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Nanotechnology in Multifunctional Anti-Dandruff Shampoos: Synergistic Role of Keratolytic, Anti-fungal, and Herbal Agents : overview

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ABSTRACT

Dandruff (pityriasis simplex) chronic and recurring scalp condition that characterised by excessive flaking, itching, and reduced quality of life ,Overactive sebaceous glands, microbial imbalance, impaired skin barrier function, and susceptibility to infection are among the overlapping causative factors that distinguish it from seborrheic dermatitis, which is limited to the scalp. *Malassezia fungi*, particularly *Malassezia pityriasis*, play a crucial role in the pathogenesis of dandruff by metabolizing lipids, releasing inflammatory mediators, and disrupting the stratum corneum barrier. Antifungal, exfoliating, and anti-inflammatory ingredients such as ketoconazole, zinc pyrithione, selenium sulfide, and salicylic acid are frequently found in conventional anti-dandruff shampoos. However, these formulations are limited by their low bioavailability, short duration on the scalp, poor penetration into the hair follicles, and the potential for irritation with prolonged use. Recent advances in nanotechnology have enabled the development of novel drug delivery systems, such as liposomes, solid lipid nanoparticles, lipid nanocarriers, polymer nanoparticles, microemulsifiers, and advanced exosome-based systems, significantly improving the effectiveness of anti-dandruff shampoos. In addition to reducing discomfort and the frequency of application, these nanocarriers enhance drug deposition in the scalp, target hair follicles, ensure controlled release, and stabilize active ingredients. Furthermore, herbal enhancers, including coconut oil, aloe vera, green tea and rosemary, possess synergistic antifungal, anti-inflammatory, antioxidant, and scalp barrier-repairing properties when added. Thus, by simultaneously addressing microbial overgrowth, inflammation, and scalp barrier damage, multifunctional, nanotechnology-enhanced shampoos offer an effective approach to tackling the multifactorial nature of dandruff. This review underscores the potential of nanoparticle-based anti-dandruff shampoos to increase therapeutic efficacy and patient adherence by highlighting recent developments, formulation considerations, evaluation techniques, and regulatory hurdles related to these products.

Keywords: Dandruff, seborrheic dermatitis , antidandruff Shampoo , Nanoparticle , Nanotechnology, Ketoconazole

INTRODUCTION

1.1 Background

Dandruff or pityriasis simplex , is a common persistent and relapsing scalp disorder that is strictly confined to the scalp; in contrast to seborrheic dermatitis (SD) which is a chronic inflammatory skin disease of body areas with high density of sebaceous glands like the scalp, axilla, or groins. ^[1] This scalp condition is characterized by the excessive shedding of dead skin cells from the scalp which cluster together because of their robust cohesive strength. It often appears as white or yellowish flakes or scales as a small patches specially on top of the hair and detach as such from the surface of the stratum corneum and may be accompanied by itching, irritation, or dryness ^[2] . In addition to mild itching, hair loss and hair thinning may also be associated with the condition.

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In the physiological spectrum of scaling about 487,000 cells/cm² get released normally after detergent treatment and their number goes up to 800,000 cells/cm² during dandruff and seborrheic dermatitis. Also dandruff can have a negative effect on patients' quality of life due to the resulting psychological stress or low self-esteem and is considered as an embarrassing disorder [3].

Although the exact etiology and pathophysiology are still unclear, fungal and bacterial colonization and imbalance of the microbiome seem to be one of the important factors involved in DF as shown in Figure 1, in these contexts the most common types of fungi on our healthy skin are lipophilic yeasts of the genus *Malassezia* [4] which have been shown to be able to penetrate the stratum corneum under suitable conditions to develop their pathogenic potential and causing visible desquamation of scalp [5]. So DF usually caused by *P. ovale* combine with multiple *Malassezia* fungus include including *Malassezia restricta*, *Malassezia sympodialis*, *Malassezia obtusa*, *Malassezia sloofiae*, *Malassezia pachydermatis*, and *Malassezia furfur* are considered the causative agent of dandruff [6]. Among them, *Malassezia furfur* is found to be the most common species, It was identified by the French scientist Louis-Charles Malassez in host factor [7].

It is commonly aggravated by exogenous factors such as the humidity, extended period of the sun exposure, trauma (scratching), and endogenous factors such as emotional stress and immune response, even season change can effect this condition. Since people prone to dandruff may see seasonal variations in their condition, frequently worsening in the winter [8]. The mechanism of dandruff formation is shown in figure 1 [9]. 50% is global prevalence of dandruff is most frequently seen between puberty and middle age groups when sebaceous gland activity is at its peak [10]. also more prevalent in males than females, due to higher testosterone levels resulting in greater oil production.

Traditional anti-dandruff formulations primarily rely on antifungal agents such as zinc pyrithione, ketoconazole, selenium sulphide, and climbazole, but these agents are limited by poor scalp penetration and retention, low bioavailability, and potential irritation or resistance after long-term use [11]. Among these, ketoconazole is considered the most effective and widely used due to its strong antifungal activity, minimal side effects when used topically, and lower recurrence rate. Ketoconazole is an azole (imidazole) antifungal agent that can be used either topically or orally. It has been approved by the U.S. FDA for the treatment of dandruff and seborrheic dermatitis of the scalp in various formulations, such as Nizoral shampoo, Xolegel gel, and Extina aerosol foam. Although KTZ has some problems, like limited solubility, high molecular weight and low percutaneous deposition in the epidermis, clinically it is relevant for certain disease states where KTZ has been shown to be efficacious. The quest for using nanoparticles has been researched to enhance a drug's permeability in the skin, which can render a drug more clinically relevant in therapy. So, nanotechnology-based formulations like ketoconazole-loaded silver, gold, and solid lipid nanoparticles (SLNs) have been developed to enhance treatment efficacy [12].

Furthermore, nano-ionization helps obtain the level of polymorphs for KTZ that result in improved permeability, solubility and dissolution. This again helps remediate the solubility of KTZ to make it a better therapeutic choice. Thus, that coating of KTZ on top of the nanoparticles will help increase solubility and efficacy of KTZ, while also having the potential of decreasing the amount of KTZ needed for efficacy in treating dandruff based on the clinical relevancy we found earlier. With nanoparticles, due to the unique functional features, epidermal penetration will also increase [13]. In addition, however, ketoconazole shampoos may occasionally cause changes in hair texture or colour, scalp irritation, blistering, and dryness [12]. In recent years, nanotechnology has emerged as a transformative approach for enhancing the performance of topical formulations and proved to be safe and effective in the targeted delivery of many medicaments.

