



International Journal of Pharmaceuticals and Health care Research (IJPHR)

IJPHR | Vol.13 | Issue 2 | Apr - Jun -2025

www.ijphr.com

DOI : <https://doi.org/10.61096/ijphr.v13.iss2.2025.222-236>

ISSN: 2306-6091

Review

Recent Nanotechnology for Transdermal Drug Delivery System

Dev Raj¹, Anjali Kumari^{2*}, Ankita², Vinay Pandit³



¹Assistant Professor, Laureate institute of Pharmacy, Jawalamukhi, Himachal Pradesh 176031

²B.Pharm Students, Laureate institute of Pharmacy, Jawalamukhi, Himachal Pradesh 176031

³HOD, Pharmaceutics Department, Laureate institute of Pharmacy, Jawalamukhi, Himachal Pradesh 176031

*Author for Correspondence: Anjali Kumari

Email: anjalichambail@gmail.com

| | |
|--|--|
|  | Abstract |
| Published on:08 May 2025 | <p>Transdermal drug delivery systems (TDDS) provide non-invasive alternative to standard administration methods, allowing for regulated drug release, increased patient compliance, and bypassing first-pass metabolism. Recent breakthroughs in nanotechnology have considerably increased the efficacy of transdermal medication delivery by bypassing the skin's barrier function, particularly the stratum corneum. This study focuses on the most recent discoveries in nanocarrier systems, such as liposomes, ethosomes, solid lipid nanoparticles, nanostructured lipid carriers, dendrimers, and microneedles, which are intended to improve drug penetration and therapeutic effects. We study a wide range of nano-enabled formulations, including ointments, patches, creams, and sprays, each customized to a unique therapeutic application, ranging from pain management and dermatological problems to chronic systemic diseases. The report also examines present obstacles and future directions in the sector, with the goal of providing a complete picture of how nanotechnology is transforming transdermal medication delivery.</p> |
| Published by: DrSriram Publications | |
| <p>2025 All rights reserved.</p>  <p>Creative Commons Attribution 4.0 International License.</p> | |
| | <p>Keywords: Transdermal drug delivery system, Nanotechnology, Nanocarriers, Regulated drug release, Microneedles.</p> |

INTRODUCTION

Nanotechnology is regarded as one among of the most auspicious technological advancements of the twenty-first century. The prefix 'nano' originated from the Greek word 'dwarf' which means something minuscule and represents 1 billionth of a meter (10^{-9} m). So, Nanotechnology is a field of science, which involves designing and creating material and devices by modifying at the nanoscale (1to100 nanometres).¹ This definition indicates two fundamental aspects of nanotechnology. The initial aspect concerns scale: nanotechnology involves manipulating frameworks by precisely shaping and sizing them with nanometre-level accuracy. The second aspect concerns innovation: nanotechnology must exploit unique properties that emerge at the nanoscale to innovate in

various application.² This technology enables scientists and engineers to make advancements in a variety of sectors, including materials science, electronics, medicine, and energy.³

Origin

Richard Feynman, an American physicist and recipient of the Nobel Prize, formally introduced the foundational concept of Nanotechnology in 1959. At the yearly conference of the American Physical Society, Feynman delivered talk named “There’s Plenty of Room at the Bottom” at the California Institute of Technology (Caltech). In his talk, Feynman speculated that, “Why is it impossible to inscribe all 24 volumes of the Encyclopaedia Britannica on the tip of a pin?” & outlined a concept of employing devices to build tiny machines. Such a novel concept showed that Feynman’s hypothesis has been validated, and for this reason, he is widely recognized as the founding figure of modern nanotechnology.

In 1974, fifteen years after Feynman's proposal, Japanese scientist Norio Taniguchi was the first to employ and define the term 'nanotechnology,' characterizing it as "Nanotechnology primarily involves the processing of separation, consolidation, and deformation of materials at the atomic or molecular level".⁴

Types of nanotechnology

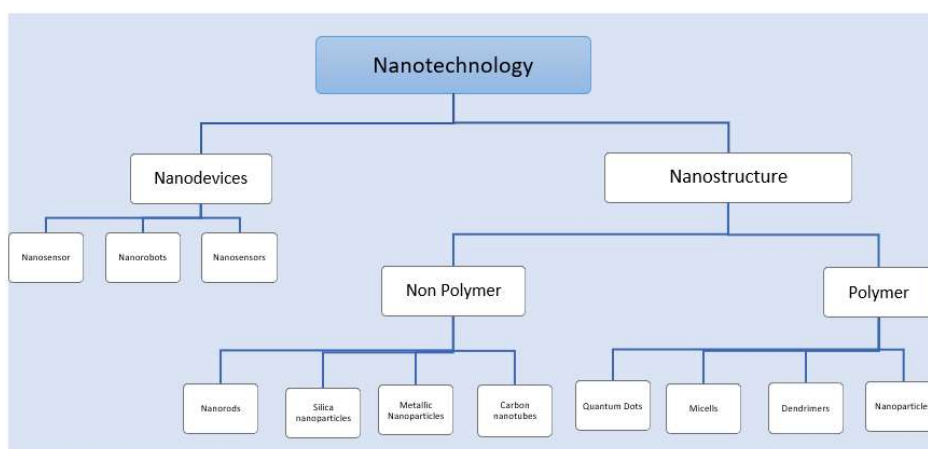


Fig 1: Types of Nanotechnology

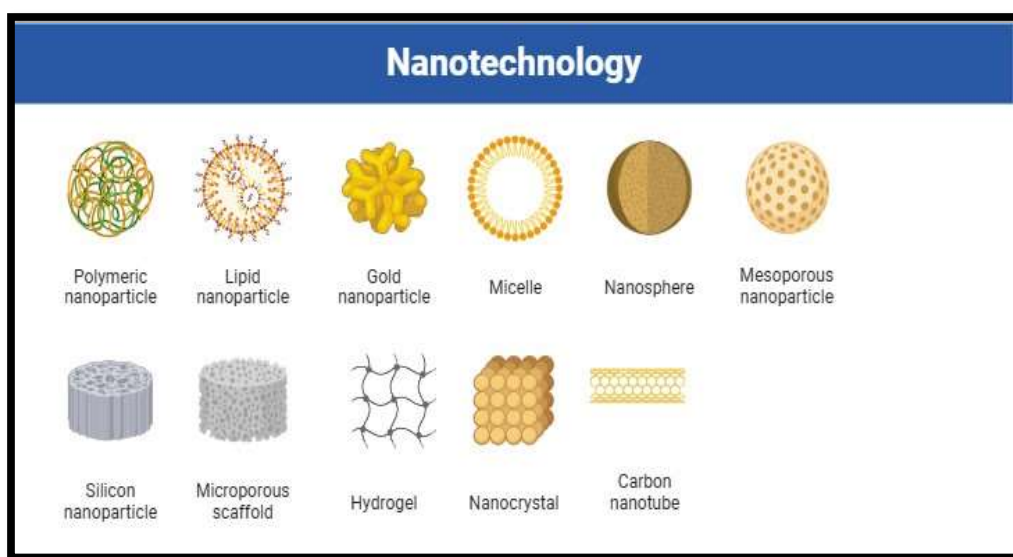


Fig 2: Structural classifications of nanotechnology-based systems

Nanoparticles

According to the International Organization for Standardization (ISO), nanoparticles are defined as nano-objects characterized by having all of their external dimensions within the nanoscale (from 1 to 100 nm). NPs can be crystalline with single or multi-crystal solids, or amorphous. It can be either loose or agglomerated.⁵ NPs might consist of many layers or be uniform. In the latter instance, the layers are frequently as follows:

