Available online on 15.09.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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# Hair Follicles: Strategic Targets for Promoting Hair Growth

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Article Info:

Article History:

Received 10 June 2025
Reviewed 23 July 2025
Accepted 19 August 2025
Published 15 Sep 2025

Cite this article as:

TUO-KOUASSI AN, N'GUESSAN-GNAMAN KC, AKA-ANY-GRAH S, ANIN AL, LIA AJ, N'GUESSAN A, DALLY I, YAO MA, KOFFI AA, Hair Follicles: Strategic Targets for Promoting Hair Growth, Journal of Drug Delivery and Therapeutics. 2025; 15(9):124-133 *DOI: http://dx.doi.org/10.22270/jddt.v15i9.7341*

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Abstract

The hair follicle is much more than a simple anchor for the hair shaft: it is a complex micro-organism, richly vascularized, with a great capacity for absorption. This unique anatomical structure has emerged as a promising pathway for the targeted delivery of active substances, particularly for treating hair disorders. Owing to its funnel-shaped architecture and its associated sebaceous and eccrine glands, the follicle provides an extensive contact surface and direct access to the dermal layer. Numerous studies have highlighted its ability to enhance skin penetration and to support the sustained release of active compounds. In addition to its structural advantages, the hair follicle exhibits dynamic biological activity, including a cyclic growth pattern that can influence the permeability and receptivity of the follicular environment. This dynamic behavior opens new avenues for timed and localized drug delivery. Furthermore, innovative carrier systems, such as nanoparticles, microparticles, liposomes, solid lipid nanoparticles, and polymer-based vehicles have been developed to optimize transfollicular targeting and improve therapeutic efficacy while minimizing systemic exposure. This article reviews the morphological and physiological characteristics of the hair follicle, its role in transfollicular uptake, and recent advances in delivery technologies that enable safe, targeted, and efficient administration of active substances to the hair and scalp, for cosmetic and medical purposes.

**Keywords:** Hair follicle**,** targeted delivery**,** carrier systems**,** transfollicular administration**,** hair disorders

## 1. Introduction

Developing effective cutaneous drug-delivery systems is a major challenge in dermatology, cosmetics and local pharmacotherapy. Long regarded as a secondary pathway, transfollicular absorption is now attractive growing interest as an alternative or complement to classical percutaneous routes. Due to its distinctive architecture and dynamic physiology, the hair follicle constitutes a privileged portal for active substances: it traverses several skin layers and is embedded in an environment rich in immune cells, accessory glands and hormonal receptors, making it a relevant target for both localized and systemic actions. Once under-utilized, this route now lies at the core of innovative strategies driven by nanotechnologies, lipid-based systems and smart polymers. This article reviews relevant aspects of the pilosebaceous unit, a complex three-dimensional and dynamic structure, while highlighting its anatomy, physiology, and highly specific growth cycle. Next, it was important to highlight the penetration mechanisms, the various investigation methods, and the relevant therapeutic target sites of the hair follicle for proper release of active ingredients and the efficacy of the innovative formulations. Finally, the non-scarring disorders encountered in general, and the state of art in local or systemic treatment associated with these various disorders were be presented[1,2].

## 2. Anatomy and Physiology

Hair follicles are skin appendages and represent complex, dynamic three-dimensional structures[3], as illustrated in Figure 1. More than 20 different cell populations contribute to the organization of the pilosebaceous unit[4], which describes the integrated structure of the hair follicle, the hair shaft, the corresponding arrector pili muscle, and the associated sebaceous gland[5]. The hair shaft is composed of the medulla, the cortex which contains melanosomes, and the cuticle, made up of flat, cornified cells.

The hair follicle itself is composed of a permanent superficial structure and a cyclic, transient component that includes the hair bulb. The permanent portion of the hair follicle, which does not undergo significant cyclic changes, can be subdivided into several sections: the infundibulum, the isthmus, and the bulge.

The infundibulum spans from the skin surface to the opening of the sebaceous gland duct into the follicular canal. The superficial part of the infundibulum (acroinfundibulum) is lined with epidermis containing a well-developed stratum corneum and granular layer. The lower part, called the infrainfundibulum, may show a progressive loss of epidermal differentiation extending toward the isthmus, making it a key entry point for applied substances[6,7,8].

