

Microneedle Therapy

A Medik8 Briefing for the Scientific Community
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Abstract

The stratum corneum is the main barrier to transdermal penetration of active ingredients in topical pharmaceuticals and cosmeceuticals. Microneedle therapy has previously only been used by dermatologists as an independent anti-ageing treatment; but new studies show that pre-treatment with microneedles will dramatically increase the penetration and therefore serum concentration and therapeutic effect of topical treatments. The following briefing outlines the findings of recent key studies and shows that not only will microneedle therapy dramatically enhance topical treatment efficacy, but it will reduce the appearance of wrinkles and scars and independently stimulate collagen production.

Introduction

Microneedle therapy (also referred to as Skin Needling) is a relatively new technology, which combines the ancient Chinese acupuncture techniques with the contemporary mesotherapy practice. One of the most remarkable discoveries in this area was probably by Dr Andre Camirand, a Canadian Plastic Surgeon, who in 1997 reported previously unforeseen and very surprising results from scar camouflage tattooing procedures with skin-colour pigment in patients with hypochromic facial scars. Camirand observed that after one to two years post procedure, the appearance of the scars was remarkably improved both in texture and in colour, although the pigment had long vanished. After thorough examination Camirand concluded that the insertion of the fine tattoo gun needles into the scar managed to break down the scar collagen and lead to a synthesis of new healthy collagen as well as to a re-stimulation of melanogenesis [1].

Since the 1990's, microneedle therapy has long been used by dermatologists in the form of Collagen Induction Therapy (CIT) to fade scars and generally as an anti-ageing treatment. Shortly afterwards smaller sizes of microneedles were recognised for their capacity to dramatically increase the bioavailability of topical treatments and further enhance their transcutaneous absorption. A key benefit from Microneedle Therapy therefore rests with increasing transdermal penetration of actives, facilitating higher serum concentrations at the dermal level. This has the potential to make topical treatments both more effective and more affordable. The second key benefit from microneedle therapy is the induction of collagen by controlled wounding. Collagen induction builds layers of the supporting intracellular matrix, promoting healthy, resilient skin that looks younger.

Penetration Enhancement

A real challenge for the manufacturers of cosmeceutical topical formulations is undoubtedly that of improving the cutaneous permeation. Cutaneous permeation occurs when an active compound is released from its delivery vehicle

(e.g. ointment, cream, liquid, gel, etc.) through the epidermal skin barrier and into the subcutaneous layers of the skin [2].

The largest limitation of the transdermal active transportation is the fact that it is principally in a form of passive diffusion, as governed by Fick's law [3]. According to Fick's law, molecules travel randomly from a region of a relatively high concentration to a region of a relatively low concentration, resulting in the complete diffusion of two substances involved. For that reason, lipid-soluble actives penetrate easily through the skin, while water-based ingredients require specialist delivery systems and penetration enhancers [4].

Thus, the physiology of the stratum corneum presents an efficient barrier to large or hydrophilic molecules [5]. At the same time, the levels of cutaneous hydration are correlated with the rate of absorption into the skin: lower hydration levels in the skin reduce the diffusion of the active ingredient from the topical formulation into the skin [6].

Additionally, it is important to note that the stratum corneum on facial areas is exposed to higher levels of UV radiation than elsewhere on the body. This has been proven to increase the lipid concentration of stratum corneum cells [7]. Removing lipids from cells increases the water and hydrophilic molecule diffusion rate coefficient by a factor of 100 [8]. Therefore the UV exposed lipid-rich cells of facial areas are much less permeable to hydrophilic compounds.

It can be easily concluded that the chief requirements of advanced skin delivery systems are enhanced penetration and increased efficacy. Some of the recent innovations to achieve these objectives are lipid systems, liposomes, microcapsules, polymers, films as well as pH adjusting ingredients and specialist penetration enhancers, such as PP-2 (INCI: PPG-12 SMDI Copolymer) or linoleic acid. It is also crucial that the ultimate skin care formulation is characterised by minimal or no irritation (e.g. due to controlled release of actives) and a longer shelf life and period after opening (e.g. due to increased stability of ingredients or separation of incompatible actives).

There are, of course, also certain cosmetic formulations, such as sunscreens, skin lightening treatments and hydrators which do not require specialist delivery systems due to the fact that they function in the upper layers of the stratum corneum.