- (a) The surface layer, which typically is composed of metal ions, polymers, surfactants, and a range of tiny molecules.
- (b) The shell layer, which differs from the core layer in terms of composition.
- (c) The core layer is the NP's central section.⁶

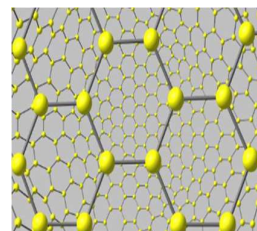


Fig 3: Nanoparticles

Dendrimers

Dendrimers are organic nanostructures with unique physicochemical properties and are biocompatible, making them useful for medication administration. The term dendrimer comes from the Greek word dendron, which means "tree," because its morphological structure is similar to that of tree branches. It also incorporates the Greek term "meros" which means "part".⁷ One of the most appealing fields of dendrimer chemistry is the use of dendrimers in pharmaceuticals and medical chemistry, as well as potential of dendrimers as drugs.⁸

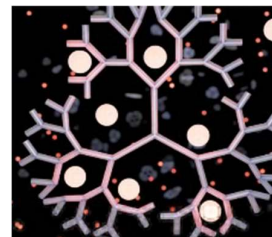


Fig 4: Dendrimers

Quantum dots

One of the inventions in nanotechnology involves nano-sized particles known as Quantum dots (QDs). Quantum dots are fluorescent semiconductor nanoparticles made up of a core substance surrounded by a shell of another semiconductor material with a diameter ranging from 2 to 10 nanometres.⁹ Carbon-based quantum dots hold promise for applications in imaging, and drug delivery due to their excellent biological properties, including low toxicity & high biocompatibility.¹⁰



Fig 5: Quantum Dots

Nanosensors

Nanosensors are now being utilized to detect and monitor physical features at the nanoscale, including temperature, chemical species, and nanoparticles. Nanoscale devices monitor and change physical quantities into discernible and measurable signals. Nanosensors are utilized in medical applications, pollutant management, disease detection, and monitoring of manufacturing and transportation activities.¹¹

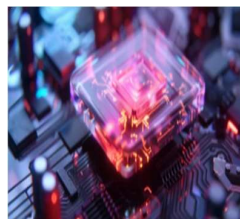


Fig 6: Nanosensors

Nanorobots

Richard Feynman initially proposed the concept of nanorobots in 1959 with his address "There's Plenty of Room at the Bottom," in which he highlighted their potential for treating heart problems.¹² Micro/nanorobots should be capable of performing tasks through the encapsulation or functionalization with therapeutic or diagnostic agents, integration with functional materials, or design into specific micro/nano structures. They must also navigate toward target sites via planned or optimized paths to carry out "delivery" and "execution" functions.¹³

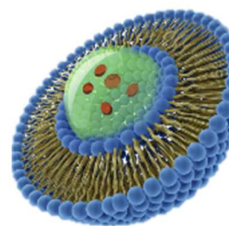


Fig 7: Liposomes

Liposomes

Liposomes are spherically shaped tiny vesicles made up of one or more phospholipid bilayer membranes. Because of their unusual structure, they can encapsulate both hydrophilic and hydrophobic molecules within their aqueous core and lipid bilayers, making them ideal carriers in drug delivery systems. Because of their biocompatibility, biodegradability, and stability, liposomes have been widely used in medical applications, particularly for targeted drug delivery.¹⁴



Fig 8: Nanorobots

Niosomes

In an aqueous environment, non-ionic surfactants and cholesterol self-assemble to form microscopic lamellar structures known as niosomes. These vesicles can hold both hydrophilic and lipophilic medicines, increasing their stability, bioavailability, and targeted delivery. Niosomes are commonly used in transdermal medication administration systems due to their biocompatibility and ability to enhance drug penetration through the skin.¹⁵

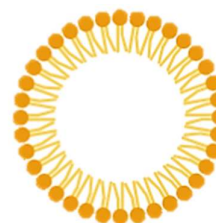


Fig 9: Niosomes

Phytosomes

Phytosomes ("Phyto-liposomes") are complexes generated by combining plant extracts or phytoconstituents (such as curcumin, quercetin, and silybin) with phospholipids (most often phosphatidylcholine). This creates a molecular complex in which the phytochemical is incorporated or attached to the lipid layer, increasing its lipophilicity and membrane permeability. Phytosomes are particularly useful for topical and transdermal applications because

- Compatible with skin lipids.
- Increased penetration into the stratum corneum.
- Potential for use with nano formulations such as liposomes, ethosomes, and transferosomes.¹⁶

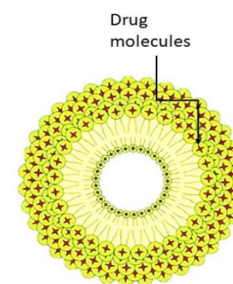


Fig 10: Phytosome

Transdermal drug delivery system

Since its inception in the late 1970s, transdermal drug delivery has been regarded as a unique and painless method of giving medication therapies, owing in great part to its non-invasiveness. It decreases the risk of medication overdoses associated with oral delivery or injection while also allowing for adequate therapeutic efficacy by preventing the drug's early metabolism by the liver.¹⁷

As the name suggests, transdermal drug delivery (TDD) utilizes the skin as the administration site, allowing active agents, such as therapeutic compounds, to penetrate the skin barrier and reach deeper tissues, ultimately exerting localized effects or achieving systemic drug distribution.¹⁸

TDDS, such as patches, allow regulated and sustained drug release, which may result in more stable plasma drug levels and longer-lasting therapeutic benefits. Recent advances in nanotechnology, particularly the incorporation of biopolymer-based nanoparticles.¹⁹

Enhancement of transdermal delivery by equipment

- Passive delivery techniques: - Nano emulsion, polymeric nanoparticles, creams, ointments, creams & gels.
- Active delivery techniques:- Iontophoresis, Sonophoresis, microneedles, electroporation, thermal ablation, photo mechanical waves.²⁰

Recent advancement in transdermal drug delivery system

Compared to traditional methods, transdermal drug delivery systems based on nanocarriers have several benefits, including improved drug physicochemical stability, higher skin penetration, enhanced biodistribution, efficient targeted accumulation, and regulated drug delivery.²¹

One important factor influencing the effectiveness of nanocarriers' transdermal treatments is their skin penetration efficiency. By altering the nano-skin interactions, it has been demonstrated that the physicochemical

characteristics of nanocarriers such as hydrophilic-lipophilic balance, size, shape, deformability, and surface charges have an impact on their penetration in extremely complex skin.²²

Nanotechnology based Transdermal drug delivery systems (TDDS) have a number of benefits over traditional techniques. Some of these are as: -

