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AN OVERVIEW OF MEDICINAL PLANTS USED FOR THE TREATMENT OF HAIR LOSS

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ABSTRACT

In the domains of cosmetics and primary healthcare, hair loss is a common and steadily rising problem. The problem at hand is widespread, having affected people of all sexes and races in differing ways throughout human history. People who are going through hair loss spend a large sum of money annually on different treatments, which include medications, dietary supplements, specialty tonics, and hair care products. Conventional approaches to treating thinning hair include medication treatments and surgical techniques like hair replacement. Two commonly recommended pharmacological medications used to promote hair growth are minoxidil and Propecia (finasteride). Scientific evidence has proven that these drugs are effective in treating alopecia in the vertex region of the scalp. Despite the efficacy of these pharmaceutical substances, there exists a prevailing sense of concern regarding its uncharted long-term consequences and potential adverse reactions. Consequently, there has been a significant surge in the prevalence of complementary therapies, with herbal therapy experiencing notable growth in popularity. This research provides a comprehensive examination of several themes pertaining to hair, encompassing origin, mechanisms of action, hair illnesses, and variables influencing hair growth, physiology and pathophysiology of hair, different types of alopecia, epidemiology, diagnosis, and possible therapies.

Keywords: Hair loss, alopecia, types of alopecia, pathophysiology, medicinal plants

INTRODUCTION

Hair is a distinctive dermal structure that serves as an identifier for individuals [1]. 88% of the composition of hair consists of proteins [2]. Comprised entirely of dermal papilla cells, the hair ultimately reaches the epidermis [3]. A prospective area for the cosmeceutical application of materials derived from nanotechnology is hair care. Hair, akin to the structure of skin and nails, comprises a keratinous filament comprising a hair follicle and shaft. Hair follicles are epidermal structures that encompass a diminutive dermal papilla at their basal region and traverse a significant portion, if not the entirety, of the depth of the skin. The hair bulb, composed of actively dividing cells, undergoes morphogenesis in close proximity to the follicle base to produce an elongated and thin hair shaft [4]. The hair coat, which provides warmth, protection from harmful elements, and dryness for the majority of highly evolved organisms, necessitates a consistent supply of fresh hairs throughout the organism's lifecycle [5].

Hair can be classified into two main varieties:

1. Vellus hair
2. Terminal follicle

Straight, vellus hairs are characterized by their slender structure and pale pigmentation. Moreover, Terminal

follicle" refers to a type of hair follicle that produces thick, coarse hair. Terminal hair has increased density and pigmentation, as well as a tendency to exhibit curliness. It is commonly observed in close proximity to the eyebrows and eyelashes. The phenomenon of shedding 70-100 hairs on a daily basis is often observed and considered to be prevalent [6].

Upon birth, individuals possess an estimated quantity of 100,000 terminal hair follicles located on the scalp. The inherent structure of these follicles facilitates the growth of hair that is both lengthy and voluminous. The process of hair growth is marked by three concurrent and different phases, namely anagen, catagen, and telogen, culminating in the shedding of hair [7-9]. Hair loss is categorized as a dermatological issue, and the continuous endeavour to discover natural ingredients that can stimulate hair growth continues. Alopecia, also referred to as hair loss, is a prevalent issue regularly mentioned by patients, which can result in significant psychological and physical distress [6]. Based on the extant body of literature, it has been firmly proven that androgenetic alopecia serves as the predominant cause responsible for the occurrence of hair loss within the human population [10]. Alopecia can be classified into various categories based on several factors, including as

disease, mechanical stress, nutritional deficiency, hormonal imbalance, and age [11]. The name "alopecia" derives from the Greek word ἀλώπηξ (alōpēx), which refers to the mammal often known as the "fox" [12].

Hair loss in humans is primarily influenced by two factors: psychoemotional stress and an imbalance in male hormone production. These factors have the potential to disturb the regular patterns of the hair cycle [13]. Hair loss refers to the gradual reduction in hair density on the scalp. Alopecia has the potential to manifest as either a transient or enduring condition. The prevailing manifestation of hair loss is a progressive process known as "androgenetic alopecia." Research suggests that over 50% of American males and 21.3% of Chinese males are prone to this condition, which is influenced by a mix of male hormones, specifically testosterone and dihydrotestosterone (DHT). Dihydrotestosterone (DHT) is a hormone primarily synthesized from testosterone by the enzymatic action of 5 α -reductase. DHT exhibits more biological activity compared to testosterone. The development of this disorder is contingent upon genetic factors, namely hereditary inheritance. Additional forms of hair loss encompass alopecia areata, which manifests as localized bald patches that often regenerate; telogen

effluvium, characterized by swift hair shedding following childbirth, illness, or abrupt weight loss; and traction alopecia, which involves hair thinning due to the strain exerted by tightly braided or pulled-back hairstyles [2, 14-15].