While Medik8 uses all of the above delivery systems to maximise the active penetration through the three natural transdermal delivery routes, that is the stratum corneum, hair follicle pores and sebaceous gland canals, we also recognise that Microneedle Therapy constitutes an alternative delivery route with the potential to even greater enhance the penetration and speed up treatment results.

In 2007, Verbaan, F.J., et al. proved in a landmark paper that microneedle arrays of 0.5mm upwards penetrate the skin sufficiently to increase the diffusion of any compound up to 72000Da, although the 72000Da compound experienced some denaturation [9]. Further tests showed Calcein, a hydrophilic molecule of 622Da, penetrated microneedle treated skin by 10^4 - 10^5 times more than intact skin [10,11] (see figure 1). Hyaluronic acid is a polymer and so potentially could be of any size, however cosmeceutically available hyaluronic acid is normally approximately 2000Da so will clearly penetrate the skin with greater efficiency and speed after the microneedle pre-treatment and will not denature so will remain biologically active. The increased penetration rate will increase serum levels of hyaluronic acid without requiring an increase in concentration beyond what is possible in terms of viscosity.

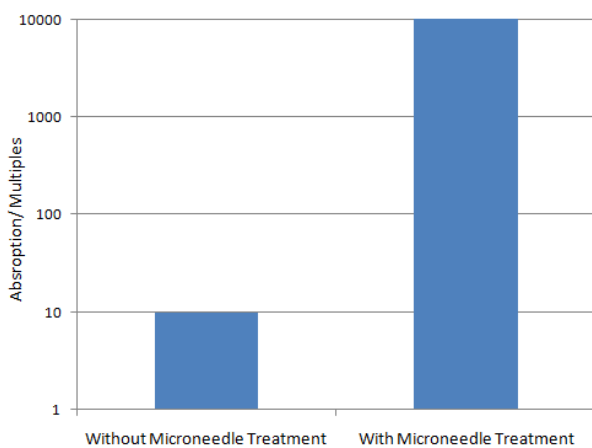


Fig 1. Logarithmic Chart Comparing Transdermal Calcein penetration with and without microneedle treatment. Conservative results used.

Using microneedle pre-treatment will increase the penetration of topical treatments dramatically.

Scar Reduction

Atrophic facial scars are one of the biggest issues for acne sufferers as they involve a loss of tissue at

the site of the scar, giving the appearance of “holes” in the skin. Previously performed aesthetic surgeries, injuries and other dermatological conditions, such as stretch marks, are also common causes of atrophic scars. These obvious scars are of serious aesthetic concern to many and microneedle treatments provide an effective solution.

Scar tissue is formed when damaged layers of epidermis are repaired rapidly in the presence of TGF- β 1 & 2. Research shows that inhibiting TGF- β 1 & 2 allows scar-free healing [11], this is correlated by the fact that scar formation occurs more often in older patients and as skin matures levels of TGF- β 1 & 2 increase. It is possible that the controlled small injuries produced by microneedling stimulate a different healing response, one that does not involve TGF- β 1 & 2 and therefore does not cause scar tissue formation.

Microneedle treatments have been shown to initiate collagen formation and the healing cascade [12], but as they act in a non-ablative manner they do not remove the epidermis and will not cause hyperpigmentation [13]. Therefore microneedle therapy promotes healing with less damage and recovery time than traditional ablative or “Re-surfacing,” techniques [14].

Microneedle therapy can therefore be used to remove and fade old scars and even prevent much of the scarring from any new surgeries. When the wounds from the surgery are closed the microneedle roller can be used safely and will encourage faster healing with less scarring.

A recent study by Imran Majid (2009) confirmed the efficacy of skin needling using a dermaroller device in the treatment of atrophic facial scars. Majid conducted the microneedling treatment on 37 patients suffering from atrophic facial scarring to a series of 3 microneedling treatments and observed any changes in the appearance of the scars, by grading the pit of the scars on numerous picture shots made throughout the course of treatments. Improvement was also assessed by patients themselves on a 1-10 scale. The results reported by Majid confirm microneedle therapy as an effective method for the treatment of atrophic facial scars. “Overall 36 out of the total of 37 patients completed the treatment schedule and were evaluated for its efficacy. Out of these 36 patients, 34 achieved a reduction in the severity of their scarring by one or two grades. More than 80% of patients assessed their treatment as 'excellent' on a 10-point scale. No significant adverse effects were noted in any patient.” [15]

Collagen Induction

Collagen Induction Therapy is based on the skin’s inherent repair response to mechanical injury [16]. Immediately after an injury occurs the damaged collagen and elastin fibres, as well as other damaged

skin components, are recycled to produce more regular layers of tissue and new collagen is synthesised. Collagen synthesis is complex and occurs in different ways in different areas of the body [17- 19], but epidermal collagen can be stimulated by injury.