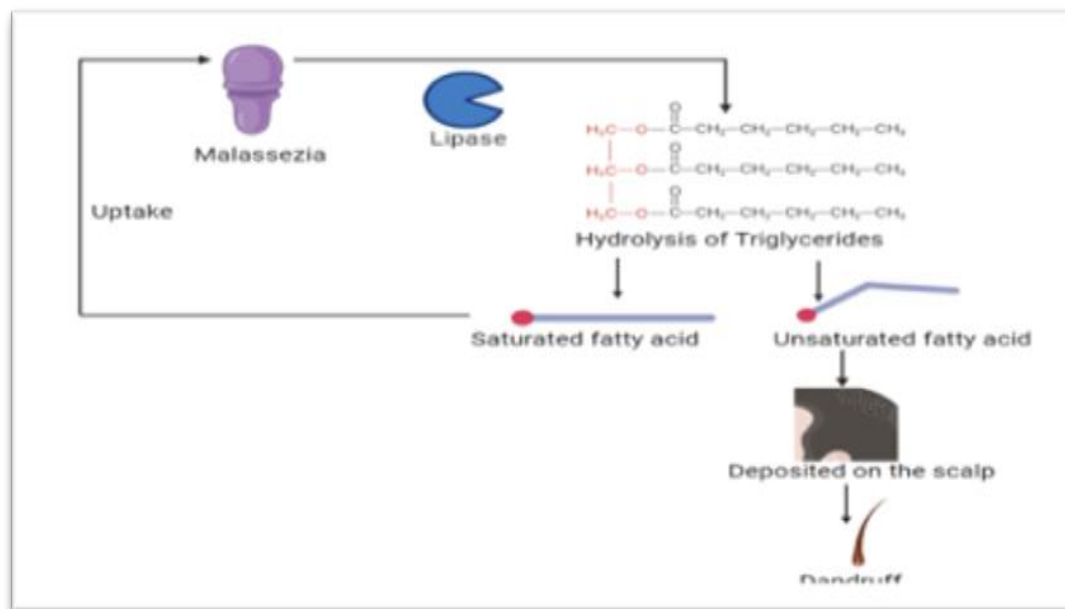


Figure 1: pathogenesis of dandruff formation

1.2 Aim of Study

- To summarize current advances in multifunctional shampoos with nanoparticle delivery and herbal enhancers.
- Objectives: permeation improvement, sustained release, synergistic effect, and natural additives.

2.Literature Review

2.1 Anatomy of the scalp and hair

The scalp consists of layers of soft tissue covering the skull. It serves as an area where hair can grow and acts as a physical barrier, protecting the cranial vault from physical trauma and potential pathogens that could cause infection ^[14]. There are five layers of the scalp: the skin, the connective tissue layer, the fascia, the loose areola, and the pericardium. The first layer is skin, which is thick and contains hair follicles and sebaceous glands. Hair follicles can extend into the dense connective tissue layer, where the nerves, lymphatic vessels, and vascular supply to the scalp are located, as shown in Figure 2. It is also worth noting that human hair grows at a rate of 0.35 mm/day, and around 100 hairs are shed daily. Human hair angiogenesis begins at about ten weeks of gestation, and final development results in the mature hair follicle ^[15]. Each follicle is part of a pilosebaceous unit, which comprises a sebaceous gland that secretes sebum to lubricate skin and hair. Sebum also provides a nutrient-rich environment that supports commensal microorganisms, including *Malassezia* species ^[16], in addition to the arrector pili muscle, which contracts to cause goosebumps, and the hair follicle.

A hair follicle is a complex mini-organ extending from the epidermis into the dermis and sometimes the subcutaneous layer and includes 3 essential hair follicle segments found on the head: the infundibulum, isthmus, and inferior segment. The infundibulum is the follicle's upper portion, beginning at the epidermal surface and extending to the sebaceous duct opening. The isthmus is the area between the sebaceous duct opening and the bulge ^[16].

The hair shaft, which is the visible, non-living part of the hair above the skin surface, is divided into three layers: the cuticle, the cortex, and the inner medulla. It is surrounded by a protective layer called the root sheath. The root sheath consists of two strata: the inner and the outer. When the hair follicle develops, blood vessels originating from the deep dermal vascular plexus surround it. These vessels nourish the hair follicle and support nutrient delivery, waste elimination, and growth. Loss of blood supply to the hair follicles is associated with some forms of hair loss. ^[17].

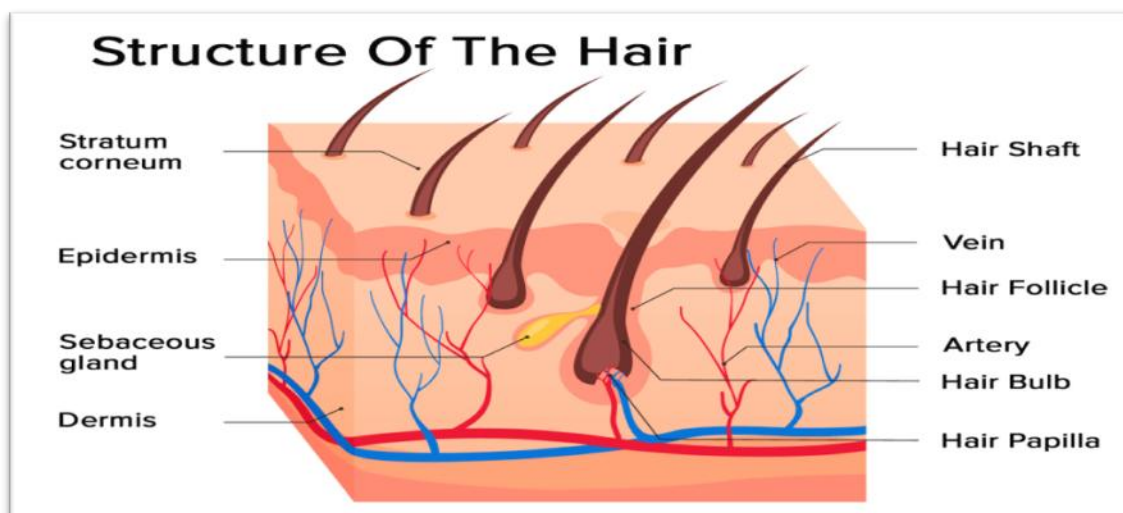


Figure 2: Structure of the hair

2.2 Etiology of dandruff and scalp disorders

Dandruff is a chronic, relapsing multifactorial scalp disorder due to an interplay among microbial dysbiosis, barrier dysfunction, sebaceous activity, and host susceptibility, in addition to interaction between biological and environmental triggers. ^[18]

Sebaceous glands of the skin secrete lipids in the first stage, which is thought to be controlled by androgens. The lipophilic *Malassezia* spp. then colonize such lipid-rich regions and use scalp lipids as an energy source. The enzyme lipase, which is secreted by *Malassezia*, hydrolyses triglycerides into free fatty acids, causing more *Malassezia* growth and possibly an inflammatory reaction and skin peeling and dandruff from an unsaturated fatty acid from *Malassezia* overgrowth that triggers inflammation and skin irritation ^[19].

