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TRANSPORTE TRANSDÉRMICO POR MEIO DE APARELHOS PORTÁTEIS: OUTRA FORMA DE APLICAR COSMÉTICOS, ENSAIO *IN VIVO*

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RESUMO: A pele é uma importante via de aplicação de fármacos. A camada mais externa da pele, o extrato córneo é a primeira porção protetora que dificulta a permeabilidade de substâncias. Métodos físicos como o peeling ultrassônico, a ionização e a eletroporação podem facilitar a entrada de substância na pele. O objetivo do estudo foi observar os efeitos do peeling ultrassônico, a ionização e a eletroporação associado com cosméticos na pele. **MÉTODOS:** Foram utilizados 6 animais da linhagem Wistar divididos aleatoriamente em 3 grupos com 2 animais cada (um grupo controle, um grupo tratado com Peeling Ultrassônico mais Fluido Nano Gold e um outro grupo tratado com Dermoroller mais Sérum Anti-wrinkle), e tratados por 10 dias consecutivos. Os dados foram analisados qualitativamente. **RESUTADOS:** As análises histológicas mostraram uma redução na camada córnea no grupo submetido ao Peeling Ultrassônico, mas no grupo da Ionização com o Fluido Nano Gold houve um aumento da epiderme. **CONCLUSÃO:** Observou-se um aumento de fibroblastos com neoformarção de colágeno no grupo tratado com o Dermaroller mais o sérum Anti-Wrinkle.

Palavras-chaves: Ionização. Eletroporação. Cosméticos.

TRANSDERMIC TRANSPORT BY PORTABLE DEVICES: ANOTHER WAY TO APPLY COSMETICS, *IN VIVO* ASSAY

ABSTRACT: The skin is an important route of drug application. The outer most layer of skin, the stratum cornea is the first protective portion that hinders the permeability of substances. Physical methods such as ultrasonic peeling, ionization and electroporation can facilitate the entry of substance in the skin. The aim of the study was observed the ultrasonic peeling, the ionization and electroporation effects associated with cosmetics in the skin. **METHODS:** Six Wistar animals were used and divided randomly into 3 groups of 2 animal seach (a control group, a treated group with ultrasonic peeling plus Nano Gold fluid and another group treated with Dermoroller plus Anti-wrinkle Serum). The treatment lasted 10 days consecutive. The data were analyzed qualitatively. **RESULTS:** The Histological analyzes showed a reduced in the cornea stratum and an increase of the epidermis in the group treated with ultrasonic peeling plus ionization and Nano Gold fluid. **CONCLUSION:** It was observed an increase in the fibroblasts with neoformation of collagen in the treated group with the Dermaroller plus serum anti-wrinkle.

Keywords: Ionization. Electroporation. Cosmetics

1. INTRODUCTION

The skin is an important route of administration of drugs, and in the previous years there has been a significant increase in the studies for the development of specific formulations for such purpose. However, just some molecules can cross the skin levels. For example, when the potent lipophilic substance permeates the skin by passive diffusion, it can have a therapeutic benefit. So, this type of the transport is slow and it requires a latency of hours.[1]

The outermost layer of skin, the cornea stratum is first protective portion. The function of it is to prevent water loss and avoid, to a certain extent, the entry of foreign bodies such as microorganisms, harmful physical agents and chemicals products including medicines. This layer contains only 20% water and therefore is a barrier extremely lipophilic[2-3].

The hard step of the dermal absorption is the permeation through the cornea stratum,[4] which because of that characteristics is the main barrier to transport molecular, allowing the passage of lipophilic molecules of low molecular weight and only small quantity[5]. Due to the limitations imposed by cornea stratum, the most part of hydrophilic substances and with intermediate or high molecular weight shows reduced permeability cross the skin[6-7].

To facilitate the permeation of substances through the skin, there are many physical methods and devices that can help this process such as ultrasonic peeling, ionization and electroporation[8].

