) from tilapia skin



Source: Chico Gadelha/Revista Pesquisa FAPESP, 2023.

Therefore, this narrative review approach aims to present the acellular protein matrix from tilapia skin as a biological graft used in corneal ulcer surgeries in veterinary medicine in small animals.

MATERIALS AND METHODS

The present study is a narrative bibliographical review, contemplating a qualitative analysis of the literature regarding the subject in question: "use of tilapia skin (*Orechromis niloticus*) in ophthalmological surgical procedures in veterinary medicine", being the only inclusion criterion in the selection.

The search for scientific articles used academic search engines (Google Scholar and ScienceDirect) as research support and MEDLINE databases and the journal directories, Pubmed Central. The following descriptors were used: "tilapia skin, *Oreochromis niloticus*, ophthalmology of veterinary medicine, biological graft and biomaterials", also translated into English.

The study was organized emphasizing all clinical studies of the Tilapia skin research that report the potential use of products from the skin of the fish used in ophthalmological surgeries in veterinary medicine. These are case studies that address the proposed theme, available in Portuguese and English.

Data collection was carried out after searching for articles and simple and expanded abstracts related to research on tilapia skin (*Oreochromis niloticus*). 35 articles were found and 33 articles were excluded, 10 simple and expanded summaries and 8 were excluded, as all were evaluated regarding the title, summary and suitability for the theme. All 3 articles within the inclusion criteria were evaluated in full. After this, the studies were arranged in a table for the final result and discussion.

RESULTS AND DISCUSSIONS

PRODUCTION OF ACELLULAR PROTEIN MATRIX FROM TILAPIA SKIN

Briefly, tilapia skins are mechanically removed from the fish in the fish farm, washed in running water, stored in sterile plastic containers and on ice. The stored skins are transported to the laboratory (clean room), where they are scraped to remove muscle remains, washed in sterile saline and frozen for storage. They are subsequently thawed and added to oxidizing solutions that ensure microbiological decontamination. The skins are incubated in surfactant solutions that guarantee their decellularization and processed in solutions that guarantee the removal of melanophores. During the process, the skins are subjected to successive washes with a saline solution containing enzymes.

APPLICABILITY OF THE ACELLULAR PROTEIN MATRIX IN OPHTHALMIC VETERINARY MEDICINE

Initially, the works available in the literature address the use of fresh tilapia skin and, later, the acellular protein matrix in small animals (dogs and cats).

Three published articles were found: 2 in a national magazine and 1 in an international magazine between 2022 and 2023; 2 simple and expanded summaries in national event annals; 1 award at a national event for best work presented and 15 mentions in the media in high-profile online magazines in the field of ophthalmic veterinary medicine. The studies present the improvement of ocular surgical techniques in animals through the use of products from tilapia skin in corneal reconstruction, according to the clinical approach (Table 1).

Table 1: Data available in scientific article databases and search platforms.

	Summaries in event annals	Clinical applicability
1	Evaluation of bacterial microbiota in dog corneal ulcers repaired with tilapia skin graft. MELO, M.S.; VIEIRA, N.C.G.; VIEIRA-NETO, A.E. In: Proceedings of the XVII Brazilian Congress of Veterinary Ophthalmology, Curitiba: Veterinary Science Archive, 2021. v. 42-42.	Evaluation of the bacterial microbiota in corneal ulcers in dogs that were repaired with tilapia skin grafts. The results showed low bacterial growth, highlighting the continued importance of care after repair with the biotechnological graft.
2	Tilapia skin graft (*Oreochromis niloticus*) in the repair of dog corneal ulcers: case report.	Fresh tilapia skin used to repair corneal ulcers in a dog.

