Available online on 15.09.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

Herbal Drug-Loaded Nanoparticles for Vitiligo Treatment: Mechanisms, Formulation Strategies, Characterization, and Therapeutic Potential

Madhuri H Rayabagi [1]*, Bijal Prajapati [2], Madhukumar H M [1], Girish Bolakatti [3]

[1] GM Institute of Pharmaceutical Sciences and Research, Davanagere-577006, Karnataka, India
[2] Faculty of Pharmacy, Parul Institute of Pharmacy, Parul University, Vadodara-391760, Gujarat, India
[3] Director, Centre for Innovation and New Product Idea, GM University, Davanagere-577006

Article Info:

Article History:

Received 13 June 2026
Reviewed 21 July 2026
Accepted 14 Aug 2026
Published 15 Sep 2026

Cite this article as:

Rayabagi MH, Prajapati B, Madhukumar H M, Bolakatti G, Herbal Drug-Loaded Nanoparticles for Vitiligo Treatment: Mechanisms, Formulation Strategies, Characterization, and Therapeutic Potential, Journal of Drug Delivery and Therapeutics. 2026; 16(9):131-142 *DOI:* https://doi.org/10.22270/jddt.v16i9.7947

For Correspondence:

Madhuri H Rayabagi, GM Institute of Pharmaceutical Sciences and Research, Davanagere-577006, Karnataka, India.

Abstract

Vitiligo is a chronic autoimmune depigmenting disorder characterized by the progressive destruction of melanocytes, resulting in the appearance of white patches on the skin. The multifactorial pathogenesis of vitiligo involves oxidative stress, autoimmune responses, inflammatory cytokines, genetic predisposition, and melanocyte apoptosis. Although conventional therapies such as phototherapy, corticosteroids, calcineurin inhibitors, and surgical interventions are available, their efficacy remains limited due to adverse effects, recurrence, prolonged treatment duration, and poor patient compliance. Herbal medicines have gained significant attention because of their antioxidant, anti-inflammatory, immunomodulatory, and melanogenesis-promoting properties. However, poor aqueous solubility, instability, low bioavailability, and inadequate skin permeation restrict their clinical application. Nanotechnology-based drug delivery systems provide an innovative platform for improving the therapeutic efficacy of herbal compounds by enhancing stability, penetration, targeted delivery, and controlled release. This review discusses the pathogenesis of vitiligo, the rationale for herbal nanoformulations, nanoparticle systems, formulation approaches, characterization parameters, biological evaluation methods, regulatory considerations, and future perspectives in vitiligo therapy.

Keywords: Vitiligo, Herbal Nanoparticles, Nanotechnology, Melanogenesis, Drug Delivery Systems, Skin Targeting, Nanomedicine.

1. Introduction

Vitiligo is a chronic, acquired depigmenting disorder characterized by the progressive loss of functional melanocytes from the epidermis, resulting in well-demarcated, milky-white macules and patches on the skin [1]. The condition affects approximately 0.5–2% of the global population, with no significant predilection for gender or race; however, its clinical visibility is often more pronounced in individuals with darker skin tones, leading to greater psychosocial burden [2,3].

The disease manifests in various clinical forms, including segmental, non-segmental (generalized), acrofacial, and universal vitiligo, depending on the distribution and progression of depigmented lesions. Although vitiligo is not life-threatening or contagious, it is associated with social stigma, significant psychological distress, and reduced quality of life, often contributing to anxiety, depression, and decreased self-esteem in affected individuals [4,5].

The exact etiology of vitiligo remains complex and multifactorial, involving an interplay of genetic predisposition, environmental triggers, immune dysregulation, and oxidative stress. Among the proposed hypotheses, the autoimmune and oxidative stress theories are the most widely accepted [6]. In the autoimmune paradigm, melanocytes are selectively targeted and destroyed by autoreactive CD8+ cytotoxic T lymphocytes, mediated through the release of pro-inflammatory cytokines such as interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α). Concurrently, oxidative stress plays a pivotal role by inducing the accumulation of reactive oxygen species (ROS), which leads to lipid peroxidation, mitochondrial dysfunction, and ultimately melanocyte apoptosis [7,8].

Recent studies have demonstrated that melanocytes in vitiligo patients exhibit impaired antioxidant defense mechanisms, including reduced levels of catalase, glutathione peroxidase, and superoxide dismutase. This imbalance between oxidants and antioxidants renders melanocytes highly susceptible to oxidative damage. Additionally, the release of damage-associated molecular patterns (DAMPs) further amplifies immune

activation, creating a vicious cycle of melanocyte destruction [9,10].

Conventional therapeutic approaches for vitiligo primarily aim at halting disease progression and promoting repigmentation [11]. These include topical corticosteroids, calcineurin inhibitors, systemic immunosuppressants, and phototherapy modalities such as narrowband ultraviolet B (NB-UVB) and psoralen plus ultraviolet A (PUVA)[12]. Although these treatments may provide symptomatic relief, their long-term use is often limited by adverse effects, including skin atrophy, irritation, carcinogenic risk, and variable therapeutic outcomes[13,14].

