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Treatment of alopecia by different novel approach

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ABSTRACT
Alopecia is a chronic dermatological illness in which people lose some or all of their hair on their head, and in severe cases, their entire body, as a result of hair follicle destruction. It's an autoimmune disease caused by a combination of inherited and environmental causes. Alopecia is a side effect of chemotherapy. When chemotherapy is stopped, hair tends to regenerate. Alopecia areata is a disorder that only affects a small part of the body. Alopecia areata is a type of hair loss that affects the scalp, face, trunk, and extremities. Hair loss caused by a combination of genes and hormones is known as androgenetic alopecia. When the hair cycle switches from the anagen (growing) to the telogen (shedding) phase, telogen effluvium occurs. A thyroid disease, such as hypothyroidism or hyperthyroidism, could cause it. It can also be brought on by stress, such as undergoing major surgery. Traumatic alopecia is similar to traction alopecia, which is most commonly seen in youngsters and is caused by forceful hair traction. Trichotillomania is a type of traumatic alopecia in which the patient pulls his or her hair continuously. The normal variety of tinea capitis (black-dots) promotes non-scarring hair loss. Other varieties of tinea capitis, such as kerion and favus, encourage scarring hair loss. Hair shedding that occurs during the anagen phase of the cell cycle is known as anagen effluvium. Cancer patients are treated with chemotherapeutic drugs. Tinea capitis (favus) is an inflammatory variant of tinea capitis that can cause alopecia scarring.) The accumulation of mucinous material in sebaceous glands and hair follicles causes alopecia mucinosa. The metastatic infiltration of malignant cells into the scalp hair is known as alopecia neoplastica. The aetiology is determined by the type of alopecia. Anagen effluvium is caused by chemotherapeutic medications and leads in hair loss.Nanotechnology has enabled the development of drug delivery methods that increase the skin's stability, pharmacokinetics, and pharmacodynamics, as well as penetration and the construction of skin depots, therapeutic adherence, and the reduction of negative effects and treatment resistance.Nanoparticles,liposomes,neosomes,ethosomes,transferosomes,cubosomes,polymeric nanoparticles,metallic nanoparticles,cyclodextrins are different novel drug delivery systems that have the ability to interact with lipids in the stratum corneum, allowing skin permeation, or through hair follicles, forming depots, have the potential to transport both lipophilic and hydrophilic Improve pharmaceutical skin penetration and bioavailability by facilitating targeted and extended drug release through the stratum corneum and aiding local depot formation.Microneedling/mesotherapy, laser-assisted hair regrowth, radio frequency, sonophoresis, iontophoresis, and nanoparticles are some of the most common alopecia treatments. Nanotechnology, in particular, is a fascinating and rapidly developing field. When used alone or in combination with other drug delivery strategies, it offers improved results and reduces the risk of systemic side effects. More research on the efficacy, safety, and long-term effects of human nanoparticles is required.

Keywords: Alopecia, therapies,nanoparticles,liposomes,niosomes,transferosomes,ethosomes,cubosomes,hair loss

I. INTRODUCTION

The hair fall is a widespread biological condition all over the world, whether it is hair fall in men or in women. The significance of hair in improving a person's overall personality cannot be overstated. Many people begin to lose their hair at very young age. Hair loss can affect everyone, regardless of their place of origin, and is caused by a range of genetic, environmental, and systemic factors. Alopecia is a chronic dermatological condition in which people lose some or all of their hair on their head and, in extreme cases, their entire body, due to the destroy of the hair follicles. The cause of alopecia and how it progresses is unknown, although it is a type of autoimmune disorder that results from a concoction of hereditary and environmental factors.

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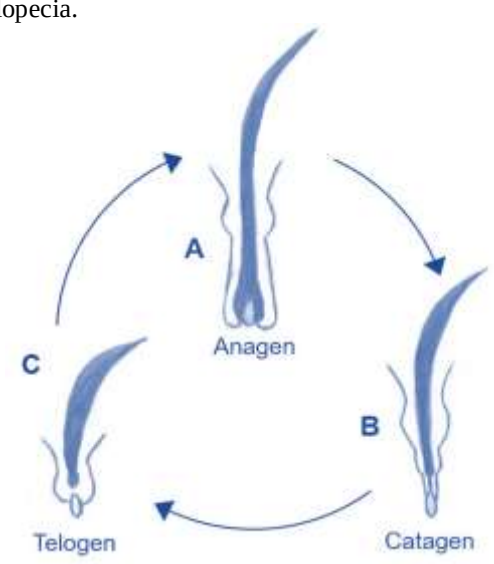
Chemotherapy can also induce alopecia. Hair tends to regrow once chemotherapy is discontinued. [1]There are three stages to the hair cycle.: anagen, catagen, and telogen. [2] Ninety percent of hair is in the anagen (growth) phase, with the remaining ten percent in the resting and shedding phases. [3] The telogen phase occurs when hair is falling out, and the hair will recycle and regrow again in the (growth) anagen phase. [4] The two most common kinds of alopecia are scarring and non-scarring alopecia.



Non-scarring or androgenetic alopecia is the most prevalent kind. Men lose hair in the front and temporal regions, but women lose hair in the center part of the scalp. Furthermore, female hair loss does not result in total baldness, whereas male hair loss can result in total baldness. [5]

ETIOLOGY

Six different types of non-scarring alopecia:

1) Alopecia areata: Hair loss that affects the scalp is known as alopecia areata, face, trunk, extremities. Alopecia areata is a condition that affects only a section of the body. Alopecia totalis is a condition that affects an entire site. Alopecia universalis is the term for hair loss that spreads across the body. [6]

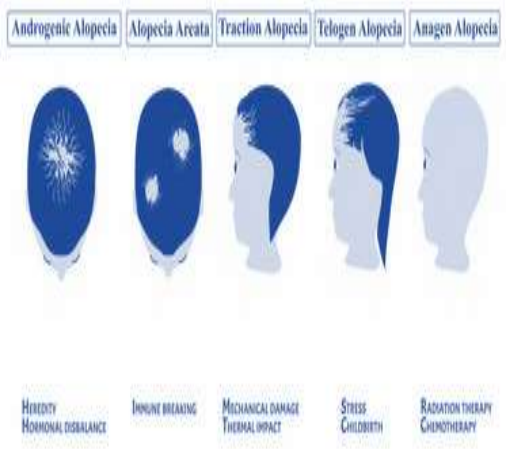
2) Androgenetic alopecia is a type of hair loss occured by a combination of genes and hormones (androgenic).

