REVIEW ARTICLE

Exploring the Role of Microneedling in Dermatology and Onco-dermatology: Current Applications, Future Directions, and Clinical Implications

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ABSTRACT:

Background: Microneedling (MN) is an innovative therapeutic technique that has gained significant prominence over the last decade. It functions by inducing controlled physical trauma via needle penetration, which activates the skin's natural wound healing processes with minimal damage to the epidermis. A key ancillary benefit is its ability to significantly enhance the transdermal absorption of topically applied medications, making it a versatile tool for dermatological treatment. **Objective:** This review aims to synthesize and evaluate the current applications of microneedling within dermatology, with a specific focus on its use for treating various skin conditions and neoplasms. A further objective is to discuss the future prospects and necessary directions for research to optimize this technology. **Methods:** This study is structured as a comprehensive narrative review, analyzing and consolidating findings from existing literature on the clinical use of microneedling. The analysis encompasses its use both as a standalone procedure and in combination with topical therapeutics. **Main Outcome Measures:** The primary outcomes assessed were the efficacy of MN in treating specific dermatological diseases and its role in enhancing drug delivery. Secondary outcomes included an evaluation of its advantages and the identification of optimal parameters for clinical use. **Results:** The review confirms that microneedling has been successfully employed to manage a wide spectrum of conditions, including psoriasis, atopic dermatitis, viral warts, scars, alopecia, pigmentation disorders, and skin tumors. Its hallmark advantages are a reduction in systemic adverse drug effects and a favorable safety profile. However, the literature reveals a lack of consensus on optimal device settings, treatment frequency, and intervals. **Conclusion:** Microneedling represents a highly promising and minimally invasive modality in dermatology. While current evidence supports its efficacy for diverse conditions, further advanced research is strongly recommended. Large-scale, precise clinical trials are essential to standardize treatment protocols and conclusively establish MN as a first-line effective treatment strategy

***Keywords**: Microneedling, Dermatological disorders, Skin tumours, pigmentary disorders*

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1. Introduction

Microneedling (MN) is a non-invasive dermatological technique that uses a variety of sterile fine needles to create controlled micro-injuries in the skin. This process induces a cascade of wound healing responses, promoting dermal remodelling and enhancing collagen and elastin synthesis [1]. Since nearly, first publication on microneedling (MN mediated medication delivery in 1998, the field has advanced dramatically, demonstrating enhanced transdermal drug penetration and therapeutic efficacy [2]. This advancement has expanded the potential for delivering a diverse range of therapeutics for and across the skin. Comprehensive research, influenced by patient-centered treatment, has led to the development of unique and sophisticated mental health systems. MN has shown promise in addressing various dermatological concerns, including wrinkles, scarring, acne, alopecia, hyperpigmentation, stretch marks, rosacea, and skin laxity, as well as promoting skin rejuvenation [3]. Microneedling enhances the penetration of therapeutic agents like topical tretinoin and vitamin C, improving their effectiveness. This technique triggers controlled micro-injuries, stimulating collagen synthesis and tissue repair. Collagen, a vital protein for skin elasticity and firmness, naturally diminishes with age, contributing to wrinkles and laxity. Additionally, collagen depletion can occur due to scars, stretch marks, and other skin damage, making microneedling a valuable approach for skin rejuvenation. Microneedling is a gradual process, requiring time for new skin regeneration. Full results typically become visible over several months as collagen production and tissue remodeling progress [4].

2. Procedure

Microneedling (MN), also known as collagen induction therapy (CIT) or percutaneous collagen induction (PCI), is the controlled generation of micro-injuries in the skin with a device containing fine surgical needles. This activates the body's natural healing reaction, which promotes the synthesis of collagen, elastin, and capillaries, so reducing fine lines, wrinkles, and acne scars. The procedure is safe for all skin types and can

be customized by adjusting needle lengths. Typically, 1 to 3 sessions are required, spaced 4 to 6 weeks apart, to achieve the desired results. Each session lasts between 30 to 60 minutes, with the needles penetrating the stratum corneum and creating micro-conduits, which minimize epidermal damage and initiate dermal regeneration [5].

