The importance of extracellular matrix (ECM) integrity in maintaining normal tissue function is demonstrated by numerous pathologies of acute or chronic injury associated with destruction or disruption of its components. Regenerating agent therapy (RGTA) showed a strong anti-oxidative and protective effect resulting in reduced inflammation in chronic periodontitis, corneal lesions, oral and skin ulcers [1-5]. Two cases of corneal healing with Cacicol®. The first one was a chemical corneal burn with persistent lesions which resulted in restitution ad integrum after treatment with Cacicol®. The second case was a contact lens wearer whose cornea had an ulcer with profuse lesions within the stromal layer and the evolution under conventional treatment for 2 weeks was insignificant and after the use of Cacicol® the lesions improved. Cacicol® is an innovative treatment that can be used in non-healing corneal lesions, e.g.: unresponsive corneal burns with conventional treatment.

Keywords: extracellular matrix (ECM), regenerating agent therapy (RGTA), corneal lesions, Cacicol®
The second case was a 35-year-old man, contact lens wearer who appeared in the ophthalmology department with ocular pain, photophobia and decreased vision, symptoms secondary to a long trip which instituted poor personal hygiene. The visual acuity was very low, the patient’s visual acuity was only hand movements. The biomicroscopic evaluation demonstrated a profound corneal ulcer with a risk of perforation. The pathogen of staphylococcus into the patients conjunctival secretions was identified.

**Results and discussions**

To the first patient the conventional treatment did not lead to the expected results, the epithelialisation was slow (3 weeks) and the stromal defect persisted. The use of a tissue regenerating agent administration - Cacicol®, one drop/week, lead to the remodeling of the cornea and to restitution ad integrum. The visual acuity progressed from 0.1 at the beginning of treatment, to 1.0 after the cessation of treatment.

To the second patient the local treatment administered was Netilmicin for 10 days, hourly for 48 hours and then every 3 hours for 7 days. Because there were stagnant secretions, the treatment was switched to Vigamox for 7 days, Tobrex ointment and Indocoll for the inflammation.

When the secretions disappeared, re-epithelisants like Thealoz duo and Corneregel were administered. The scar was severe, that is why the RGTA were administered, one drop of Cacicol® per week for 5 weeks. The result was total epithelialization after 2 weeks. Figures 1 and 2 demonstrate the favorable evolution of the scar.

![Fig. The aspect of the cornea before the treatment with Cacicol](image)

![Fig. 2. The aspect of the cornea after the treatment with Cacicol](image)

There was insignificant evolution to conventional treatment in these cases, so, the therapeutic alternative to favor and ameliorate the scar was the Cacicol® matrix therapy. The chronic inflammatory component was associated with the lesion. Pain relief was alleviated after 2 weeks under the new RGTA treatment with the restoration of the extracellular matrix which surrounds the sensitive nerve endings onto the cornea. The restitution ad integrum was gained at the end of the therapy in the first case. In the second case, the improvement in visual acuity was 80% and the patient did not have any pain. The superior and paracentral parts of the cornea remain leukemic, under supervision.

The new therapeutic class of RGTA is a new and different promising healing agent from any product on the current market and their innovation consist in creating a new micro-environment because of their content in heparin-sulphates [8].

The idea of recreating a new micro-environment due to the heparin-sulphates is a real innovation. RGTA regeneration agents replace the degraded glycosaminoglycans such as heparin-sulphates and will furthermore settle on the matrix proteins and are resistant to the remodeling enzymes because they are not destroyed by proteolytic enzymes such as heparinases, thus providing protection for the stromal extracellular matrix environment and other components involved in tissue healing [9].

The RGTA attached to the matrix proteins will allow the growth factors and cytokines to act on the injured area leading to the restoration of the matrix comparable to physiological conditions. Heparin-sulphate and their analogues obstruct in vivo the proteolytic enzymes like elastase, plasmin, cathespisin G [10,11].

RGTA have the potential of healing chronic wound problems of the entire body [12]. In order to promote epithelial wound healing, they contour a bio-skeleton which will activate cell adhesion and will be ready for the adhesion of growth factors onto the surface. RGTA job is to link different structural proteins such as collagen, elastin and fibronectin, thus assisting in the formation of the corneal matrix architectonics and can also restore the intercellular communication for the normal tissue regeneration, thus providing a strong mechanical protection for degradation. By this way, restoration of ECM (stromal extracellular matrix) scaffold properties and process take place and the RGTA reestablish the micro-environment.

Thus, this bio-skeleton being made, the micro-environment is just perfect to promote the healing through re-epithelialization and to secure the stromal extracellular matrix plan which will alleviate the pain. An anti-fibrotic response is done by decreasing the synthesis of collagen type III, decreasing the tissue edema and inflammation and reforming the collagen reorganization [13].

Oral mucositis is a complication of cancer treatment. Chemotherapy and radiation treatment cause oral mucosal atrophy and ulcerations, increasing the risk of infection and affecting the quality of life. RGTA prevented mucositis in 50% of treated hamsters and significantly reduced the mean lesion volume in the remaining animals [2].

**Conclusions**

The conventional treatment given in both cases did not lead to the expected results, which warranted new RGTA treatment, Cacicol®, which was introduced and the improvement of the lesion was immediate and evident through the alleviation of the pain and the evolution of the scar. Cacicol® was very well tolerated, did not have any local or general allergic reaction, nor side effects. The intraocular pressure remained within normal values and other components involved in tissue healing [9,14].

RGTA by its mode of action, its glucose-based structure, its ability to specifically localize to sites of injury where it is retained throughout the restoration process, and its natural elimination as a matrix element with no evidence of toxicity, makes it a safe product [15-17].

RGTA controls ocular surface inflammation and enhances corneal healing. As a result, RGTA are the best choice to use for long-lasting corneal lesions [18-21].
Studies demonstrate that RGTA matrix based therapy is an efficacious and non-invasive approach to treat various injuries affecting the cornea, muscle injuries, acute or chronic ulcers, oral mucositis, reduced bone loss in chronic periodontitis [18-25].

References

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Manuscript received: 4.10.2018

REV.CHIM.(Bucharest) ♦ 70 ♦ No.5 ♦ 2019 http://www.revistadechimie.ro 1807