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AN UPDATE ON ETIOPATHOGENESIS AND MANAGEMENT OF ALOPECIA

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ABSTRACT

Alopecia, a common dermatological condition characterized by hair loss, affects individuals worldwide, impacting their physical appearance and psychological well-being. The therapeutic approaches used to treat alopecia, encompassing both natural and synthetic interventions. In the pursuit of effective treatments, researchers and practitioners have explored both natural and synthetic therapies for alopecia. Natural therapies, often derived from botanical sources, have long been used in traditional medicine systems across cultures. On the other hand, synthetic therapies have emerged as a result of cutting-edge research and technological advancements. These synthetic interventions have shown varying degrees of success, but their use is often accompanied by potential adverse effects, emphasizing the importance of careful monitoring and patient education. This article aims to provide an in-depth exploration of natural and synthetic therapeutic approaches for alopecia. We will discuss their mechanisms of action, potential benefits, limitations, and the current state of research in this field. By examining the interplay between these two categories of treatments, we hope to shed light on the diverse options available for individuals seeking to address hair loss.

Keywords: Alopecia, Natural treatment, Herbal treatment, Synthetic drug.

INTRODUCTION:

Alopecia, a condition characterized by hair loss, can significantly affect a person's sense of self, emotional health, and general quality of life. It is a distressing condition that

affects millions of individuals worldwide [1]. It affects both men and women, and while it is more commonly associated with aging, it can occur at any stage of life. It can manifest in various forms, including androgenetic alopecia (pattern hair loss), alopecia areata (patchy hair loss), and telogen effluvium (excessive shedding) [2]. The causes of alopecia are multifactorial, involving genetic predisposition, hormonal imbalances, autoimmune disorders, nutritional deficiencies, stress, and environmental factors [3]. However, the evidence supporting their effectiveness is limited, necessitating further research and clinical trials. On the other hand, synthetic therapeutic strategies for alopecia include medications like Minoxidil, corticosteroids, and Immunosuppressant's [4]. Herbal Remedies give information on Traditional botanical remedies, Key plant extracts and their properties, Mechanisms of action and potential efficacy [5]. Essential Oils give information on Essential oils for hair growth and follicle stimulation, Promising botanical extracts used in aromatherapy, and scientific evidence supporting their use [6]. Nutritional Supplements give information on Micronutrients essential for hair health and Role of vitamins, minerals, and antioxidants [7]. Scalp Massage and Acupuncture give information on Stimulating blood circulation and promoting hair growth, Traditional practices, and their

modern applications, and Clinical evidence supporting their effectiveness [8]. Synthetic Therapeutic Approaches has Topical Medications, Oral Medications, Platelet-Rich Plasma (PRP) Therapy, and Hair Transplantation [9]. Combining Natural and Synthetic Approaches has Complementary Therapies, Personalized Treatment Plans [10].

Data base Resources:

Excel conducted a methodical literature review. Utilising keywords, study exploration was carried out using internet databases Pub Med, Google Scholar, and Science Direct. Alopecia, herbal treatments, synthetic drugs, Saw Palmetto, Rosemary, Minoxidil, Finasteride, Pumpkin Seed etc. Literature focuses on herbal and natural treatment alternatives to synthetic drugs.

Alopecia

Androgenetic alopecia: This is the most prevalent type of alopecia, sometimes known as male or female pattern baldness. It is characterized by gradual hair thinning and loss, typically starting at the temples or crown of the head [11].

Alopecia areata: Patchy hair loss is a common symptom of this kind of alopecia, frequently in small, circular or oval-shaped regions. Alopecia areata can proceed to entire body or scalp baldness (alopecia totalis or alopecia universalis), respectively [12].

Telogen Effluvium: Because of a disruption in the hair development cycle, this is a transient form of hair loss. It can be triggered by factors such as physical or emotional stress, illness, hormonal changes, certain medications, or nutritional deficiencies [13, 14].

Traction alopecia: This form of hair loss is brought on by severe hair tugging or strain, sometimes as a result of hairstyles that draw the hair back firmly or entail the use of weaves or hair extensions [15, 16].