1. Enhance skin penetration
 - Bypassing the stratum corneum barrier of the skin, nanocarriers such as liposomes, niosomes, nanoemulsions, and solid lipid nanoparticles (SLNs) can increase medication penetration.
 - Hydrophilic or high molecular weight medications are frequently difficult for conventional TDDS to distribute through the skin.²³
2. Enhanced Bioavailability
 - Drugs are better soluble and protected from deterioration by nanoparticles, which increases systemic absorption.
 - Due to inadequate skin penetration, conventional patches may have low bioavailability.
3. Extended and Controlled Release:
 - Because of their extended release, nanoparticles lower the frequency of doses while preserving therapeutic levels.
 - SLN-based insulin patches had a longer duration of action than standard patches.²⁴
4. Localized and targeted delivery
 - To lessen off-target effects, functionalized nanoparticles can be made to target particular tissues or cells. In order to improve the distribution of medications to deeper layers of the skin and increase the effectiveness of treatment for illnesses like psoriasis and acne
 - Invasomes vesicles that include phospholipids, ethanol, and terpenes—have been used.²⁵
5. A higher capacity for loading drugs
 - While nanoparticles effectively transport both hydrophilic and lipophilic medicines, conventional transdermal patches frequently have trouble with hydrophilic medications.
 - Ethosomal gels for insulin enhanced transdermal absorption when compared to standard insulin patches.²⁶

Nanotechnology-based transdermal formulations in various physical forms

Nano-ointment

Transdermal ointments are formulations that transport medications into the bloodstream via the skin. Unlike topical therapies, which operate locally, transdermal ointments allow regulated medication release, increasing patient compliance while bypassing gastrointestinal metabolism. They're commonly utilized in hormone therapy, pain management, and cardiovascular treatments. Permeation enhancers promote drug absorption through the skin barrier, maximizing therapeutic results.²⁷

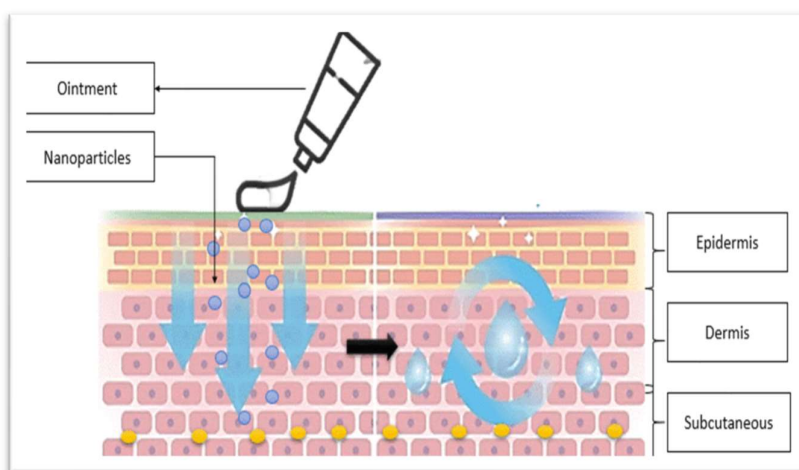


Fig 11: Pharmacological mechanism of nano-formulated ointments.

Nano-ointments have different advantages over traditional, here are some of them.

- Nano ointments include nanoparticles (usually <100 nm) that penetrate deeper into epidermal layers, improving medication delivery.²⁸
- Nano ointments provide regulated and prolonged medication release, reducing dose frequency.²⁹
- Nano formulations improve medication bioavailability through better solubility and stability.³⁰

- Targeted delivery minimizes impact on healthy tissues, thereby reducing systemic side effects.

Table 1: Various nanotech-based ointments, detailing their target diseases, nanocarrier types, and mechanisms of action.

| Nanotechnology-Based Ointment | Disease | Nanocarrier Type | Mechanism/Benefit | Reference |
|---|---|----------------------------------|---|-----------|
| Niosomal Minoxidil Ointment | Androgenetic Alopecia | Niosomes | Enhanced drug retention in the skin. | 31 |
| SLN-based Clotrimazole Ointment | Treat tinea corporis | Solid Lipid Nanoparticles (SLNs) | Higher antifungal action. | 29 |
| Nanoemulsion-based Ketoprofen Ointment | Osteoarthritis and Musculoskeletal Pain | Nanoemulsions | Increased skin penetration and quick beginning of action. | 32 |
| Nanoparticle-based Terbutaline Sulfate Ointment | Asthma | Polymeric Nanoparticles | Controlled medication release and enhanced stability. | 33 |
| Nanoemulgel-based Methoxsalen Ointment | Psoriasis | Nanoemulgel | Enhanced penetration and accumulation in skin layers | 34 |
| Nanogel-based Lidocaine Ointment | Local Anesthesia | Nanogels | Anesthesia develops quickly and lasts a long time. | 35 |
| Nanoparticle-based Amphotericin B Ointment | Fungal Infections | Liposomes | Improved penetration irrespective of molecular weight. | 36 |
| Nanoparticle-based Hydrocortisone Ointment | Eczema and Dermatitis | Polymeric Nanoparticles | Reduced dosage frequency and sustained release. | 37 |
| Nanoemulsion-based Ibuprofen Ointment | Inflammatory Pain Conditions | Nanoemulsions | Increased solubility and skin permeability. | 32 |
| Nanogel-based Testosterone Ointment | Hypogonadism | Nanogels | Controlled release and higher absorption. | 38 |
| Nanogel-based Clobetasol Ointment | Psoriasis and Eczema | Nanogels | Enhanced delivery to deeper skin layers. | 39 |
| Nanoparticle-based Mupirocin Ointment | Bacterial Skin Infections | Solid Lipid Nanoparticles (SLNs) | Improved antibacterial action. | 29 |
| Nanoparticle-based Resveratrol Ointment | Skin Aging and Oxidative Stress | Polymeric Nanoparticles | Increased skin penetration and antioxidant activity. | 29 |

Nanogels

Nanogels are three-dimensional hydrogel networks made from crosslinking polymer chains at the nanoscale. These structures are very hydrophilic and can retain large amounts of water without dissolving, making them ideal drug transporters.⁴⁰

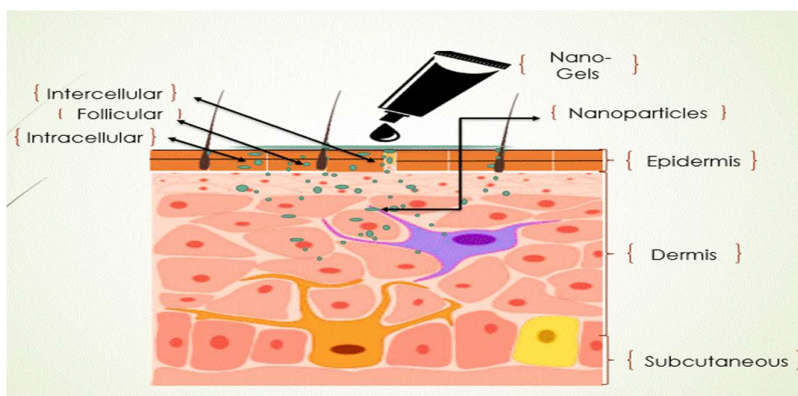


Fig 12: Pharmacological mechanism of nano-formulated gels.