	MELO, M.S.; VIEIRA-NETO, A.E.; MORAES-FILHO, M.O. In: Proceedings of the XVII Brazilian Congress of Veterinary Ophthalmology, Curitiba: Veterinary Science Archive, 2021. v. 90-90.	The tilapia skin graft promoted favorable healing of the cornea, resulting in greater transparency, absence of melanosis, low vascularization and good lubrication.
Articles in national and international magazines		Clinical applicability
1	Tilapia skin graft (*Oreochromis niloticus*) in repair of dog corneal ulcer: case report. MELO, M.S. et al., Brazilian Journal of Animal and Environmental Research, v. 5, p. 367-375, 2022.	Use of a tilapia (*Oreochromis niloticus*) skin graft to repair an ulcer on a dog's cornea. The graft demonstrated efficacy and presented itself as a promising option for the treatment of corneal ulcers in dogs.
2	Acellular dermal matrix from tilapia skin in feline corneal repair: case report. MELO, M.S. et al., Multidisciplinary Health Journal, 2023, 4(3), 397–402. doi.org:10.51161/conais2023/21951	Use of acellular dermal matrix from tilapia skin in the repair of a lesion on the cornea of a feline. The study highlighted the effectiveness of this approach in recovering feline eye health.
3	Use of occlusive tilapia skin dressing in corneal perforation with luxation and extravasation of the crystalline in a puppy of dog: case report. MELO, M.S. et al. Contemporary Journal 3(11): 20142-20149, 2023.	Use of tilapia skin cellular dermal matrix in a 4-month-old Shitzu dog with a serious eye injury. In the surgical procedure, the technique used was the third eyelid flap. Post-surgical evaluation showed complete restructuring of the cornea, with healing, restoration of vision and shape of the eye, indicating success in the innovative grafting technique for extravasation of the lens.
National awards		
1	XVII Brazilian Congress of Veterinary Ophthalmology - 2021 in Foz do Iguaçu with the presentation of the work entitled Tilapia Skin Graft in Corneal Ulcers in Dogs	Description of the first case of use of fresh tilapia skin in dog eye lesions.
2	IV CONAIS - National Congress on Health Innovation – 2023 in Fortaleza, Brazil, with the presentation of the work entitled Acellular Dermal Matrix of Tilapia Skin in Feline Corneal Repair: Case Report	Description of the first case of use of the acellular protein matrix from tilapia skin in an adult cat, 4 years old, diagnosed with a corneal ulcer.
3	IV International Meeting on Biotechnology in Human and Animal Health: Biotechnological Advances and Trends for Human and Animal Health - 2023 in Maceió, Brazil, with presentations of studies entitled (1) Revolutionary Biotechnological Graft for Felines: Acellular Dermal Matrix of Tilapia Skin - Case report and (2) Tilapia Skin as a Graft in the Repair of Corneal Ulcers: Case Report with Biotechnological Derivatives in Dogs.	Description of the use of acellular protein matrix from tilapia skin in dogs and cats and the adaptation of the surgical technique.
Repercussion and citations in the media		
2021		
1	UFC Translational Medicine, November 2021. New UFC studies guarantee three more national awards for research with tilapia skin. “Veterinary use – The third award was given to the first research that uses tilapia skin for ophthalmic use. ” Award for best work II Brazilian Congress of Veterinary Ophthalmology, the study Tilapia skin graft in dog corneal ulcer. Available at: https://medicinatranslacional.ufc.br/pt/novos-estudos-da-ufc-garantem-mais-tres-premios-nacionais-para-as-pesquisas-com-pele-de-tilapia/	

