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Emerging smart microneedle technologies in psoriasis: convergence of nanocarriers, machine learning, and personalized delivery

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Psoriasis is a long-term autoimmune disorder that causes an excessive growth of keratinocytes in the skin. A mix of immune system irregularities, environmental influences, and genetic predisposition triggers it. The condition significantly impacts the quality of life of those affected. Histopathological investigation and clinical evaluation are two of the current diagnostic techniques; One method used to assess the severity of psoriasis is the Psoriasis Area and Severity Index (PASI). Topical medications and systemic therapy are examples of traditional treatments; nevertheless, they frequently do not offer long-lasting comfort and may have unfavourable side effects. Recent developments in targeted psoriasis therapy highlight the potential of microneedle technology, particularly nanoparticulate microneedle formulations, which allow improved drug administration and decreased systemic toxicity. Further, incorporating artificial intelligence (AI) and machine learning (ML) into microneedle-based formulations is rising as a powerful tool to predict optimal design parameters, mechanical properties, and drug release profiles, thereby speeding research and enhancing therapeutic precision. This review delves into the pathophysiology, diagnosis, and treatment of psoriasis, focusing on novel microneedle approaches and AI, ML-based optimisation. We also examined ongoing studies, treatment patterns, and regulatory issues. We highlight patents about microneedles and how they could revolutionise the way psoriasis is treated.

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1. Introduction

Psoriasis, an autoimmune inflammatory chronic condition, is characterised by erythematous and scaly skin lesions that can appear anywhere on the scalp, knees, elbows, or anywhere else.[1–3] Psoriasis manifests in different ways, including inverse psoriasis, guttate psoriasis, palmoplantar psoriasis, pustular psoriasis, and erythrodermic psoriasis.[4,5] An individual can exhibit several phenotypes, with psoriasis vulgaris being the most prevalent form. Itching, burning, and discomfort are frequent complaints across all phenotypes. There is variation in the level of skin involvement. The majority of psoriasis types follow a periodic course, peaking for a few weeks or months, then fading temporarily or perhaps entering a remission phase.[2,4,5]

Psoriasis affects individuals globally, according to a global report on psoriasis that the World Health Organisation issued on October 26, 2016.[6] Prevalence estimates range from 0.09 to 11.4%, with potential increases noted (impact is detected even with a small body surface area affected). The incidence of psoriasis has been the subject of limited research, with estimates of 0.60 per 1000 person-years in the US and 15.04 per 1000 in North Africa. There are also ethnic differences; in the US, Caucasians are more common than other ethnicities. Although it might be challenging to identify trends, certain nations exhibit a noticeable rise in prevalence over time. Recent global data from a large-scale 2023 study covering 20 countries reported an overall adult psoriasis prevalence of 4.4%, with regional variations: 5.7% in Asia, 4.6% in Europe and Australia, 4.9% in the Middle East, 3.7% in North America, 3.1% in Latin America, and the lowest at 1.7% in Africa.[7] With disability-adjusted life years (DALYs) reaching 1 050 660 in 2010, psoriasis poses a substantial worldwide burden, with the 50–69 age group being particularly impacted. Psoriasis burden increases with age, with slightly higher DALYs in adult males than females up to 75 years. The Global Burden of Disease Study may underestimate the psychosocial impact, emphasising the need for a balanced understanding of both objective and subjective burdens in psoriasis.[6]

Over time, oral, topical, and parenteral medicines are utilised to manage psoriasis. Patients with constructive damage from psoriasis are also treated with systemic medications, physiotherapy, and topical drugs.[8,9] Consequently, topical treatments have drawbacks such as greasiness, dullness, slipperiness, and delayed processes.[4,10,11] Dermatologists focus more

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on topical formulations, while formulation scientists have more explored transdermal drug delivery methods based on microneedles (MN) to address medicine permeability issues. MNs became prominent for treating psoriasis due to their higher patient compliance and improved skin penetration for therapeutic actives.[12–14] Because they have fewer side effects and are made of polymers like maltose[15] and ceramics,[16] solid MNs provide a noninvasive method with lower systemic toxicity and patient compliance. Rapid advancements in psoriasis treatment have been demonstrated by the decline in dependence on transdermal patches and hypodermic needles brought about by MN-based transdermal drug delivery system (TDDS).[4]

Fig. 1 presents data from ScienceDirect, PubMed, and clinical trials over the last five years. Panel (a) shows the number of publications related to psoriasis and psoriasis + microneedles, with a sharp reduction when combining topics. Panel (b) focuses on clinical trials for psoriasis, where 35.6% are completed, and 49.8% are industry-sponsored, with most being interventional (75%). Panel (c) highlights microneedle-based clinical trials, where 30.4% are completed, 63% are industry-sponsored, and 87% are interventional. This comparison underscores the limited integration of microneedles in psoriasis research and highlights the need for further investigation to bridge this gap and explore therapeutic advancements. Understanding the complex pathophysiology of chronic skin conditions is crucial for comprehending and examining the use of MNs in treating psoriasis.

Getting through the complex pathophysiology of chronic skin conditions is crucial for exploring the use of MNs in managing psoriasis. Recent research also showed the integration of artificial intelligence (AI) and machine learning (ML) to design the microneedles, predict drug release profiles, and stratify patients based on personalised therapy. AI algorithms such as ConvNeXt and ResNet, and random forest models have been utilised in MN fabrication to control geometry for improved skin penetration, and modulated controlled pharmacokinetic profiling. For example, studies have employed AI-integrated microneedle platforms for psoriasis treatment, and deep machine learning models have been used to guide manufacturing targeted therapies. Understanding every detail of psoriatic pathology, AI/ML, will help us appreciate how vital MN technology is for delivering specific treatment options. This review, therefore, discusses the role of AI and ML in MN development, providing insights into their integration for design optimisation and personalised treatment approaches. The focus of this review is to investigate the molecular and immunological elements that underlie psoriasis thoroughly. This will thoroughly examine the developments and difficulties that arise when utilizing MNs as a revolutionary method for treating psoriasis.

2. Pathogenesis of psoriasis

The skin, the body's outermost layer, is a key component of the integumentary system. It weighs approximately seven percent of the total body weight and covers approximately two square meters.[17] It shields the body from microbial infections,

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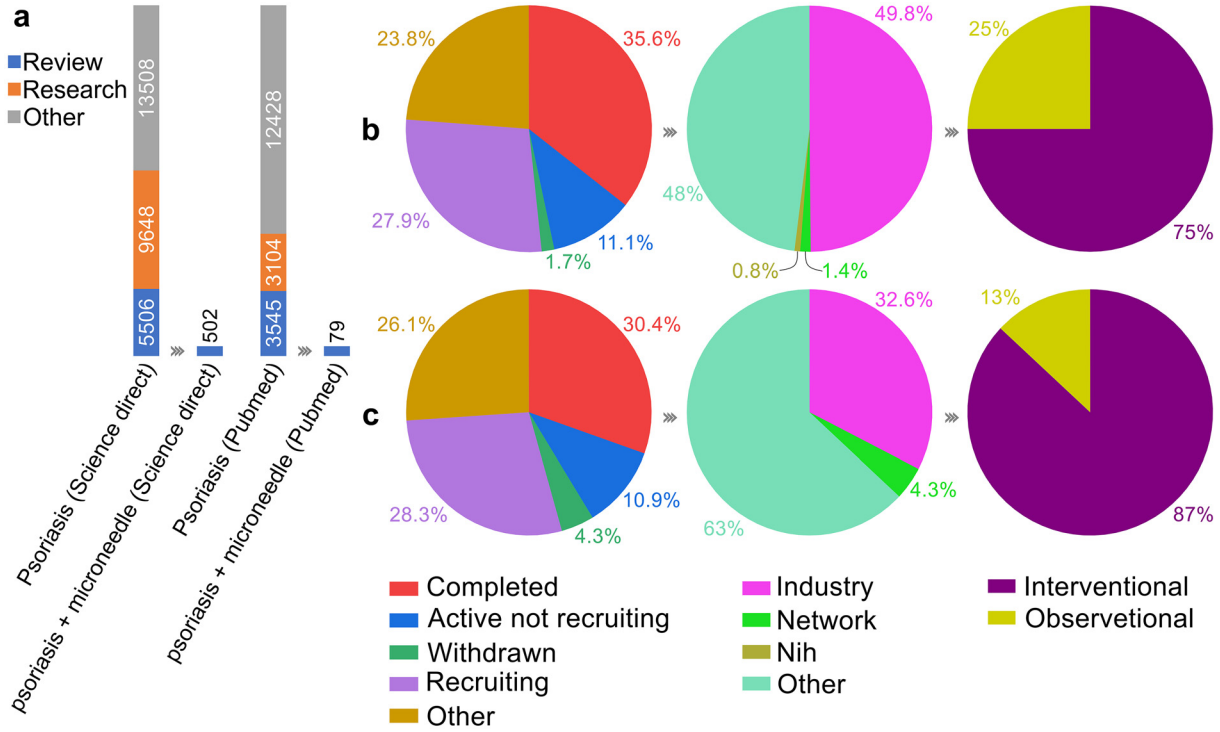

Fig. 1 Data overview from the past five years on psoriasis and microneedles, compiled from multiple sources: (a) publications retrieved from PubMed and ScienceDirect, (b) clinical trials conducted on psoriasis, and (c) clinical trial data related to microneedle technology (source: National Library of Medicine, clinicalTrials.gov) (access date: 15th Jan 2025).

extremes of temperature, and dehydration. Exacerbations of psoriasis can be triggered by various factors, including trauma (known as the Koebner phenomenon), infections, physiological stress, and metabolic syndrome. These variables influence the skin's innate and adaptive immune systems indirectly.[2,17] The following sections address the primary pathogenic pathways associated with psoriasis.

2.1. Genetic contribution

A complicated genetic architecture typifies a chronic autoimmune skin condition with polygenic involvement, psoriasis. More than sixty-three genetic risk loci associated with psoriasis have been identified by genome-wide association studies (GWASs); these loci together account for around 28% of the heritability of the condition, though the estimate of the total genome-wide heritability is 50%.[18,19] The significant genetic locus overlap amongst various groups is noteworthy, with 11 risk loci exhibiting noticeable changes between Han Chinese and Caucasians. Major risk alleles within primary histocompatibility complex class I (MHC-I), such as HLA-C*12:03, HLA-C*06:02, HLA-B*38:01, HLA-B*57:01, and HLA-A*02:01, contribute significantly to the pathogenesis of psoriasis and emphasise the significance of presenting antigens in the immune response. Specific coding mutations associated with psoriasis vulgaris are found in ERAP1 and ERAP2, two crucial participants in antigen processing.

Loci within NF-κB spread over the genetic landscape and become important regulators influencing keratinocyte differentiation and proliferation, TH-17 pathway proinflammatory cytokine production, T-cell clonal expansion, and Wnt signalling pathway modulation.[20] This thorough comprehension of the complex genetic interactions offers essential insights into the molecular mechanisms underlying psoriasis. It presents prospects for focused therapeutic interventions and the creation of individualised treatment plans catered to the unique genetic profiles of afflicted people.

2.2. Environmental triggers

Current research clarifies the intricate relationships that psoriasis has with different environmental factors. In psoriasis, smoking appears to be a risk factor that is influenced by genetic factors such as HLA-C*06:02 and CYP1A1; also, the role of alcohol use is less clear.[20–22] Several drugs, such as NSAIDs and β-blockers, have been linked to the induction and aggravation of psoriasis, demonstrating the complex relationship between drugs and skin disorders.[20,23] Diet and obesity are modifiable risk factors; research indicates that specific dietary components may have an impact on the severity of psoriasis in addition to a higher prevalence of obesity in people with the illness.[24] Biomechanical stress becomes apparent as an essential microenvironmental element, influencing osteoclasts, T cells, and the course of arthritis.[25] Numerous infections are known triggers for psoriatic disorders, including streptococcal pharyngitis and HIV.[26] This highlights the significance of treating both systemic and localised infections. The microbiome plays a critical role in developing diseases, especially the skin microbiota, with changes in bacterial com-

position linked to the development of psoriasis. The potential for novel treatment approaches is highlighted by ongoing clinical trials examining probiotics, faecal microbiota transplantation (FMT), and other microbiome-targeted medicines.[20]

2.3. Immune response

The self-immune system misinterprets signals, which leads to psoriasis. Keratinocytes usually mature and shed once every 35–40 days. However, in the case of psoriasis, they proliferate quickly, emerging from the basal layer and reaching the skin's surface in 6–8 days. Rather than being shed, these cells build up on the epidermis and cause discernible sores.[8] There are many theories that try to explain the pathophysiology of psoriasis, but the most well-recognised one focuses on the role of circulating and/or activated immune cells, including T cells, macrophages, dendritic cells, neutrophils, and macrophage-derived products.[27] This section provides more explanations of the molecular processes that occur throughout the pathogenesis of psoriasis, as seen in Fig. 2c and Table 1.

Immune cell infiltration into the dermis and epidermis leads to the release of proinflammatory cytokines, thereby extending and intensifying inflammation.[28] The pathogenesis of psoriasis is influenced mainly by dendritic cells (especially CD11c+ myeloid dendritic cells and Langerhans cells), CD8+ T lymphocytes, and CD4+ T cells. When dendritic cells' major histocompatibility complex (MHC) molecules recognise antigens, T lymphocytes become activated.[1]

Numerous synapses and co-stimulation pathways are involved in the interaction between myeloid dendritic cells (MDCs) and naive CD4+ T cells, which results in Th1, Th17, and Th22 cell polarization.[29] The function of plasmacytoid dendritic cells (pDCs) in lymphoid organs and blood is vital. When stimulated by antimicrobial peptides, pDCs emit interferon-alpha (IFN-α), which has been linked to psoriasis triggers including as trauma, infections, and stress. IFN-α reactions support the co-stimulation of MDC/T cells, which may result in autoimmunity.[30,31] A key player in the pathophysiology of psoriasis is the LL-37-IFN-Th17/Th22 axis, which involves keratinocytes, cytokines (IL-22, IFN-γ, and IL-17), and chemokines.[30] Traditionally overlooked, CD8+ T cells are found to be a source of proinflammatory cytokines (IL-17, IL-13, IFN-γ, and IL-22). Activated by CD1d identification on keratinocytes and MDCs, natural killer-T (NK-T) cells may produce IFN-γ and IL-13, which could aid in the formation of psoriatic plaque.[31,32]

The first stage is when autoantigens – from environmental or genetic sources – activate antigen-presenting cells, especially dendritic cells. These autoantigens cause antigen-presenting cells to migrate to lymph nodes to initiate a subsequent immune response by activating the major histocompatibility complex (MHC) on their surface.[33] Natural killer T cells, keratinocytes, macrophages, and plasmacytoid dendritic cells are essential for this process because they produce proinflammatory cytokines, including IL-6, TNF, and IL-1β together. These cytokines cause the release of IL-23 and IL-12 by stimulating myeloid dendritic cells. T-helper 1 (TH-1) cells are stimulated by IL-12, which causes them to secrete TNF and IFN-gamma. T-helper 17 (TH-17) cells are stimulated by IL-23, which causes them to release IL-22 and IL-17. Psoriatic plaques develop as a result of the hyperproliferation of keratinocytes induced by these processes.[34]

The inflammatory response induced by IL-12 and IL-23 is mediated by essential signalling pathways, especially those involving TYK-JAK2 and STAT3 as autoantigen-carrying infected cells go to lymph nodes, where they interact with healthy T-cells and sustain the immune response; the autoimmune cascade advances. The circulating system then receives the activated immune cells, which aid in the spread of the autoimmune response throughout the body. The distinctive psoriatic lesions are caused by the hyperproliferation of keratinocytes, which is induced by the return of these immune cells to the epidermis at various places.[33,34]

3. Diagnosis, associated comorbidities and management

psoriasis diagnosis primarily relies on clinical observation, with various less common forms such as inverse, pustular, guttate, erythrodermic, and annular psoriasis distinguished by their distinct morphologies (Fig. 2b).[40] Chronic plaque psoriasis, which affects 80% to 90% of patients, is the most common clinical type. It is identified by distinct, symmetrical, reddish plaques covered with silvery scales, typically appearing on the scalp, trunk, buttocks, and limbs.[33] Nail involvement may occur independently of plaques, and active lesions may cause itching or pain. Psoriasis may present as an isomorphic response, where new lesions develop on previously uninvolved skin following trauma. Disease severity, categorised as mild, moderate, or severe, aids in treatment decisions.[41] Atypical presentations may warrant differential diagnoses such as contact dermatitis, atopic dermatitis, secondary syphilis, lichen planus, tinea corporis, mycosis fungoides, and pityriasis rosea, often confirmed through careful observation or, in rare cases, by skin biopsy (Table 2).[40,42]

