



## Alopecia Areata: An Updated Review

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### Abstract:

There are diverse types of alopecia and each call for a specific treatment. Regrettably there is no curative solution to the problem of alopecia as most drugs target its management. The purpose of the review is to explore the different types of alopecia and how each affect hair appearance and growth. The review begins by describing hair structure and hair physiological changes during life progression. A detailed description of conventional medication prescribed for alopecia and associated adverse effects are also pronounced in this review. Both approved (minoxidil and finasteride) and unapproved medications indicated for the condition are discussed to expose voids, which need to be filled by future drug development. The review also discusses the prospective future therapies of alopecia as directed by current research and technological advancement.

Androgenetic alopecia is a patterned hair loss disorder affecting approximately 73% of men and 57% of women in their lifetime, this affection can cause psychological effects like low self-esteem and depression diminishing the quality of life. Currently, finasteride and minoxidil are the only two drugs approved by the food and drug administration (FDA), and devices of low-level laser therapy are FDA cleared. Alternative therapies for androgenetic alopecia treatment include a drug like dutasteride, botulinum toxin A, cell-based therapies like adipose-derived stem cell conditioned medium and platelet-rich plasma protocols. A combination of two or more therapies can be found in the literature, the general consent indicates that any combination has higher efficiency than a single therapy. Finasteride is in less use due to the related sexual side effects, some adjuvant techniques have emerged to improve the delivery and effectiveness of minoxidil, i.e. micro needling. The surgical approach is mainly focused on hair transplant surgery, which offers relatively less invasive procedures and is a more suitable option for long time results, however, it is expensive. Recently, drug-assisted delivery techniques have emerged to improve the efficiency of conventional drugs; transdermal drug delivery through ultrasound pressure waves means creating diffusion channels, increasing skin permeability and stimulating cell differentiation and growth factor utilization along with minoxidil absorption. Another approach for drug-assisted delivery is the embodiment of finasteride in polymer-based microspheres aiming for a sustained and controlled delivery, which can be beneficial to reduce the regular doses decreasing adverse effects.

**Keywords:** alopecia, hair growth minoxidil, finasteride.

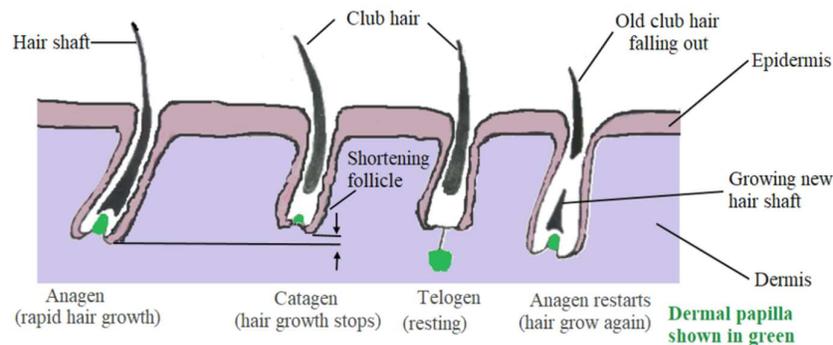
## 1. Introduction

Alopecia is a condition, which results in loss of hair from one's head or other body parts where hair is naturally supposed to be found. The distressful condition causes low self-esteem affecting patients psychologically and socially.<sup>1</sup> There are diverse categories of alopecia but the commonest are androgenic alopecia (common baldness), alopecia areata and chemotherapy induced alopecia.<sup>2</sup> Causes of the conditions are many including

stress, heredity, hormonal, nutrition, some sickness as well as certain medications like those prescribed for cancer.<sup>3-4</sup> Although the FDA sanctioned only two serendipitous drugs (finasteride and minoxidil) for the management of alopecia, there are many unapproved medications which are claimed to reverse the condition.<sup>5</sup> Other products that are claimed to reverse hair loss lack persuading proof from controlled scientific experiments, thereby hindering wider use and commercialization.