Oxidative degradation of sebum, particularly peroxidation of squalene through lipid peroxides, generates bioactive metabolites, including squalene monohydroperoxide (SQOOH), that compromise the barrier and elicit inflammation, leading to an impaired epidermal barrier characterised by increased transepidermal water loss, with altered ceramide composition and disrupted stratum corneum lipid lamellae ^[20]. This barrier defect promotes the penetration of *Malassezia* and enhances inflammatory responses.

Moreover, individual susceptibility to *Malassezia*-derived inflammatory metabolites varies. Unregulated levels of pro-inflammatory cytokines such as IL-1 α , IL-8, and TNF- α , as well as antimicrobial peptides, have also been observed in skin affected by dandruff. It is also worth noting that genetic susceptibility influences the severity and recurrence of the disease ^[21]. Ultimately, external factors, including cold seasons, stress, harsh grooming routines, and pollution, can make symptoms worse. Seasonal fluctuation, especially winter worsening, has been well documented in studies conducted between 2020 and 2023 ^[22].

2.3 Active Agents in Anti-Dandruff Shampoos

There are two strategies for dandruff treatment, either by treating the cause using antifungal medications like zinc or by managing the symptoms. Pyrithione, ketoconazole, selenium sulphide, climbazole, etc., or by treating symptoms through utilizing antiproliferatives like coal tar and keratolytic substances such as salicylic acid as shown in table 1 ^[23].

A variety of therapeutic agents exist for the treatment of dandruff. Table 1 summarize the main therapeutic agents that are utilized today as shampoos to manage scalp dandruff.

Table 1: Topical therapeutic agent for dandruff

Class	Drug	Formulations Available
Antifungal Agents	Ketoconazole	1%, 2% Shampoo
	Ciclopirox	1% Shampoo
	Ciclopirox olamine	1%, 1.5% Shampoo
	Piroctone olamine	1% Shampoo
	Zinc pyrithione (ZPT)	1%, 2% Shampoo
	Selenium sulfide	1%, 2.25%, 2.5% Shampoo
Keratolytic Agents	Salicylic acid	2%, 3%, 4% Shampoo
	Salicylic acid + Sulfur	2% + 2% Shampoo; 3% + 5% Shampoo
	Coal tar preparations	0.5–7% Coal tar shampoos
Antifungal (Allylamine)	Terbinafine	1% Shampoo
Miscellaneous	Propylene glycol	15% Shampoo / Solution

From a treatment perspective, the recommended duration of treatment with topical anti-dandruff or anti-SD agents, according to clinical guidance and dermatologic practice, is generally up to 4 weeks, due to this anticipated time frame correlating with both a return to normal keratinocyte turnover as well as reduction in *Malassezia* density and improvement in stratum corneum intactness [24].

2.3.1 Keratolytic agents

Salicylic Acid (SA)

Salicylic acid is a potent keratolytic β -hydroxy acid that decreases corneocyte adhesion by solubilising intercellular cement, thereby stimulating desquamation of compacted scales and benefiting scalp flaking [25]. Furthermore, the lipophilic properties of SA enhance penetration into areas rich in sebaceous glands, thus improving clinical efficacy for patients with moderate dandruff. Studies suggest that the partnership of SA combined with antifungal agents promotes more efficacy than SA alone since its incorporation of removing the keratin layer facilitates more access of topical antifungals into the stratum corneum [26].

Sulphur

Sulphur has been described as mildly keratolytic, antifungal, and antibacterial. Newer formulations may use micro-encapsulated sulphur to reduce odor and potential irritation while improving deposition on the scalp surface. Though sulphur is less commonly used than SA, it is still effective in reducing scaling and flaking, especially at low, effective doses (1–5%) [27].

2.3.2 Antifungal/Antimicrobial Agents

Zinc pyrithione

Zinc pyrithione is derived from pyrithione (1-hydroxy-2-pyridinthione) and is synthesised from the antimicrobial metabolite aspergillilic acid of the fungus *Aspergillus flavus* [28]. Several shampoos containing 0.3–2% zinc pyrithione have been used over the counter to treat dandruff. Although zinc pyrithione (Figure 3) is commonly used as an antidandruff agent, its mechanism of action against *Malassezia*, particularly restricted *Malassezia*, remains unclear; only physiological data on the qualification of *Malassezia* contributors by zinc pyrithione (ZPT) have been reported [29]. Recent nanotechnology-enhanced ZPT formulations demonstrate improved scalp deposition, prolonged retention, and enhanced antifungal efficacy compared to conventional particles [30].

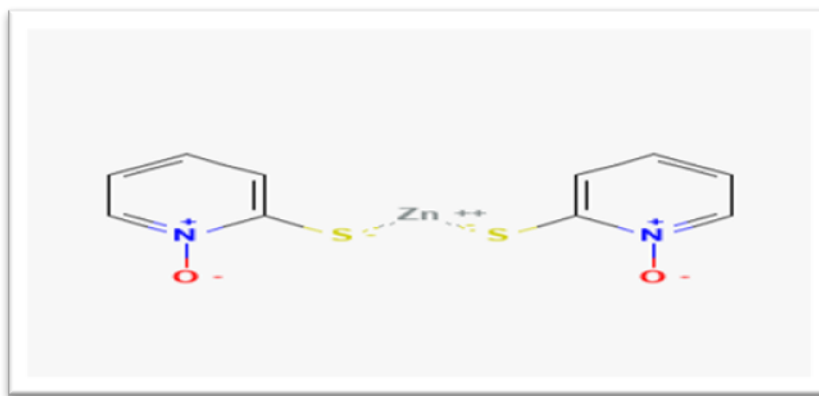


Figure 3: Zinc pyrithione structure

Ketoconazole (KTZ)

Ketoconazole (Figure 4) is an imidazole antifungal that acts by inhibiting lanosterol 14- α -demethylase and preventing the formation of ergosterol in fungal membranes. Ketoconazole is regarded as one of the most effective treatment options for moderate to severe dandruff and seborrhoeic dermatitis.

