World Journal of Pharmaceutical and Life Sciences

www.wjpls.org

Impact Factor: 8.21 Coden USA: WJPLA7

NANOCARRIER-BASED DELIVERY OF MINOXIDIL: CURRENT PERSPECTIVES AND FUTURE DIRECTIONS IN ALOPECIA THERAPY

Sukhpreet Kaur*[1], Gurpreet Kaur[2], Lekesh Kumar[3]

[1,2,3]School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh.

***Corresponding Author: Sukhpreet Kaur**

School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh.

DOI: https://doi.org/10.5281/zenodo.19883346

How to cite this Article: Sukhpreet Kaur*[1], Gurpreet Kaur[2], Lekesh Kumar[3]. (2026). Nanocarrier-Based Delivery of Minoxidil: Current Perspectives And Future Directions In Alopecia Therapy. World Journal of Pharmaceutical and Life Sciences, 12(5), 04–15.

Article Received on 24/03/2026 **Article Revised on 15/04/2026** **Article Published on 01/05/2026**

ABSTRACT

The predominant type of hair loss, androgenetic alopecia (AGA), is genetically inherited and primarily affects the frontal and central scalp. AGA develops when the enzyme 5-Alpha Reductase (5-AR) converts testosterone to Dihydrotestosterone (DHT), leading to shrinking hair follicles. Currently, the FDA has approved finasteride and minoxidil for treatment, but their limitations have prompted investigation into advanced drug delivery methods. Nanocarriers such as liposomes, solid lipid nanoparticles, and transferosomes show potential for targeted delivery in treating AGA. They enhance drug stability, target delivery, and sustained release while reducing systemic exposure. Innovations like antioxidant formulations and spironolactone-loaded nanoparticles aim to combat AGA by reducing oxidative stress and blocking androgen receptors. Despite promising preclinical results, challenges in clinical translation include the need for reliable trials, funding, and regulatory approval. This review underscores the necessity for clinical validation and scalable production in realizing the transformative potential of nanotechnology for AGA treatment.

KEYWORDS: Androgenetic alopecia, Nanotechnology, Nanostructured lipid carriers, Liposomes, Polymeric nanoparticles, Transferosomes, Drug delivery.

1. INTRODUCTION

Alopecia, commonly referred to as hair loss, is a multifactorial condition affecting millions of individuals worldwide, leading not only to aesthetic concerns but also to profound psychological distress. Among the various forms, androgenetic alopecia (AGA) is the most prevalent, accounting for over 90% of hair loss cases in both men and women (Trueb, 2017). Other variants, including alopecia areata and telogen effluvium, are also widespread, further highlighting the growing clinical importance of effective therapeutic interventions. Despite the availability of multiple treatment strategies, topical minoxidil remains the first-line pharmacological agent approved by the U.S. Food and Drug Administration (FDA) for alopecia management (Suchonwanit et al., 2019).

Minoxidil, a piperidinopyrimidine derivative, was originally developed as an oral antihypertensive agent due to its potent vasodilatory action. Serendipitously, patients treated with oral minoxidil exhibited hypertrichosis, which led to the development of its topical formulations for alopecia treatment (Vañó-Galván et al., 2018). The drug acts primarily by opening ATP-sensitive potassium (K^+) channels, enhancing blood flow to hair follicles, and stimulating follicular cell proliferation. It also promotes vascular endothelial growth factor (VEGF) expression and prolongs the anagen (growth) phase of the hair cycle, resulting in improved hair density and thickness (Randall et al., 2019).

Despite its proven efficacy, the therapeutic performance of conventional topical minoxidil formulations is limited by multiple challenges. The drug exhibits poor aqueous solubility, low permeability across the stratum corneum, and rapid clearance from the scalp surface, leading to suboptimal drug retention and inconsistent therapeutic

outcomes (Torky et al., 2021). The commonly used hydroalcoholic vehicle (ethanol–propylene glycol–water) may enhance penetration but often causes irritation, dryness, and dermatitis, reducing patient compliance (Lalloo et al., 2020). Furthermore, the conventional solution fails to achieve sufficient follicular targeting, which is crucial since hair follicles act as a primary drug reservoir and entry route for transdermal absorption.

Recent advances in nanotechnology have opened new frontiers for optimizing minoxidil delivery. Nanocarrier-based systems offer distinct advantages, including enhanced solubility, increased follicular penetration, controlled release, and improved scalp retention (Ghosh et al., 2020). These systems enable localized delivery of minoxidil directly to the hair follicles, minimizing systemic absorption and side effects. Various nanocarriers such as liposomes, niosomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), polymeric nanoparticles, and nanoemulsions have been extensively explored to overcome the pharmacokinetic limitations of conventional formulations (Sutradhar & Amin, 2021). The nanoscale size, large surface area, and tunable physicochemical properties of these systems contribute to better interaction with scalp lipids and follicles, thus enhancing the therapeutic efficacy of minoxidil.

Moreover, nanocarrier-based formulations can be engineered for sustained or controlled release, allowing longer drug residence at the target site and reducing the frequency of application. Studies have demonstrated that lipid-based nanocarriers enhance minoxidil retention within the follicular ducts, while polymeric nanoparticles offer gradual release, maintaining effective drug concentration over an extended period (Singh et al., 2022). The incorporation of nanotechnology into alopecia therapy therefore represents a promising step toward improving both efficacy and patient adherence.

2. Pharmacological Profile and Mechanism of Action of Minoxidil

Properties	Details
Name	Minoxidil (MXD)
CAS Registration Number	38304-91-5
CID	4201
Category	Antihypertensives & Vasodilator
LD50	1321-3492mg/kg
Molecular formula	$C_9H_{15}N_5O$
Relative molecular mass	219.31 g/mol
Log P	3.0
pKa	4.61(at25℃)
Solubility	Soluble in Alcohol and in Propylene Glycol; soluble in Methanol; slightly soluble in Water; practically insoluble in Chloroform, in Acetone, in Ethyl Acetate And in Hexane.
Water solubility	100%Ethanol(29mg/ml), Acetone(25mg/ml), Propylene glycol(12mg/ml), Methanol(10mg/ml), DMSO (6.5mg/ml), and, Water(2.2mg/ml).
BCS Class	III
Melting point	248
Storage	2-8℃,protectfromlight
Color	White
Synonyms	Loniten, Rogaine, MXDum, Alopexil,
Dosage forms	Tablet, Topical Solutions, Foams

Minoxidil, chemically known as 2,4-diamino-6-piperidinopyrimidine 3-oxide, is a potent vasodilator originally introduced for the treatment of hypertension. Its unexpected hypertrichotic effect in patients led to its repositioning as a therapeutic agent for alopecia. The pharmacological action of minoxidil is closely linked to its ability to enhance hair follicle activity, prolong the anagen phase, and stimulate follicular proliferation (Suchonwanit et al., 2019).