TYPES OF ALOPECIA

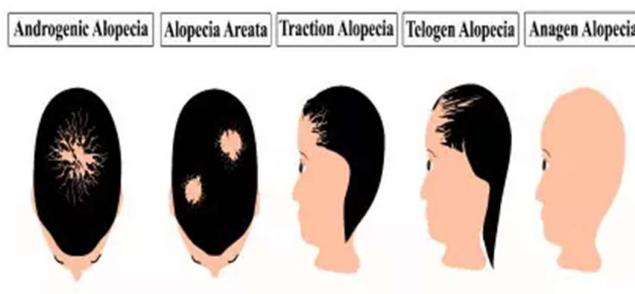


Figure 1: Types of Alopecia

Risk factors

Alopecia's precise causes are not well understood, however a number of things might hasten its onset:

- **Genetic Predisposition:** Family history plays a significant role in androgenetic alopecia. If your parents or close relatives have experienced hair loss, you may have a higher risk of developing it [17].
- **Autoimmune Factors:** The immune system incorrectly attacks the hair follicles in alopecia areata, causing hair loss. Autoimmune diseases and a family history

of autoimmune conditions may increase the risk [18].

- **Hormonal Changes:** Hormonal imbalances, such as those that occur during pregnancy, childbirth, menopause, or thyroid disorder, can contribute to hair loss [19].
- **Environmental and Lifestyle Factors:** Excessive heat styling, chemical treatments, poor nutrition, and emotional stress can contribute to hair loss or exacerbate existing conditions [20].

PATHWAYS OF ALOPECIA:

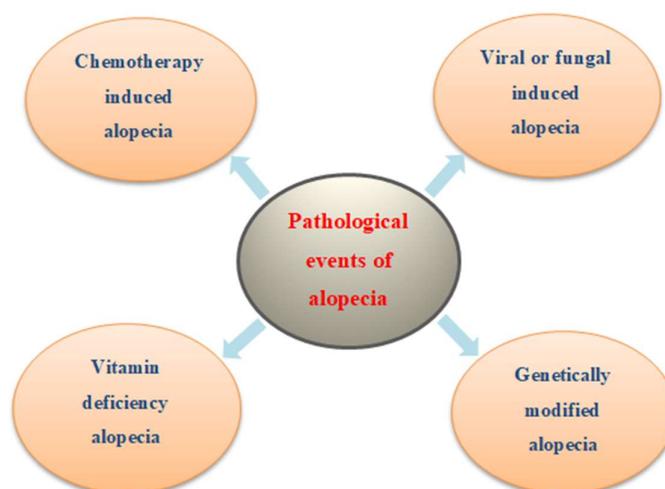


Figure 2: Pathological events of Alopecia

Chemotherapy induced alopecia:

8% of patients decline chemotherapy treatments because they fear losing their hair. According to reports, 80% of alopecia is caused by anti-microtubule drugs, 60% to 100% by topoisomerase inhibitors, >60% by alkylators, and 10% to 50% by antimetabolites. Monotherapy have lower incidence compared to poly therapy. The alopecia also associated to aromatase inhibitor such as letrozole and anastrozole. The decrease in oestrogen production is thought to be the pathogenic mechanism for this particular form of hair loss. Alopecia, which is brought on by the drugs doxorubicine, epirubicine, and docetaxel, has shown the best outcomes, but it should be avoided in cases of haematological malignancies because to the possibility of scalp skin metastases.

Bacteria induced alopecia:

Scarring alopecia can be produced by Staphylococcus bacteria grown up middle-aged. Alopecia has been linked to Staphylococcus infections in sheep, dogs, and horses. The strain of salmonella was associated with hair loss in guineapig.

Fungal infections:

Pruritis is connected to fungi infections that can result in hair loss. Either Trichophyton tonsurans or Microsporum canis are the fungi that cause alopecia. Rhesus monkeys, chimpanzees, and gibbons have all been found to develop fungal infections, which are often brought on by M. canis.

Vitamin deficiency:

When the immune system assaults the hair follicle, alopecia areata (AA) develops. According to studies, AA and low vitamin D levels are related. If levels are low, vitamin D supplements should be used. Eight water-soluble vitamins make up the vitamin B complex: thiamine (vitamin B1), riboflavin

(vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), vitamin B6, biotin (vitamin B7), folate, and vitamin B12. Only vitamin B12, biotin, riboflavin, and folate deficits have been linked to hair loss. Women with hair loss frequently lack iron. A dietary deficit that causes hair loss is low serum ferritin levels. A recognised indicator of established zinc insufficiency is alopecia.

Genetically modified:

The adult hair follicle's (HF) development cycle, which comprises of growth, regression, and rest stages, is regulated by the hairless gene (Hr; formerly known as hr), which encodes a 130-kDa protein (HR), a transcriptional co-repression.

Chemotherapeutic drugs:

Chemotherapeutic drugs available are bleomycin, epirubicine or doxorubicin, oral cyclophosphamide, fluorouracil, capecitabine, gemcitabine, melphalan, methotrexate, mitomycin, mitoxantrone, topotecan and the platinum drugs (oxaliplatin, cisplatin, and carboplatin).

