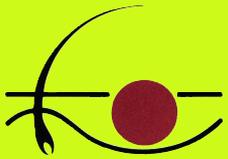


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▶ **A new
transdermal
delivery for
cosmetics
(TMT system®)
Electroporation
for photodamaged
skin, stretch marks
and cellulitis**

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TIRÉ À PART

Arnette

Transdermal systems provide the transepidermal passage of active molecules, drugs or cosmetics. There are a great many such systems as they have been developing for over 15 years in different fields of medicine.

They may involve the optimisation of cosmetic formulations, the use of laser micro-needles, micro-incisions, radiofrequency or the molecules may be transported by different energy channels: iontophoresis, electroporation, sonophoresis, microwave or photomechanics.

Skin electroporation aims at applying an electrical field at the skin surface, to transepidermally transport charged macromolecules.

The diffusion of the electroporation is homogenous within a skin surface. Different factors may modify skin electroporation such as the type of current applied, the concentration of the molecule, its ionic charge, the pH of the solution as well as its viscosity. Different factors affecting the charge, size and structure and the lipophilicity of the molecule may also modify the transepidermal passage. Finally, skin factors such as the permeability, presence of pores and skin thickness, in particular that of the stratum corneum, may also modify the passage.

The barrier function is mainly provided by the stratum corneum. Within it “micropaths” called

ultramicropores form, allowing for the transepidermal and then transdermal passage of molecules. The electric currents used range from 100 to 1000 volts with a frequency of 1 Hz and from 1 to 100 milliseconds. It consists of high voltages and short times, differing electrophoresis from iontophoresis using low voltages with longer times, or even continuous currents.

Material and methods

The purpose of this study is to provide the first results obtained with a system of electroporation and check the cosmetological efficacy of different preparations associating a transport gel called Mesogel® and a solution containing active cosmetic ingredients in different skin cosmetology indications.

The product in solution is applied using a roll-on (**Fig. 1**) called the anode while the patient holds the cathode to allow the current to circulate. The ionisation of the molecules occurs on the skin surface. The application of these short voltages on the cells and tissues induces modifications in the cell membranes and intercellular spaces.

The ultramicropores increase the skin and cell permeability and create a concentration gradient that favours the passage of ionised and non ionised molecules. The resulting concentration gradient increases the penetration by electroosmosis and electrophoresis.

Thirty female volunteers, 32 to 65 years old, were used in the study. All phototypes, according to Fitzpatrick’s classification, were included.

Ten patients received 10 sessions of electroporation in each of 3 indications: wrinkles, stretch marks and cellulitis (**Fig. 2-4**).

The criteria for inclusion required, for the wrinkles, a maximum Fitzpatrick score of 2, for stretch marks a maximum width of 4 mm and stage 1 for cellulitis.

The methods of assessment included a visual analogue scale of the main clinical signs by the



Figure 1 :
Roll'on

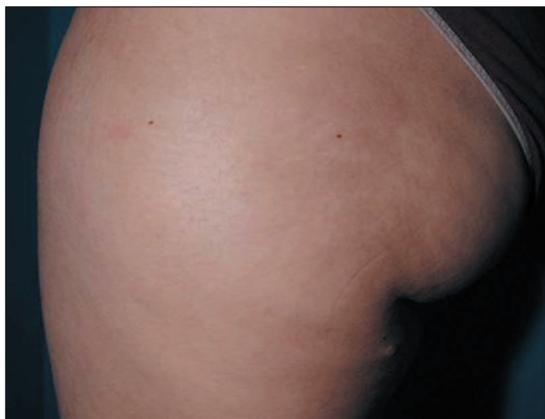
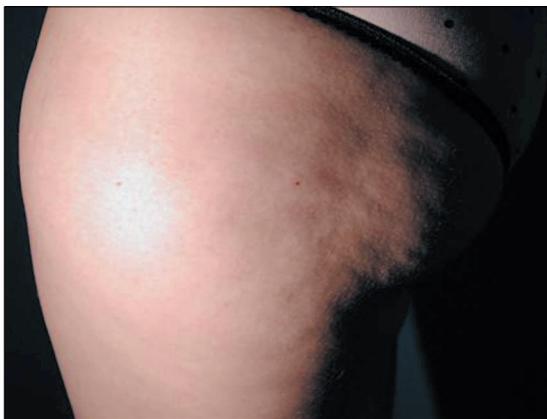
KEY WORDS • Transepidermic system (TMT® System)
• Skin ageing • Stretch mark • Cellulitis