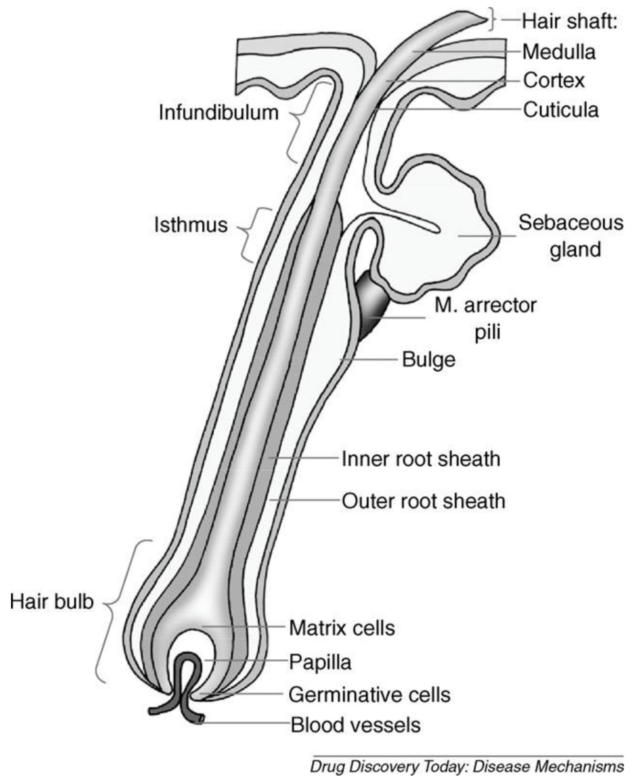


**Figure 1: Morphology of the human hair follicle[9]**

The isthmus is the segment between the sebaceous gland duct and the follicular bulge, which houses stem cells[4] and precursors of skin mast cells[10]. This bulge marks the end of the permanent portion of the follicle[11]. The dermal papilla is connected to blood vessels, which nourish the lower follicle, and the fibrous sheath, separated from the epithelial root sheath by a glassy or basal membrane. The epithelial hair bulb surrounds the dermal papilla and contains matrix and germinative cells. Through continuous cell division during the anagen phase, the hair shaft and inner root sheath are generated, with the latter ending halfway up the follicle. The outer root sheath is a partially keratinized layer that continues from the epidermis and serves to protect the inner follicular layers[9]. Sebaceous glands secrete sebum, a fungistatic and bacteriostatic mixture of short-chain fatty acids that lubricates hair and skin, repelling water and microorganisms. Sebum is released into the upper third of the follicular canal[5]. Structurally and functionally, a distinction exists between vellus hair and terminal hair, differing in shaft diameter, length, and pigmentation. Androgen-independent hairs (eyebrows, eyelashes) and hormonally influenced hairs (scalp, beard, chest, armpits, pubic area) are typically terminal hairs: long (>2 cm), thick (>50 µm), pigmented, and usually contain a medullary cavity[9,12,13,14]. The medulla is found in large terminal hair fibers, but most scalp hairs are not medullated[15]. Terminal hairs often extend over 3000 µm into the hypodermis[9,16]. In contrast, non-pigmented vellus hairs are shorter (<2 cm), thinner (<30 µm), and extend less than 1000 µm into the dermis[4,5]. Each hair follicle is associated with one or more sebaceous glands, epithelial cell outgrowths.

On the scalp, hair follicles typically form a follicular unit consisting of 1–4 terminal hairs and 1–2 vellus hairs, surrounded by the arrector pili muscle[5,9,17].