3. Applications of MN in Dermatological disorders

Various (MN) therapies have been developed to reduce wrinkles and scars, stimulate skin regeneration, and enhance overall skin look[13]. Recent clinical trials have expanded the applications of microneedling (MN) beyond cosmetic use to include the treatment of actinic keratosis (AK), pigmentation problems, hyperhidrosis, and striac[14]. Furthermore, the potential of MN to cure hair pathology has drawn attention recently due to its potential to activate dermal papilla stem cells, enhance blood supply to hair follicles, and attract growth factors and signalling pathways that promote hair regrowth [15]. Normal wound healing is believed to be induced by MN breaks collagen strands in the superficial dermis and induces collagen synthesis immediately below the epidermis[16]. MN is utilized for treating various skin tumors by enhancing the local delivery of anticancer drugs into the tumor site. This mechanism also underlies its application in scar treatment across different etiologies [10]. In this review we will provide an overview of several dermatological diseases in which the drug delivery can be achieved by MN.

3.1. Psoriasis

Psoriasis, a chronic papulosquamous disease, occurrence rate is from 1 to 2% in the overall populace [17]. Psoriasis is not only restrained to the dermis, but it can also affect the nails and joints as well [18]. The disease is characterized by hyperkeratosis of the stratum corneum, acanthosis (epidermal thickening), and scaly plaque with variable degrees of pruritus on the elbow, scalp and knee[19].

Methotrexate either orally or parenterally used in the management of psoriasis which eventually causes side effects [21]. Efforts have been directed toward intradermal delivery of methotrexate at psoriatic sites to minimize systemic exposure. The efforts were made to deliver methotrexate topically via the solid maltose MN in combination with iontophoresis According to a study, using iontophoresis and microneedles together can synergistically improve methotrexate administration to the skin in vivo by a factor of 25 [22]. To support this, the skin administration of methotrexate in cadavers of pigs and humans is enhanced by applying polylactic-co-glycolic acid (PLGA) MN using the poke and patch techniques. However, Pre-treatment with laser ablation significantly enhanced methotrexate penetration across the skin compared to PLGA MN pre-treatment [14]. The ease of applying a microneedle patch on the site, might be more clinically adaptable.

Anti–TNF–α antibody therapy has proven effective in managing psoriasis by significantly reducing epidermal inflammation in psoriatic lesions. This chimeric monoclonal antibody works by neutralizing both the transmembrane-bound and soluble forms of circulating TNF-α, leading to rapid alleviation of inflammation [23]. MN can be used for local delivery of anti– TNF–α using carboxymethyl cellulose dissolving MN [24].

It has been demonstrated that mate tea extract contains a molecule termed pentaerythritol tetrakis (3,5-di-tert-butyl-4-hydroxyhydrocinnamate) (PTTC), which possesses anti-psoriatic properties. Although PTTC has the ability to treat psoriasis, PTTC has a very high Log P that is 23 that causes deprived solubility and apportioning into the stratum corneum [24]. MN was used to Promote the intradermal administration of PTTC for psoriasis therapy. To enhance PTTC's intradermal distribution for the treatment of psoriasis, MN was employed. Additionally, the compound's effectiveness was demonstrated utilizing 3D psoriatic cell culture, which also revealed decreased production of interleukin-6 (IL-6), a cytokine that is normally upregulated in lesions associated with psoriasis [25].

Microneedles (MN) coated with hydroxypropyl cellulose (HPC) have been investigated for the intradermal delivery of Cyclosporin A (CyA), a hydrophobic drug with a high molecular weight, aimed at treating psoriasis. Pharmacokinetic investigations on eight-week-old Sprague-Dawley (SD) rats revealed that intradermal administration of CyA significantly reduced systemic toxicity compared to oral delivery. This was attributable to the sluggish absorption of CyA from the delivery location which allowed for localized treatment of psoriasis while minimizing the adverse effects commonly associated with systemic drug distribution [26].

Hyaluronic acid was employed to fabricate the microneedle patch which was used in combination with a topical gel containing the active ingredients calcipotriol and betamethasone dipropionate. This formulation aimed to enhance the delivery of the therapeutic agents to the skin for improved treatment outcomes [27].