Psoriasis frequently coexists with a range of comorbidities that have a substantial influence on many areas of health. The systemic aspect of psoriasis is shown by the increased vulnerability to several diseases that is linked to both pre- and post-psoriatic circumstances. Psoriatic Arthritis (PsA), a disorder characterised by inflammation affecting tendons, ligaments, and joints, is one of the noteworthy comorbidities associated with psoriasis.[43] Morning stiffness, nail pitting, arthralgia, and joint swelling are some of the early symptoms. Psoriasis Epidemiology Screening Test (PEST) is one instrument used for PsA screening.[44] Early onset of psoriasis is associated with an increased risk of cardiovascular illnesses, similar to that seen in people with type 2 diabetes. Research has demonstrated a connection between peripheral vascular disease, atherosclerosis, myocardial infarction, and psoriasis.[45] Interestingly, children who are obese have a higher risk of having moderate to severe psoriasis, which adds to the range

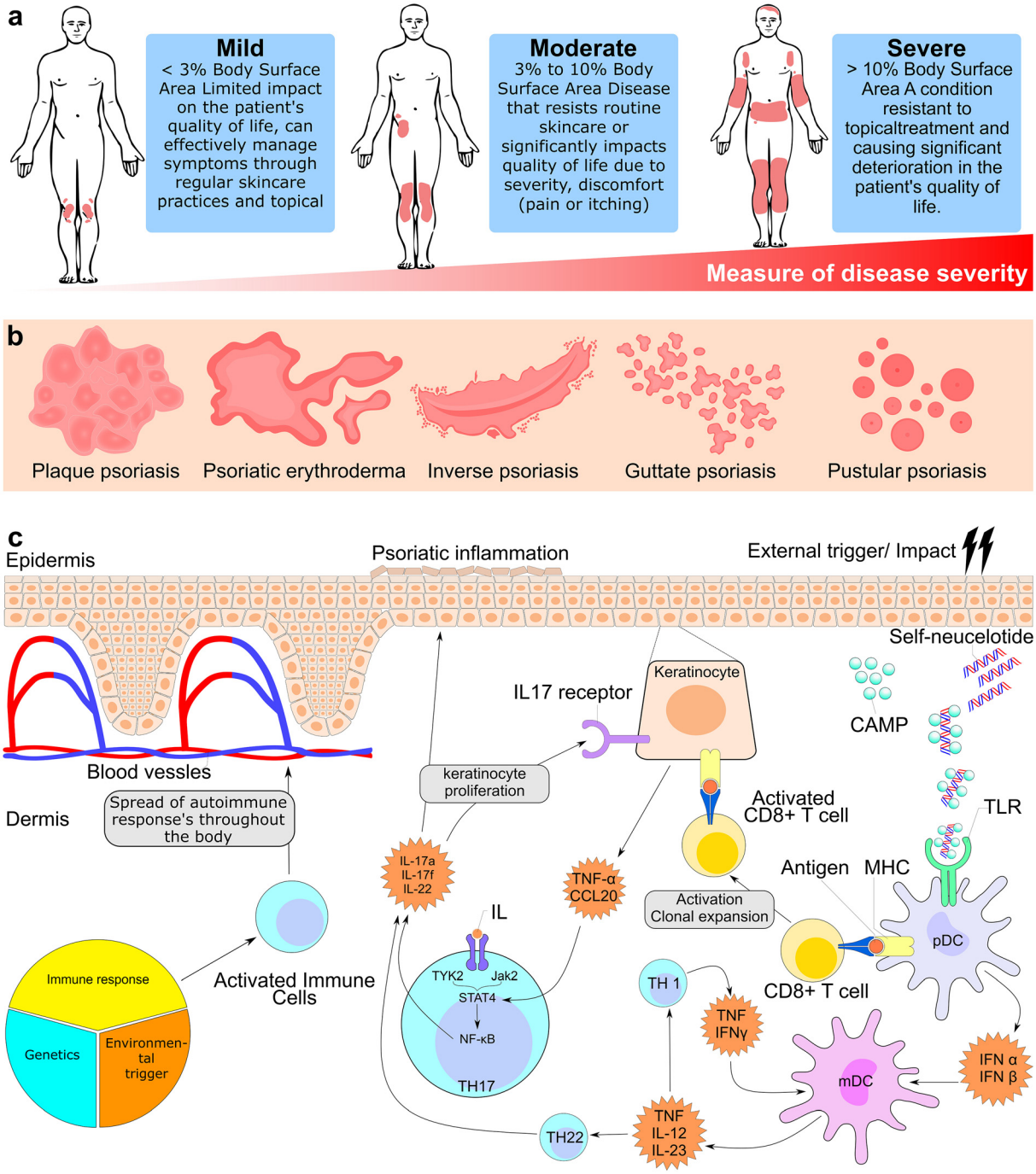

Fig. 2 Skin lesion types and severity of psoriasis. (a) It shows how psoriasis can range from mild to severe depending on skin involvement. (b) Displays diverse skin lesions in different forms of psoriasis. (c) Psoriasis-related pathogenesis pathways. When dendritic cells get activated, the immune system is triggered, activating Th1 and Th17 cells by producing interleukin (IL)-12 and IL-23, respectively. Th17 cells secrete IL-17, whereas Th1 cells generate the inflammatory cytokines tumour necrosis factor (TNF)-α and interferon (IFN)-γ. These cytokines cause inflammation, keratinocyte proliferation, and neovascularisation by further inducing macrophage accumulation and cytokine production.

of morbidities linked to metabolic syndrome.[42] Furthermore, psoriasis has a significant psychological impact, with patients reporting greater rates of anxiety, melancholy, and even suicidal ideation. To address these components of patient treatment, routine psychological well-being screening with standard anxiety and depression scales is advised.[46] Psoriasis is linked to inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, which occur four times more frequently in individuals with psoriasis compared to the general population. These conditions are in addition to cardiovascular

Table 1 Key players in the pathogenesis of psoriasis[35–39]

Sr. no.	Category	Key players	Role in psoriasis pathogenesis
1	Cells	Dendritic cells	Antigen presentation and secretion of cytokines
		Keratinocytes	Abnormal differentiation and hyperproliferation
		T cells (Th1, Th17, Th22)	Secretes IL-17, IL-22, IFN-γ, and promotes inflammation
2	Cytokines	IFN-γ	Promote inflammation
		IL-23	Help to stabilise Th17 cells
		IL-22	Promotes keratinocyte proliferation
		IL-17A	Induces keratinocyte activation and release of chemokines
		TNF-α	Activates dendritic cells and keratinocytes
3	Pathways	JAK-STAT	Mediates cytokine signalling in inflammation
		NF-κB	Regulation of inflammatory gene expression

Table 2 Differential diagnosis of psoriasis based on clinical features and available treatment options

Sr. no.	Differential diagnosis	Clinical features	Diagnostic test	Treatment options
1	Atopic dermatitis	Main symptom of itching with typical presentation: flexural lichenification in adults and older children; facial and extensor papules and vesicles in infants.[49]	Physical examination, family background, and patch test.[50]	Emollients,[51] topical corticosteroids (hydrocortisone,[52] desoximetasone,[53] clobetasol propionate,[54] mometasone furoate,[53] betamethasone[55]), antihistamines (cetirizine,[56] fexofenadine,[57] Acrivastine[58] and loratadine[59])
2	Secondary syphilis	Copper-toned lesions often affect the palms and soles.[60]	Rapid plasma reagin (RPR), Venereal Disease Research Laboratory (VDRL) test.[61]	Penicillin, doxycycline.[62]
3	Contact dermatitis	Patches or plaques with sharp margins, angular corners, and geometric outlines, depending on the nature of exposure to the irritant or allergen.[63]	Patch test[64]	Avoidance of irritants, topical steroids.[63]
4	Tinea corporis	Reduced number of lesions with a ring-shaped configuration.[65]	Examination of skin scrapings on potassium hydroxide wet mount[66]	Topical treatment (itraconazole,[67] terbinafine,[68] and fluconazole[69])
5	Lichen planus	Purple lesions and frequent mucosal involvement[70]	Immunofluorescence, biopsy.[71]	Topical corticosteroids, systemic steroids (Prednisone),[72] retinoids (Tazarotene, Acitretin).[73]
6	Mycosis fungoides	Irregularly shaped lesions with uneven distribution, distinct colour, and wrinkling caused by epidermal atrophy.[74]	Fine-needle aspiration (FNA) biopsy combined with immunophenotyping.[75]	Photodynamic therapy, radiation therapy, chemotherapy, and immunotherapy.[76]
7	Psoriasis	Plaque psoriasis, characterised by red, scaly patches, varies in coverage across patients. Guttate psoriasis presents as small, red spots mainly on the trunk and limbs.[77] Inverse psoriasis appears as scale-free, red lesions in skin folds. Pustular psoriasis manifests as white blisters surrounded by red skin.[78] Erythrodermic psoriasis, rare and severe, results in widespread redness and heat loss through the skin.[79]	Skin biopsy, physical examination.	Corticosteroids (topical),[80] vitamin D analogs (calcitriol, calcipotriene, tacalcitol, maxacalcitol),[81] retinoids (tretinoin, tazarotene, bexarotene, Adapalene, etretinate, Acitretin),[82] phototherapy (psoralen, 5-aminolevulinic acid),[83] JAK inhibitors (tofacitinib, baricitinib),[84] monoclonal antibodies (certolizumab, Infliximab, golimumab, etanercept, Ustekinumab, ixekizumab, Adalimumab).[2]

and psychological disorders.[47] In general, complete healthcare management of people with psoriasis depends on identifying and treating these comorbidities. It highlights how crucial it is to take a comprehensive approach that takes into account not just the dermatological features of the disorder but also the systemic effects it has on different organ systems and mental health.

Although there is no known cure for psoriasis, topical therapy for mild to moderate instances and phototherapy or systemic therapy for moderate-to-severe cases are effective treatments. Body surface area involvement determines severity; psoriasis classified as moderate-to-severe occurs when 5–10 percent of the body is affected. For mild to moderate cases, topical therapy is the norm of care; for severe problems, sophisticated options are taken into consideration.[48] Patients frequently use topical medications even while undergoing systemic therapy. Effective psoriasis management depends on adjusting treatment according to the severity of the condition (Fig. 2a).[8]

4. Current trends for treatment of psoriasis

The location, severity, and, most importantly, the presence of any comorbidities, such as psoriatic arthritis, must all be carefully taken into account when choosing the best course of treatment for psoriasis.[85] Since psoriasis is an incurable chronic condition that necessitates long-term management, pharmaceutical compatibility, tolerability, and efficacy for individual patients are important considerations in therapy recommendations.[42] Apart from these factors, there are three primary methods of treating psoriasis depending on how severe it is: phototherapy, topical therapy, and systemic therapy (Table 3).

4.1. Photo therapy

Due to its cost-effectiveness when compared to biologics, phototherapy is typically recommended as a first-choice treatment for moderate to severe instances of psoriasis, while it is still a secondary option for mild-to-moderate cases.[86] The idea behind phototherapy is to cause keratinocytes and T-cells in the epidermis to undergo apoptosis, which will prevent psoriatic plaques from forming.[87] In general, phototherapy can be divided into three primary types: excimer lamp/laser (at 308 nm),[88] psoralen plus ultraviolet A (PUVA) (range from 320 to 400 nm),[89] and narrowband ultraviolet B (NB-UVB) (at 311 nm).[90] However, patients frequently become non-compliant when required to visit medical institutions multiple times over a period of years for phototherapy treatments.

Although phototherapy is an effective treatment, the lack of tailored photo-irradiation and the limited penetration of topically applied photosensitizers can lead to a variety of adverse effects, making the therapeutic outcomes variable when compared to systemic treatments.[87] By enabling the precise delivery of photosensitizers deep into the dermal layers, MNs (MNs) provide a viable answer to these problems, efficiently dissolving thick plaques without inducing pain or discomfort.[42,91] This development could improve phototherapy's effectiveness and tolerability in the treatment of psoriasis.

Table 3 Currently available products in the market for psoriasis treatment[94]

Sr. no.	Route of administration	Brand name	Formulation type; active moiety
1	Topical	CLOBEX	Lotion, shampoo, spray; clobetasol propionate
		IMPOYZ	Cream; clobetasol propionate
		BRYHALI	Lotion; halobetasol propionate
		DUOBRII	Lotion; halobetasol propionate; tazarotene
		LEXETTE	Aerosol, foam; halobetasol propionate
2	Oral	OTEZLA	Tablet; Apremilast
		ROCALTROL	Capsule; calcitriol
		JYLAMVO	Solution; methotrexate

4.2. Systemic therapy

The care of moderate-to-severe psoriasis is commonly believed to be anchored by systemic therapy. In order to effectively treat psoriasis, this method involves administering anti-psoriatic drugs orally or parenterally, which allows for their distribution throughout the systemic circulation.[92] Regardless of the afflicted body surface area, systemic therapy emerges as the major therapeutic method when psoriasis persists in difficult places such as the scalp, ears, genitalia, or other inaccessible regions where topical therapy and phototherapy may not be possible.[93]

When treating severe cases of psoriasis, it is frequently advised to use a multimodal approach that incorporates topical, systemic, and phototherapy treatments at the same time. This multimodal approach seeks to accelerate the patient's recuperation while optimising therapeutic efficacy.[42] Based on the routes of delivery, systemic therapy can be further divided into two primary classes: parenteral and oral. Every route has unique benefits and factors to take into account, providing flexibility and customised treatment plans to meet the demands of each patient and the severity of the disease.

4.3. Topical therapy

Topical therapy is the mainstay of care for mild to moderate psoriasis; however, there are regional differences in the classification of mild to moderate Psoriasis. While some dermatologists consider the infected body surface to be as moderate as 3–5%, others consider it to be as high as 10%.[33,95] Applying different therapeutic agents to the affected skin using traditional formulations such as ointment, gel, lotion, cream, soap, tape, spray, shampoo, and oil includes applying corticosteroids, calcineurin inhibitors, vitamin D analogues, coal tar, keratolytics, and more.[42,85,95] Unfortunately, because of skin barriers, particularly the stratum corneum, which prevents deep penetration into the dermis and limits the effectiveness of various therapeutic agents on psoriasis, their effectiveness is highly dependent on delivery vehicles. The efficacy of current topical therapy for psoriasis is further undermined by issues such as sticky textures, greasiness, susceptibility to accidental removal, slow skin penetration resulting in delayed activity, and poor patient compliance.[96]

Microneedles represent a topical or transdermal drug delivery approach that enables the efficient administration of therapeutic agents directly into the dermis without pain, by minimally breaching the stratum corneum. This novel strategy may be able to overcome the drawbacks of traditional delivery methods and formulations, providing a technique to optimise treatment effectiveness for psoriasis patients.

5. Microneedle strategies for the treatment

Martin S. Gerstel and Virgil A. pioneered a novel way to medication delivery with MNs, which range in size from 25 to 2000 μm.[97] This innovative technology makes it easier to create

tiny skin holes that promote transcutaneous drug delivery, which is especially advantageous for medications with larger molecular masses.[98] Combining the advantages of both invasive and non-invasive methods, MNs offer a promising new strategy for drug delivery. Especially, their microscopic size allows for an affordable translation to the commercial scale.[99] Clinical trials and animal research have demonstrated their potential in treating psoriasis, with recent improvements highlighting increased drug penetration and therapeutic effects. In order to highlight their adaptability and potential for specialised pharmaceutical applications, MNs are classed according to the kind of material utilised, the technique of manufacture, and the drug release mechanism. The first reported pharmaceutical application of microneedles was seen in 1998, there is still no marketed microneedle product overseas for therapeutic use in health sector.[100] This indicates, although extensive research has shown benefits of MNs in disease management and drug delivery, challenges revolve around large-scale manufacturing, sterility, storage stability, and meeting strict regulatory requirements, as discussed further in a separate section. Therefore, further focused research on scalable fabrication, stability optimisation, and clinical translation is urgently needed to use the full potential of microneedles as a revolutionary therapy for psoriasis and other chronic skin conditions. In the parts of this article that follow, we will examine several kinds of MNs made specially to cure psoriasis.