## 3. Hair Growth Cycle

Hair follicles undergo a growth cycle consisting of three main phases: anagen, catagen, and telogen. The anagen phase is the growth phase, during which cells proliferate rapidly and continuously to form the inner root sheath and migrate upward to form the hair shaft. The catagen phase is a transitional phase characterized by the cessation of mitosis, cellular resorption, and apoptosis of the lower follicular segment. The telogen phase is the resting stage that precedes hair shedding[5]. Recently, two additional stages of the hair cycle have been described. The exogen phase, which involves the release of telogen hair fibers from the follicle. The kenogen phase, a latency period between the exogen phase and the development of new anagen hair fibers[18]. Typically, 85-90% of scalp follicles are in the anagen phase, which can last from 2 to 6 years. Approximately 1–2% are in the catagen phase, about 2 weeks and around 10% in the telogen phase, lasting 2 to 4 months[18,19]. The hair shaft elongation rate is estimated at 0.3 to 0.4 mm per day, though some sources report 0.5 mm per day[19]. This rate depends on the proliferation and subsequent differentiation of matrix keratinocytes within the hair bulb. The thickness of the hair shaft is related to the size of the hair bulb[18,19]. Most hair growth disorders stem from alterations in the hair cycle. For example, androgenetic alopecia results from a shortened anagen phase, leading to increased hair loss and the transformation of terminal follicles into vellus follicles (miniaturization). Conversely, a prolonged anagen phase with conversion of vellus follicles to terminal follicles can occur in hypertrichosis and hirsutism[19,20]. Certain locally active inhibitors regulate the hair cycle. These compounds accumulate during the anagen phase and eventually trigger the onset of catagen[5]. It is important to note that the duration of each growth phase and the percentage of hairs in each phase differ significantly between vellus and terminal hairs.

## 4. Follicular Penetration

Researchers have recently taken an interest for using hair follicles as pathway for intra- and transdermal drug delivery. For a long time, intercellular penetration was considered the only relevant route of skin absorption. However, follicular penetration is now recognized as a complex process whose effectiveness depends on various factors such as follicle density and size, the activity status of the follicles, and the physicochemical properties of the penetrating substance.

### 4.1 Density, Size, and Follicular Reservoir

It is widely known that the density and size of hair follicles vary greatly depending on the body site. As early as 1967, Feldman observed that absorption rates are highest in skin areas where follicles are more densely packed[21]. Additionally, it is important to consider that hair follicles are epidermal invaginations that extend deep into the dermis, thereby providing a larger actual absorption surface area[22]. The surface of follicular openings is initially keratinized, while in the lower infundibulum, the corneocytes are smaller, more fragile, and more permeable[4], revealing the interruption of the skin barrier in this region. The stratum corneum reservoir is rather transient, as most of the topically applied substance remains in contact with superficial skin layers and is thus vulnerable to rubbing off, washing, and desquamation. In contrast, substances stored within hair follicles are relatively protected. Once absorbed, only the slow processes of sebum secretion and hair growth can exhaust the follicular reservoir[23]. Lademann et *al.,* showed that for a formulation containing 320 nm particles, the follicular storage time was 10 times longer than that of the stratum corneum[24]. Ethnic variations in follicle size and distribution must also be considered: African-American individuals have lower follicle density and volume depending on body region[25].

### 4.2Hair Follicle Activity

Not all hair follicles facilitate substance penetration equally[24,26]. Active or open follicles, which show sebum flow and/or hair growth, are more receptive to topically applied substances. In contrast, inactive or closed follicles do not exhibit these signs and are less permeable.

