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Review

Nanotechnology-Based Cosmetics for Hair Care

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Abstract: Hair is a significant indicator of health and can have a major impact on an individual's cosmetic appearance. Research within the cosmetics industry has revealed that when nanomaterials are engineered into hair care, they can enhance the benefits of active ingredients in order to improve hair cosmesis. Within the cosmetics arena, the unique size and intrinsic properties of nanoparticles can be tailored to target the hair follicle and shaft. This review aims to provide an overview of cosmetic nanocarriers that can be employed to improve the appearance of hair.

Keywords: nanotechnology; nanomaterials; hair follicle; hair shaft; hair cosmetics; hair cosmesis; hair color; hair growth

1. Introduction

Hair, while not a vital organ, can be an indicator of individual health and have a major impact on cosmetic appearance. A variety of conditions including androgenic alopecia, hirsuitism, and loss of hair color can have a significant impact on the quality of life of patients, evoking cosmetic concerns as well as inducing a loss of self-esteem, a sense of social inadequacy, and feelings of helplessness [1].

Accordingly, hair quality is considered to be a significant marker of health [2]. For example, brittle hair may be a marker for thyroid disease or nutritional deficiency, what may be perceived as "dry scalp" may in fact be primary skin disease ranging from psoriasis to tinea capitis, and thinning hair may signify hormonal imbalances. Considering the impact of hair on quality of life, it is no surprise that consumers attempt to alter their hair for a variety of aesthetic reasons [3]. For example, since the Greco–Roman time, a mixture of lead minerals and slaked lime was used to color grey hair black [3]. However, the use of hair dye is limited given the low penetration and low stability of bioactive species. Furthermore, throughout the 20th century, there has been increasing concern over the adverse effects of such dyes including genetic and carcinogenic reactions against human cell lines. Within this setting, the cosmetics industry and biomedical field has turned towards emerging delivery platforms.

Nanotechnology is one such avenue—a scientifically diverse discipline that exploits the complex and remarkably unique properties of matter at the nanoscale. Nanomaterials have been extensively researched and used as a vehicle for the delivery of bioactive agents to the skin within the cosmetic arena [4,5]. Nanotechnology confers small size ranging from 1 to 100 nm and a very large surface area-to-volume ratio, facilitating their interaction with the target organ—the skin. Nanomaterials can also be designed to deliver established or developing formulations of drugs in a sustained, controlled and targeted manner to avoid adverse systemic side effects. This liberation system not only allows for the enhanced delivery of active substances to the epidermis of the skin, but also permits prolonged contact at the site of action—properties that bring a variety of benefits to cosmetic products. Furthermore, due to their small size, their optical transparency enhances their cosmetic appeal. Therefore, because of their unique and intrinsic properties, nanomaterials are being increasingly exploited in the development of advanced skin care products, specifically targeting the hair follicle and shaft.

2. Hair Anatomy

2.1. Hair Follicle

Hair is composed of two structures: the hair follicle and the hair shaft (Figure 1). The hair follicle is arranged in a stocking-like configuration, containing several layers of structures. The hair follicle contains an upper segment (infundibulum), a middle segment (isthmus) and lower segment (bulb and suprabulb). The infundibulum, extending from the opening of the follicular orifice to the sebaceous gland, is the major interface between epithelium and the environment, harboring residential microflora with its own specialized immune system and innate defenses [6]. Within the cosmetic space, the infundibulum accumulates the majority of topically applied products (*i.e.*, nanoparticles) between the infundibular walls and the hair shaft. The middle segment extends down from the bottom of the sebaceous gland duct (which releases sebum into the hair follicle canal) to the insertion of the arrector pilli muscle. The bulge region is located below the sebaceous gland and houses the epithelial stem cells responsible for growth of a new hair shaft and melanocyte precursors. The hair bulb, resembling the bulb of a tulip, actively produces a particularly sized and pigmented hair shaft. The bulb encloses the follicular dermal papilla and a single capillary loop. It is an essential source of growth factors that are critical for hair growth and melanogenesis. Hair color is determined by the melanocytes located in the bulb region, responsible for the pigmentation of initial hairs, and the melanocyte stem cells located in the bulge region, responsible for the maintenance of the hair follicle pigments in subsequent hair cycles.