Hair grows in a cyclic manner comprising of four phases namely anagen, catagen, telogen and exogen.<sup>6</sup> These four phases keep on recurring as long as the person's follicles are capable of producing hair. The most active phase of hair growth, commonly known as the anagen last for a period of 2 to 7 years and about 90 % of hair in a healthy scalp are in this phase.<sup>7</sup> The anagen phase becomes shorter progressively after each cycle causing the production of weaker and villus hair. The phases which follow after the anagen are characterized by hair recession and are shorter in a healthy scalp.<sup>8</sup>

Androgenetic alopecia (AGA) also known as hair loss pattern baldness is a common condition affecting not only men but women, causing hair loss in well-defined patterns. This genetic condition affects 58% of men and 21% of women, and its effects increase with age.<sup>1</sup> The main cause related to androgenetic alopecia is the abundance of dihydrotestosterone (DHT), a strong form of testosterone produced by the action of the two types (I and II) of the enzyme 5 $\alpha$ -reductase, DHT cause miniaturization of the follicles leading to hair transformation into vellus hair.<sup>2</sup> AGA can also cause psychological distress leading to low self-esteem and depression, making people have a low-quality life, androgenetic alopecia affects around 80 million people just in the United States.<sup>3-5</sup> Due to the importance of this disorder, the research for therapeutic options to prevent hair loss caused by androgenetic alopecia has derived in a wide variety of treatments of different nature from oral drugs to surgical approaches. The most used treatments for AGA include oral drugs like finasteride and topical administration of minoxidil, however, the effectiveness of these conventional therapies is low. In recent years, new therapies have become available including phototherapy techniques like low-level laser therapy (LLLT), cell-based therapies like cell stem therapy (platelet-rich plasma, adipose-derived stromal vascular cells, and human follicle mesenchymal stem cells), and surgical approaches like hair transplant and hairline-lowering surgeries. Furthermore, alternative therapies using combinations of techniques have raised to improve the delivery and bioavailability of minoxidil, for instance, oral administration of minoxidil, Low frequency dual-frequency ultrasound-mediated microbubble cavitation for transdermal minoxidil delivery and micro needling followed by topical administration of minoxidil.



## Types of alopecia and their causes

There are many different types of alopecia as there are different causes of the condition. Common types are androgenic alopecia, alopecia areata, chemotherapy induced alopecia (CIA), anagen effluvium, telogen effluvium traction alopecia and trichotillomania. The condition can be classified into two categories; scarring alopecia (instigated by swelling responses to follicle damage) and most common non-scarring alopecia caused by many factors such as hormones, medication, nutrition and certain illnesses.

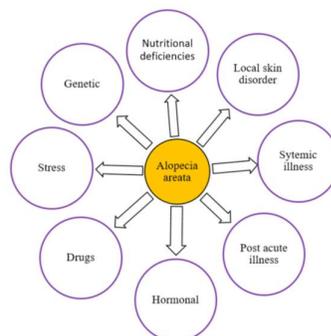
## Androgenic alopecia

This is common baldness affecting both male (male pattern baldness) and female (female pattern baldness). It affects mostly men as compared to women because men produce more of the causative male sex hormone testosterone. In women, the condition has a different phenotypical expression depicted as scalp hair thinning unlike the hairline recession in men.<sup>10</sup> The metabolism of testosterone in the gonads and other parts of the body such as the liver and brain by an enzyme called 5-alpha reductase produces a strong androgen called dihydrotestosterone (DHT). About 10 % of the testosterone produced in the body gets converted to DHT.<sup>11</sup> DHT, also a sex steroid like testosterone, accelerates baldness more compared to other androgens targeting the same receptor sites with a higher binding affinity (binds easily lasting for 53 minutes whereas testosterone lasts for only 35 minutes). The binding of androgen to hair follicle receptors causes progressive shrinkage and weakening of follicles causing destruction of follicle cells. The interface of hair follicle with androgens results in reduced anagen lifespan and prolonged telogen lifespan. According to Urysiak-Czubatka et al<sup>12</sup>, androgenic alopecia affects 70 % of all men and about 40 % of ladies in their entire lifespan. Male individuals who do not develop baldness generally produce less quantities of the 5-alpha reductase enzyme. Androgenic alopecia affects people of Caucasian origin more than other races.<sup>11,13,14</sup> Prevalence of this condition across gender and race are depicted on Table

### **Alopecia areata**

Alopecia areata is a non-scarring autoimmune condition, which results in loss of hair in one's scalp or any other body parts.<sup>15</sup> The causative of the condition is still obscure; with some speculations reporting it to be an organ-explicit immune system infection interceded by T lymphocytes coordinated at hair follicles.<sup>16</sup> Other reports say hereditary predisposition and natural variables may instigate the sickness.<sup>17</sup> The condition is characterized by the presence of scattered bald patches around the affected area, usually the scalp. The scalp patches can develop into bigger ones if the condition is not suppressed. The condition affected both male and female equally but most popular in infants.<sup>18</sup>