2	Diário do Nordeste, November 2021. Research with tilapia skin developed in Ceará wins three awards this month. Available at: https://diariodonordeste.verdesmares.com.br/metro/pesquisas-com-pele-de-tilapia-desenvolvidas-no-ceara-ganham-tres-premios-neste-mes-1.3165107
2023	
1	Dogs&Cats, May 2023. Technique with tilapia skin treats serious corneal injuries in dogs and cats. In ophthalmology, the skin's dermal matrix can restore the vision of pets. Available at: https://caesegatos.com.br/tecnica-com-pele-de-tilapia-trata-lesoes-graves-de-cornea-em-caes-e-gatos/
2	Brazilian Communication Company (EBC), Our animals, on air in May 2023. Tilapia skin is used in the ophthalmological treatment of dogs. Available at: https://radios.ebc.com.br/nossos-bichos/2023/05/pele-de-tilapia-usada-tratamento-oftalmologico-de-caes
3	TV Ceará, TV Pet Show Program, May 2022. Ophthalmological treatment with tilapia skin in animals. Available at: https://www.youtube.com/watch?v=FsBZ8SWzoHs
4	Scientific and technological dissemination stand, May 2023. Anclivepa Brazilian Congress (CBA). Available at: https://cba2023.com.br/
5	GCmais, May 2023. Surgery on pet eyes with tilapia skin can be applied to humans. Available at: https://gcmais.com.br/noticias/2023/05/23/cirurgia-em-olhos-de-pets-com-pele-de-tilapia-podera-ser-aplicada-em-humanos/? amp=1
6	Power in the square, May 2023. Surgery on pet eyes with tilapia skin can be applied to humans. Available at: https://podernoquadrado.com/cirurgia-em-olhos-de-pets-com-pele-de-tilapia-podera-ser-aplicada-em-humanos/
7	Sobral online, May 2023. Surgery on pet eyes with tilapia skin can be applied to humans. Available at: https://sobralonline.com.br/cirurgia-em-olhos-de-pets-com-pele-de-tilapia-podera-ser-aplicada-em-humanos/
8	City newspaper, May 2023. Surgery on pet eyes with Tilapia skin can be applied to humans. Available at: https://www.youtube.com/watch?v=rpJw5UcDNck
9	O Optimista, Panorama, July, 2023. UFC: tilapia skin is used in dog cornea surgery Available at: https://ootimista.com.br/panorama/ufc-pele-da-tilapia-e-usada-em-cirurgia-de-corneas-de-cachorros/
10	Fortaleza City Council (CMFor), July 2023. Tilapia skin is used in dog cornea surgery. Tilapia skin can, at low cost, speed up the recovery process of patients, avoiding contamination. Available at: https://www.cmfor.ce.gov.br/2023/07/25/pele-da-tilapia-e-usada-em-cirurgia-de-corneas-de-cachorros/
11	Jornal Jangadeiro, July 2023. Tilapia skin in corneal surgeries in dogs and cats. Available at: https://www.youtube.com/live/CgB7xpPuFlA?feature=share
12	Search FAPESP 331, p. 65 to 67, September 2023. The vision of dogs/Biotechnology, Biocurative originating from tilapia skin helps in the recovery of animals that have suffered serious corneal injuries. Available at: https://revistapesquisa.fapesp.br/wp-content/uploads/2023/08/065-067_tilapia_331.pdf
13	Gizmodo, Uol, by magazine Search FAPESP, published in September 2023. Tilapia skin is an option for treating corneal injuries in dogs. Available at: https://gizmodo.uol.com.br/pele-de-tilapia-e-opcao-para-tratar-lesoes-de-cornea-em-caes/
14	Institute ProSilvestre, September 2023. Operation of owl 61 at Institute Prosilvestre at Eye Center Dra. Mirza Melo. Available at: social network - Institutoprosilvestre
15	Tv Globo, Globo Rural Program, September 2023. Tilapia skin is used to treat corneal injuries in dogs. Available at: https://globorural.globo.com/pecuaria/peixe/noticia/2023/10/pele-de-tilapia-e-utilizada-para-tratar-lesao-de-cornea-em-caes.ghtml

Source: data available in the literature.