Recent clinical trials of KTZ 1–2% Shampoo has indicated statistically significant reductions in *Malassezia* loads and lower recurrence rates compared to either selenium sulphide or ZPT [31]. Nano carrier-based KTZ formulations (e.g., liposomes, solid lipid nanoparticles, and polymeric nanoparticles) also enhance fungal penetration into follicles and minimise irritation [32].

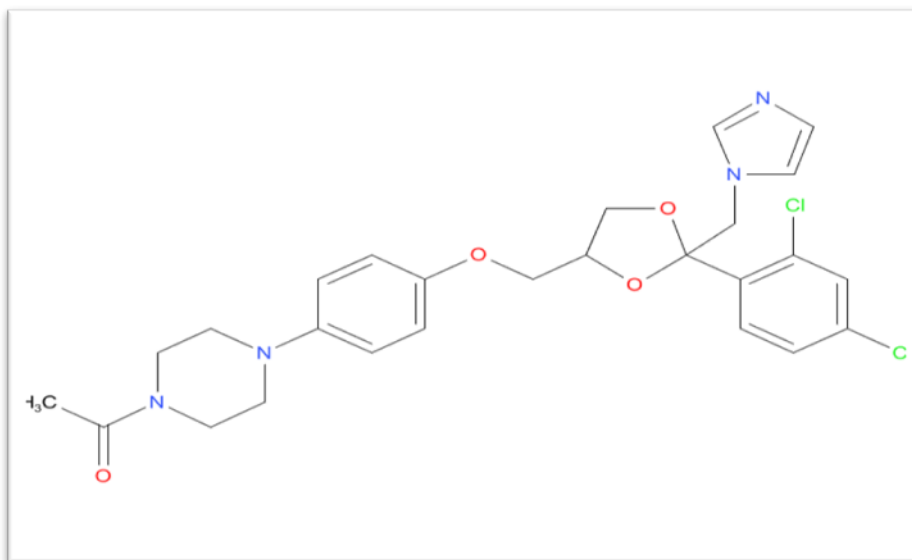


Figure 4: Ketoconazole structure

Selenium Sulphide (SeS₂)

Selenium sulphide is cytostatic and antifungal, decreasing epidermal cell turnover while inhibiting *Malassezia* growth. Although it is effective, its prolonged use can be limited due to scalp irritation, including

redness, dryness, and even a burning sensation on the scalp, potentially leading to further damage to the skin barrier and/or odor. Low-dose SeS₂ formulations recently developed since 2020 can enhance tolerability without sacrificing effectiveness^[33].

2.1.3 Anti-Inflammatory Agents

Inflammation is a key event in the pathogenesis of dandruff, which may be perpetuated by irritant-free fatty acids such as oleic acid released from *Malassezia* lipase activation. The effectiveness of anti-inflammatory agents in the treatment of dandruff has also improved with the combination of anti-inflammatory agents in the shampoo, which can improve pruritus, erythema, and barrier disruption.

Common agents include:

- Zinc derivatives (e.g., zinc gluconate) decrease the release of inflammatory cytokines.
- Nicotinamide (Vitamin B3) enhances barrier recovery and down regulates NF-κB-mediated inflammation.
- Pyridoxine (vitamin B6) has been demonstrated to balance sebum production and reduce irritation.
- Mild topical corticosteroids (e.g., low-potency hydrocortisone) are primarily used in combination products to manage flares.

Furthermore, herbal anti-inflammatory ingredients, such as aloe vera polysaccharides and green tea catechins, have become popular due to their antioxidant, soothing, and barrier-restoring capabilities, with a lower risk of side effects^[34].

2.4 Nanoparticle-Based Delivery Systems in Shampoos

There has been an emergence of nanotechnology as a transformative vehicle for enhancing anti-dandruff shampoo formulations, leading to improvements in drug penetration, retention on the scalp, controlled release, and decreased irritation. Standard antidandruff agents typically have low follicular delivery, short contact time, and limited bioavailability from rinsing. However, nanocarrier-based systems provide better deposition in hair follicles and sebaceous-rich regions of the scalp and stratum corneum. As a result, therapeutic performance is elevated while limiting systemic exposure and undesirable drug events^[35]. These nanocarrier systems are particularly useful for poorly soluble, highly lipophilic, and irritating actives like ketoconazole, zinc pyrithione, and herbal extracts^[36].

2.5 Type of Nanoparticle

Liposomes

Liposomes are vesicular systems derived from phospholipids laying horizontally alongside each other, able to entrap both hydrophilic and lipophilic active agents. The bilayer structure is similar to that of biological membranes, allowing for better delivery by penetrating and depositing into the stratum corneum and avoiding or minimizing the area around the follicular openings. Liposomal shampoos have increased retention of active drug delivery, less irritation and better moisturisation due to their biocompatibility. Recently, it has been shown that liposomal ketoconazole, a common antifungal agent in the treatment of seborrhoeic dermatitis, has significantly decreased barrier disruption with improved antifungal activity compared to traditional formulations^[37]. However, their clinical application may be limited by stability issues and high production cost, which can restrict large-scale use.

Solid lipid nanoparticles (SLNs)

Solid lipid nanoparticles (SLNs) are sub-micron colloidal carriers with a solid lipid core stabilized with a surfactant or surfactants. The significant advantages of SLNs for use in antidandruff therapies include high entrapment efficiency, occlusive properties and sustained release of active ingredients. The solid lipid matrices also allow for increased adhesion to the scalp and improved residence time, which would help *Malassezia* be

exposed to antifungal and antimicrobial drugs for a longer period of time as they reside on the surface of a liquid, solid or semi-solid lipid matrix. Due to these features, SLN-based shampoos containing actives such as ketoconazole, selenium sulphide, and herbal oils have improved antifungal activity and reduced irritation in recent trials [38].

Nanostructured lipid carriers (NLCs)

Colloid systems made up of a fluid lipid phase embedded in a solid lipid matrix or localized at the surface of solid platelets and the surfactant layer are known as nanostructured lipid carriers (NLC) [39]. A crystal lattice with several gaps is formed by the structural flaws of solid lipids when liquid lipid is incorporated. In comparison to SLN, this configuration improves stability, increases space, and permits a greater drug loading capacity [40].