5.1. Types of microneedles

The six types of MNs (Fig. 3) that facilitate medication distribution are solid (SMNs),[101] coated (CMNs),[102] dissolving (DMNs),[103] sweallable MN, hydrogel MN and hollow (HMNs).[104] SMNs produce skin microchannels that facilitate patch administration of a future medication, improving drug transfer and lowering the risk of infection. We call this technique "poke and patch".[101] High molecular weight medications like proteins and vaccinations can be delivered by HMNs, which resemble hypodermic needles and have a central channel. For effective distribution, they can also be integrated with drug reservoirs or microfluidic devices.[104] Through injection, CMNs quickly deliver big molecules like DNA and vaccinations by introducing the covering material into the skin. The amount of medication that can be coated is restricted by their small surface area, notwithstanding their efficiency.[102] Drug loss during coating and injection is reduced by taking certain precautions. Made of polymers or polysaccharides, DMNs dissolve when injected, releasing the medication. These needles enable effective skin penetration because they are usually less than 1000 μm in height and less than 50 μm in tip diameter. DMNs are progressively dissolved by the interstitial fluid of the skin, allowing the medication to enter the bloodstream.[103] Based on the types of microneedles discussed above and in Fig. 3, the following Table 4 summarises their respective strengths and weaknesses.

5.2. Materials for microneedles

Silicon, metal, ceramics, glass, and carbohydrates are some of the materials used to make MNs (Fig. 3g). Every material has specific benefits and drawbacks when it comes to MN fabrication. Because of its precise production capabilities, crystalline structure, and flexibility, silicon was the first material to be used in the creation of MNs. However, the usage of silicon is limited due to its high cost, challenging production process, brittleness, and problems with biocompatibility.[98] The recommended materials for MNs are metals like titanium and stainless steel because of their superior mechanical strength, biocompatibility, and dependability. Titanium served as a potent substitute for the first metal, stainless steel.[113] Ceramics, such as calcium phosphate and alumina, are made using affordable micro-moulding techniques and are stable and resistant to chemicals. Although silica glass is brittle and mostly utilised in experiments, it may take on a variety of morphologies.[114] MNs also involve the use of carbohydrates, particularly maltose and other sugars. These are made using metal or silicon templates, and they dissolve over time to release the medication. Carbohydrates are inexpensive and non-toxic; however, they have a problem with degrading at high temperatures, which makes their production more difficult.[110]

5.3. Methods of preparation for microneedles

Achieving needle geometry consistency and repeatability at the micron-scale resolution is the primary objective of MN production, but it is difficult because of the conical 3D structure and larger aspect ratio of MNs. Micro molding is one of the most commonly used fabrication procedures. It involves depositing a polymeric solution onto microstructured molds using techniques such as casting, followed by vacuum application to remove air bubbles, drying to solidify the polymer, and demolding to extract intact MN arrays (Fig. 4a).[115] By introducing the polymeric solution into molds using atomised spraying, difficulties associated with micromolding, such as incomplete cavity filling and dependence on centrifugation or vacuuming, are overcome (Fig. 4b).[116] After cleaning, bending, and electro-polishing, metallic sheets are laser-cut into MN shapes designed *via* AutoCAD using infrared lasers (Fig. 4d).[117] Laser ablation, a subtractive top-down technique employing focused ultrafast laser pulses, enables direct fabrication of MNs with precise control over tip sharpness, height, and array density, particularly for metal MNs requiring high mechanical strength (Fig. 4c).[118]

High-precision hollow MN arrays are created using deep X-ray lithography (LIGA), which entails applying a thick photoresist layer on a substrate, patterning it using vertically penetrating synchrotron X-rays, and electroplating to build metal MNs with excellent aspect ratios and smooth sidewalls (Fig. 4c).[115] Through photo-polymerisation, micro-stereolithography (Micro-SL) produces intricate 3D microstructures by layer-by-layer curing of liquid resins with UV lasers, allowing fabrication of MNs with complex geometries and internal channels. Droplet-born air blowing (DAB), a novel mild fabrication method, shapes polymer droplets into MNs by applying controlled air flow to elongate them into sharp projections,

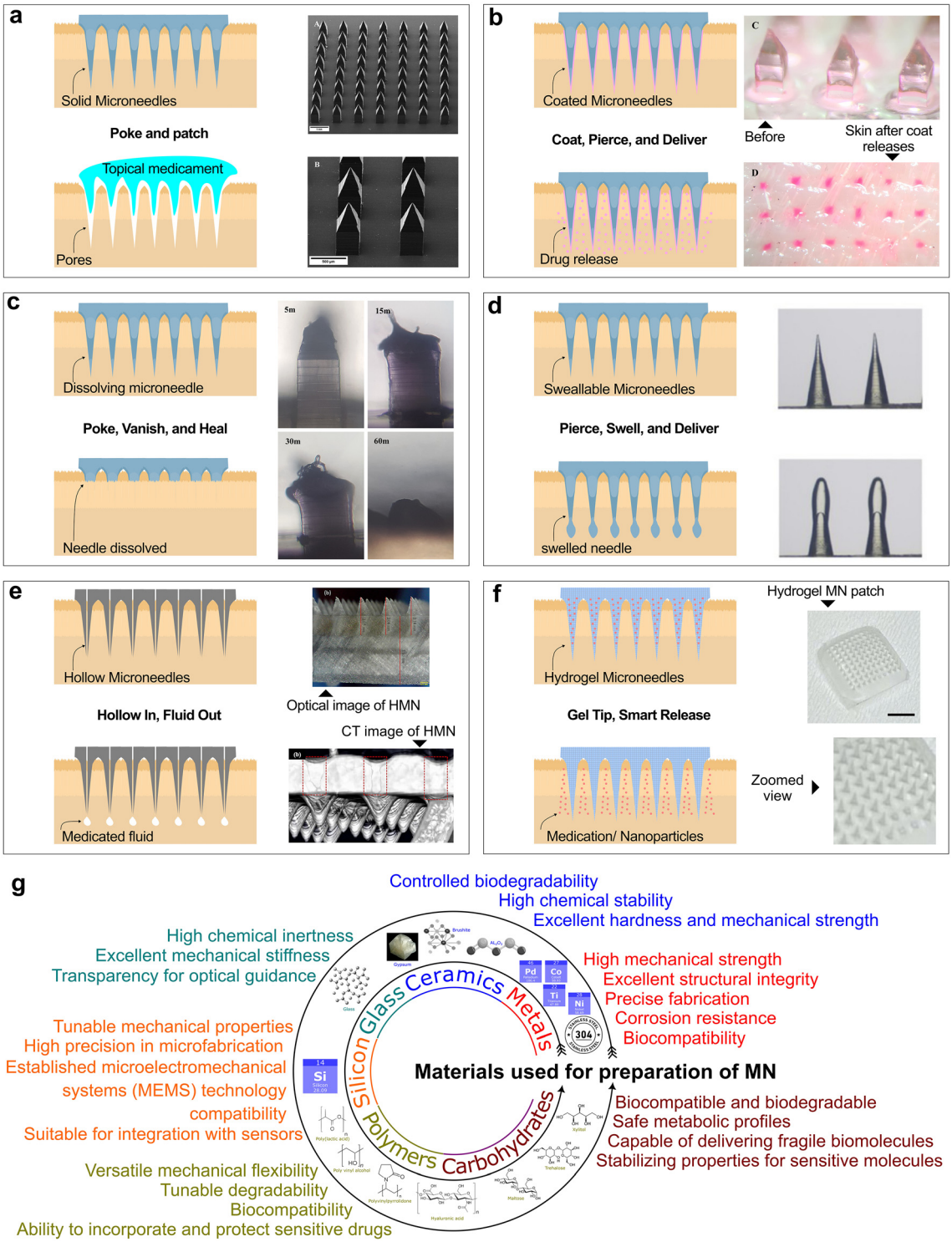

Fig. 3 Schematic and photographic representations of various microneedles illustrating their structure, mechanism of drug delivery, and interactions with skin layers: (a) solid microneedles, reproduced (or adapted) from Shahriari *et al.*, with permission from Elsevier, copyright 2024;[106] (b) coated microneedles, reproduced (or adapted) from Shahriari *et al.*, with permission from Elsevier, copyright 2024;[106] (c) dissolving microneedles, reproduced (or adapted) from Shahriari *et al.*, with permission from Elsevier, copyright 2024;[106] (d) swellable microneedles, reproduced (or adapted) from Zhao *et al.*, with permission from American Chemical Society, copyright 2024;[111] (e) hollow microneedles, reproduced (or adapted) from Kawre *et al.*, with permission from Elsevier, copyright 2024;[112] (f) hydrogel-forming microneedles, reproduced (or adapted) from Zheng *et al.*, with permission from American Chemical Society, copyright 2022;[109] and (g) key materials used in microneedle fabrication along with their advantages.

Table 4 Strengths and limitations of various microneedle types[104–110]

Sr. no.	Type of microneedle	Strengths	Weaknesses
1	Solid	Easy manufacturing, high mechanical strength for skin penetration	Require an additional step of drug application, limited or no drug capacity
2	Coated	Immediate drug introduction at the site, precise drug delivery is possible, suitable for biological delivery	Limited drug delivery due to thin coat size, hard to attain uniform coating thickness
3	Dissolving	Completely dissolves in skin, single-step application, suitable for hydrophilic medicated moieties	Lower mechanical strength, moisture sensitivity
4	Hollow	Can be used for liquid formulations, suitable for biologicals and vaccines	High coat and complex manufacturing process require precise application
5	Hydrogel	Good biocompatibility, sustained release	Slower onset and complex optimisation procedures are needed

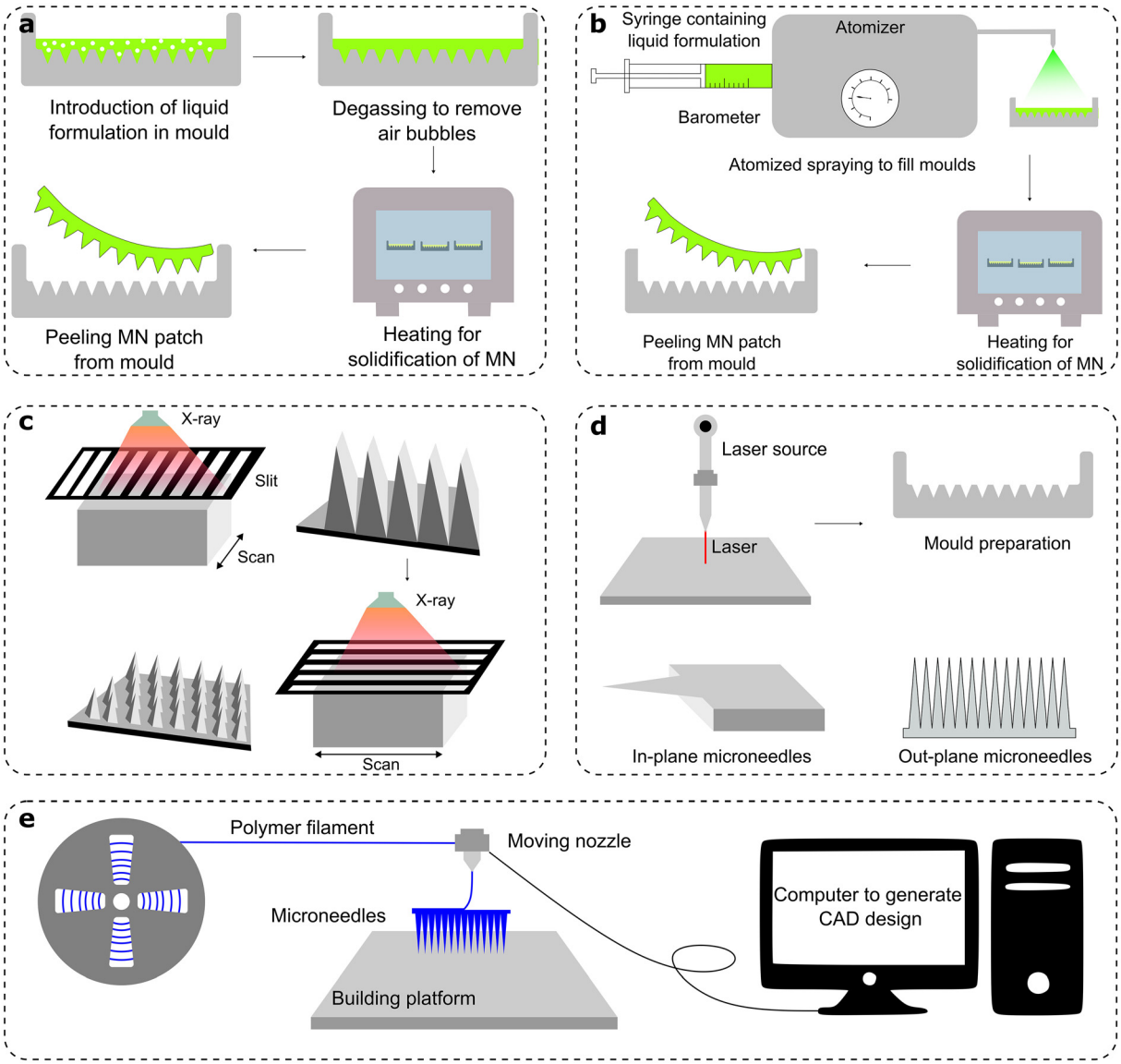

Fig. 4 Techniques for fabricating microneedles. (a) A polymeric solution is deposited into a mold during the micromolding process, which is then vacuum applied, dried, and extracted. (b) Atomised spraying to injecting the polymeric solution into molds. (c) Deep X-ray lithography to produce MN arrays. (d) Metallic sheets a laser-cut into MN forms. (e) 3D printing, with improved micro-stereolithography, to produce high-resolution MN production.

avoiding UV or heat exposure and thus preserving the bioactivity of incorporated drugs.[119]

To create MNs, microfabrication technology (MEMS) combines etching (wet chemical or dry plasma), patterning (photolithography), and deposition (chemical or physical vapour deposition), enabling fabrication of silicon or metal MNs with high precision and reproducibility. Finally, high-resolution additive manufacturing using 3D printing (Fig. 4e), an advanced form of Micro-SL, offers rapid prototyping, geometric customisation, cost-effectiveness, and scalability by directly printing MN arrays with diverse designs for patient-specific applications.[119] Each fabrication method is chosen based on desired MN characteristics such as tip sharpness, mechanical strength, drug loading capability, and application type, underscoring the critical role of precise manufacturing in advancing MN-based therapeutic systems.

5.4. AI, ML-assisted design and optimisation of microneedles

AI and ML usage in MN development and production has emerged as a transformative way to accelerate research, increase precision, and ensure quality of production. Traditional MN manufacturing often involves time-consuming trial-and-error procedures, but AI/ML approach uses data-driven systemic decision-making throughout the design-to-production.[120,121] The Quality by Design (QbD) approach has been widely accepted in pharmaceutical research for systematic product development, including in dermatological applications.[122] In skin disease research, QbD gives robust design of topical, transdermal, and microneedle arrays by finding critical material attributes and process parameters that influence product quality, efficacy, and patient safety. By using design of experiments (DoE) within QbD, researchers can optimise MN geometry, mechanical strength, and drug entrapment for enhanced skin penetration and therapeutic outcomes in psoriasis and other skin conditions.[123–125] However, while QbD ensures quality-based formulation development, the next generation of optimisation involves integrating AI and ML approaches based on complex biological datasets, thereby complementing and advancing the QbD framework towards intelligent, patient-specific microneedle-based therapies.

ML algorithms, such as gradient boosting, random forests, and advanced deep learning models like graph attention networks (GAT), have been used to predict mechanical behaviours based on input data including type of material, needle shape, size, and mesh-derived strain.[126] For example, a GAT model trained on a comprehensive simulation dataset was able to predict stress distribution patterns in MNs with high accuracy (mean squared error of 8.3×10^{-5} MPa), significantly reducing the need for physical prototyping and mechanical testing. Deep learning models like ConvNeXt and ResNet have been used for defect detection in 3D-printed MN arrays. These convolutional neural networks were trained on thousands of annotated MN images and demonstrated high reliability (up to 96% classification accuracy) in distinguishing defective from non-defective needles.[126] Moreover, in order to fine-tune the microstructure and improve mechanical integrity in 3D printing of MN, ML techniques are increasingly used for optimisation of 3D printing parameters, including etching conditions, layer thickness, and curing time.[127] By adjusting CAD-derived features and real-time printing data, ML algorithms can predict production outcomes and adjust manufacturing settings dynamically. This predictive capacity supports the development of novel MN geometries tailored to specific drug delivery goals, along with an improvement in manufacturing efficiency.[128] In future, AI and ML will provide exciting opportunities for inverse design, digital twins, and patient-centric MN development. But, obstacles such as limited high-quality datasets, the need for model interpretability, and regulatory integration must be addressed to ensure a marketed product launch. Nonetheless, AI/ML-driven strategies are poised to redefine the landscape of MN innovation by enabling faster, smarter, and more reliable transdermal drug delivery systems.

AI and ML application in MN research is geometrical optimisation for biosensing and therapy in various disease treatment.[128] The height of the needle, needle diameter, tip angle, wall thickness in case of hollow MN, and placement of needle maintaining a specific distance are critical determinants of microneedle performance. This parameter can affect skin penetration efficiency, mechanical failure probability, and drug release kinetics.[126] Old design processes rely on trial-and-error prototyping, which is time-consuming and resource-intensive. And here, ML techniques give a high-throughput method to simulate the influence of design parameters to predict the performance of MNs.