### 4.3Physicochemical Factors Affecting Follicular Penetration

Both active compounds and their vehicles influence the efficiency of follicular penetration. The penetration mechanism of several compounds including minoxidil has been studied[27,28]. In terms of vehicles, studies have shown that ethanol, dimethyl sulfoxide, and propylene glycol, as well as lipophilic vehicles rather than hydrophilic ones, can enhance follicular penetration[5]. In recent years, micro/nanoparticles and liposomes have attracted attention for their ability to improve follicular penetration. Liposomes are vesicular structures with a lipid bilayer membrane enclosing an aqueous core[29]. They can carry both hydrophilic and lipophilic drugs: hydrophilic ones inside the core, and lipophilic ones in the membrane. Liposome-based formulations have shown improved skin penetration of various actives[28] and are useful for follicular targeting of drugs[27,30,31]. Nanoparticles have also been proposed for prolonging sunscreen contact time on the stratum corneum[32] and for delivering vitamin A into superficial skin layers[33]. Several studies have pointed out that the follicular penetration of particles is highly dependent on their size. Schaefer et *al.,* concluded that particles smaller than 1 µm can be found in the superficial layers of the stratum corneum and follicular orifices, while particles between 3 and 10 µm are only visible in the follicular orifices[6]. Larger particles, over 10 µm in size, remained completely on the skin surface. Toll et *al.,* demonstrated that 750 and 1500 nm particles penetrated more deeply into the terminal hair follicles of the scalp than those between 3000 and 6000 nm[34]. Vogt et *al.,* found that 750 nm particles remained in the superficial parts of the infundibulum, while 40 nm particles penetrated deep into the follicular canal[35]. Lademann et *al.,* compared 320 nm particles with non-particulate systems and found a threefold deeper penetration of the particle-containing formulation into the hair follicle[36]. These results suggest that particulate systems can be used to target specific regions within the follicular canal[35]. Although it has been suggested that particles generally penetrate the compartment between the cuticle and the inner root sheath layer[34], the exact mechanism of penetration is still unclear. According to Lademann et *al.,* the influence of size could be explained by the structure of the hair surface[36]. As the cuticle is made up of superimposed 500-800 nm cells, which form a kind of zigzag structure, it is assumed that the follicles act as pumps during the hair movement that occurs *in vivo* and can be mimicked by the application of massage *in vitro*[37]. It has been suggested that the most effective penetration can be achieved with nanoparticles, whose size matches that of cuticle cells[23]. In addition, follicular penetration can be enhanced by various means[34]. Studies suggest that the follicular route, unlike the conventional epidermal route, is particularly favorable to particulate systems[38]. Vogt et *al.,* have shown that particulate systems can be used as vehicles for active compounds in the hair follicle duct, but also that nanoparticles can be used to target active compounds directly into the cells[35]. Studies of nanoparticles that can reach the deepest parts of follicles after a short time prove that their penetration process outpaces sebum flow[24]. Table 1 show different compound delivery systems and their follicular penetration depth. The results presented differ from one another, as there are a variety of techniques used to study follicular penetration.

**Table 1: Particulate systems used for follicular penetration (Wosicka et al., 2010)**

| Carrier | Size (μm) | Maximum penetration depth (μm) | Skin source | Massage/CSSS | Ref. |
|---|---|---|---|---|---|
| Nanoparticles from Resomer (labeled with 5-fluoresceinamine) | 0.32 | 1500<br>300 | Pig ear skin | +/−<br>−/− | [46] |
| Nanoparticles | 1.5<br>0.75<br>0.04 | Superficial aggregation in the follicle openings<br>225 | Human skin | −/+ | [45] |
| Polystyrene microspheres | 0.75<br>1.50<br>3.00<br>6.00 | 2000–2300<br>1700–2000<br>1100–1400<br>1700–2000 | Human skin | +/+ | [31] |
| Titanium dioxide particles | 0.02 lateral<br>0.10 length | 400 | Porcine skin<br>Human skin | +/− | [43] |
| Podophyllotoxin-loaded solid lipid nanoparticles | 0.07 | 275 | Abdomen porcine skin | −/− | [48] |
| Nile red-labeled solid lipid nanoparticles | 0.484 | 900 | Human scalp skin | −/− | [37] |
| Amphoteric and cationic unilamellar liposomes | Extruded through 400 nm pores of polycarbonate filters | 69% of mean follicle length | Pig ear skin | −/− | [50] |

### 4.4 Investigation of Follicular Penetration

Historically, the main challenge in evaluating follicular penetration was the lack of a quantitative model system that was truly devoid of follicles, while still preserving the structural, biochemical, and barrier properties of normal skin[5]. Although various attempts were made, most failed to meet these combined criteria. Wahlberg compared hairy and hairless skin areas in guinea pigs[39]. Other authors compared healthy skin to scar tissue devoid of appendages[40,41], or to newborn rat skin, which lacks follicles[42]. Barry introduced the "sandwich model", using Franz diffusion cells where two skin membranes were superimposed[43]. However, none of these methods enabled selective and quantitative determination of follicular penetration, because the results showed overlapping effects between intercellular and follicular routes. To address these limitations, two *in vivo* methods have been introduced. Firstly, selective Hair Follicle Blocking[44]. This method consists in blocking hair follicles on a defined skin area using micro-droplets of a varnish-wax mixture. Then, penetration results from this treated area are compared to unblocked skin. This approach demonstrated that hair follicles allow rapid penetration of topically applied caffeine[7,45]. Secondly, the differential tape stripping method was developed[46]. This technique allows for the assessment of substance penetration into hair follicles by combining two approaches: tape stripping, which removes the stratum corneum and cyanoacrylate surface biopsy, which extracts the follicular contents. The two resulting layers are then quantified separately, providing precise insights into the substance's penetration behavior. This method revealed that the *in vitro* follicular reservoir of excised human skin represented only 10% of the *in vivo* reservoir of the same volunteers and skin site. This suggests that elastic fibers contract around follicles after skin excision, thereby impeding follicular penetration. These findings are crucial for interpreting previous and future skin penetration studies. It can thus be assumed that excised skin models are only partially suitable for studying drug penetration, since follicular absorption is significantly reduced due to fiber contraction following excision[47].