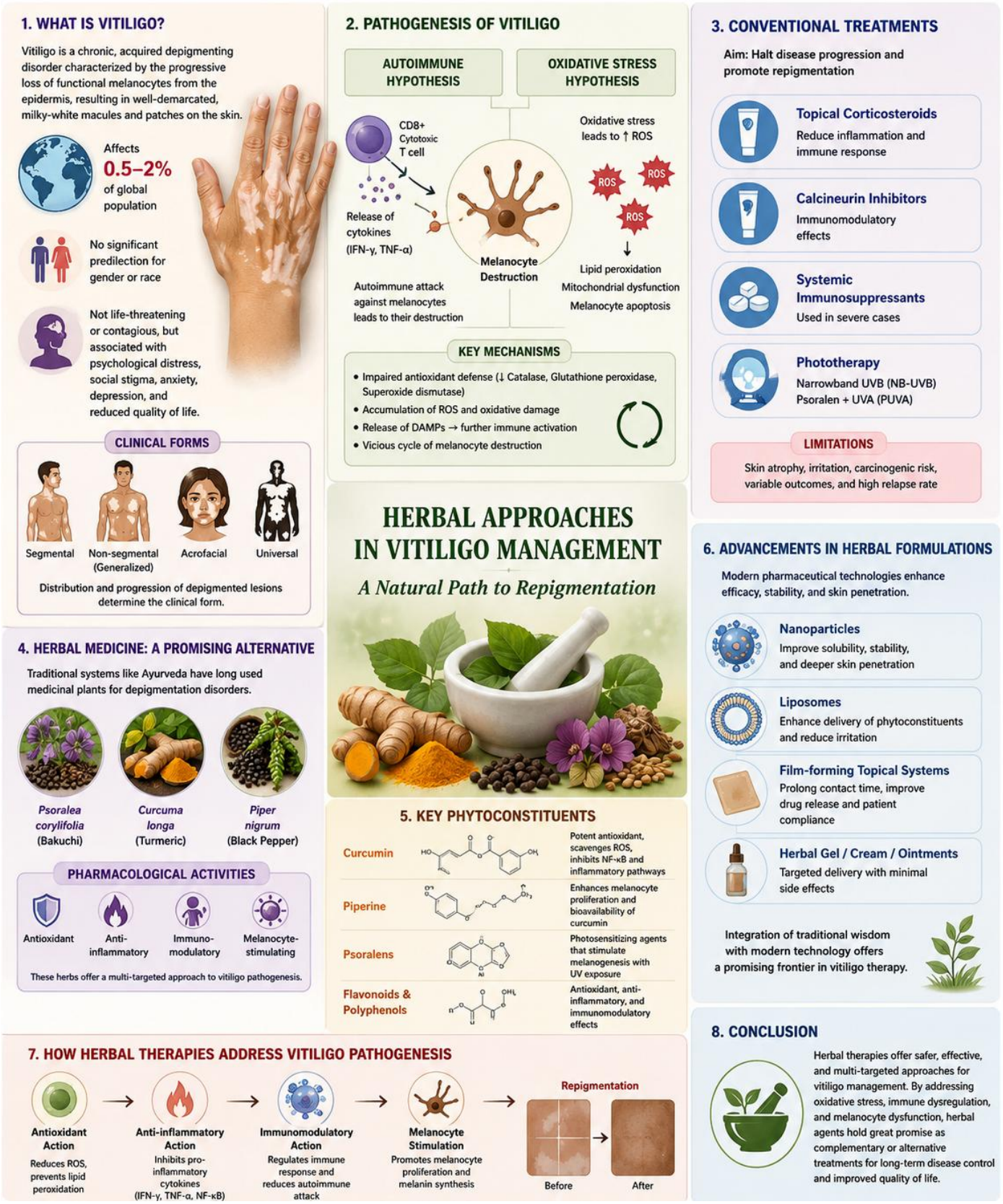

Figure 1. Overview of Vitiligo Pathogenesis, Conventional Therapies, and Herbal Approaches for Repigmentation

In recent years, there has been a growing interest in herbal and plant-based therapies as alternative or complementary approaches for vitiligo management. Traditional systems of medicine, particularly Ayurveda, have long utilized medicinal plants such as *Psoralea corylifolia* (Bakuchi) [15], *Curcuma longa* (turmeric) [16], and *Piper nigrum* (black pepper)[17] for the treatment of depigmentation disorders. These herbal agents possess a wide spectrum of therapeutic activities, including anti-inflammatory, antioxidant, immunomodulatory, and melanocyte-stimulating properties. Phytoconstituents such as curcumin, piperine, psoralens, flavonoids, and polyphenols have been extensively studied for their potential role in modulating key pathways involved in vitiligo pathogenesis. For instance, curcumin exhibits potent antioxidant activity by scavenging ROS and inhibiting inflammatory signaling pathways such as NF-κB, while piperine enhances melanocyte proliferation and improves the bioavailability of curcumin. Similarly, psoralens act as photosensitizing agents that stimulate melanogenesis upon exposure to ultraviolet radiation.

Furthermore, advancements in pharmaceutical technology have facilitated the development of novel herbal formulations, including nanoparticles, liposomes, and film-forming topical systems, which enhance drug stability, skin penetration, and therapeutic efficacy. These innovative delivery systems represent a promising frontier in the integration of traditional herbal medicine with modern dermatological therapeutics [18]. Therefore, this review aims to provide a comprehensive overview of herbal approaches in vitiligo management, focusing on their mechanisms of action, key phytoconstituents, and recent advancements in formulation strategies. Emphasis is placed on understanding how herbal therapies can address the multifactorial nature of vitiligo and offer safer, effective alternatives to conventional treatments.

2. Vitiligo: Disease Overview

Vitiligo is a chronic acquired depigmenting disorder characterized by the selective destruction or dysfunction of melanocytes, resulting in the appearance of depigmented macules and patches on the skin [19,20]. The disease affects individuals of all ages and ethnic groups and is associated with considerable psychological and social burden. Clinical presentation and disease progression vary among patients, leading to the classification of vitiligo into different clinical subtypes.

Table 1. Clinical Characteristics and Classification of Vitiligo

Parameter	Description
Etiology	Multifactorial disorder involving autoimmune, oxidative stress, inflammatory & genetic mechanisms.
Prevalence	Affects approximately 0.5–2% of the global population.
Main Clinical Feature	Loss of skin pigmentation due to melanocyte depletion.
Disease Nature	Chronic, progressive, and non-contagious disorder.
Impact on Patients	Causes cosmetic disfigurement, psychological stress, anxiety, and reduced quality of life.

Table 1 summarizes the general characteristics of vitiligo, including its definition, etiology, prevalence, and clinical significance. Vitiligo is a multifactorial disorder primarily associated with melanocyte loss and remains one of the most common acquired depigmenting diseases worldwide.

Table 2. Clinical Manifestations of Vitiligo

Clinical Manifestation	Description
White Macules and Patches	Well-defined depigmented areas resulting from melanocyte destruction.
Symmetrical Distribution	Lesions frequently occur symmetrically on both sides of the body.
Leukotrichia	Depigmentation of hair present within vitiliginous lesions.
Mucosal Involvement	Depigmentation may affect oral, genital, or other mucosal surfaces.
Progressive Enlargement	Existing lesions may increase in size and number over time.
Koebner Phenomenon	Development of lesions at sites of trauma or skin injury.

Table 2 highlights the major clinical manifestations of vitiligo. The disease typically presents as depigmented macules and patches that may gradually enlarge and affect both cutaneous and mucosal tissues.