A deteriorating scenario for alopecia areata is when patients end up with an absolutely hairless scalp (alopecia totalis). Alopecia areata can also result in loss of hair on the whole body, a condition known as alopecia universalis. Alopecia areata may not ordinarily lead to death of hair follicle cells as hair often grows after recovery when proper body signals are assumed. Plenty products have been purported to reverse alopecia areata but none stood the test of time because of ineffectiveness and side effects. Interventions with products such as zinc, cortocosteroids, dithranol, tretinoin, azelaic acid, systematic cortisone, minoxidil and immuno-suppressive remedies have been widely used with limited success to combat alopecia areata. There is still need to find reliable cure for alopecia areata. Other causes of alopecia areata as adopted from Amin and Sachdeva<sup>15</sup> are summarized on Figure 2.



### **Chemotherapy induced alopecia**

Loss of scalp hair is one of the dreaded adverse effects of chemotherapy causing some patients to deny or omit treatment.<sup>19</sup> Chemotherapy treatments attack fast growing cell types and not only neoplastic cancer cells. This leads to the attack of fast-growing hair fiber keratinocytes in the active growth phase leading to loss of hair.<sup>20</sup> Hair matrix keratinocytes at the anagen stage are the absolute quickest multiplying cells in the body, about 60%

of them stay in the synthesis (S) stage. Chemotherapeutic medications target rapid growing neoplastic malignancy cells and, in the process, destroying fast growing hair matrix keratinocytes in anagen growth phase.<sup>21</sup> Consequently, the follicles in the anagen stage are exposed to a faster dystrophic catagen phase followed by the breaking of hair and its subsequent shading.

After chemotherapy, 90 % of hairs in the anagen stage (majority of scalp hair) are transformed to telogen and consequently shade off as club hair but without replacement. This triggers longer telogen phases and shortens anagen phases in the hair cycle. In most cases, hair lost after chemotherapy regrows when the patient stops taking the medication because cycling follicular stem cells are usually not affected by the treatment and will generate a new hair follicle, which will produce a new hair strand later. Decent upkeep of hair follicles during chemotherapy requires therapeutic tactics such as telogen arresting and catagen inhibition. This could be solved by treatment with follicle keratinocytes apoptosis obstructive agents.<sup>20</sup> Regrettably at present there are no apoptosis obstructive agents or telogen arresting remedies to give to patients. It is desirous to come up with treatments for fortifying hair healthy during chemotherapy.

### **Anagen effluvium**

The condition results in the shading off of growing hair in the anagen stage (anagen arrest).<sup>22</sup> Just like chemotherapy induced alopecia the anagen effluvium can be triggered by chemotherapy or other medications.<sup>23</sup> The condition leads to loss of anagen hair causing very long telogen phase, which lasts for as long the treatment is being administered to the patient. Excessive use of medications like blood thinners, birth control pills, diuretics, and acne drugs is also believed to prompt the disorder. Even though in most cases the condition can be reversed and hair grows back after a period of up to 3 months, the condition can be irreversible leading to psychological torture impacting negatively to the patient's sensitivity of appearance.<sup>24</sup>

### **Telogen effluvium**

Telogen effluvium denotes to non-scarring hair loss due to untimely pushing of hair follicles into the inactive telogen stage.<sup>24</sup> The disorder is common to the old aged, physical and emotional stressed people, as well as thyroid or other hormonal irregularities.<sup>25-26</sup> The level of effluvium relies upon the gravity and duration of exposure to the causative agent as opposed to the agent itself. Telogen effluvium can be critical (going on for below six months), chronic (more than six months) or chronic repetitive.<sup>26</sup>

### **Traction alopecia**

Traction alopecia is typically instigated by tensional straining activities on hair leading to its breakage.<sup>27</sup> Middle aged ladies are mostly affected because of the high desire to look presentable by trying varying hair styles. Hair styles such as braiding, tight pig tails, repeated chemical treatments like hair bleaching and dying are the basic reasons for traction alopecia.<sup>28</sup> Traction alopecia happens in people of various cultural origins and is the after effect of a person's hair styling and hair care practices.