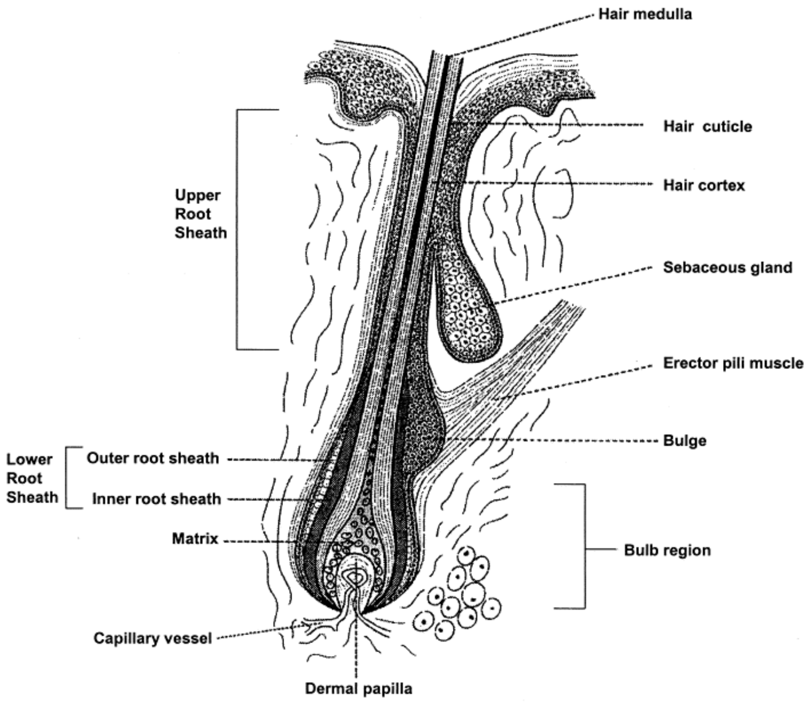


Figure 1. Hair shaft and follicle anatomy. Reprinted with permission from [7], published by Oxford University Press, 2002.

2.2. Hair Shaft

The hair shaft is composed of dead, keratinized cells. The shaft is subdivided of three concentric regions: the cuticle, cortex and medulla. The cuticle is the outermost layer of the hair, formed by flat overlapping cells in a scale-like or tessellated pattern. A healthy cuticle gives a shiny, elastic and brilliant look to hair. Overbrushing, excess heat or the use of chemicals such as hair dyes can injure the cuticle, resulting in the loss of its natural glow. The cortex lies between the medulla and the cuticle and is composed of hardened fibrous cells that are twisted into bundles. The cortex contains pigment granules (melanin) that give hair its natural color. When the cuticle is injured, the cortex is exposed, increasing follicular water loss and entry of foreign material, which can go on to damage the rich disulfide bonded network. The medulla is the innermost layer of hair and functions to support the structure of the hair. The diameter of the medulla varies according to the thickness of the hair. Interestingly, the medulla can be absent or interrupted without altering the hair strength.

3. Follicular Targeting with Nanoparticles

Topical drug therapy allows for the delivery of substantial amounts of drug to the site of disease, though poor and erratic drug absorption and active ingredient stability often confound delivery. Recent progress in nanotechnology allows for the development of carriers with enhanced ability to penetrate and permeate the skin. The stratum corneum, the lipid rich, tightly bonded outermost layer of the epidermis, is a direct barrier to ingredient penetration, preventing passage through the layers of the epidermis to the dermis [8]. While cosmetic products are not intended for systemic absorption, their efficacy depends on entry through this armor. Despite its efficient barrier function, some nanomaterials will be able to penetrate this obstacle, depending on their size and structure. There are three routes by which nanoparticles gain penetration: (1) intercellular, (2) transcellular, and (3) follicular permeation. Intercellular permeation is very difficult and depends on the solutes ability to penetrate the hydrophilic pores of the skin, whose size is estimated to be less than 36 nm [9]. Transcellular permeation is also highly unlikely given the tight matrix of corneocytes. However, the presence of hair follicles significantly contributes to the penetration and permeation of topically applied nanosized particles. In the past, it was thought that appendageal offices occupy 0.1% of the skin surface [8]. However, new evidence has suggested that follicular distribution is body-region-dependent, with some body regions (*i.e.*, forehead) harboring a significantly increased number of follicular orifices [10]. This suggests that while follicular openings may serve as a gateway for nanoparticulate drugs to be transported into the hair follicle, there may be significant differences in percutaneous absorption of appendage-free and abundant areas.

