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Nanotechnology and Vitiligo: an integrative review of emerging therapeutic strategies

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Abstract. Vitiligo is an acquired chronic dermatological disorder characterized by the selective destruction of epidermal melanocytes, resulting in hypopigmented or depigmented macules on the skin and mucous membranes. It is a multifactorial disease whose pathophysiology involves autoimmune mechanisms, genetic predisposition, oxidative stress, and alterations in the cutaneous microenvironment. This article aims to conduct a literature review on the application of nanotechnology in the treatment of vitiligo, addressing the main pathophysiological mechanisms of the disease, the nanoengineered systems currently under investigation, and their potential advantages over conventional therapies.
To achieve this objective, a descriptive and exploratory literature review was carried out based on national and international scientific publications indexed in the Scopus, Web of Science, PubMed, and SciELO databases. The search strategy employed the descriptors “vitiligo,” “nanotechnology,” and “treatment,” as well as their corresponding terms in English, combined using Boolean operators. Initially, 126 publications were identified, of which 72 fully met the eligibility criteria after duplicate removal, title and abstract screening, and critical appraisal of the full texts. Original research articles and review papers addressing the pathophysiological aspects of vitiligo and the therapeutic applications of nanotechnology were included. The analyzed studies demonstrated that conventional treatments included topical corticosteroids, calcineurin inhibitors, and narrowband ultraviolet B (NB-UVB) phototherapy, whereas non-conventional approaches encompassed the use of plant extracts, cell-based therapies, platelet-rich plasma (PRP), microneedle systems, and nanotechnology-based platforms. These strategies have emerged as promising alternatives for enhancing repigmentation and modulating the pathophysiological mechanisms involved in vitiligo. Furthermore, nanoengineered systems have shown significant potential to overcome the limitations associated with conventional topical formulations. It can be concluded that nanotechnology represents an innovative and highly promising strategy for the treatment of vitiligo, enabling more precise drug delivery, improved therapeutic efficacy, and reduced adverse effects associated with conventional therapies. Advances in nanoengineered delivery systems suggest considerable potential for the development of personalized treatments capable of simultaneously targeting the immunological, oxidative, and regenerative mechanisms involved in the disease.
Keywords: Repigmentation, nanosistems, melanocytes.

Introduction

Vitiligo is an acquired autoimmune cutaneous disorder characterized by the selective loss of epidermal melanocytes, resulting in the progressive development of achromic or hypochromic macules, affecting approximately 0.5% to 2% of the global population (Padmakar, 2023). Although often underestimated as a merely aesthetic disturbance, vitiligo imposes substantial psychosocial burdens, including stigmatization, anxiety, depression, and suicidal ideation (Ezzedine, 2021). The etiology of the disease is multifactorial, involving a complex interplay of genetic predisposition, oxidative stress, environmental triggers, and profound immune dysregulation, primarily mediated by the activation of cytotoxic CD8+ T lymphocytes and the signaling of pro-inflammatory cytokines such as IFN-γ, TNF-α, IL-6, and IL-17 (Parga, 2025).

Therapeutic management of this chronic and unpredictable condition aims to halt the autoimmune response and stimulate cutaneous

repigmentation from melanocyte reservoirs located in hair follicles (Ju, 2024). First-line conventional approaches include high-potency topical corticosteroids, calcineurin inhibitors (e.g., tacrolimus and pimecrolimus), and narrowband ultraviolet B (NB-UVB) phototherapy. More recently, Janus kinase (JAK) inhibitors, such as ruxolitinib and tofacitinib, have emerged as promising biologic therapies capable of disrupting the inflammatory cytokine cascade in both localized and generalized forms of the disease (Moghadam, 2023; Spritz, 2021).

Nevertheless, standard-of-care treatments face significant limitations that compromise patient adherence and long-term therapeutic outcomes (Rosmarin, 2020). Prolonged topical corticosteroid use induces notable local adverse effects, including skin atrophy and telangiectasias, while systemic JAK inhibitor administration raises concerns regarding overall patient safety (Howell, 2019). From a pharmaceutical standpoint, the primary obstacle lies in the impermeability of the stratum corneum, which restricts drug penetration to the deeper epidermal layers and pilosebaceous units at effective concentrations, resulting in suboptimal clinical responses and high relapse rates upon treatment discontinuation (Gupta, 2021).

Given these challenges, nanotechnology has established itself as an innovative platform in dermatological medicine by enabling the development of delivery systems capable of overcoming the skin's biological barriers (Kang, 2024). The engineering of materials at the nanoscale allows for the modulation of physicochemical properties of therapeutic systems to efficiently traverse the stratum corneum, directing active compounds toward follicular and epidermal reservoirs (Raszewska-Famielec and Flieger, 2022; Qadir, 2022; Jain, 2012). Drug encapsulation protects labile molecules from degradation, enables controlled release kinetics, and enhances local bioavailability, thereby reducing required dosages and minimizing systemic absorption and associated toxicities (Sun, 2020; Waghule, 2020). Recent evidence has demonstrated the superiority of nanocarriers such as liposomes, ethosomes, nanoemulsions, and nanostructured lipid carriers in the delivery of tacrolimus, tofacitinib, silymarin, and statins, outperforming conventional formulations in modulating oxidative stress, suppressing IFN-γ signaling, and promoting repigmentation (Parga, 2025; Erf, 2019).

Thus, the present work aims to conduct a comprehensive literature review on the pathophysiology of vitiligo, with an emphasis on autoimmune mechanisms and oxidative stress, and to comparatively analyze conventional therapies versus non-conventional approaches, particularly the pharmacological potential of plant-derived extracts and the development of nanotechnology-based delivery systems.

Methodology

This study comprises a descriptive and exploratory literature review, grounded in a qualitative and retrospective analysis of the scientific literature. The bibliographic survey was designed to map the current state of the art and technological advances related to the proposed theme. Data collection was performed through consultations of internationally and nationally recognized indexed databases, specifically Scopus, Web of Science, and PubMed. Search strategies were delimited using controlled descriptors and free terms based on the core keywords of the study, combined through Boolean operators AND and OR. The search strategy employed the following terms in both Portuguese and their English counterparts: vitiligo and treatment, vitiligo and nanotechnology. Inclusion criteria comprised original research articles and review papers published in peer-reviewed journals, with no strict language restrictions. Exclusion criteria encompassed conference abstracts, book chapters, dissertations, theses, and studies that did not directly address the correlation between the established thematic axes.

Contextualization and Analysis

Epidemiology of Vitiligo

Vitiligo is a pigmentary dermatosis of worldwide distribution, with an estimated global prevalence ranging from 0.5% to 2%, although epidemiological studies reveal significant geographic variations, with higher frequencies observed in certain populations from South Asia and other specific regions (Kumar, 2024; Haulrig, 2024). The condition affects individuals of all ages, races, ethnicities, and skin phototypes. However, individuals with darker skin tones (e.g., African and Asian descent) often face greater stigmatization, discrimination, and potentially more severe psychosocial repercussions (Pandya, 2025).

Vitiligo affects both sexes equally, with no consistent gender-based differences in prevalence. Nevertheless, several studies indicate that women tend to seek dermatological care more frequently and report a higher psychosocial impact from the disease, including impairments in self-esteem, quality of life, and emotional well-being. This phenomenon may be attributed both to greater concerns regarding physical appearance and to sociocultural factors influencing disease perception and coping strategies (Alikhan, 2011).

The onset of vitiligo predominantly occurs in younger individuals. Recent epidemiological data indicate that a substantial proportion of cases manifest during childhood and adolescence, with the disease commonly presenting before the age of 30. Furthermore, population-based studies have demonstrated heterogeneous age distribution, with onset patterns varying across different age groups and among distinct ethnic populations (Haulrig et al., 2024; Lee et al., 2015).

A notable epidemiological feature of vitiligo is its association with genetic factors. Familial aggregation has been well documented, with first-

degree relatives exhibiting a higher likelihood of developing the disease compared to the general population (Zhang, 2012; Tenesa & Haley, 2013). Additionally, individuals with vitiligo present an increased frequency of comorbid autoimmune conditions, including type 1 diabetes, systemic lupus erythematosus, rheumatoid arthritis, pernicious anemia, and Addison's disease, reinforcing the existence of a shared immunogenetic basis (Baldini, 2017).