### **Trichotillomania**

This type of alopecia emanates from frequent self-plucking of hair from one's scalp resulting in hair loss or damage. In most cases it is associated with children or psychiatric patients who routinely pluck off their hair.<sup>29</sup> Interventions in such conditions involve psychiatric treatment for adults and in young children; the habit may disappear as the child grows.<sup>30</sup>

## **DRUG THERAPIES**

Finasteride was the first drug approved by the FDA for androgenetic alopecia treatment in 1997, an inhibitor of type II 5 $\alpha$ -reductase enzyme responsible for the conversion of testosterone in dihydrotestosterone.<sup>6</sup> DHT is a strong androgen that induces follicle miniaturization and decreases the hair growth rate, which appears to be the

main cause of AGA. Since its approval, the use of this drug raised concerns regarding sexual adverse effects (decrease in libido and erectile dysfunction), despite all the controversies around it, finasteride has shown the effectiveness of up to 60%.<sup>7</sup> The dose recommended for patients of each gender is 1 mg/day for men and 5 mg/day for women, a recent study showed that this treatment should be intended for women in the pre and post-menopausal stage were proved to have more efficiency.<sup>8</sup> Dutasteride is an inhibitor of the two types of 5 $\alpha$ reductase, this drug has been used for AGA treatment since 2009.<sup>9</sup> As an inhibitor of the two types of the enzyme, a better result would be expected compared to finasteride. A comparison study of finasteride versus dutasteride at different doses was conducted by Gubelin Harcha et al they found that similar results were obtained for 1 mg/day of finasteride and 0.2 mg/day of dutasteride, however, at a higher dose of dutasteride (0.5 mg/day) a significant increase in hair count was obtained in comparison to regular treatment of finasteride.<sup>10</sup> Although no sexual adverse effects are claimed by different authors, the same concerns as those found for finasteride are related to the dutasteride treatment. Minoxidil is the only topical drug approved by the FDA for androgenetic alopecia treatment, the effect of this drug seems to have several contributions in the biological response; increases blood flow, increases the mitosis of hair matrix keratinocytes and promotes growth hair faster and thicker; prolongs the anagen phase, and stimulates the kenogen follicles to initiate a new hair growth cycle.<sup>3,11</sup> Typical minoxidil treatment consists in topical application of 2-5% solution, showing better results with the application of 5% solution twice a day for men while having similar results in women using both solution concentrations (recommended dose for women is topical application of 2% solution once a day).<sup>12</sup> In new studies, the oral administration of minoxidil was proposed as an alternative, showing similar results than those obtained for topical administration in men, however, side effects like hypertrichosis (93%) and pedal edema (10%) can appear even at doses as low as 0.25mg/day. <sup>13,14</sup> A more recent approach consists in a combination of oral administration of finasteride (1 mg/day) along with a topical application of 5% minoxidil solution (6), although the drug combination has shown better results than either of the two drugs alone, more research is needed to determine the most suitable doses to avoid side effects as much as possible. More complex treatments like that reported by Tanaka et al using different ways of administration and combination of minoxidil and finasteride seem to show good results aiming only for Asian men, however, stronger evidence is needed to determine the reliability of this study.<sup>15</sup>

## **PHOTOTHERAPY**

The low-level laser therapy (LLLT) is a technique used to generate an overall effect in the human body called photo biomodulation (PBM), this therapy is also known with the names of low-level light therapy, red light therapy, and soft laser. PBM is the effect caused by low laser beams, which improve wound healing and stimulate hair growth.<sup>16</sup> Although the mechanism of action of LLLT is not clear, it has been gaining popularity and recognition as a suitable treatment for AGA, in fact, there are several FDA-cleared devices using low-level laser therapy.<sup>17</sup> Some of the effects of this phototherapy are accelerated mitosis of keratinocytes and fibroblast, inhibition of nitric oxide production by the cytochrome C oxidase and decrease of inflammation.<sup>17</sup>