As a proof of concept and by using AI/ML, Tarar *et al.* designed MNs for enhanced interstitial fluid (ISF) collection.[129] This study utilises finite element methods (FEM) with various ML algorithms to decide the geometrical parameters that maximise fluid uptake during a single MN insertion, thereby offering a more efficient and data-driven design approach. Using COMSOL Multiphysics, the researchers performed a detailed parametric sweep across a wide range of geometrical and other variables like MNs inlet/outlet diameter, length, thickness of wall, curvature, material properties and skin types. Almost 48 000 simulation scenarios were analysed to set a large dataset describing the volumetric flow rate (VFR) of ISF through the MNs. Linear regression, support vector regression (SVR), Gaussian process regression (GPR), neural networks (NNR), and decision tree regression (DTR) models were trained and evaluated for multiple regression values using the fed dataset. Out of this, DTR emerged as the most accurate predictor with an $R^2 \approx$ of 0.9999 and minimal error (MSE $\approx 3.2 \times 10^{-6}$), eliminating more complex models like neural networks. The study underscores the predictive power of ML in MN design and also presents a user-friendly graphical interface (Fig. 5a) for real-time design optimisation of MN. This combination of ML and AI holds significant promise for the rational design of transdermal delivery systems, enhancing both clinical efficacy and patient comfort.

In another study by Tarar *et al.*, a novel method using Bayesian ML was introduced to optimize MN design (Fig. 5b) for efficient biological fluid sampling, particularly ISF.[130] This

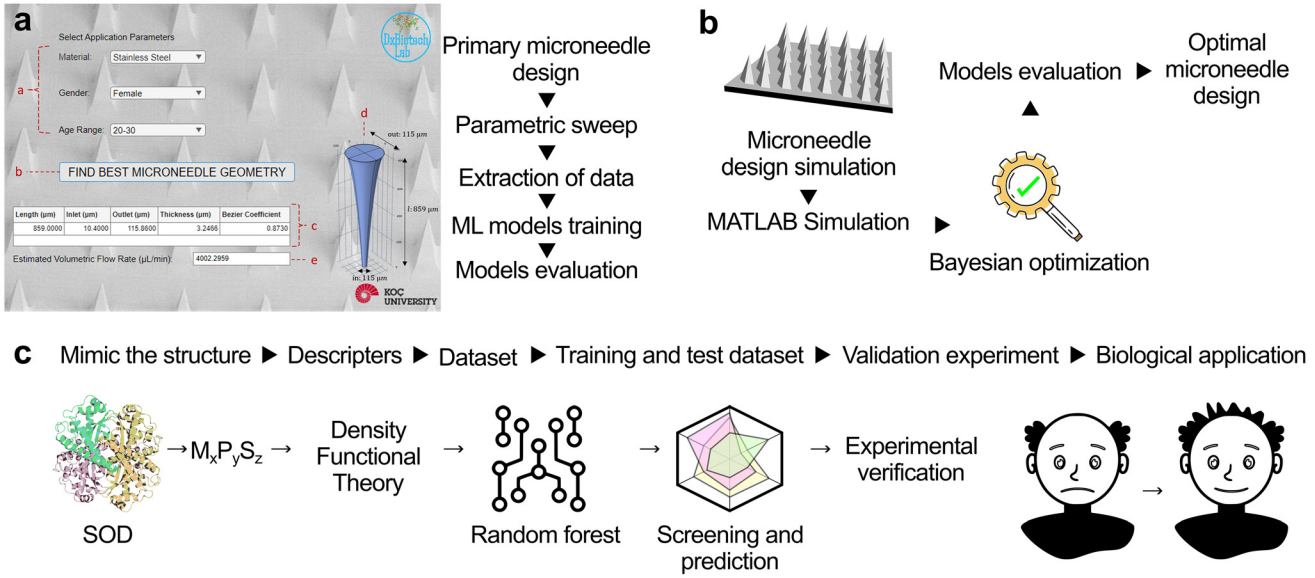

Fig. 5 (a) ML-optimized sweeping microneedle for ISF collection; reproduced (or adapted) from Tarar *et al.*, with permission from American Chemical Society, copyright 2023.[129] (b) Bayesian ML-optimized microneedle for fluid sampling; adapted from Tarar *et al.*, with permission from Royal Society of Chemistry, copyright 2023.[130] (c) ML-guided SOD nanozyme for alopecia; adapted from Zhang *et al.*, with permission from American Chemical Society, copyright 2022.[131]

study showed an "online" optimization program that eliminates the need for a prefeed dataset by directly using computational fluid dynamics (CFD) simulations in COMSOL Multiphysics with Bayesian optimization in MATLAB. The optimization mainly focuses on five key parameters like needle length, inlet and outlet diameters, thickness of wall, and curvature to maximize the volumetric flow rate (VFR) of extracted ISF. The Bayesian algorithm collectively selected design configurations based on the expected improvement criterion, balancing the various design parameters within the design space. This method gained a maximum flow rate of 21.16 mL min^{-1}, a 60% increase compared to trial-and-error-based designs. An outcome of this study was the demonstration of the superior performance of Bayesian optimization by employing adaptive probabilistic modelling and sampling strategies. This research exemplifies the growing potential of integrating physics-based modelling with AI/ML to get rational, rapid, and scalable MNs design.

In a treatment personalisation, Zhang *et al.* used ML algorithms to design MnPS3 (Fig. 5c), a superoxide dismutase-mimicking nanozyme incorporated into dissolvable MNs, for the treatment of androgenetic alopecia.[131] The authors managed a library of 91 transition-metal thiophosphates (MxPySz), selected for their potential to exhibit mixed valence states conducive to redox activity. By sorting physicochemical and structural factors like formation energy, bandgap, and coordination number while applying a range of supervised ML algorithms, they systemically modelled the connection between material features and SOD-like activity. The RF model showed the best predictive fit ($R^2 \approx 0.7$), and was used to select manganese thiophosphite ($MnPS_3$) as a leading candidate. This prediction was validated experimentally, with $MnPS_3$ exhibiting strong reactive oxygen species (ROS) scavenging capacity and superior SOD-mimetic kinetics. Significantly, the study explains the use of ML not only as a data analysis tool but as a predictive engine capable of shortening complex chemical spaces to identify functionally relevant materials. The addition of ML with density functional theory (DFT) calculations provided mechanistic insight into the redox cycling of Mn(II)/Mn(III) states and the associated energetics of $^{\bullet}O_2^-$ dismutation. Overall, this work exemplifies a data-driven, AI-assisted paradigm in nanozyme discovery, offering a blueprint for future efforts aimed at developing next-generation therapeutics through computationally guided materials innovation.

In the study by Xue *et al.*, AI played an important role in showing a path to the identification of therapeutic targets and moieties for diabetic wound healing, demonstrating how ML can advance precision medicine.[132] They employed AI-assisted bioinformatics to mine high-throughput transcriptomic data from dataset GSE144441, which includes gene expression profiles from skin samples of diabetic and non-diabetic patients. Using ML-based methods such as CGPS (gene set analysis incorporating prioritisation and sensitivity) and platforms like KOBAS-i, they selected differentially expressed genes (DEGs) with high statistical significance. These DEGs were then examined through Gene Ontology (GO) and KEGG pathway enrichment analyses, revealing key biological processes involved in diabetic wound pathology. A complex innovation was the integration of these DEGs into the Connectivity Map (CMap) database, which utilises AI algorithms to predict potential therapeutic agents based on gene expression signatures. Using this approach, Trichostatin A (TSA) was found as the top candidate compound capable of reversing the diabetic wound gene expression profile. Next, AI-based network analysis tools like STRING and CytoHubba (*via* Cytoscape) were employed to pin-

Table 5 MN as a treatment option for psoriasis

Sr. no.	Therapeutic moiety	MNs type	Significance of formulation	Ref.
1	Methotrexate	Tip-swellable microneedle array patch	Enables efficient, localised, and sustained delivery of MTX with minimal drug wastage, prolonged skin retention, deep insertion into skin lesions, and superior therapeutic efficacy compared to traditional drug delivery.	11
2	Reactive oxygen and nitrogen species (RONS)	Plasma-activated ice microneedle	Patch enables transdermal delivery of RONS, inducing ROS-activated keratinocyte apoptosis, reducing hyperproliferation and inflammation; shows significant therapeutic efficacy and biosafety.	133
3	Biguanide chitosan	DMN	Clear cfDNA and reduce inflammation in psoriasis, high DNA-binding, biocompatibility, and anti-inflammatory effects. Simple, scalable method addresses drug permeability challenges. Minimises side effects such as immune suppression and skin irritation.	134
4	Methotrexate	DMN (hyaluronic acid-coated liposomes)	HA-CD44 interaction increases cell adhesion, promoting apoptosis in HaCaT cells. Reduces skin erythema, scaling, and thickening in psoriasis. Lowers proinflammatory cytokines (IL-17A, IL-23, TNF-α) and Ki67 expression. Adequate mechanical properties, minimal skin irritation, controlled drug release, and avoids systemic MTX toxicity.	135
5	Budesonide	Multifunctional structural colour triboelectric MN	Made of budesonide-encapsulated PAM-PEGDA-LiCl ionic hydrogel with an inverse opal scaffold structure. Charge generation allows efficient, controllable drug release *via* electrostatic repulsion, reduces skin fibrosis and promotes angiogenesis, aiding psoriasis treatment. Visual monitoring of drug release. Good *in vivo* performance in psoriasis treatment, indicating strong potential for practical use.	136
6	Tofacitinib citrate	Iontophoretic DMN	Increased drug delivery 28-fold to 314.7 μg per sq cm. Delivered 18.56 μg per sq cm and 62.07 μg per sq cm at 0.1 and 0.5 mA per sq cm. Achieved the highest delivery of 566.59 μg per sq cm, showing a synergistic effect and reduced lag time. Combined MNs and iontophoresis significantly enhance tofacitinib citrate delivery, demonstrating potential for effective transdermal therapy.	137
7	Glycyrrhiza glabra extract (GgE)	Hydrogel MN	Conical and sharp (400–500 μm diameter, 700–900 μm height). Showed notable swelling (2-fold in 5 minutes) and good degradability (30 minutes), indicating burst release. No cytotoxicity against the fibroblast cell line L929. Effective GgE delivery, reducing cell population as shown by AO and DAPI staining. Useful for controlling cell proliferation in skin disorders.	138
8	Methotrexate	Hollow MN	Utilised high-precision 3D printed master mold and dual-molding process for customizable HMNs. HMNs feature varied shapes, heights, and diameters to suit different drug delivery requirements. Reusable molds reduce production costs significantly. Demonstrated effective treatment of psoriasis in mice, achieving similar efficacy with a 0.1-fold oral dose, minimizing side effects and toxicity.	139

point HDAC4 as a central hub gene—providing a rational molecular target for TSA. So, AI here served as a hypothesis-generating engine that enabled the discovery of a novel drug–target pair (TSA-HDAC4), limiting experimental workload, and streamlined the drug development pipeline.

Suriyaamporn *et al.* used AI to optimise the formulation of hydrogel MNs patches (cHMNs) for the transdermal delivery of 5-fluorouracil (5-FU) in non-melanoma skin cancer.[107] The authors used ML algorithms to predict and control critical hydrogel properties like swelling and erosion behaviour dependent on crosslinking temperature and duration. A dataset of 75 experimental formulations was used to train multiple predictive models, with Gaussian Process Regression (GPR) achieving superior performance (R^2 > 0.93). This AI-driven method allowed for the rational selection of formulation parameters to achieve optimal drug release kinetics and mechanical strength of MNs. Next, the final formulation combined 5-FU-hydroxypropyl-β-cyclodextrin inclusion complexes loaded in flexible PEGylated liposomes, enhancing skin permeation and cellular uptake while minimising toxicity. This study highlights the effective use of AI in accelerating formulation screening, reducing resource-intensive experimentation, and precision in designing advanced drug delivery platforms.

AI in MN technology include a combination of learning for autonomous design optimisation, generative adversarial networks (GANs) for developing novel MN geometries, and federated learning systems that allow mixed model training across researchers without compromising proprietary data. Advances in natural language processing (NLP) may also be harnessed to extract insights from unstructured literature, further accelerating MN innovation for the management of psoriasis.

5.5. Synergy of microneedles in the treatment of psoriasis

Microneedles and nanoparticulate medication are two novel delivery methods for psoriasis treatment. Their combination is beneficial because it opens up pores in the skin that allow nanoparticles to enter the upper layers of the skin. Furthermore, nanoparticulate systems provide a host of advantages, including specific delivery and controlled drug release.

Table 5 summarises related examples; this section outlines their applications in treating psoriasis.

5.5.1. Nanoparticle-loaded microneedle. A type of MN technology, known as nanoparticle-loaded MNs, employs nanoparticles for drug delivery and therapeutic applications. These nanoparticles are either loaded onto or coated on MNs, combining the benefits of both technologies and creating synergy for psoriasis therapy.

The Gao *et al.* study created a novel open-loop therapy with MNs to treat a combination of diabetes and psoriasis, which are linked by the NF-κB signalling pathway to inflammation and insulin resistance.[140] This medication combines two different kinds of "microneedles": long-range metformin (Met) for systemic hypoglycemia effects and short-range curcumin nanoparticles (Cur NPs) for targeted, extended psoriasis treatment. Because the hydrophobic PLGA core of Cur NPs keeps them within the psoriatic skin, they can release curcumin gradually to stop the growth of keratinocytes. In order to control blood glucose levels, metformin enters the systemic circulation by penetrating the skin deeply. Together, the two drugs block the NF-κB pathway, which lowers inflammatory cytokines (TNF-α, IL-1β, IL-23, IL-17A, and IL-6) at the protein and gene levels. Pharmacodynamic experiments with IMQ-induced psoriasis in diabetic and non-diabetic mice showed a significant reduction in inflammatory responses and symptoms. With its deep penetrating ability, the dual drug load that combines anti-inflammatory and antihyperglycemic qualities synergises the effect, and this comorbidity of psoriasis and diabetes may be effectively managed with an MN formulation.

Zhou *et al.* developed a methotrexate (MTX) prodrug (MTX-TK-HA) that is reactive to reactive oxygen species (ROS) and is intended to target hyperproliferative keratinocytes through CD44-mediated means.[141] This is a novel method of treating psoriasis. They used nano-precipitation to manufacture MTX-TK-HA with PLA-mPEG into nanoassemblies, which they then loaded into dissolving MNs. These MNs' robust mechanical characteristics and hyaluronic acid matrix allowed them to efficiently pierce psoriatic skin. Intracellular uptake was facilitated by CD44-mediated endocytosis, and ROS stimulation caused the release of MTX, which inhibited the NF-κB pathway to limit keratinocyte growth. Here, researchers have used the prodrug approach and deep-penetrating power of MNs to get a synergistic effect in disease treatment. As a proof of concept of this work, they tested this in an animal model, and this approach significantly lowered the inflammation associated with psoriasis, suggesting potential for better transdermal medication delivery in psoriasis and other ROS-responsive diseases.

In order to effectively deliver ginsenoside Rg3 (Rg3), a substance having anti-inflammatory and immune-regulating qualities, to particular sites and achieve stable release while enhancing permeability, Huang *et al.* created a cholesterol-free liposome-in-microneedle.[142] Hyaluronic acid (HA)-based MNs (Rg3-MNs) were modified to integrate Rg3-loaded liposomes, which showed enough mechanical strength (0.59 N per needle) to pierce the epidermis. Rg3-MNs were tested in mice with IMQ-induced psoriasis-like dermatitis, and they dramatically decreased cutaneous edema and epidermal thickness by blocking the STAT3/p-STAT3 signalling pathway and lowering levels of TNF-α, IL-23, and IL-17. When compared to liposomes alone, this approach demonstrated an additive effect of skin retention and bioavailability of Rg3 with less discomfort. Furthermore, this platform may be able to load additional anti-psoriasis medications such as methotrexate and calcitriol, providing a synergistic treatment alternative for psoriasis.

In order to treat psoriasis, Wang *et al.* developed a hyaluronic acid (HA)-based microneedle (MN) patch that delivers methotrexate (MTX)-containing human serum albumin nanoparticles (HSA NP) to lymph nodes (LNs).[143] The results of the study showed that the MN patch penetrated the skin well and improved medication administration. The patch prevented the disease from progressing in a mouse model of psoriasis by considerably reducing erythema and skin thickness. The therapy raised MTX accumulation in LNs while lowering the percentages of T and dendritic cells in LNs. Furthermore, the patch lowered the skin's levels of IL-6 and TNF-α. According to this study, the HM/MN patch is a viable alternative treatment for psoriasis that may find use in clinical settings due to hyaluronic acid-based MN and drug load synergism.