Although the genetic contribution is significant, environmental factors also play a crucial role in modulating disease risk and age of onset. Studies suggest that environmental changes over time may influence patterns of vitiligo onset, underscoring its multifactorial nature as a result of the interaction between elevated genetic predisposition and environmental influences (Zeng, 2004; Spritz & Santorico, 2021). Figure 1 summarizes the main etiological factors leading to skin depigmentation or hypopigmentation.

Pathophysiology of Vitiligo

The pathophysiology of vitiligo is multifactorial and strongly associated with autoimmune mechanisms that result in the selective destruction of epidermal melanocytes. Compelling evidence indicates that vitiligo is predominantly mediated by autoreactive cytotoxic CD8+ T lymphocytes, which recognize melanocyte-specific antigens and promote melanocyte apoptosis through the release of perforin, granzymes, and activation of Fas/FasL-dependent pro-apoptotic pathways (Wang, 2025). Central to this immune process is the inflammatory axis driven by interferon-gamma (IFN-γ), a key cytokine in vitiligo pathogenesis. IFN-γ activates the JAK–STAT signaling pathway, inducing the expression of chemokines such as CXCL9 and CXCL10, which sustain the continuous recruitment of CD8+ T cells to the epidermis. This inflammatory loop contributes to lesion progression, disease chronicity, and impaired spontaneous repigmentation (Zhang, 2021).

Parallel to the adaptive immune response, oxidative stress plays a primary role in disease pathophysiology. Melanocytes exhibit heightened susceptibility to the accumulation of reactive oxygen species (ROS) due to their deficient antioxidant defense mechanisms. In this oxidative milieu, cells undergo dysfunction, mitochondrial damage, and release of damage-associated molecular patterns (DAMPs), such as HSP70 and HMGB1, which amplify cutaneous inflammation and enhance melanocyte immunogenicity (Cui, 2019; Speeckaert, 2019). The inflammatory microenvironment in vitiligo-affected skin is further characterized by the presence of resident memory T cells (TRM), which are activated by dermal dendritic cells, migrate to the epidermis, and persist even after melanocyte elimination. These cells are implicated in lesion recurrence and therapeutic resistance, as they sustain local IFN-γ production and perpetuate immune recruitment. Additionally, a quantitative and functional reduction in regulatory T cells (Tregs) has been observed, compromising peripheral immune tolerance and favoring persistent autoimmunity (Rashid, 2023), as illustrated in Figure 2.

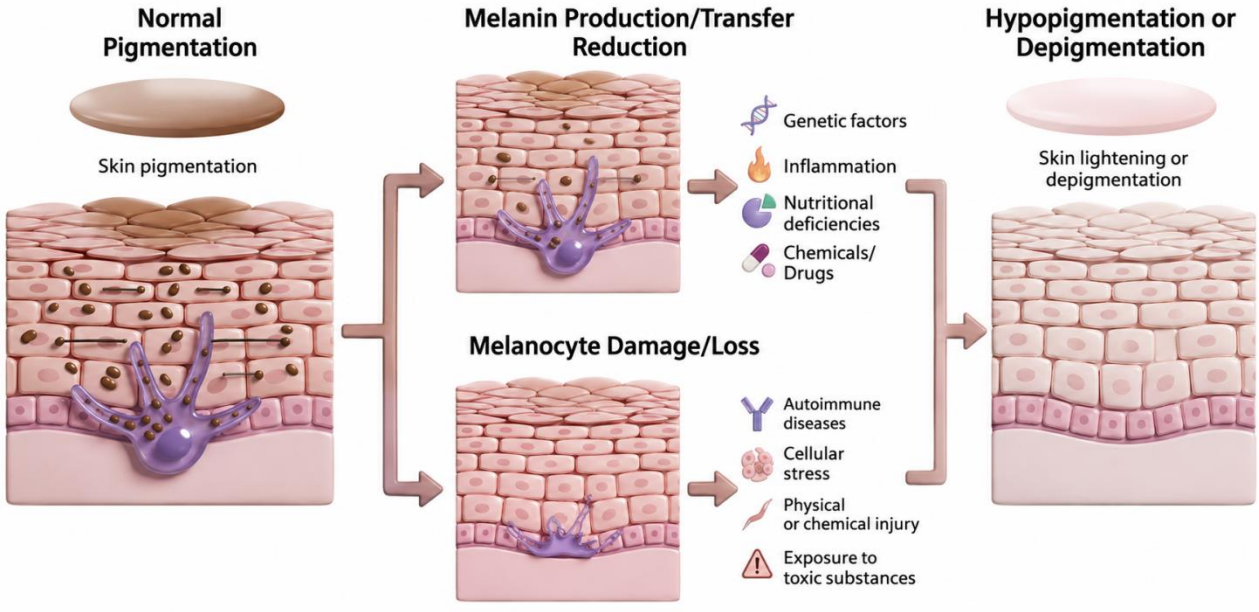

Figure 1. Schematic representation of the two primary cellular mechanisms leading to reduced or absent skin pigmentation, contrasted with normal pigmentation patterns. Normal pigmentation. Under physiological conditions, melanocytes in the basal layer synthesize melanin and transfer it via dendritic processes to adjacent keratinocytes (arrows), ensuring homogeneous skin pigmentation. Reduced melanin production/transfer. In this pathway, melanocytes remain present in the tissue but become hypofunctional, exhibiting decreased melanin synthesis or impaired melanin transfer to keratinocytes, resulting in partial pigment reduction. Associated etiologies include genetic factors,

inflammatory processes, enzymatic deficiencies (e.g., tyrosinase dysfunction), and exposure to chemical agents or pharmaceuticals. This mechanism typically leads to hypopigmentation (partial loss of color). Melanocyte destruction/loss. In this pathway, melanocytes are eliminated or undergo disappearance, leading to an absence of melanin production. Associated causes include autoimmune disease (as in vitiligo), cellular injury, post-injury tissue repair processes, and exposure to toxic substances. This mechanism typically results in depigmentation (complete loss of color). Both pathways converge toward the same macroscopic outcome — skin lightening or depigmentation — as illustrated on the right by the marked reduction of melanin in histological sections. Image created with BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Recent advances have highlighted the role of exosomes in the pathophysiology of vitiligo. Exosomes released by immune system cells can transport regulatory microRNAs capable of modulating inflammatory, apoptotic, and oxidative stress pathways in melanocytes (Ma, 2025). These microRNAs actively participate in melanocytic destruction and the amplification of the autoimmune response, suggesting a novel level of intercellular communication involved in disease progression (Li, 2024).