The current pharmaceutical interventions available for the management of alopecia include medications like as Minoxidil® and Finasteride®. In recent years, there has been a notable increase in the availability of herbal topical preparations within the commercial market [16].

This article offers a thorough analysis of plant species that have been found for their potential in stimulating hair growth. Furthermore, this study delves into the myriad of factors that contribute to hair loss, recognizing that the basic mechanisms of this phenomenon remain incompletely understood. A variety of treatments are currently available to address the issue of hair loss, scientifically referred to as alopecia. These treatment options span a wide spectrum of choices, encompassing both natural and synthetic remedies.

Hair-related issues

- Hair Loss
- Gray Hair
- Dandruff
- Frizzy Hair
- Dull Hair

- Androgenic Alopecia
- Alopecia Areta
- Telogen Effluvium [3].
- Fibroblast growth factor-5 (FGF-5)
- Epidermal growth factor (EGF)
- Wingless-related integration site (WNT)

Factors affecting hair growth

- Insulin-like GrowthFactor (IGF)
- Vascular endothelial growth factor (VEGF)
- Fibroblast growth factor-2 (FGF-2)
- Prostaglandin (PGD)
- Transforming growth factor beta (TGF-) (Figure. 1) [3].

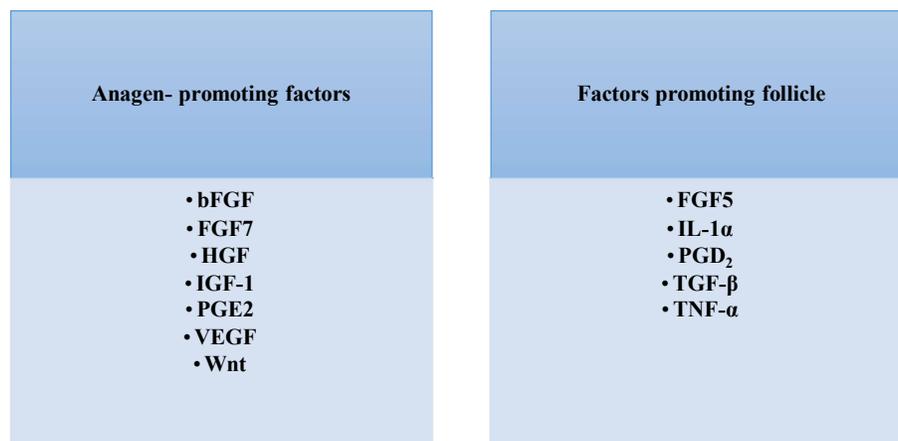


Figure 1: Factors affecting hair growth [12]

Physiology of hair growth

In humans, it has been shown that there are approximately 100,000 terminal hair follicles on the scalp at the time of birth. These particular hair follicles have a natural inclination to generate abundant and lengthy hair. Hair undergoes a well-defined and simultaneous growth cycle that encompasses three main phases:

- Anagen is active for two to eight years (approximately eighty to ninety percent of hairs).
- Catagen phase lasts for two to three weeks (less than 1% to 2% of hairs degenerate).
- Telogen is approximately three months long (10–20% of hairs at rest). Hair loss occurs throughout the telogen phase. A daily hair loss of one hundred is regarded normal (Figure 2) [7, 12, 17, 18].