3) Telogen effluvium: occurs when the hair cycle shifts from the anagen (growing) phase to the telogen (shedding) phase. It could be occured by a thyroid disorder such as hypothyroidism or hyperthyroidism. It can also be caused by stress, such as severe surgery. A crash diet, inadequate nutrition, or medications can all contribute to telogen effluvium. [7]

4) Traumatic alopecia: This is related to traction alopecia, which is usually observed in children and results from violent traction of the hair. Trichotillomania is a kind of traumatic alopecia in which the patient continuously pulls on his or her hair. [8]

5) Tinea capitis: Unlike other varieties of tinea capitis, such as kerion and favus, the typical type of tinea capitis (black-dots) promotes non-scarring hair loss.

6) Anagen effluvium: Anagen effluvium is hair shedding that happens during the cell cycle's anagen phase. Chemotherapeutic chemicals are used to treat cancer patients.



Scarring alopecia can be devided into three categories:

1) Tinea capitis (favus): is an inflammatory form of tinea capitis that can lead to scarring alopecia.

2) Alopecia mucinosa: This is caused by the accumulation of mucinous material in sebaceous glands and hair follicles. The mucinous substance triggers an inflammatory reaction that prevents hair development.

3) Alopecia neoplastica: Alopecia neoplastica is the metastatic infiltration of malignant cells into the scalp hair.

PATHOPHYSIOLOGY

The type of alopecia determines the pathogenesis. It is unknown in alopecia areata, admitting the famous theory involves autoimmunity in the form of a T-cell–mediated

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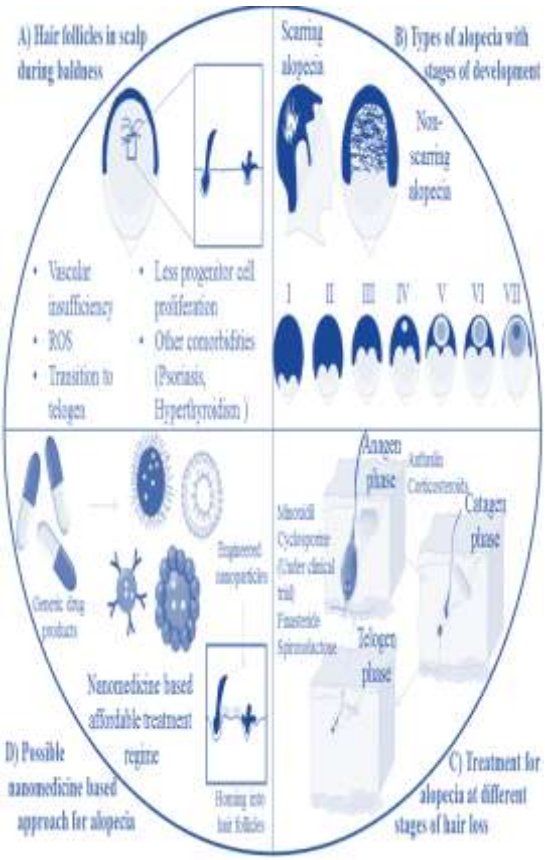
route. Androgens, both hereditary and hormonal, play a role in the pathophysiology of androgenetic alopecia. The losing of hair in telogen effluvium is influenced by hormones or stress, but the cause is not always evident. [9] Hair loss in tinea capitis is caused by a dermatophyte infection. Chemotherapeutic drugs cause anagen effluvium, which results in hair shedding. Alopecia mucinosa is caused by the invasion of the scalp by abnormal cells.[10]



Gross representation of alopecia progress with existing treatment and advancing nano-approaches. **A**) Microenvironment at hair follicle during the progression of alopecia. **B**) Types of alopecia and stages of development. **C**) Existing treatment strategies for alopecia at the several stages of hair development.**D**) Engineering nanoparticles in achieving possible nanomedicine and nano-theranostics approach for alopecia.

Treatments based on nanotechnology for alopecia

So far, nanotechnology has enabled the creation of drug delivery systems that improve stability, pharmacokinetic and pharmacodynamic characteristics of the skin,penetration and creation of skin depots therapeutic adherence, and reduce harmful effect and treatment resistance [24]. As a result, nanotechnology-based formulations enable smart distribution at lower dosages while maximising therapeutic benefits and providing a more desirable release profile. Some Nanotechnology-Based Formulations are listed below.

Nanoparticles with Vesicular Structure

Nanoparticles with vesicular structures are a type of lipid-based nanoparticle that has the potential to transport both lipophilic and hydrophilic drugs., improving drug-targeted delivery and bioavailability [11]. Because of their ability to solubilize drug into the lipidic matrix, promoting localised depots and facilitating skin absorption via the follicular pathway, these nanotechnology-based formulations have been extensively studied as topical delivery systems and are also regarded as permeation enhancers.[12,13].

Liposomes

Liposomes are phospholipid bilayer structures with an aqueous centre in which hydrophilic or lipophilic medicines can be put in the core or trapped between the phospholipid bilayers. [14,15]. Liposomes have the ability to interact with lipids in the stratum corneum, allowing skin permeation, or through hair follicles, forming depots, due to their phospholipid composition [16]. Liposomes are biocompatible and biodegradable, and they can stay in the bloodstream for a long time. However, aggregation, drug leakage, hydrolysis, and particle size changes limit their use [15,17]. According to reports, drug-loaded liposomes significantly improved skin penetration and depot formation by the stratum corneum pathway. Liposomes, on the another hand, may cause systemic side effects including

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headaches or hypotension due to their capacity to reach the bloodstream.PEVs, or Vesicles containing various penetration enhancers can also boost cutaneous medication bioavailability by improving drug accumulation in the higher skin layers without reaching systemic circulation.