The ultrasonic peeling promotes a cleaning in general, is nothing more that permanent disposal of a contaminant from substrate, which may be the surface of any object. To accomplish cleaning, you must have a job to remove contaminants, breaking their chemical bonds, overcome the force of electrical attraction and Van der Waals, ensuring that removal is permanent, preventing that the electric force would be redeposited to the contaminantes[8]. Thus, the cleaning of a substrate is not an easy task, especially if the need for cleaning is high, if the contaminants are chemically inert, if the object to be cleaned have holes or cavities and cannot undergo abrasion, chemical or mechanics. In the ultrasonic cleaning systems, the work to remove and keep contaminants away from the substrate (usually with chemical help) is performed by the phenomena of the propagation of high-intensity sound: cavitation and transfer time. The macroscopic manifestations of those phenomenon in the cleaning process are: the dispersion and an increased dissolution of solid and liquid films, erosion, fatigue and the degradation of contaminants and the eliminating of air bubbles in the cavities[9-10]. This way, it tries to reduce the excess waste and keratin of skin of the cornea stratum to facilitate the permeation of substances.

Iontophoresisis a technique to promote permeation used widely. It is the combinations of an electric continue current or electric alternating current with topical drug, which enhances the transdermal release through the cornea stratum, increasing the therapeutic efficacy of many treatments. A drug with positive polarity, for example, it should be placed in a positive electrode to repel the like charges to put the drug to into in the skin toward the site wished, when electrical current is triggered[11]. There are several clinical applications of Iontophoresis as transdermal transport[12-13].

Electroporation is another type of physical permeation promoter that consists in the use of short pulses (microseconds to milliseconds) of high voltage 100-1000 V/cm, which goes to

beyond the membrane barrier providing for a structural rearrangement of this membrane, and making it highly permeable to exogenous molecules[14]. This structural rearrangement creates temporary aqueous channels (pores) due to application of electric field[15-16].This phenomenon is a non-invasive process, reversible and not alter the biological structure or target cell function[17].

The electric field used in the electroporation process is obtained normally by applying tension pulses between two electrodes, in which there is a suspension of cells (in vitro) or a region of a tissue of a patient (in vivo), and it has the effect changing the potential difference across the lipid double layer. When this transmembrane potential reaches critical intensity, the electroporation started, and the permeates area is increased by the duration of the voltage pulse and the frequency of repetition[18].

Platinum Anti Wrinkleis a multiaction serum used for the treatment of premature aging and expression lines. This consists mainly of Copper Tripeptide 1 (GHK-Cu) a peptide expression promotes cell growth factors,more regularly collagen synthesis, elastin, proteoglycans, glycosaminoglycans production and anti-inflammatory and antioxidant responses[19-20] Acetyl Hexapeptide 8 (Argireline®) a synthetic peptide that is especially marketed as a component of eye care products and patterned from the N-terminal end of the protein SNAP-25 that inhibits SNARE complex formation and catecholamine release[21] and Platinumnanospheres.

Nano Gold Fluid is another multi fluid action topical application, indicated to promote cell renewal.This consists of various peptides and vitamins, being its main components Gold nanospheres, application to the skin has shown positive effects on low blood-flow skin ulcers, findings showed a significant improvement in mouth legions and skin ulcers with no adverse reactions observed[22]. Copper Tripeptide 1 (GHK-Cu) and Ceramide 3 are the most abundant ceramide in healthy human and important factor in maintaining the hydration and skin barrier[23-24].

Due toall these possibilities of fluids and permeation, this study aimed to observe the effects of ultrasonic peeling, the ionization and electroporation associated with the cosmetics in the skin.

2. METHODS

This is an experimental study, the research population was Wistar rats (Rattos norvegicos albinus) males. The study sample consisted of 6 animals weighing between 250 g and 300g, coming from the vivarium of Universidade Potiguar (UnP).