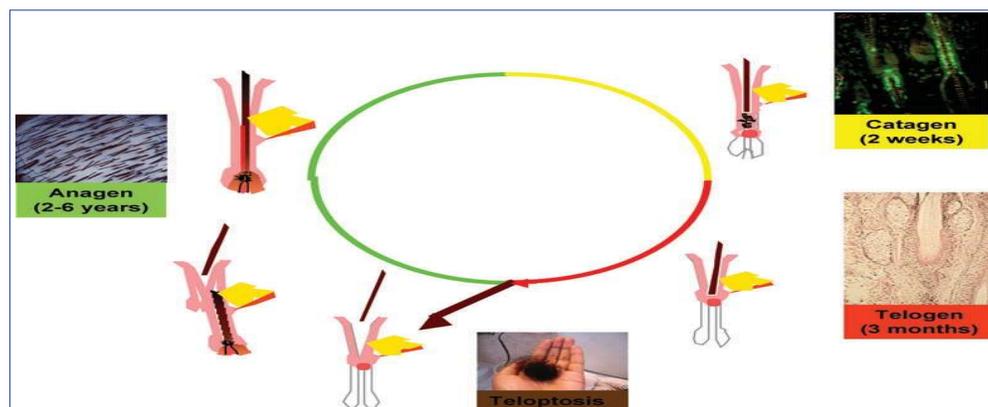


Figure 2: Physiology of hair growth [17]

RISK FACTORS FOR HAIR LOSS

- Giving birth
- Infection
- Severe long-term sickness
- Extreme psychological tension
- Extensive surgery
- Being either hyperthyroid or hypothyroid
- Anemia due to a lack of iron
- Abrupt diets
- Medications
- Stressful emotions
- Neurologic conditions
- Growing Older
- Imbalance of hormones
- Degraded surroundings
- Toxic materials
- Harm and detriment
- Radiance
- Inflammatory diseases of the scalp
- Environmental elements
- Shifting ways of living
- The autoimmune disease
- Index of body mass
- Glucose fasting
- Adolescence
- Quantity of births
- Oral contraceptive use for longer than a year
- Ladies who are nursing
- Exposure to sun
- Periodic table
- Higher exposure to estrogen
- Polycystic ovary syndrome (PCOS) [2, 3, 17, 19, 20].

MECHANISM OF ACTION

Androgenic alopecia (AGA) is a commonly observed form of hair loss (HL) that presents itself in persons of diverse age groups, encompassing both males and females. The regulation of vellus hair transitioning into terminal hair is governed

by androgen, a hormone that facilitates the growth of hairs that are longer, thicker, and darker in appearance. Androgenetic alopecia is distinguished by a progressive transformation of terminal hair follicles into vellus hair that is shorter, thinner, and shallower, along with a substantial decrease in the anagen phase. Hair loss is closely associated with testosterone, a prominent male androgen.

The enzymatic process of converting testosterone into dihydrotestosterone (DHT), a more potent androgen, is accelerated by the enzyme known as 5 α -reductase. There are two separate types of 5-alpha reductase (5-AR) that exist. Type 1 is observed in diverse cellular populations, encompassing keratinocytes, fibroblasts, sweat glands, and sebocytes. In contrast, Type 2 is predominantly situated within the dermis and the internal root sheath of hair follicles. The engagement of Type 2 with the androgenic receptor necessitates the presence of NADPH as a cofactor. The binding affinity of dihydrotestosterone (DHT) to the androgen receptor (AR) is estimated to be roughly five times higher compared to testosterone. Following this, the binding of dihydrotestosterone (DHT) to the androgen receptor (AR) leads to the regression of hair follicles through the upregulation of inhibitory molecules associated with hair development, such as

dikkopf-related protein 1 (DKK-1), interleukin-6 (IL-6), and transforming growth factor (TGF- β) (**Figure. 3**) [8, 23].

Androgenetic alopecia (AGA) is distinguished by the participation of androgens in the regulation of hair follicle (HF) growth cycles. More precisely, androgens play a role in the reduction of the anagen phase, resulting in a rise in the quantity of hair follicles transitioning into the catagen and telogen phases. Furthermore, it has been observed that androgens exert an inhibitory effect on the transition from the telogen to anagen phase. The period during which the hair follicle remains unoccupied is commonly known as the kenogen phase. The regions that have been impacted demonstrate a gradual decrease in the density of capillaries. Androgens exert a significant influence on diverse physiological mechanisms inside the human skin, including the regulation of sebaceous gland proliferation and differentiation, hair growth, and the process of wound healing. Although other hormones such as thyroid hormones and glucocorticoids have a part in the process, androgens are widely regarded as the principal regulators of human growth. The given data consists of a pair of coordinates, specifically [12, 21].