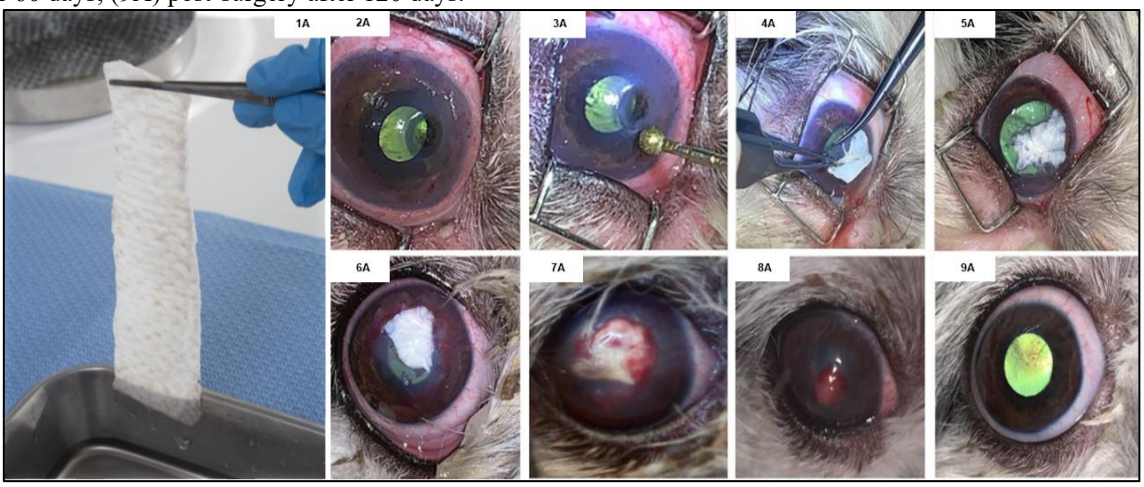
Fresh tilapia skin was used in corneal repair surgery on a shih-tzu in 2019, demonstrating great effectiveness. The excellent results rewarded researcher Mirza Melo under the guidance of prof. Dr. Odorico Moraes, as the best work presented at the II Brazilian Congress of Veterinary Ophthalmology - 2021, entitled "Tilapia skin graft in dog corneal ulcers." With the application of the heterologous skin graft to the animal, it was observed easy conservation and manipulation during surgery, excellent corneal repair and a pain-free post-surgical period, absence of infections or complications after application of the skin. Similar results to the use of tilapia skin in glycerol used as a regenerative device for the treatment of wounds and burns in humans, which presents a lower pain threshold, fewer dressing changes and, consequently, fewer inputs and less work by the clinical team (Lima-Junior *et al*., 2019; 2020).

In all cases, the skin is fully adhered to the wound or lesion bed, functioning as a tissue framework for the injured tissue to be regenerated (Lima-Junior *et al*., 2020). Also, in traumatic wounds of horses, tilapia skin in glycerol presented a healing response no inferior to that of a product on the market that is known to have a favorable effect on healing, providing health and well-being to the animal (Costa *et al.*, 2023). Furthermore, it significantly reduced inputs and working hours. Products from tilapia skin are widely studied in various areas of human and animal medicine. However, veterinary use in ophthalmology had never been carried out, making researcher Mirza Melo a pioneer in this area.

The results demonstrating the effectiveness of tilapia skin even in its raw material form (*in natura*) with a preparation similar to other biological membranes, made it possible to expand the research horizons with the use of the acellular protein matrix. In ophthalmology, similarities are highlighted between the corneal healing process and the skin healing process, namely: healing phases - inflammation, proliferation and remodeling, collagen deposition and wound healing. Collagen is the fundamental component in this biological action, guiding and giving shape to most tissues. The scaffold presented itself as a new graft alternative for corneal keratoplasties in dogs and other species (Mendoza, 2019; Silva, 2023). The *scaffold*, when used to treat the cornea in dogs, demonstrated excellent healing and corneal transparency, absence of excessive pigmentation, low blood vessel formation and adequate ocular lubrication (Melo *et al*., 2021). The biological device was effective in repairing the cornea, maintaining its transparency and preserving vision, representing an innovative approach in veterinary ophthalmology.

Currently, the use of the *scaffold* has excellent results in relation to its use in repairing corneal ulcers in dogs. All procedures are carried out under the coordination of veterinarian Mirza Melo, at the Veterinary Eye Center, located in Fortaleza, Ceará. The results obtained were positive in more than 420 operated eyes (Figure 4) (Melo *et al*., 2022).