All rats were fasted for 12 hours, and then the rats were anaesthetized with Zoletil 50, intramuscularly in the left quadriceps at a dosage calculated according to the animal weight (50 to 75 mg/kg).

It was performed shaving the back of the animals 3x5 cm² (LXA) and divided randomly in to three groups with two animals each: a control group without treatment, a group with Labelle®, ultrasonic peeling system (view Figure 1) plus 3 drops of Nano Gold fluid associated with ionization and a group with the pen Dermaroller® (view Figure 2) in average intensity associated with 3 drops of Platinum Anti Wrinkle serum. Ten applications were performed

once daily in the morning for 10 days, with an exposure time of 3 minutes each procedure. On the day 11, the animals were sacrificed in CO_2 chamber and with drew an area of 2x2 cm^2 biopsy histology analyses.

The data were analyzed qualitatively.

The statistical analysis was made by the test t student with ⊠=10%.

3. RESULTS

According to the analyzes of the Figures 1 and 2 it is possible to compare groups looking to the epithelial tissues, particularly in relation to the cornea stratum. In the control group (view Figure 3) as there was not intervention not only the cornea stratum, but also everything is normal. In the treated group (view Figure 4) that received the ultrasonic peeling plus Nano Gold fluid there was a decrease in the thickness of the cornea stratum by the breaking of chemical bonds and the proper action of "cleaning"[9]. In this increase of lenses was not observed any changes in the use of ionization plus Nano Gold fluid.

Figure 1. - Labelle®(Ultrasonic Peeling System)

Figure 2. - Dermaroller® Pen (Portable Electroporation System)

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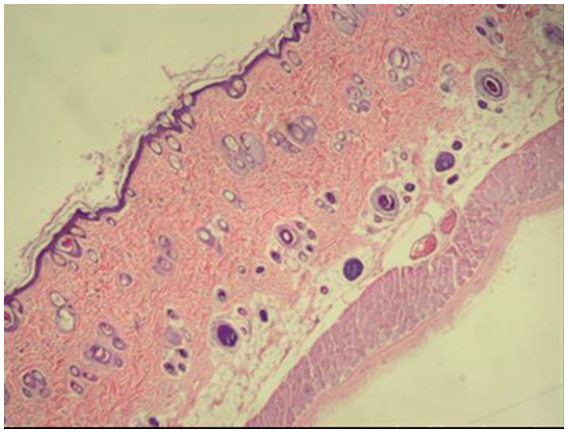

Figure 3. - Photomicrograph HE 40x: normal epidermis and presence of cornea stratum.

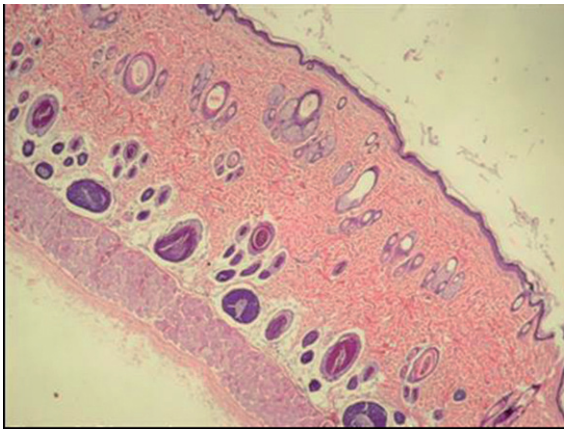

Figure 4. - Photomicrograph HE 40x: Thin epidermis with less cornea stratum due to use of ultrasonic peeling.

On a larger increase was observed as shown in the images below an increase in the thickness of the epidermis in the control group (view figure 5) compared with the treated group with Ultrasonic Peeling plus Nano Gold fluid (view figure 6) that may have occurred due to the use of Nano Gold fluid and again the decrease of the cornea stratum previously described.