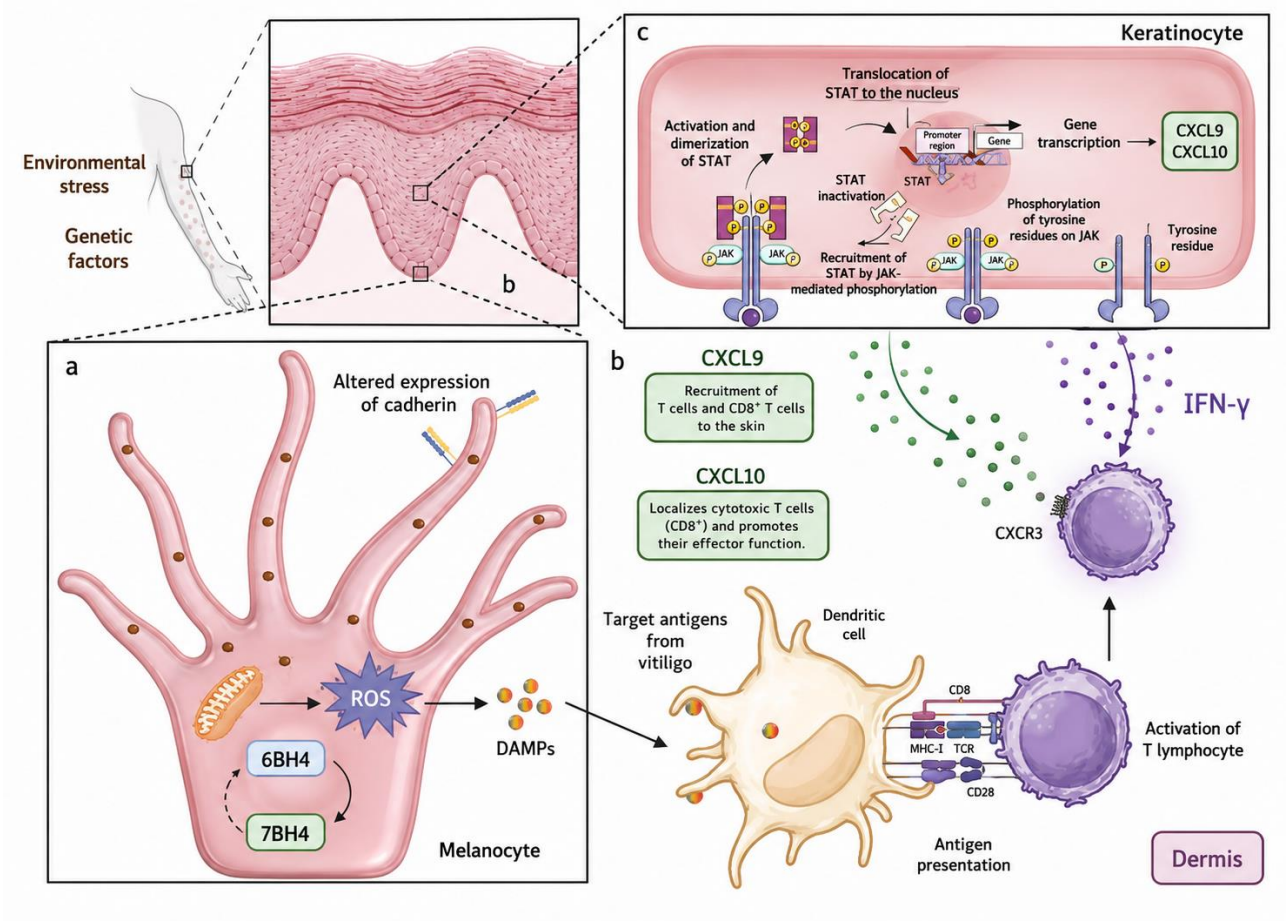

Figure 2. Integrated schematic of the interactions among melanocytes, dendritic cells, cytotoxic CD8⁺ T lymphocytes, and keratinocytes in the pathophysiology of vitiligo. The process is initiated by the convergence of environmental stress and genetic factors, leading to melanocyte damage and the establishment of an amplified autoimmune response in the skin. (a) Oxidative stress in the melanocyte (epidermis). In stressed melanocytes, mitochondrial dysfunction promotes the accumulation of reactive oxygen species (ROS), exacerbated by an imbalance in tetrahydrobiopterin metabolism, with conversion of the natural 6BH4 isoform to the 7BH4 isomer, which perpetuates oxidative damage. This altered redox environment leads to aberrant cadherin expression — compromising melanocyte adhesion — and to the release of damage-associated molecular patterns (DAMPs), which signal cellular injury. (b) Antigen presentation and lymphocyte activation (dermis). Released DAMPs and vitiligo target antigens are captured by dendritic cells, which present them via MHC-I to the T-cell receptor (TCR) of CD8⁺ T lymphocytes, with CD28-mediated co-stimulation, resulting in cytotoxic T-cell activation. Activated T lymphocytes then secrete IFN-γ, a central cytokine in amplifying the immune response. (c) IFN-γ/JAK-STAT signaling in keratinocytes. IFN-γ acts on keratinocytes by activating the JAK-STAT pathway: phosphorylation of JAK tyrosine residues promotes STAT recruitment and phosphorylation, followed by dimerization and nuclear translocation, where it induces gene transcription of the chemokines CXCL9 and CXCL10. CXCL9 recruits CD8⁺ T lymphocytes to the skin, whereas CXCL10, through binding to its receptor CXCR3, localizes cytotoxic T lymphocytes and potentiates their effector function — establishing a feedback loop that perpetuates melanocyte destruction and the characteristic depigmentation of the disease. Abbreviations: ROS, reactive oxygen species; DAMPs, damage-associated

molecular patterns; MHC-I, major histocompatibility complex class I; TCR, T-cell receptor; IFN-γ, interferon-gamma; JAK, Janus kinase; STAT, signal transducer and activator of transcription; CXCL9/CXCL10, CXC motif chemokine ligands 9 and 10; CXCR3, CXC chemokine receptor type 3. Image created with BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Classification and Diagnosis of Vitiligo

Vitiligo exhibits broad clinical heterogeneity and is classified according to the pattern of distribution, extent, and evolution of depigmented lesions. Currently, vitiligo is categorized into non-segmental vitiligo (NSV), segmental vitiligo (SV), mixed vitiligo (MV), and unclassified vitiligo (UCV), in accordance with the nomenclature proposed by the Vitiligo Global Issues Consensus Conference and subsequently ratified by the International Vitiligo Task Force (Ezzedine, 2012; Van Geel, 2023). NSV represents the most common form of the disease and is characterized by generally bilateral and symmetrical lesion distribution, encompassing the acrofacial, mucosal, generalized, universal, and mixed subtypes. Additional less frequent variants include focal, punctate, hypochromic, and follicular vitiligo, which differ in terms of location, morphology, and clinical behavior. Recognition of these subtypes is fundamental for diagnosis, prognostic assessment, and the definition of the most appropriate therapeutic strategies for each patient.

SV, in turn, presents with unilateral distribution following dermatomal patterns or cutaneous mosaicism, typically with early onset, rapid initial progression, and subsequent stabilization. It may exhibit focal, unisegmental, bi-segmental, or multisegmental patterns.

MV represents the coexistence of segmental and non-segmental vitiligo in the same patient, whereas UCV encompasses less frequent forms, such as focal vitiligo and isolated mucosal vitiligo, whose clinical features do not always allow definitive inclusion in the aforementioned categories. This classification holds clinical and therapeutic relevance, as the different subtypes exhibit distinct evolutionary trajectories, prognostic outcomes, and treatment responses, and is currently adopted as the international reference standard for both research and clinical practice (Van Geel, 2023). These forms present distinct therapeutic responses, as outlined in Figure 3.

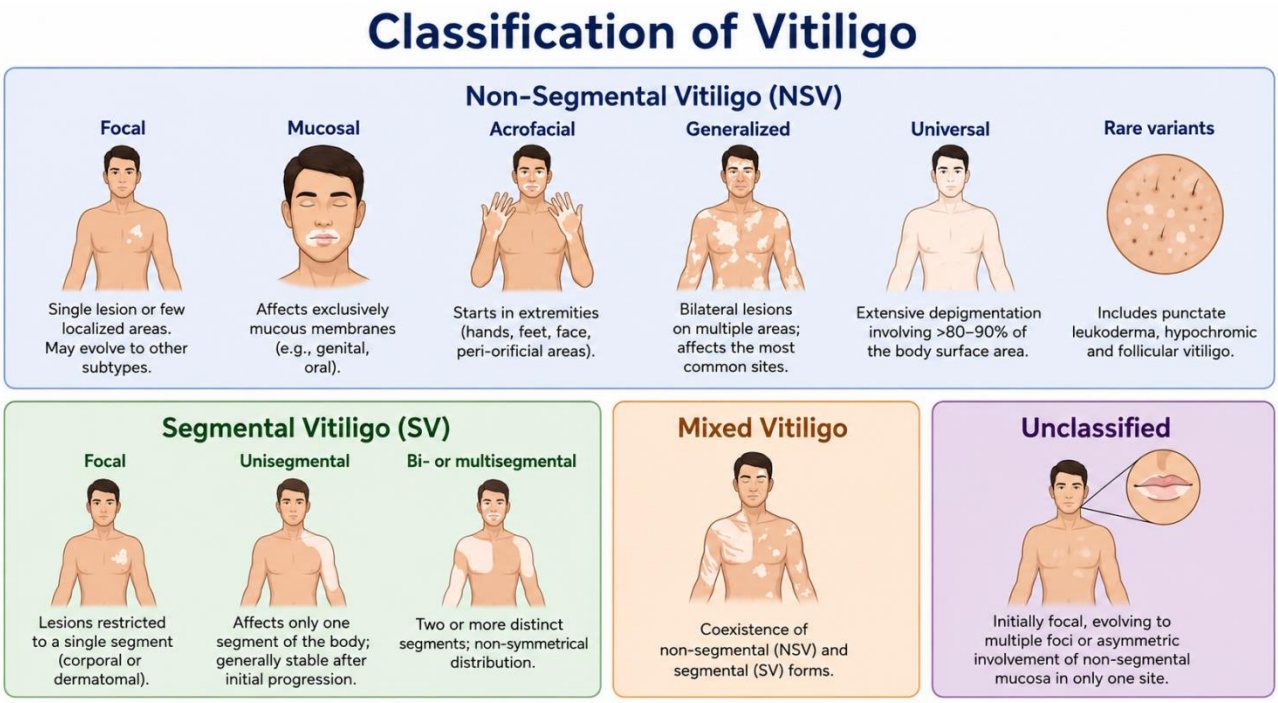

Figure 3. Classification and clinical presentation forms of vitiligo. Schematic representation of the main vitiligo subtypes according to the distribution and extent of depigmented lesions, organized into four major categories. Non-Segmental Vitiligo (NSV). Form characterized by typically bilateral and symmetrical lesions, subdivided into: focal, presenting a single lesion or a few localized macules, which may progress to other subtypes; mucosal, affecting exclusively the mucous membranes (e.g., genital and oral); acrofacial, with onset at the extremities (hands, feet, and perioral/periorbital regions); generalized, with widespread and symmetrical lesions, corresponding to the most common form; universal, with extensive depigmentation involving more than 80–90% of the body surface area; and rare variants, including punctate leukoderma, hypochromic vitiligo, and follicular vitiligo. Segmental Vitiligo (SV). Form with unilateral distribution, restricted to body segments or dermatomes, subdivided into: focal, with lesions limited to a single body segment or