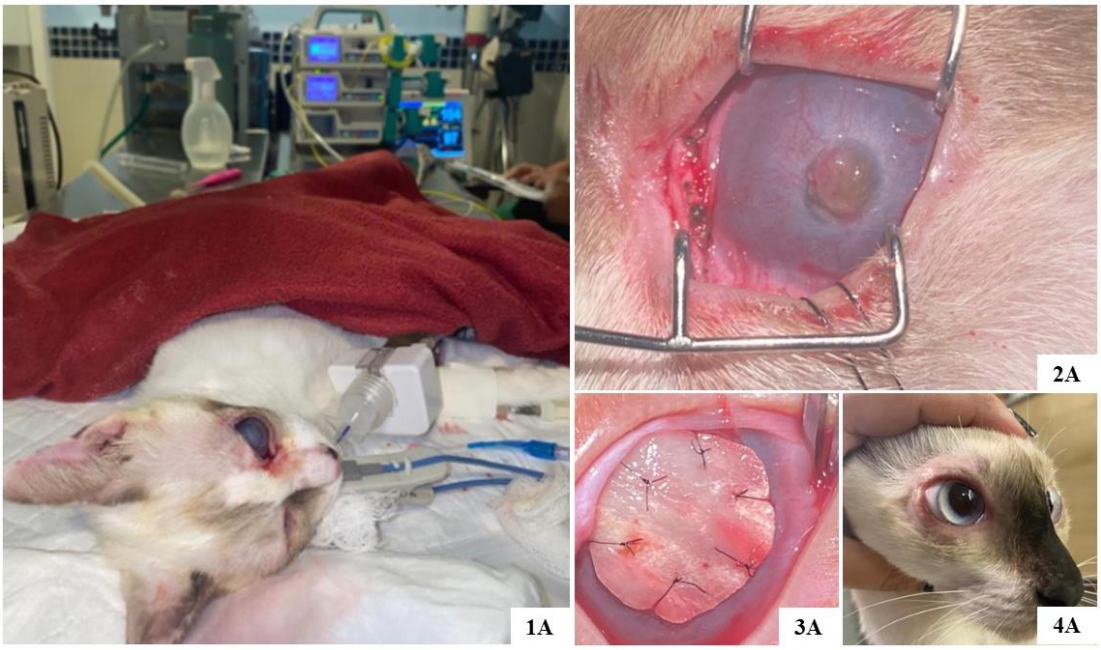
Figure 4: Applicability of the acellular protein matrix in dog corneal ulcer repair: 1A: Acellular protein matrix from tilapia skin. 2A to 9A: Keratoplasty with Tilapia skin in a dog, images of scar evolution from the initial moment until 120 days of evolution: (2A) corneal lesion on day 1; (3A) initial transsurgical appearance; (4A) intermediate transsurgical aspect; (5A) final transsurgical appearance; (6A) post-surgery after 10 days; (7A) 30 days post-surgery; (8A) post-surgery after 60 days; (9A) post-surgery after 120 days.



Source: Melo et al., 2022.

Furthermore, it is noteworthy that it was necessary to adapt ophthalmic surgical techniques during the applicability of products from tilapia skin, specifically, with the use of the *scaffold*. Melo and collaborators (2023), reports that the *scaffold* was used as an alternative to the pedicled conjunctival flap technique, aiming to evaluate the parameters of ocular health recovery in an adult cat, mixed breed. The medical device was fixed to the cornea with 9.0 nylon suture in separate simple stitches, ensuring precise accommodation and effective adherence to the underlying cornea. Furthermore, the graft was combined with the third eyelid flap technique to protect the area and create pressure between the graft and the cornea, which proved to be essential to facilitate graft adhesion and material absorption (Figure 5).

Figure 5: Trans and post-surgical procedure of an adult feline animal, mixed breed, female, aged 4 years, demonstrating the adaptations of the surgical technique with the use of scaffold made from tilapia skin: 1A: after sedation and anesthetic protocol for keratoplasty with scaffold from tilapia skin; 2A: transsurgical view before debridement (initial appearance); 3A: immediate transsurgery after suturing the scaffold graft; 4A: 30 days post-surgery showing complete re-epithelialization of the cornea, with good lubrication and transparency.