## **CELL-BASED THERAPIES**

Stem cell therapy (SCT) is one of the more recent and promising approaches to treat androgenetic alopecia. SCT uses exogenous cells, clinical trials can use both allogenic and autologous cell sources. Adult stem cells can be harvested from different tissues including fat, scalp, bonemarrow and peripheral blood.<sup>19</sup> Bone marrow stem cells (BMSC) have been used for its relatively easy and fast harvesting, however, the procedure to obtain them is invasive and causes pain to the donor, also the low yields of cell detachment conventions make BMSC not the best option for hair loss treatment. Owing to the constraints of the use of BMSC, the adipose-derived stem cells

have been proposed due to their ability to differentiate into mesenchymal lineage cells and the release of several growth factors.<sup>20</sup> Fat tissue is harvested in a less invasive way (i.e. liposuction) and in more abundant quantities than other stem cell tissues. Adipose-derived stem cell-conditioned medium contains growth factors such as vascular endothelial growth factor, hepatocyte growth factor, platelet-derived growth factor, and insulin-like growth factor 1.<sup>21</sup>

### **MICRONEEDLING**

The microneedling procedure consists of making small holes in the scalp with a dermaroller containing titanium needles until mild erythema is reached, the preferred needle size used for AGA treatment is 1.5 mm in length. It is worthy to mention that microneedling is considered an adjuvant technique, this implies that its application has as a goal to help improve the effectiveness of the main treatment (i.e. topical minoxidil administration). Microneedling acts through the stimulation of the stem cells and activation of growth factors, which also stimulate the dermal papillae.<sup>23</sup> In recent work, Kumar et al performed a comparative study of 5% topical minoxidil plus microneedling (once a week) and minoxidil alone. The results of this study indicate that the topical minoxidil plus microneedling treatment has a significant effect on hair growth, the patients reported up to 50% improvement versus the treatment with minoxidil alone.<sup>24</sup> Microneedling has also been used along with PRP+topical minoxidil and compared to the topical minoxidil treatment alone, the results in such a study showed significant improvement in the patients in the group receiving the microneedling+PRP+5% minoxidil versus the patients under the minoxidil alone.<sup>25</sup> Another study reported the comparison of microneedling+5% minoxidil treatment against microneedling+PRP, in that case, both treatments showed similar results been both effective in AGA treatment.<sup>26</sup>

### **Medication for alopecia**

There are several remedies to manage alopecia albeit plenty reports of adverse reactions and ineffectiveness. Both natural and synthetic remedies are reported although there are only two drugs, (topical minoxidil and oral finasteride) which were sanctioned for hair regrowth by FDA. Due to diversified alopecia types, alopecia drugs are not universally prescribed but rather target a specific type.

#### **Minoxidil (Rogaine)**

Minoxidil, commercial name rogaine is the only FDA sanctioned topical application drug against alopecia. Minoxidil is a pyrimidine derivative originally used as an orally administered treatment for hypertension.<sup>31</sup> The hair growth promotion popularly known for minoxidil was discovered serendipitously as its side effect for the treatment of hypertension.<sup>32</sup> Prescriptions for minoxidil are normally packaged in strengths of 5% (for male use) and 2% for female use. The drug's mechanism of stimulating hair regrowth remains elusive up to now, although it is a well-known potassium channel opener that is responsible for hyperpolarization of cell membranes. The hyperpolarization causes vasodilation, angiogenesis, and opening of potassium channels thereby facilitating the entrance of more oxygen, blood, and food nutrients to the follicles.<sup>33-34</sup> Thus, the provision of nutrients and good blood supply is suspected to have some significant contribution to hair rejuvenation by minoxidil. Minoxidil facilitates the transformation of follicles in telogen phase back to anagen. A prolonged active growth phase has also been reported after treatment with topical minoxidil.

#### **Finasteride (Propecia)**

Finasteride (synthetic 4-azasteroid compound) is one of the FDA sanctioned drugs for the treatment of alopecia. Like minoxidil, finasteride was also serendipitously discovered as a hair growth promoter. Prior to its use in trichology, finasteride was used to treat prostate enlargement in men.<sup>35</sup> Apparently, the drug is prescribed to male patients experiencing hair loss only. Finasteride works by inhibiting 5 alpha reductase, an enzyme that catalyzes the metabolism of testosterone into dihydrotestosterone (DHT). The use of finasteride competitively

inhibits the 5 alpha reductase enzymes on the androgen receptors thereby preventing the conversion of testosterone into DHT. Effective results in the handling of androgenic alopecia with finasteride are observed when the drug is administered early or before the death of hair follicles. Unlike minoxidil, which can be used by both male and female patients, finasteride is contraindicated to female patients, particularly pregnant ones due to its teratogenic effect.<sup>36</sup> Treatment for androgenic alopecia with finasteride often yield reversible hair loss because the drug does not address the genetic cause of the condition and thus hair loss will likely recur. The two approved drugs, minoxidil and finasteride were reported to have side effects in some cases (Table 2).