dermatome; unisegmental, affecting only one body segment and typically stabilizing after initial progression; and bi- or multisegmental, involving two or more distinct segments with asymmetrical distribution. Mixed Vitiligo. Simultaneous coexistence of non-segmental (NSV) and segmental (SV) forms in the same patient. Unclassified Vitiligo. Initially focal presentation that evolves into asymmetrical multifocal non-segmental lesions, or isolated mucosal involvement restricted to a single site, not fulfilling the criteria for the other categories. Abbreviations: NSV, non-segmental vitiligo; SV, segmental vitiligo. Image created with BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Diagnosis of Vitiligo

The diagnosis of vitiligo is based on the observation of depigmented macules with well-defined borders, generally distributed symmetrically. These lesions tend to expand over time and may affect any body region, particularly sun-exposed areas and sites subject to repeated trauma, as observed in the Koebner phenomenon (Rashid, 2023).

Although no definitive clinical diagnostic test exists for vitiligo, several complementary resources may be employed to aid in the assessment of the possible disease. One method used to differentiate vitiligo from other dermatoses is dermoscopy, which allows for detailed analysis of melanocytes and structural alterations in depigmented areas. The combination of this examination with Wood's lamp contributes to the detection of depigmenting disorders not visible to the naked eye. Dermoscopy provides insight into the status of melanocytes and the distinctive features of vitiligo patches (Tatte, 2014).

Skin biopsy and histological examination are also utilized to assess the condition of pigmentary cells. Biopsy is an invasive procedure; therefore, it is not employed in routine diagnosis. Commonly, the clinical diagnosis of vitiligo relies on a combination of physical examination, dermoscopy, and Wood's lamp examination (Van Geel, 2023).

The differential diagnosis of vitiligo is broad, as many cutaneous conditions present areas of depigmentation that may mimic vitiligo. It is necessary to differentiate vitiligo from melanoma-associated leukoderma, to avoid misdiagnosis as vitiligo, particularly because it may precede melanoma detection. Although clinically similar, antibodies against the melanoma antigen recognized by T cells 1 (MART-1) in melanoma-associated leukoderma may help distinguish it from vitiligo (Teulings, 2014). Nevus depigmentosus is a segmental hypopigmentation typically present at birth or detectable within the first year of life. It is stable, although it may enlarge proportionally to the child's growth. It is a common differential diagnosis of segmental vitiligo (SV), but nevi generally contain a normal number of melanocytes with reduced melanin production (Kim, 2008). Under Wood's lamp examination, the contrast between lesional and normal skin is less pronounced than in vitiligo (Mosher, 2003). Given this scenario, Table 1 presents the breadth of the differential diagnosis of vitiligo, compiling conditions that may mimic the characteristic depigmented pattern of the disease.

Conventional Treatments

Conventional treatments for vitiligo aim to stimulate skin repigmentation and abrogate the immune response. Topical corticosteroids and calcineurin inhibitors are commonly used, and for extensive forms of the disease, narrowband UVB (NB-UVB) phototherapy is employed (Alghamdi, 2012).

Topical Corticosteroids

Topical corticosteroids are considered one of the main therapeutic approaches in the management of vitiligo, particularly in localized and active-phase cases. In this context, corticosteroids act by promoting local immunosuppression, reducing the production of pro-inflammatory cytokines, such as interferon-gamma and tumor necrosis factor-alpha (TNF-α), which are implicated in the pathophysiology of depigmentation, as illustrated in Figure 2 (Ezzedine, 2015; Passeron and Bergqvist, 2022).

The most commonly used agents include clobetasol propionate, mometasone furoate, and betamethasone valerate. These agents demonstrate greater efficacy when employed in recent lesions, particularly in areas such as the trunk and proximal limbs. Clinical studies indicate that partial repigmentation may be observed after 2 to 3 months of continuous use, with therapeutic response varying according to anatomical location and disease duration (Taieb, 2013).

Despite its efficacy, the prolonged use of topical corticosteroids is associated with cutaneous adverse effects, such as epidermal atrophy, telangiectasias, striae, and perilesional hypopigmentation. For this reason, their use in intermittent regimens or for a limited duration, with regular dermatological monitoring, is recommended. In areas of thin skin, such as the face and intertriginous regions, the risk of adverse effects is higher, which restricts their prolonged use in these areas (Alghandi, 2017).

The literature reinforces that topical corticosteroids remain the first-line therapy for localized vitiligo, especially in the early stages. However, their isolated efficacy may be limited in extensive or long-standing cases, and they are frequently combined with phototherapy to enhance clinical outcomes (Taieb, 2013; Das, 2025).

Table 1. Differential diagnosis of vitiligo: conditions that mimic the depigmented pattern

Classification category	Causes or triggers	Clinical features and history	Diagnostic methods	Conditions and examples
Genetic Syndromes	Genetic mutations and hereditary inheritance.	Depigmentation present since birth or early childhood, frequently associated with other systemic alterations.	Physical exam, family history, and Wood's lamp.	Piebaldism; Ito hypomelanosis; tuberous sclerosis; Waardenburg syndrome; Hermansky-Pudlak syndrome; Menkes syndrome; Ziprkowski-Margolis syndrome; Griscelli syndrome.
Autoimmune / Inflammatory	Autoimmune response mediated by T lymphocytes against melanocytic antigens in genetically susceptible individuals (HLA association); possible infectious or environmental triggers.	Depigmentation (vitiligo/poliosis) that may accompany systemic manifestations — in VKH, ocular (uveitis), auditory, and meningeal involvement.	Multisystem clinical assessment, ophthalmologic exam, imaging/laboratory tests, and Wood's lamp.	Vogt-Koyanagi-Harada syndrome; halo nevus (Sutton's nevus).
Chemically Induced Leukoderma	Phenols and other phenolic derivatives.	Acromic patches similar to vitiligo, appearing at sites of contact with specific chemical substances; may present with irregular borders.	Dermoscopy and Wood's lamp.	Occupational leukoderma.
Drug-Induced	Systemic drugs (immune checkpoint inhibitors), immunomodulators, or topical application of medications.	Cutaneous pigment loss triggered after the initiation of specific drug therapies, often mimicking vitiligo.	Clinical history, dermoscopy, and Wood's lamp.	Depigmentation by topical or systemic drugs (e.g., ipilimumab, pembrolizumab, nivolumab, and imiquimod).
Post-Inflammatory Hypopigmentation	Previous cutaneous inflammatory processes, allergic reactions, phototherapy, or radiotherapy.	Light or hypochromic patches that appear after the resolution of inflammatory, eczematous, or traumatic lesions.	Dermoscopy (to assess residual pigment) and Wood's lamp.	Pityriasis alba; atopic dermatitis; allergic contact dermatitis; psoriasis; lichen planus, and post-traumatic reactions.