Source: Melo et al., 2023. *Images authorized by the animal's owner.

The flap technique depends on the needs of the patients, specific medical conditions and the assessment of the ophthalmic surgeon (Santhiago, 2020). However, they may present some disadvantages: greater complexity, increased surgical time, more surgical inputs, possible risks of complications in the healing process (infection and displacement of the flap); and, consequently, difficulty in healing, patient limitations and discomfort. Using the scaffold as a flap replacement resulted in a greater cost/benefit ratio, excellent biocompatibility, reduced surgical time, rapid healing without complications, without graft rejection and greater animal well-being (**Figure 5**) (Melo *et al*., 2023).

Given the excellent results, it can be highlighted that the surgical adaptations regarding the use of the flap, relatively, demonstrated greater comfort and well-being for the animal, minimizing pain and suffering. Furthermore, antibiotics were used to minimize the risk of local infection after repair, as in previous studies (Bertolino *et al*., 2022; Melo *et al*., 2023). Even with the use of the tilapia skin *scaffold*, the use of antibiotics to aid recovery is recommended, as there are cases in which the patient's condition is more delicate. Professional monitoring is also essential for the effectiveness of the procedure, even post-surgery (Vieira, 2023).

Furthermore, the scaffold has recently been used on other species: birds (owl, parrot) and reptiles (snake). Post-surgical monitoring of the animals is still being carried out. However, information from the personal research archive already points to successful results with the applicability of the biomaterial. Therefore, reaffirming the high biocompatibility and potential in the

healing process arising from the richness of collagen that makes up the acellular protein matrix. Products from tilapia skin have great potential and socio-financial, innovative and technological impact with a view to application in the most diverse areas of regenerative medicine.

FUTURE PERSPECTIVES AND SOCIO-FINANCIAL IMPACT OF THE APPLICABILITY OF THE ACELLULAR PROTEIN MATRIX FROM TILAPIA SKIN IN VETERINARY OPHTHALMOLOGY

Given the excellent clinical results presented in veterinary ophthalmology, the future perspective is for the acellular protein matrix from tilapia skin to be used in clinical routine. However, it is worth highlighting that products made from tilapia skin are not yet commercially available. The second product - freeze-dried tilapia skin, is still in the process of technological transfer to the industry. Its availability on the market is expected to be available in the coming years. However, the scaffold, even in animal studies, has already demonstrated results that have a significant impact on animal ophthalmology. At the same time, its use in future studies on humans is already being considered.

With a view to the socio-financial sector, the biological device presents itself as an innovative technology with an excellent cost/benefit ratio. In veterinary ophthalmology studies, it showed a significant improvement in the quality of life of pets who previously suffered from serious eye conditions, such as corneal ulcers. In a relevant way, it contributed to animal welfare and, consequently, enabled the satisfaction of its owners. Also, cost reduction was observed during surgical treatment compared to some traditional techniques. The scaffold is a technology developed in the state of Ceará, Brazil, which means that in the future, it will be a more accessible product for both professionals and pet owners, given the reduction in import costs.

Among the countless benefits with the future use of tilapia skin grafts in veterinary ophthalmology, it is important to highlight animal refinement. In animals that present severe injuries, as in the cases already mentioned, the high biocompatibility of the graft reduced the need for euthanasia; once the animal had access to effective and quick treatment. It is also noteworthy that the excellent results boost research into new innovative ophthalmological treatments for animals, as well as creating new opportunities in veterinary medicine. A new surgical technique was developed and optimized surgical time for the professional.

Studies with the scaffold produced great social benefit, enabling effective treatment and improving the health and well-being of pets. It is a viable alternative, having all the characteristics of a good biomaterial to be used as a biological graft in the clinic. Tilapia is the most cultivated fish in Brazil and has excellent market acceptance. Most of the skin is a waste by-product in the food industry, which makes it a low-cost and readily available raw material. Therefore, devices produced

from tilapia skin are accessible, tend to be cheap and biosustainable, with the potential to generate relevant socio-financial impact in Brazil.