Table 3. Classification of Vitiligo

Type	Subtype	Characteristics
Non-Segmental Vitiligo (NSV)	Generalized Vitiligo	Most common form; widespread symmetrical lesions.
Non-Segmental Vitiligo (NSV)	Acrofacial Vitiligo	Involves face, hands, fingers, and feet.
Non-Segmental Vitiligo (NSV)	Universal Vitiligo	Extensive depigmentation involving more than 80–90% of body surface area.
Non-Segmental Vitiligo (NSV)	Mucosal Vitiligo	Limited primarily to mucosal surfaces.
Segmental Vitiligo (SV)	Unilateral Vitiligo	Lesions occur on one side of the body following a dermatomal pattern.
Segmental Vitiligo (SV)	Early-Onset Vitiligo	Typically develops at a younger age.
Segmental Vitiligo (SV)	Stable Vitiligo	Exhibits rapid progression followed by stabilization.

Table 3 presents the major classifications of vitiligo. Non-segmental vitiligo is the predominant form and is generally associated with autoimmune mechanisms, whereas segmental vitiligo usually demonstrates unilateral distribution and earlier stabilization [5,6].

4. Role of Herbal Therapeutics in Vitiligo

Vitiligo is a multifactorial pigmentary disorder involving oxidative stress, autoimmune dysregulation, inflammatory responses, melanocyte apoptosis, and impaired melanogenesis. Since multiple pathogenic pathways are involved simultaneously, therapeutic agents capable of acting on several targets are highly desirable. Herbal therapeutics contain diverse phytoconstituents such as polyphenols, flavonoids, alkaloids, terpenoids, glycosides, and phenolic compounds that exhibit antioxidant, anti-inflammatory, immunomodulatory, anti-apoptotic, melanogenic, and photoprotective activities [21,22,23].

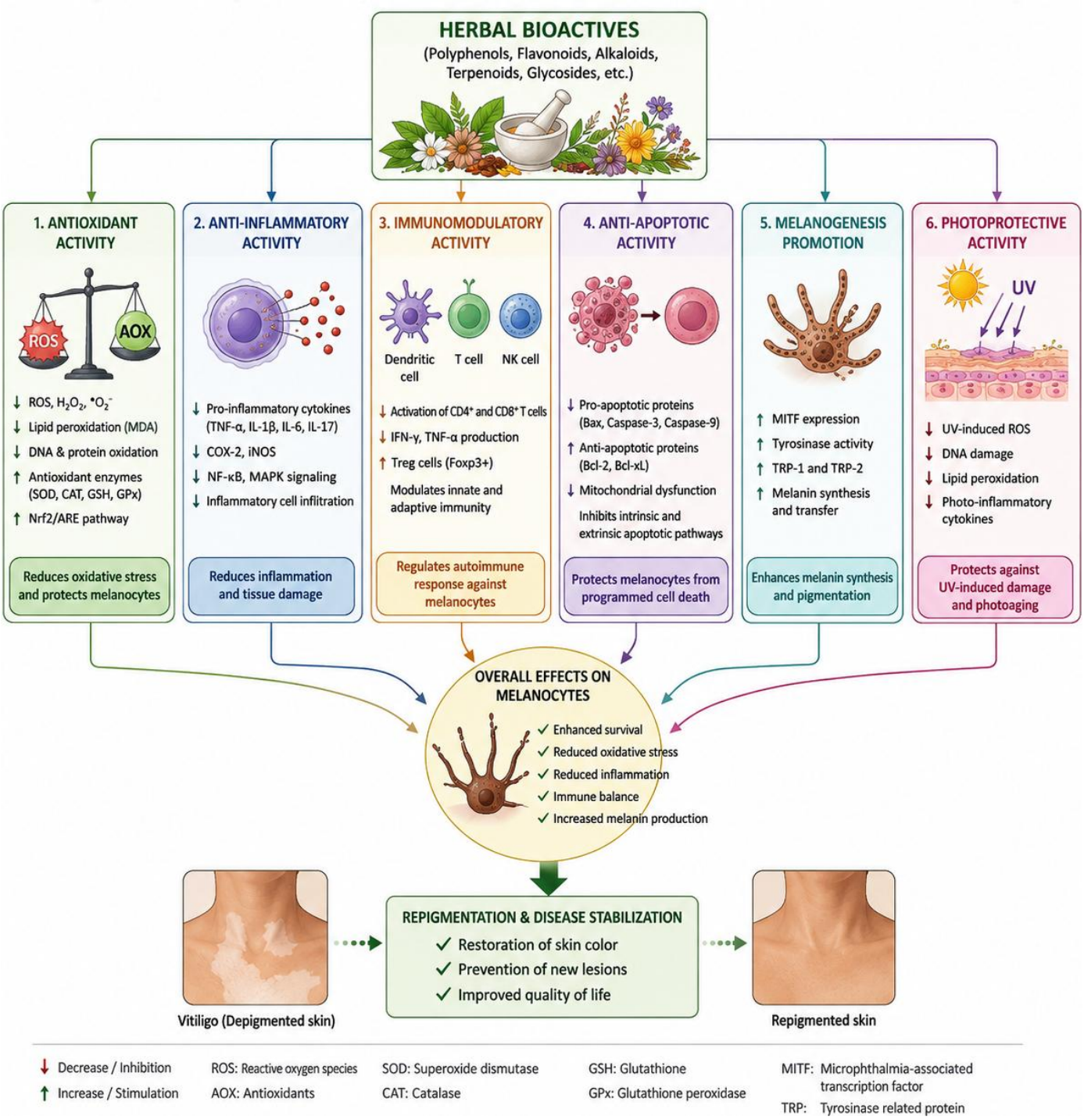

Figure 2. Major Therapeutic Mechanisms of Herbal Bioactives in Vitiligo

Unlike conventional therapies that generally focus on a single mechanism, herbal therapeutics can exert pleiotropic effects by regulating multiple cellular pathways involved in melanocyte survival and pigmentation. These properties make herbal bioactives attractive candidates for the management of vitiligo.

Figure 2 illustrates the multi-target therapeutic actions of herbal bioactives in vitiligo. By simultaneously reducing oxidative stress, inflammation, immune-mediated melanocyte destruction, and apoptosis while promoting melanogenesis, herbal therapeutics contribute to repigmentation and disease stabilization.