In addition, the transcription of genes that are dependent on androgens is

responsible for the manifestation of baldness. Hence, a viable approach for addressing hair loss is the inhibition of 5α -reductase enzyme activity, resulting in an anti-androgenic impact and consequent decrease in hair loss. Finasteride is

commonly used as the primary pharmacological intervention for the treatment of alopecia, as it acts as an inhibitor of 5α -reductase type II (Figure 3) [22].

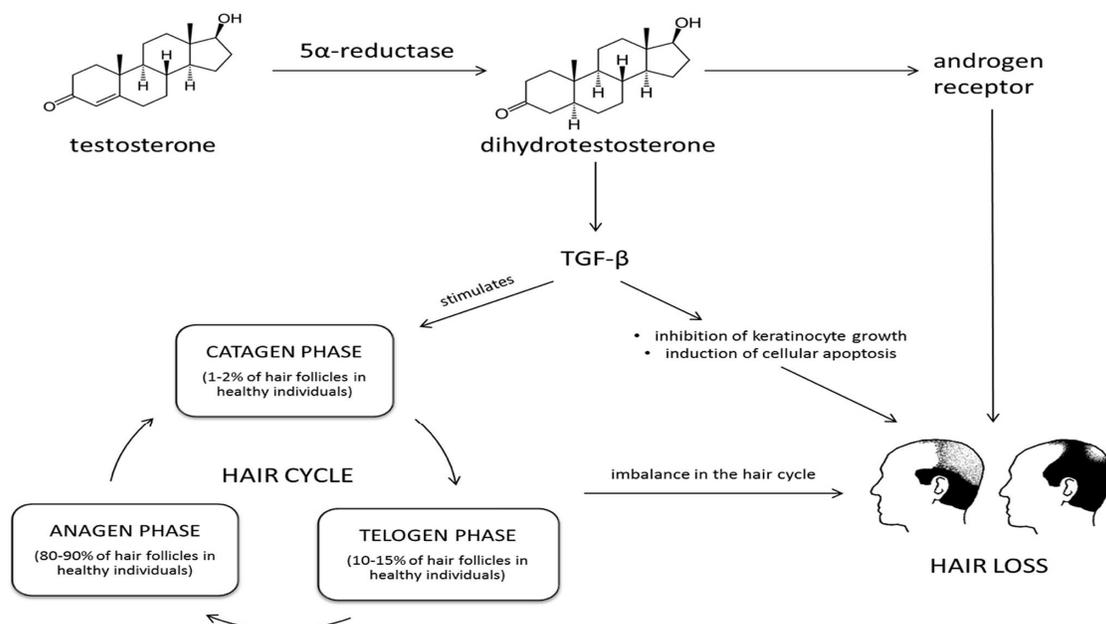


Figure 3: The effect of the 5α -reductase enzyme, dihydrotestosterone, and the growth factor TGF- β on hair loss [24].

TYPES OF HAIR LOSS

The onset of male pattern hair loss is commonly characterized by the initial recession of hair at the temples, referred to as bitemporal recession. This is followed by a more widespread thinning of hair across the crown region of the scalp. Over a period of time, the condition gradually advances to the development of total hair loss at the crown of the head, accompanied by a narrow band of hair forming a horseshoe-shaped pattern along the sides and back of the skull. In addition, female hair loss is distinguished

by a diffuse reduction in hair volume and a decline in hair density, particularly in the centre area of the scalp, while the frontal hairline remains unaffected [8].

For simplicity, alopecia can be primarily divided into 2 general sub-types, namely:

- Scarring (cicatricial)
- Non-scarring (non-cicatricial).

Various types of alopecia had been known including

- Alopecia universalis,
- Androgenic alopecia (AGA)
- Alopecia areata (AA)

- Syphilitic alopecia
- Telogen effluvium
- Stress, immune-related alopecia
- Chemotherapy-related alopecia [25].

Classification of Male pattern hair loss

- Beek 1950
- Hamilton 1951
- Ogata 1953
- Setty 1970
- Norwood 1975
- Bouhanna 1976
- Blanchard 1984
- Dynamic classification of Dardour and Bouhanna 1996
- Koo 2000

Classification of Female pattern hair loss

- Ludwig 1977
- Ebling and Rook 1975
- Savin 1992
- Olsen 1994
- Sinclair 2004

Classification Irrespective of sex

- Bouhanna 2000
- Basic and specific classification 2007 [27].