The hair follicle represents interruptions in the potent skin barrier that serve not only as an entry point for these topically applied compounds but also as an important reservoir, which significantly contributes to the transport of drugs and cosmetics into the skin [11]. For example, a study by Tenjarla *et al.* found the penetration of corticosteroids was considerably increased in haired skin compared to hairless skin [12]. It has been suggested that the size of a particle determines the depth of follicular penetration [13]. Much research has demonstrated that the smaller the size of particle, the greater its ability to penetrate the follicular canal (Figure 2) [4,14,15]. Interestingly, a study by Patzelt *et al.* found that the optimal size for follicular penetration ranged from 400 to 700 nm, each size capable of selectively targeting different structures within the hair follicle [16]. Authors found that by selecting 230 nm particles they could target the sebaceous gland and by selecting 643 nm particles they could target the bulge region. It is noteworthy that these particles were capable of penetrating follicular orifices that are presumed to be no larger than 200 nm in diameter. While these results stand in contrast to prior work, it may be explained by a mechanical effect rather than an effect specific to particle size. It was even hypothesized by Lademann *et al.* that hair movement may act to pump the nanoparticles deeper within the hair follicles [17]. Therefore, by modifying the size of the particles, a diverse range of cosmetic modalities can be utilized to selectively target the structures within the follicle. Additionally, nanoparticles have demonstrated superiority over non-particle formulations in terms of storage behavior; one study found that the movement of particles out of the follicular unit was delayed, suggesting its enhanced storage within the hair follicle [18].

While the retention of particles within the hair follicle has been well researched, the behavior of the particles with respect to penetration beyond the stratum corneum is not entirely clear. Follicular depletion can only be achieved by penetration into the deeper layers of the stratum corneum or by exiting the hair follicle via sebum flow and hair growth. This is in contrast to the relatively short storage of substances within the stratum corneum due to its continuous desquamation and turnover. Nevertheless, it has been shown that nanoparticles, while capable of deeper penetration than their non-nano counterparts, are unable to penetrate beyond the stratum corneum. In fact, titanium dioxide microparticles, the particles frequently used in sunscreens, are capable of penetrating the hair follicle, yet deeper penetration of the particles into viable skin tissue is not detected [19]. Labouta *et al.*

reviewed 125 different permeation/penetration experiments finding that particulate substances are not able to overcome the intact skin barrier *in vivo* [20]. The authors comment, however, that a distinct size threshold below which transfollicular or intercellular penetration and absorption is permitted, is unknown [20,21]. There are a few studies that do report the penetration of very small particles. One study found that gold nanoparticles, with a hydrodynamic diameter of 11.6 nm, were capable of crossing the stratum corneum, spreading widely within the epidermis and dermis [22]. Authors hypothesize that nanoparticles that are engineered to an exceedingly low size (1–10 nm) acquire unique properties that can induce lipid-modulation and subsequent skin penetration.