Neoplasms	Neoplastic processes, malignant infiltration, or immune response against tumor cells.	Depigmented areas that may precede, accompany, or arise at sites distant from the primary tumor (perilesional in the case of melanoma).	Anti-MART1 (Melan-A) immunohistochemistry, skin biopsy, and Wood's lamp.	Melanoma-associated leukoderma; mycosis fungoides (cutaneous T-cell lymphoma).
Infections	Infectious agents (fungi, bacteria, or parasites).	Pigment alterations associated with infectious/contagious conditions; may present with changes in sensation (leprosy) or fine scaling (pityriasis).	Clinical exam, specific laboratory tests, mycological exam, or serological tests.	Leprosy; pityriasis versicolor; leishmaniasis; onchocerciasis; treponematoses (pinta and syphilis).
Congenital	Anomalies in melanocytic, vascular development, or melanocyte maturation.	Stable lesions present since birth; they do not present the complete achromia of vitiligo (the depigmented nevus has normal melanocytes, but low melanin).	Diascopy (vitropression maneuver) and Wood's lamp (less marked contrast than in vitiligo).	Anemic nevus; depigmented nevus (nevus depigmentosus).
Idiopathic	Unknown cause; possibly photoaging or constitutional factors.	Small rounded white patches (guttate) or pale/poorly defined patches on the trunk, with slow progression.	Dermoscopy and Wood's lamp.	Idiopathic guttate hypomelanosis; progressive macular hypomelanosis.
Trauma or Radiation-Induced	Physical trauma, ionizing radiation, or light therapy.	Areas of hypochromia located at sites of prior tissue injury.	Clinical exam and history of trauma.	Scars; depigmentation induced by phototherapy or radiotherapy.

Legend: The table systematizes, across five dimensions, the main categories of conditions capable of mimicking vitiligo depigmentation. For each category (row), the underlying causes or triggers, the inferred clinical features that aid in differentiation, the related diagnostic methods, and representative conditions and examples are presented. The categories covered are: genetic syndromes (depigmentation present since birth or early childhood, hereditary in nature and frequently syndromic); autoimmune/inflammatory (T-cell-mediated melanocytic destruction, as in Vogt-Koyanagi-Harada syndrome and halo nevus); chemically induced leukoderma (achromic macules in areas of contact with phenols and phenolic derivatives); drug-induced (systemic drugs — especially immune checkpoint inhibitors — or topical drugs); post-inflammatory hypopigmentation (hypochromic macules following inflammatory, eczematous, or traumatic lesions); neoplasms (leukoderma associated with melanoma and mycosis fungoides); infections (fungal, bacterial, or parasitic agents); congenital (stable nevoid lesions present since birth, without complete achromia); idiopathic (idiopathic guttate hypomelanosis and progressive macular hypomelanosis); and trauma- or radiation-induced (hypochromia at sites of previous tissue injury). Dermoscopy and Wood's lamp stand out as cross-cutting tools in distinguishing between true depigmentation and hypopigmentation. Source: Prepared by the author (2026).

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs), such as tacrolimus and pimecrolimus, represent an important therapeutic alternative, particularly in sensitive areas. These drugs act by blocking the enzyme calcineurin, preventing the activation of T lymphocytes and reducing the production of inflammatory cytokines involved in melanocyte destruction (Das, 2025).

Unlike corticosteroids, TCIs do not induce cutaneous atrophy, which makes them especially indicated for application on the face, eyelids, and cervical region. Studies demonstrate that 0.1% tacrolimus presents repigmentation rates comparable to those of medium-potency corticosteroids, mainly in facial lesions (Rosenbach, 2021).

Therapeutic response tends to be more evident after 3 to 6 months of continuous use. Adverse effects are generally mild, including a transient burning or pruritus sensation at the application site. Safety in prolonged use has been confirmed, including in the pediatric population (Alghamdi, 2017).

Narrowband UVB Phototherapy (NB-UVB)

Narrowband ultraviolet B phototherapy (NB-UVB) is currently considered the gold standard for the treatment of generalized vitiligo. Its mechanism involves direct stimulation of the proliferation and migration of residual melanocytes from hair follicles, in addition to exerting an immunomodulatory effect by reducing the activity of cytotoxic T lymphocytes (Ezzedine, 2015).

The therapeutic protocol generally includes sessions performed two to three times per week, for a minimum period of six months. Repigmentation tends to occur initially in a perifollicular pattern, with centrifugal progression. Studies indicate that approximately 40% to 60% of patients present significant repigmentation after one year of regular treatment (Taieb, 2013). However, the response varies according to the location of the lesions, with acral and periungual areas being less responsive. Treatment adherence also constitutes a challenge, due to the need for multiple weekly sessions and prolonged follow-up (Figure 4).

Non-Conventional Treatments

Non-conventional treatments for vitiligo comprise therapeutic approaches that are not part of the classic first-line protocol (topical corticosteroids, calcineurin inhibitors, and NB-UVB phototherapy). They are considered complementary or alternative strategies. These modalities include phytotherapy, regenerative therapies, advanced drug delivery techniques, cell-based therapies, platelet-rich plasma, and phytotherapy. In general, such interventions seek to optimize repigmentation through immunomodulatory, antioxidant, or regenerative mechanisms.

Use of Plant Extracts

In elucidating the pathogenesis of vitiligo, therapies based on natural products have sparked scientific interest due to the need to mitigate the oxidative stress and autoimmune response that culminate in melanocyte apoptosis (Chen, 2023) (Table 2).

Among the promising phytotherapeutic approaches, the standardized extract of Ginkgo biloba stands out — a compound derived from leaves widely used in traditional Chinese medicine. This extract exhibits significant antioxidant properties, acting as a scavenger of reactive oxygen species (ROS) and activating the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, in addition to exerting immunomodulatory, neuroprotective, and platelet aggregation-modulating effects (Wang, 2019). Seminal clinical evidence demonstrates that daily oral administration of 120 mg of this extract in patients with slowly spreading non-segmental vitiligo promoted a significant halt in the progression of depigmentation and induced repigmentation when compared to the placebo group (Parsad; Pandhi; Juneja, 2003). Subsequent studies and systematic reviews corroborate the safety profile and clinical efficacy of the phytocomplex, positioning it as a viable therapeutic alternative with low adverse impact for the management and clinical stabilization of vitiligo (Qadir, 2022; Giovanelli, 2025).

Nigella sativa extract has demonstrated scientific relevance in the treatment of vitiligo due to its multi-target pharmacological properties, which encompass well-documented antioxidant, anti-inflammatory, and immunomodulatory activities (Tavakoli, 2022). In clinical trials aimed at evaluating this substance, the diagnosis and mapping of achromic lesions are rigorously outlined through fluorescence examination under Wood's lamp (Ghorbanibirgani, 2014). In the intervention protocol established by researchers in the field, patients were instructed to topically apply Nigella sativa cream or oil to the affected macules twice daily (morning and evening) for a continuous six-month interval, under strict restriction of concomitant use of any other topical or systemic therapy (Sarac, 2019). As a clinical outcome, treatment with the phytocomplex promoted a statistically significant repigmentation rate, with pronounced improvement evidenced in anatomically challenging regions such as the distal extremities (hands), face, and genital areas (Ghorbanibirgani, 2014; Koshak, 2023). Given these findings, the essential oil or lipophilic extract of N. sativa seeds consolidates itself as an alternative, safe, and promising therapeutic option for the clinical management of vitiligo (Sarac, 2019; Balić, 2021).

Additionally, Centella asiatica stands out as a promising phytocomplex in the therapeutic management of vitiligo. This plant species, widely renowned in traditional Asian medicines, possesses pharmacological properties grounded in its triterpene fractions, which exert significant wound-healing, anti-inflammatory, and antioxidant

bioactivities (Zhou, 2022; Rachmawati, 2024). In the pathophysiological context of vitiligo, the extract acts directly on the attenuation of cellular oxidative stress, mimicking endogenous enzymatic systems to neutralize reactive oxygen species (ROS). This cytoprotection preserves the viability and ultrastructural integrity of melanocytes in the epidermal melanin unit, attenuating apoptotic triggers and favoring melanogenesis mechanisms and subsequent cutaneous repigmentation (Ahmed, 2025).

Clinical investigations grounded in dermatological phytotherapy demonstrate that the hydrophilic extract of Polypodium leucotomos, a fern native to tropical and subtropical regions of the Americas, exhibits intrinsic antioxidant, immunomodulatory, and systemic photoprotective properties. The underlying molecular mechanisms involve the direct scavenging of reactive oxygen species (ROS), the blockade of lipid photodegradation, and the preservation of Langerhans cells, mitigating cellular damage and oxidative stress induced by ultraviolet (UV) radiation in the melanin unit (Mulero, 2008; Mulero, 2006).