**Table 3** Summarized table of unapproved drugs used for the treatment of alopecia

Drug	Proposed mechanism	Type and of condition alopecia	Author	Year
Dutasteride	Inhibition of 5 $\alpha$ -reductase	Extensive condition	Levy and Emer40	2013
Photochemotherapy (PUVA)	Immunomodulatory	Patchy surface alopecia areata	Amin and Sachdeva41	2013
Ketoconazole	Antrogen receptor blocker	Patchy/moderate androgenic alopecia	Fields et al.42	2020
Diphencyprone (DPCP)	Antigen competition	Extensive alopecia areata	Wiseman et al.43	2001
Cimetidine	Antiandrogenic	Patchy/moderate androgenic alopecia	Park et al.44	2018
Oral prednisolone	Multiple mechanisms	Extensive condition alopecia areata	Efentaki et al.45	2009
Flutamide	Antiandrogen	Patchy alopecia areata	Lourith and Kanlayavattanakul46	2013
Sulfasalazine	immunosuppressive and immunomodulatory	Moderate alopecia areata	Alsantali18	2011
Dithranol (anthralin)	Immunomodulatory	Extensive alopecia areata	Khan and Chandra47	2017
Cyclosporine (CsA)	A inhibition of T-cell activation	Moderate alopecia areata	Amin and Sachdeva41	2013

## 2. Herbal remedies for alopecia

Currently no herbal treatment has been approved for the treatment of alopecia but several studies have shown that some phytochemicals have the propensity to stimulate hair growth on *in vitro* and *in vivo* models (Table 4).

Name of herb	Proposed mechanism	Active phytochemicals	Author	Year
<i>Platyclus orientalis</i>	Hair growth promoter	sesquiterpene	Zhang et al <sup>48</sup>	2018
<i>Glycyrrhiza glabra</i>	Inhibition of 5 $\alpha$ reductase	Coumarines, Phytosterols, Flavonoids	Saumendu et al <sup>49</sup>	2014
<i>Dicerocaryum senecioides</i>	Hair growth promotion	Flavonoid glycosides	Rambwawasvika et al <sup>50</sup>	2019
<i>Cyperus rotundus</i>	Hair growth promotion	Alkaloids, Tannins, glycosides,	Jain et al. <sup>25</sup>	2016
<i>Rosmarinus officinalis</i>	Hair growth promoter	12-methoxycarnosic acid	Murata et al. <sup>51</sup>	2013
<i>Urtica dioica</i>	Hair growth promoter	flavonoid glycosides	Semalty et al. <sup>10</sup>	2011
<i>Ginkgo biloba</i>	Hair growth promoter	Flavonol glycosides, terpene trilactones	Kobayashi et al <sup>52</sup>	1993
<i>Allium cepa (onion)</i>	Hair growth stimulator	Flavonoids	(Dorsch <sup>53</sup>	1997
<i>Carthamus tinctorius</i>	Follicle cells proliferation	Quinochalcones, Flavonoids	Junlatat and Spripanidkulchai <sup>54</sup>	2014
<i>Zizyphus jujube</i>	Hair growth promoter	Essential oils	(Yoon et al. <sup>55</sup>	2010
<i>Vitis vinifera (grape)</i>	Proliferation of hair follicles	Polyphenolic, proanthocyanidins	Pietta et al. <sup>56</sup>	1998
<i>Lavenda</i>	Hair growth promoter	Essential oils	(Lee et al. <sup>57</sup>	2016
<i>Hibiscus rosa-sinensis</i>	Hair growth promoter	Essential oils	Adhirajan et al. <sup>58</sup>	2003

### Surgical hair transplant

Hair transplant involves the surgical removal of hair bearing scalp tissue from a donor or other regions of the same scalp to the hairless portion of the body. The practice is mostly done to reverse male pattern baldness compared to other types of alopecia.<sup>34,59</sup> The temporal and occipital regions of the scalp are not normally affected by androgens and can be a source for hair bearing tissue to be transplanted to bald portions of the same scalp. The two most prevalent surgical procedures are follicular unit strip surgery (FUSS) and follicular unit extraction (FUE).<sup>60-61</sup> Another challenge of surgical hair transplant is the meticulous care needed for an operation and this calls for experienced medical practitioners who sometimes are hard to come by. Furthermore, there is no assurance that the transferred follicles will stay for a longer duration in the treated person's head before reaching telogen stage.<sup>62</sup> Other challenges to the patient during hair transplant include excessive bleeding,

infection and severe pain. Thus, most people shy away from the process because of these challenges and therefore the need to develop other alternative drugs still stand.