Dai *et al.* examined a novel method of treating psoriasis by combining calcipotriol monohydrate (CPM) in nanosuspensions (NSs) with trilayer dissolving microneedle patches (MAPs).[144] The NSs have an average PS of 211 ± 2 nm. The PVP and PVA needle arrays with a polylactic acid backing layer that was 3D printed were used to create the MAPs. These patches demonstrated effective insertion capabilities, strong mechanical qualities, and quick tip disintegration. When the MAPs were tested on Sprague-Dawley rats that had psoriasis caused by imiquimod, they showed efficacy that was on par with commercial ointments, improving patient compliance and drug delivery.

5.5.2. Nanoparticle-free microneedle. A type of MN technology called nanoparticle-free MNs is made without the use of nanoparticles for medication delivery and medicinal uses. These biocompatible and biodegradable MNs are designed to administer medications, vaccinations, or other therapeutic agents straight into the skin.

Bi *et al.* created a new MN patch that improves psoriasis treatment by combining MTX and epigallocatechin-3-gallate (EGCG).[145] The detachable, H_2O_2-responsive gel matrix of these MN patches was intended to improve local medication administration and extend therapeutic effects. EGCG was used as an anti-inflammatory medication and as a cross-linking agent at the tips of the polymer gel needles. The two-step casting technique used to generate the patches produced a structure where EGCG, a marker of psoriatic inflammation, was sustainably released in response to ROS, while MTX was rapidly released to provide immediate therapeutic effects. Gel needle tips were inserted, broke from their supporting arrays, and inflated when they came into touch with interstitial skin fluid. This resulted in the formation of drug reservoirs that allowed for regulated release. Through downregulation of the

NF-κB pathway in keratinocytes, the MNs displayed efficient skin retention for around four days, providing sustained ROS scavenging and anti-inflammatory action. When compared to patches loaded with either MTX or EGCG alone, this combination therapy produced better results in animal models of psoriasis and prophylactic psoriasis. The prolonged release of EGCG produced ongoing anti-inflammatory effects, while the quick release of MTX reduced keratinocyte hyperproliferation. The gel-based MN patch appears to be a viable therapy option for persistent skin conditions, as evidenced by the dual-release system's improvement in treatment efficacy and prolongation of therapeutic advantages. The study demonstrated how synergistic effects can be utilized to create responsive, intelligent drug delivery systems that enhance patient outcomes.

In order to treat psoriatic skin lesions, Wang *et al.*'s work presents a unique supramolecular dissolving microneedle (DMN) patch made of hydroxypropyl β-cyclodextrin (HPCD), which effectively delivers triamcinolone acetonide (TA), a hydrophobic glucocorticoid.[146] Because psoriasis thickens the stratum corneum, traditional glucocorticoid creams have trouble penetrating, whereas conventional DMNs have trouble effectively encasing hydrophobic medications. These problems are resolved by the TA-loaded HPCD DMN (TAMN) created in this work, which greatly increases the solubility and bioavailability of TA by generating water-soluble complexes through host–guest interactions. TAMN exhibits strong mechanical strength, which enables it to efficiently puncture the thicker skin of psoriatic lesions. TAMN has a stronger inhibitory effect on immortalized human keratinocyte (HaCaT) cells, according to *in vitro* research. *In vivo*, TAMN, applied two times in a week, was more effective than daily usage of commercial TA cream in reducing psoriatic symptoms in imiquimod-induced psoriasis-like mice. Additionally, TAMN had a considerable anti-inflammatory effect on the lesions as seen by the reduction of IL-23, Ki67, and IL-17 expression. This revolutionary DMN platform expands the variety of medications that can be administered by DMNs and the applications of supramolecular materials in transdermal drug administration. It also offers a potential, minimally invasive alternative for psoriasis therapy.

6. Regulatory considerations for development and manufacturing of microneedles

Enhanced drug absorption, increased patient compliance, and specified distribution are just a few of the possible benefits that come with using MNs, a novel way of medicine delivery. Key considerations for developing transdermal products are detailed in the FDA's guidance documents, specifically "Transdermal and topical delivery systems – product development and quality considerations guidance for industry" and "Regulatory considerations for microneedling products guidance for industry and food and drug administration staff (document issued on November 10, 2020)".[147,148]

To guarantee their quality, safety, and efficacy, MNs used for medicine administration must adhere to strict regulatory standards, just like any medical device. The Food and Drug Administration (FDA) in the United States classifies combination products, which include MNs used for medicine delivery. Products made up of any combination of a medication, device, or biological product are referred to as combination products under FDA regulations (21 CFR 3.2(e)). When MNs are made to administer medications through the skin, they are usually regarded as drug-device combination products. MNs' primary mode of action and intended usage determine their classification and regulatory process. The Centre for Drug Evaluation and Research (CDER) or the Centre for Biologics Evaluation and Research (CBER) will be the main regulatory bodies if the main function of the MN device is to provide medication. Device restrictions from the FDA, such as design controls, quality system regulations (QSR), and potentially premarket notification (510(k)) or premarket approval (PMA) requirements, must be followed by the device component of such combination goods.

The FDA's regulatory classification and approval of MNs for medical use are heavily reliant on their technological features and design. One important factor to take into account is the features of the needles: MNs need to be carefully crafted in order to effectively pass through the skin barrier and enable efficient medication administration. The length, sharpness, and placement of the needles are important factors that affect how well the device delivers medications to the targeted layers of skin. Medication compatibility is another important factor to consider. The materials used in the production of MNs must be carefully chosen to ensure that they are compatible with the medicine being administered. This will maintain the drug's stability, efficacy, and safety. The regulatory filing process requires both confirmation of medication delivery performance and compatibility studies. Furthermore, biocompatibility and safety are first. To prove biocompatibility and safety, MNs must go through extensive testing that includes evaluations for tissue responses, irritation, and sensitization. In order to ensure patient safety during device application, these thorough investigations are necessary to make sure that MNs not only administer medications efficiently but also meet the strict safety criteria needed to receive regulatory approval.

The FDA might need evidence from both non-clinical and clinical studies to justify the approval of MNs for use in medicine. Clinical data is essential for proving the safety, effectiveness, and ability of the device to administer medications as planned. Enrolling participants who are representative of the intended patient population is crucial for clinical research in order to guarantee that the findings accurately reflect real-world circumstances. Efficacious endpoints must to be precisely specified, with an emphasis on therapeutic outcomes or pharmacokinetic profiles as indicators of the effectiveness of drug delivery. To produce trustworthy efficacy data, robust study designs and validated measurement instruments are necessary. Furthermore, thorough safety evaluations are essential to examine possible negative outcomes connected to the

usage of MNs, including localized skin reactions, systemic impacts, and issues related to the device.

The FDA's Quality System Regulation (21 CFR Part 820), which establishes strong quality requirements to assure product uniformity, reliability, and traceability throughout the manufacturing process, must be strictly followed while manufacturing MNs for medical use. The first important factor to take into account is material selection. Materials used to fabricate MNs must be biocompatible and go through extensive testing to ensure their performance and safety. Validated sterilisation techniques and suitable packaging solutions are necessary to preserve product sterility and integrity until use. Sterilisation and packaging are crucial stages in this process. In order to reduce patient hazards, it is also important to have thorough and clear labelling that includes directions for handling, disposing of, and using MN items. These elements are essential to building strong QMSs that maintain safety and efficacy requirements needed for market approval and regulatory compliance.

In order to assure compliance with FDA regulations, the development and production of MNs for medical use necessitate negotiating complicated regulatory procedures. Through the thoughtful evaluation of essential factors such as manufacturing standards, data needs, regulatory classification, and design features, developers can expedite the regulatory

Table 6 Covering patents, products, and ongoing clinical trials for microneedles

	Title	Description/beneficial effects	Ref.
Patents	Transdermal double-layer MN based on hydrogen producing probiotics and its preparation method and application	Publication number: US20240091514. Inventors: Bin Zheng (Tianjin), Qinglu Guo (Tianjin), Yulin Cao (Beijing), Shixiang Cheng (Tianjin), Zhihui Bai (Beijing). MNs encapsulate hydrogen-producing bacteria safely with pore sizes smaller than bacteria, preventing leakage, and minimizes side effects. Hyaluronidase-loaded MN tips enhance tissue penetration for improved treatment efficacy. Target applications include psoriasis and other inflammatory skin diseases.	150
	MN patches, systems, and methods	Publication number: JP2024037953A. Current assignee: Georgia Tech Research Corp. The versions provide MN patches with a tab for handling in addition to a system with a tray for storage. Indicators providing feedback during application are included, improving usability and guaranteeing efficient distribution of drugs to the skin.	151
	Microneedle array with active ingredient	Publication number: JP2024023486A. Inventor: Futian Liu, Xiaojie Yu, Guang Wei Lu, M. Hughes Patrick, Neervannan Sesha, E. Steward Lance. The procedure involves filling a MN array mold with two fluids, one containing an active substance and dissolvable polymer in the lower wells and just dissolvable polymer in the higher wells. MNs that emerge from a base layer can be formed by heating or by drying at room temperature.	152
	Microneedle array device, methods of manufacturing and use thereof	Publication number: US20240075267A1. Inventor: Chihwei Chang. Three-layered MN arrays—a base layer, a separation layer, and a bioactive layer—are used in the system. When physiological conditions are encountered, the separating layer disperses or dissolves. This procedure makes it possible to remove the foundation layer while keeping the bioactive layer firmly affixed to the skin's surface, which promotes the efficient distribution of bioactive substances.	153
Marketed products	MicronJet® 600	The MicronJet patch, developed by NanoPass Technologies, is a MN-based vaccination delivery system for influenza vaccinations.	154
	INTRAcel™ PRO	The INTRAcel premium gadget is designed to provide electrocoagulation and hemostasis during general surgical procedures and dermatological procedures. Jeisys Medical Inc., a manufacturer of medical aesthetic devices, sponsored the device's FDA registration.	155
	AdminPatch®	Made of SS316L stainless steel, intended for diagnosis, treatment, cure and prevention of disease. Product covered by US patent no. 7658728, 7785301, 8414548, and patents pending in the U.S. and other countries.	156
	BD Soluvia™	Becton Dickinson designed BD Soluvia, a product for microinjecting medications and vaccinations into the skin's dermal layer.	157
Clinical trials	NCT02955576	The Catholic University of Korea led this clinical trial, which looked into the effectiveness of a MN patch in treating psoriatic plaques. The study, which included 20 individuals, contrasted three groups: one that used ointment as the sole treatment, another that used hyaluronic acid patches without MNs, and a third that used HA patches with MNs. With a main completion date of February 2017, the trial's objectives were to monitor side effects and evaluate changes in psoriasis severity.	158 and 159
	NCT03795402	The goal of the Janssen Research & Development-sponsored clinical trial, which involved Innovaderm Research Inc., was to use a MN device to take and examine skin samples from people with mild chronic plaque psoriasis. With its completion in December 2019, this observational research included 11 participants. The main objective was to compare the efficiency of RNA extraction between standard punch biopsies and MN device sampling using these samples for transcriptomics profiling. The goal of the study was to develop a less intrusive technique for taking skin samples for psoriasis research and genetic analysis.	159 and 160

approval process and successfully launch novel MN technologies. Following legal requirements not only protects patients but also makes it easier for clinical practice to accept and use MNs for improved drug delivery.

7. Patented, marketed and products under clinical trial

Microneedles have drawn a lot of interest in medication delivery and therapy throughout the last 10–15 years. Their popularity for transdermal drug delivery stems from their ability to address issues such as needle pain and limitations associated with oral treatment.[149] Although there aren't many psoriasis-specific patents or products, MNs are being investigated for a number of different medicinal uses. Current MN developments are summarized in Table 6, covering patents, products, and ongoing clinical trials.

8. Clinical translational challenges

Despite having various advantages, microneedle systems face several critical translational challenges. In case of psoriasis, it often affects large and multiple body areas based on severity, as mentioned in Fig. 2a, raising concerns on the practicality of MN application. While larger MN patches could be developed, their fabrication and patient tolerability remain challenging, suggesting that current MN systems may be more suited for mild to moderate localised psoriasis lesions.[110,161,162] In case of severe lesions, as illustrated in Fig. 2a, it becomes impractical to use multiple MN patches due to coverage limitations, focusing the need for alternative or combinational treatment strategies along with a special applicator. Furthermore, uniform application force is important for perfect skin penetration; thus, self-application without an applicator may result in variability and incomplete dosing. Applicator devices can ensure reproducible insertion depth and enhance patient compliance, and it opens wide area for research in medical devices. Additionally, applying MNs to difficult-to-reach areas, presents a big challenge, requiring either assistance from professionals or specially designed applicator. While MNs are designed for self-use, initial guidance by healthcare professionals is enough to educate patients on correct application techniques. Solving these translational issues through device optimisation, patient education, and clinical validation is essential to advance MN-based psoriasis therapies from experimental settings to real-world dermatological practice.

9. Conclusion

Novel approaches utilizing MNs have encouraging opportunities for improving targeted therapy in the management of psoriasis. Future research and development have interesting opportunities due to the combination of microneedle technology with new advances in material science, drug delivery systems, and pathogenesis of psoriasis understanding. Future developments in microneedle design, like the creation of biodegradable and dissolvable materials, will improve patient compliance and reduce tissue injury. Recent advancements in the manufacturing of microneedles, including as 3D printing and laser-assisted techniques, hold promise for optimizing production procedures and facilitating the creation of customized designs that meet patient requirements while adhering to regulatory requirements. Furthermore, the integration of AI and ML approaches into microneedle research can accelerate formulation optimization by predicting critical attributes such as mechanical strength, dissolution behaviour, and drug release kinetics. Improving standards and regulatory frameworks for the development of microneedles will be essential to bringing these discoveries from the lab to the patient. In short, even though there are still obstacles to overcome in terms of increasing production volume, guaranteeing formulation stability over time, and proving clinical effectiveness through reliable trials, AI-assisted microneedle design and development present an advanced strategy for achieving customized, effective, and patient-friendly psoriasis treatments, the continued development of microneedle-based treatments presents a promising path towards customized and successful psoriasis treatment, one that could soon change the face of dermatological care.

Author contributions

A. D. S.: conceptualization, writing – original draft, visualization. R. S.: conceptualization, writing – review & editing, supervision.

Conflicts of interest

The authors declare no competing interests.

Data availability

Data will be made available on request.

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References

1 M. Sala, A. Elaissari and H. Fessi, Advances in Psoriasis Physiopathology and Treatments: Up to Date of Mechanistic Insights and Perspectives of Novel Therapies

Based on Innovative Skin Drug Delivery Systems (ISDDS), *J. Controlled Release*, 2016, **239**, 182–202, DOI: 10.1016/j.jconrel.2016.07.003.

2 J. E. Greb, A. M. Goldminz, J. T. Elder, M. G. Lebwohl, D. D. Gladman, J. J. Wu, N. N. Mehta, A. Y. Finlay and A. B. Gottlieb, Psoriasis, *Nat. Rev. Dis Primers*, 2016, **2**(1), 16082, DOI: 10.1038/nrdp.2016.82.

3 M. Xue, Q. Deng, L. Deng, T. Xun, T. Huang, J. Zhao, S. Wei, C. Zhao, X. Chen, Y. Zhou, Y. Liang and X. Yang, Alterations of Gut Microbiota for the Onset and Treatment of Psoriasis: A Systematic Review, *Eur. J. Pharmacol.*, 2025, 177521, DOI: 10.1016/j.ejphar.2025.177521.

4 S. H. Shravanth, R. A. M. Osmani, S. L. Jyothi, V. P. Anupama, M. Rahamathulla and H. V. Gangadharappa, Microneedles-Based Drug Delivery for the Treatment of Psoriasis, *J. Drug Delivery Sci. Technol.*, 2021, **64**, 102668, DOI: 10.1016/j.jddst.2021.102668.

5 H.-J. Lee and M. Kim, Challenges and Future Trends in the Treatment of Psoriasis, *Int. J. Mol. Sci.*, 2023, **24**(17), 13313, DOI: 10.3390/ijms241713313.

6 I. M. Michalek, B. Loring and S. M. John, World Health Organization. *Global Report on Psoriasis*.

7 C. Skayem, C. Taieb, B. Halioua, C. Baissac and M. Saint Aroman, Epidemiology, of Psoriasis: A Worldwide Global Study, *Acta Derm.-Venereol.*, 2025, **105**, adv42945, DOI: 10.2340/actadv.v105.42945.