EPIDEMIOLOGY

Based on existing scholarly sources, it is evident that the prevailing kind of hair loss is androgenic alopecia, with a prevalence rate of 30.7% among females and 86.4% among males. Subsequently, the occurrence of telogen effluvium is observed in 9.8% of females and 9.3% of males, while alopecia

areata affects 7.0% of females and 40% of males. A plausible correlation exists between the presentation of symptoms related to COVID-19 and the presence of androgenetic alopecia as a preexisting disorder. Therefore, it can be demonstrated that COVID-19 is commonly linked to the onset of new cases of telogen effluvium, constituting around 93.6% of such occurrences. Moreover, those who have pre-existing medical conditions demonstrate an increased probability, estimated at 95%, of acquiring alopecia areata [3].

The study revealed that the occurrence of female pattern hair loss in women below the age of 50 was determined to be 6%, a figure that notably escalated to 38% in those aged 70 years and above. A significant proportion of women who were diagnosed with female-pattern hair loss demonstrated hair densities that fell within the lower half of the normal distribution (28). The research encompassed a predominant proportion of individuals in their third and fourth decades of life, with 65.1% of males and 56.68% of females falling inside this specific age bracket [29]. Persons of Chinese, Japanese, and African American heritage demonstrate a relatively reduced level of susceptibility when compared to persons of Caucasian ancestry. The frequency of this phenomena has been observed to increase in tandem with the progression of age [23].

Female pattern hair loss (FPHL) is commonly acknowledged as the primary cause of diffuse hair loss in women, with a prevalence rate of 32% among Caucasian women aged 20 and older. The occurrence of hair loss in women is frequently observed beyond the age of 50, although it can initiate at any time after the onset of menstruation. By the age of 70, almost half of women will display symptoms of female pattern hair loss (FPHL). Twin studies have yielded empirical support for the heritability of graying and frontotemporal hairline recession in females. Nevertheless, further investigation is required to ascertain the extent to which genetics affects female pattern hair loss (FPHL) in a manner comparable to its impact on male pattern hair loss (MPHL) [30].

In 2006, a census was done by the Brazilian Society of Dermatology, with a sample size of 36,253 female patients. The findings indicated that nonscarring alopecia

(unspecified) ranked among the top 10 most prevalent diagnoses. A study conducted in the United States in 2001 examined a sample of 1,008 women of Caucasian descent. Moreover, the research results revealed a significant correlation between the age of the participants and the frequency of occurrence, with older individuals demonstrating elevated levels. The prevalence rates observed in a population survey conducted in 2010, which utilized a sample of 8446 Chinese women, exhibited similarities to the rates reported in the Korean study. According to the findings presented in **(Table. 1)**, the prevalence of female pattern hair loss (FPHL) appears to be lower among individuals of Caucasian ethnicity. This observation is based on a recent study conducted in Taiwan, which involved a substantial sample size of 26,226 women [12].

Table 1: The study examines the frequency of Female Pattern Hair Loss across different age groups [12]

Study	Country	n	Age groups					
			20-29	30-39	40-49	50-59	60-69	>69 [#]
Norwood, 2001	USA	1008	3	17	16	23	25	29
Birch, 2001	England	377	3	10	5	14	33	38
Gan, 2005	Australia	717	12	17	25	28	41	56
Wang, 2010	China	8446	1	2	5	8	10	12
Pai, 2001	South Korea	4601	-	2	4	7	12	25
Su, 2013	Taiwan	26226	-	6	10	12	13	15

DIAGNOSIS

The physician will likely conduct a physical examination and inquire about your hair care regimen, nutrition, and medical and family history prior to formulating a diagnosis. You may also be required to take the following tests:

- Blood analysis.
- Perform a pull test.
- A scalp biopsy was performed.
- Light microscopy (LMA) [31, 32].

TREATMENT

Currently, there are several therapy techniques available that aim to promote hair regrowth or prevent hair loss. The treatment options for androgenic alopecia and anagen effluvium include the use of topical minoxidil at concentrations of 2% or 5%. Minoxidil is a compound known as 2,4-di-amino-6-piperidinopyrimidine-3-oxide and has been found to be effective in androgenic alopecia by prolonging the growth phase of hair follicles (anagen), shortening the resting phase (telogen), and promoting the enlargement of miniaturized hair follicles. Triamcinolone acetonide is specifically designed for the treatment of alopecia areata. In cases of tinea capitis, antifungal agents such as itraconazole, griseofulvin, or fluconazole are commonly used.