In the management of vitiligo, a randomized controlled trial evaluated the efficacy of this approach in a group of 25 adult patients with generalized non-segmental vitiligo. The therapeutic protocol consisted of oral administration of 250 mg of P. leucotomos extract (or placebo), three times daily, combined with narrowband ultraviolet B (NB-UVB) phototherapy performed twice a week, over a period of 25 to 26 weeks. The clinical outcomes revealed a statistically significant increase in the repigmentation rate, with marked anatomical responsiveness evidenced in the head and neck region (Mohammad, 2025). However, scientific evidence emphasizes that the therapeutic efficacy of the phytocomplex is related to its synergistic and adjuvant use with phototherapy, not demonstrating the same clinical performance when used as a monotherapy regimen alone (Giovanelli, 2025).

Linear furanocoumarins such as psoralen and bergapten (5-methoxypsoralen) are widely employed in photochemotherapy protocols, such as PUVA therapy (Psoralen combined with Ultraviolet A radiation) for the treatment of chronic dermatological disorders, including vitiligo. In the scenario of Brazilian botanical biodiversity, the extract of Brosimum gaudichaudii Trécul (Moraceae), popularly known as mama-cadela, stands out as an easily found source, obtained mainly from the bark of its roots and stem, exhibiting proven pharmacological activities (Jacomassi, 2007; Souza, 2024). The phototherapeutic mechanism of action is based on the ability of these hydrophobic molecules to intercalate between the base pairs of nuclear DNA in melanocytes and keratinocytes. After activation by specific wavelengths in the UVA range (320–400 nm), psoralens establish covalent bonds with pyrimidine bases, forming monofunctional and bifunctional adducts (cross-links), which stimulate melanocytic proliferation, melanin synthesis, and the subsequent migration of melanocytes to the depigmented areas (Sumorek-Wiadro, 2020; Oliveira, 2025).

Additionally, isolated bergapten is commonly incorporated into topical formulations, such as ointments and gels, acting as a localized photosensitizing agent to induce tissue repigmentation with a lower incidence of systemic side effects. In pharmacotechnical development and clinical practice, these topical preparations are frequently optimized or associated with vitamin complexes (including vitamins B1, B6, and A) to act synergistically, aiding in epidermal trophism and cellular protection against severe oxidative damage. Thus, the standardized extract of B. gaudichaudii is consolidated in the scientific literature as a therapeutic input with high phytopharmaceutical potential and documented clinical efficacy in the management of vitiligo (Sumorek-Wiadro, 2020; Silva, 2026).

In addition to the phytocomplexes previously discussed, the extract of Aloe vera (L.) Burm. stands out for its broad spectrum of bioactivities, encompassing anti-inflammatory, antimicrobial, immunomodulatory, and wound-healing properties. The chemical composition of its mucilaginous parenchyma is highly complex, consisting of polysaccharides (such as acemannan), glycoproteins, minerals, enzymes, and both lipo- and water-soluble vitamins (Sanches, 2014; Sánchez-Munoz, 2024). In the pathophysiological context of vitiligo, the synergistic action of its antioxidant components, combined with the supply of essential micronutrients, acts on the modulation of the epidermal microenvironment, aiding in the mitigation of oxidative stress and potentially favoring the melanocytic differentiation and migration processes required for cutaneous repigmentation. Currently, preclinical investigations and exploratory trials seek to consolidate the exact molecular mechanisms and the clinical efficacy of Aloe vera as a therapeutic agent targeted at vitiligo (Karagoz, 2023; Ansari, 2025).

The incorporation of standardized botanical extracts into the therapeutic arsenal against vitiligo is consolidating itself as a promising alternative strategy to conventional therapies, such as phototherapy and topical corticosteroids. However, for the validation of these plant matrices in dermatological routine, it is imperative to ensure pharmacotechnical quality control, which includes the standardization of chemical markers, the reproducibility of inputs, and the rigorous determination of safety and efficacy profiles through robust clinical trials (Karagoz, 2023; Giovanelli, 2025).

Table 2. Plant extracts employed as complementary therapies in the treatment of vitiligo.

Plant Extract	Plant Part Used	Pharmacological Mechanism	Dosage	Clinical Effect
Ginkgo biloba	Leaves	Antioxidant, immunomodulatory	Oral (120 mg/day)	Reduction in progression and depigmentation
Nigella sativa	Seeds	Antioxidant, anti-inflammatory	Topical	Repigmentation on hands, face, and genital areas
Centella asiatica	Whole plant	Antioxidant, healing	Topical (1%)	Melanocyte protection and repigmentation
Polypodium leucotomos	Fern	Antioxidant, photoprotective	Oral + NB-UVB	Greater repigmentation on head and neck
Brosimum gaudichaudii	Root	Photosensitizing	Topical/oral	Stimulation of repigmentation
Aloe vera	Leaf gel	Anti-inflammatory, antioxidant	Topical	Potential repigmentation

Legend: The table outlines the characteristics of six plant extracts studied as complementary/adjuvant approaches in the management of vitiligo. For each extract, the plant part used, the proposed pharmacological mechanism, the reported dosage, and the observed clinical effect are indicated. The six extracts covered are: Ginkgo biloba (leaves; antioxidant and immunomodulatory action; oral use, 120 mg/day; associated with reduced progression of depigmentation); Nigella sativa (seeds; antioxidant and anti-inflammatory action; topical use; repigmentation reported on hands, face, and genital areas); Centella asiatica (whole plant; antioxidant and healing action; topical use at 1%; melanocyte protection and repigmentation); Polypodium leucotomos (fern; antioxidant and photoprotective action; oral use associated with NB-UVB; greater repigmentation on the head and neck); Brosimum gaudichaudii (root; photosensitizing action; topical or oral use; stimulation of repigmentation); and Aloe vera (leaf gel; anti-inflammatory and antioxidant action; topical use; potential for repigmentation). Source: Prepared by the author (2026). Image created with the assistance of ChatGPT and BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Cell Therapy

Cell therapy, particularly with mesenchymal stem cells derived from adipose tissue, has been the subject of studies as an alternative for melanocyte regeneration. These melanocytes can be induced to differentiate into pigmentary lineages, enabling the capacity to restore melanocytic function in depigmented areas. This ultimately contributes to more durable and physiologically integrated skin repigmentation (Yang, 2023).

Among the techniques described in the literature, the transplantation of autologous melanocyte and keratinocyte suspension (non-cultured epidermal cell suspension) is one of the most studied and practiced. In this procedure, a small sample of the patient's healthy skin is collected, processed to obtain a cell suspension rich in melanocytes and keratinocytes, and applied to the depigmented area previously prepared by dermabrasion or laser. Clinical studies have demonstrated that this method can lead to a significant increase in the melanin index and a reduction in the contrast between the treated area and normal skin after several months of follow-up, indicating measurable clinical repigmentation (Nilforoushzadeh, 2022).

Another important piece of evidence lies in the analysis of autologous melanocyte transplantation, which showed that both cultured cells and non-cultured suspensions can promote repigmentation in stable vitiligo.

Cell therapy is a strategy that differs from conventional therapies not only by modulating the immune response but also by introducing functional cells directly into the affected skin, considering that the destruction or deficiency of melanocytes is the main mechanism of vitiligo depigmentation.

Microneedles

Microneedles are microsystems of microneedles that allow the minimally invasive intradermal delivery of medications. This type of treatment can be used to transport antioxidants or immunomodulators directly to the dermis, promoting localized action and more positive repigmentation (Zhang, 2025). The application of microneedles in the treatment of vitiligo represents an innovative and highly promising strategy in the field of pharmaceutical technology and dermatology, overcoming the anatomical barrier imposed by the stratum corneum. Solid or hollow microstructured devices act through a purely mechanical approach, creating transient microchannels in the epidermis

without reaching the nociceptors (pain receptors) of the superficial dermis. This controlled microtrauma induces minimal tissue injury that stimulates the release of local growth factors and activates the physiological inflammatory cascade, favoring the migration of functional melanocytes from adjacent follicular niches to the depigmentation zone, resulting in the stimulation of melanogenesis (Figure 4) (Chang; Xu; Li, 2025; Yu, 2024).

In addition to the mechanical inducing effect, microneedles have been widely investigated as transdermal delivery systems for drugs and bioactive compounds aimed at modulating the immunological microenvironment of vitiligo. The pathogenesis of the disease involves a pathological triad characterized by intracellular oxidative stress with accumulation of reactive oxygen species (ROS), followed by cytotoxic lymphocytic infiltration (CD8+ T cells) that destroys melanocytes. Advanced polymeric systems, such as hyaluronic acid-based soluble microneedles, enable the local targeting of bioinspired antioxidant nanoparticles and exosomes, modulating crucial signaling pathways such as the Nrf2/HO-1 pathway, reducing cellular apoptosis, and restoring epidermal redox homeostasis (Chang; Xiang; Zhang, 2026; Jiang, 2025).