Optical techniques have also been introduced for *in vivo* analysis of skin penetration. Grams et *al.,* demonstrated rapid intrafollicular transport of a lipophilic tracer from an aqueous solution using confocal laser scanning microscopy (CLSM)[48]. Other promising tools include the combination of confocal Raman spectroscopy with CLSM[49], as well as optical coherence tomography (OCT)[50].

### 4.5Target Sites within the Hair Follicle

The topical delivery of active substances to specific target sites within the skin such as different types of hair follicles or specific compartments and cells inside the follicle offers a valuable opportunity to develop new strategies for the prevention and treatment of follicle-related conditions. Follicular targeting opens avenues not only for hair therapy and the treatment of follicle-associated diseases, but also for gene therapy and immunotherapy[51]. Four main therapeutic targets can be identified in human hair follicles, as shown in Figure 2: the infundibulum, the sebaceous glands, the bulge region and the follicular matrix cells.

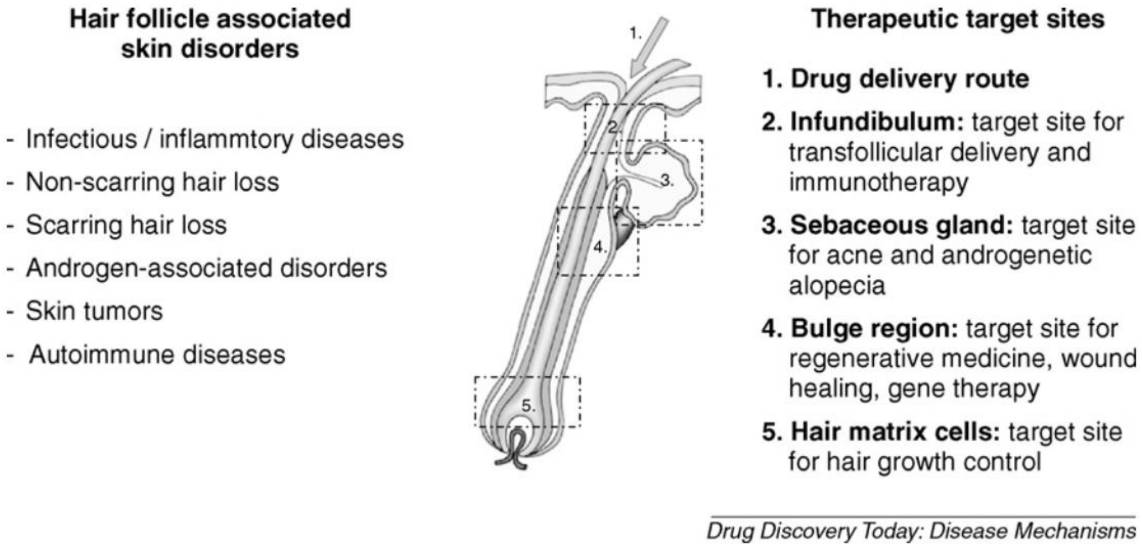


**Figure 2: The hair follicle and its relevant therapeutic targets (Patzelt et al., 2008a)**

The infundibulum, particularly its lower part, the infundibulum constitutes an interrupted barrier zone, offering enhanced permeability. Due to these barrier disruptions, a high density of antigen-presenting cells, mast cells, and other immune cells, can be found in this upper follicular region[4,51]. This makes the infundibulum a promising target for topical vaccination[52]. Furthermore, the upper dermal vasculature provides a rich capillary network that nourishes the upper follicles. This may allow hair follicles to function as transport shunts, enabling topically applied drugs to cross the continuous stratum corneum and reach either the viable skin layers, or the systemic circulation[5]. There is also evidence that drugs can cross the junction between the inner and outer root sheaths, before diffusing through the outer sheath and into the dermis[53].