Herbal drugs:

Curcuma aeruginosa (pink and blue ginger), Serenoa repens (palmetto), Cucurbita pepo (pumpkin), Trifolium pratense (red clover), and Panax ginseng (Chinese red ginseng) are all herbal treatments for alopecia.

Table 1: Characteristics of Herbal drugs

Drug	Route of administration	Results	Mechanism of Action
<i>Allium cepa</i>	Topical	Hair growth, increased number of hair	Onion juice may cause a minor type of dermatitis that stimulates the growth of hair.
<i>Allium sativum L. (garlic)</i>	Topical	A markedly higher total number of hairs	Modulatory impact on the immune system.
<i>Camellia sinensis (green tea)</i>	Topical	33% of the mice had noticeable hair growth [21]	ECGC stimulate hair expansion via its proliferative.
<i>Cucurbita pepo L. (pumpkin)</i>	Topical	Positive anabolic effect of hair growth	Inhibition of 5 alpha reductase.
<i>Pink and blue ginger, or Curcuma aeruginosa Roxb.</i>	Topical	Accelerated hair growth and reduced hair loss	Inhibition of 5 alpha reductase.
<i>Ginseng, Panax ginseng C. A. Meyer</i>	Topical	Enhanced proliferation of hair matrix keratinocytes in-vitro	Enhancing human dermal papilloma cells. [22]
<i>Palmetto Serenoa repens (W. Bartram)</i>	Topical	Stimulated proliferation of hair keratinocytes	Anti-androgenic action [23]
<i>Sophora flavescens Aiton (sophora)</i>	Topical	Stimulated proliferation of hair keratinocytes	Inhibition of 5 alpha reductase.
<i>Essential Oils</i>	Topical	Reduced hair loss	-
<i>Procyanides</i>	Topical	Similar to minoxidil	Inducing the catagen phase, anti-oxidant properties.
<i>Trifolium pratense L/ red clover</i>	Topical	Increase the number of hair	Inhibition of 5-alpha reductase, Anti-inflammatory activity.
<i>Aloe Vera</i>	Topical	Hydration of scalp, maintain healthy hair follicles, promotes hair growth [24]	-
<i>Rosemary</i>	Topical	Stimulate the hair follicles, promote the hair growth	Exhibits anti-inflammatory properties that can help alleviate inflammation of the scalp [25]
<i>Licorice</i>	Both topical and oral	Promote hair growth by stimulation hair follicles	Inhibition of 5-alpha reductase, anti-inflammatory property [26]
<i>Phyllanthus Emblica</i>	Both topical and oral	Maintain scalp health by preventing microbial infections and reducing dandruff	Antioxidants help neutralize harmful free radicals in the body [27]

Current therapeutic drugs

Minoxidil

Alopecia, a disorder marked by hair loss or thinning, is frequently treated with the drug minoxidil. Originally developed as an oral medication for hypertension, it was later discovered to have a beneficial effect on hair growth. Minoxidil is now primarily available as a topical solution or foam for application to the scalp. It is not completely understood how Minoxidil works to promote hair growth [28]. However, it has several effects on the hair follicles, which are responsible for producing and maintaining hair [29]. The exact signalling pathways involved in these processes are still being investigated, but Minoxidil is known to activate adenosine triphosphate (ATP)-sensitive potassium channels. This activation leads to the opening of these channels, which subsequently promotes hair follicle growth [30]. Furthermore, Minoxidil may have an effect on the dermal papilla cells, which are specialized cells located at the base of the hair follicles. These cells play a crucial role in regulating hair growth and follicle development [31]. Minoxidil is believed to counteract the effects of DHT by promoting hair growth and preventing further hair loss [32]. While Minoxidil can be effective in stimulating hair growth, it is not a permanent solution. If treatment with Minoxidil is discontinued, the benefits may gradually diminish, and hair loss may

resume. Therefore, it is generally recommended to continue using Minoxidil regularly to maintain the desired results [33].

Finasteride

Finasteride is an oral medication approved for the treatment of androgenetic alopecia in men. The enzyme 5-alpha-reductase, which turns testosterone into DHT, is inhibited by it [34]. Finasteride helps to slow down hair loss and encourage hair regeneration by lowering DHT levels. But it's crucial to remember that. Finasteride is not recommended for women of childbearing age due to potential risks during pregnancy [35].