2.1 Pharmacokinetic and Physicochemical Properties

Minoxidil is a weak base (pKa ≈ 4.6) and exhibits low aqueous solubility (~2 mg/mL), which limits its efficient penetration through the stratum corneum, the primary barrier of the scalp (Lalloo et al., 2020). When applied topically, only 1–2% of the dose typically penetrates the skin, resulting in limited drug availability at the follicular site (Torky et al., 2021). The drug is metabolized in the liver to its active form, minoxidil sulfate, via sulfotransferase enzymes (SULT1A1). However, the expression level of these enzymes varies among individuals, influencing treatment responsiveness (Vañó-Galván et al., 2018).

The short half-life (4–6 hours) and rapid clearance of minoxidil from the scalp necessitate twice-daily

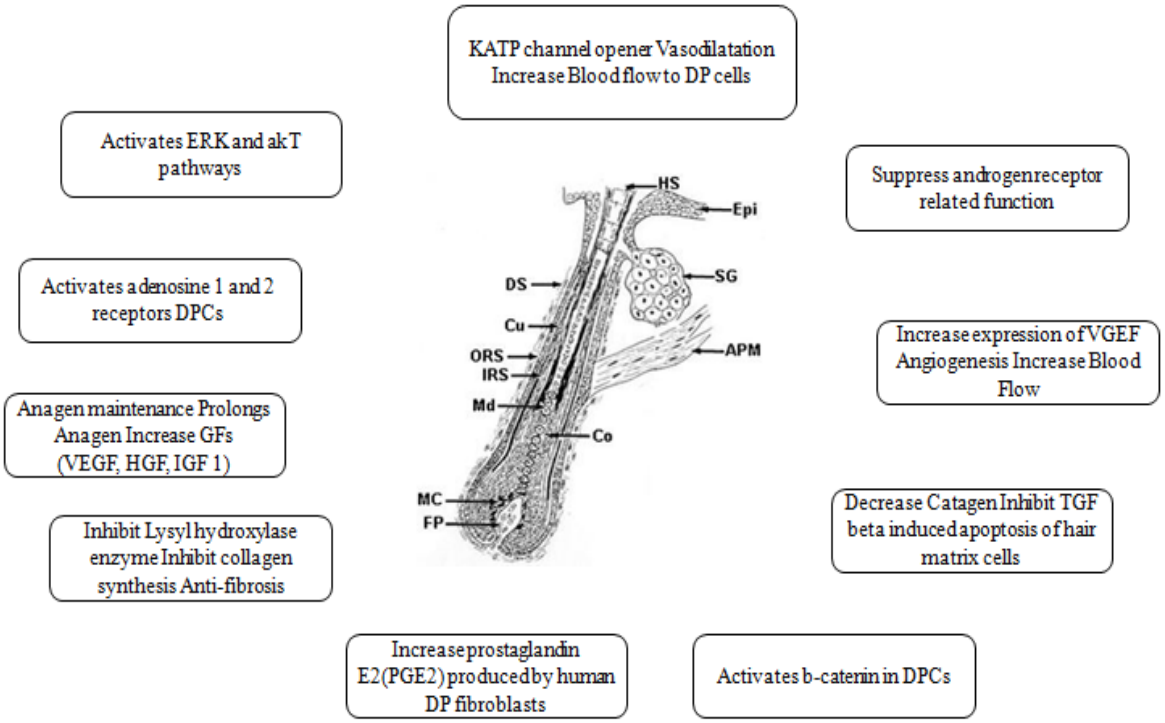
application, which often compromises patient compliance. Additionally, its limited scalp retention and high volatility contribute to low bioavailability and suboptimal therapeutic outcomes. These pharmacokinetic limitations have driven the exploration of nanotechnology-based systems that can enhance its solubility, scalp adhesion, and controlled release profile.

2.2 Mechanism of Action in Hair Growth Stimulation

The mechanism by which minoxidil promotes hair growth is multifactorial and not yet fully elucidated. However, several well-established biochemical and physiological pathways have been proposed (Randall, 2019; Trueb, 2017):

1. Vasodilation and Enhanced Follicular Blood Flow

MXD is proposed to promote the survival of human dermal papillary cells (DPCs) or hair cells by activating both extracellular signal-regulated kinase (ERK) and Akt and by preventing cell death by increasing the ratio of BCl2/Bax. MXD may stimulate the growth of human hairs by prolonging anagen through these proliferative and antiapoptotic effects on DPCs. MXD, when used as a vasodilator, acts by opening adenosine triphosphate-sensitive potassium channels in vascular smooth muscle cells. This vasodilation may also improve the viability of hair cells or hair follicles (Sattur and Sattur 2021).



2. Pharmacodynamics

MXD is an orally effective direct acting peripheral vasodilator that reduces elevated systolic and diastolic blood pressure by decreasing peripheral vascular resistance. MXD is also used topically to treat androgenetic alopecia (Wester, Maibach et al. 1984). Microcirculatory blood flow in animals is enhanced or forearm blood flow increases while renal blood flow and glomerular filtration rate are preserved. The predominant site of MXD action is arterial. However, Vasodilation does not occur with MXD (Clissold and Heel 1987).

2.3 Limitations of Conventional Minoxidil Formulations

Minoxidil is a major treatment for alopecia, yet traditional formulations have notable drawbacks. Low follicular targeting hampers its efficacy, as much is lost on the scalp surface or evaporates before reaching hair follicles. Moreover, minoxidil's poor solubility and chemical instability in aqueous conditions limit effective dose delivery. Scalp irritation and dermatitis are common adverse effects due to the ethanol-propylene glycol base used, impacting patient adherence. The short retention time on the scalp necessitates frequent applications, complicating consistent use. Individual variability in enzymatic conversion to the active metabolite limits therapeutic response. Addressing these issues requires innovative nanocarrier formulations to improve solubility, release control, follicular penetration, and reduce adverse reactions.

