

Transdermal Delivery of Medications for Aesthetics

By Bob Kronemyer, Associate Editor

Transdermal drug administration has obvious potential advantages over oral, injection, or intravenous drug delivery. Many aesthetic applications seek to deliver ingredient molecules to a specific depth in tissue to rejuvenate photo-aged skin, minimize or eliminate hyperpigmentation, smooth tissue areas impacted by cellulite or mobilize localized fat deposits. Conventionally applied topical medications, used for aesthetic treatments, are limited in their ability to penetrate to any significant depth in tissue. Injection mesotherapy does deliver an ingredient mix to a specific required depth but suffers from the disadvantage of variable technique, non standardized formulas and poor patient acceptance.

Advantages of transdermal delivery techniques relate to convenience, patient comfort, minimal trauma and possible delegation of treatments to ancillary personnel. Highly localized administration is possible, and delivery can be achieved through absorption by dermal blood supply and distribution via the lymphatic system.

The DermaWave No-Needle Mesotherapy System uses four sequences of electrical waveforms to deliver topical ingredients transdermally.

However, the principle barriers to transcutaneous drug delivery are the protective properties of the stratum corneum. Absorption may be increased by removal of the stratum corneum via dermabrasion, excimer laser ablation, solvents and the use of penetration enhancers like dimethyl sulfoxide.

New methods of transdermal delivery focus on techniques that are efficient at delivering molecules to an appropriate treatment site avoiding the risk of a poor outcome. Disruption of the stratum corneum can be achieved by electroporation or the creation of water channels or microconduits. In electroporation,

ions and molecules move through the stratum corneum by diffusion and electromotive or electro-osmotic transport.

The DermaWave No-Needle Mesotherapy System™ uses four sequences of electrical waveforms to deliver topical ingredients transdermally. On the direction of a physician, a prescription conducting active gel may be used to address the underlying factors contributing to the formation of cellulite, hyperpigmentation, photo-aging and fat deposits.

Electroporation differs from iontophoresis. Studies comparing iontophoresis with electroporation show that iontophoresis delivers 100 times less drug than injections but provides higher local concentrations than oral administration. In iontophoresis, the pathways that ingredients take are restricted with the drug permeating the skin via appendageal pores. These routes account for about 0.1% of the skin's surface, making drug delivery via iontophoresis inefficient for large tissue areas. Appendageal penetration is slow, so dilution is a factor influencing success. In contrast, the number of transdermal pathways available via electroporation is 500 times greater than with iontophoresis.

Methylene Blue (MB) delivered by electroporation showed much greater penetration than dye delivered by iontophoresis. Delivery is enhanced by energy in the form of pulses, and even at low electroporation levels delivery of MB was dramatically higher than with iontophoresis.

Double-blind studies, conducted at major universities confirm the benefits of the DermaWave approach and allow objective comparisons of needle and No-Needle techniques.

Radioisotope lymphography is used to establish molecule penetration and retention time in tissue and employs a tagging technique to trace ingredient passage through an intact stratum corneum to sites in the extracellular matrix and dermis. This technique monitors the retention of ingredients in tissue at specified times as well as their presence in the lymphatic system.

Radioisotope lymphography showed that all patients receiving non-active ultrasound gel showed minimal penetration –

with most of the tagged material residing in the upper epidermis. 100% of the group receiving the permeation enhanced active material showed transdermal penetration through an intact stratum corneum to the extracellular matrix of the dermis in less than 20 minutes and even distribution and retention in tissue up to 24 hours.

An *in vivo* study from the University of Pretoria, South Africa, observed the effects of the DermaWave No-Needle Mesotherapy System on photo-aging using agents such as hyaluronic acid (HA), retinoic acid (RA) and dimethylaminoethanol (DMAE). All volunteers showed a reduction in photo-aging. The system successfully increased transdermal delivery and was described as a safe, effective alternative to painful needle mesotherapy.

DermaWave's electroporation delivery of the combination drug, containing DMAE, RA and HA, resulted in a significant reduction of coarse wrinkles after five treatments (one treatment per week) – comparably better than reported results with mesotherapy.

In vitro effects from the combination of agents on collagen synthesis and cell proliferation were also studied. HA, RA, DMAE and the combination drug reduced the effects of photo-aging. HA, DMAE and the combination drug increased collagen synthesis.

In the case of cellulite formation, it is important to address the visible result of the condition as well as the underlying cause. Cellulite deposits occur as the result of biochemical and metabolic alterations at an interstitial matrix and connective structures level. Reduced collagen, elastin and deposits of monosaccharide occur and extracellular matrix changes result in a structure that is more gel like than liquid. Tissue acidity increases and changes occur in oxy-reduction mechanisms. There is a pronounced slow-down in arteriole and vascular flow and permeability of the capillaries and lymphatic drainage system are severely compromised. Fat cells are displaced into the lower dermis. Fibrous bands, responsible for the maintenance of skin tension, become less elastic and trap the displaced cells.

Current strategies for reduction of cellulite are focused on treatments to reduce the external appearance of the disease. Reduction of external dimpling represents only one aspect of cellulite formation and does not address the many underlying causes of the condition.

Practitioners employing a single strategy to improve the appearance of dimpled skin may be limited in offering patients a viable long-term solution to their problem.

Protocols employing traditional endermology require an initial series of 16 sessions followed by frequent follow-up visits. Patients can expect to spend at least \$2,000 for their initial series of 16 sessions and an additional \$2,000 for maintenance visits in a single year. Cost factors play an important role in determining patient satisfaction especially in older patients presenting more difficult to resolve grades of cellulite.

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Injection mesotherapy is criticized for its lack of scientific proof, but the electroporation technique is well supported by scientific literature. Transdermal delivery of medications is a major thrust to the world's pharmaceutical companies with upwards of 40% of new drugs being developed for this method. No-Needle Mesotherapy is expected to transition from exclusively aesthetic applications to other areas of interest in medicine.