Androgenetic alopecia, a frequent kind of hair loss in both men and women, is largely treated with finasteride. It is a member of the pharmacological class known as 5-alpha-reductase inhibitors [36]. Finasteride is most commonly prescribed for male pattern baldness, but it may also be used off-label for female pattern hair loss. The target enzyme 5-alpha-reductase is targeted and inhibited by finasteride as part of its mechanism of action [37]. Dihydrotestosterone (DHT) is produced by this enzyme from the male hormone testosterone, a more potent androgen responsible for the miniaturization of hair follicles in androgenetic alopecia. By inhibiting 5-alpha-reductase, Finasteride reduces the levels of DHT in the scalp,

helping to slow down hair loss and promote hair regrowth [38]. It typically takes several months of continuous use to see noticeable improvements in hair density and regrowth. Results can vary among individuals, and the drug may not work for everyone. While Finasteride is generally well-tolerated, some people may get adverse effects from it. The most frequent adverse effects include breast soreness or enlargement and sexual dysfunction (such as lower libido, erectile dysfunction, or reduced ejaculate volume). These side effects are usually reversible upon discontinuation of the medication, but it's important to discuss any concerns with a healthcare professional [39].

Corticosteroids and immunomodulators

Corticosteroids and immunomodulators are two commonly used classes of medications for the treatment of alopecia, a condition characterized by hair loss. These medications work by targeting the underlying immune response that contributes to the development of alopecia. Corticosteroids are anti-inflammatory medications that imitate the effects of cortisol, a hormone that the adrenal glands naturally produce [40]. They can be administered topically, orally, or through injections, depending on the severity and location of hair loss. When used in alopecia

treatment, corticosteroids suppress the immune response that mistakenly attacks the hair follicles, leading to hair loss. However, it is believed that they exert their effects by reducing inflammation and inhibiting the immune system's activity [41]. Corticosteroids inhibit the creation of cytokines and other pro-inflammatory compounds, which are involved in the immunological response. By suppressing inflammation, corticosteroids help to prevent further damage to the hair follicles and promote hair regrowth.

In alopecia, JAK inhibitors target the immune cells that mistakenly attack the hair follicles, leading to hair loss. By inhibiting the JAK enzymes, these medications interrupt the Signalling pathways that drive inflammation and immune cell activation [42]. However, it's important to note that JAK inhibitors are relatively new, and their long-term safety and efficacy are still being studied. Corticosteroids and immunomodulators, such as JAK inhibitors, are two classes of medications commonly used in the treatment of alopecia [43]. Corticosteroids work by suppressing inflammation and the immune response, while JAK inhibitors target specific enzymes involved in immune cell activation [44].

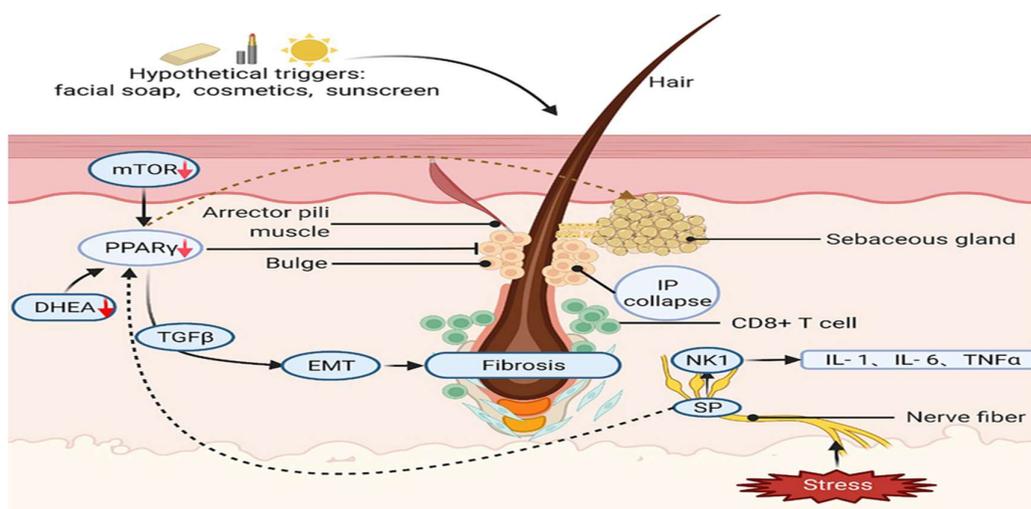


Figure 3: MOA of alopecia develops

CONCLUSION:

In conclusion, alopecia presents a multifaceted challenge that necessitates a holistic approach to treatment. While natural therapeutic options show promise in providing alternative and potentially safer interventions, further research is needed to establish their effectiveness. Synthetic therapies, on the other hand, offer immediate relief and have a more extensive body of evidence supporting their use. By combining these therapeutic modalities and individualizing treatment plans, clinicians can optimize outcomes and enhance the standard of living for alopecia sufferers.

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