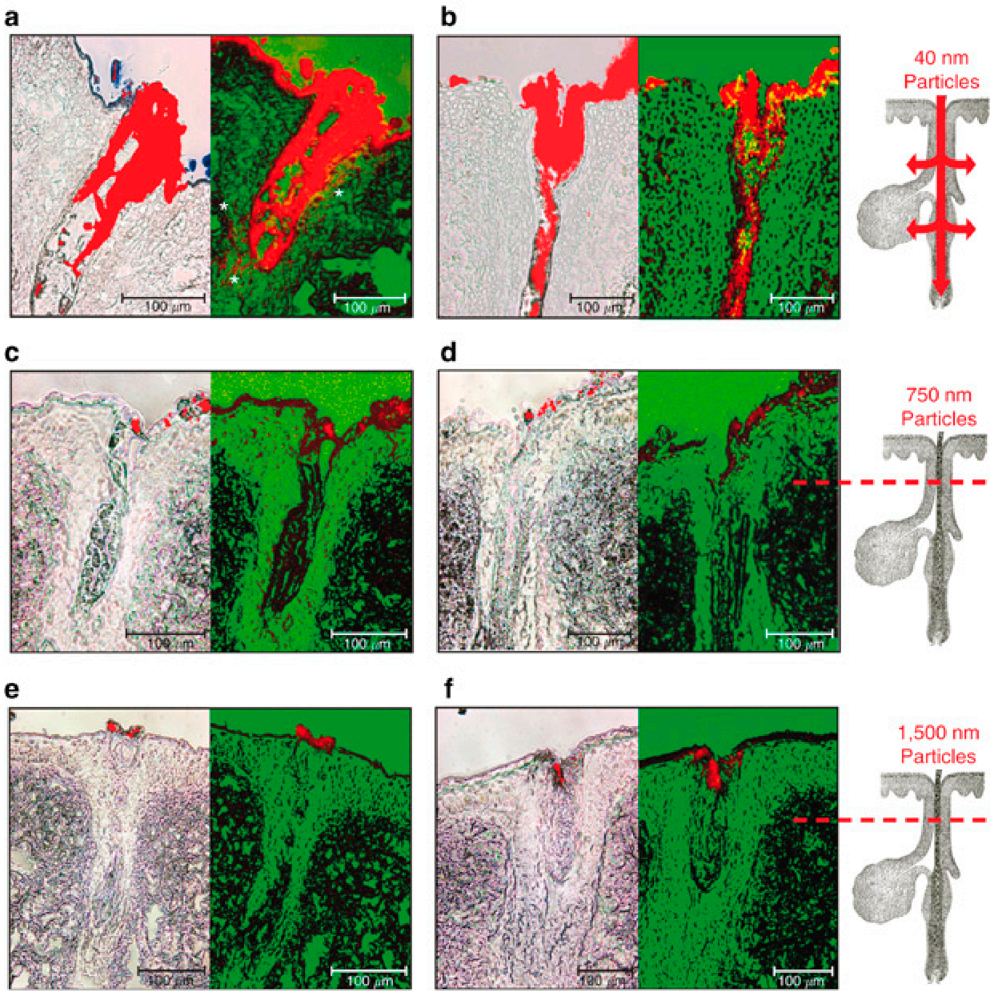


Figure 2. Penetration of variably sized nanoparticles via the hair follicle. Laser scan microscopy was performed on skin samples treated with variably size particles. It was found that 40 nm particles (**a**,**b**) penetrated deep into hair follicles. In contrast, 750 nm particles (**c**,**d**) and 1500 nm particles (**b**,**f**) aggregated in the infundibulum. Reprinted with permission from [15], published by Nature Publishing Group, 2006.