Microneedle therapy allows for the controlled induction of the skin's self repair mechanism, by creating micro injuries in the skin, which induce new collagen synthesis to a controlled degree.

To confirm the collagen induction benefit of the microneedle therapy in vivo, Aust et al. conducted a retrospective study of 480 patients in South Africa and Germany. Individuals with wrinkles, scars and stretch marks were treated with 1 up to 4 sessions of the microneedle therapy. Pre-operative skin preparation involved application of topical vitamin A and C for at least 4 weeks before the procedure(s). Subjective evaluation by German patients revealed a 60-80% improvement in the appearance of their skin, while empirical evidence by histological examination in 20 patients demonstrated a significant new collagen and elastin deposition at 6 months post-treatment and a 40 % increase in the epidermal thickness at 1 year post treatment [14,16].

Medik8 Titanium Dermaroller

The Medik8 Titanium Dermaroller has several unique differences to other rollers for dermatological use. To allow it to be used more effectively and intensively on the facial skin on a regular basis, several key innovations have been necessary.

Titanium Needle Composition

Because the Medik8 Titanium Dermaroller can be used more intensively than previous dermatological versions, the needles benefit from being manufactured from Titanium and not stainless steel. Titanium gives a finer edge that lasts much longer, preventing excess irritation caused by blunted needles. The needles are manufactured in Sweden as engineering parts, not in China or Korea where many skin models are manufactured.

The titanium needles are also gold-plated to help inhibit microbial growth and maintain sterility. The gold coating also prevents oxidation and pitting of the surface even with long term use. This is especially important for non-single-use products that penetrate the skin's surface.

A sanitising solution is also available and is recommended for sanitising rollers pre-use.

Optimum Needle Length

Studies indicate microneedle roller needles need to penetrate the upper layer of skin for best results.

The Medik8 Titanium Dermaroller has a variety of needle lengths for optimum results without appreciable pain or injury.

The genuine Medik8 Titanium Dermaroller is available in two versions for personal use. A 0.2mm version is recommended for patients with very thin, delicate or pain sensitive skin, as well as for skin needling beginners. A 0.3mm personal version is available for tougher skin types or those who are not new to microneedle rollers and would like to obtain more spectacular results.

Longer needles can cause more damage and extend healing time, plus they can be painful to use when not in the expert hands of a trained aesthetician, nurse, dermatologist or surgeon. Longer needled versions of the Medik8 Titanium Dermaroller at 0.5mm, 1.0mm, 1.5mm, 2.0mm and 3.0mm are available for professional use only, and can be used with P-graded topical anaesthetics such as 4% Lidocaine for patient comfort.

Painless Application

According to their published papers, some researchers experimented with fixed microneedle arrays; however these arrays require more pressure for the microneedles to enter the skin, causing more pain for the same penetration depth.

The Medik8 Titanium Dermaroller requires very little pressure, and will not cause appreciable pain, unlike a fixed array.

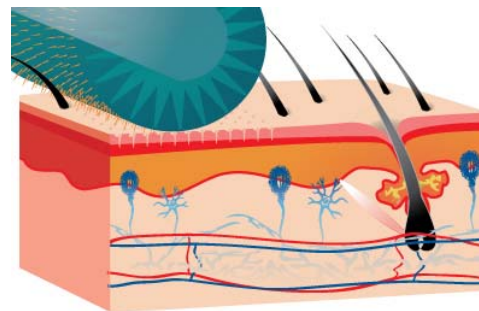


Fig 2. Diagram showing the Personal Medik8 Titanium Dermaroller penetrating the epidermis but not blood vessels or sensory nerves.

Daily Use

Treatments can be applied as part of a daily routine and so the Medik8 Titanium Dermaroller can be used daily as well to enhance the penetration of certain treatments. To begin with, the Medik8 Titanium Dermaroller should only be used twice a week, so that the amount of penetration is controlled and the healing time is kept to a minimum.