Finasteride is occasionally administered to patients who exhibit

resistance to minoxidil in the management of androgenic alopecia, due to its capacity to impede the enzymatic conversion of testosterone into dihydrotestosterone. On the other hand, these drugs demonstrate significant adverse effects and have limited therapeutic efficacy. For example, although minoxidil aids in the renewal of hair, its benefits are temporary and prolonged administration is required to observe any noticeable improvement. Male patients who are taken finasteride, a medication known for its capacity to block the enzyme 5-alpha-reductase and thus hinder the conversion of testosterone to dihydrotestosterone (DHT), may experience adverse effects such as decreased sexual desire, erectile dysfunction, and the development of breast tissue (gynecomastia).

Likewise, it is widely recognized that antifungal medications have the potential to adversely affect hepatic function. A randomized clinical experiment has demonstrated that the microinjection of stromal vascular fraction cells (SVFs) and adipose-derived mesenchymal stem cells (AD-MSCs) can effectively induce hair growth and promote the proliferation of epidermal stem cells in individuals suffering from androgenic alopecia. However, it is essential to note that a substantial proportion of these individuals require regular

microinjections to sustain hair growth [19, 22, 30, 33- 36].

The utilization of low-intensity light treatment in 2007, the Food and Drug Administration (FDA) provided permission for the utilization of low-level light therapy (LLLT) as a therapeutic intervention for the treatment of hair loss. Photobiomodulation, biostimulation, low level laser therapy (LLLT), red light treatment, cooled laser, and soft laser are synonymous terms used interchangeably to refer to the same therapeutic modality. Low-level laser therapy (LLLT) was initially employed subsequent to its identification in the 1960s [23].

The integration of herbal nanomedicine into cosmetics is a common practice owing to its little negative consequences. The accessibility of herbal drugs for the prevention and treatment of hair loss has been enhanced as a result of advancements in our comprehension of their mechanisms of action and improvements in quality control [3].

Several other medications are available for the treatment of hair issues.

- Biotin
- Caffeine
- Cimetidine
- Ferritin
- Melatonin
- Zinc [3].

Alimentary deficiencies possible to underlie hair disorders

- Protein
- Vitamin C
- Biotin
- Vitamin B
- Zinc
- Niacin
- Iron [30].

Medications for female pattern hair loss

- Cyproterone
- Dutasteride
- Estrogens
- Finasteride
- Fluridil
- Flutamide
- Ketoconazole
- Latanoprost
- Minoxidil
- Spironolactone [30].

Treatments in general for hair loss

- Finasteride 1mg
- Dutasteride
- Topical finasteride
- Topical minoxidil
- Oral minoxidil (2.5-5mg daily)
- Topical Prostaglandins (topical bimatoprost 0.03% lotion, latanoprost 0,1%, topical 1% cetirizine)
- Oral prostaglandin (setipiprant 500mg twice a day)
- topical valproic acid

- Serenoa Repens/Saw Palmetto
- Physical therapies (Growth factors, Micro-needling)
- Laser therapy (Low level laser therapy (LLLT))
- Surgical treatment (Hair transplantation) [32, 36].

HERBAL MEDICINE

Herbal formulations that are natural products are commercially accessible and are utilized for various purposes, including but not limited to hair cleansing, antidandruff, hair tonic, hair growth promotion, hair conditioner, and the treatment of parasites and alopecia [9].

Researchers are currently engaged in the development of nano-formulations derived from herbal sources, with the aim of providing assistance to persons with hair-related concerns. A diverse range of hair products, encompassing oils, serums, conditioners, hair colorants, cleansers, gels, and wax formulations, have been formulated to effectively target and alleviate a wide array of hair-related issues. Globally, a substantial number of herbal treatments and phytoconstituents are employed for the purpose of addressing hair-related concerns. With the advancement in understanding the mechanisms of action and quality control of herbal remedies, it has become increasingly viable to identify herbal drugs that can effectively address and mitigate hair loss

[3]. The aforementioned solutions offer a multitude of advantages, such as the utilization of natural components, a notable degree of safety, cost-effectiveness, patient-friendly use, the incorporation of therapy and recuperation, and the capacity to address several facets of hair growth stimulation or hair loss management (Figure. 4) [16].