8 M. Pradhan, A. Alexander, M. R. Singh, D. Singh, S. Saraf, S. Saraf and Ajazuddin, Understanding the Prospective of Nano-Formulations towards the Treatment of Psoriasis, *Biomed. Pharmacother.*, 2018, **107**, 447–463, DOI: 10.1016/j.biopha.2018.07.156.

9 A. Drakos, T. Torres and R. Vender, Emerging Oral Therapies for the Treatment of Psoriasis: A Review of Pipeline Agents, *Pharmaceutics*, 2024, **16**(1), 111, DOI: 10.3390/pharmaceutics16010111.

10 P. Tapfumaneyi, M. Imran, Y. Mohammed and M. S. Roberts, Recent Advances and Future Prospective of Topical and Transdermal Delivery Systems, *Front. Drug Delivery*, 2022, **2**, DOI: 10.3389/fddev.2022.957732.

11 P. Zhao, Z. Li, Z. Ling, Y. Zheng and H. Chang, Efficient Loading and Sustained Delivery of Methotrexate Using a Tip-Swellable Microneedle Array Patch for Psoriasis Treatment, *ACS Biomater. Sci. Eng.*, 2024, **10**(2), 921–931, DOI: 10.1021/acsbiomaterials.3c01810.

12 G. J. P. Fernando, J. Hickling, C. M. Jayashi Flores, P. Griffin, C. D. Anderson, S. R. Skinner, C. Davies, K. Witham, M. Pryor, J. Bodle, S. Rockman, I. H. Frazer and A. H. Forster, Safety, Tolerability, Acceptability and Immunogenicity of an Influenza Vaccine Delivered to Human Skin by a Novel High-Density Microprojection Array Patch (NanopatchTM), *Vaccine*, 2018, **36**(26), 3779–3788, DOI: 10.1016/j.vaccine.2018.05.053.

13 V. K. Rapalli, T. Waghule, S. Gorantla, S. K. Dubey, R. N. Saha and G. Singhvi, Psoriasis: Pathological Mechanisms, Current Pharmacological Therapies, and Emerging Drug Delivery Systems, *Drug Discovery Today*, 2020, **25**(12), 2212–2226, DOI: 10.1016/j.drudis.2020.09.023.

14 H. X. Nguyen and A. K. Banga, Advanced Transdermal Drug Delivery System: A Comprehensive Review of Microneedle Technologies, Novel Designs, Diverse Applications, and Critical Challenges, *Int. J. Pharm.*, 2025, **670**, 125118, DOI: 10.1016/j.ijpharm.2024.125118.

15 C. S. Kolli and A. K. Banga, Characterization of Solid Maltose Microneedles and Their Use for Transdermal Delivery, *Pharm. Res.*, 2008, **25**(1), 104–113, DOI: 10.1007/s11095-007-9350-0.

16 K. Ita, Ceramic Microneedles and Hollow Microneedles for Transdermal Drug Delivery: Two Decades of Research, *J. Drug Delivery Sci. Technol.*, 2018, **44**, 314–322, DOI: 10.1016/j.jddst.2018.01.004.

17 G. J. Tortora and B. Derrickson, *Principles of Anatomy and Physiology*, ed. B. Roesch, L. Elfers and K. Trost, Wiley, USA, 14th edn, 2014.

18 Q. Li, V. Chandran, L. Tsoi, D. O'Rielly, R. P. Nair, D. Gladman, J. T. Elder and P. Rahman, Quantifying Differences in Heritability among Psoriatic Arthritis (PsA), Cutaneous Psoriasis (PsC) and Psoriasis Vulgaris (PsV), *Sci. Rep.*, 2020, **10**(1), 4925, DOI: 10.1038/s41598-020-61981-5.

19 L. C. Tsoi, P. E. Stuart, C. Tian, J. E. Gudjonsson, S. Das, M. Zawistowski, E. Ellinghaus, J. N. Barker, V. Chandran, N. Dand, K. C. Duffin, C. Enerbäck, T. Esko, A. Franke, D. D. Gladman, P. Hoffmann, K. Kingo, S. Kõks, G. G. Krueger, H. W. Lim, A. Metspalu, U. Mrowietz, S. Mucha, P. Rahman, A. Reis, T. Tejasvi, R. Trembath, J. J. Voorhees, S. Weidinger, M. Weichenthal, X. Wen, N. Eriksson, H. M. Kang, D. A. Hinds, R. P. Nair, G. R. Abecasis and J. T. Elder, Large Scale Meta-Analysis Characterizes Genetic Architecture for Common Psoriasis Associated Variants, *Nat. Commun.*, 2017, **8**(1), 15382, DOI: 10.1038/ncomms15382.

20 D. Yan, J. E. Gudjonsson, S. Le, E. Maverakis, O. Plazyo, C. Ritchlin, J. U. Scher, R. Singh, N. L. Ward, S. Bell and W. Liao, New Frontiers in Psoriatic Disease Research, Part I: Genetics, Environmental Triggers, Immunology, Pathophysiology, and Precision Medicine, *J. Invest. Dermatol.*, 2021, **141**(9), 2112–2122, DOI: 10.1016/j.jid.2021.02.764.

21 U. Krämer and C. Esser, Cigarette Smoking, Metabolic Gene Polymorphism, and Psoriasis, *J. Invest. Dermatol.*, 2006, **126**(3), 693–694, DOI: 10.1038/sj.jid.5700161.

22 V. Richer, C. Roubille, P. Fleming, T. Starnino, C. McCourt, A. McFarlane, S. Siu, J. Kraft, C. Lynde, J. E. Pope, S. Keeling, J. Dutz, L. Bessette, W. P. Gulliver, B. Haraoui and R. Bissonnette, Psoriasis and Smoking, *J. Cutaneous Med. Surg.*, 2016, **20**(3), 221–227, DOI: 10.1177/1203475415616073.

23 D. M. Balak and E. Hajdarbegovic, Drug-Induced Psoriasis: Clinical Perspectives, *Psoriasis*, 2017, **7**, 87–94, DOI: 10.2147/PTT.S126727.

24 A. W. Armstrong, C. T. Harskamp and E. J. Armstrong, The Association between Psoriasis and Obesity: A Systematic Review and Meta-Analysis of Observational Studies, *Nutr. Diabetes*, 2012, **2**(12), e54–e54, DOI: 10.1038/nutd.2012.26.
25 J. Belasco and N. Wei, Psoriatic Arthritis: What Is Happening at the Joint?, *Rheumatol. Ther.*, 2019, **6**(3), 305–315, DOI: 10.1007/s40744-019-0159-1.
26 M. Ceccarelli, E. Venanzi Rullo, M. Vaccaro, A. Facciolà, F. d'Aleo, I. A. Paolucci, S. P. Cannavò, B. Cacopardo, M. R. Pinzone, G. F. Pellicanò, F. Condorelli, G. Nunnari and C. Guarneri, HIV-Associated Psoriasis: Epidemiology, Pathogenesis, and Management, *Dermatol. Ther.*, 2019, **32**(2), e12806, DOI: 10.1111/dth.12806.
27 M. Kamata and Y. Tada, Dendritic Cells and Macrophages in the Pathogenesis of Psoriasis, *Front. Immunol.*, 2022, **13**, 941071, DOI: 10.3389/fimmu.2022.941071.
28 L. M. Johnson-Huang, M. A. Lowes and J. G. Krueger, Putting Together the Psoriasis Puzzle: An Update on Developing Targeted Therapies, *Dis. Models Mech.*, 2012, **5**(4), 423–433, DOI: 10.1242/dmm.009092.
29 A. Chiricozzi, P. Romanelli, E. Volpe, G. Borsellino and M. Romanelli, Scanning the Immunopathogenesis of Psoriasis, *Int. J. Mol. Sci.*, 2018, **19**(1), DOI: 10.3390/ijms19010179.
30 A. Wang and Y. Bai, Dendritic Cells: The Driver of Psoriasis, *J. Dermatol.*, 2020, **47**(2), 104–113, DOI: 10.1111/1346-8138.15184.
31 M. Vičić, M. Kaštelan, I. Brajac, V. Sotošek and L. P. Massari, Current Concepts of Psoriasis Immunopathogenesis, *Int. J. Mol. Sci.*, 2021, **22**(21), 11574, DOI: 10.3390/ijms222111574.
32 P. Zhang, Y. Su, S. Li, H. Chen, R. Wu and H. Wu, The Roles of T Cells in Psoriasis, *Front. Immunol.*, 2023, **14**, DOI: 10.3389/fimmu.2023.1081256.
33 C. E. M. Griffiths, A. W. Armstrong, J. E. Gudjonsson and J. N. W. N. Barker, Psoriasis, *Lancet*, 2021, **397**(10281), 1301–1315, DOI: 10.1016/S0140-6736(20)32549-6.
34 X. Zhou, Y. Chen, L. Cui, Y. Shi and C. Guo, Advances in the Pathogenesis of Psoriasis: From Keratinocyte Perspective, *Cell Death Dis.*, 2022, **13**(1), 81, DOI: 10.1038/s41419-022-04523-3.
35 A. M. Goldminz, S. C. Au, N. Kim, A. B. Gottlieb and P. F. Lizzul, NF-KB: An Essential Transcription Factor in Psoriasis, *J. Dermatol. Sci.*, 2013, **69**(2), 89–94, DOI: 10.1016/j.jdermsci.2012.11.002.
36 X. Zhou, Y. Chen, L. Cui, Y. Shi and C. Guo, Advances in the Pathogenesis of Psoriasis: From Keratinocyte Perspective, *Cell Death Dis.*, 2022, **13**(1), 81, DOI: 10.1038/s41419-022-04523-3.
37 L. Xia, H. Li, L. Long, W. Ruan, J. Ma, S. Xu and D. Qiao, Research Progress on the Pathogenesis of Psoriasis and Its Small Molecule Inhibitors, *Arch. Pharm.*, 2025, **358**(1), DOI: 10.1002/ardp.202400621.
38 I. Sieminska, M. Pieniawska and T. M. Grzywa, The Immunology of Psoriasis—Current Concepts in Pathogenesis, *Clin. Rev. Allergy Immunol.*, 2024, **66**(2), 164–191, DOI: 10.1007/s12016-024-08991-7.
39 K. Shivhare and N. K. Satija, Acute Myeloid Leukemia–Osteoblast Interaction Mediated Autophagy Induction Protects Against Cytarabine Induced Apoptosis, *Cell Biochem. Funct.*, 2025, **43**(2), DOI: 10.1002/cbf.70055.
40 W. B. Kim, D. Jerome and J. Yeung, Diagnosis and Management of Psoriasis, *Can. Fam. Physician*, 2017, **63**(4), 278–285.
41 K. Papp, W. Gulliver, C. Lynde, Y. Poulin and J. Ashkenas, Canadian Psoriasis Guidelines Committee. Canadian Guidelines for the Management of Plaque Psoriasis: Overview, *J. Cutaneous Med. Surg.*, 2011, **15**(4), 210–219, DOI: 10.2310/7750.2011.10066.
42 B. H. J. Gowda, M. G. Ahmed, U. Hani, P. Kesharwani, S. Wahab and K. Paul, Microneedles as a Momentous Platform for Psoriasis Therapy and Diagnosis: A State-of-the-Art Review, *Int. J. Pharm.*, 2023, **632**, 122591, DOI: 10.1016/j.ijpharm.2023.122591.
43 M. Haroon, B. Kirby and O. FitzGerald, High Prevalence of Psoriatic Arthritis in Patients with Severe Psoriasis with Suboptimal Performance of Screening Questionnaires, *Ann. Rheum. Dis.*, 2013, **72**(5), 736–740, DOI: 10.1136/annrheumdis-2012-201706.
44 O. FitzGerald, A. Ogdie, V. Chandran, L. C. Coates, A. Kavanaugh, W. Tillett, Y. Y. Leung, M. deWit, J. U. Scher and P. J. Mease, Psoriatic Arthritis, *Nat. Rev. Dis. Primers*, 2021, **7**(1), 59, DOI: 10.1038/s41572-021-00293-y.
45 M. S. Garshick and J. S. Berger, Psoriasis and Cardiovascular Disease-An Ounce of Prevention Is Worth a Pound of Cure, *JAMA Dermatol.*, 2022, **158**(3), 239–241, DOI: 10.1001/jamadermatol.2021.4723.
46 T. L. Hedemann, X. Liu, C. N. Kang and M. I. Husain, Associations between Psoriasis and Mental Illness: An Update for Clinicians, *Gen. Hosp. Psychiatry*, 2022, **75**, 30–37, DOI: 10.1016/j.genhosppsych.2022.01.006.
47 C. R. H. Hedin, E. Sonkoly, M. Eberhardson and M. Ståhle, Inflammatory Bowel Disease and Psoriasis: Modernizing the Multidisciplinary Approach, *J. Intern. Med.*, 2021, **290**(2), 257–278, DOI: 10.1111/joim.13282.
48 G. Hari, A. Kishore and S. R. P. Karkala, Treatments for Psoriasis: A Journey from Classical to Advanced Therapies. How Far Have We Reached?, *Eur. J. Pharmacol.*, 2022, **929**, 175147, DOI: 10.1016/j.ejphar.2022.175147.
49 C. Ahn and W. Huang, *Clinical Presentation of Atopic Dermatitis*, 2024, pp. 37–44. DOI: 10.1007/978-3-031-54513-9_4.
50 S. Weidinger, A. Nosbaum, E. Simpson and E. Guttman, Good Practice Intervention for Clinical Assessment and Diagnosis of Atopic Dermatitis: Findings from the Atopic Dermatitis Quality of Care Initiative, *Dermatol. Ther.*, 2022, **35**(3), DOI: 10.1111/dth.15259.
51 Y. Zhong, M. Samuel, H. van Bever and E. H. Tham, Emollients in Infancy to Prevent Atopic Dermatitis: A Systematic Review and Meta–analysis, *Allergy*, 2022, **77**(6), 1685–1699, DOI: 10.1111/all.15116.

52 A. A. Mohamed, R. El Borolossy, E. M. Salah, M. S. Hussein, N. M. Muharram, N. Elsalawy, M. G. Khalil, M. O. Mahmoud, R. Y. El-Amir, H. M. A. Elsanhory, N. Ahmed, A. S. Adaroas, M. Montaser and A. A. El Kholy, A Comparative Randomized Clinical Trial Evaluating the Efficacy and Safety of Tacrolimus versus Hydrocortisone as a Topical Treatment of Atopic Dermatitis in Children, *Front. Pharmacol.*, 2023, **14**, DOI: 10.3389/fphar.2023.1202325.

53 K. Lahiri, S. Barua, B. V. R. Babu, S. Tahiliani, K. Godse and K. R. Kulkarni, Assessment of Safety and Effectiveness of Desoximetasone Emollient Cream 0.25% in Comparison to Mometasone Cream 0.1% in Indian Patients with Eczema, *Int. J. Res. Med. Sci.*, 2022, **10**(3), 688, DOI: 10.18203/2320-6012.ijrms20220519.

54 M. Jing, Q. Yu, B. Zhu, F. Yuan, J. Zhang, L. Peng, W. Lin and M. Chen, Topical 0.05% Clobetasol Cream in the Treatment of Chronic Hand Eczema, *Medicine*, 2021, **100**(10), e24418, DOI: 10.1097/MD.0000000000024418.

55 K. P. Debes, N. A. Evdina, A. Laigaard, J. M. Larsen, L. F. Zachariassen, C. H. F. Hansen and A. K. Hansen, Betamethasone Treatment for Atopic Dermatitis in Gut Microbiota Transplanted Mice, *Comp. Med.*, 2020, **70**(1), 6–15, DOI: 10.30802/AALAS-CM-18-000136.

56 G. F. Parisi, S. Leonardi, G. Ciprandi, A. Corsico, A. Licari, M. Miraglia del Giudice, D. Peroni, C. Salpietro and G. L. Marseglia, Cetirizine Use in Childhood: An Update of a Friendly 30-Year Drug, *Clin. Mol. Allergy*, 2020, **18**(1), 2, DOI: 10.1186/s12948-020-00118-5.

57 A. Ningombam, S. Handa, N. Srivastava, R. Mahajan and D. De, Addition of Oral Fexofenadine to Topical Therapy Leads to a Significantly Greater Reduction in the Serum Interleukin-31 Levels in Mild to Moderate Paediatric Atopic Dermatitis, *Clin. Exp. Dermatol.*, 2022, **47**(4), 724–729, DOI: 10.1111/ced.15032.

58 P. Phinyo, P. Koompawichit, S. Nochaiwong, N. Tovanabutra, S. Chiewchanvit and M. Chuamanochan, Comparative Efficacy and Acceptability of Licensed Dose Second-Generation Antihistamines in Chronic Spontaneous Urticaria: A Network Meta-Analysis, *J. Allergy Clin. Immunol.: Pract.*, 2021, **9**(2), 956–970, DOI: 10.1016/j.jaip.2020.08.055.