Neosomes

Niosomes are non-ionic surfactant-based vesicular nanotechnology formulations that can accommodate either hydrophilic or hydrophobic pharmaceuticals.By facilitating targeted and extended drug release through the stratum corneum and supporting local depot building, niosomes can improve medication skin penetration and bioavailability. Furthermore, niosomes have higher stability and a better cost-effective ratio than liposomes [18,19], as well as biocompatible and biodegradable features. These nanotechnology-based formulations have not been connected to irritating or immunogenic responses in comparison to conventional topical formulations, allowing for enhanced therapeutic adherence due to a reduction in the greasy sensation after application. The ability of drugs entrapped in niosomes to reach deeper skin layers and establish drug depots improved therapeutic adherence and sustained release.[20,21]

Ethosomes

Ethosomes are lipid-rich vesicular nanotechnology-based compositions with high ethanol concentrations. Ethosomes have been demonstrated to boost drug skin penetration in various studies due to their interaction with the stratum corneum's lipids and elevation of both the cellular membrane's fluidity and permeability. [23,25]. Ethosomes, as opposed to liposomes, allow for better drug transport effectiveness and stability via the skin [22,23,24]. Liposomes, on the other hand, penetrate the skin less deeply and prevent accumulating in deeper layers.Because the medication could reach deeper skin layers after being put into ethosmomes, skin penetration was improved. [22].

Transferosomes

an aqueous core is surrounded by a phospholipid bilayer with edge activators. Those structures are differentiated by their ability to deform and infiltrate through the epidermal layers without significantly reducing particle size, allowing them to reach the deep levels of the stratum corneum [27]. Edge activators, which work by modifying interfacial tension and allowing these vesicular nanoparticles to "squeeze" through intercellular gaps without losing their structure, are responsible for transferosomes' ability to deform [26]. Transferosomes are more adaptable than liposomes and may be more resistant to stress [28]. Transferosome deformation is problematic when a hydrophilic drug is present due to a loss in vesicular flexibility, which might lead to transferosomal disruption.

Cubosomes

Cubosomes are crystalline bilayer vesicular nanoparticles with a liquid honeycomb lattice on the inside and specialised surfactants on the exterior that self-assemble [29]. On the interior, there are two water channels, and on the exterior, there are particular surfactants. Honeycomb is a bi-continuous three-dimensional form that improves surface area. Because of their improved durability, biodegradability, and encapsulation efficiency, cubosomes are a viable method for prolonged and targeted drug release [30]. They have demonstrated their ability to reduce the skin's barrier function, enhancing skin penetration and hair follicle depots, allowing them to reach deeper skin layers and permitting continuous release. Cubosomes, however, produce greater Drug quantities due to their increased loading capacity, which may enter the systemic circulation.

Polymeric nanoparticles

Polymeric nanoparticles are biocompatible colloidal systems composed of natural or synthetic polymers with particle sizes ranging from 200 to 300 nm [32]. Polymeric nanoparticles as topical administration strategies are among the most studied and developed topical drug delivery systems, forming drug depots that allow for sustained and targeted drug release due to their ability to reduce drug degradation and enhance drug skin permeation through the stratum corneum and follicular accumulation. Polymer-based synthetic nanotechnology-based formulations, which may transport the drug dispersed in the matrix, adsorbed at the surface, or encapsulated, improve drug hair follicle accumulation [35]. Polymeric nanoparticles are being developed and tested for AGA therapy [31,24]. Depending on the polymer, polymeric nanoparticles can be structured as nano capsules or nanospheres.

Metallic Nanoparticles

Due to the incorporation of metal or metal oxide compounds, metallic nanoparticles are hard inorganic structures with antibacterial, anti-inflammatory, healing, and antioxidant capabilities. The medication may be adsorbed or conjugated at the surface, depending on the activity. Metallic nanoparticles, on the other hand, are commonly utilised as colouring or physical agents in a variety

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of cosmetics pipelines. Sun blockers include silver, gold, zinc, titanium, and silica [38]. Zircon-based nanoparticles for medication delivery have boosted the expression of the VEGF and IGF-1 genes, as well as their mRNA levels, in the current AGA scenario. As a result, there was significant hair growth, improved hair bulb retention, and no erythema or discomfort [37].

Cyclodextrins

Cyclodextrins (CDs), which are cyclic polysaccharides containing six to eight glucopyranose units, are an enzymatic result of starch breakdown [36]. Alpha, beta, and gamma are three non-synthetic CDs that differ solely in the number of D-glucose units they contain. CDs assist in ensuring that a medicine is released in a controlled and consistent manner. CDs carry medicine to the hair follicle, ensuring drug stability and minimising oxidative, thermal, and photolytic degradation, as well as enhancing drug water solubility [31,40]. CD/Drug inclusion complexes have been developed in the past to boost drug diffusion coefficients and influx through the skin, resulting in higher accumulation at the application site. [39]

Current Technique

It is employed to cope with the existing problems of alopecia. Modern techniques have been developed and are covered further below.

Micro needling/Mesotherapy

Micro needling is a common treatment for skin rejuvenation, striae and scar reduction, and, more recently, hair loss therapy. The stimulation of the Wnt/B-catenin pathway may be the mechanism of action when given alone. This treatment enhances medicine penetration by creating microchannels through the top layers of the epidermis and the superficial dermis [42]. Solid, hollow, coated, and dissolving microneedles are among the various shapes and sizes available [43]. Solid microneedles are often used in dermatology, and their penetration depth and/or number of microneedles vary depending on the equipment used, such as a derma roller or an electric pen. For scalp delivery, a depth of 1.2 to 1.5mm is ideal [44].

Chandrashekar et al were the first to report that microneedling followed by topical triamcinolone acetonide treatment successfully treated two patients with alopecia areata (AA) who were resistant to topical therapy in 2014 [42]. Jha et colleagues found statistically significant differences in pull test, terminal/vellus hair ratio, and patient satisfaction while treating patients with microneedling and platelet rich plasma (PRP) combined with topical minoxidil compared to PRP or minoxidil alone [45].