Polymeric nanoparticles (PNPs)

Polymeric nanoparticles (PNPs) are made using biodegradable polymers such as polylactic-co-glycolic acid (PLGA), chitosan, or Eudragit®. Their structural stability allows them to control release profiles and improve protection of unstable therapeutics. Chitosan nanoparticles also exhibit intrinsic antimicrobial activity and electrostatic adhesion to negatively charged scalp surfaces and a greater ability to penetrate into pointing hair follicles. Polymer-based nanocarriers have been used to enhance delivery of zinc pyrithione and ketoconazole, demonstrating significant reductions in *Malassezia furfur* density and improvement in clinical scaling scores [41].

microemulsion/nanoemulsion

Nanoemulsions are thermodynamically unstable dispersions with a mean droplet size of about 1 to 100 nm that typically need a cosurfactant for stabilization because of their higher free energy, while microemulsions are thought to be thermodynamically stable dispersions with a mean droplet size of about 100–400 nm [42]. The average particle diameter and poly-dispersity index of this kind of emulsion are influenced by both its quantitative and qualitative makeup. The small size and homogeneity of the droplet, which vary depending on the mode of administration and the target cells for which it is intended, are crucial for drug delivery [43]. The particle size range increases with a higher poly-dispersity index, making the emulsion more heterogeneous. Another essential factor for the thermodynamic stability of emulsions is the zeta potential [44]. In this sense, the repulsion between the suspended particles increases with the zeta potential value's absolute distance from zero.

They are an appealing alternative for improved cutaneous and transdermal delivery of both hydrophilic and lipophilic medicines, as well as offering regulated or sustained drug release properties. They have been extensively researched to improve the bioavailability of poorly soluble medications [45]. In order to guarantee effective drug concentration levels in the skin following dermal administration, microemulsions have been employed as carriers for antifungal medications. Azole antifungals such as ketoconazole [46, 47], clotrimazole [48], fluconazole [49], and miconazole and allylamine/benzylamine antifungals terbinafine [51] have been developed in a number of microemulsion-based gels. The combined effects of the lipophilic and hydrophilic domains of microemulsions may be responsible for the higher drug penetration-enhancing activity of microemulsions, whereas the increased antifungal activity may result from improved drug-containing microemulsion oil globule penetration through the fungal cell wall [52].

Topical treatments for dandruff and SD have included salicylic acid (SA), a keratolytic agent with antibacterial properties. However, using SA topically is linked to irritation and a burning feeling. A microemulsion loaded with SA was created to reduce skin irritation and boost SA solubility, offering a superior topical administration method with improved solubility in all investigated concentrations [53]. Another study created a microemulsion with 12% salicylic acid and 4% lactic acid. This was made up of castor oil, ethyl alcohol, filtered water, propylene glycol as a co-surfactant, and Tween 80 as a surfactant. The microemulsion region grows as the concentration of surfactant or co-surfactant increases. For the topical treatment of psoriasis, scaly patches, dandruff, corns, calluses, and warts on the hands or feet, such a microemulsion may be an appropriate vehicle [54].

An alternative to corticosteroids in the treatment of SD, topical calcineurin inhibitors tacrolimus and pimecrolimus have demonstrated safety and effectiveness. A lipophilic medication called tacrolimus is marketed as a lipophilic cream. To increase tacrolimus's cutaneous availability, a microemulsion-based hydrogel and colloidal carrier were created [55].

Exosome-Based Therapies

Exosomes are cell-secreted nano-sized extracellular vesicles that are tiny and have a diameter of between 30 and 150 nanometers. They are essential for intercellular communication and the movement of bioactive chemicals. Numerous cell types secrete them, and their varied roles in health and illness have shown promise as novel therapeutic tools in a number of medical specialities, including dermatology, which has garnered significant attention [56]. In dermatology, engineered exosomes containing therapeutic compounds provide improved targeted delivery and may be used to treat localized skin infections, including fungal infections [57].

The unique properties of exosomes, such as their capacity to transport bioactive compounds and promote intercellular communication, have created new opportunities for the development of cutting-edge therapies for dermatological disorders.

Exosomes have anti-inflammatory properties and, in addition, can control immunological responses, which may help treat inflammatory skin diseases, including dermatitis and eczema [58]. People with alopecia or other hair diseases may benefit from exosomes that include growth factors and signalling molecules because they have the ability to stimulate hair follicles and promote hair growth [59].

2.6 Advantage in Shampoo Formulation

Therapeutic agents are incorporated into numerous pharmaceutical formulations, including liquid pharmaceutical dosage forms (such as solutions, shampoos, lotions, emulsions, and hair oils) or semisolids (ointments, creams, and gels) that ease application to a multitude of sites while maintaining the required functionality of the active agent. Even so, shampoos, medicated foams, and lotion-based formulations are the most common, as they are optimal for delivering effective treatments of dandruff and scalp seborrhoeic dermatitis (SD) due to their enhanced spreading, rinsability, and uniform delivery of active agents across the hair-bearing scalp (including the follicular openings).

Generally, shampoos may be described as cosmetic preparations required for the washing of hair and scalp and impart gloss to the hair as well as maintain the manageability and oiliness of hairs. Its primary function is to cleanse the hair of accumulated sebum, scalp debris and residues of hair grooming preparations. The added functions of shampoo include lubrication, conditioning, body building, prevention of static charge buildup, medication and so on, and it is packed in a form which is convenient for use. However, it has some unwanted effects, like drying and irritation on eyes. The drying effect of shampoo causes the hair to be too dry and cannot be handled by a comb; hence, it becomes obligatory for conditioning of the hair [60]. On the other hand, anti-dandruff shampoo has some specific function other than cleansing action. Shampoo generally contains an anti-dandruff agent as well as some other medicinal agent like vitamins, amino acids, plant extracts, antibacterial agents, etc. [61].

Two types of anti-dandruff shampoos are available commercially

1. Synthetic anti-dandruff shampoos (based on ingredients of chemical origin)
2. Herbal anti-dandruff shampoos (based on plant ingredients)

When included in anti-dandruff shampoos, nanoparticles have several formulation and therapeutic benefits. Their Small size allows them to penetrate deeply into hair follicles, which are recognized as key sites of *Malassezia* colonization. The nanoparticles can be captured in the follicular duct, which enhances localized delivery of antifungals and improves retention on the scalp, leading to improved performance over traditional formulations [62].