The technological versatility of microneedles also allows their association with conventional and surgical therapies, synergistically optimizing repigmentation rates in cases of stable and refractory vitiligo. Clinical studies demonstrate that the combined use of microneedles with narrowband ultraviolet B (NB-UVB) phototherapy, or associated with non-cultured autologous epidermal cell suspension transplantation, significantly enhances the engraftment, viability, and uniform distribution of grafted melanocytes. This hybrid approach minimizes the risks of scarring and infectious processes observed in traditional ablative laser methods, consolidating microneedles as a minimally invasive platform with high clinical adherence for cutaneous pigmentary rehabilitation (Yu, 2024; Wu, 2026).

Platelet-Rich Plasma (PRP)

Platelet-rich plasma is known as a regenerative approach that provides a concentrated source of growth factors, favoring the cutaneous microenvironment and stimulating repigmentation (Da Silva, 2023). The combination with other therapies, such as microneedling or phototherapy, has shown good results, potentiating therapeutic effects and promoting more efficient repigmentation. The controlled release of these cytokines and protein fractions by activated platelets acts directly on the chemotaxis, proliferation, and differentiation of functional melanocytes from adjacent hair follicle niches. Furthermore, PRP exerts important local immune modulation, reducing the levels of pro-inflammatory cytokines that mediate cell destruction, which decisively contributes to the stabilization of active lesions (Santos; Mendes, 2024; Gupta, 2025). The development of hybrid formulations and the advancement in polymeric matrices for the sustained release of these biological components represent the biotechnological frontier for optimizing the residence time of PRP in the lesioned tissue (Gupta, 2025; Reis, 2026).

Nanotechnology

Nanotechnology has established itself as an advanced strategy in dermatology through the development of controlled drug delivery systems capable of overcoming inherent limitations of conventional topical formulations (Sun, 2020). In the context of vitiligo, the skin barrier represents a significant obstacle to the efficacy of therapeutic agents, limiting their penetration and retention in the epidermal layers where residual melanocytes are located. In this scenario, nanostructured systems, including lipid nanoparticles, liposomes, ethosomes, niosomes, and nanofibers, have received increasing attention due to their ability to improve cutaneous permeation, increase drug stability, promote sustained release, and reduce systemic toxicity (Darvishi, 2025; Pareek, 2025).

Unlike conventional therapies, which exhibit limited efficacy, side effects, and require prolonged treatment, nanotechnology-based strategies have demonstrated greater specificity and improved cutaneous penetration of drugs in a controlled manner. This allows for an increase in therapeutic response and a reduction in systemic adverse effects, making it a safer approach for the patient (Tiwari, 2025).

Nanomaterials exhibit intrinsic properties due to their nanometric size, possessing a high surface-area-to-volume ratio and the ability to cross biological barriers. Furthermore, they can be functionalized for selective targeting, with controlled drug release to increase the stability of more unstable therapeutic molecules. These characteristics make nanoparticles ideal for vitiligo treatments, providing greater drug retention on the skin surface and improved local bioavailability (Abdel-Mottaleb; Lamprecht, 2016).

Among the nanostructured systems applied to vitiligo are liposomes, polymeric nanoparticles, solid lipid nanoparticles (SLNs), dendrimers, and nanogels. All of these nanomaterials allow for the encapsulation of therapeutic agents such as corticosteroids, immunosuppressants, antioxidants, and growth factors, protecting them from degradation, improving their penetration, and ensuring sustained release (Dowling A et al., 2011; Tiwari, 2025).

The use of nanostructured systems, such as liposomes, niosomes, nanocapsules, and smart hydrogels, has shown potential for increasing the bioavailability of active agents and improving cutaneous penetration, as shown in Figure 5 (Zaher, 2020).

Lipid nanoparticles, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), have proven to be matrices capable of mimicking stratum corneum lipids and promoting follicular targeting, which maximizes active retention

in melanocytes and reduces systemic toxicity (Garg, 2023; Darvishi; Chekeni, 2026).

Liposomes are vesicles formed by one or more phospholipid bilayers and are used in the treatment of vitiligo (Batista, 2007; Kulkarni, 2018). These systems allow for the encapsulation of hydrophilic and/or lipophilic drugs, increasing cutaneous penetration and prolonging therapeutic action (Bellefroid, 2019). Studies state that liposomal formulations of corticosteroids, calcineurin inhibitors, and natural compounds can improve repigmentation and reduce lesion progression, with a lower risk of systemic adverse effects (Kaushik, 2020; Patel, 2022). Recent studies have demonstrated innovative nanotechnology-based solutions for vitiligo, with results superior to conventional formulations. For example, the use of liposomes and ethosomes loaded with tacrolimus showed repigmentation rates of up to 60%, compared to only 35% for common ointments, due to better follicular penetration.

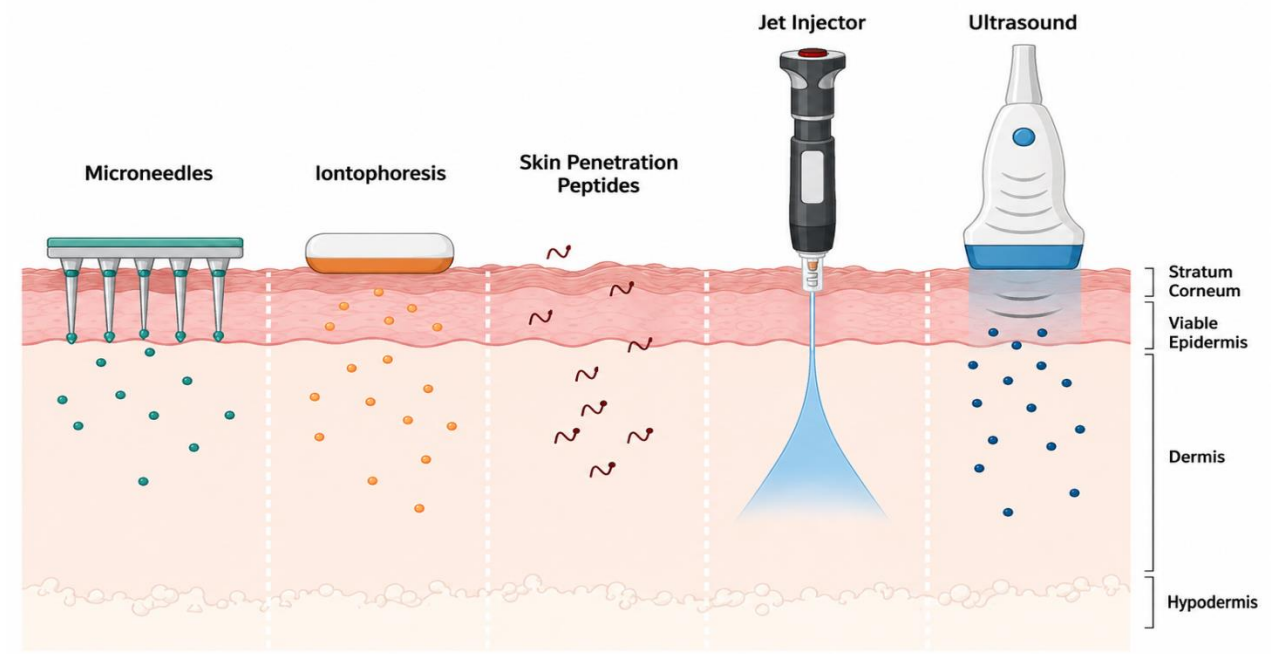

Figure 4. Physical and technological methods for enhancing cutaneous drug penetration. Schematic representation of five strategies employed to overcome the stratum corneum barrier and increase the transdermal permeation of drugs into the viable epidermis and dermis. From left to right: microneedles create mechanical microchannels that cross the stratum corneum, depositing the drug into the viable layers; iontophoresis applies a low-intensity electrical current that drives ionized molecules through the skin; cell-penetrating peptides act as carriers that facilitate the translocation of their cargo across the stratum corneum; the jet injector (needle-free device) propels a high-pressure liquid jet that deposits the drug into deeper layers; and ultrasound (sonophoresis) generates acoustic waves whose cavitation transiently disorganizes the stratum corneum, enhancing permeation. The colored dots represent the drug molecules distributed at different depths (stratum corneum, viable epidermis, dermis, and hypodermis). Image created in BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Furthermore, nanoemulsions containing tofacitinib showed efficacy in reducing oxidative stress and modulating IFN-γ mRNA expression in experimental models. Other approaches include silymarin nanomicelles, which surpassed clobetasol in melanocyte activation.