Table 4. Therapeutic Actions of Herbal Bioactives in Vitiligo

Therapeutic Activity	Mechanism of Action	Target Molecules/Pathways	Expected Outcome
Antioxidant Activity	Neutralization of reactive oxygen species and free radicals	ROS, H_2O_2, MDA, Nrf2, SOD, Catalase, GSH	Reduced oxidative stress and melanocyte protection
Anti-inflammatory Activity	Suppression of inflammatory mediator production	TNF-α, IL-1β, IL-6, IL-17, NF-Kb	Reduced inflammation and lesion progression
Immunomodulatory Activity	Regulation of immune cell activation and cytokine release	CD4+ T cells, CD8+ T cells, Dendritic cells, IFN-γ	Prevention of autoimmune melanocyte destruction
Anti-apoptotic Activity	Inhibition of apoptosis signaling pathways	Bax, Caspase-3, Caspase-9, Bcl-2	Enhanced melanocyte survival
Melanogenesis Promotion	Stimulation of melanin synthesis pathways	MITF, Tyrosinase, TRP-1, TRP-2	Increased melanin production and repigmentation
Photoprotective Activity	Protection against UV-induced oxidative injury	ROS, DNA damage pathways	Prevention of melanocyte damage and phototoxicity

Table 10 summarizes the major therapeutic actions of herbal bioactives in vitiligo. These compounds exert beneficial effects through multiple biological pathways, making them attractive candidates for multifunctional vitiligo therapy.

4.1 Antioxidant Activity

Excessive accumulation of reactive oxygen species (ROS) results in cellular damage and melanocyte destruction.Herbal bioactives possess strong free-radical scavenging activity and enhance endogenous antioxidant defense systems. They reduce oxidative damage by increasing the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase and catalase [10].

Table 5. Role of Antioxidant Activity in Vitiligo Management

Oxidative Stress Factor	Effect on Melanocytes	Protective Effect of Herbal Bioactives
Reactive Oxygen Species (ROS)	Cellular damage	Free radical scavenging
Hydrogen Peroxide (H_2O_2)	Mitochondrial dysfunction	Detoxification of oxidative species
Lipid Peroxidation	Membrane damage	Preservation of membrane integrity
DNA Damage	Cellular dysfunction	DNA protection and repair support
Protein Oxidation	Loss of protein function	Prevention of oxidative protein modifications

Table 5 demonstrates how antioxidant-rich herbal compounds counteract oxidative stress-mediated melanocyte damage, thereby preventing disease progression.

4.2 Anti-inflammatory Activity

Chronic inflammation contributes significantly to melanocyte destruction. Activated immune cells release pro-inflammatory cytokines that perpetuate tissue damage. Herbal bioactives suppress inflammatory pathways, particularly NF-κB and MAPK signaling, leading to reduced cytokine production and inflammatory cell infiltration.

Table 6. Anti-inflammatory Effects of Herbal Therapeutics

Inflammatory Mediator	Role in Vitiligo	Effect of Herbal Bioactives
TNF-α	Induces melanocyte apoptosis	Downregulation
IL-1β	Promotes inflammation	Inhibition
IL-6	Stimulates immune activation	Reduction
IL-17	Enhances chronic inflammation	Suppression
NF-κB	Controls inflammatory gene expression	Inactivation

Table 6: highlights the ability of herbal therapeutics to suppress inflammatory mediators involved in melanocyte destruction.

4.3 Immunomodulatory Activity

Vitiligo is widely recognized as an autoimmune disorder in which immune cells target melanocytes as foreign antigens.

Herbal therapeutics help restore immune balance by regulating T-cell responses and reducing excessive cytokine secretion.

Table 7. Immunomodulatory Effects of Herbal Bioactives

Immune Component	Role in Disease Progression	Therapeutic Effect
CD8+ T Cells	Direct melanocyte destruction	Reduced activation
CD4+ T Cells	Cytokine production	Immune regulation
Dendritic Cells	Antigen presentation	Suppressed activation
Natural Killer Cells	Cytotoxic activity	Controlled immune response
IFN-γ	Autoimmune signaling	Downregulation

Table 7 summarizes the role of herbal bioactives in regulating immune responses and minimizing autoimmune-mediated melanocyte damage.

4.4 Anti-apoptotic Activity

Melanocyte apoptosis is a major pathological event responsible for depigmentation. Herbal bioactives inhibit apoptotic signaling pathways by suppressing pro-apoptotic proteins while enhancing anti-apoptotic protein expression.

Table 8. Anti-apoptotic Mechanisms of Herbal Therapeutics

Apoptotic Marker	Biological Function	Effect of Herbal Bioactives
Bax	Promotes apoptosis	Downregulated
Caspase-3	Execution of apoptosis	Inhibited
Caspase-9	Initiates apoptosis	Reduced
Bcl-2	Prevents apoptosis	Upregulated
Bcl-xl	Supports cell survival	Increased expression

Table 8 demonstrates the protective role of herbal compounds in preserving melanocyte viability through modulation of apoptosis-related proteins.

4.5 Melanogenesis Promotion

Melanogenesis refers to the synthesis of melanin within melanocytes. Enhancing melanin production is essential for achieving repigmentation in vitiligo.

Herbal bioactives stimulate melanogenic pathways by increasing the expression of melanogenesis-associated genes and enzymes.

Table 9. Melanogenesis-Promoting Effects of Herbal Bioactives

Melanogenic Marker	Function	Therapeutic Outcome
MITF	Master regulator of melanogenesis	Increased melanocyte activity
Tyrosinase	Rate-limiting enzyme in melanin synthesis	Enhanced melanin production
TRP-1	Melanin biosynthesis	Increased pigmentation
TRP-2	Melanin maturation	Improved pigment stability

Table 9 describes key molecular targets involved in melanogenesis that are stimulated by herbal bioactives, resulting in enhanced pigmentation.

4.6 Photoprotective Activity

Ultraviolet radiation can induce oxidative stress and melanocyte damage. Herbal bioactives provide photoprotection through antioxidant and anti-inflammatory mechanisms.

Table 10. Photoprotective Effects of Herbal Therapeutics

UV-Induced Damage	Consequence	Protective Action
ROS Generation	Oxidative stress	Free radical scavenging
DNA Damage	Cell death	DNA protection
Lipid Peroxidation	Membrane damage	Membrane stabilization
Inflammatory Response	Tissue injury	Cytokine suppression

Table 10 illustrates the photoprotective effects of herbal bioactives that help protect melanocytes from UV-induced cellular damage.