Another key benefit is the improved deposition of actives onto the scalp and stratum corneum. Nanoparticles have enhanced interactions with cutaneous lipids and corneocyte surfaces, leading to improved adhesion of actives to the scalp and reduced wash-away during rinsing. This ultimately improves the bioavailability of antifungal or anti-inflammatory agents, as well as the duration of action of the actives post-shampoo application [63]. Nanoparticle-based systems can also provide sustained and controlled release of incorporated drugs, which has benefits in managing dandruff and seborrhoeic dermatitis, requiring prolonged antifungal activity to suppress *Malassezia* growth and restore barrier function. Lipid-based nanoparticles or

polymeric nanocarriers may provide sustained drug release profiles, which may help minimise frequency of dosing and reduce the potential for irritating the scalp from high peaks in concentration associated with multiple dosing of actives [64].

Nanocarrier systems provide many pros that directly improve the performance of antidandruff formulations. First, they enhance the stability of labile compounds, protecting active ingredients such as ketoconazole, selenium sulphide, and herbal bioactive from oxidative, photolytic, and thermal degradation, thereby extending shelf-life while maintaining therapeutic efficacy [65]. Second, encapsulation with nanoparticles improves tolerability, since it reduces direct interaction of irritating agents with the epidermis, assisting in reducing erythema, dryness, and irritation often associated with traditional antidandruff ingredients, such as sulphur and zinc pyrithione [66]. Third, nanoparticles improve solubility and dispersion of hydrophobic drugs, achieving a more uniform distribution across the scalp and subsequently improving the efficacy profile of lipophilic antifungal agents [67]. Last, nanocarriers facilitate the development of multifunctional formulations, allowing simultaneous delivery of antifungal, anti-inflammatory, and antioxidant agents in a single platform, which is especially advantageous to countering the multifactorial course of dandruff (microbial dysbiosis, inflammation, and barrier disruption) [68].

2.7 Herbal enhancers in hair care

Due to their relative safety, biocompatibility, and multifunctional advantageous action, herbal ingredients are often included in shampoos designed to treat dandruff and related conditions. These plant-derived ingredients provide moisturizing, anti-inflammatory, antimicrobial, and antioxidant properties that complement the actions of traditional antifungal medications and keratolytic agents and are increasingly being incorporated into modern all-in-one formulations [69]. Recent investigations have documented several herbs with added benefits for scalp and scalp hair disorders to promote their use in anti-dandruff evidence-based therapies [70].

Coconut Oil (*Cocos nucifera*)

Coconut oil is a processed natural oil obtained from mature coconut kernels. In vivo, it exhibits a number of biological activities, including anticancer, antibacterial, analgesic, antipyretic, and anti-inflammatory qualities. Coconut oil has historically been used to cure and moisturize skin infections [71] and is a superior natural emollient that may assist in maintaining scalp hydration and minimizing dryness, resulting in scalp flaking. Its high affinity to scalp hair proteins may enhance the structural integrity of the hair shaft and aid in lessening friction and irritation from curling, drying, and styling products. Coconut oil also exhibits mild antimicrobial tendencies relative to *Malassezia* species and may enhance the cutaneous penetration and bioavailability of co-administered antifungal agents to optimize therapeutic effects in treating dandruff [72-74].

Sidr Powder (*Ziziphus spina-christi*)

From the Rhamnaceae family, this tropical evergreen tree exhibits exfoliating, antimicrobial, and antioxidant effects and can effectively prevent corneocyte accumulation while also suppressing *Malassezia* growth. Bioactive compounds such as flavonoids and tannins can help strengthen the scalp barrier while reducing oxidative inflammation, which supports its traditional use as a scalp soother and cleansing herbal remedy [75].

Also, it has been shown that many saponin glycosides found in sidr can help get rid of extra sebum and have antibacterial and antifungal properties, so they make them very valuable for usage in cosmetics. The multi-target effects of Sidr supplement its usage alongside chemical agents for effective control of dandruff [76, 77].

Green tea (*Camellia sinensis*):

Popular beverage worldwide, and its potential beneficial effects, such as its anti-cancer and antioxidant properties, are thought to be mediated by epigallocatechin-3-gallate (EGCG), a major constituent of polyphenols in green tea selectively inhibiting activity of 5 α -reductase hair loss-related enzymes, thus useful in treating androgenic alopecia [78].

Green tea is a rich source of antioxidants, such as flavonoids, which have been shown to increase hair growth, as well as protecting hair follicles from oxidative stress [79].

Aloe Vera (*Aloe barbadensis miller*):

The succulent plant in Figure 5, which is well-known for its many uses, has drawn a lot of interest in the field of hair cosmetics because of its varied composition and advantageous qualities. Numerous components make up aloe vera, such as polysaccharides, enzymes, vitamins (A, C, E, and B12), minerals (calcium, magnesium, and zinc), amino acids, and phytochemicals (anthraquinones and flavonoids). Its nutritional profile contains vital minerals and vitamins that support healthy hair.

Anthraquinones and other phytochemicals have anti-inflammatory, antioxidant, and antibacterial qualities, and the gel's pharmacological and medical qualities help to calm the scalp, contribute to a healthier scalp environment and encourage hair development. The complex mixture of polysaccharides in the gel includes acemannan, which has therapeutic and moisturizing properties. Aloe vera's amino acids help keep hair strands strong and intact. Additionally, it feeds hair follicles, revitalises the scalp, lessens dandruff, and increases the strength and lustre of hair ^[80].



Figure 5: aloe vera plants

Rosemary (*Rosmarinus officinalis*):

Rosemary (Figure 6) belongs to the mint family (Lamiaceae) and is a perennial evergreen shrub with a unique aromatic scent. Extensive scientific evidence supports its anti-inflammatory, antimicrobial, wound-healing, and anticancer properties in dermatological practice. It also shows promise in treating alopecia areata. This is attributed to its content of carnosol/carnosic acid and ursolic acid, which give rosemary its antioxidant and anti-inflammatory properties ^[81].

Rosemary has been used in traditional medicine, as well as in the pharmaceutical and cosmetic industries. In addition to its medicinal benefits, rosemary can be used in cosmetic formulations to treat both pathological and non-pathological conditions such as aging, baldness, and scalp disorders, in addition to its various medicinal properties, including those related to hair health ^[82].