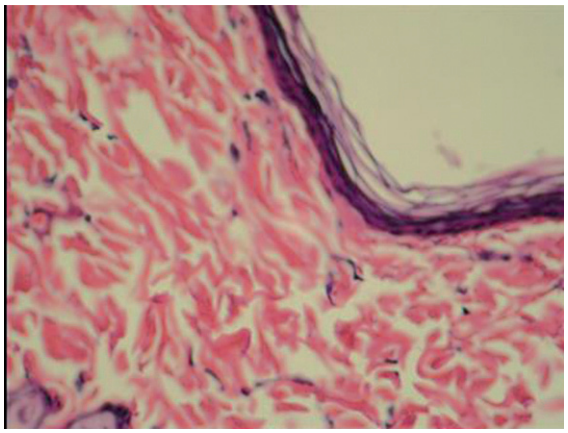

Figure 5. Photomicrograph HE 400x: normal epidermis and presence of stratum cornea.

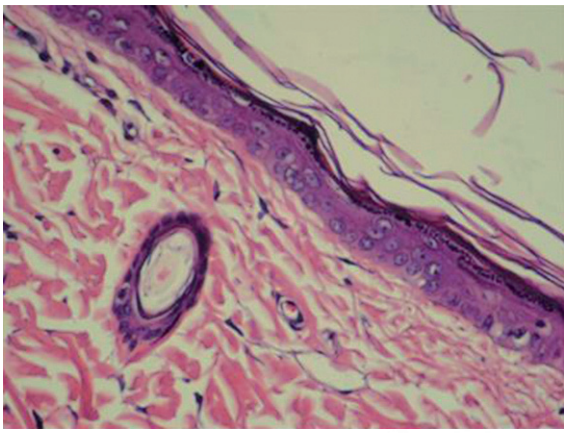

Figure 6. - Photomicrograph HE 400x: Thick epidermis with less cornea stratum due to use of fluid Nano Gold plus ultrasonic peeling

In the figures below, comparing the control group (Figure 7) with the group treated with the Dermaroller® plus Platinum Anti-wrinkle Serum (Figure 8). It can notice a large number of fibroblasts with collagen neoformation in the treated group, electroporation facilitated the entry of Platinum Anti-wrinkleSerum[17,18] activating the neoformation of collagen making the skin stronger after 10 treatment sessions.

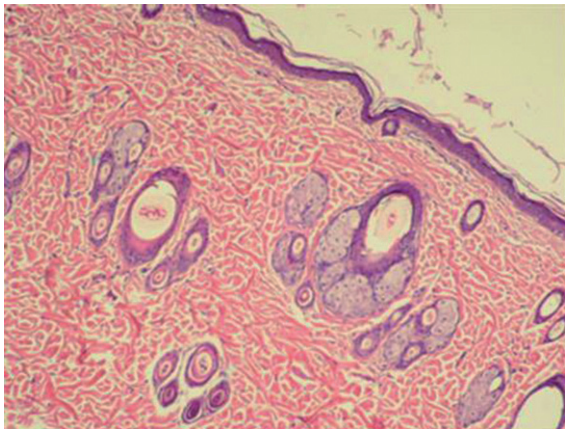

Figure 7. Photomicrograph HE 100x: Presence of collagen normal tissue, group without treatment.

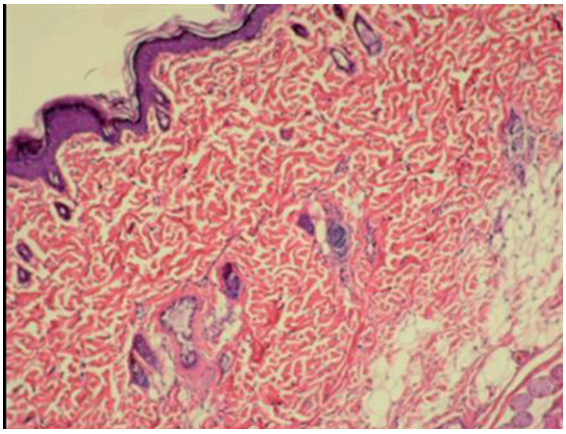

Figure 8. - Photomicrograph HE 100x: Presence of fibroblasts and collagen neoformation after 10 sessions of Dermaroller plus serum Anti-wrinkle

By increasing the images on 400x is clear the presence of larger number of fibroblasts in the group treated with the Dermaroller plus Platinum Anti Wrinkle Serum (view Figure10) compared with the control group (view Figure 9), what can improve the skin appearance due to fibroblastic activity with the treatment maintenance.