3. Nanocarrier-Based Drug Delivery Systems for Minoxidil

Conventional topical formulations of minoxidil often suffer from limited scalp penetration, poor follicular localization, and short residence time, which restrict therapeutic efficiency. To overcome these challenges, nanocarrier-based drug delivery systems have been

developed to enhance the bioavailability, controlled release, and follicular targeting of minoxidil. These nanocarriers improve physicochemical stability, reduce systemic absorption, and ensure localized, sustained drug action (Sutradhar & Amin, 2021).

Nanocarrier systems are engineered at the nanometer scale (10–1000 nm) and are capable of encapsulating lipophilic or hydrophilic drugs while modulating their pharmacokinetic behavior. The most studied systems for minoxidil delivery include liposomes, niosomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), polymeric nanoparticles, and nanoemulsions.

Sr. No.	Formulation	Inference	Reference
1	Prepared nanotechnology- based Minoxidil cubosomes by melt dispersion emulsification technique	To increase penetration and deposition of the drug in the skin while minimizing its adverse reactions with alcohol And propylene glycol.	(Santos, Pereira-Silva et al. 2020)
2	Nanotechnology-based formulation For transdermal delivery of minoxidil	The potential use was limited by its low drug content (*DC*) and entrapment efficiency(*EE*)	(Baptista 2018)
3	MXD/HP-β-CDGEL, Alginate Gel, Solid inclusion complex between hydroxypropyl-β-cyclodextrin (HP-β-CD) And minoxidil (MXD prepared by freeze drying.	Enhanced minoxidil delivery to hair follicles and safety	(Tricarico, Maqoudetal. 2018)
4	Minoxidil nanovesicles with oleic acid	Enhanced follicular delivery and reduced side effects, the follicular deposition of MXD was10-foldhigher for vesicular Gel than the control	(Kumar, Singh et al. 2018)
5	Developed topical gel of minoxidil using model polymers such as Hydroxypropyl methylcellulose, K4M (HPMC K4M) and Hydroxypropyl cellulose (HPC) at different concentrations(1,2 and 3%) individually and in Combination	This combination offers advantages of enhanced stability, controlled release, and improved penetration for effective treatment.	(Parhi, Terapalli et al. 2014)
6	Minoxidil Emulgels	Safe topical delivery systems For the Treatment of androgenic alopecia	(Mathewand Saral 2024)
7	Microneedles coated with Minoxidil	Enhance permeation of drug with the aid of micro needles, thus reducing the concentration of alcohol and damage of scalp Cells	(Kim, Seonget al. 2022)
8	Microemulsions and Microemulsion based Hydrogel systems (MEHs)	Increased percutaneous penetration of minoxidil	(Sunitha, Jitendra et al. 2013)
9	Minoxidil gel for enhanced topical drug delivery. Formulations were prepared by using Natrosol, Carbopol 974 and HPMC K100 (hydroxylpropylmethyl cellulose) as viscosity Enhancing agents	Provides superior topical drug delivery through improved stability, viscosity, and controlled release	(Gupta, Shahi et al. 2012)
10	Minoxidil foamable emu oil Emulsion	Reduce skin irritation and Increase patient compliance	(Shatalebi and Rafiei2014)
11	Minoxidil vesicles, double emulsions, and an inclusion complex with hydoxypropyl-β-cyclodextrin (HP-β-CD)	Skin retention studies, Retention was the highest when the drug was encapsulated in cationic vesicles	(Kim, Lee et al. 2003)
12	Minoxidil complex (minoxidil, methyl-β-cyclodextringel)with calcium alginate, sodium alginate, carbopol 934 and hydroxyethylcellulose	Best performance was observed For the calcium alginate formulation	(Lopedota, Cutrignelli et al. 2015)
13	Nanostructured lipid carrier (NLC) Minoxidil gel	Minoxidil-NLC were prepared using solid and liquid lipids with Cholesterol and Soya lecithin in different concentrations by the melt dispersion ultrasonication, Faster onset yet prolonged action as evident from *in-Vitro* release	(Silva, Santos et al. 2009)

Topical marketed formulations of MXD

The only topical drug approved by the FDA to treat androgenetic alopecia (AGA), a frequent cause of hair loss in both men and women, is minoxidil (MXD). Topical MXD formulations that are now on the market are usually aqueous solutions with 2% or 5% minoxidil by weight as depicted. Twice a day, these compositions are applied straight to the scalp. Traditional MXD

formulations have drawbacks, even though they work well for some individuals. These include low penetration through the scalp, which reduces efficacy, the solvent base's potential to cause scalp irritation, and a very short half-life that requires frequent application. These drawbacks emphasize the necessity of developing better topical administration methods for minoxidil in order to maximize its therapeutic potential for the treatment of AGA.

Brand Name	Constituents	Minoxidil (%)	Type of Formulation	Mechanis m of Action	Uses	Side Effects
Mintop Forte5% Solution	Minoxidil	5%	Topical solution	Vasodilator (increases Blood flow)	Male pattern baldness	Temporary hair fall, scalp irritation
Men's Rogaine 2%,5% Aerosol	Minoxidil	2%, 5%	Aerosol	Vasodilator (increases blood flow)	Male pattern baldness	Chest pain, rapid heartbeat, dizziness, weight gain, scalp irritation, unwanted facial hair growth
Equate2%, 5%topical solution	Minoxidil	2%, 5%	Topical solution	Vasodilator (increases Blood flow)	Male pattern baldness	Scalp irritation (alcohol)
Inoxi10% Solution	Minoxidil	10%	Topical solution	Vasodilator (increases Blood flow)	Male pattern baldness	Not evaluated for women and Children
Inoxi Forte 5%Lotion	Minoxidil	5%	Lotion	Vasodilator (increases blood flow)	Androgenic alopecia; Hereditary hair loss problems	Increased heart rate, chest pain, breast tenderness, palpitations
Minch3%, 12.5%(w/v)	Minoxidil	3%, 12.5%	Topical solution	Vasodilator (increases blood flow)	Male pattern baldness	Scalp irritation, itching, headache
Radixil 2%, 5%,10%	Minoxidil	2%, 5%, 10%	Topical solution	Vasodilator (increases blood flow)	Male pattern baldness	Irregular heartbeat, weight gain, shortness of breath, skin redness, eye Irritation
Pilogro	Minoxidil	2%, 5%	Topical solution	Vasodilator (increases blood flow)	Male pattern baldness	Sleepiness, shortness of breath, chest pain, weight gain, Irregular heartbeat
Regero	Minoxidil	2%	Topical solution	Vasodilator (increases blood flow)	Male pattern baldness	Itching, headache, irritation, chest pain, unwanted hair growth, swollen hands and Feet
Retreat	Minoxidil	5% (w/w)	Topical gel	Vasodilator (increases blood flow)	Male pattern baldness	Scalp irritation
Stonark	Minoxidil	5% (w/v)	Solution	Vasodilator (increases Blood flow)	Male pattern baldness	Not evaluated
Ximinox	Minoxidil	2%, 5%	Lotion	Vasodilator (increases	Male pattern	Irritation, itching,