3.2. Atopic dermatitis

Atopic dermatitis is a widespread chronic inflammatory disorder, characterized by severe itching, dry skin, scaling, and inflammation of the lips, significantly impacting patient quality of life. The disorder causes sleep disturbance, and affects the private relations [29]. The treatment of this worse disease is the use of Corticosteroids. Nevertheless, the long-term application of topical steroids to treat atopic dermatitis causes tachyphylaxis [30]. Owing to tachyphylaxis the quantity as well potency is required to increase drastically, which enhances the propensity of the negative consequences [31]. Furthermore, topical pimecrolimus and other calcineurin inhibitors and tacrolimus are drug of choice. This class of drugs is also linked to adverse effects, including localized irritation and a temporary burning sensation during application [32]. Consequently, a great deal of work has gone into investigating various therapeutic options for the control and therapy of atopic dermatitis.

Recently, it was discovered that plant flavonoids such resveratrol, chrysanthemin, tannic acid, quercetin, and naringenin are potential options for treating atopic dermatitis[33]. These compounds have demonstrated anti-inflammatory, anti-allergic, and antioxidant qualities that have shown substantial benefits in the treatment of atopic dermatitis. These flavonoids are water soluble; this solubility is the one of the problems to deliver it orally and topically as well. The application of MN to improve the delivery of flavonoids to the viable epidermis, which is the main site of action, would be of great value [34]. To address this issue, a strategy was developed to deliver lipid microparticles (LM) loaded with quercetin into pig skin punctured with microneedles. With localization in the viable epidermis, the main site of action, this method improved quercetin penetration into the stratum corneum[35].

3.3. Viral warts

Benign epidermal proliferations known as viral warts are brought on by an infection with the human papillomavirus (HPV). The prevalence of HPV is 7–12% in the general population [37]. *Verucca vulgaris* is the most common to cause warts. Plantar warts, which typically manifest as hyperkeratotic plaques on the foot, are frequently seen on the hands, while genital warts are typically spread during intercourse. It is transmitted via touch [38]. Salicylic acid, lactic acid, podophyllin, and 5-FU preparation are the most common topical preparations used to treat viral warts. These preparations chemically destroy the infected epidermal cells while reducing the hyperkeratotic epidermis[39]. There have been reports that bleomycin works better than cryotherapy [42]. For the treatment of warts local therapy is observed to be most effective.

The first proper MN design consists of poly-lactic-acid (LPLA) solid MN coated with bleomycin.[14].

3.4. Scars

Skin biopsies were taken for a study both before and after using a Derma roller. An increase in the synthesis of different forms of collagen that is statistically significant, including those essential for skin structure including, type I, III, and VII was observed, accompanied by a decrease in overall elastin levels [45].

MN, and a 15% trichloroacetic acid peel in the treatment of 50 patients with atrophic acne vulgaris scars. The complete reduction was confirmed in all patients with Grade 2 scars and in 22.7% of patients with Grade 3 scars. Overall, 100% of patients had unprejudiced improvement in scars by at least 1 grade [47]. Results indicated significant improvements in scar appearance, with enhanced skin texture and reduced scar depth. In a study focused on patients with darker skin tones, the effectiveness of MN combined with 35% glycolic acid peels for acne scar treatment was examined. Participants were divided into two groups: one group received MN treatment alone, while the other group underwent a combination of MN treatment and glycolic acid peels. The combination treatment resulted in more noticeable improvements in skin texture, scar reduction, and a decrease in post-inflammatory hyperpigmentation (PIH) when compared to the group that received only MN treatment. This suggests that combining MN with glycolic acid peels may enhance the outcomes for patients with acne scars [50]. MN has also been used to improve the treatment of hypertrophic surgical scars by increasing the distribution of topical medicines into the dermis[51]. A study demonstrated the effectiveness of MN as an alternative treatment for hypertrophic scars in burn patients [52].

3.5. Alopecia

MN has been recommended as a second line of therapy for alopecia. The effective use of MN in both androgenetic alopecia (AGA) and alopecia areata (AA) has been addressed and demonstrated in recent years.