The sebaceous gland is connected to the follicle via the follicular canal located in the lower infundibulum. It is implicated in the pathogenesis of acne[54], androgenetic alopecia[5] and other sebaceous gland dysfunctions. As it expresses 5-α-reductase, especially in facial and scalp regions, it converts testosterone into the more potent 5-α-dihydrotestosterone (5-α-DHT)[5,15]. This makes it an important therapeutic target for hormonal and sebaceous regulation.

The Bulge Region, located 500-800 µm below the skin surface[55]. This area of the outer root sheath is the insertion point for the arrector pili muscle and harbors epithelial stem cells[11]. It is responsible for follicle regeneration and is therefore another key therapeutic target. It contains multipotent stem cells with high proliferative capacity. These cells are targeted in gene therapy to enable long-term correction of congenital hair disorders or genetic skin diseases. The bulb region, including the matrix cells, regulates both hair growth and hair pigmentation[5,14,56,57]. The follicular papilla and matrix cells are therefore strategic targets for managing hair loss, promoting hair regrowth, and influencing color and cycling dynamics[5].

## 5 Non-Scarring Follicular Disorders in Women

A wide range of disorders are linked to the hair follicle, likely due to its complex structure and cellular organization. Generally, follicle-related conditions can be grouped into two categories. Irreversible destruction of regenerative cell populations, leading to scarring alopecia. Reversible disorders of the normal hair cycle are the focus of our analysis. Common causes of these reversible disorders include: telogen effluvium, androgenetic alopecia, alopecia areata and traction alopecia[1,9,58].

### 5.1 Telogen Effluvium

Hair loss is perhaps the most frequent symptom associated with hair follicles. Various internal factors may interfere with the hair cycle, causing an abnormally high number of hairs to enter the telogen resting phase simultaneously[9,59]. In telogen effluvium, hair shedding typically begins around three months after the triggering event. Besides physiological forms such as neonatal or postpartum telogen effluvium, it also occurs in systemic illnesses, endocrine disorders (thyroid, parathyroid, or pituitary diseases), and in association with certain medications such as retinoids, anticonvulsants, antithyroid agents, anticoagulants, β-blockers[9,59]. By contrast, when metabolic and mitotic activity of the follicular epithelium is suppressed, this may lead to a premature discontinue of the anagen phase. In such cases, the connection between the hair shaft and the inner root sheath is weakened, and hairs are lost during anagen phases. Causes include: chemotherapy, radiation therapy, thallium poisoning, and inflammatory diseases such as secondary syphilis and, more rarely, systemic lupus erythematosus[9,59].

### 5.2 Androgenetic Alopecia (AGA)

The most frequent cause of hair loss in women is androgenetic alopecia[60,61]. The roles of androgens and heredity remain unclear in many women with non-scarring, patterned scalp hair loss, especially in early or late-onset subtypes[62].

For men, pattern hair loss may be the result of a normal phenomenon, but women believe just the opposite. Many authors have discussed that patients' reactions to their diagnosis have more to do with self-perception than the objective clinical course because of the aforementioned feelings and the effects AGA has on women's self-image. AGA occurs in ~12% of young women under age 30, and 30–40% of women aged 60–69[63].

In patients with early-onset AGA, the clinical progression is generally more severe. Both frequency and severity increase with age[64]. Androgens affect several skin functions: sebaceous gland differentiation, hair growth, epidermal barrier homeostasis, wound healing[65].

Changes in isoenzyme levels or androgen receptor activity may significantly contribute to hyperandrogenism and associated skin conditions such as: acne, hirsutism, and androgenetic alopecia[65]. Interestingly, androgens stimulate terminal hair growth in androgen-sensitive areas (e.g. beard, axilla, pubic region), but inhibit hair growth and promote follicular miniaturization in the scalp, resulting in patterned hair loss or common hereditary baldness[59].

Most women with hereditary baldness have normal circulating androgen levels. However, severely progressive alopecia may occur in women with elevated androgens.