				Blood flow)	baldness	Headache
Gaine Hair	Minoxidil	2%	Topical solution	Vasodilator (increases blood flow)	Male pattern baldness	Headache, allergic reaction, rashes on the skin, chest Pain
Hair4U2% Lotion	Minoxidil	2% w/v + Diaminopy ridineoxide1.5% w/v	Lotion	Not evaluated	Male pattern baldness	Headache, skin rashes, edema, dermatitis
Hair4U Spray	Minoxidil	2%, 5%, 10% + Diaminopy ridineoxide1.5%	Spray	Not evaluated	Male pattern baldness	Headache, skin rashes, edema, dermatitis
RadixilA	Minoxidil	5% + Diaminopy ridine 1.5	Topical solution	Not evaluated	Male pattern baldness	Redness, dryskin, change in hair Color and texture
RadixilF	Minoxidil	5% + 0.1% Finasteride	Topical solution	Not evaluated	Male pattern baldness	Redness, dryskin, change in hair Color and texture
Stonark-AX	Minoxidil	2% w/w + Diaminopy ridineoxide1.5% w/w	Topical solution	Not evaluated	Male pattern baldness	Not evaluated
Stonark-2AX	Minoxidil	2%w/v+ Aminexil 1.5% w/v	Topical solution	Not evaluated	Male pattern baldness	Notevaluated
Hairslim-F Topical Solution	Minoxidil	5% w/v + Finasteride 0.1% w/v	Topical solution	Not evaluated	Male pattern baldness	Dryskin, tingling, headache, dermatitis, erythema, Dizziness
Keshgaine-5%	Minoxidil	5%	Solution	Not evaluated	Male pattern baldness	Not evaluated
Regenepure Precision Minoxidil 5%Spray	Minoxidil	5%	Spray	Not evaluated	Male pattern baldness	Not evaluated
MX-2 Solution	Minoxidil	2%	Solution	Vasodilator (increases blood flow)	Male pattern baldness	Not evaluated
Coverit5%	Minoxidil	5%	Solution	Vasodilator (increases blood flow)	Male pattern baldness	Skin redness, weight gain, headache, Irregular heart rate
Exidil5% Solution	Minoxidil	5%	Solution	Vasodilator (increases bloodflow)	Male pattern baldness	Not evaluated
Rootz5% Solution	Minoxidil	5%	Solution	Vasodilator (increases blood flow)	Male pattern baldness	Not evaluated
Tinfal	Minoxidil	5% (w/v)	Solution	Vasodilator (increases bloodflow)	Male pattern baldness	Not evaluated
Tinfal Plus	Minoxidil	5% +	Solution	Not	Male	Not evaluated

		Aminexil 1.5%		evaluated	pattern baldness	
Lipogaine (Men)	Minoxidil	5% with Biotinyl-tripeptide, Niacin, Apple Polyphenol	Serum	Not evaluated	Male pattern baldness	Not evaluated
Lipogaine (Women)	Minoxidil	2%	Serum	Not evaluated	Female pattern baldness	Not evaluated
Imxia	Minoxidil	5%	Solution	Vasodilator (increases Blood flow)	Male pattern baldness	Not evaluated
Minokem	Minoxidil	2%, 5% (60 mL)	Spray	Vasodilator (increases Blood flow)	Male pattern baldness	Weight gain, eye irritation, chest pain, skin redness
Minotreat	Minoxidil	5%	Lotion	Vasodilator (increases Blood flow)	Male pattern baldness	Not evaluated
Proanagen Solution	Diaminopyrimidine oxide topical solution (1.5%)	1.50%	Solution	Not evaluated	Hair loss due to premature exhaustion of hair root	Not evaluated
Keraglo Eva	Biotin (10mg), Folic Acid (300mcg), Selenium(40 mcg), Gamma Linolenic Acid	-	Tablets	Not applicable	Hair loss	No side effects reported at appropriate doses

5. Mechanistic Insights: How Nanocarriers Enhance Minoxidil Delivery

Nanocarriers have emerged as a transformative strategy for enhancing the topical delivery of Minoxidil (MNX), particularly for the treatment of conditions such as Androgenetic alopecia. Through tailoring size, surface properties, and release profiles, nanocarriers overcome many of the limitations associated with conventional formulations. The mechanistic underpinnings of how they achieve improved MNX delivery can be grouped into five phenomena: reduced particle size and diffusion, increased surface area and contact, occlusive film formation, controlled-release kinetics, and follicular targeting.

Firstly, the dramatic reduction in particle size inherent to nanocarriers enables more efficient diffusion through both intercellular and follicular pathways. Conventional MNX topical formulations often struggle to penetrate effectively via the stratum corneum, leading to sub-optimal drug delivery and retention. Nanoparticles, by virtue of their diminutive dimensions, are better able to navigate between corneocytes and enter the hair follicle canal, bypassing or reducing the barrier effect of the outer skin layers. For example, the review by Santos et al. (2020) highlights that MNX-loaded nanotechnology formulations can accumulate in hair follicles via the trans-appendageal route.