Table 2: Various ointment formulations, including disease indication, nanocarrier type, and mechanism of therapeutic action.

| Nanogel-Based Gel | Disease/Condition | Nanocarrier Type | Mechanism/Benefit | Reference |
|---------------------------------|------------------------------|------------------|---|-----------|
| Nanogel-based Insulin Gel | Diabetes Mellitus | Nanogels | Promotes transdermal delivery. | 42 |
| Nanogel-based Diclofenac Gel | Inflammatory Pain Conditions | Nanogels | Diclofenac has better skin penetration and a longer duration of action. | 31 |
| Nanogel-based Clobetasol Gel | Psoriasis and Eczema | Nanogels | Improved distribution to deeper skin layers. | 39 |
| Nanogel-based Lidocaine Gel | Local Anesthesia | Nanogels | Anesthesia develops quickly and lasts a long time. | 35 |
| Nanogel-based Testosterone Gel | Hypogonadism | Nanogels | Testosterone is released under control and absorbed more efficiently. | 38 |
| Nanogel-based Dexamethasone Gel | Inflammatory Skin Conditions | Nanogels | Sustained release and focused distribution. | 43 |
| Nanogel-based Methotrexate Gel | Psoriasis | Nanogels | Enhanced skin penetration and less side effects. | 31 |

Transdermal patches

A Nanopatch is a micro-or nano structured patch used to deliver therapeutic agents such to deliver medicines, vaccination, or proteins directly through the skin(transdermal) or mucosal surface.

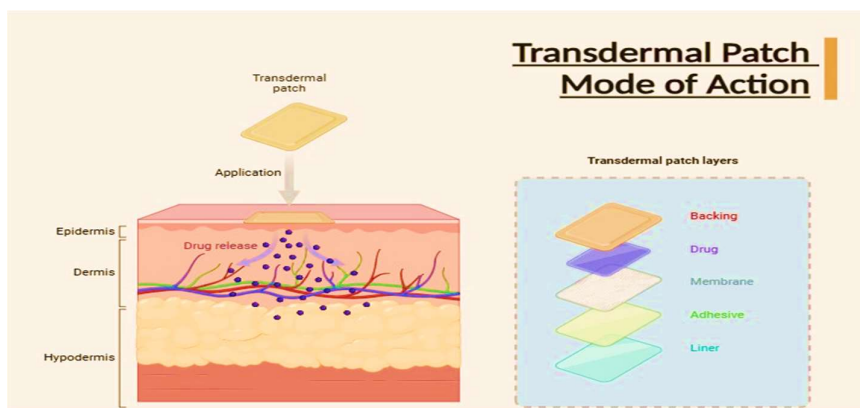


Fig 13: Advanced nanopatch technology facilitating transdermal delivery pharmaceuticals

A nanopatch is a micro- or nanostructured patch used to deliver therapeutic agents such as medicines, vaccinations, or proteins directly through the skin (transdermal) or mucosal surfaces. These patches are a subclass of microneedle technology and frequently contain hundreds to thousands of microscopic projections on a small patch, each smaller than a human hair.⁴⁴

Nano patches are a substantial advancement over traditional transdermal drug delivery devices. Traditional patches are primarily based on passive diffusion, which limits their efficacy to medications that are tiny, lipophilic, and can cross the skin barrier. Nanopatches, on the other hand, use nanoscale carriers such liposomes, solid lipid nanoparticles, & polymeric nanoparticles to improve therapeutic solubility, stability, and stratum corneum penetration.⁴⁵

Table 3: Various nanotech-based patches detailing their target diseases, nanocarrier types, and mechanisms of action.

| Nano-patches | Disease/ Condition | Nanocarrier Type | Mechanism/Benefit | Reference |
|-----------------------|---------------------------------|--|--|-----------|
| Pirfenidone | Pulmonary Fibrosis | Chitosan-Sodium Alginate Nanogel | Enhances skin permeation and provides sustained drug release. | 35 |
| Artemether | Malaria | Chitosan-Chondroitin Sulfate Nanoparticles | Improves stability and encapsulation efficiency, facilitating controlled release. | 35 |
| Methyl Salicylate | Pain Relief | Chitosan-Nanoemulsion Films | Increases drug loading capacity. | 35 |
| Estradiol | Menopausal Symptoms | Niosomes | Provides controlled and sustained hormone release for hormone. | 46 |
| Testosterone | Hypogonadism | Liposomes | Enhances solubility and stability, enabling steady hormone levels. | 47 |
| Tacrolimus | Atopic Dermatitis | Liposomes | Improves skin penetration and prolongs anti-inflammatory effects. | 48 |
| 5-Fluorouracil (5-FU) | Skin Cancer | Liposomes | Enables localized and controlled release of chemotherapy agents. | 49 |
| Rizatriptan Benzoate | Migraine | Nano Lipid Carriers | Provides sustained drug release to maintain steady-state concentration, enhancing therapeutic effects | 50 |
| Penbutolol Sulfate | Hypertension | Iontophoretic Delivery System | Uses electric current to enhance skin permeability and deliver ionized drug molecules effectively | 51 |
| Ranitidine | Gastroesophageal Reflux Disease | Iontophoretic Delivery System | Enhances transdermal delivery of ionized ranitidine using electric current for paediatric applications | 51 |
| Lidocaine | Local Anaesthesia | Iontophoretic Delivery System | Uses electric current to enhance delivery of lidocaine for rapid onset anaesthesia | 52 |
| Fentanyl | Chronic Pain | Iontophoretic Delivery System | Provides controlled delivery of fentanyl for long-term pain management | 51 |
| Sumatriptan | Migraine | Iontophoretic Delivery System | Enhances transdermal delivery for rapid relief from migraine symptoms | 51 |
| Allopurinol | Gout | Nanostructured Lipid Carriers | Sustains drug release to manage uric acid levels effectively | 51 |

| | | | | |
|----------------------------|--------------|----------------------------|---|---------------|
| Carvedilol | Hypertension | Nanolipid Transfersomes | Enhances skin penetration and provides controlled release for blood pressure management | ⁵¹ |
| Diltiazem Hydrochloride | Hypertension | Solid Nanoparticles | Lipid Provides sustained release and improves bioavailability for effective hypertension treatment | ⁵¹ |
| Curcumin | Inflammation | Chitosan Nanoparticles | Enhances skin penetration and provides sustained release of curcumin to reduce inflammation | ⁵³ |

Nano-creams

Nano-creams topical formulations enhanced with nanoparticles to improve the delivery and efficacy of active ingredients through the skin. By incorporating nanoparticles, these overcome the skin's natural barrier, allowing for deeper penetration and targeted delivery of therapeutic agents.⁵⁴

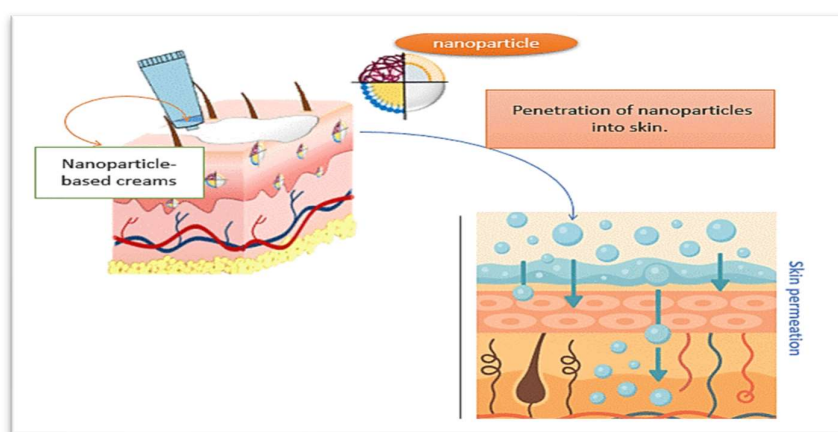


Fig 14: Advanced nano-creams technology facilitating transdermal delivery.