Mesotherapy is a treatment in which medications and/or vitamin combinations are injected into the skin. Moftah et al showed a substantial improvement in female pattern hair loss (FPHL) when comparing mesotherapy with a dutasteride-containing solution (dutasteride 0.5 mg, biotin 20 mg, pyridoxin 200 mg, and D-panthenol 500 mg) to normal saline [46].

Mesotherapy with a minoxidil-finasteride blend (1 ml minoxidil 0.5 percent, 1 ml finasteride 0.05 percent, 2 ml biotin 5mg/ml, and 2 ml Dpanthenol 50mg/ml) exhibited excellent hair regrowth when utilised as adjuvant therapy in the treatment of a patient with androgenetic alopec Microinfusing drugs into the skin with hollow microneedles from professional tattoo machines is another novel skin delivery technology. The sole data on alopecia is a case report of two people with AGA who improved after having a 5 percent Minoxidil micro infusion [48]. The advantage of this procedure over intralesional injection is that a small amount of medicine can be applied consistently and at the same depth into the skin, improving drug delivery to the target (s).ia (AGA) [47].

(DMN) are drug-encapsulating tiny needles that release drug into the skin once the needles' polymers have decomposed entirely [49]. This technique has been tested for wrinkle treatment with ascorbic acid [50], pruritus treatment with capsaicin [51], and keloid treatment with Re-188 [52], but it has not yet been used in people to treat hair loss. After using valproic acid coated dissolving micro needles, Shaman et al. discovered enhanced expression of the Wnt/bcatenin pathway and activation of hair regeneration in mice [53].

Laser-assisted hair regrowth

Alopecia areata and other kinds of alopecia have lately been treated with lasers, both ablative and non-ablative, including fractional lasers. The SC is disturbed, allowing medicines to reach the hair follicles more effectively [54]. Furthermore, by establishing a favourable wound-healing environment, the minor lesions induced by these therapies may encourage hair formation [55]. In a randomised controlled split-scalp study (N=10 men), Cho,2016 et al discovered an increase in hair density and shaft diameter using the Thulium laser (1,927 nm) followed by topical growth agents (GF). Among the chemicals in the GF were

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keratinocyte growth factor, human cord blood cell-conditioned medium (which largely contained platelet-derived growth factor, vascular endothelial growth factor, hepatocyte growth factor, insulin-like growth factor 1, and fibroblast growth factor), and genistein.

Hair growth was enhanced in all treatment groups in a prospective case study of 88 shaved mice treated with Er:YAG laser (2,940 nm) alone or in combination with topical minoxidil, however anagen re-entry was significantly faster in the combined group. These findings could be explained by the increased absorption of minoxidil following ablative fractional Er: YAG laser (2,940 nm) therapy [56].

Radio-frequency

In radio-frequency (RF) cell-ablation, microelectrodes are used to deliver an alternating electrical current through the skin at a frequency of 100–500 kHz. The ions in the cells near the microelectrodes oscillate as a result of the change in electrical potential. Classification of Accepted Manuscript Information: Heat creation, evaporation of water, cell apoptosis, and, eventually, skin damage The Wnt/bcatenin pathway activation could be the mechanism. Inflammation can cause hair regeneration in thermal injury wounds by increasing blood flow, follicular vascularization, inflammatory cells, and cytokines. Yu et al. used a combination of fractional radiofrequency micro needling and 5% topical minoxidil to study split-scalp hair loss in 19 Chinese men with male pattern hair loss (MPHL). After 5 months, the combined-therapy group had significantly more hair count and thickness.

Sonophoresis

The use of ultrasound to increase the skin's permeability (sonophoresis) allows for the transfer of a variety of substances [58]. There are two types of ultrasonic treatments: "high" power and "low" power (ultrasound frequencies below 100 kHz) [59] Low-power ultrasounds can be used for sonophoresis, sonoporation, gene therapy, and bone regeneration [5,27]. Mitragotri et al. used low-frequency ultrasound (20 KHz) in vitro to increase the transport of low-molecular-weight drugs (like salicylic acid and corticosterone) and high-molecular-weight proteins (like insulin, interferon, and erythropoietin) across human cadaver skin. The most important ultrasound-related phenomena in sonophoresis is cavitation, which is the acoustically driven creation and oscillation of gas bubbles [58]. When compared to therapeutic ultrasound, low-frequency ultrasound induces a 1000-fold increase in transdermal enhancement [58] and improves skin permeability to a wide range of medicinal compounds, including both hydrophilic and macromolecules [60].

Santoianni P et al used low-frequency sonophoresis in vivo to give methylprednisolone ointment and cyclosporine solution intradermally as a treatment for patchy alopecia areata (30 patients). The drugs were given three times a week for three months after 10 minutes of sonophoresis (25 KHz). Both treatments resulted in a significant increase in hair growth [59].

Iontophoresis (IP)

In the iontophoretic technique, a small electric current (up to 0.5 mA/cm2) is administered to a drug reservoir on the skin's surface. An electrode with the same charge as the drug/solute generates repulsion forces, which drive the solute molecules across the SC towards an electrode with the opposite charge. When an electric field is applied to a charged ion solution, the charged ions are propelled in the direction of the field. Iontophoresis can also increase the penetration of uncharged molecules into the skin, resulting in electroosmosis, because the entire solution experiences a convective flow due to viscous forces [57,60]. This delivery system increased the amount of medication reaching the follicular infundibula by 5-fold as compared to the usual technique. conveyance of information in a passive manner Iontophoresis was revealed to greatly increase the transport and storage of nutrients in an in vitro investigation on rat skin by Gelfuso et al. [61]. When ultrasound and iontophoresis are used together, the optimum results can be achieved. Each strategy leads in a 10-fold increase in penetration when used alone. The use of ultrasonic pretreatment has also been shown to reduce voltage by lowering skin resistance. This delivery system increased the amount of medication reaching the follicular infundibula by 5-fold as compared to the usual technique. conveyance of information in a passive manner Iontophoresis was revealed to greatly increase the transport and storage of nutrients in an in vitro investigation on rat skin by Gelfuso et al. [61]. When ultrasound and iontophoresis are used together, the optimum results can be achieved. Each strategy leads in a 10-fold increase in penetration when used alone. The use of ultrasonic pretreatment has also been shown to reduce voltage by lowering skin resistance.