Secondly, nanocarriers provide dramatically increased surface area relative to bulk delivery systems. This enhanced surface contact translates into improved drug–tissue interaction, greater solubilisation of the lipophilic MNX, and better wetting and adhesion to scalp tissue. The higher interface area enhances solubility and facilitates closer contact with the skin and follicular epithelium, thereby improving uptake and bioavailability. As a broader formulation principle, nanocarriers outperform traditional dosage forms by virtue of their high surface-to-volume ratios.

Thirdly, some nanocarriers form semi-occlusive or occlusive films on the scalp surface, which then enhance local hydration and prolong the residence of the formulation. When applied topically, an occlusive film reduces transepidermal water loss, swells the stratum corneum, increases its permeability, and hence increases drug retention in local tissue. In the context of MNX delivery, the lipid-based nanoparticles (such as solid lipid nanoparticles, SLNs, or nanostructured lipid carriers, NLCs) can reorganise the lipids in the stratum corneum, enhance hydration, and lead to depot formation within the skin. For example, MNX-loaded NLCs

showed enhanced in-vitro skin retention in ex-vivo models.

Fourthly, nanocarriers can be engineered to release MNX in a controlled fashion rather than the rapid burst typical of simple solutions or conventional gels. Controlled release kinetics mean that the drug is gradually liberated over a longer period, maintaining effective local concentrations for extended times, reducing dosing frequency, and potentially lessening systemic absorption or local irritation. In topical hair-loss therapy, sustained release means that MNX remains present at the follicular site for longer, increasing exposure of the follicular dermal papilla cells and enhancing therapeutic effect. Santos et al. (2020) describe how MNX-nanocarrier systems allowed depot formation in the follicles and prolonged action.

Finally, nanocarriers enable improved follicular targeting due to a combination of size, surface charge, and other physicochemical properties. The hair follicle offers a "shortcut" pathway to deeper skin layers. Nanoparticles in optimal size ranges may preferentially accumulate in follicles rather than dispersing across the broader skin surface. Additionally, electrostatic interactions (for example, positively charged carriers interacting with the slightly negative follicular duct environment) can enhance retention. The review by Andrade et al. (2025) emphasises this capacity of nanocarriers to deliver MNX into follicles and thereby improve localisation of drug deposition.

Integrating these mechanisms, we see a coordinated enhancement of topical MNX therapy: smaller particles reach deeper and more directly; increased surface area enhances solubilisation and contact; occlusive behaviour improves retention; controlled release sustains local concentrations; and follicular-targeting ensures drug is delivered where it matters most. These effects combined promise greater efficacy, fewer side-effects, and potentially lower doses of MNX. Nevertheless, it's important to recognise the challenges: for example, many studies on MNX-nanocarriers have not fully quantified follicular vs interfollicular drug accumulation, and long-term safety of these nano-systems remains under-explored (Andrade et al., 2025).

6. Comparative Evaluation of Nanocarrier Systems

Nanocarrier System	Key Feature	Main Advantage	Limitation
Liposomes	Phospholipid vesicles	Biocompatible and effective for deep penetration	Instability and high cost
Niosomes	Non-ionic surfactant vesicles	Cost-effective and stable	Limited hydrophobic drug loading
SLNs	Solid lipid core	Controlled release and occlusive effect	Low drug loading
NLCs	Solid + liquid lipid blend	Higher loading and sustained action	Formulation complexity
Polymeric Nanoparticles	Polymer-based matrix	Controlled and targeted release	Expensive and possible toxicity
Nanoemulsions	Oil-in-water dispersion	High solubility and cosmetic appeal	Risk of surfactant irritation

7. Safety, Toxicity, and Regulatory Considerations

Safety, toxicity, and regulatory considerations are critical aspects in the development of lipid and polymeric nanocarriers for topical applications. A comprehensive safety evaluation is essential to ensure that these nanocarriers do not induce adverse effects upon skin contact or systemic absorption. Commonly employed in vitro assays such as the MTT assay and LDH release test assess cytotoxicity by evaluating cell viability and membrane integrity, respectively. Additionally, skin irritation tests using reconstructed human epidermis models or animal skin help determine dermal compatibility. Long-term safety concerns focus on the biodegradability and biocompatibility of carrier materials, as incomplete degradation or accumulation may lead to inflammatory or immunogenic responses. Despite their potential benefits, the absence of standardized testing and regulatory guidelines for nanocarriers in topical formulations presents significant challenges. Moreover, differentiating between cosmetic and pharmaceutical classifications adds complexity, as regulatory pathways vary in stringency depending on the intended use and therapeutic claims. Therefore, harmonized international regulations and validated testing protocols are urgently needed to ensure the safe and effective use of nanocarrier-based formulations in dermatological and cosmetic applications.

8. Future Directions and Emerging Trends

Future directions and emerging trends in minoxidil nanoformulations focus on advancing efficacy, safety, and sustainability. Green nanotechnology is gaining attention through the use of plant-derived surfactants and lipids to create eco-friendly, biocompatible carriers that minimize toxicity and environmental impact. The development of 3D follicular modeling represents another significant innovation, enabling predictive in vitro testing of drug penetration and follicular uptake

before clinical trials. Additionally, integrating minoxidil delivery with bioactive molecules such as growth factors or stem cell-derived exosomes offers synergistic effects that can enhance hair follicle regeneration and prolong the anagen phase. Smart nanocarriers responsive to physiological stimuli like pH or temperature are being explored for on-demand, controlled drug release, optimizing therapeutic outcomes while reducing side effects. Furthermore, efforts are being directed toward translating these promising laboratory formulations into clinically viable products by overcoming regulatory, scalability, and stability challenges. The commercialization of advanced minoxidil nanoformulations will depend on establishing standardized manufacturing processes, long-term safety data, and effective delivery systems that align with patient compliance and market demands. Collectively, these emerging strategies highlight a multidisciplinary approach toward the next generation of nanotechnology-based hair restoration therapies.

9. CONCLUSION

Nanocarrier-based delivery systems represent a paradigm shift in alopecia management, offering enhanced bioavailability, sustained drug action, and reduced side effects of minoxidil. Among all systems, lipid-based nanocarriers and nanoemulsions show the most promising results in improving follicular targeting and therapeutic outcomes. However, challenges related to scale-up, regulatory approval, and long-term safety must be addressed before their widespread clinical adoption. Future research focusing on biocompatible, patient-friendly, and cost-effective nanocarriers will define the next generation of topical hair growth therapies.