Figure 6: Rosemary leaves

Synergistic Effects with Chemical Actives

Herbal extracts may work synergistically with traditional chemical agents for dandruff by improving penetration into the follicle, improving retention of drugs, and minimizing the irritative potential of chemical actives such as ketoconazole or zinc pyrithione. Their anti-inflammatory and antioxidant benefit helps restore the homeostasis of the scalp and provides multiple benefits to bacterial and fungal components of the dandruff syndrome. This information aids in developing leading-edge multifunctional applications for shampoo ^[83, 84].

2.8 Formulation consideration

The base formulation of any shampoo—including nanotechnology-enhanced, multifunctional anti-dandruff systems—must be carefully designed to ensure cleansing efficacy, scalp tolerance, delivery of actives, and product stability. Surfactants, viscosity modifiers, and preservatives are the main parts of the base ^[85]. Surfactants are the primary cleansing agents that lower the surface tension between the hair/scalp and oils or dirt, enabling effective removal of sebum and dandruff flakes. Surfactants can be anionic, like sodium lauryl sulphate, amphoteric, like cocamidopropyl betaine, or nonionic, like decyl glucoside. Contemporary studies underscore the incorporation of gentler and naturally derived surfactants, such as glycosides and saponins from botanical origins, to mitigate the irritation associated with harsh anionic surfactants ^[85-87].

Hydroxyethylcellulose, xanthan gum, and guar derivatives are examples of viscosity modifiers that change the thickness and flow of the shampoo base. These modifiers also affect the stability of nanoparticle dispersion, the quality of the foam, and the way it feels in nano-enabled systems. A higher viscosity helps control the deposition of nanoparticles and herbal extracts on the scalp ^[85, 87]. To stop microbes from growing in water-based systems, preservatives are very important. To keep the shelf life without hurting the health of the scalp, you should use natural preservatives (like rosemary extract) or safer synthetic ones. The best preservative should work well with nanoparticles and herbal actives. This is because some preservatives can make lipid or polymeric nanocarriers unstable ^[85, 87].

Interaction problems happen when surfactant micelles and nanoparticles attract or repel each other through electrostatic forces. This can change the size and spread of nanoparticles. For instance, anionic surfactants might push away negatively charged nanoparticles unless charge-modifying excipients are used to stop this from happening. Coating nanoparticles with biocompatible polymers, like chitosan, is one way to make them more stable and compatible with herbal polysaccharides ^[89-90]. 6.3 Strategies for Improving Performance The goal of optimizing nano-enabled shampoo formulations is to make sure that the actives are released slowly, that they penetrate the target sites in a controlled way, and that they are safe without causing irritation ^[88-91]. Sustained release is necessary to keep therapeutic levels of antifungal and keratolytic agents on the scalp for a long time. Nanocarrier systems, including polymeric nanoparticles and lipid nanocarriers, can encapsulate active substances and release them slowly. This means that you don't have to apply them as often, which makes it easier to follow the instructions ^[88-90].

In order to prevent excessive systemic absorption, controlled penetration guarantees that active ingredients reach their intended targets, such as hair follicles or the stratum corneum. Because of improved uptake and diffusion pathways, nanocarriers smaller than about 200 nm exhibit better follicular targeting. To maximize

targeted delivery, optimisation frequently entails modifying particle surface charge, nanocarrier composition, and surfactant concentration [89, 90]. Optimizing safety entails modifying excipient concentrations to reduce irritation of the scalp. For instance, the risk of sensitization can be reduced by substituting milder surfactants for harsh ones, particularly when combined with nanoparticles and herbal extracts, which occasionally have unpredictable interactions [85, 91].

2.9 Assessment Techniques

In Vitro Research

Before moving on to biological or human testing, in vitro assessments are essential for comprehending how the shampoo formulation behaves [92-93]. Measurements of particle size and dispersion (e.g., using dynamic light dispersion) are important because size affects release rate, follicular penetration, and stability; narrow size distributions are recommended [92].

The percentage of the active ingredient successfully encapsulated within the nanocarrier, compared to the total additive, is measured by encapsulation efficiency (EE). Improving the delivery of expensive active ingredients and reducing their waste is associated with high encapsulation efficiency [92-93].

To simulate the speed and reliability of active ingredient release from nanocarriers, release profile studies are conducted in simulated aqueous or oily environments. Controlled and sustained release profiles indicate the superiority of these formulations over conventional shampoos [92-93].

Scalp and in vivo penetration research

In vivo scalp penetration assessments bridge the gap between in vitro and clinical testing using the scalp or removed skin [93-95]. Dandruff scoring systems use standardized clinical scales to measure the degree of visible flaking or scaling both before and after treatment.

The effectiveness of the anti-dandruff ingredients in the nano-shampoo formulation is confirmed by these scores [95]. Measurements of scalp hydration and transepidermal water loss (TEWL) evaluate moisture retention and barrier integrity. Higher hydration and lower TEWL are signs of better scalp health, particularly in products that contain humectant and keratolytic ingredients [95-96]. Sensitization or negative reactions can be found with the use of irritation tests, such as controlled patch testing. Because the presence of nanoparticles can occasionally change the dynamics of skin interaction when compared to conventional products, nanotechnology formulations need to be closely watched [96].

Safety and Legal Aspects

Irritation and Toxicity Cytotoxicity, sensitization potential, and long-term scalp compatibility are all included in safety assessment [97-99].

Initial information about the formulation's effect on cellular health is obtained through cytotoxicity tests on keratinocyte or fibroblast cell lines. Prior to clinical use, these studies aid in the screening of potentially hazardous combinations [97]. In order to ascertain whether the formulation causes allergic reactions, sensitisation assessment uses repeated exposure models (such as in vivo or reconstructed human epidermis). Sensitisation studies are especially crucial because nanocarriers may enable deeper penetration [97-98]. Studies on long-term scalp compatibility assess whether frequent use has an impact on microbial flora, sebum balance, or scalp integrity. Keratolytics and antifungals used in anti-dandruff shampoos must strike a careful balance between their therapeutic effects and the maintenance of normal scalp ecology [98-99].

Aspects of Regulation

Safety, quality, and labelling transparency are the main requirements for cosmeceuticals using nanotechnology, while regulatory compliance varies by area [99-100]. Strong safety data is required for products

enabled by nanotechnology by regulatory agencies, including the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA). This comprises stability information, toxicity assessment, and nanoparticle characterization (size, shape, and surface characteristics). In order to inform customers, clear labelling of nano-materials is increasingly becoming commonplace in many jurisdictions [99]. The potency, consistency of bioactivity, and lack of pollutants (such as pesticides and heavy metals) of herbal actives must all be standardized and tested. Documented proof of safety and effectiveness is frequently required by regulatory bodies, especially when using innovative nanocarriers [99–100].