The utilization of herbal remedies to stimulate hair growth and mitigate hair loss.

- *Abrus precatorius*
- *Aconiti ciliare tuber*
- *Allium tuberosum rottler ex spreng*
- *Asiasari radix*
- *Boehmeria nipononivea*
- *Eclipta alba*
- *Glycyrrhiza glabra*
- *Hordeum vulgare*
- *Ishige sinicola*
- *Lycopersicon esculentum*
- *Lygodium japonicum*
- *Mentha piperita oil.*
- *Oryza sativa*
- *Piper nigrum*
- *Platycarya strobilacea*
- *Thuja orientalis*
- *Carthamus tinctorius*
- *Phyllanthus emblica*
- *Rhinacanthus nasutus*
- *Chrysanthemum zawadskii,*
- *Polygonum multiflorum* [37, 38].

The botanical substances employed in the management of alopecia Please provide one of the following options:

- The provision of dietary assistance to meet the nutritional needs of individuals.
- Two types of medications commonly used in the treatment of hair loss are DHT blockers and 5- α -Reductase blockers.

- The relationship between aromatherapy and enhanced circulation of blood in the scalp has been explored [6].

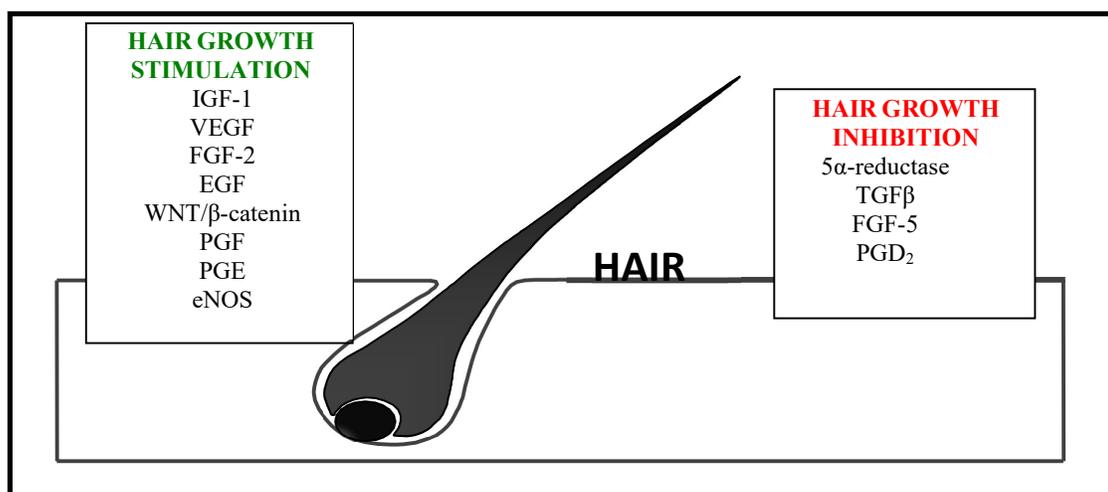


Figure 4: Mechanism of action of herbs for hair loss and hair growth [38]

CONCLUSION

Hair loss is a prevalent issue that has been observed in both males and females over an extended period of time. The phenomenon under consideration remains incompletely comprehended and remains the subject of ongoing investigation, with numerous therapeutic options available, including those derived from natural or synthetic sources. However, there is a growing trend towards the utilization of natural materials, particularly formulations including plant extracts. Due to the potential adverse effects on human health, synthetic-

based products may pose various risks and induce a range of side effects. Given the growing prevalence of herbal pharmaceuticals in the field of hair care, it would be prudent to undertake a comprehensive examination into the effectiveness of these treatments and their methods of manufacture. In prospective times, there exists the potential for the discovery of several novel plant species that possess commercially valuable extracts. Additionally, assertions on the efficacy of various widely distributed herbs may be substantiated by empirical evidence.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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Author Contribution

The authors confirm contribution to the paper as follows: study conception and design: Glena AH, Sakthi PS; data collection: Glena AH; analysis and interpretation of results: Glena AH, Sakthi PS, Kamaraj R; draft manuscript preparation: Glena AH, Sakthi PS. All authors reviewed the results and approved the final version of the manuscript.

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