5. Limitations of Herbal Drugs in Vitiligo Therapy

Despite their significant therapeutic potential, herbal bioactives face several pharmaceutical and biopharmaceutical challenges that limit their clinical effectiveness. These limitations often result in insufficient drug concentrations reaching the target site, thereby reducing therapeutic outcomes [24].

Table 11. Major Limitations of Herbal Drugs and Their Impact on Therapeutic Efficacy

Limitation	Description	Consequence
Poor Aqueous Solubility	Inability to dissolve efficiently in biological fluids	Low absorption and reduced efficacy
Chemical Instability	Susceptibility to oxidation, hydrolysis, and photodegradation	Drug degradation during storage and application
Poor Skin Permeability	Limited penetration through stratum corneum	Reduced delivery to melanocytes
Low Bioavailability	Inadequate systemic or local drug concentration	Limited therapeutic response
Rapid Metabolism	Fast enzymatic degradation	Short biological half-life
Poor Targeting	Non-specific distribution	Drug wastage and reduced effectiveness

Table 11 summarizes the major formulation challenges associated with herbal bioactives. These limitations significantly restrict their therapeutic potential and necessitate the development of advanced delivery systems.

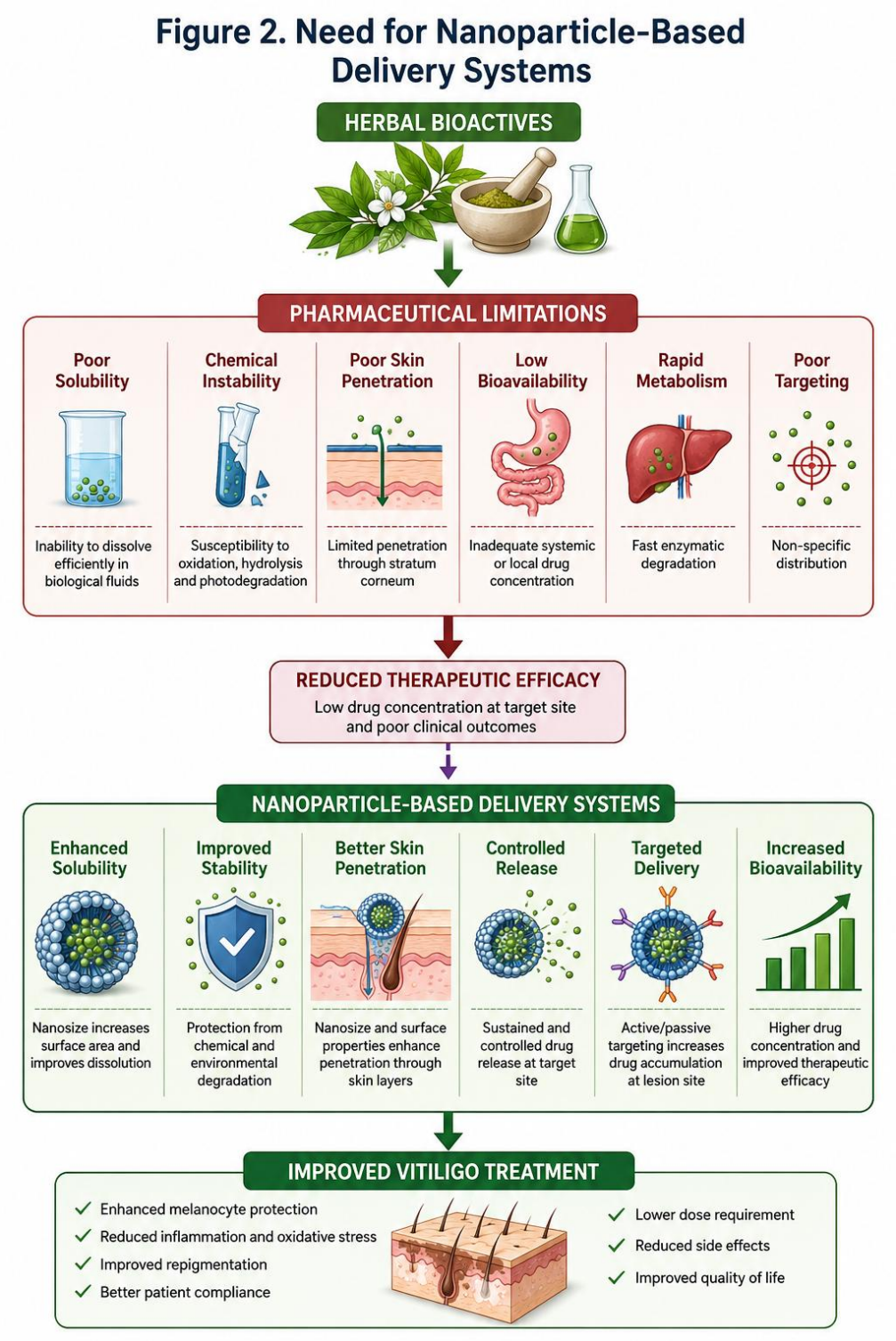

Figure 3. Need for Nanoparticle-Based Delivery Systems

Figure 3 demonstrates how nanoparticle-based delivery systems overcome the major pharmaceutical limitations of herbal bioactives. By enhancing solubility, stability, penetration, and bioavailability, nanotechnology significantly improves the therapeutic effectiveness of herbal treatments for vitiligo.

6. Rationale for Nanoparticle-Based Herbal Delivery

Herbal bioactives possess significant therapeutic potential for vitiligo management; however, their clinical efficacy is often limited by poor solubility, instability, inadequate skin penetration, and low bioavailability. Nanotechnology-based delivery systems can effectively overcome these barriers by improving drug stability, targeted delivery, and sustained release. Nanoparticles facilitate enhanced accumulation of bioactive compounds within vitiliginous lesions, thereby improving therapeutic outcomes.