Summary: Skin electroporation has been shown to enhance transdermal drug delivery by several orders of magnitude and to transiently permeabilize cells tissue. A new approach consisting of delivering active cosmetics ingredients to the dermis in various clinical conditions. This study aimed to determine the efficacy of this technique of electroporation using clinical assessment over a 5-month period. The TMT® System (Bodyestetic laboratories, Barcelona, Spain) used one roll-on electrode directly applied on the skin to deliver with square wave pulses a solution dedicated to 3 applications: early photodamage, early and white stretch marks, cellulite with orange-peel aspect. 10 sessions were

achieved in all applications over a 5 weeks period with a 3-months follow-up. 10 subjects of phototypes I to V was enrolled and received 2 treatments by week. We observed that the wrinkles were improved with 4 treatments less than roughness and tone of the skin. Stretch marks are improved after the 8th sessions in length and color. Orange peel was improved dramatically without improvement of fat body volume with a stabilized weight. A stinging sensation without pain is described during the session. A slight erythema is observed just after the session. The clinical assessment confirms that TMT® System is a non invasive, user-friendly method for dermal cosmetic delivery. We will discuss the transportation of macromolecules. Further clinical studies will explore further dermatological applications.



Figures 2 : Small wrinkles : before and after treatment



Figures 3 : Cellulitis : before and after treatment



Figures 4 :
Stretch marks :
before and after treatment

investigator, an evaluation of the clinical tolerance during the treatment and at the end of the study. The study follow-up period was 5 months. The sessions lasted for 10 to 15 minutes, generating a transient erythema with a stinging

sensation without pain or muscular contraction. Pregnant women and patients with a pace-maker were excluded. We did not note any irritation after the session or at the end of the study.

Results

Statistically, the results show an improvement in wrinkles according to the Glogau stage although the improvement is not significant. However, a significant improvement in the elastose stage is noted in all of the patients. Skin roughness decreases and the surface improves as does the grain of the skin.

The results on stretch marks reveal an unpleating and a contraction reducing the visibility of it in width.

As for the cellulitis, the orange skin appearance decreases.

Discussion

The delivery of topics by electroporation above all corresponds to the permeation of the main barrier (the stratum corneum) through the application of high voltages in short times.

This increase in permeability also reaches the cells of the stratum corneum in addition to the interkeratinocyte spaces. Besides different substances such as vitamin C, macromolecules may also cross the stratum corneum. Electroporation, as opposed to iontophoresis, induces intrakeratocyte cell permeability.

The association of two methods demonstrated a synergic effect of the transport of macromolecules if electroporation comes before iontophoresis.

The association with sonophoresis does not usually provide any synergy in the transport of macromolecules. The application of ultrasounds may allow for a reduction in the voltages. This study corresponds to the first application of cosmetic macromolecules by electroporation. The skin modifications due to electroporation by high voltage pulses are moderate and quickly reversible. These short electric pulses provoke a very high drop in the electrical resistance responsible for skin permeability. Electroporation changes skin hydration, induces a disorganisation of the double lipid layer of the stratum corneum, a transient loss of barrier function with a transient increase in the blood flow.

The safety is total and the skin tolerance is good since the different currents are restricted to the stratum corneum and the superficial parts of the skin.

The pain is extremely modest and mainly corresponds to sensations of electrical stinging that does not require a local anaesthetic.

Active cosmetic ingredients known to act on skin ageing, cellulitis (orange skin) and stretch marks, found in the solution to apply certainly penetrate more than by passive diffusion.

The first clinical effects attest to this.

Electroporation is a non invasive method to deliver macromolecules to the skin. It is promising for macromolecules of at least 40 kda and provokes a fast, continuous or pulsed, delivery of substances.

It is possible to modulate the pharmacokinetics of substances using appropriate currents. The control of the pulses and the form of electrodes can be used to control the main adverse reaction, muscular contraction, that we have not encountered.

Other studies, in particular by marking, will provide objective traceability of the molecules transported. ●

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