Products made from tilapia skin have the prospect of contributing significantly to reducing the cost of regenerative devices, democratizing access to innovative surgical methods and modern therapies for reparative surgeries. In practical terms, the scaffold will provide a significant increase in the animals' quality of life at a reduced cost, as the device uses as its raw material a waste by-product largely produced by the Brazilian food industry, one of the largest in the world.

In veterinary ophthalmology studies, the acellular protein matrix from tilapia skin presents itself as an excellent grafting alternative, as it optimizes animal comfort and well-being, high biocompatibility, absence of rejection, in addition to a good cost/performance ratio. benefit. All the success of its applicability in small animals makes it possible to use it in other species. Additionally, it brings the idealization closer to its use in human ophthalmology, given the high scientific, technological and innovative potential for regenerative medicine.

ACKNOWLEDGMENT

All studies were supported by the Center for Research and Development in Medicines (NPDM) of the Federal University of Ceará (UFC) and developed at the Veterinary Eye Center: Exams, Veterinary Ophthalmology, Fortaleza, Ceará, Brazil.

REFERENCES

1. Afonso, I. S. D. (2017). *Ocular Emergencies in Small Animals: Retrospective Study of 72 Cases* [Doctoral thesis, University of Lisbon (Portugal)].

2. Bertolino, B. F., de Oliveira, D., Costa, G. L., & Albuquerque, A. C. (2022). Study of biological membranes for the repair of corneal lesions in dogs and cats. *Brazilian Journal of Development*, 58579-58585.

3. Borges, L. F. A., Brito, F. G., & Silva, R. A. (2021). Therapeutic aspects of keratoconjunctivitis sicca in dogs: Literature review. In *Current Affairs in Tropical Medicine in South America, Veterinary* (Chap. 8, pp. 125-144).

4. De Miranda, L. G., Nascimento, P. R., & Souza, L. R. (2023). Eosinophilic keratoconjunctivitis in feline: Case report. *Pubvet, 17*(06), e1404-e1404.

5. Forrester, J. V., Dick, A. D., McMenamin, P. G., & Roberts, F. (2020). *The Eye E-Book: Basic Sciences in Practice*. Elsevier Health Sciences.

6. Gervasio, K. A., Chambers, C. B., & Hall, T. M. (2022). *Wills Eye Hospital Manual of Eye Diseases: Diagnosis and Treatment in the Office and Emergency*. Artmed Editora.

7. Machado, A. K. F. (2019). *Perception of Dog and Cat Owners in the Federal District on the Principles of Responsible Ownership and Their Influence on Animal Welfare and Public Health* [Undergraduate course completion work, University of Brasília, Faculty of Agronomy and Veterinary Medicine].

8. Mannis, M. J. M. D., & Holland, E. J. (2016). *Kanski's Clinical Ophthalmology: A Systematic Approach* (8th ed.). Elsevier.

9. Melo, M. S., Dias, L. G., Freitas, A. B., & Silva, A. F. (2023). Use of occlusive tilapia skin dressing in corneal perforation with dislocation and extravasation of the lens in a puppy: Case report. *Contemporânea - Journal of Ethics and Political Philosophy, 3*, 20142-20149.

10. Queiroz, O., & Reis, A. (2023). Corneal ulcer: Literature review (veterinary medicine). *Institutional Repository, 2*(1).

11. Ross, M. H., Pawlina, W., & Barnash, T. A. (2016). *Atlas of Descriptive Histology*. Artmed Editora.

12. Santhiago, M. R. (Ed.). (2020). *Refractive Surgery*. Editora Cultura Médica.

13. Sousa, J. M. (2023). *Use of Platelet-Rich Fibrin in Corneal Ulcers in Dogs* [Master's thesis, Animal Biotechnology, Universidade Estadual Paulista (Unesp)].

14. Vieira, L. S. (2023). *Supervised Internship Report in Veterinary Medicine: Small Animal Clinic and Surgery*. Ânima University Repository (RUNA).