59 Y. Xie, S. Irwin, A. Chupina Estrada, B. Nelson, A. Bullock, L. Fontenot, H. Feng, M. Sun and H. W. Koon, Loratadine as an Anti-Inflammatory Agent Against *Clostridium Difficile* Toxin B, *J. Infect. Dis.*, 2024, DOI: 10.1093/infdis/jiae021.

60 D. Moino and S. Ros, Syphilis in Pregnancy: Fetal and Neonatal Complications, *NeoReviews*, 2024, **25**(6), e375–e379, DOI: 10.1542/neo.25-6-e375.

61 D. Solaimalai, S. Rathore, M. M. Beck, A. Regi, B. L. Yesudhason, B. Veeraraghavan and J. A. J. Prakash, Enzyme–linked Immunosorbent Assay (ELISA) versus Venereal Disease Research Laboratory Test (VDRL) and Rapid Plasma Reagin Test (RPR) for Screening of Syphilis in Pregnant Women, *Int. J. Gynecol. Obstet.*, 2020, **150**(1), 103–107, DOI: 10.1002/ijgo.13154.

62 H. Tong, A. Heuer and N. Walker, The Impact of Antibiotic Treatment for Syphilis, Chlamydia, and Gonorrhoea during Pregnancy on Birth Outcomes: A Systematic Review and Meta-Analysis, *J. Global Health*, 2023, **13**, 04058, DOI: 10.7189/jogh.13.04058.

63 M. Tramontana, K. Hansel, L. Bianchi, C. Sensini, N. Malatesta and L. Stingeni, Advancing the Understanding of Allergic Contact Dermatitis: From Pathophysiology to Novel Therapeutic Approaches, *Front. Med.*, 2023, **10**, DOI: 10.3389/fmed.2023.1184289.

64 J. G. DeKoven, E. M. Warshaw, M. J. Reeder, A. R. Atwater, J. I. Silverberg, D. V. Belsito, D. Sasseville, K. A. Zug, J. S. Taylor, M. D. Pratt, H. I. Maibach, J. F. Fowler, B. L. Adler, M.-C. Houle, C. M. Mowad, N. Botto, J. Yu and C. A. Dunnick, North American Contact Dermatitis Group Patch Test Results: 2019–2020, *Dermatitis®*, 2023, **34**(2), 90–104, DOI: 10.1089/derm.2022.29017.jdk.

65 A. K. Leung, J. M. Lam, K. F. Leong and K. L. Hon, Tinea Corporis: An Updated Review, *Drugs Context*, 2020, **9**, DOI: 10.7573/dic.2020-5-6.

66 U. Khurana, A. Marwah, V. Dey, U. Uniya and R. Hazari, Evaluating Diagnostic Utility of PAS Stained Skin Scrape Cytology Smear in Clinically Suspected Superficial Cutaneous Mycoses: A Simple yet Unpracticed Technique, *J. Fam. Med. Primary Care*, 2022, **11**(3), 1089, DOI: 10.4103/jfmpc.jfmpc_959_21.

67 A. Khurana, A. Agarwal, D. Agrawal, S. Panesar, M. Ghadlinge, K. Sardana, K. Sethia, S. Malhotra, A. Chauhan and N. Mehta, Effect of Different Itraconazole Dosing Regimens on Cure Rates, Treatment Duration, Safety, and Relapse Rates in Adult Patients With Tinea Corporis/Cruris, *JAMA Dermatol.*, 2022, **158**(11), 1269, DOI: 10.1001/jamadermatol.2022.3745.

68 S. Brigida and A. A. Elizabeth, A Comparative Study of Efficacy of Oral Terbinafine and Oralitraconazole in Tinea Corporis/Tinea Cruris Infection, *J. Pharm. Res. Int.*, 2021, 94–105, DOI: 10.9734/jpri/2021/v33i20A31352.

69 P. Salunke, S. Someshwar and M. Bhobe, Efficacy of Daily Oral Terbinafine versus Pulse Fluconazole Therapy in the Treatment of Tinea Corporis, Tinea Cruris, and Tinea Faciei: A Comparative Study, *MGM J. Med. Sci.*, 2020, **7**(1), 10, DOI: 10.4103/mgmj.MGMJ_30_20.

70 P. R. M. Souza, L. Dupont and D. D. R. de Souza, Lichen Planus, in *Dermatology in Public Health Environments*, Springer International Publishing, Cham, 2023, pp. 559–568. DOI: 10.1007/978-3-031-13505-7_22.

71 M. B. S. Cerqueira, L. M. P. Ramalho, S. Arruda, L. D. A. Melo and M. C. M. C. Pereira, IMMUNOFLUORESCENCE AS A DIAGNOSTIC TOOL FOR ORAL LICHEN PLANUS, *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.*, 2020, **130**(3), e196, DOI: 10.1016/j.oooo.2020.04.409.

72 S. J. Kia, M. Basirat, T. Mortezaie and M.-S. Moosavi, Comparison of Oral Nano-Curcumin with Oral Prednisolone on Oral Lichen Planus: A Randomized Double-Blinded Clinical Trial, *BMC Complementary Med. Ther.*, 2020, **20**(1), 328, DOI: 10.1186/s12906-020-03128-7.

73 A. Andabak-Rogulj, E. Vindiš, L. Aleksijević, I. Škrinjar, D. Juras, A. Aščić and B. Brzak, Different Treatment Modalities of Oral Lichen Planus—A Narrative Review, *Dent. J.*, 2023, **11**(1), 26, DOI: 10.3390/dj11010026.
74 J. M. Jung, D. J. Lim, C. H. Won, S. E. Chang, M. W. Lee and W. J. Lee, Mycosis Fungoides in Children and Adolescents, *JAMA Dermatol.*, 2021, **157**(4), 431, DOI: 10.1001/jamadermatol.2021.0083.
75 M. P. Feletti, V. M. Novo, A. M. de A. Ramos, B. S. Costa, E. F. da P. Scardua, D. R. Camisasca and T. R. Grão-Velloso, MYCOSIS FUNGOIDES: A MULTIDISCIPLINARY TEAM APPROACH, *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.*, 2024, **137**(6), e153–e154, DOI: 10.1016/j.oooo.2023.12.026.
76 K. Wojewoda, M. Gillstedt, H. Englund, S. Ali, C. Lewerin and A. Osmancevic, Diagnostic Outcomes and Treatment Modalities in Patients with Mycosis Fungoides in West Sweden—A Retrospective Register-Based Study, *Cancers*, 2022, **14**(19), 4661, DOI: 10.3390/cancers14194661.
77 P. Gisondi, F. Bellinato and G. Girolomoni, Topographic Differential Diagnosis of Chronic Plaque Psoriasis: Challenges and Tricks, *J. Clin. Med.*, 2020, **9**(11), 3594, DOI: 10.3390/jcm9113594.
78 M. Knabel and K. Mudaliar, Histopathologic Features of Inverse Psoriasis, *J. Cutaneous Pathol.*, 2022, **49**(3), 246–251, DOI: 10.1111/cup.14142.
79 K. A. Reynolds, D. J. Pithadia, E. B. Lee, W. Liao and J. J. Wu, A Systematic Review of Treatment Strategies for Erythrodermic Psoriasis, *J. Dermatol. Treat.*, 2021, **32**(1), 49–55, DOI: 10.1080/09546634.2019.1689228.
80 M. Zhang, X. Bai, W. Cao, J. Ji, L. Wang, Y. Yang and H. Yang, The Influence of Corticosteroids, Immunosuppressants and Biologics on Patients With Inflammatory Bowel Diseases, Psoriasis and Rheumatic Diseases in the Era of COVID-19: A Review of Current Evidence, *Front. Immunol.*, 2021, **12**, DOI: 10.3389/fimmu.2021.677957.
81 A. M. A. Stanescu, A. A. Simionescu and C. C. Diaconu, Oral Vitamin D Therapy in Patients with Psoriasis, *Nutrients*, 2021, **13**(1), 163, DOI: 10.3390/nu13010163.
82 N. Kanda, T. Hoashi and H. Saeki, Nutrition and Psoriasis, *Int. J. Mol. Sci.*, 2020, **21**(15), 5405, DOI: 10.3390/ijms21155405.
83 S. Makuch, M. Dróżdż, A. Makarec, P. Ziółkowski and M. Woźniak, An Update on Photodynamic Therapy of Psoriasis—Current Strategies and Nanotechnology as a Future Perspective, *Int. J. Mol. Sci.*, 2022, **23**(17), 9845, DOI: 10.3390/ijms23179845.
84 M. Nogueira, L. Puig and T. Torres, JAK Inhibitors for Treatment of Psoriasis: Focus on Selective TYK2 Inhibitors, *Drugs*, 2020, **80**(4), 341–352, DOI: 10.1007/s40265-020-01261-8.
85 K. Walter, Psoriasis, *J. Am. Med. Assoc.*, 2022, **327**(19), 1936, DOI: 10.1001/jama.2022.5270.
86 A. W. Armstrong and C. Read, Pathophysiology, Clinical Presentation, and, Treatment of Psoriasis: A Review, *J. Am. Med. Assoc.*, 2020, **323**(19), 1945–1960, DOI: 10.1001/jama.2020.4006.
87 P. Zhang and M. X. Wu, A Clinical Review of Phototherapy for Psoriasis, *Lasers Med. Sci.*, 2018, **33**(1), 173–180, DOI: 10.1007/s10103-017-2360-1.
88 D. Mehta and H. W. Lim, Ultraviolet B Phototherapy for Psoriasis: Review of Practical Guidelines, *Am. J. Clin. Dermatol.*, 2016, **17**(2), 125–133, DOI: 10.1007/s40257-016-0176-6.
89 S. Ahmed Asim, S. Ahmed and N. Us-Sehar, Psoralen-Ultraviolet A Treatment with Psoralen-Ultraviolet B Therapy in the Treatment of Psoriasis, *Pak. J. Med. Sci.*, 2013, **29**(3), 758–761, DOI: 10.12669/pjms.293.2622.
90 P. G. Calzavara-Pinton, R. Sala, M. Arisi, M. T. Rossi, M. Venturini and B. Ortel, Synergism between Narrowband Ultraviolet B Phototherapy and Etanercept for the Treatment of Plaque-Type Psoriasis, *Br. J. Dermatol.*, 2013, **169**(1), 130–136, DOI: 10.1111/bjd.12277.
91 Y. Zhang, J. Yu, A. R. Kahkoska, J. Wang, J. B. Buse and Z. Gu, Advances in Transdermal Insulin Delivery, *Adv. Drug Delivery Rev.*, 2019, **139**, 51–70, DOI: 10.1016/j.addr.2018.12.006.
92 P. Gisondi, M. Del Giglio and G. Girolomoni, Treatment Approaches to Moderate to Severe Psoriasis, *Int. J. Mol. Sci.*, 2017, **18**(11), 2427, DOI: 10.3390/ijms18112427.
93 B.-X. Yan, X.-Y. Chen, L.-R. Ye, J.-Q. Chen, M. Zheng and X.-Y. Man, Cutaneous and Systemic Psoriasis: Classifications and Classification for the Distinction, *Front. Med.*, 2021, **8**, 649408, DOI: 10.3389/fmed.2021.649408.
94 *USFDA approved drugs*. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 2024-06-04).
95 J.-T. Maul, F. Anzengruber, C. Conrad, A. Cozzio, P. Häusermann, A. Jalili, A. G. A. Kolios, E. Laffitte, A.-K. Lapointe, C. Mainetti, C. Schlapbach, R. Trüeb, N. Yawalkar, M. Dippel and A. A. Navarini, Topical Treatment of Psoriasis Vulgaris: The Swiss Treatment Pathway, *Dermatology*, 2021, **237**(2), 166–178, DOI: 10.1159/000512930.
96 K. S. Paudel, M. Milewski, C. L. Swadley, N. K. Brogden, P. Ghosh and A. L. Stinchcomb, Challenges and Opportunities in Dermal/Transdermal Delivery, *Ther. Delivery*, 2010, **1**(1), 109–131, DOI: 10.4155/tde.10.16.
97 J. Halder, S. Gupta, R. Kumari, G. D. Gupta and V. K. Rai, Microneedle Array: Applications, Recent Advances, and Clinical Pertinence in Transdermal Drug Delivery, *J. Pharm. Innovation*, 2021, **16**(3), 558–565, DOI: 10.1007/s12247-020-09460-2.
98 P. Arora and R. Shukla, Microneedles along with Conventional Therapies: An in-Depth Observational Review in Alopecia Areata Treatment, *J. Drug Delivery Sci. Technol.*, 2024, **95**, 105627, DOI: 10.1016/j.jddst.2024.105627.
99 R. F. Donnelly and M. R. Prausnitz, The Promise of Microneedle Technologies for Drug Delivery, *Drug Delivery*

Transl. Res., 2024, **14**(3), 573–580, DOI: 10.1007/s13346-023-01430-8.

100 S. Henry, D. V. McAllister, M. G. Allen and M. R. Prausnitz, Microfabricated Microneedles: A Novel Approach to Transdermal Drug Delivery, *J. Pharm. Sci.*, 1998, **87**(8), 922–925, DOI: 10.1021/js980042+.

101 N. Tariq, M. W. Ashraf and S. Tayyaba, A Review on Solid Microneedles for Biomedical Applications, *J. Pharm. Innovation*, 2022, **17**(4), 1464–1483, DOI: 10.1007/s12247-021-09586-x.

102 B. Z. Chen, M. C. He, X. P. Zhang, W. M. Fei, Y. Cui and X. D. Guo, A Novel Method for Fabrication of Coated Microneedles with Homogeneous and Controllable Drug Dosage for Transdermal Drug Delivery, *Drug Delivery Transl. Res.*, 2022, **12**(11), 2730–2739, DOI: 10.1007/s13346-022-01123-8.

103 T. Bauleth-Ramos, N. El-Sayed, F. Fontana, M. Lobita, M.-A. Shahbazi and H. A. Santos, Recent Approaches for Enhancing the Performance of Dissolving Microneedles in Drug Delivery Applications, *Mater. Today*, 2023, **63**, 239–287, DOI: 10.1016/j.mattod.2022.12.007.

104 S. Gade, K. Glover, D. Mishra, S. Sharma, O. Guy, R. F. Donnelly, L. K. Vora and R. R. S. Thakur, Hollow Microneedles for Ocular Drug Delivery, *J. Controlled Release*, 2024, **371**, 43–66, DOI: 10.1016/j.jconrel.2024.05.013.

105 E. D. Ozyilmaz, A. Turan and T. Comoglu, An Overview on the Advantages and Limitations of 3D Printing of Microneedles, *Pharm. Dev. Technol.*, 2021, **26**(9), 923–933, DOI: 10.1080/10837450.2021.1965163.

106 M. H. Shahriari, H. Salmani, M. Akrami and Z. Salehi, Development of a Facile, Versatile and Scalable Fabrication Approach of Solid, Coated, and Dissolving Microneedle Devices for Transdermal Drug Delivery Applications, *Giant*, 2024, **18**, 100284, DOI: 10.1016/j.giant.2024.100284.

107 P. Suriyaamporn, C. Pornpitchanarong, T. Charoenying, K. Dechsri, T. Ngawhirunpat, P. Opanasopit and B. Pamornpathomkul, Artificial Intelligence-Driven Hydrogel Microneedle Patches Integrating 5-Fluorouracil Inclusion Complex-Loaded Flexible Pegylated Liposomes for Enhanced Non-Melanoma Skin Cancer Treatment, *Int. J. Pharm.*, 2025, **669**, 125072, DOI: 10.1016/j.ijpharm.2024.125072.

108 W.-D. Yao, J.-N. Zhou, C. Tang, J.-L. Zhang, Z.-Y. Chen, Y. Li, X.-J. Gong, M.-Y. Qu, Q. Zeng, Y.-L. Jia, H.-Y. Wang, T. Fan, J. Ren, L.-L. Guo, J.-F. Xi, X.-T. Pei, Y. Han and W. Yue, Hydrogel Microneedle Patches Loaded with Stem Cell Mitochondria-Enriched Microvesicles Boost the Chronic Wound Healing, *ACS Nano*, 2024, **18**(39), 26733–26750, DOI: 10.1021/acsnano.4c06921.

109 H. Zheng, A. GhavamiNejad, P. GhavamiNejad, M. Samarikhalaj, A. Giacca and M. Poudineh, Hydrogel Microneedle-Assisted Assay Integrating Aptamer Probes and Fluorescence Detection for Reagentless Biomarker Quantification, *ACS Sens.*, 2022, **7**(8), 2387–2399, DOI: 10.1021/acssensors.2c01033.