Nano-creams have substantial advantages over traditional topical creams because of their nanoscale formulation, which improves skin penetration, nanoemulsions, and solid, lipid nanoparticles to encapsulate active medicines and transport them across the skin barrier.⁵⁵

Table 4: Presents various nanotech-based creams, detailing their target diseases, nano-carrier types, and mechanisms of action.

| Nano-creams | Disease/Condition | Nanocarrier Type | Mechanism/Benefit | Reference |
|---------------------------|---------------------------------|------------------|--|---------------|
| Acyclovir | Herpes Simplex Virus Infections | Nanocrystals | Enhances skin permeation and bioavailability. | ⁵⁶ |
| Azithromycin | Skin Infections Post-Tick Bites | Nanocrystals | Increases saturation solubility and skin bioavailability, enhancing antibacterial effects. | ⁵⁷ |
| Ganoderma lucidum Extract | Frostbite-Related Infections | Nanogel | Improves skin penetration and retention, promoting wound healing. | ⁵⁸ |
| Meloxicam | Pain & inflammation | Nanocrystals | Enhances transdermal permeability and plasma concentration. | ⁵⁹ |
| Flurbiprofen | Pain & Inflammation | Nanocrystals | Increases skin penetration and anti-inflammatory effects. | ⁵⁸ |
| Diclofenac | Pain & Inflammation | Nanocrystals | Enhances skin penetration and deposition, improving therapeutic outcomes. | ⁶⁰ |

| | | | | |
|-----------------------------|---------------------------|-------------------------|---|----|
| Apremilast | Psoriasis | Nanocrystals | Increases saturation solubility. | 61 |
| Methotrexate | Psoriasis | Nanocrystals | Provides targeted delivery and prolonged intradermal release, reducing systemic side effects. | 62 |
| Azelaic Acid | Acne Vulgaris | Nanocrystal Hydrogel | Improves rheological properties and drug delivery, enhancing therapeutic efficacy. | 63 |
| Fusidic Acid | Bacterial Skin Infections | Nanocrystals | Enhances antibacterial properties and wound healing. | 64 |
| Nitrofurazone | Bacterial Skin Infections | Nanocrystals | Improves dissolution and skin penetration, enhancing antibacterial efficacy. | 65 |
| Silver Sulfadiazine | Bacterial Skin Infections | Nanocrystals | Provides enhanced antibacterial properties and promotes wound healing. | 66 |
| Luliconazole | Fungal Infections | Nanocrystals | Increases solubility and antifungal activity. | 67 |
| Clotrimazole | Fungal Infections | Nanocrystal Nanogel | Enhances skin penetration and antifungal efficacy. | 58 |
| Beclomethasone Dipropionate | Eczema | Nanocrystals | Increases saturation solubility and skin accumulation, enhancing anti-inflammatory effects. | 68 |
| Caffeine | Skin Aging | Nanocrystals | Enhances skin permeation, providing anti-aging effects. | 58 |
| Glabridin | Hyperpigmentation | Nanocrystals | Improves skin penetration, reducing pigmentation effectively. | 69 |
| Diosmin | Diabetic Foot Ulcer | Nanocrystals | Provides high porosity and mucoadhesion. | 70 |
| Tretinoin | Acne Vulgaris | Polymeric Nanoparticles | Increases skin accumulation and reduces systemic absorption. | 58 |

Nano- sprays

Nano sprays are a novel way to transdermal drug delivery that use nanotechnology to improve therapeutic agent penetration into the skin. Nano sprays, unlike traditional delivery methods, can encapsulate both hydrophilic and lipophilic medications within nanoparticles, allowing them to move more easily across the stratum corneum. This procedure provides a non-invasive alternative to standard methods, which may improve patient compliance and provide more constant drug absorption.⁷¹

Table 5: Various nanotech-based sprays, detailing their target diseases,nano-carrier types, and mechanisms of action.

| Nano-sprays | Disease/Condition | Nanocarrier Type | Mechanism/Benefit | Reference |
|-------------|---|-------------------------|--|-----------|
| Levodopa | Parkinson's Disease | Polymeric Nanoparticles | Enhances brain delivery via intranasal route, bypassing the blood-brain barrier. | 72 |
| Curcumin | Lung Inflammation | Liposomes | Provides anti-inflammatory effects in airway inflammation | 73 |
| Budesonide | Asthma | Liposomes | Improves lung inflammation and reduces toxicity of inhaled steroids | 74 |
| Amikacin | Nontuberculous Mycobacterial Lung Disease | Liposomes | Enhances drug accumulation in lungs and reduces systemic side effects | 75 |

| | | | | | |
|---------------------|------------------------|----------|----------------------------------|--|----|
| Fasudil | Pulmonary Hypertension | Arterial | Starch-Coated Magnetic Liposomes | Enhances absorption in pulmonary artery smooth muscle cells, reducing proliferation | 76 |
| Cisplatin | Lung Cancer | | Liposomes | Enhances drug accumulation in lungs and reduces systemic toxicity | 77 |
| Salbutamol Sulphate | Asthma | | Liposomes | Increases concentration and retention time in lungs, prolonging anti-asthmatic effects | 78 |
| Paclitaxel | Lung Cancer | | Liposomes | Reduces tumour foci in lungs and prolongs survival | 78 |
| Doxorubicin | Lung Cancer | | Liposomes | Extends retention time in lungs and enhances efficacy | 79 |
| Clodronate | Lung Cancer | | Liposomes | Reduces number of macrophages and attenuates tumor cell proliferation | 80 |
| Rivastigmine | Alzheimer's Disease | | Polymeric Nanoparticles | Enhances brain delivery and provides controlled release | 81 |
| Galantamine | Alzheimer's Disease | | PLGA Nanoparticles | Provides sustained drug release and preserves pharmacological activity | 82 |
| Dextrans | Respiratory Diseases | | Octaarginine-Coated Liposomes | Increases intracellular targeting and improves cellular uptake | 83 |

Future Perspectives

Future research is expected to concentrate on the creation of intelligent, stimuli-responsive nanocarriers, bioinspired delivery systems, and integration with digital health technologies as Nanotechnology is steadily transforming the field of transdermal drug delivery systems (TDDS). These new approaches seek to increase patient adherence, accuracy, and therapeutic efficacy.