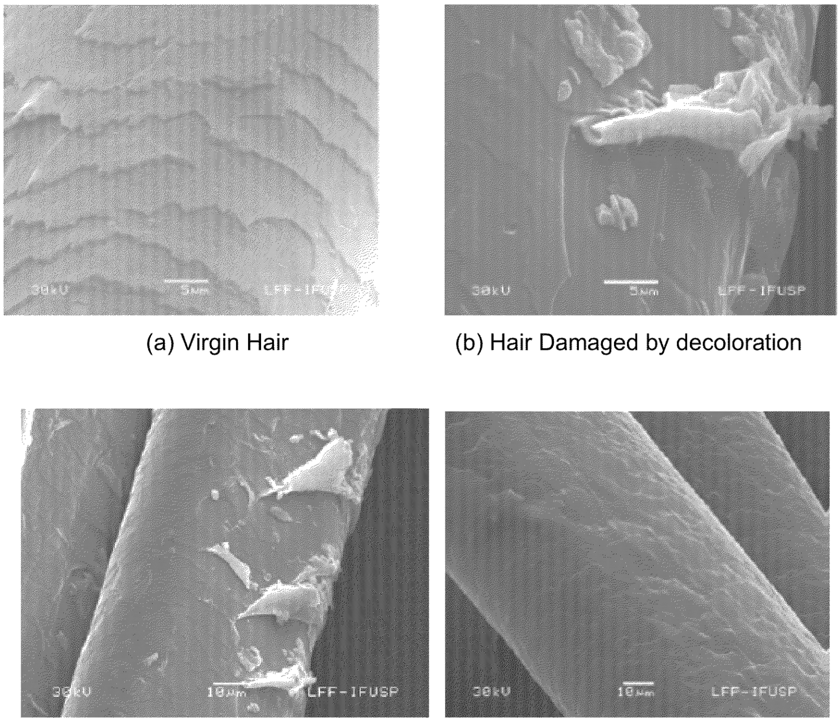
It must be noted that analysis of penetration and storage requires utilizing measuring techniques that accurately differentiate between follicular penetration and other routes of entry. One such technique utilized by many of the aforementioned experiments is cyanoacrylate skin surface stripping, which has been found to improve follicular penetration of a variety of transcutaneously applied compounds by removing the horny layer as well as contents of the upper follicular orifice [15]. While this model is a valuable tool to assess penetration into the hair follicle, it effectively opens hair follicles and increases the reservoir function of the hair follicle, which may not translate into intact human skin [23]. Furthermore, *in vitro* investigations on excised human skin demonstrated a significantly higher amount of drug penetration and storage as compared to *in vivo* conditions [24]. This effect was due to strong contraction of the elastic fibers around the hair follicle post-biopsy. Taken together, it is important to consider study design when evaluating the results of follicular penetration and storage and results must be interpreted with caution. The development of new methods to assess permeation and penetration of nanomaterials may help to further elucidate toxicological data and alleviate concerns about systemic absorption. A variety of vehicles aimed specifically at the hair follicle and shaft allow for the delivery of sufficient concentrations of active compounds into the interior these structures, allowing for the improved penetration of molecules intended to improve hair cosmesis. The following review provides an overview of cosmetic nanocarriers that are employed to deliver a variety of molecules to the hair follicle and shaft, intended to improve the appearance of the user.

4. Nanoparticles in Hair Cosmeceuticals

4.1. General Appearance

Hair is a signal of youth, with hair quality being positively correlated with good health [25]. Therefore, it is no surprise that an estimated 83.1 billion dollars will be spent in the hair care market in 2016 [26]. Nanotechnology-based innovations are aimed at improving the stability of cosmetic ingredients, enhancing the aesthetic appearance of products and targeting active ingredients to the focal structures with controlled release and sustained effects [27]. Much research has focused on the ways in which nanomaterials can be used to improve hair cosmesis—maintaining shine, silkiness and health of hair. Here, we have outlined a few ways through which nanomaterials have potentially changed the ways in which hair cosmetics provide their benefits.

Research demonstrates that nanomaterials have entered just about every personal hair care product on the market [28]. Shampoos have incorporated nanomaterials in order to optimize resident contact time with the scalp and hair follicle, allowing active agents time to form a protective film, sealing moisture within the cuticles (*i.e.*, preventing transfollicular water loss). Typically, during washing, the cuticle layer is opened by hot water, exposing the hydrolipid emulsion layer, whose function is to enable external water absorption and prevent internal water loss. In traditional shampoos, silicone will accumulate on the scalp rather than penetrate the hair given its hydrophobic characteristics. However, when silicone oil is incorporated into nanomaterials, it can rapidly diffuse into hair fibers given its small size. This results in improved hair moisture, gloss and lubrication [29]. The advantage of this formulation is that it does not destroy the cuticle of the hair fibers, but rather its nanosize allows for penetration into the hydrolipid emulsion layer. In contrast to shampooing, whose primary goal is to cleanse the hair, conditioning is responsible for reintroducing the materials necessary for proper growth, texture and health. Seracin, derived from silkworm, has been incorporated into conditioning agents as cationic nanoparticles and proven useful in repairing damaged cuticles, restoring gloss and texture (Figure 3) [30]. Another study found that cationic nanoemulsions (emulsions with a droplet diameter less than 100 nm) significantly improved dry hair, even after repeated shampooing [31]. The emulsion allowed for hair to appear shiny, less brittle and non-greasy. Another compound containing nanoparticles of oxides, hydroxides, carbonates, silicates and phosphates was able control the grease of hair [32]. Lastly, the use of zinc and chitin nanofibril complexes were able to reduce hair flakes (as measured by the corneocyte count) and sebum (as measured by milligrams of superficial lipids per square centimeter of skin surface) both *in vitro* and *in vivo* [33]. Incorporation of nanomaterial into this formulation improves ingredient deposition into the hair and directly impacts amino acid synthesis and keratin formation in order to repair the damaged cuticle and cortex. Within this setting, nanomaterials hold the potential to improve hair cosmesis by promoting increased contact with the hair shaft and follicle, increasing the quantity of incorporated active ingredients reaching the target site. Encapsulation of ingredients within nanomaterials optimizes penetration and allows for the delivery of previously insoluble compounds [34]. Thus, this platform has many features that are advantageous for topical application, representing an innovative technology that should be continuously exploited for commercial cosmetic products.