Nanoparticles

In a range of therapeutic uses, including topical administration for hair loss therapy,

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nanoparticle systems use molecular-sized particles loaded with various medicines and compounds. Liposomes, solid lipid nanoparticles, nanoemulsions, natural and synthetic polymer-based nanoparticles, and gold/silver nanoparticles are all good choices for follicular delivery. Nanoparticles with a diameter of 230 nm were shown to be more effective at targeting sebaceous glands, whereas particles with a diameter of 643 nm were found to be more effective at targeting the hair follicle bulge area. [62].Only a few human studies have been undertaken to determine the efficacy of nanosystems for hair loss therapy at this time. Several animal studies, on the other hand, have convincingly established that nanoparticles have improved medicine penetration, longer drug delivery, and less systemic side effects than typical topical drug administration [63]. These features allow for longer-lasting pharmaceutical administration, fewer systemic side effects, and less skin irritation, all of which should help patients comply.Drugs can be delivered to the follicles using lipid nanosystems that interact with sebum. Liposomes have showed significant diffusion into hair follicles due to their lipophilic and hydrophilic properties.These features allow for longer-lasting pharmaceutical administration, fewer systemic side effects, and less skin irritation, all of which should help patients comply.Drugs can be delivered to the follicles using lipid nanosystems that interact with sebum. Liposomes have showed significant diffusion into hair follicles due to their lipophilic and hydrophilic properties.[64].Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NSLC), which comprise a combination of unsaturated and liquid lipid components, also showed efficient drug release at higher drug concentrations. NSLC has the advantage of maintaining high drug stability, allowing for a prolonged shelf life.[65].Polymeric nanoparticles made from natural and manmade biocompatible materials are being studied, and they have been found to be safe. [66].Nanoparticles encapsulated in minoxidil have been studied using animals. When compared to a standard minoxidil solution, percutaneous administration of minoxidil encapsulated poly(L-lactide-co-glycolide) nanoparticles (PLLGA) synthesised by water-in-oil-in-water solvent evaporation (W/O/W) and sonification resulted in 2.5 times hair follicle delivery. [67]. A 5-fold longer release period than minoxidil solution and a two-fold increase in effectiveness Chitosan, a natural polymeric nanoparticle, was Nanoparticles also demonstrated a lower irritating impact than commercial shown to enhance minoxidil in hair follicles when applied to pig ear skin[68,69].Lipid nanoparticles have been developed as carriers for topical finasteride and minoxidil delivery and they have been demonstrated to have great stability and can be stored for at least 28 days.[70].Despite the lack of data on nanoparticle delivery in humans, a small non-controlled prospective study found that topical application of a solution containing 5% NanoxidilR (a nanosome-based preparation of Pyrrolidinyl Diaminopyrimidine Oxide, a potassium channel opener, Azelaic acid, Copper Tripeptide-1, Lysophosphatidic acid) and several hair growth promoters such as myristoyl pentapeptide-17, adenosine[71].Inhibitors of the 5-Alpha Reductase enzyme could likewise be delivered via nanoparticles. Nanoparticles containing finasteride and dutasteride have the advantage of lowering medication penetration and thereby systemic side effects.[72]. Finasteride-encapsulated nanoparticles have also been studied extensively in animal models and have shown to offer similar benefits to minoxidil-encapsulated nanoparticles, such as longer drug release and enhanced stability. We got testosterone-induced AGA in mice after 10 weeks of finasteride PLLGA nanoparticle therapy and discovered that 93.3 percent of total hair growth was achieved, compared to 86.7 percent with oral finasteride, with the added benefit of improved apoptosis suppression[73].The only human study was a small retrospective case series including 2.5 percent finastride in a liposome formulation in males with AGA. At six months, 11 patients (39.2%) showed moderate improvement in their overall photography, whereas 14 patients showed limited progress (50 percent). The therapy was well tolerated and easy to use by the patients.[74].In addition to the most regularly used hair loss treatments like minoxidil and 5 alpha reductase inhibitors, nanoparticle technology has been employed to deliver Quercetin, fibroblast growth factor 2 containing dalteparin/protamine, Ruxolitinib, Arginine, Flutamide, and Fullerene. Nanoparticle delivery has showed promise in animal models and may provide another medicine delivery alternative with less systemic absorption and associated side effects [75-80].

Best of current technique

Healthcare practitioners should consider not just the medicine but also the mode of administration while treating alopecia. In our literature review, we looked into novel

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technologies for improving alopecia therapy delivery, including as micro needling, laser-assisted, radiofrequency, sonophoresis, iontophoresis, and nanoparticles. The results are promising, despite the fact that most technologies have only been evaluated in animal models so far. Nanotechnology, in particular, is a fascinating and rapidly developing field. When used alone or in combination with other drug delivery strategies, it offers improved results and reduces the risk of systemic side effects. More research on the efficacy, safety, and long-term effects of human nanoparticles is required.

II. CONCLUSION

Novel therapeutics are extremely important in the treatment of alopecia. While reducing side effects and hazardous consequences, a novel drug delivery system can improve poor bioavailability, therapeutic efficacy, dose frequency, patient adherence, and patient quality of life. When employed alone or in combination with other medication delivery systems, nanotechnology offers improved results and reduces the danger of systemic side effects. More research on the efficacy, safety, and long-term effects of human nanoparticles is required.