Smart and Stimuli-Responsive Systems

Stimuli-responsive nanocarriers, which can release medications in response to particular physiological or environmental stimuli like pH, temperature, enzymes, redox potential, light, or ultrasound, will be progressively incorporated into future TDDS. By providing exact spatiotemporal control over medication delivery, these devices reduce systemic side effects and improve therapeutic results.⁸⁴

Combining Wearable Technology with Microneedles

Nanocarriers and microneedle arrays have demonstrated significant potential in enhancing medication penetration while preserving non-invasiveness. By rupturing the stratum corneum, microneedles can create microchannels that enable nano formulations to penetrate deeper.⁸⁵

Gene and Peptide Delivery

Previously thought to be difficult because of problems with molecular size and stability, nanocarrier systems are being developed to trans dermally deliver more sensitive and complex biomolecules, including proteins, nucleic acids, and peptides.⁸⁶

CONCLUSION

Nanotechnology is a revolutionary approach to drug delivery that manipulates materials at the nanoscale to improve therapeutic effectiveness. Nanotechnology is critical in transdermal drug delivery systems (TDDS) because it helps to overcome the skin's natural barrier, notably the stratum corneum, allowing for better drug penetration, prolonged release, and focused action. Nanocarriers such as liposomes, niosomes, solid lipid nanoparticles (SLNs), and nano emulsions have demonstrated substantial advantages in topical formulations, including improved solubility, stability, adverse effects reduction, and bioavailability.

In summary, the table's data offers a varied range of nanotechnology-based formulations, which are categorized systematically by formulation name, targeted disease, nanocarrier type, and mechanism of action. The study emphasizes nanocarriers' developing function in topical drug delivery systems, as well as their growing usefulness in treating a variety of dermatological and systemic disorders.

In the future, nanotechnology in transdermal therapy will be based on the development of smart, stimuli-responsive delivery systems as well as the integration of developing tools like as microneedle arrays and wearable technology. While problems like as regulatory approval, scalability, and long-term safety persist, continued research and innovation are critical to realize the full therapeutic promise of nanotechnology-based transdermal formulations.

REFERENCES

1. Kumar, R., Kumar, M. & Luthra, G. Fundamental approaches and applications of nanotechnology: A mini review. *Mater. Today Proc.* (2023) doi:10.1016/j.matpr.2022.12.172.
2. Bayda, S., Adeel, M., Tuccinardi, T., Cordani, M. & Rizzolio, F. The History of Nanoscience and Nanotechnology: From Chemical–Physical Applications to Nanomedicine. *Molecules* 25, 112 (2019).
3. Barhoum, A. *et al.* Review on Natural, Incidental, Bioinspired, and Engineered Nanomaterials: History, Definitions, Classifications, Synthesis, Properties, Market, Toxicities, Risks, and Regulations. *Nanomaterials* 12, 177 (2022).
4. Hulla, J., Sahu, S. & Hayes, A. Nanotechnology. *Hum. Exp. Toxicol.* 34, 1318–1321 (2015).
5. Joudeh, N. & Linke, D. Nanoparticle classification, physicochemical properties, characterization, and applications: a comprehensive review for biologists. *J. Nanobiotechnology* 20, 262 (2022).
6. Khan, Y. *et al.* Classification, Synthetic, and Characterization Approaches to Nanoparticles, and Their Applications in Various Fields of Nanotechnology: A Review. *Catalysts* 12, 1386 (2022).
7. Sarode, R. J. & Mahajan, H. S. Dendrimers for drug delivery: An overview of its classes, synthesis, and applications. *J. Drug Deliv. Sci. Technol.* 98, 105896 (2024).
8. Wang, J., Li, B., Qiu, L., Qiao, X. & Yang, H. Dendrimer-based drug delivery systems: history, challenges, and latest developments. *J. Biol. Eng.* 16, 18 (2022).
9. Pechnikova, N. A. *et al.* Carbon Quantum Dots in Biomedical Applications: Advances, Challenges, and Future Prospects. *Aggregate* (2024) doi:10.1002/agt2.707.
10. Guan, X. *et al.* Emerging Trends of Carbon-Based Quantum Dots: Nanoarchitectonics and Applications. *Small* 19, (2023).
11. Javaid, M., Haleem, A., Singh, R. P., Rab, S. & Suman, R. Exploring the potential of nanosensors: A brief overview. *Sensors Int.* 2, 100130 (2021).
12. Weeraratna, I. N., Kumar, P., Dzoagbe, H. Y. & Kiwanuka, L. Advancements in Micro/Nanorobots in Medicine: Design, Actuation, and Transformative Application. *ACS Omega* (2025) doi:10.1021/acsomega.4c09806.
13. Zhou, H., Mayorga-Martinez, C. C., Pané, S., Zhang, L. & Pumera, M. Magnetically Driven Micro and Nanorobots. *Chem. Rev.* 121, 4999–5041 (2021).
14. Guo, M., He, Z., He, X. & Song, X. Surface Modification of Liposomes Using Folic Acid. in 191–196 (2023). doi:10.1007/978-1-0716-2954-3_16.
15. Moammeri, A. *et al.* Current advances in niosomes applications for drug delivery and cancer treatment. *Mater. Today Bio* 23, 100837 (2023).
16. Alharbi, W. S. *et al.* Phytosomes as an Emerging Nanotechnology Platform for the Topical Delivery of Bioactive Phytochemicals. *Pharmaceutics* 13, 1475 (2021).
17. Richard, C., Cassel, S. & Blanzat, M. Vesicular systems for dermal and transdermal drug delivery. *RSC Adv.* 11, 442–451 (2021).
18. Qin, H. *et al.* Advances of transdermal drug delivery system based on extracellular vesicles. *J. Drug Deliv. Sci. Technol.* 105, 106647 (2025).
19. Tahir, D., Ardiansyah, A., Heryanto, H., Noor, E. E. M. & Mohamed, M. A. Chitosan-based hydrogels: A comprehensive review of transdermal drug delivery. *Int. J. Biol. Macromol.* 298, 140010 (2025).
20. Jeong, W. Y., Kwon, M., Choi, H. E. & Kim, K. S. Recent advances in transdermal drug delivery systems: a review. *Biomater. Res.* 25, (2021).
21. Vyas, A., Kumar Sonker, A. & Gidwani, B. Carrier-Based Drug Delivery System for Treatment of Acne. *Sci. World J.* 2014, 1–14 (2014).
22. Qu, F., Geng, R., Liu, Y. & Zhu, J. Advanced nanocarrier- and microneedle-based transdermal drug delivery strategies for skin diseases treatment. *Theranostics* 12, 3372–3406 (2022).
23. Tiwari, N. *et al.* Nanocarriers for Skin Applications: Where Do We Stand? *Angew. Chemie Int. Ed.* 61, (2022).
24. Ciftci, F. *et al.* Advances in Drug Targeting, Drug Delivery, and Nanotechnology Applications: Therapeutic Significance in Cancer Treatment. *Pharmaceutics* 17, 121 (2025).
25. Babaie, S., Bakhshayesh, A. R. Del, Ha, J. W., Hamishehkar, H. & Kim, K. H. Invasome: A Novel Nanocarrier for Transdermal Drug Delivery. *Nanomaterials* 10, 341 (2020).
26. Shen, S., Wu, Y., Liu, Y. & Wu, D. High drug-loading nanomedicines: progress, current status, and prospects. *Int. J. Nanomedicine* Volume 12, 4085–4109 (2017).