REFERENCES

1. Ghosh, A., Patra, P., & Mitra, S. Nanotechnology in dermatological therapy: Opportunities and challenges. Current Pharmaceutical Design, 2020; 26(34): 4417–4430.
2. Lalloo, R., Naidoo, S., & Pillay, V. Advances in topical delivery systems for alopecia treatment: A focus on minoxidil. Journal of Controlled Release, 2020; 327: 732–747.
3. Randall, V. A. The biology of hair growth: Mechanisms of minoxidil action. Clinical and Experimental Dermatology, 2019; 44(8): 924–931.
4. Singh, R., Patel, K., & Gupta, N. Nanocarrier-mediated dermal delivery of minoxidil: Advances and future outlook. Drug Development and Industrial Pharmacy, 2022; 48(5): 207–218.
5. Suchonwanit, P., Thammarucha, S., & Leerunyakul, K. Minoxidil and its use in hair disorders: A review. Drug Design, Development and Therapy, 2019; 13: 2777–2786.
6. Sutradhar, K. B., & Amin, M. L. Nanotechnology-based topical drug delivery systems for alopecia treatment: Current scenario and prospects. Nanomedicine: Nanotechnology, Biology and Medicine, 2021; 38: 102439.
7. Torky, A., ElMeshad, A., & Abdel-Mottaleb, M. M. Formulation and evaluation of minoxidil nanostructured lipid carriers for improved follicular targeting. International Journal of Pharmaceutics, 2021; 598: 120348.
8. Trueb, R. M. Molecular mechanisms of androgenetic alopecia. Experimental Gerontology, 2017; 92: 47–54.
9. Vañó-Galván, S., Rodrigues-Barata, A. R., & Hermosa-Gelbard, Á. Minoxidil in alopecia treatment: Past, present, and future. Dermatologic Therapy, 2018; 31(4): e12640.
10. Lalloo, R., Naidoo, S., & Pillay, V. Advances in topical delivery systems for alopecia treatment: A focus on minoxidil. Journal of Controlled Release, 2020; 327: 732–747.
11. Randall, V. A. The biology of hair growth: Mechanisms of minoxidil action. Clinical and Experimental Dermatology, 2019; 44(8): 924–931.
12. Suchonwanit, P., Thammarucha, S., & Leerunyakul, K. Minoxidil and its use in hair disorders: A review. Drug Design, Development and Therapy, 2019; 13: 2777–2786.
13. Sutradhar, K. B., & Amin, M. L. Nanotechnology-based topical drug delivery systems for alopecia treatment: Current scenario and prospects. Nanomedicine: Nanotechnology, Biology and Medicine, 2021; 38: 102439.
14. Torky, A., ElMeshad, A., & Abdel-Mottaleb, M. M. Formulation and evaluation of minoxidil nanostructured lipid carriers for improved follicular targeting. International Journal of Pharmaceutics, 2021; 598: 120348.
15. Trueb, R. M. Molecular mechanisms of androgenetic alopecia. Experimental Gerontology, 2017; 92: 47–54.
16. Vañó-Galván, S., Rodrigues-Barata, A. R., & Hermosa-Gelbard, Á. Minoxidil in alopecia treatment: Past, present, and future. Dermatologic Therapy, 2018; 31(4): e12640.
17. Bozzuto, G., & Molinari, A. Liposomes as nanomedical devices. International Journal of Nanomedicine, 2015; 10: 975–999.
18. Lalloo, R., Naidoo, S., & Pillay, V. Advances in topical delivery systems for alopecia treatment: A focus on minoxidil. Journal of Controlled Release, 2020; 327: 732–747.
19. Patel, K. P., Singh, M., & Desai, T. R. Polymeric nanoparticle-based delivery systems for enhanced follicular targeting of minoxidil. Drug Delivery, 2019; 26(1): 963–975.
20. Rai, V. K., Mishra, N., & Yadav, K. S. Nanoemulsion as an efficient topical delivery vehicle for minoxidil: A mechanistic approach. Colloids and Surfaces B: Biointerfaces, 2018; 167: 394–404.
21. Singh, S., Kaur, J., & Kumar, P. Development and evaluation of minoxidil nanoemulsion gel for enhanced hair follicle delivery. AAPS PharmSciTech, 2020; 21(7): 251.