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REFERENCES

[1]. Madani S, Shapiro J. Alopecia areata update. J Am Acad Dermatol.2000; 42:549-66.
[2]. Monib KME, Hussein MS, Kandeel WS. The relation between androgenetic thin hair diagnosed by trichoscope and benign prostatic hyperplasia. J Cosmet Dermatol. 2018 Dec 05;
[3]. Gordon SC, Abudu M, Zancanaro P, Ko JM, Rosmarin D. Rebound effect associated with JAK inhibitor use in the treatment of alopecia areata. J EurAcad Dermatol Venereol. 2019 Apr33;4:156-157
[4]. Spaich S, Kinder J, Hetjens S, Fuxius S, Gerhardt A, Sütterlin M. Patient Preferences Regarding Chemotherapy in Metastatic Breast Cancer-A Conjoint Analysis for Common Taxanes. Front Oncol. 2018; 8:535.
[5]. Li J, Kong XB, Chen XY, Zhong WZ, Chen JY, Liu Y, Yin P, Fang SL. Protective role of α2-macroglobulin against jaw osteoradionecrosis in a preclinical rat model. J Oral Pathol Med. 2019 Feb;2:166-173.
[6]. Lee YB, Jun M, Lee WS. Alopecia areata and poliosis: A retrospective analysis of 258 cases. J Am Acad Dermatol. 2019 Jun;6:1776-1778.
[7]. Liu LY, King BA. Response to tofacitinib therapy of eyebrows and eyelashes in alopecia areata. J Am Acad Dermatol. 2019 Jun;6:1778-1779.
[8]. Chen P, Chen F, Zhou B. The risk of dermatological toxicities of combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma patients: a systematic review and meta-analysis. CutanOculToxicol. 2019 Jun;2:105-111.
[9]. Yu L, Lu Z. Linear alopecia areata. JAAD Case Rep. 2018 Nov4;10:1072-1073.
[10]. Davey L, Clarke V, Jenkinson E. Living with alopecia areata: an online qualitative survey study. Br J Dermatol. 2019 Jun;6:1377-1389.
[11]. Modi C.D,Bharadia P.D. Transfersomes: New Dominants for Transdermal Drug Delivery. Am. J. Pharm.Tech. Res. **2012**; 2: 71–91.
[12]. Muzzalupo R, Tavano L, Cassano R,Trombino S, Ferrarelli T, Picci N.Anew approach for the evaluationof niosomes as effective transdermal drug delivery systems. Eur. J. Pharm. Biopharm. 2011;79: 28–35.
[13]. Choi M.J, Maibach H.I. Liposomes and niosomes as topical drug delivery systems. Skin Pharmacol. Physiol.2005;18:209–219.
[14]. Escobar-Chavez, J,Díaz-Torres R,Rodríguez-Cruz I, Domínguez-Delgado C,Morales R,Ángeles-Anguiano E, Melgoza-Contreras L. Nanocarriers for transdermal drug delivery. Res. Rep.Transdermal. Drug Deliv. 2012;1: 3–17.
[15]. Abdel-Mottaleb, M.M.A.; Try, C.; Pellequer, Y.; Lamprecht, A. Nanomedicine strategies for targeting skin inflamation. Nanomedicine 2014, 9, 1727–1743.
[16]. Barua, S.; Mitragotri, S. Challenges associated with Penetration of Nanoparticles across Cell and TissueBarriers: A Review of Current Status and Future Prospects. Nano Today 2014, 9, 223–243.
[17]. Bakowsky, H.; Richter, T.; Kneuer, C.; Hoekstra, D.; Rothe, U.; Bendas, G.;

Ehrhardt, C.; Bakowsky, U.Adhesion characteristics and stability assessment of lectin-modified liposomes for site-specific drug delivery. Biochim. Biophys. Acta **2008**, 1778, 242–249.

[18]. Mali, N.; Darandale, S.; Vavia, P. Niosomes as a vesicular carrier for topical administration of minoxidil:Formulation and in vitro assessment. Drug Deliv. Transl. Res. **2013**, 3, 587–592.

[19]. Moghassemi, S.; Hadjizadeh, A. Nano-niosomes as nanoscale drug delivery systems: An illustrated review.J. Control. Release **2014**, 185, 22–36.

[20]. Uchechi, O.; Ogbonna, J.D.N.; Attama, A.A. Nanoparticles for Dermal and Transdermal Drug Delivery.Appl. Nanotechnol. Drug Deliv. **2014**, 4, 193–227.

[21]. Rajera, R.; Nagpal, K.; Singh, S.K.; Mishra, D.N. Niosomes: A Controlled and Novel Drug Delivery System.Biol. Pharm. Bull. **2011**, 34, 945–953.

[22]. Lopez-Pinto, J.M.; Gonzalez-Rodriguez, M.L.; Rabasco, A.M. E_ect of cholesterol and ethanol on dermaldelivery from DPPC liposomes. Int. J. Pharm. **2005**, 298, 1–12.

[23]. Touitou, E.; Dayan, N.; Bergelson, L.; Godin, B.; Eliaz, M. Ethosomes—Novel vesicular carriers for enhanceddelivery: Characterization and skin penetration properties. J. Control. Release **2000**, 65, 403–418.

[24]. Carter, P.; Narasimhan, B.; Wang, Q. Biocompatible nanoparticles and vesicular systems in transdermal drugdelivery for various skin diseases. Int. J. Pharm. **2019**, 555, 49–62.

[25]. Touitou, E.; Godin, B.;Weiss, C. Enhanced Delivery of Drugs Into and Across the Skin by Ethosomal Carriers.Drug Dev. Res. **2000**, 50, 406–415.

[26]. Bibi, N.; Ahmed, N.; Khan, G.M. Nanostructures in Transdermal drug Delivery Systems; Elsevier: Amsterdam,Netherlands, 2017; pp. 639–668.

[27]. Hua, S. Lipid-based nano-delivery systems for skin delivery of drugs and bioactives. Front. Pharmacol.**2015**, 6, 219.

[28]. Rajan, R.; Jose, S.; Mukung, V.P.B.; Vasudevan, D.T. Transferosomes—A vesicular transdermal deliverysystem for enhanced drug permeation. J. Adv. Pharm. Technol. Res. **2011**, 2, 138–143.

[29]. Karami, Z.; Hamidi, M. Cubosomes: Remarkable drug delivery potential. Drug Discov. Today **2016**, 21,789–801.