Table 12. Advantages of Nanoparticle-Based Herbal Delivery Systems in Vitiligo

Advantage	Mechanism	Therapeutic Benefit
Enhanced Solubility	Reduction in particle size, increases surface area and dissolution rate	Improved absorption and bioavailability
Improved Skin Penetration	Facilitates transport through stratum corneum, hair follicles, and sweat glands	Enhanced delivery to melanocytes
Controlled Release	Sustained release of encapsulated compounds over time	Reduced dosing frequency and prolonged action
Improved Stability	Protects bioactives from oxidation, hydrolysis, and photodegradation	Enhanced shelf-life and therapeutic efficacy
Targeted Delivery	Selective accumulation at depigmented lesions	Increased local drug concentration
Reduced Side Effects	Minimizes systemic drug exposure	Improved safety profile and patient compliance

Table 12 summarizes the major advantages of nanoparticle-mediated herbal delivery. These systems significantly improve the pharmaceutical and therapeutic performance of herbal bioactives by enhancing solubility, penetration, stability, and targeting efficiency.

7. Types of Nanoparticles Used in Vitiligo Therapy

Various nanoparticle systems have been explored for topical vitiligo treatment owing to their ability to improve drug delivery and skin retention [25].

Table 13. Types of Nanoparticles Used for Herbal Delivery in Vitiligo

Nanoparticle Type	Composition	Advantages	Limitations
Polymeric Nanoparticles	Biodegradable polymers	Sustained release, high stability, controlled delivery	Complex manufacturing
Solid Lipid Nanoparticles (SLN)	Solid lipids and surfactants	Skin hydration, occlusive effect, enhanced penetration	Limited drug loading
Nanostructured Lipid Carriers (NLC)	Solid and liquid lipids	High drug loading, better stability, controlled release	Formulation optimization required
Liposomes	Phospholipid vesicles	Biocompatibility, improved permeation, reduced irritation	Physical instability
Nanoemulsions	Oil-water dispersions	Rapid absorption, enhanced solubilization	Possible phase separation
Nanogels	Hydrogel-based nanoparticles	Moisturization, prolonged skin retention	Lower mechanical stability

Table 13 compares the major nanoparticle systems investigated for vitiligo treatment. Lipid-based systems and polymeric nanoparticles are the most widely studied due to their superior skin-targeting properties.

8. Formulation Development of Herbal Nanoparticles

Formulation development begins with preformulation studies to evaluate the physicochemical characteristics of herbal bioactives and their compatibility with formulation excipients.

Table 14. Comprehensive Evaluation Parameters for Herbal Nanoparticle-Based Vitiligo Therapy

Category	Evaluation Parameter	Purpose/Significance	Method/Instrument	Ideal Outcome/Criteria
Preformulation Studies	Solubility Analysis [26]	Selection of suitable formulation components	Solubility studies in water, buffers, oils, solvents	Maximum solubility achieved
	FTIR Analysis[26]	Drug-excipient compatibility	FTIR Spectroscopy	No significant interaction
	DSC Analysis[27]	Thermal behavior and stability	Differential Scanning Calorimetry	Stable thermal profile
	XRD Analysis [28]	Crystallinity determination	X-Ray Diffractometer	Reduced crystallinity/amorphous conversion
Physicochemical Characterization	Particle Size [29]	Influences penetration, release, uptake	Dynamic Light Scattering (DLS)	50–300 nm
	Polydispersity Index (PDI)[30]	Particle size distribution	DLS	< 0.3
	Zeta Potential [30]	Colloidal stability	Zeta Analyzer	±30 mV or above
	Entrapment Efficiency (%EE) [31]	Drug encapsulation efficiency	Centrifugation + UV/HPLC	>70%
	Drug Loading Capacity (%DL)[31]	Amount of drug loaded	UV/HPLC	High drug loading
	pH[32]	Skin compatibility	Digital pH Meter	5.0–7.0
	Viscosity[32]	Rheological behavior	Brookfield Viscometer	Suitable topical application
Morphological Characterization[33]	Surface Morphology	Shape and aggregation	SEM	Smooth, spherical particles
	Internal Structure	Nanostructure confirmation	TEM	Uniform nanoparticles
	Surface Roughness	Topographical analysis	AFM	Homogeneous surface
Thermal & Crystallinity Analysis[33]	Melting Point	Thermal stability	DSC	Stable thermal behavior
	Crystallinity	Physical state determination	XRD	Amorphous or reduced crystallinity
In Vitro Drug Release[34]	Initial Burst Release	Immediate drug availability	Dialysis Bag Method	Controlled release
	Sustained Release	Prolonged therapeutic action	Diffusion Studies	Extended-release profile
	Cumulative Drug Release (%)	Total release efficiency	UV/HPLC Analysis	>80% release

	Zero-Order Kinetics	Constant drug release	Mathematical modeling	Desired release pattern
	First-Order Kinetics	Concentration-dependent release	Mathematical modeling	Mechanistic evaluation
	Higuchi Model	Diffusion-controlled release	Mathematical modeling	Drug diffusion assessment
	Korsmeyer-Peppas Model	Release mechanism identification	Mathematical modeling	Fickian/non-Fickian release
Skin Permeation Studies [35]	Flux (J)	Drug permeation rate	Franz Diffusion Cell	High permeation
	Permeability Coefficient (Kp)	Skin penetration efficiency	Franz Diffusion Cell	Increased permeability
	Drug Retention	Drug retained in skin	Skin extraction method	High local retention
Biological Evaluation[31]	Cytotoxicity Assay	Cellular safety assessment	MTT Assay	Cell viability >80%
	Cytotoxicity Assay	Metabolic activity assessment	Alamar Blue Assay	Cell viability >80%
	Cellular Uptake	Nanoparticle internalization	Fluorescence Microscopy	Enhanced uptake
	Cellular Uptake	Intracellular localization	Confocal Microscopy	Efficient internalization
	ROS Assay	Antioxidant activity	DCFH-DA Assay	Reduced ROS levels
Anti-Vitiligo Evaluation[36]	Melanin Content Assay	Pigmentation assessment	Spectrophotometric Analysis	Increased melanin content
	Tyrosinase Activity Assay	Melanogenesis evaluation	Enzyme Activity Assay	Increased activity
	MITF Expression	Melanocyte regulation	RT-PCR/Western Blot	Upregulated
	TYR Expression	Melanin synthesis	RT-PCR/Western Blot	Upregulated
	TRP-1 Expression	Melanogenesis marker	RT-PCR/Western Blot	Upregulated
	TRP-2 Expression	Pigment maturation	RT-PCR/Western Blot	Upregulated
	Nrf2 Expression	Antioxidant defense	RT-PCR/Western Blot	Upregulated
	HO-1 Expression	Cytoprotection	RT-PCR/Western Blot	Upregulated
	Bax Expression	Pro-apoptotic marker	RT-PCR/Western Blot	Downregulated
	Bcl-2 Expression	Anti-apoptotic marker	RT-PCR/Western Blot	Upregulated
	Caspase-3 Expression	Apoptosis marker	RT-PCR/Western Blot	Downregulated
	TNF-α, IL-6, IFN-γ	Inflammatory markers	ELISA	Reduced levels
In Vivo Evaluation[36]	Chemically Induced Vitiligo Model	Disease simulation	Animal Study	Repigmentation observed
	UV-Induced Vitiligo Model	Repigmentation evaluation	Animal Study	Enhanced pigmentation