22. Sutradhar, K. B., & Amin, M. L. Nanotechnology-based topical drug delivery systems for alopecia treatment: Current scenario and prospects. Nanomedicine: Nanotechnology, Biology and Medicine, 2021; 38: 102439.
23. Torky, A., ElMeshad, A., & Abdel-Mottaleb, M. M. Formulation and evaluation of minoxidil nanostructured lipid carriers for improved follicular targeting. International Journal of Pharmaceutics, 2021; 598: 120348.
24. Yadav, K., Saini, V., & Singh, G. Niosomal formulations for enhanced topical delivery of minoxidil. Journal of Drug Delivery Science and Technology, 2020; 57: 101654.
25. Andrade, J. F. M., Verbinnen, A., Bakst, A., Cunha-Filho, M., Gelfuso, G. M., & Gratieri, T. An update on nanocarriers for follicular-targeted drug delivery for androgenetic alopecia topical treatment. Expert Opinion on Drug Delivery, 2025; 22(3): 367–381. https://doi.org/10.1080/17425247.2025.2457950
26. Santos, A. C., Pereira-Silva, M., Guerra, C., Costa, D., Peixoto, D., Pereira, I., Pita, I., Ribeiro, A. J., & Veiga, F. Topical Minoxidil-Loaded Nanotechnology Strategies for Alopecia. Cosmetics, 2020; 7(2): 21.
27. Khairnar, T. D. Recent trends in nanocarrier formulations of actives. Trends in Drug Formulation & Delivery, 2024. doi:10.1016/j.tdfd.2024.100.
28. Güngör, S. (2021). Nanocarriers Mediated Cutaneous Drug Delivery. Advanced Drug Delivery Reviews.
29. Adil, A. and M. Godwin. "The effectiveness of treatments for androgenetic alopecia: a systematic review and meta-analysis." Journal of the American Academy of Dermatology, 2017; 77(1): 136-141. e5.
30. Anastassakis, K. "Hormonal and genetic etiology of male androgenetic alopecia." Androgenetic Alopecia From A to Z: Vol. 1 Basic Science, Diagnosis, Etiology, and Related Disorders, 135-180.
31. Aslani, F. S., L. Dastgheib, et al. "Hair counts in scalp biopsy of males and females with androgenetic alopecia compared with normal subjects." Journal of cutaneous pathology, 2009; 36(7): 734-739.
32. Bao, P., J. Luo, et al. "The seasonal development dynamics of the yak hair cycle transcriptome." BMC genomics, 2020; 21: 1-13.
33. Barry, B. W. "Drug delivery routes in skin: a novel approach." Advanced drug delivery reviews, 2002; 54: S31-S40.
34. Bater, K. L., M. Ishii, et al. "Perception of hair transplant for androgenetic alopecia." JAMA facial plastic surgery 18(6): 413-418. Batrinos, M. L. "The endocrinology of baldness." Hormones, 2016; 13: 197-212.
35. BjÃ¶rklund, S., J. Engblom, et al. "A water gradient can be used to regulate drug transport across skin." Journal of controlled release 143(2): 191-200.
36. Blume, U., J. Ferracin, et al. "Physiology of the vellus hair follicle: hair growth and sebum excretion." British Journal of Dermatology, 1991; 124(1): 21-28.
37. Blumeâ€•Peytavi, U., A. Blumeyer, et al. "S1 guideline for diagnostic evaluation in androgenetic alopecia in men, women and adolescents." British Journal of Dermatology, 164(1): 5-15.
38. Botchkarev, V. A. and R. Paus. "Molecular biology of hair morphogenesis: development and cycling." Journal of Experimental Zoology Part B: Molecular and Developmental Evolution, 2003; 298(1): 164-180.
39. Brain, K. R. and R. P. Chilcott. "Physicochemical factors affecting skin absorption." Principles and practice of skin toxicology, 2008; 83-92.
40. Buffoli, B., F. Rinaldi, et al. "The human hair: from anatomy to physiology." International journal of dermatology 53(3): 331-341.
41. Buhse, L., R. Kolinski, et al. "Topical drug classification." International journal of pharmaceutics, 2005; 295(1-2): 101-112.
42. Caputo, M. and C. Cametti "Diffusion through skin in the light of a fractional derivative approach: progress and challenges." Journal of Pharmacokinetics and Pharmacodynamics, 48(1): 3-19.
43. Carter, P., B. Narasimhan, et al. "Biocompatible nanoparticles and vesicular systems in transdermal drug delivery for various skin diseases." International journal of pharmaceutics, 555: 49-62.
44. Chase, H. B., H. Rauch, et al. "Critical stages of hair development and pigmentation in the mouse." Physiological Zoology, 1951; 24(1): 1-8.
45. Devjani, S., O. Ezemma, et al. "Androgenetic alopecia: therapy update." Drugs, 83(8): 701-715.
46. Ebling, F. J. G. "The hair cycle and its regulation." Clinics in dermatology, 1988; 6(4): 67-73.
47. Ekman, D. R., D. M. Skelton, et al. "Metabolite profiling of fish skin mucus: a novel approach for minimally-invasive environmental exposure monitoring and surveillance." Environmental science & technology, 49(5): 3091-3100.
48. Ellis, J. A., R. Sinclair, et al. "Androgenetic alopecia: pathogenesis and potential for therapy." Expert reviews in molecular medicine, 2002; 4(22): 1-11.
49. Franbourg, A., P. Hallegot, et al. "Current research on ethnic hair." Journal of the American Academy of Dermatology, 2003; 48(6): S115-S119.
50. Galliker, N. A. and R. M. TrÃ¼eb "Value of trichoscopy versus trichogram for diagnosis of female androgenetic alopecia." International journal of trichology, 4(1): 19-22.
51. Garg, T., G. Rath, et al. "Comprehensive review on additives of topical dosage forms for drug delivery." Drug delivery, 22(8): 969-987.
52. GoroÅ¡ovÃ¡, A., E. Matalova, et al. "Langerhans cells in feline foetal epidermisImmunohistochemical study of spatial distribution." Acta Veterinaria Brno, 2008; 77(3): 307- 312.