110 K. Ita, Transdermal Delivery of Drugs with Microneedles—Potential and Challenges, *Pharmaceutics*, 2015, **7**(3), 90–105, DOI: 10.3390/pharmaceutics7030090.

111 P. Zhao, Z. Li, Z. Ling, Y. Zheng and H. Chang, Efficient Loading and Sustained Delivery of Methotrexate Using a Tip-Swellable Microneedle Array Patch for Psoriasis Treatment, *ACS Biomater. Sci. Eng.*, 2024, **10**(2), 921–931, DOI: 10.1021/acsbiomaterials.3c01810.

112 S. Kawre, P. Suryavanshi, D. S. Lalchandani, M. K. Deka, P. Kumar Porwal, S. Kaity, S. Roy and S. Banerjee, Bioinspired Labrum-Shaped Stereolithography (SLA), Assisted 3D PrVinted Hollow Microneedles (HMNs) for Effectual Delivery of Ceftriaxone Sodium, *Eur. Polym. J.*, 2024, **204**, 112702, DOI: 10.1016/j.eurpolymj.2023.112702.

113 R. Ali, P. Mehta, M. Arshad, I. Kucuk, M.-W. Chang and Z. Ahmad, Transdermal Microneedles—A Materials Perspective, *AAPS PharmSciTech*, 2020, **21**(1), 12, DOI: 10.1208/s12249-019-1560-3.

114 L. Bao, J. Park, G. Bonfante and B. Kim, Recent Advances in Porous Microneedles: Materials, Fabrication, and Transdermal Applications, *Drug Delivery Transl. Res.*, 2022, **12**(2), 395–414, DOI: 10.1007/s13346-021-01045-x.

115 C. Oliveira, J. A. Teixeira, N. Oliveira, S. Ferreira and C. M. Botelho, Microneedles' Device: Design, Fabrication, and Applications, *Macromolecules*, 2024, **4**(2), 320–355, DOI: 10.3390/macromol4020019.

116 S. C. Park, M. J. Kim, S.-K. Baek, J.-H. Park and S.-O. Choi, Spray-Formed Layered Polymer Microneedles for Controlled Biphasic Drug Delivery, *Polymers*, 2019, **11**(2), 369, DOI: 10.3390/polym11020369.

117 E. Albarahmieh, L. AbuAmmouneh, Z. Kaddoura, F. AbuHantash, B. A. Alkhalidi and A. Al-Halhouli, Fabrication of Dissolvable Microneedle Patches Using an Innovative Laser-Cut Mould Design to Shortlist Potentially Transungual Delivery Systems: In Vitro Evaluation, *AAPS PharmSciTech*, 2019, **20**(5), 215, DOI: 10.1208/s12249-019-1429-5.

118 F. K. Aldawood, A. Andar and S. Desai, Investigating Laser Ablation Process Parameters for the Fabrication of Customized Microneedle Arrays for Therapeutic Applications, *Pharmaceutics*, 2024, **16**(7), 885, DOI: 10.3390/pharmaceutics16070885.

119 M. Olowe, S. K. Parupelli and S. Desai, A Review of 3D-Printing of Microneedles, *Pharmaceutics*, 2022, **14**(12), DOI: 10.3390/pharmaceutics14122693.

120 G. Zhong, Q. Liu, Q. Wang, H. Qiu, H. Li and T. Xu, Fully Integrated Microneedle Biosensor Array for Wearable Multiplexed Fitness Biomarkers Monitoring, *Biosens. Bioelectron.*, 2024, **265**, 116697, DOI: 10.1016/j.bios.2024.116697.

121 R. X. Gao, J. Krüger, M. Merklein, H.-C. Möhring and J. Váncza, Artificial Intelligence in Manufacturing: State of the Art, Perspectives, and Future Directions, *CIRP Ann.*, 2024, **73**(2), 723–749, DOI: 10.1016/j.cirp.2024.04.101.

122 M. Behera, P. Mahale, A. Gowtham, A. D. Sutar, R. K. Kaundal and R. Shukla, Quality by Design Based

Hydrogel Formulation of 4-Octyl Itaconate-Loaded Nanostructured Lipid Carriers for Epidermal Restoration in Atopic Dermatitis, *J. Pharm. Invest.*, 2025, DOI: 10.1007/s40005-025-00748-4.

123 D. A. Castilla-Casadiego, H. Carlton, D. Gonzalez-Nino, K. A. Miranda-Muñoz, R. Daneshpour, D. Huitink, G. Prinz, J. Powell, L. Greenlee and J. Almodovar, Design, Characterization, and Modeling of a Chitosan Microneedle Patch for Transdermal Delivery of Meloxicam as a Pain Management Strategy for Use in Cattle, *Mater. Sci. Eng., C*, 2021, **118**, 111544, DOI: 10.1016/j.msec.2020.111544.

124 S. Kumar and R. Shukla, Advancements in Microneedle Technology: Current Status and next-Generation Innovations, *J. Microencapsulation*, 2024, **41**(8), 782–803, DOI: 10.1080/02652048.2024.2418613.

125 A. D. Sutar, R. K. Verma and R. Shukla, Quality by Design in Pulmonary Drug Delivery: A Review on Dry Powder Inhaler Development, Nanotherapy Approaches, and Regulatory Considerations, *AAPS PharmSciTech*, 2024, **25**(6), 178, DOI: 10.1208/s12249-024-02900-z.

126 W. He, S. Kong, R. Lin, Y. Xie, S. Zheng, Z. Yin, X. Huang, L. Su and X. Zhang, Machine Learning Assists in the Design and Application of Microneedles, *Biomimetics*, 2024, **9**(8), 469, DOI: 10.3390/biomimetics9080469.

127 M. Elbadawi, L. E. McCoubrey, F. K. H. Gavins, J. J. Ong, A. Goyanes, S. Gaisford and A. W. Basit, Harnessing Artificial Intelligence for the next Generation of 3D Printed Medicines, *Adv. Drug Delivery Rev.*, 2021, **175**, 113805, DOI: 10.1016/j.addr.2021.05.015.

128 G. D. Goh, S. L. Sing and W. Y. Yeong, A Review on Machine Learning in 3D Printing: Applications, Potential, and Challenges, *Artif. Intell. Rev.*, 2021, **54**(1), 63–94, DOI: 10.1007/s10462-020-09876-9.

129 C. Tarar, E. Aydın, A. K. Yetisen and S. Tasoglu, Machine Learning-Enabled Optimization of Interstitial Fluid Collection via a Sweeping Microneedle Design, *ACS Omega*, 2023, **8**(23), 20968–20978, DOI: 10.1021/acsomega.3c01744.

130 C. Tarar, E. Aydın, A. K. Yetisen and S. Tasoglu, Bayesian Machine Learning Optimization of Microneedle Design for Biological Fluid Sampling, *Sens. Diagn.*, 2023, **2**(4), 858–866, DOI: 10.1039/D3SD00103B.

131 C. Zhang, Y. Yu, S. Shi, M. Liang, D. Yang, N. Sui, W. W. Yu, L. Wang and Z. Zhu, Machine Learning Guided Discovery of Superoxide Dismutase Nanozymes for Androgenetic Alopecia, *Nano Lett.*, 2022, **22**(21), 8592–8600, DOI: 10.1021/acs.nanolett.2c03119.

132 Y. Xue, C. Chen, R. Tan, J. Zhang, Q. Fang, R. Jin, X. Mi, D. Sun, Y. Xue, Y. Wang, R. Xiong, H. Lu and W. Tan, Artificial Intelligence-Assisted Bioinformatics, Microneedle, and Diabetic Wound Healing: A "New Deal" of an Old Drug, *ACS Appl. Mater. Interfaces*, 2022, **14**(33), 37396–37409, DOI: 10.1021/acsami.2c08994.

133 T. Wu, J. Zhang, X. Jing, Z. Wang, Z. Wu, H. Zhang, D. Liu, M. Rong and P. K. Chu, Multiple RONS-Loaded Plasma-Activated Ice Microneedle Patches for Transdermal Treatment of Psoriasis, *ACS Appl. Mater. Interfaces*, 2024, **16**(35), 46123–46132, DOI: 10.1021/acsami.4c10067.

134 Z. Liu, Y. Wang, Y. Zhang, L. Hu, B. Chen, Y. Li, X. Guo, B. Yu and F.-J. Xu, Biguanide Chitosan Microneedles with Cell-Free DNA Scavenging Ability for Psoriasis Therapy, *Bioact. Mater.*, 2024, **33**, 497–505, DOI: 10.1016/j.bioactmat.2023.11.015.

135 S. Shen, X. Zheng, X. Dong, M. Fang, A. Wan, T. Zhu, Q. Yang, J. Xie and Q. Yan, Methotrexate-Loaded Hyaluronan-Modified Liposomes Integrated into Dissolving Microneedles for the Treatment of Psoriasis, *Eur. J. Pharm. Sci.*, 2024, **195**, 106711, DOI: 10.1016/j.ejps.2024.106711.

136 Y. Wang, X. Zhang, G. Chen, M. Lu and Y. Zhao, Multifunctional Structural Color Triboelectric Microneedle Patches for Psoriasis Treatment, *Matter*, 2023, **6**(5), 1555–1568, DOI: 10.1016/j.matt.2023.03.005.

137 A. A. Dandekar, H. T. Garimella, C. L. German and A. K. Banga, Microneedle Mediated Iontophoretic Delivery of Tofacitinib Citrate, *Pharm. Res.*, 2023, **40**(3), 735–747, DOI: 10.1007/s11095-022-03190-5.

138 A. Khorshidian, N. Sharifi, F. Choupani Kheirabadi, F. Rezaei, S. A. Sheikholeslami, A. Ariyannejad, J. Esmaeili, H. Basati and A. Barati, In Vitro Release of Glycyrrhiza Glabra Extract by a Gel-Based Microneedle Patch for Psoriasis Treatment, *Gels*, 2024, **10**(2), 87, DOI: 10.3390/gels10020087.

139 Y. Ren, J. Li, Y. Chen, J. Wang, Y. Chen, Z. Wang, Z. Zhang, Y. Chen, X. Shi, L. Cao, J. Zhang, H. Dong, C. Yan and Z. Li, Customized Flexible Hollow Microneedles for Psoriasis Treatment with Reduced–dose Drug, *Bioeng. Transl. Med.*, 2023, **8**(4), DOI: 10.1002/btm2.10530.

140 X. Gao, F. Zhang, Y. Huang, W. Hu, Y. Chen, L. Jiang, X. Pan, C. Wu, C. Lu and T. Peng, Site-Specifically Launched Microneedles for the Combined Treatment of Psoriasis-Diabetic Comorbidity, *ACS Appl. Mater. Interfaces*, 2023, **15**(40), 46613–46625, DOI: 10.1021/acsami.3c08358.

141 Y. Zhou, L. Yang, Y. Lyu, D. Wu, Y. Zhu, J. Li, D. Jiang, X. Xin and L. Yin, Topical Delivery of ROS-Responsive Methotrexate Prodrug Nanoassemblies by a Dissolvable Microneedle Patch for Psoriasis Therapy, *Int. J. Nanomed.*, 2023, **18**, 899–915, DOI: 10.2147/IJN.S394957.

142 C. Huang, K. Gou, X. Yue, S. Zhao, R. Zeng, Y. Qu and C. Zhang, A Novel Hyaluronic Acid-Based Dissolving Microneedle Patch Loaded with Ginsenoside Rg3 Liposome for Effectively Alleviate Psoriasis, *Mater. Des.*, 2022, **224**, 111363, DOI: 10.1016/j.matdes.2022.111363.

143 H. Wang, Z. Zhao, C. Wu, X. Tong, Y. Shi and S. Chen, Microneedle Patch Delivery of Methotrexate-Loaded Albumin Nanoparticles to Immune Cells Achieves a Potent Antipsoriatic Effect, *Int. J. Nanomed.*, 2022, **17**, 3841–3851, DOI: 10.2147/IJN.S371183.

144 X. Dai, A. D. Permana, M. Li, Habibie, M. Nur Amir, K. Peng, C. Zhang, H. Dai, A. J. Paredes, L. K. Vora and

R. F. Donnelly, Calcipotriol Nanosuspension-Loaded Trilayer Dissolving Microneedle Patches for the Treatment of Psoriasis: In Vitro Delivery and In Vivo Antipsoriatic Activity Studies, *Mol. Pharm.*, 2024, **21**(6), 2813–2827, DOI: 10.1021/acs.molpharmaceut.3c01223.

145 D. Bi, F. Qu, W. Xiao, J. Wu, P. Liu, H. Du, Y. Xie, H. Liu, L. Zhang, J. Tao, Y. Liu and J. Zhu, Reactive Oxygen Species-Responsive Gel-Based Microneedle Patches for Prolonged and Intelligent Psoriasis Management, *ACS Nano*, 2023, **17**(5), 4346–4357, DOI: 10.1021/acsnano.2c08979.

146 H. Wang, Y. Fu, P. Liu, F. Qu, S. Du, Y. Li, H. Du, L. Zhang, J. Tao and J. Zhu, Supramolecular Dissolving Microneedle Patch Loading Hydrophobic Glucocorticoid for Effective Psoriasis Treatment, *ACS Appl. Mater. Interfaces*, 2023, **15**(12), 15162–15171, DOI: 10.1021/acsami.3c00058.

147 FDA. *Contains Nonbinding Recommendations Regulatory Considerations for Microneedling Products Guidance for Industry and Food and Drug Administration Staff Preface Public Comment*; 2020. https://www.regulations.gov.

148 Fda; Cder; hillsi. *Transdermal and Topical Delivery Systems-Product Development and Quality Considerations Guidance for Industry DRAFT GUIDANCE*. https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

149 B. H. J. Gowda, M. G. Ahmed, A. Sahebkar, Y. Riadi, R. Shukla and P. Kesharwani, Stimuli-Responsive Microneedles as a Transdermal Drug Delivery System: A Demand-Supply Strategy, *Biomacromolecules*, 2022, **23**(4), 1519–1544, DOI: 10.1021/acs.biomac.1c01691.

150 B. Zheng, Q. Guo, Y. Cao, S. Cheng and Z. Bai, Transdermal Double-Layer Microneedle Based on Hydrogen Producing Probiotics and Its Preparation Method and Application, US20240091514A1, 2022.

151 D. McAllister, M. Prausnitz, S. Henry and J. J. Norman, MICRONEEDLE PATCHES, SYSTEMS, AND METHODS, JP2024037953A, 2022.

152 F. Liu, X. Yu, L. E. Steward, G. W. Lu, P. M. Hughes and S. Neervannan, Microneedle Array with Active Ingredient, JP2024023486A, 2022.

153 C. Chang, MICRONEEDLE ARRAY DEVICE, METHODS OF MANUFACTURING AND USE THEROF, US20240075267A1, 2023.

154 Y. Levin, E. Kochba and R. Kenney, Clinical Evaluation of a Novel Microneedle Device for Intradermal Delivery of an Influenza Vaccine: Are All Delivery Methods the Same?, *Vaccine*, 2014, **32**(34), 4249–4252, DOI: 10.1016/j.vaccine.2014.03.024.

155 *Dr EMMA clinics*. https://dr-emma.co.uk/treatment/intracel-pro/ (accessed 2024-06-20).

156 *AdminMed*. https://www.adminmed.com/microneedlearrays (accessed 2024-06-20).

157 *Words pharmaceutical frontiers*. https://www.worldpharmaceuticals.net/companies/becton-dickinson/ (accessed 2024-06-20).

158 F. Qu, R. Geng, Y. Liu and J. Zhu, Advanced Nanocarrier- and Microneedle-Based Transdermal Drug Delivery Strategies for Skin Diseases Treatment, *Theranostics*, 2022, **12**(7), 3372–3406, DOI: 10.7150/thno.69999.

159 *ClinicalTrials.gov*. https://clinicaltrials.gov/ (accessed 2024-06-20).

160 P. K. Yadav, S. Das and M. K. Das, 3D-Microneedles: A Novel Approach for Skin Directed Delivery and Its Application, *Polym.-Plast. Technol. Mater.*, 2023, **62**(11), 1364–1393, DOI: 10.1080/25740881.2023.2207203.

161 S. Indermun, R. Luttge, Y. E. Choonara, P. Kumar, L. C. du Toit, G. Modi and V. Pillay, Current Advances in the Fabrication of Microneedles for Transdermal Delivery, *J. Controlled Release*, 2014, **185**, 130–138, DOI: 10.1016/j.jconrel.2014.04.052.

162 F. Moawad, R. Pouliot and D. Brambilla, Dissolving Microneedles in Transdermal Drug Delivery: A Critical Analysis of Limitations and Translation Challenges, *J. Controlled Release*, 2025, **383**, 113794, DOI: 10.1016/j.jconrel.2025.113794.