### 5.3 Alopecia Areata

Alopecia areata, also known as spot baldness, is a non-scarring, autoimmune, and inflammatory hair loss disorder. Histologically, it is characterized by: an increased number of follicles in the catagen and telogen phases, and also a lymphocytic infiltrate around the peribulbar region[66]. Clinically, it most often manifests as: sudden loss of hair in well-circumscribed patches, usually localized on the scalp. Severe presentations include: alopecia areata totalis, complete loss of scalp hair and alopecia areata universalis, complete loss of scalp and body hair including eyebrows, eyelashes, etc. The exact cause remains partly unknown, although several hypotheses exist. Strong indicators of an autoimmune origin include: lymphocytic infiltrates in hair follicles, increased autoantibody levels found in other autoimmune conditions, a higher prevalence of autoimmune comorbidities, detection of autoantibodies against anagen hair follicles, increased CD4/CD8 T lymphocytes, and cytokine abnormalities. Then, these findings support the notion that alopecia areata is a follicle-specific autoimmune disorder[66].

### 5.4 Traction Alopecia

Traction alopecia (Figure 3) affects approximately one-third of women of African descent[67] who wear various types of traumatic hairstyles over prolonged periods. This is especially problematic on hair that has reduced resistance to mechanical stress[68]. The risk of developing traction alopecia increases with the degree and duration of tension applied to the hair, and the use of chemical hair relaxers[69,70].

**Figure 3: Frontotemporal traction alopecia[71]**

Hairstyles most at risk include: tight buns or ponytails, sewn-in weaves or hair extensions, tight braids such as dreadlocks. In early stages, patients typically present with hair loss patches without scarring along the frontal scalp margin or the area subjected to traction. Hair loss can occur in any area of the scalp, depending on the configuration of the hairstyle. Broken hairs and follicular pustules are often present[2]. If the traumatic hairstyle persists without proper intervention, the condition can progress to irreversible scarring alopecia (cicatricial). Patients may also report scalp tenderness, itching, paresthesia, or even headaches[2]. Currently, there is no curative treatment once the damage becomes irreversible.

## 6. Existing Treatments

### 6.1 Telogen Effluvium

The effectiveness of treatment depends mainly on the identification of the specific cause, and the possibility of eliminating the triggering factor. In most cases, complete recovery occurs within 4 to 6 months, provided the underlying cause has been resolved[58].

### 6.2 Androgenetic Alopecia (AGA)

Treatment of AGA can be medical, or surgical. Only two drugs have demonstrated proven efficacy and are officially indicated for AGA: oral finasteride, and topical minoxidil[58].

Finasteride, contraindicated in women of childbearing age due to the risk of external genital malformations in male fetuses. Randomized controlled trials have not confirmed efficacy in postmenopausal women, especially at the commonly prescribed dose of 1 mg/day orally.

Topical Minoxidil 2%, caused minimal regrowth in 50% of women, and moderate regrowth in 13%[58]. Side effects were 7% reported irritation (burning, itching, redness), 3–5% developed facial hypertrichosis, unwanted facial hair growth. The 5% minoxidil solution is more effective than the 2% formulation.

Treatment with finasteride or minoxidil must be continued indefinitely to maintain any clinical benefit.

In the women's category, systemic anti-androgens such as spironolactone (50 to 200 mg/day), cyproterone acetate, flutamide, may help reduce hair thinning, but clinical data is insufficient to confirm efficacy[58,72].

Surgical Approach involves hair transplantation, typically by relocating permanent follicles to bald scalp areas. It usually requires two to four sessions to achieve adequate hair density. The use of mini- and micrografts, instead of larger punch grafts, has revolutionized the cosmetic result, yielding a more natural appearance, avoiding "tufts" or "plugs". Treatment algorithms for AGA are generally based on clinical stage[58].

### 6.3 Treatment of Alopecia Areata

Treatment depends largely on two factors: the extent of the disease, and the patient's age.

In localized Alopecia Areata (Small Patches), the treatment of choice is intra-lesional corticosteroids. A typical protocol involves injection of triamcinolone acetonide suspension diluted to 5 mg/mL, directly into bald patches at 0.1 mL per injection site, spaced out across the affected area. Maximum dose is 10 mg (i.e. 2 mL of 5 mg/mL solution) per visit. Injections repeated every 4–6 weeks. If hair regrowth is observed, treatment continues. If no regrowth is seen after 3 months, injections should be discontinued[58]. Other Treatment for localized cases include topical corticosteroids, topical minoxidil, anthralin. Topical minoxidil and corticosteroids have been supported by clinical trials[58].