53. Guarrera, M., P. Cardo, et al. "Reliability of hamilton-norwood classification." International journal of trichology, 2009; 1(2): 120-122.
54. Gupta, A. K., M. A. Bamimore, et al. "Efficacy of non-surgical treatments for androgenetic alopecia in men and women: a systematic review with network metaanalyses, and an assessment of evidence quality." Journal of Dermatological Treatment, 33(1): 62-72.
55. Harrison, S. and R. Sinclair. "Hair colouring, permanent styling and hair structure." Journal of cosmetic dermatology, 2003; 2(3â€•4): 180-185.
56. Headington, J. T. "Hair follicle biology and topical minoxidil: possible mechanisms of action." Dermatologica, 1987; 175(2): 19-22.
57. Illouz, Y. G. "Study of subcutaneous fat." Aesthetic plastic surgery, 1990; 14: 165-177.
58. Jhawat, V. C., V. Saini, et al. "Transdermal drug delivery systems: approaches and advancements in drug absorption through skin." Int J Pharm Sci Rev Res., 20(1): 47-56.
59. Jones, L. N. "Hair structure anatomy and comparative anatomy1." Clinics in dermatology, 2001; 19(2): 95-103.
60. Kaliyadan, F., A. Nambiar, et al. "Androgenetic alopecia: an update." Indian journal of dermatology, venereology and leprology, 79: 613.
61. Kanitakis, J. "Anatomy, histology and immunohistochemistry of normal human skin." European journal of dermatology, 2002; 12(4): 390-401.
62. Kao, J., J. Hall, et al. "In vitro percutaneous absorption in mouse skin: influence of skin appendages." Toxicology and applied pharmacology, 1988; 94(1): 93-103.
63. Kasting, G. B. "Kinetics of finite dose absorption through skin 1. Vanillylnonanamide." Journal of pharmaceutical sciences, 2001; 90(2): 202-212.
64. Katzer, T., A. Leite Junior, et al. "Physiopathology and current treatments of androgenetic alopecia: Going beyond androgens and antiâ€ androgens." Dermatologic therapy, 32(5): e13059.
65. Kaufman, K. D. "Androgens and alopecia." Molecular and cellular endocrinology, 2002; 198(1-2): 89-95.
66. Khiao In, M., K. C. Richardson, et al. "Histological and functional comparisons of four anatomical regions of porcine skin with human abdominal skin." Anatomia, histologia, embryologia, 48(3): 207-217.
67. Kim, B. J., J. Choi, et al. "Modified basic and specific (BASP) classification for pattern hair loss." International journal of dermatology, 59(1): 60-65.
68. Kim, K.-w., H.-y. Choi, et al. "Compensation on impedance of the stratum corneum." Journal of Electrical Engineering and Technology, 2008; 3(3): 444-449.
69. Koch, K., B. Bhushan, et al. "Diversity of structure, morphology and wetting of plant surfaces." Soft matter, 2008; 4(10): 1943-1963.
70. Kolarsick, P. A. J., M. A. Kolarsick, et al. "Anatomy and physiology of the skin." Journal of the Dermatology Nurses' Association, 3(4): 203-213.
71. Kuczara, A., A. WaÅ›kiel-Burnat, et al. "Trichoscopy of Androgenetic Alopecia: A Systematic Review." Journal of Clinical Medicine, 13(7): 1962.
72. Kumar, S., A. Wahid, et al. "Physiology and anatomy of hair in drug abusing cases." IJMTFM, 2: 153-9.
73. Lau, W. M. and K. W. Ng "Finite and infinite dosing." Percutaneous penetration enhancers drug penetration into/through the skin: methodology and general considerations, 35-44.
74. Lim, K.-M. "Skin epidermis and barrier function." International journal of molecular sciences, 22(6): 3035.
75. Marwah, H., T. Garg, et al. "Permeation enhancer strategies in transdermal drug delivery." Drug delivery, 23(2): 564-578.
76. McGrath, J. A., R. A. J. Eady, et al. "Anatomy and organization of human skin." Rookâ€™s textbook of dermatology, 2004; 1: 3.2-3.80.
77. Menon, G. K. and A. M. Kligman. "Barrier functions of human skin: a holistic view." Skin pharmacology and physiology, 2009; 22(4): 178-189.
78. Messenger, A. G. and R. Sinclair. "Follicular miniaturization in female pattern hair loss: clinicopathological correlations." British Journal of Dermatology, 2006; 155(5): 926- 930.
79. Montagna, W. The structure and function of skin, Elsevier. Monteiro-Riviere, N. A. (2001). Structure and function of skin. Toxicology of the Skin, CRC Press, 2015; 15-32.
80. Murphrey, M. B., J. H. Miao, et al. "Histology, stratum corneum."
81. Naito, A., T. Midorikawa, et al. "Lipid peroxides induce early onset of catagen phase in murine hair cycles." International journal of molecular medicine, 2008; 22(6): 725-729.
82. Nestor, M. S., G. Ablon, et al. "Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and ethics." Journal of cosmetic dermatology, 20(12): 3759-3781.
83. Nguyen, B. and A. Tosti "Alopecia in patients with COVID-19: A systematic review and meta-analysis." JAAD international, 7: 67-77.
84. Ohyama, M., Y. Zheng, et al. "The mesenchymal component of hair follicle neogenesis: background, methods and molecular characterization." Experimental dermatology, 19(2): 89-99.
85. Ovcharenko, Y. and O. Salyenkova "Modern concept of the etiology and pathogenesis of androgenetic alopecia." The Journal of VN Karazin Kharkiv National University, series" Medicine"(42).
86. Ozturk, P., E. Kurutas, et al. "BMI and levels of zinc, copper in hair, serum and urine of Turkish male patients with androgenetic alopecia." Journal

of Trace Elements in Medicine and Biology, 28(3): 266-270.
87. Paik, J. H., J. B. Yoon, et al. "The prevalence and types of androgenetic alopecia in Korean men and women." British Journal of Dermatology, 2001; 145(1): 95-99.
88. Paus, R. "Principles of hair cycle control." The Journal of dermatology, 1998; 25(12): 793-802.
89. Peus, D. and M. R. Pittelkow. "Growth factors in hair organ development and the hair growth cycle." Dermatologic clinics, 1996; 14(4): 559-572.
90. Piccini, I., M. Sousa, et al. "Intermediate hair follicles from patients with female pattern hair loss are associated with nutrient insufficiency and a quiescent metabolic phenotype." Nutrients, 14(16): 3357.
91. Prie, B. E., L. Iosif, et al. "Oxidative stress in androgenetic alopecia." Journal of medicine and life, 9(1): 79.
92. Purba, T. S., L. Brunken, et al. "A primer for studying cell cycle dynamics of the human hair follicle." Experimental dermatology, 25(9): 663-668.
93. Raina, N., R. Rani, et al. "New insights in topical drug delivery for skin disorders: from a nanotechnological perspective." ACS omega, 2022; 8(22): 19145-19167.
94. Rebora, A. "Pathogenesis of androgenetic alopecia." Journal of the American Academy of Dermatology, 2004; 50(5): 777-779.
95. Anwar, M., Warsi, M. H., Akhter, S., & Ahmad, M. Z. Formulation strategies to improve solubility and dermal delivery of minoxidil: An updated review. Journal of Drug Delivery Science and Technology, 2022; 71: 103278.
96. Moeineddine, F., & Reynolds, A. J. The role of minoxidil in hair loss treatment: Mechanisms, efficacy, and limitations. Dermatologic Therapy, 2020; 33(6): e14016.
97. Murtaza, G., Ahmad, M., & Shafiq, N. Development of novel minoxidil formulations for improved hair regrowth and patient compliance. Pharmaceutical Development and Technology, 2020; 25(7): 843–853.
98. Sutradhar, K. B., & Amin, M. L. Topical minoxidil delivery systems: Problems and progress. International Journal of Pharmaceutics, 2021; 607: 120978.
99. Vaidya, A., Desai, B., & Khopade, S. Stability and formulation challenges of topical minoxidil preparations: An overview. Journal of Cosmetic Dermatology, 2021; 20(12): 4039–4048. (https://doi.org/10.1111/jocd.14495)