	Repigmentation Rate (%)	Pigment recovery	Image Analysis	Increased pigmentation
	Histopathology	Tissue architecture	H&E Staining	Normal skin morphology
	Melanocyte Count	Melanocyte restoration	Histological Analysis	Increased melanocytes
	Inflammatory Infiltration	Immune response assessment	Histopathology	Reduced infiltration
Stability Studies [37]	Particle Size Stability	Physical stability	DLS	No significant change
	PDI Stability	Uniformity maintenance	DLS	<0.3 maintained
	Zeta Potential Stability	Colloidal stability	Zeta Analyzer	Stable charge
	Drug Content Stability	Chemical stability	HPLC/UV	>90% retained
	Drug Release Stability	Functional stability	Release Studies	Similar release profile
	Physical Appearance	Visual stability	Visual Inspection	No aggregation/separation
	pH Stability	Formulation compatibility	pH Meter	Stable pH
	Long-Term Stability	Shelf-life determination	25°C ± 2°C / 60% RH ± 5% RH	Stable for 12 months
	Accelerated Stability	Predict formulation robustness	40°C ± 2°C / 75% RH ± 5% RH	Stable for 6 months
Future Evaluation	Stimuli-Responsive Behavior	Triggered drug release	pH/Temperature Studies	Controlled release
	Follicular Targeting	Delivery to melanocyte reservoir	Skin Distribution Studies	Enhanced follicular deposition
	Gene-Based Evaluation	Melanocyte regeneration potential	Molecular Biology Techniques	Improved gene regulation

This comprehensive table 14 summarizes all critical parameters involved in the development and evaluation of herbal nanoparticle formulations for vitiligo therapy. It encompasses preformulation studies, physicochemical characterization, morphology, thermal behavior, drug release kinetics, skin permeation, biological safety, anti-vitiligo efficacy, in vivo performance, stability assessment, and future nanomedicine approaches. These parameters collectively determine the quality, safety, efficacy, and clinical translation potential of nanoparticle-based herbal therapeutics for vitiligo management.

Conclusion

Herbal drug-loaded nanoparticles represent a promising next-generation therapeutic strategy for vitiligo management. By addressing the fundamental limitations of conventional herbal formulations, nanoparticle systems improve solubility, stability, skin penetration, controlled release, and targeted delivery. Comprehensive characterization involving particle size, zeta potential, entrapment efficiency, morphology, thermal behavior, drug release, skin permeation, cytotoxicity, melanogenesis, gene expression, and stability studies is essential for successful formulation development. Future advances in nanotechnology, follicular targeting, and precision medicine are expected to transform herbal nanoparticle-based therapies into clinically effective treatments for vitiligo, offering safer and more efficient alternatives to conventional approaches.

References

1. Vitiligo. Available from: http://www.herbsandcures.com/2007/May. Accessed July 17, 2009.

2. Vitiligo treatment. Available from: http://pushpakaran.shoutpost.com/archives/2007/May. Accessed July 17, 2009.

3. Hearing VJ. Biochemical control of melanogenesis and melanosomal organization. J Invest Dermatol Symp Proc. 1999;4(1):24-28. https://doi.org/10.1038/sj.jidsp.5640176 PMid:10537003

4. Taieb A. Intrinsic and extrinsic pathomechanisms of vitiligo. Pigment Cell Res. 2000;8:41. https://doi.org/10.1034/j.1600-0749.13.s8.9.x PMid:11041356

5. Nordlund JJ, Lerner AB. Vitiligo-it is important. Arch Dermatol. 1982;118:5-8. https://doi.org/10.1001/archderm.1982.01650130009007

6. Ezzedine K, Lim HW, Suzuki T, Katayama I, Hamzavi I, Lan CCE, et al. Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. Pigment Cell Melanoma Res. 2012;25:E1-E13. https://doi.org/10.1111/j.1755-148X.2012.00997.x PMid:22417114 PMCid:PMC3511780

7. Kemp EH, Waterman EA, Weetman AP. Autoimmune aspects of vitiligo. Autoimmunity. 2001;34:65-77. https://doi.org/10.3109/08916930108994127 PMid:11681494

8. Dwivedi M, Kemp EH, Laddha NC, Mansuri MS, Weetman AP, Begum R. Regulatory T cells in vitiligo: implications for pathogenesis and therapeutics. Autoimmun Rev. 2015;14:49-56. https://doi.org/10.1016/j.autrev.2014.10.002 PMid:25308528

9. Boniface K, Seneschal J, Picardo M, Taieb A. Vitiligo: focus on clinical aspects, immunopathogenesis, and therapy. Clin Rev Allergy Immunol. 2018;54:52-67. https://doi.org/10.1007/s12016-017-8622-7 PMid:28685247

10. Arora AK, Kumaran MS. Pathogenesis of vitiligo: an update. Pigment Int. 2017;4:65. https://doi.org/10.4103/2349-5847.219673

11. Garg BJ, Saraswat A, Bhatia A, Katare OP. Topical treatment in vitiligo and potential uses of new drug delivery systems. Indian J Dermatol Venereol Leprol.