(a) Virgin Hair (b) Hair Damaged by decoloration

(c) Hair Damaged by discoloration (d) Hair treated with sericin cationic nanoparticles

Figure 3. Images of virgin hair (**a**), hair damaged by coloring agents (**b**,**c**) and hair treated with seracin cationic nanoparticles (**d**) [30].

4.2. Hair Color

Permanent hair dyes are extensively used by around one-third of the general population, with hair dye manufacturing developing into a multi-billion dollar industry [35]. The majority of consumers purchase permanent hair dyes, a product that has gained significant popularity due to its lasting effect, ease of application and changeability (*i.e.*, allows any color to be achieved). However, the use of synthetic dyes has been associated with adverse events including hypersensitivity reactions. Several epidemiologic studies have even associated their use with an increased risk of non-Hodgkin's lymphoma and multiple myeloma [36]. In light of this, the cosmetics industry has turned towards the development of new dyes and precursors as an alternative to permanent hair dyes. The use of nanotechnology to color hair dates back to when Greek and Roman civilizations were able to synthesize quantum dots within the hair shaft using a recipe of litharge, slaked lime and water to blacken hair [3]. More recently, an alkaline solution of $HAuCl_4$ allowed for the synthesis of gold nanoparticles inside human hair [3]. In this study, white hair fibers treated with this solution gave different shades (ranging from pale yellow to deep brown) in a time-dependent manner, with color remaining even after repeated washing (Figure 4). Another study found that incorporating *p*-phenylenediamine (PDA), the principle chemical involved in permanent hair dye, into hyaluronic nanoparticles successfully reduced toxicity and increased cell viability compared PDA alone [37]. Interestingly, 206 nm silica colored nanoparticles were only able to penetrate the cuticle and cortex of bleached hair fibers [38]. Authors postulated that bleaching destroys the disulfide bonds in the cuticle and cortex layers of the hair, destroying the bond between the lipids and the protein-rich surface. This allows the proteinaceous surface of hair to interact with nanoparticles, allowing for the diffusion of the silica nanoparticles into the hair fibers. Gourlaouen and Lee describe a method for coloring or lightening keratin fibers using quantum dot luminescent nanoparticles, capable of emitting visible light [39]. The nanoparticles provide a lasting, wash-resistant color without destruction of the keratin fibers. Lastly, carbon nanotubes enhance the affinity of carbon black for hair fibers [40]. Carbon black, a pigment used in a variety of cosmetic formulations for dying white/grey hair black has many limitations given its weak interaction with hair, ultimately staining other contacting surfaces (*i.e.*, combs, brushes, clothing, scalp). The small size and increased surface area-to-volume-ratio of carbon nanotubes results in enhanced affinity and interaction with hair fibers for a lasting effect.