The combination of MN and minoxidil demonstrated a significant enhancement in the rate of hair regrowth compared to minoxidil alone[54]. Specifically, the MN-assisted delivery of minoxidil appeared to accelerate

the onset of new hair growth, with improvements becoming evident within 6 weeks, as opposed to the 10 weeks required for noticeable effects in the minoxidil-only group. Furthermore, the treatment showed promising results, with 80% of participants reporting noticeable improvements in hair growth, underscoring the potential of combining MN with minoxidil for more effective treatment of hair loss. [55].

The primary treatment for alopecia areata (AA) remains intralesional corticosteroids. However, microneedling (MN) has been proposed as a complementary approach, offering collagen induction that may counteract steroid-induced atrophy, with the added benefit of causing less pain compared to injections. [57]. A case study demonstrated successful treatment of corticosteroid-resistant AA with MN combined with topical corticosteroids. Two male patients, unresponsive to corticosteroids, topical steroids, and 5% minoxidil, were treated with topical triamcinolone and MN using a Derma roller. Both patients reported "excellent" hair regrowth and showed no recurrence at the 3-month follow-up. However, the study had limitations, including an inability to assess common adverse effects of steroid treatment, such as atrophy, scarring, and heightened infection risk.

Table:1 Table showing the drugs that are delivered in the form of microneedle (MN) dosage form.

Sr. No	Drug	Coated	Indication	References
1.	Methotrexate	Maltose	Psoriasis	[58]
2.	Methotrexate	Polylactic-co-glycolic acid	Psoriasis	[59]
3.	anti– TNF–α	Carboxymethyl cellulose	Psoriasis	[60]
4.	Pentaerythritol tetrakis	Uncoated	Psoriasis	[61]
5.	Cycloserine A	hydroxypropyl cellulose	Psoriasis	[62]
6.	Calcipotriol and betamethasone dipropionate	Hyloronic acid	Psoriasis	[63]
7.	Tacrolimus	Uncoated	Atopic dermatitis	[32]
8.	Pimecrolimus	Uncoated	Atopic dermatitis	[64]
9.	Quercetin	Lipid microparticles	Atopic dermatitis	[65]

10.	Chrysanthemin	Lipid microparticles	Atopic dermatitis	[3]
11.	Tannic Acid	Lipid microparticles	Atopic dermatitis	[66]
12.	Naringenin	Lipid microparticles	Atopic dermatitis	[67]
13.	Resveratrol	Lipid microparticles	Atopic dermatitis	[68]
14.	Bleomycin	Poly-Lactic-Acid	Viral warts	[69]
15.	Trichloroacetic Acid (15 %)	Uncoated	Scars	[70]
16.	Glycolic Acid	Uncoated	Scars	[71]
17.	4-Butylresorcinol	Uncoated	Melesma	[72]
18.	Imiquimod	Uncoated	Basal cell carcinoma	[73]
19.	5 Flurouracil	Uncoated	Basal cell carcinoma	[74]
20.	5 Aminolevulinic Acid	Solid Silicon	Photosensitizing agent	

21.	Methyl aminolevulinic acid	Uncoated	Skin tumours	
22.	Meso-Tetra (N-Methyl-4-Pyridyl) Porphinetetratosylate (Tmp)	Uncoated	Skin tumours	
23.	Itraconazole	Uncoated	Skin tumours	

3.6. Pigmentary disorders

Multiple studies have suggested MN as a potential alternative to traditional treatments for pigmentation disorders in individuals with darker skin tones, such as melasma, leukoderma, and periorbital hyperpigmentation.

3.7. Melasma

The increased transdermal drug delivery enabled by MN has shown greater effectiveness than standalone skin-lightening agents in treating melasma [75]. When treating 60 patients with moderate to severe melasma, topical tranexamic acid was used instead of tranexamic acid microinjections [45]. In a pilot study, 20 female patients with melisma (Fitzpatrick Skin Type III–IV) were compared to those receiving treatment with depigmentation serum and MN (MN + serum) in combination. The depigmentation serum alone comprised 4-butylresorcinol and sophora-alpha (prenylated flavonoids from the roots of Sophora flavescens). [75]. In the MN and serum group, the baseline mean MASI score reduced by 9.9 points ($p < 0.001$), whereas the serum-only group exhibited a reduction of 7.1 points ($p < 0.05$) two months after therapy.