In extensive Alopecia Areata (>50% of scalp), the treatment of choice is topical immunotherapy with the contact allergen diphenylcyclopropenone (DPCP). Some studies report 40% hair regrowth rates[58]. Other options imply systemic corticosteroids and PUVA phototherapy (psoralens + UVA light). Systemic corticosteroid use is controversial, long-term use leads to significant side effects, and hair loss tends to recur quickly after withdrawal. Despite their potency, systemic steroids should be used with caution, and only in severe and resistant cases. Table 2 lists treatments for alopecia areata.

**Table 2: Treatment of alopecia areata[58]**

| Patient Type | Hair Loss Severity | Treatment Options |
|---|---|---|
| **Adults** | < 50% hair loss | - Observe 2–3 weeks<br>- Intralesional corticosteroids<br>- 5% Minoxidil ± corticosteroid cream or anthralin |
| | > 50% hair loss | - Topical immunotherapy (DPCP)<br>- PUVA phototherapy<br>- 5% Minoxidil ± corticosteroid cream or anthralin |
| Children | Any severity | - 5% Minoxidil ± corticosteroid cream or anthralin |

### 6.4. Treatment of Traction Alopecia (TA)

Most cases of traction alopecia (TA) can be reversed if appropriate action is taken at an early stage. Therefore, clinicians must be proactive and vigilant, especially when caring for at-risk patients[2,73]. The key intervention, regardless of disease stage is the relief of mechanical tension on the hair shaft. This means loosening or stopping traumatic hairstyles, avoiding chemical and heat treatments, and not combining chemically/thermally treated hair with tight styling[74]. Early clinical sign is perifollicular erythema (redness around hair follicles), which may evolve into folliculitis, characterized by pustules and papules[71].

Initial medical management is topical or intralesional corticosteroids applied to the hairline or affected margin, topical and oral antibiotics, to treat or prevent infection[2,74,75].

Several reports show promising results in advanced stages of TA for using Topical Minoxidil (2%). Khumalo et *al.,* reported two cases of women with long-standing traction alopecia who experienced visible regrowth after 3 months, and significant improvement after 6 and 9 months, with 2% topical minoxidil application[76]. These women had no regrowth after 1-2 years of abstaining from harmful styling practices. Topical minoxidil can be proposed as a supportive measure, typically for a few months, because facial hypertrichosis, excess hair growth on the face, may occur, especially in dark-skinned individuals. Patients should be warned about this possible side effect and the dose adjusted as needed[76]. Callender et *al.,* also reported that 2% topical minoxidil was effective in some TA patients[73].

When traction alopecia progresses to scarring, and follicular atrophy, medical treatment becomes ineffective, and surgical intervention may be considered. Documented surgical techniques include punch grafts with rotation flaps[2], micrografts (1–2 follicular units), minigrafts (3–4 follicular units)[2,77].

Before opting for hair transplantation, patients must receive realistic expectations, and be informed of the need for multiple sessions to achieve cosmetically acceptable results.

Clinicians educating and treating patients with traction alopecia must remain culturally sensitive, especially regarding the importance of certain hairstyling practices that may be culturally or socially significant.

## Conclusion

Hair follicles represent more than mere structural components of the skin, they are dynamic microenvironments essential for maintaining hair growth, responding to hormonal and immunological signals, and serving as gateways for therapeutic intervention. As demonstrated throughout this review, their complex anatomy, regenerative cycle, and accessibility via transfollicular delivery make them particularly valuable targets for localized and systemic drug administration. Understanding the biological behavior of hair follicles, especially the roles of the infundibulum, sebaceous glands, bulge stem cells, and hair matrix opens promising therapeutic avenues for managing a wide range of non-scarring alopecias, from androgenetic alopecia to traction and autoimmune forms such as alopecia areata. Furthermore, advances in nanoformulations and targeted delivery systems such as liposomes, microparticles and nanoparticles enhance the potential for precise, deep, and sustained follicular drug deposition. Future research should prioritize the development of multi-targeted strategies that integrate pharmacological innovation, patient-specific factors, and follicular biology to optimize hair regeneration therapies. Ultimately, by leveraging the unique properties of the hair follicle, science is better positioned to offer personalized, effective, and less invasive solutions for individuals affected by hair growth disorders.

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