### **Psychological and behavioral therapy**

Like any other social and psychological ills, alopecia patients need counseling to enable them to bear with their conditions. The level of low self-esteem may lead to even fatal cases of suicide as the affected persons fail to accept the condition.<sup>63</sup> Counseling is crucial especially to adolescence and young ladies who feel like their condition can have negative influence on their sexuality and acceptance in relationships.<sup>64</sup> In a study done by Lemieux et al.<sup>63</sup> to investigate the psychological influence of hair loss in cancer patients undergoing chemotherapy, patients with hair loss had stress, low self-esteem and poor body image compared with those without Chemotherapy Induced Alopecia. In a separate study on chemotherapy patients by Rivitti,<sup>65</sup> cases of psychiatric disorder were more in alopecia patients as compared to a group without alopecia. Thus, psychological support is crucial in the fight against alopecia. Behavioral remedies such as the wearing of wigs, tattoos and hats can also be suggested to patients during counselling.<sup>66</sup>

### **Nutritional effects in alopecia**

Nutrition has also been found to contribute significantly to hair growth and hair healthy. Apart from the protein needed for hair growth, several nutrients are required in the scalp to facilitate healthy hair growth. Some valuable nutrients and their effect in hair growth are given in Table 5.

**Table 5** Nutrients important for healthy hair growth<sup>44,67,68</sup>

Nutrient	Effect on hair growth
Zinc	Indicated to patchy surface alopecia
Iron	Carries oxygenated blood to the hair follicle cells
Selenium	Needed for a healthy scalp
Silica	Development of strong hair
Copper	Production of antioxidant superoxide dismutase needed for healthy hair
Potassium	Moisture and pH maintenance
Magnesium	Strengthens hair and facilitate faster growth
Calcium	Fast hair growth
Vitamin A	Prevents free radicals and inflammation on follicles
Vitamin B	Improves shininess and helps grow thick hair
Vitamin C	Facilitates faster growth of strong hair and helps absorption of iron
Vitamin D	Facilitates hair follicle cycling
Vitamin E	Improves circulation of blood and volume reaching the follicles.

#### Prospective future treatment for alopecia

Technological advancement in drug delivery systems together with the prospect of discovering novel alopecia therapeutics promises better medication for hair loss in future. This is going to be fostered by the high demand of hair growth products and rewarding monetary value offered for alopecia

**Table 6** Prospective future treatments for alopecia

Prospect treatment	Treatment mechanism	References	Year
Herbal remedies	Diverse mechanisms depending on phytochemicals used	Jain et al.25	2017
Stem cell therapy	Self-renew follicle cells. Elongated anagen phase of hair growth	Li et al.71	2015

Blended medicines	Diverse mechanisms depending on treatments mixed	Sheikh et al.72	2015
Enhancing transdermal drug delivery systems	Facilitate the penetration of hair growth stimulants to target receptors	Ramkanth et al.73	2018
Gene therapy	inserting explicit genes, which will prompt the body to start the healing process to patients	Meidan and Touitou74	2001

#### 4. Conclusion

In this review, diverse types of alopecia have been discussed with prominence given to their effect on hair follicle and hair growth cycle. Causes of alopecia such as genetic predisposition, medication, diet, stress, auto immune disorder and prolonged sickness together with their mechanism of reducing hair growth have been discussed. A comprehensive discussion of the existing approved and unapproved medication for alopecia together with their pros and cons has been indicated. The review also discussed on the mechanism of action of common drugs used or purported to treat the condition. The last segment of the review was dedicated to giving possible ways by which prospective future therapies must arrest shortcomings of conventional medication using the available knowledge base and technological advancement. Prospect drug discoveries ought to focus not only on developing new alopecia treatments but also refining and adjusting the current drugs to advance hypertrichotic ability as well as reducing adverse effects.

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