3.8. Vitiligo

The effectiveness of MN as part of combination therapy for vitiligo remains inconclusive. A study evaluated repigmentation outcomes in patients with treatment-resistant bilateral symmetrical vitiligo by comparing the effects of narrowband ultraviolet B and topical 0.005% latanoprost solution, administered either with or without Dermaroller. Repigmentation was achieved in 17 patients from each group, accounting for 37.8% of treated lesions. However, only 8.8% of repigmented lesions exhibited more than 50% repigmentation. Notably, the comparison between the groups revealed no statistically significant difference in repigmentation outcomes [78].

Periorbital hyperpigmentation has been successfully treated with Periorbital melanosis MN therapy. A male patient exhibited significant improvement, ranging from approximately three-fourths to nearly complete recovery, after undergoing 12 sessions of DermaFrac treatment. This approach combined MN with active ingredients such as kojic acid and a specialized nti-aging serum comprising biologically active peptides, including myristoyl pentapeptide-17, acetyl octapeptide-3, palmitoyl pentapeptide-4, acetyl hexapeptide-8, and a chemically produced tripeptide combination[79]. To establish its therapeutic potential more definitively, well-designed randomized controlled trials with larger and more diverse patient populations are essential for further evaluation of MN in treating pigmentation disorders in skin of color.

3.9. Verruca

A study investigated the advantages of MN as a technique of medicine delivery in verruca accomplishing comprehensive cure in three patients. In this study, MN was utilized in conjunction with 0.2–0.5 mL of topical bleomycin at a concentration of 1 unit/mL, administered over an average of four treatment sessions to enhance therapeutic outcomes [43]. MN holds potential as an effective approach for achieving 100% cure rates in plantar warts by improving bleomycin delivery to lesions. However, to establish its precise therapeutic role in the treatment of verruca, well-designed clinical trials with larger sample sizes are necessary.

3.10. Actinic keratosis (AK)

Patients with actinic keratosis (AK) have exhibited variable outcomes when MN is used as an adjunct to standard treatment modalities. In a split-face study, the administration of MN following methyl aminolevulinate photodynamic treatment (MAL-PDT) in 10 patients with AK as opposed to MAL-PDT without MN [81]. For every evaluated metric, MAL-PDT with Derma roller (MN-MAL-PDT) improved more than MAL-PDT alone [82].. In their split-facial study, twenty patients with at least four non-hyperkeratotic AK on each side of their face were randomly assigned to undergo either ALA-PDT with MN

therapy with Eclipse Micropen EliteTM or ALA-PDT alone. Twelve organ transplant recipients who had 59 cases of AK that did not respond to traditional PDT therapy also had their usage of MN for treatment reviewed. Patients underwent three sessions of cyclic photodynamic therapy (PDT) using the Dermaroller MC905™ before the topical application of 16% methyl aminolevulinate (MAL). However, the absence of a PDT-only comparison group limited the ability to determine the specific benefits of MN in treating recurrent AK. Overall, MN demonstrates potential as an adjunctive therapy for managing refractory AK [85].

3.11. Skin cancer

Skin cancer is the most prevalent malignancy in humans, with its incidence rising rapidly worldwide. Various risk factors contribute to its development, including genetic predisposition, prolonged Exposure to sunlight, immunosuppression, human papillomavirus infection, photosensitizing medication, and tobacco usage. Significant attempts have been made to lessen the prevalence and impact of the condition particularly through extensive skin screening programs Skin cancer is commonly divided into two types: non-melanoma skin cancer (NMSC) and malignant melanoma (MM). NMSC is further classified into basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) each with distinct pathological and clinical characteristics[86].