The development of liquid crystal platforms for the topical delivery and protection of biomolecules, such as interfering RNA (siRNA), aiming at the silencing of pro-inflammatory cytokines directly in the epidermal melanin unit, is being developed in parallel with the encapsulation of linear furanocoumarins, immunomodulators such as tacrolimus, and antioxidant phytotherapeutics (including fractions of Ginkgo biloba, Nigella sativa, Centella asiatica, and Polypodium leucotomos) in nanostructured matrices. This has proven to increase chemical stability, solubilize hydrophobic compounds, and provide controlled release of these inputs, potentiating the tissue repigmentation rate with a lower frequency of clinical application (Qadir, 2022; Giovanelli, 2025).

Solid lipid nanoparticles (SLNs), in turn, present an important approach, especially in the delivery of corticosteroids and drug combinations. These nanoparticles show improved cutaneous penetration, thereby reducing the frequency of application and decreasing local side effects, such as skin atrophy (Souto, 2008; Garg, 2023).

An emerging field of nanotechnology also involves the use of polymeric nanofibers as vehicles for topical drug release. Studies published in 2025 highlight that nanofibers can be produced from biocompatible polymers to increase skin adhesion

and facilitate the incorporation of drugs with different mechanisms of action (Pareek, 2025). Polymeric nanomaterials, generally produced from biodegradable polymers such as chitosan and poly(lactic-co-glycolic acid) (PLGA), offer greater stability and controlled release (Tiwari, 2025). They prove to be effective mainly in the delivery of immunomodulators such as tacrolimus and pimecrolimus, increasing cutaneous penetration and prolonging the duration of action (Kaur; Mehta, 2021; Luan, 2021).

Dendrimers, which are highly branched macromolecules, possess encapsulation capacity and surface functionalization, allowing for cellular targeting and high interaction with biological tissues. For vitiligo, these nanomaterials are being used to deliver genes, antioxidants, and immunosuppressants directly to depigmented areas, favoring repigmentation and cellular protection processes (Raj, 2020; Namazi; Hamishehkar, 2021). Nanogels also stand out as promising carriers, as they present a hydrated structure with high biocompatibility and responsiveness to stimuli such as pH, temperature, or light (Sultana, 2021). These nanogels can encapsulate proteins, peptides, and nucleic acids, allowing for prolonged and effective release into the skin (Kulkarni, 2018).

It is important to note that, although a large part of the literature is still in the preclinical phase or in early stages of development, the results suggest that nanotechnology can significantly improve repigmentation rates, reduce systemic adverse effects associated with traditional treatments, and offer greater precision in the delivery of therapeutic agents. Consequently, nanotechnology represents not only an alternative but also a potential evolution of conventional topical treatments for vitiligo, with the potential to integrate future personalized therapeutic protocols (Darvishi, 2025; Pareek et al., 2025).

Thus, nanotechnology provides excellent tools to optimize the efficacy of vitiligo treatments, offering greater specificity, safety, and tolerability.

Predictions for the future indicate a significant evolution of treatments that combine traditional drugs and natural substances with advances in nanotechnology, expanding the treatment options for vitiligo.

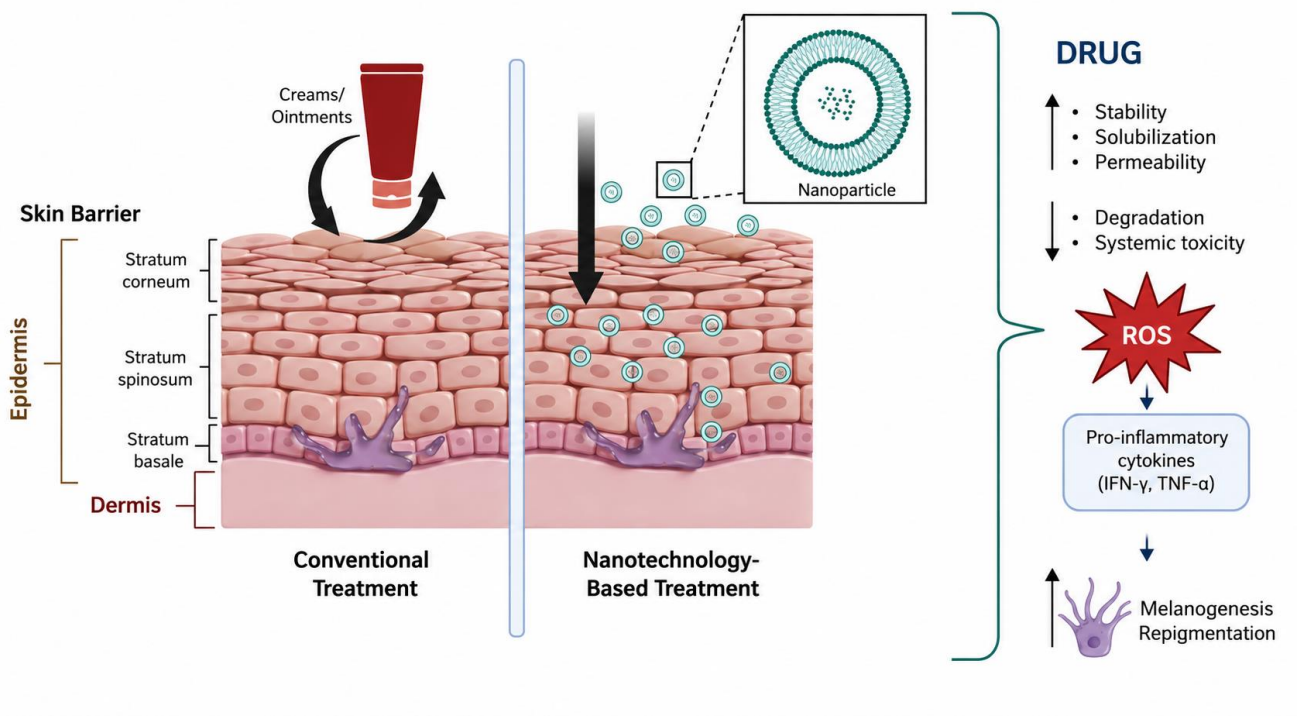

Figure 5. Conventional treatment versus nanotechnology in the cutaneous delivery of drugs for vitiligo. Comparison between conventional topical therapy and the nanotechnology-based approach, with their respective pharmacological and mechanistic impact. On the left, conventional treatment (creams and ointments) encounters the skin barrier: permeation through the stratum corneum is limited, and the drug tends to remain superficial. On the right, nanotechnology-based treatment employs the drug encapsulated in nanoparticles/liposomes — whose lipid bilayer structure is detailed in the inset — allowing for deeper and more effective penetration into the viable epidermis and the basal layer, where melanocytes reside. The column on the right summarizes the advantages for the drug: increased stability, solubilization, and permeability, with reduced degradation and systemic toxicity. These properties culminate in a therapeutic cascade: reduction of reactive oxygen species (ROS) → reduction of pro-inflammatory cytokines (IFN-γ and TNF-α) → stimulation of melanogenesis and repigmentation. Image created in BioRender. Ciambarella, B. (2026) https://BioRender.com/5aivzrs.

Conclusion

It is concluded that the treatment of vitiligo is progressing toward a promising therapeutic transition with the integration of non-conventional approaches, overcoming the clinical bottlenecks and adverse reactions associated with corticosteroid therapy and classical immunosuppressants. The consolidation of the data indicates that, while biological and regenerative therapies—such as autologous cell transplantation, soluble microneedles, and platelet-rich plasma—act on direct rehabilitation and mechanical stimulation of melanocyte niches, nanotechnological matrices establish a new standard of pharmacotechnical efficacy. Polymeric and lipid-based nanostructured systems demonstrate superior viability by mimicking the lipids of the stratum corneum, promoting follicular targeting, and enabling the controlled release of both synthetic drugs and botanical active compounds. Therefore, although the expansion of robust clinical trials is mandatory to endorse the safety and large-scale reproducibility of these formulations, nanotechnology consolidates itself as an indispensable vector for the design of personalized, multifactorial dermatological protocols with high cellular specificity for cutaneous repigmentation.

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