[30]. Pan, X.; Han, K.; Peng, X.; Yang, Z.; Qin, L.; Zhu, C.; Huang, X.; Shi, X.; Dian, L.; Lu, M.; et al. Nanostructuredcubosomes as advanced drug delivery system. Curr. Pharm. Des. **2013**, 19, 6290–6297.

[31]. Fang, C.-L.; Alju_ali, I.A.; Li, Y.-C.; Fang, J.-Y. Delivery and targeting of nanoparticles into hair follicles.Ther. Deliv. **2014**, 5, 991–1006.

[32]. Alvarez-Roman, R.; Naik, A.; Kalia, Y.N.; Guy, R.H.; Fessi, H. Skin penetration and distribution of polymericnanoparticles. J. Control. Release **2004**, 99, 53–62.

[33]. Li, J.; Qiao, Y.;Wu, Z. Nanosystem trends in drug delivery using quality-by-design concept. J. Control. Release**2017**, 256, 9–18.

[34]. Ramezanli, T.; Kilfoyle, B.E.; Zhang, Z.; Michniak-Kohn, B.B. Polymeric nanospheres for topical delivery ofvitamin D3. Int. J. Pharm. **2017**, 516, 196–203.

[35]. Zhang, Z.; Tsai, P.-C.; Ramezanli, T.; Michniak-Kohn, B.B. Polymeric nanoparticles-based topical deliverysystems for the treatment of dermatological diseases. Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol.**2013**, 5, 205–218.

[36]. Sakamoto, K.; Lochhead, R.; Maibach, H.; Yamashita, Y. Cosmetic Science and Technology: Theoretical Principlesand Applications; Elsevier: Amsterdam, Netherlands, 2017; Volume 813.

[37]. Nagai, N.; Iwai, Y.; Sakamoto, A.; Otake, H.; Oaku, Y.; Abe, A.; Nagahama, T. Drug Delivery System Basedon Minoxidil Nanoparticles Promotes Hair Growth in C57BL/6 Mice. Int. J. Nanomed. **2019**, 14, 7921–7931.

[38]. Borowska, S, Brzoska, M.M. Metals in cosmetics: Implications for human health. J. Appl. Toxicol.**2015**; 35: 551–572.

[39]. Lopedota, A,Denora N, Laquintana V,Cutrignelli A, Lopalco A ,Tricarico, D.; Maqoud, F.;Curci, A.; Mastrodonato, M.; la Forgia, F.; et al. Alginate-Based Hydrogel Containing

[40]. Minoxidil/Hydroxypropyl-beta-Cyclodextrin Inclusion Complex for Topical Alopecia Treatment. J. Pharm.Sci. **2018**; 107:1046–1054.

[41]. Tarimci N. Cyclodextrins in the Cosmetic Field, in Cyclodextrins in Pharmaceutics,

Cosmetics, and Biomedicine:Current and Future Industrial Applications; Bilensoy, E., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2011.

[42]. Arshdeep, Sendhil Kumaran M. Platelet-rich plasma in dermatology: Boon or a bane? Indian J. Dermatol. Venereol. Leprol. 2014; 80:5–14.

[43]. Mysore V, Chandrashekar B, Yepuri V. Alopecia areata-successful outcome with microneedling and triamcinolone acetonide. J. Cutan. Aesthet. Surg. 2014; 7:63.

[44]. Ita K. Transdermal delivery of drugs with microneedles—potential and challenges. Pharmaceutics. 2015; 7:90–105.

[45]. Buchi N. Nalluri, Sai Sri V. Anusha, Sri R. Bramhini, J. Amulya, Ashraf S.K. Sultana, Chandra U. Teja and Diganta B. Das, "In Vitro Skin Permeation Enhancement of Sumatriptan by Microneedle Application", Current Drug Delivery (2015) 12: 761.

[46]. Jha AK, Vinay K, Zeeshan M, et al. Platelet-rich plasma and microneedling improves hair growth in patients of androgenetic alopecia when used as an adjuvant to minoxidil. J. Cosmet. Dermatol. 2019;1–6.

[47]. Moftah N, Moftah N, Abd-Elaziz G, et al. Mesotherapy using dutasteride containing preparation in treatment of female pattern hair loss: Photographic,morphometric and ultrustructural evaluation. J. Eur. Acad. DermatologyVenereol. 2013; 27:686–693.

[48]. Melo DF, de Mattos Barreto T, Plata GT, et al. Excellent response to mesotherapy as adjunctive treatment in male androgenetic alopecia. J. Cosmet. Dermatol. 2019;1–3.

[49]. Contin LA. Alopecia androgenéticamasculinatratada com micro agulhamentoisolado e associado a minoxidil injetável pela técnica de microinfusão de medicamentos pela pele. Surg. Cosmet. Dermatology. 2016; 8:158–161

[50]. Lahiji SF, Dangol M, Jung H. A patchless dissolving microneedle delivery system enabling rapid and efficient transdermal drug delivery. Sci. Rep. 2015; 5:1–7.

[51]. Lee C, Yang H, Kim S, et al. Evaluation of the anti-wrinkle effect of an ascorbic acid-loaded dissolving microneedle patch via a double-blind, placebo controlled clinical study. Int. J. Cosmet. Sci. 2016; 38:375–381.

[52]. Misery L, Erfan N, Castela E, et al. Successful treatment of refractory neuropathic pruritus with capsaicin 8% patch: A bicentric retrospective study with long-term follow-up. Acta Derm. Venereol. 2015; 95:864–865.

[53]. Bhusari P, Shukla J, Kumar M, et al. Noninvasive treatment of keloid using customized Re-188 skin patch. Dermatol. Ther. 2017; 30:1–4.

[54]. FakhraeiLahiji S, Seo SH, Kim S, et al. Transcutaneous implantation of valproic acid-encapsulated dissolving microneedles induces hair regrowth. Biomaterials [Internet]. 2018; 167:69–79.