Targeted and immunotherapeutic agents, including BRAF inhibitors (vemurafenib, dabrafenib), immune checkpoint inhibitors (ipilimumab), and alkylating agents (dacarbazine), are commonly utilized for managing metastatic malignant melanoma (MM) [87]. Two commonly used topical treatments for non-melanoma skin cancer (NMSC) are imiquimod and 5-fluorouracil (5-FU). MN-facilitated delivery of imiquimod has been utilized in the treatment of basal cell carcinoma (BCC). In contrast, 5-fluorouracil (5-FU) functions as an antimetabolite, undergoing intracellular conversion to fluorodeoxyuridine monophosphate (FdUMP). This active metabolite binds to the nucleoside-binding site of thymidylate synthase, inhibiting its activity and subsequently reducing the synthesis of thymidine, a nucleoside essential for DNA replication

In their initial research, they utilized solid silicon MNs in combination with bio-adhesive patches loaded with 19 mg/cm² of 5-aminolevulinic acid (ALA). Employing the "poke and patch" technique in a nude mouse model, they successfully enhanced ALA penetration into the skin, facilitating optimal drug concentration in targeted lesions [92]. Following this study, several research organizations investigated alternative micro needle designs for delivering a variety of ACD to the skin. Examples of such ACD comprise methyl aminolevulinic acid (MAL), cationic photosensitizer meso-tetra (N-methyl-4-pyridyl) porphinetetratosylate (TMP), and antifungal medication itraconazole [93] and 5-FU [94]. A microneedle coated with 5-aminolevelunic acid (5-ALA) enhances the dermal distribution of the photosensitizer for treating skin tumors. Moreover, studies utilizing a murine model have demonstrated the potential of solid MNs to increase the intradermal delivery of 5-FU for skin tumor treatment [95]. In vitro experiments revealed a 4.5-fold enhance in 5-FU penetration when the drug was applied to MN-treated mouse skin vs. intact skin. likewise, in vivo investigations employing a mouse model with B16-F10 melanoma tumors revealed that topical treatment of 5% 5-FU cream on MN-perforated skin resulted in considerable tumor suppression compared to application on untreated skin. [96]. It has been proposed that delivering anticancer drugs (ACDs) into superficial skin tumors using dissolving MNs may offer greater efficacy compared to nanosized carriers. The microscale structure of MNs allows for prolonged retention of chemotherapeutic agents at tumor sites, potentially enhancing therapeutic outcomes [95]. In this setting, MN-based treatment should be viewed as an addition to normal MM care. Therefore, continued research is essential to determine the optimal MN dosage for cancer therapy. If this approach proves ineffective, future investigations into microneedle-based treatments should prioritize more localized tumors, such as basal cell carcinoma (BCC) or specific variants of squamous cell carcinoma (SCC).

4. Conclusion

MN is novel drug system has vast potential to be the prospects for the delivery of local acting drugs including the analgesics, anaesthetics and antiseptics. Although, efforts are made to deliver ACD by this route especially in skin tumours. Still there is huge vacuum to flourish and establish this route for drug delivery. Certain scientist had tried to use this route for the vaccinations, but still notable success had not achieved yet. It is only lately that there has been a paradigm change toward the use of MN for the treatment of dermatological disorders, notwithstanding the impact of MN in transdermal administration. Numerous research employing MN systems intended for more targeted medication administration to treat skin diseases show that MNs are gradually having an influence on the field of dermatology. However, it is evident that certain dermatological conditions, such as skin cancers and cutaneous infections, receive greater attention due to their severity and high prevalence. For microneedles to make a meaningful impact in the management of severe skin disorders, it is crucial to raise awareness among clinicians, particularly dermatologists, about their potential applications. Additionally, fostering collaborative research partnerships between dermatologists, academic institutions, and the pharmaceutical industry is essential to advancing microneedle research and facilitating its integration into clinical dermatology. It is crucial to remember that case reports, case series, or tiny randomized controlled trials have comprised most of the comparative research on MN. To validate MN as more than just a cosmeceutical therapy and as an evidence-based therapeutic option for individuals with a variety of dermatologic illnesses, substantial controlled clinical studies investigating the usefulness of MN are essential. Finally, further research is needed to clarify the precise mechanisms underlying MN therapy, particularly in the treatment of alopecia and pigmentary disorders. While the creation of micro-conduits and enhanced dermal drug delivery are key factors, they may not be the sole contributors to the observed therapeutic effects. A deeper understanding of these mechanisms could optimize MN-based treatments and expand their clinical applications.

Ethics approval and consent to participate

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Competing interests

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