With practice, as the skin's healing mechanisms become stimulated, rolling multiple times per week will be possible as the skin will be able to heal fully inside 24 hours.

Sanitizing

Before every use rinse the Medik8 Titanium Dermaroller with the sanitising solution. The sanitising solution provides a powerful and instant antimicrobial disinfectant with oil-removing properties. There is no need to rinse with water before use (which could potentially re-contaminate the roller) as the solution evaporates completely. Due to rapid evaporation, the roller needles are cooled for more comfortable application and importantly virtually no alcohol is transferred to the skin.

18. Hulmes, D.J., *Building collagen molecules, fibrils, and suprafibrillar structures*. Journal of Structural Biology, 2002. **137**(1-2): p. 2–10
19. Hulmes, D.J., *The collagen superfamily—diverse structures and assemblies*. Essays in Biochemistry. 1992. **27**: p. 49–67

References

1. Camirand A. Douchet J, *Needle Dermabrasion*. Aesthetic Plast Surg.1997; 21:48-51
2. Higuchi, T. 1960. *Physical chemical analysis of precutaneous absorption process from creams and ointments*. J Soc Cosmet Chem 11:85-97).
3. W.F. Smith, *Foundations of Materials Science and Engineering 3rd ed.*, McGraw-Hill (2004)
4. Wille J. J. 2006. *Skin Delivery Systems: Transermals, Dermatologicals, and Cosmetic Actives*. Blackwell Publishing, First edition, p.173-5
5. Birchall, J.C., *Stratum Corneum Bypassed or Removed*. Enhancement in Drug Delivery, 2006: p. 337.
6. Doyle D., Hanks G., Cherny N. I., Calman K. 2005. *7 Principles of drug delivery in Palliative Medicine*. Oxford textbook of palliative medicine. Oxford University Press.Third Edition, p: 219
7. Wefers, H., et al., *Influence of UV irradiation on the composition of human stratum corneum lipids*. Journal of Investigative Dermatology, 1991. **96**(6): p. 959-962.
8. Schwindt, D.A., K.P. Wilhelm, and H.I. Maibach, *Water diffusion characteristics of human stratum corneum at different anatomical sites in vivo*. Journal of Investigative Dermatology, 1998. **111**(3): p. 385-389.
9. Verbaan, F.J., et al., *Assembled microneedle arrays enhance the transport of compounds varying over a large range of molecular weight across human dermatomed skin*. Journal of Controlled Release, 2007. **117**(2): p. 238-245.
10. Oh, J.H., et al., *Influence of the delivery systems using a microneedle array on the permeation of a hydrophilic molecule, calcein*. European Journal of Pharmaceutics and Biopharmaceutics, 2008. **69**(3): p. 1040-1045.
11. Ferguson MW., & O'Kane S., *Scar-free healing: from embryonic mechanisms to adult therapeutic intervention*. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences 2004 **29**;359(1445):839-50.
12. Wu, Y., et al., *Microneedle-based drug delivery: studies on delivery parameters and biocompatibility*. Biomedical Microdevices, 2008. **10**(5): p. 601-610.
13. Cho, S.B., et al., *The treatment of burn scar-induced contracture with the pinhole method and collagen induction therapy: a case report*. Journal of the European Academy of Dermatology & Venereology, 2008. **22**(4): p. 513.
14. Aust, M.C., et al., *Percutaneous Collagen Induction: Minimally Invasive Skin Rejuvenation without Risk of Hyperpigmentation-Fact or Fiction?* Plastic and Reconstructive Surgery, 2008. **122**(5): p. 1553.
15. Majid I. *Microneedling therapy in atrophic facial scars: An objective assessment*. Cutis Skin and Laser Clinic, Govt Medical College, Srinagar, India. 2009 2(1):p. 26-30
16. Aust, M.C., et al., *Percutaneous Collagen Induction Therapy: An Alternative Treatment for Scars, Wrinkles, and Skin Laxity*. Plastic and Reconstructive Surgery, 2008. **121**(4): p. 1421-9.
17. Fernandes D, Signorini M. *Combating photoaging with percutaneous collagen induction*. Clinics in Dermatology. 2008. **26**(2):p. 192-9.