12. Pasricha JS, Khaitan BK. Oral mini-pulse therapy with betamethasone in vitiligo. Int J Dermatol. 1993;32:753-757. https://doi.org/10.1111/j.1365-4362.1993.tb02754.x PMid:8225724

13. Akdeniz N, Yavuz IH, Gunes Bilgili S, Ozaydin Yavuz G, Calka O. Efficacy of narrowband UVB therapies in vitiligo. J Dermatol Treat. 2014;25:196-199. https://doi.org/10.3109/09546634.2013.777381 PMid:23441902

14. Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: a comprehensive overview. J Am Acad Dermatol. 2011;65:473-491. https://doi.org/10.1016/j.jaad.2010.11.061 PMid:21839315 PMCid:PMC12847362

15. Parsad D, Pandhi R, Juneja A. Effectiveness of Ginkgo biloba in vitiligo. Clin Exp Dermatol. 2003;28(3):285-287. https://doi.org/10.1046/j.1365-2230.2003.01207.x PMid:12780716

16. Asawanonda P, Klahan SO. Tetrahydrocurcuminoid cream with NB-UVB therapy in vitiligo. Photomed Laser Surg. 2010;28(5):679-684. https://doi.org/10.1089/pho.2009.2637 PMid:20961233

17. Dessai S, Bhutekar S. Formulation and evaluation of psoralen herbal cream for vitiligo. Int J Pharm Res Appl. 2023;8(2):437-444.

18. Rayabagi MH, Prajapati B. Herbal Nanoparticle-Embedded Film-Forming Spray: A Novel Topical Delivery System for Vitiligo Management. Indian J of Pharmaceutical Education and Research. 10.5530/ijper.20262653.

19. Jayaprakasam A, Darvay A, Osborne G, McGibbon D. Assessment of severity and quality of life in cutaneous disease. Clin Exp Dermatol. 2002;27:306-308. https://doi.org/10.1046/j.1365-2230.2002.01025.x PMid:12139677

20. Jowett S, Ryan T. Skin disease and handicap: impact of skin conditions. Soc Sci Med. 1985;20:425-429. https://doi.org/10.1016/0277-9536(85)90021-8 PMid:3158080

21. Jeong YM, Choi YG, Kim DS, et al. Cytoprotective effect of green tea extract and quercetin. Arch Pharm Res. 2005;28(11):1251-1256. https://doi.org/10.1007/BF02978208 PMid:16350851

22. Becatti M, Prignano F, Fiorillo C, et al. Protective effects of curcumin in vitiligo keratinocytes. Antioxid Redox Signal. 2010;13(9):1309-1321. https://doi.org/10.1089/ars.2009.2779 PMid:20085492

23. Bedi KL, Zutshi U, Chopra CL, et al. Picrorhiza kurroa, an ayurvedic herb, may potentiate photochemotherapy in vitiligo. J Ethnopharmacol. 1989;27(3):347-352. doi:10.1016/0378-8741(89)90009-3. https://doi.org/10.1016/0378-8741(89)90009-3 PMid:2615440

24. Bhatia S. Nanoparticles: types, classification, characterization, fabrication methods and drug delivery applications. Springer Sci Rev. 2016;33-93. https://doi.org/10.1007/978-3-319-41129-3_2 PMid:28298942 PMCid:PMC5334270

25. Guterres SS, Alves MP, Pohlmann AR. Polymeric nanoparticles, nanospheres and nanocapsules for cutaneous applications. Drug Target Insights. 2007;2:117739280700200002. https://doi.org/10.1177/117739280700200002

26. Wadher KJ, Kakde RB, Umekar MJ. Formulation and evaluation of sustained release tablets of metformin hydrochloride using hydrophilic and hydrophobic polymers. Indian J Pharm Sci. 2011;73(2):208-215. https://doi.org/10.4103/0250-474X.91579 PMid:22303065 PMCid:PMC3267306

27. Cho E, Cho W, Cha KH, Park J, Kim MS, Kim JS, et al. Enhanced dissolution of megestrol acetate microcrystals prepared by antisolvent precipitation using hydrophilic additives. Int J Pharm. 2010;396:91-98. https://doi.org/10.1016/j.ijpharm.2010.06.016 PMid:20558265

28. Moin A, Deb TK, Osmani RA, Bhosale RR, Hani U. Fabrication, characterization, and evaluation of microsponge delivery system for facilitated fungal therapy. J Basic Clin Pharm. 2016;7:39. https://doi.org/10.4103/0976-0105.177705 PMid:27057125 PMCid:PMC4804404

29. Kocbek P, Baumgartner S, Kristl J. Preparation and evaluation of nanosuspensions for enhancing dissolution of poorly soluble drugs. Int J Pharm. 2006;312(1-2):179-186. https://doi.org/10.1016/j.ijpharm.2006.01.008 PMid:16469459

30. Detroja C, Chavhan S, Sawant K. Enhanced antihypertensive activity of candesartan cilexetil nanosuspension. Sci Pharm. 2011;79(3):635-652. https://doi.org/10.3797/scipharm.1103-17 PMid:21886909 PMCid:PMC3163369

31. Li W, Yang Y, Tian Y, Xu X, Chen Y, Mu L, et al. Preparation and in vitro/in vivo evaluation of revaprazan hydrochloride nanosuspension. Int J Pharm. 2011;408(1 2):157-162. https://doi.org/10.1016/j.ijpharm.2011.01.059 PMid:21295124

32. Londhe VY, Umalkar KB. Formulation development and evaluation of fast dissolving film of telmisartan. Indian J Pharm Sci. 2012;74(2):122-6. https://doi.org/10.4103/0250-474X.103842

33. Pandya VM, Patel JK. Formulation and optimization of nanosuspensions for enhancing simvastatin dissolution. Dissolut Technol. 2011;18(3):40-45. https://doi.org/10.14227/DT180311P40

34. Mandal B, Alexander KS, Riga AT. Sulfacetamide-loaded Eudragit RL100 nanosuspension for ocular delivery. J Pharm Pharm Sci. 2010;13(4):510-523. https://doi.org/10.18433/J3SW2T PMid:21486528

35. Grodowska K, Parczewski A. Analytical methods for residual solvents determination in pharmaceutical products. Acta Pol Pharm. 2010;67(1):13-26.

36. Zhu YP, Wang SQ, Xu AE. A mouse model of vitiligo induced by monobenzone. Exp Dermatol. 2013;22:499-501. https://doi.org/10.1111/exd.12184 PMid:23800067

37. Jyothi VGSS, Pawar J, Fernandes V, et al. Film forming topical dermal spray of meloxicam attenuated pain and inflammation in carrageenan-induced paw oedema in Sprague Dawley rats. J Drug Deliv Sci Technol. 2022;70:103195. https://doi.org/10.1016/j.jddst.2022.103195