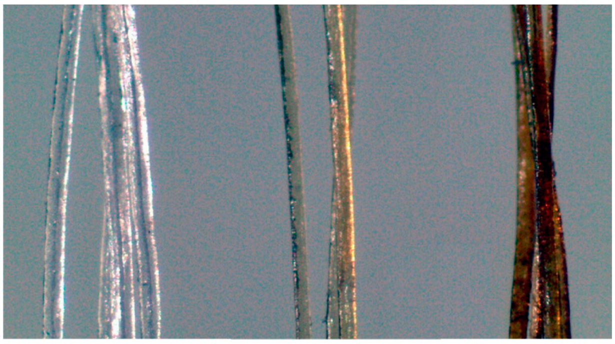


Figure 4. Color of hair is altered with gold nanoparticles in a time-dependent manner. Reprinted with permission from [3], published by American Chemical Society, 2012.

In addition to the hair shaft, hair follicles provide an additional target site of therapeutic interest. As mentioned above, it may be possible to selectively target specific sites within the hair shaft by manipulating the particle size. For example, topical liposome-entrapped melanin demonstrated the ability to modify the pigment of the hair follicle via delivery to the bulge region [41]. Therefore, developments in nanotechnology are providing new possibilities for hair dye applications, enhancing its lasting effect while limiting the toxicities.

4.3. Hair Growth and Removal

Androgenic alopecia (male pattern hair loss) is the most common form of human hair loss, affecting around 50% of adult men by the age of 50 and almost all Caucasian men by age 80 [42,43]. Furthermore, it is the result of the interplay between genetic and aging factors without any underlying disease process. Nevertheless, despite its prevalence, male-pattern baldness has a negative impact on socioemotional events (self-consciousness, helplessness, envy, *etc.*) with increased cognitive preoccupation and psychosocial distress [44,45]. While there are a variety of topical therapeutics available, drug permeability through the keratin layer is slow given the obstruction of follicular pores by horny and sebum plugs. Nanotechnology has become a promising drug delivery system, allowing for enhanced permeation into the hair pores with sustained effects. Zhou *et al.* reported that fullerene nanomaterials were capable of potentiating new hair growth and inducing new hair follicle formation within the dermis in murine and human skin [46]. The effect is thought to be due to the ability of fullerenes to scavenge free radicals, inhibiting the oxidative stress associated with hair follicle apoptosis and aging.

Currently, minoxidil and finasteride are the only two treatments approved by the US Food and Drug Administration for hair loss. One study found that encapsulating minoxidil into solid lipid nanoparticles showed similar skin penetration to commercial solutions without the corrosive potential (*i.e.*, dryness, irritation, burning, *etc.*) [47]. Finasteride, a 5-α reductase inhibitor preventing the peripheral conversion of testosterone to dihydrotestosterone, has a variety of unwanted side effects following oral administration; encapsulation of finasteride into topical liquid crystalline nanoparticles has been proposed as a viable alternative to oral administration in order to maintain high skin retention in the scalp, enable a lower dosing frequency and minimize significant side effects including mood disturbances, gynecomastia and erectile dysfunction [48]. Furthermore, poly(lactic-*co*-glycolic acid) nanoparticles loaded with a variety of hair growing ingredients (hinokitiol, gylcyrrhetinic acid and *6*-Benzylaminopurine) exerted a 2–2.5 fold greater scalp-pore permeability compared to controls and enhanced hair growth by accelerating the transition from the telogen to anagen phase of the hair cycle (Figure 5) [49]. In a second study, nanocapsules containing hinokitiol infused into a hair cleansing shampoo or hair tonic resulted in significantly higher degree of hair growth *in vivo* compared to saline and minoxidil solution controls [50].

In contrast, unwanted or excess hair can also have adverse psychological effects and impair quality of life. Given its widespread influence, people often turn towards contemporary measures for hair removal including shaving, waxing and depilatory creams. Laser hair removal has been highly publicized and has gained significant popularity for its therapeutic and cosmetic utility. Laser hair removal is a well-established method for permanent destruction of hair follicles, however current procedures require repeated treatments with exceedingly high costs and low rates of efficacy at removing lighter colored hair (grey, white, blonde and red). Recently, a patent was issued for the development of nanoparticles capable of removing unwanted hair [51]. The patent claims that the topical application of plasmonic nanoparticles, localized to target structures within the hair follicle, can be activated by light to localize thermal damage. Taken together, these results suggest that topically applied nanomaterials are successful carriers for hair-altering ingredients, representing a potentially new therapeutic opportunity for hair loss and hair removal.