[55]. [19Dabek RJ, Austen WG, Bojovic B. Laser-assisted Hair Regrowth. Plast.Reconstr. Surg. - Glob. Open. 2019;7: e2157.

[56]. Yu AJ, Luo YJ, Xu XG, et al. A pilot split-scalp study of combined fractional radiofrequency microneedling and 5% topical minoxidil in treating male pattern hair loss. Clin. Exp. Dermatol. 2018; 43:775–781.

[57]. Ke J, Guan H Lis, et al. Erbium: YAG laser (2,940 nm) treatment stimulates hair growth through upregulating Wnt 10b and β-catenin expression in C57BL/6 mice. Int. J. Clin. Exp. Med. 2015; 8:20883–20889.

[58]. Lavon I Kost J. Ultrasound and transdermal drug delivery. Drug Discov.Today. 2004; 9:670–676.

[59]. Mitragotri S, Blankschtein D, Langer R. Transdermal drug delivery using low frequency sonophoresis. Pharm. Res. 1996; 13:411–420.

[60]. Santoianni P, Nino M, Calabro G. Intradermal drug delivery by low-frequency sonophoresis (25 kHz). Dermatol. Online J. 2004. p. 24.

[61]. Watanabe S, Takagi S, Ga K, et al. Enhanced transdermal drug penetration by the simultaneous application of iontophoresis and sonophoresis. J. Drug Deliv. Sci. Technol. 2009; 19:185–189.

[62]. Gelfuso GM, Gratieri T, Delgado-Charro MB, et al. Iontophoresis-Targeted, Follicular Delivery of Minoxidil Sulfate for the Treatment of Alopecia. J. Pharm.Sci. [Internet]. 2013; 102:1488–1494.

[63]. Patzelt A, Richter H, Knorr F, et al. Selective follicular targeting by modification of the particle sizes. J. Control. Release [Internet]. 2011; 150:45–48.

[64]. Papakostas D, Rancan F, Sterry W, et al. Nanoparticles in dermatology. Arch.Dermatol. Res. 2011; 303:533–550.
[65]. Jung S, Otberg N, Thiede G, et al. Innovative liposomes as a transfollicular drug delivery system: Penetration into porcine hair follicles. J. Invest. Dermatol. 2006; 126:1728–1732.
[66]. Das S, Ng WK, Tan RBH. Are nanostructured lipid carriers (NLCs) better than solid lipid nanoparticles (SLNs): development, characterizations and comparative evaluations of clotrimazole-loaded SLNs and NLCs? Eur. J.Pharm. Sci. 2012; 47:139–151.
[67]. Roque L V, Dias IS, Cruz N, et al. Design of Finasteride-Loaded Nanoparticles for Potential Treatment of Alopecia. Skin Pharmacol. Physiol. 2017; 30:197–204.
[68]. Takeuchi I, Hida Y, Makino K. Minoxidil-encapsulated poly(L-lactide-coglycolide) nanoparticles with hair follicle delivery properties prepared using W/O/W solvent evaporation and sonication. Biomed. Mater. Eng.2018; 29:217–228.
[69]. Matos BN, Reis TA, Gratieri T, et al. Chitosan nanoparticles for targeting and sustaining minoxidil sulphate delivery to hair follicles. Int. J. Biol. Macromol. 2015; 75:225–229.
[70]. Padois K, Cantieni C, Bertholle V, et al. Solid lipid nanoparticles suspension versus commercial solutions for dermal delivery of minoxidil. Int. J. Pharm. 2011; 416:300–304.
[71]. Gomes MJ, Martins S, Ferreira D, et al. Lipid nanoparticles for topical and transdermal application for alopecia treatment: development, physicochemical characterization, and in vitro release and penetration studies. Int. J.Nanomedicine. 2014; 9:1231–1242.
[72]. Vincenzi C, Marisaldi B, Tosti A, et al. Effects of a New Topical Treatment Containing Several Hair Growth Promoters in Women with Early Female Pattern Hair Loss. Ski. Appendage Disord. 2019; 5:146–151.
[73]. Madheswaran T, Baskaran R, Yoo BK, et al. In Vitro and In Vivo Skin Distribution of 5alpha-Reductase Inhibitors Loaded into Liquid Crystalline Nanoparticles. J. Pharm. Sci. 2017; 106:3385–3394.
[74]. Kim JH, Na J, Bak D-H, et al. Development of finasteride polymer microspheres for systemic application in androgenic alopecia. Int. J. Mol. Med. 2019; 43:2409–2419.
[75]. C. Vincenzi, B. Marisaldi, A.Tosti et al. Efficacy and safety of topical finasteride in a new delivery system, poster in WCD 2019
[76]. Das L, Kaurav M, Pandey RS. Phospholipid-polymer hybrid nanoparticle mediated transfollicular delivery of quercetin: prospective implement for the treatment of androgenic alopecia. Drug Dev. Ind. Pharm. 2019; 45:1654–1663.
[77]. Takabayashi Y, Nambu M, Ishihara M, et al. Enhanced effect of fibroblast growth factor-2-containing dalteparin/protamine nanoparticles on hair growth. Clin. Cosmet. Investig. Dermatol. 2016; 9:127–134.
[78]. Boca S, Berce C, Jurj A, et al. Ruxolitinib-conjugated gold nanoparticles for topical administration: An alternative for treating alopecia? Med. Hypotheses. 2017; 109:42–45.
[79]. Yazdani-Arazi SN, Ghanbarzadeh S, Adibkia K, et al. Histological evaluation of follicular delivery of arginine via nanostructured lipid carriers: a novel potential approach for the treatment of alopecia. Artif. cells, nanomedicine, Biotechnol. 2017; 45:1379–1387.
[80]. Hamishehkar H, Ghanbarzadeh S, Sepehran S, et al. Histological assessment of follicular delivery of flutamide by solid lipid nanoparticles: potential tool for the treatment of androgenic alopecia. Drug Dev. Ind. Pharm. 2016; 42:846–853.
[81]. Zhou Z, Lenk R, Dellinger A, et al. Fullerene nanomaterials potentiate hair growth. Nanomedicine. 2009; 5:202–207.