27. Brito, S., Baek, M. & Bin, B.-H. Skin Structure, Physiology, and Pathology in Topical and Transdermal Drug Delivery. *Pharmaceutics* 16, 1403 (2024).
28. Antonio, J. R., Antonio, C. R., Cardeal, I. L. S., Ballavenuto, J. M. A. & Oliveira, J. R. Nanotechnology in Dermatology. *An. Bras. Dermatol.* 89, 126–136 (2014).
29. Goyal, R., Macri, L. K., Kaplan, H. M. & Kohn, J. Nanoparticles and nanofibers for topical drug delivery. *J. Control. Release* 240, 77–92 (2016).
30. Batheja, P., Sheihet, L., Kohn, J., Singer, A. J. & Michniak-Kohn, B. Topical drug delivery by a polymeric nanosphere gel: Formulation optimization and in vitro and in vivo skin distribution studies. *J. Control. Release* 149, 159–167 (2011).
31. Liu, L. et al. Functional nano-systems for transdermal drug delivery and skin therapy. *Nanoscale Adv.* 5, 1527–1558 (2023).
32. Tapfumaneyi, P., Imran, M., Mohammed, Y. & Roberts, M. S. Recent advances and future prospective of topical and transdermal delivery systems. *Front. Drug Deliv.* 2, (2022).
33. Teklehaimanot, Y. Nanotechnology-Enhanced Controlled Release Systems in Topical Therapeutics. *Precis. Nanomedicine* 7, (2024).
34. Bhardwaj, S., Gaur, P. K. & Tiwari, A. Development of Topical Nanoemulgel Using Combined Therapy for Treating Psoriasis. *Assay Drug Dev. Technol.* 20, 42–54 (2022).
35. Leong, M. Y. et al. Recent Development of Nanomaterials for Transdermal Drug Delivery. *Biomedicines* 11, 1124 (2023).
36. Jansook, P., Fülöp, Z. & Ritthidej, G. C. Amphotericin B loaded solid lipid nanoparticles (SLNs) and nanostructured lipid carrier (NLCs): physicochemical and solid-solution state characterizations. *Drug Dev. Ind. Pharm.* 45, 560–567 (2019).
37. Rosado, C., Silva, C. & Reis, C. P. Hydrocortisone-loaded poly(ϵ -caprolactone) nanoparticles for atopic dermatitis treatment. *Pharm. Dev. Technol.* 18, 710–718 (2013).
38. Gaikwad, S. S., Akalade, N. V. & Salunkhe, K. S. Nanogel Development and its Application in Transdermal Drug Delivery System. *Curr. Nanomedicine* 12, 126–136 (2022).
39. Botha, N. L., Mushonga, P. & Onani, M. O. Review on nanogels and their applications on dermal therapy. *Polym. Polym. Compos.* 31, (2023).
40. Soni, K. S., Desale, S. S. & Bronich, T. K. Nanogels: An overview of properties, biomedical applications and obstacles to clinical translation. *J. Control. Release* 240, 109–126 (2016).
41. S, F., Umashankar, M. S. & Narayanasamy, D. A Comprehensive Review of Nanogel-Based Drug Delivery Systems. *Cureus* (2024) doi:10.7759/cureus.68633.
42. Mohammed, V., Kalarani, I. B. & Veerabathiran, R. Nanomedicine in Neuroscience: An Application Towards the Treatment of Various Neurological Diseases. *Curr. Nanomedicine* 12, 84–92 (2022).
43. Wu, W.-S., Wang, F.-S., Yang, K. D., Huang, C.-C. & Kuo, Y.-R. Dexamethasone Induction of Keloid Regression through Effective Suppression of VEGF Expression and Keloid Fibroblast Proliferation. *J. Invest. Dermatol.* 126, 1264–1271 (2006).
44. Mohammadpour, R. & Ghandehari, H. Mechanisms of immune response to inorganic nanoparticles and their degradation products. *Adv. Drug Deliv. Rev.* 180, 114022 (2022).
45. Lu, H., Zhang, S., Wang, J. & Chen, Q. A Review on Polymer and Lipid-Based Nanocarriers and Its Application to Nano-Pharmaceutical and Food-Based Systems. *Front. Nutr.* 8, (2021).
46. Rungseewijitprapa, W., Yingngam, B. & Chaiyasut, C. Improvement of Biophysical Skin Parameters of Topically Applied Fermented Soybean Extract-Loaded Niosomes with No Systemic Toxicity in Ovariectomized Rats. *Pharmaceutics* 13, 1068 (2021).
47. Mohammadzadeh, M., Rezaei Kakhkha Zhaleh, M., Hamishehkar, H. & Talebi, A. Effect of Testosterone and Antioxidant-Loaded Nanoliposomes on the Performance of Normozoospermic Samples: A Case-Control Study. *Int. J. Basic Sci. Med.* 9, 15–24 (2024).
48. Lin, X. et al. Inhibition of Neovascularization and Inflammation in a Mouse Model of Corneal Alkali Burns Using Cationic Liposomal Tacrolimus. *Front. Bioeng. Biotechnol.* 9, (2021).
49. Valencia-Lazcano, A. A. et al. 5-Fluorouracil nano-delivery systems as a cutting-edge for cancer therapy. *Eur. J. Med. Chem.* 246, 114995 (2023).
50. Bhattacharyya, S. & Nanjareddy, L. Assessment of Nano Lipid Carrier Loaded Transdermal Patch of Rizatriptan Benzoate. *Drug Metab. Bioanal. Lett.* 15, 101–115 (2022).
51. Uchida, N., Yanagi, M. & Hamada, H. Physical Enhancement? Nanocarrier? Current Progress in Transdermal Drug Delivery. *Nanomaterials* 11, 335 (2021).
52. Djabri, A., Guy, R. H. & Delgado-Charro, M. B. Transdermal iontophoresis of ranitidine: An opportunity in paediatric drug therapy. *Int. J. Pharm.* 435, 27–32 (2012).
53. Nawaz, A. et al. Formulation and Characterization of Ethyl Cellulose-Based Patches Containing Curcumin-Chitosan Nanoparticles for the Possible Management of Inflammation via Skin Delivery. *Gels* 9, 201 (2023).