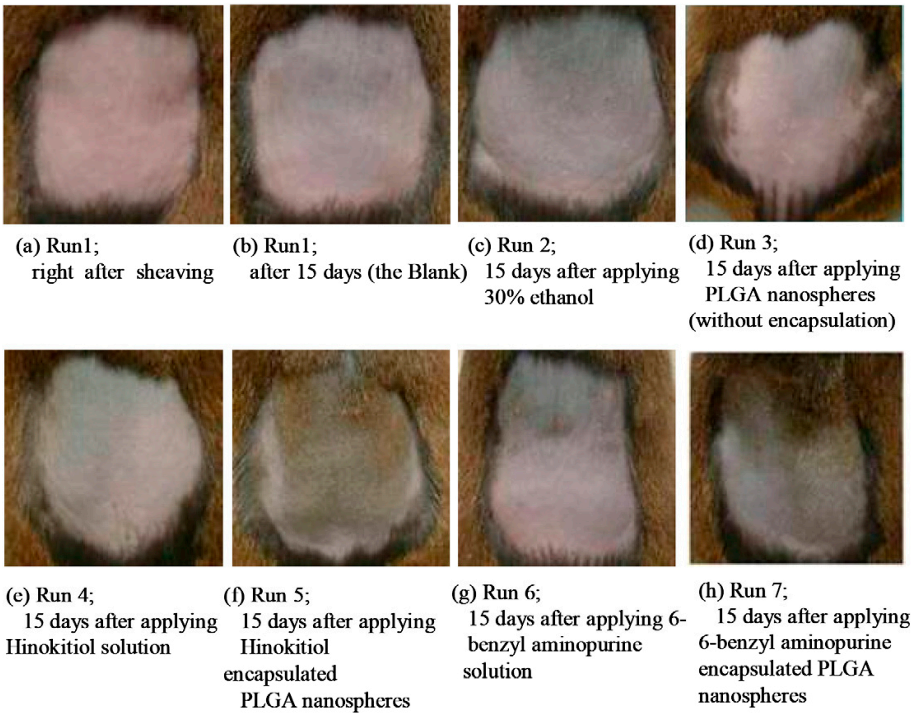


Figure 5. Evaluation of hair growth after application of a variety of hair growing ingredient encapsulated PLGA nanospheres. Mice are shown just after shaving (**a**) without applying any test liquid for 15 days (**b**) and 15 days after applying 30% ethanol (**c**), empty PLGA nanospheres (**d**), hinkokitiol solution (**e**), PLGA nanospheres encapsulated with hinkokitiol (**f**), 6-benzyl aminopurine solution (**g**), and PLGA nanospheres encapsulated with 6-benzyl aminopurine solution (**h**). Fur growth index (mean ± SD) was 1.1 ± 0.33 (**b**), 1.5 ± 0.075 (**c**), 1.7 ± 0.75 (**d**), 1.5 ± 0.50 (**e**), 2.3 ± 0.47 (**f**), 1.5 ± 0.76 (**g**) and 2.3 ± 1.11 (**h**). Reprinted with permission from [49], published by Elsevier Ltd., 2007.

5. Conclusion

The widespread influence of nanotechnology within the cosmetic arena is due to the unique properties exhibited by particles at the nanoscale. Research within the cosmetics industry has revealed that when nanomaterials are engineered into hair care, they can enhance the benefits of active ingredients. Enhanced knowledge of the composition of the hair fiber and an understanding of follicular targeting pathways are assisting the development of tailored products and new technologies capable of achieving improved hair cosmesis. Although there has been some preliminary success in the development of a variety of nanotechnology platforms for the delivery of hair care products, further research and a better understanding of toxicity are essential before the technology is readily available to the consumer.

Author Contributions

Jamie Rosen was involved in development, preparation, research, and writing of the manuscript. Angelo Landriscina made a substantial contribution in terms of review and editing the content of the manuscript. Adam J. Friedman was involved in all aspects of manuscript preparation.

Conflicts of Interest

The authors declare no conflicts of interest.

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