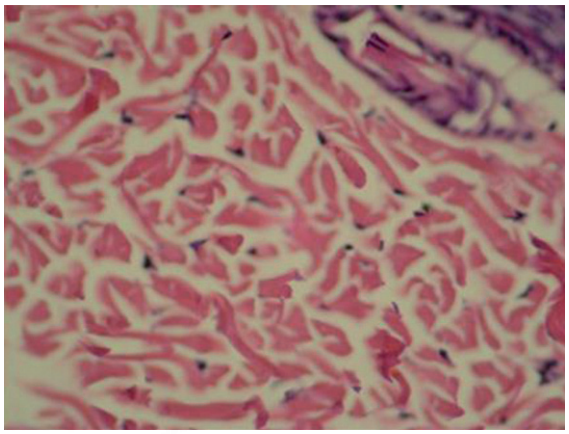

Figure 9. Photomicrograph HE 400x: Presence of minor amount of fibroblasts in the group control.

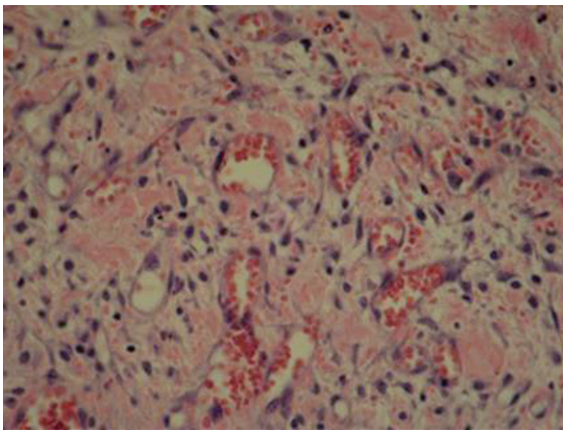

Figure 10. - Photomicrograph HE400x: Presence of much fibroblasts in the group treated with Dermaroller plus Platinum Anti Wrinkle Serum.

The result does not show significance in the statistical analysis, but it may be considered the suitable variations described.

4. DISCUSSION

The ultrasonic peeling is able to promote a reduction in the thickness of cornea stratum, making thinner and, thereby it decreases the barrier of permeation of substances.

Electroporation has proven to be a promising method to transport substances across the skin. The technique allows the carrying of macromolecules with different polarity (hydro-

philic or lipophilic) and also it provides synergistic combinations with other techniques such as iontophoresis.

This research shows that, despite of the advances in electrical behavior, the influence of physicochemical characteristics of the substances and of the formulation, there is still the lack of conclusive studies on the permeation/ retention skin, the time required for the substance permeates and the concentrations obtained in the skin layers and underlying tissues.

The Nano Gold fluid and the Platinum Anti Wrinkle Serum showed effects on the skin, but more studies should be done regarding the different types of skin, because besides the complications of penetration of substances in the skin, there are many types of epithelia that depends of morphological conditions (thickness and photo type), which may or not derail the study.

The portable devices can be another way to apply cosmetics in the skin. But more studies should be done to make the physiology of the substances clear through them.

It is suggested further studies with isolated substances of high ionic power and low molecular size in different types of skin to display the permeation and their effects in the skin. In time, it will possible in new studies to specify separate aspects of the skin like fiber elastic and other structures, despite the fact that there were this limitation in the research, including the small sample.

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