54. Raszevska-Famielec, M. & Flieger, J. Nanoparticles for Topical Application in the Treatment of Skin Dysfunctions—An Overview of Dermo-Cosmetic and Dermatological Products. *Int. J. Mol. Sci.* 23, 15980 (2022).
55. Giuli, M. V. et al. Current Trends in ATRA Delivery for Cancer Therapy. *Pharmaceutics* 12, 707 (2020).
56. Hasanovic, A., Zehl, M., Reznicek, G. & Valenta, C. Chitosan-tripolyphosphate nanoparticles as a possible skin drug delivery system for aciclovir with enhanced stability. *J. Pharm. Pharmacol.* 61, 1609–1616 (2009).
57. Koppa Raghu, P. et al. Evolution of Nanotechnology in Delivering Drugs to Eyes, Skin and Wounds via Topical Route. *Pharmaceutics* 13, 167 (2020).
58. Alnaim, A. S. Nanocrystals in Dermal Drug Delivery: A Breakthrough for Enhanced Skin Penetration and Targeted Skin Disorder Treatments. *Pharmaceutics* 16, 1561 (2024).
59. Berkowitz, R. D., Mack, R. J. & McCallum, S. W. Meloxicam for Intravenous Use: Review of its Clinical Efficacy and Safety for Management of Postoperative Pain. *Pain Manag.* 11, 249–258 (2021).
60. Pireddu, R. et al. Novel nanosized formulations of two diclofenac acid polymorphs to improve topical bioavailability. *Eur. J. Pharm. Sci.* 77, 208–215 (2015).
61. Parmar, P. K. & Bansal, A. K. Novel nanocrystal-based formulations of apremilast for improved topical delivery. *Drug Deliv. Transl. Res.* 11, 966–983 (2021).
62. Tekko, I. A. et al. Localised and sustained intradermal delivery of methotrexate using nanocrystal-loaded microneedle arrays: Potential for enhanced treatment of psoriasis. *Eur. J. Pharm. Sci.* 152, 105469 (2020).
63. Tomić, I. et al. Preparation of in situ hydrogels loaded with azelaic acid nanocrystals and their dermal application performance study. *Int. J. Pharm.* 563, 249–258 (2019).
64. Ahmed, I. S., Elnahas, O. S., Assar, N. H., Gad, A. M. & El Hosary, R. Nanocrystals of Fusidic Acid for Dual Enhancement of Dermal Delivery and Antibacterial Activity: In Vitro, Ex Vivo and In Vivo Evaluation. *Pharmaceutics* 12, 199 (2020).
65. Shen, C., Shen, B., Liu, X. & Yuan, H. Nanosuspensions based gel as delivery system of nitrofurazone for enhanced dermal bioavailability. *J. Drug Deliv. Sci. Technol.* 43, 1–11 (2018).
66. Gao, L. et al. Evaluation of genipin-crosslinked chitosan hydrogels as a potential carrier for silver sulfadiazine nanocrystals. *Colloids Surfaces B Biointerfaces* 148, 343–353 (2016).
67. Garg, A. K. et al. Solubility enhancement, formulation development and antifungal activity of luliconazole niosomal gel-based system. *J. Biomater. Sci. Polym. Ed.* 32, 1009–1023 (2021).
68. Assem, M., Khowessah, O. M. & Ghorab, D. Nano-crystallization as a tool for the enhancement of beclomethasone dipropionate dermal deposition: Formulation, in vitro characterization and ex vivo study. *J. Drug Deliv. Sci. Technol.* 54, 101318 (2019).
69. Parveen, N., Abourehab, M. A. S., Thanikachalam, P. V., Khar, R. K. & Kesharwani, P. Nanocrystals as an emerging nanocarrier for the management of dermatological diseases. *Colloids Surfaces B Biointerfaces* 225, 113231 (2023).
70. Giradkar, V., Mhaske, A. & Shukla, R. Nanocrystals: A Multifaceted Regimen for Dermatological Ailments. *Part. Part. Syst. Charact.* 41, (2024).
71. Ghasemiyeh, P. & Mohammadi-Samani, S. Potential of Nanoparticles as Permeation Enhancers and Targeted Delivery Options for Skin: Advantages and Disadvantages. *Drug Des. Devel. Ther.* Volume 14, 3271–3289 (2020).
72. Kapoor, A., Hafeez, A. & Kushwaha, P. Nanocarrier Mediated Intranasal Drug Delivery Systems for the Management of Parkinsonism: A Review. *Curr. Drug Deliv.* 21, 709–725 (2024).
73. Ng, Z. Y. et al. Assessing the potential of liposomes loaded with curcumin as a therapeutic intervention in asthma. *Colloids Surfaces B Biointerfaces* 172, 51–59 (2018).
74. Konduri, K. S., Nandedkar, S., Rickaby, D. A., Düzgüneş, N. & Gangadharam, P. R. J. The Use of Sterically Stabilized Liposomes to Treat Asthma. in 413–427 (2005). doi:10.1016/S0076-6879(05)91023-9.
75. Olivier, K. N. et al. Randomized Trial of Liposomal Amikacin for Inhalation in Nontuberculous Mycobacterial Lung Disease. *Am. J. Respir. Crit. Care Med.* 195, 814–823 (2017).
76. Nahar, K., Absar, S., Patel, B. & Ahsan, F. Starch-coated magnetic liposomes as an inhalable carrier for accumulation of fasudil in the pulmonary vasculature. *Int. J. Pharm.* 464, 185–195 (2014).
77. Wittgen, B. P. H. et al. Phase I Study of Aerosolized SLIT Cisplatin in the Treatment of Patients with Carcinoma of the Lung. *Clin. Cancer Res.* 13, 2414–2421 (2007).
78. Luo, M.-X., Hua, S. & Shang, Q.-Y. Application of nanotechnology in drug delivery systems for respiratory diseases (Review). *Mol. Med. Rep.* 23, 325 (2021).
79. Kim, I. et al. Doxorubicin-loaded highly porous large PLGA microparticles as a sustained- release inhalation system for the treatment of metastatic lung cancer. *Biomaterials* 33, 5574–5583 (2012).
80. Mochalova, E. N. et al. Comparative Study of Nanoparticle Blood Circulation after Forced Clearance of Own Erythrocytes (Mononuclear Phagocyte System-Cytoblockade) or Administration of Cytotoxic

- Doxorubicin- or Clodronate-Loaded Liposomes. *Int. J. Mol. Sci.* 24, 10623 (2023).
81. Rompicherla, S. K. L., Arumugam, K., Bojja, S. L., Kumar, N. & Rao, C. M. Pharmacokinetic and pharmacodynamic evaluation of nasal liposome and nanoparticle based rivastigmine formulations in acute and chronic models of Alzheimer's disease. *Naunyn. Schmiedeberg's. Arch. Pharmacol.* 394, 1737–1755 (2021).
82. Sadiq, A. H. et al. Enhancing Galantamine Distribution in Rat Brain Using Microplasma-Assisted Nose-to-Brain Drug Delivery. *Int. J. Mol. Sci.* 26, 1710 (2025).
83. Lin, L. et al. Vascular Endothelial Growth Factor A Contributes to Increased Mammalian Respiratory Epithelial Permeability Induced by *Pasteurella multocida* Infection. *Microbiol. Spectr.* 11, (2023).
84. Mi, P. Stimuli-responsive nanocarriers for drug delivery, tumor imaging, therapy and theranostics. *Theranostics* 10, 4557–4588 (2020).
85. Yu, J. et al. Microneedle-array patches loaded with hypoxia-sensitive vesicles provide fast glucose-responsive insulin delivery. *Proc. Natl. Acad. Sci.* 112, 8260–8265 (2015).
86. Gupta, M., Agrawal, U. & Vyas, S. P. Nanocarrier-based topical drug delivery for the treatment of skin diseases. *Expert Opin. Drug Deliv.* 9, 783–804 (2012).