2.10 Challenge and consideration

While nanoparticle-based systems provide important benefits in anti-dandruff shampoos, there are still some challenges that must be resolved for stability, safety, and formulation quality. Stability concerns remain paramount, as nanoparticles can aggregate, fuse, sediment, and leak drug content during storage. Lipid-based carriers, for example, SLNs and NLCs, can be affected by polymorphic transitions, and polymer-based nanoparticles can also degrade via hydrolysis, both of which can result in changes to drug release behaviour [101].

Toxicity considerations are equally important. The relatively small size and minimized reactivity associated with nanoparticles can occasionally elicit a cytotoxic, inflammatory or oxidative response to scalp cells. The effect of composition, surface charge, and concentration of nanoparticles can also alter the potential for skin irritation, and, therefore, biocompatibility and dermal penetration testing are warranted [102].

Furthermore, potential interactions between the nanoparticles and other excipients (surfactants, emulsifiers, thickeners and pH adjusters) in the shampoo may destabilize nanoparticles or induce drug leakage, leading to reduced therapeutic activity. Consequently, a suitable combination of formulation excipients needs to be investigated further to ensure smooth nanoparticle performance throughout the shelf life of the product [103].

Despite these limitations, a careful control of physicochemical properties and other structural interactions will in turn have the potential to develop nanocarrier systems into deliverable anti-dandruff shampoo products [104].

However, several research gaps remain. Limited clinical evidence is available to confirm the long-term efficacy and safety of these systems. Furthermore, challenges related to large-scale production, cost-effectiveness, and regulatory approval require further investigation. Future research should prioritize well-designed clinical trials and comprehensive evaluation of long-term safety.

CONCLUSION

Dandruff is a complex scalp condition requiring a multifaceted approach that goes beyond traditional washing and antifungal treatments. While conventional anti-dandruff shampoos are effective, they have limited penetration, short contact time, and undesirable side effects. Nanoparticle-based delivery methods offer targeted action on hair follicles, sustained release, stability, and reduced irritation for potent medications like ketoconazole and zinc pyrithione. The use of herbal enhancers further improves treatment efficacy by combining antibacterial, anti-inflammatory, and antioxidant properties, while also enhancing scalp tolerance and user acceptance. Although some stability, safety, and regulatory compliance issues remain, careful formulation design and rigorous evaluation can help overcome these limitations. Overall, multifunctional shampoos enhanced with nanotechnology hold great promise for the future of effective, safe, and easy-to-use treatment for dandruff and other scalp conditions.

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تقنية النانو في شامبوهات متعددة الوظائف مضادة للقشرة: الدور التآزري للعوامل الكيراتوليتية والمضادة للفطريات والعشبية: نظرة عامة

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الخلاصة:

قشرة الرأس (النخالية البسيطة) حالة مزمنة ومتكررة تصيب فروة الرأس، وتتميز بنقشر مفرط وحكة شديدة وانخفاض جودة الحياة. من بين العوامل المسببة المتداخلة التي تميزها عن التهاب الجلد الدهني، الذي يقتصر على فروة الرأس، فرط نشاط الغدد الدهنية، واختلال التوازن الميكروبي، وضعف وظيفة حاجز الجلد، وزيادة القابلية للعدوى. تلعب فطريات الملاسيزية، وخاصة الملاسيزية النخالية، دورًا حاسمًا في إمراضية قشرة الرأس من خلال استقلاب الدهون، وإطلاق وسائط التهابية، وتعطيل حاجز الطبقة القرنية. غالبًا ما توجد مكونات مضادة للفطريات، ومقشرة، ومضادة للالتهابات، مثل الكيتوكونازول، وبيريثيون الزنك، وكبريتيد السيلينيوم، وحمض الساليسيليك، في أنواع الشامبو التقليدية المضادة للقشرة. مع ذلك، تُعاني هذه التركيبات من محدودية فعاليتها، كإخفاض توافرها الحيوي، وقصر مدة بقائها على فروة الرأس، وضعف اختراقها لبصيلات الشعر، واحتمالية تسببها في تهيج فروة الرأس مع الاستخدام المطول. وقد أتاحت التطورات الحديثة في تقنية النانو ابتكار أنظمة جديدة لإيصال الأدوية، مثل الليبوسومات، وجزيئات الدهون النانوية الصلبة، وحوامل الدهون النانوية، وجزيئات البوليمر النانوية، والمستحلبات الدقيقة، وأنظمة الإكسوزومات المتقدمة، مما حسن بشكل ملحوظ من فعالية شامبوهات مكافحة القشرة. إضافة إلى تقليل الشعور بالانزعاج وتكرار الاستخدام، تُعزز هذه الحوامل النانوية ترسب الدواء في فروة الرأس، وتستهدف بصيالات الشعر، وتضمن إطلاقًا مُحكَّمًا به، وتُنَبِّت المكونات الفعالة. علاوةً على ذلك، تُضفي المُعززات العشبية، بما في ذلك زيت جوز الهند، والصابر، والشاي الأخضر وإكليل الجبل، خصائص مُضادة للفطريات، ومُضادة للالتهابات، ومُضادة للأكسدة، ومُرَمِّمة لحاجز فروة الرأس، عند إضافتها. وبالتالي، من خلال معالجة فرط نمو الميكروبات والالتهاب وتلف حاجز فروة الرأس في آن واحد، تُقدِّم أنواع الشامبو متعددة الوظائف والمعززة بتقنية النانو نهجًا فعالًا للتعامل مع الطبيعة متعددة العوامل لقشرة الرأس. تُسلِّط هذه المراجعة الضوء على إمكانات أنواع الشامبو المضادة للقشرة القائمة على الجسيمات النانوية في زيادة الفعالية العلاجية والتزام المرضى بالعلاج، وذلك من خلال إبراز التطورات الحديثة، واعتبارات التركيب، وتقنيات التقييم، والعقبات التنظيمية المتعلقة بهذه المنتجات.

الكلمات المفتاحية: القشرة، التهاب الجلد الدهني، شامبو مضاد للقشرة، جسيمات نانوية، تكنولوجيا النانو، الكيتوكونازول