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PHYTOCHEMICALS: AN HERBAL REMEDIES FOR ALOPECIA

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ABSTRACT

Although hair does not perform a vital physiological purpose in homo sapiens, it is significant to our self-worth. The two most prevalent types of hair loss are androgenic baldness and alopecia areata. There are several therapeutic active substances with synthetic origins, but they have a variety of drawbacks. Their efficacy, safety, and the length of time required to have the desired effect are all debatable. There has prompted interest in developing an alternate treatment against loss of hair using preparations including plants and/or their separated active components. Research has been conducted on plants and products manufactured from plants to support their efficacy in treating hair loss. Pink and blue ginger, Green tea, Pumpkin, Red clover, and Chinese red ginseng are the herbs with the most substantial evidence-based effects against alopecia. Inhibition of 5α-reductase is thought to be the main mechanism of action, with better nutritional maintenance and scalp blood flow.

Keywords: Herbal, Alopecia, Hair loss, Alopecia Areata, Androgenic Baldness

INTRODUCTION

Hair serves no important physiological purposes in contemporary humans. Despite this, it significantly affects our sense of self. Hair loss does not have numerous negative impacts, but it may have emotional impacts which include elevated levels of apprehension and depression **[1]**. The main protein in hair, keratin, is a collagenous structure that makes up the hair. The tubular, cone-shaped organs called hair follicles are

the source of these hairs. The development of the scapus pili begins with the matrix of the hair bulb and various types of skin cells. The proliferation of cells in the hair follicle divides relatively quickly to generate the hair. The freshly generated keratinocytes are stratified, keratinized, and tinted to form a lifeless hair shaft in a hair cavity. Hair also encompasses moisture, fats, elements, and the tint melanin combined with keratin, which contains a significant amount of the cysteine amino acid. Six concentric layers grow from the matrices of the hair bulb at the base of the hair cavity. The outer thick layer called cortex, the cuticle (which serves to provide strength), the inner and outer root covering, the medulla (whose purpose is uncertain), and the cortex are all located from the center outward **[2]**. The hair, which may be inherently curly or straight, angular, worn, split, sheared, etc.is made up of root, shaft, and hair. The dermal papilla, a collection of keratinocytes that swirl around the hair follicle's epithelial region, is the only dermal component present. It is in charge of regulating the hair cycle. The dimension of the papilla has a direct impact on the diameter of the resultant hair. The dermal papilla can stop growing if it is removed. The morphology of the papilla does not significantly alter over the course of cycle **[3]**. The hair growth cycle comprises three stages: the initial stage is the anagen stage, which lasts, on average, between three and six years **[4-6]** is accompanied by a catagen stage that lasts for about two weeks **[7]**, during which development activity reduces and eventually ends. The morphology of the hair changes during this time. The telogen stage, often known as the sleeping stage, is the last stage before the anagen stage, which lasts for roughly three months. While hair is in the telogen stage, it progressively grows out and falls out. Because new hair is already forming in the follicle at such a moment, pulling out hair at that time is painless, as when brushing **[2]**. 80–90% of follicles in healthy people are in the anagen stage, compared to 1 percent in the catagen phase and 15 percent in the telogen stage. A trichogram, which is a microscopic scaled examination of depilated hair amplified from 10 to 30 times, can be used to evaluate the connection between different stages of hair follicles. According to studies, the proportion of telogen stage follicles increases while the proportion of anagen and catagen stage follicles decreases **[8]**. This ratio is altered in the case of many hair illnesses, and the trichogram may show dystrophic hair.

A healthy person loses 100–150 hairs daily on average **[2]**. Increased hair loss can be brought on by severe and protracted infections, extreme stress, diet, malnourishment, drug side effects, as well as chemical as well as mechanical hair strain

[9]. Hormonal changes brought on by pregnancies and menopause, thyroid conditions, inflammatory conditions of the body, and immune system dysfunction are internal variables that can potentially have an impact on hair loss. Many skin conditions and the follicles' incapacity to ever start the development phase again are the two main causes of permanent hair loss **[2]**. Along with familial susceptibility, hormonal imbalance, localized micro-inflammation **[10]**, and loss of the follicular bulb's extracellular matrix are some of the main causes of baldness.

The androgenic hormones, which are significant hair growth regulators, have a special impact on male pattern baldness. Baldness is more prevalent in individuals with higher levels of the 5-reductase enzyme in their hair cells, which converts testosterone into the more potent androgen-signaling dihydrotestosterone (DHT). Dihydrotestosterone activates transforming growth factor-β (TGF-β) in subcutaneous follicular cells also have effect on follicular nuclear receptors. As a result, the proliferation of keratinocytes is inhibited, and cellular apoptosis is induced, which causes hair follicle to shed **[11]**. Inflammation also comes from transforming growth factor-β's abnormal expression **[12]**. Transforming growth factor-β is also a catagen phase inducer in the physiology of the hair and scalp **[13]**. Increased amounts of dihydrotestosterone and uncontrolled transforming growth factor-β signaling were found in the balding crown due to enhanced 5α-reductase activity **[14]**.

Androgenic baldness and Alopecia areata are the two types of baldness that are most prevalent. The first is distinguished by the hair follicles' high sensitivity to dihydrotestosterone, whereas the second is brought on by an immunological response **[15, 16]**. Moreover, hair has an immune system of its own, and when it malfunctions, it can cause alopecia areata. Synthetic drugs which produce dilatation in hair follicles' blood vessels are the most often used treatments for hair loss like potassium channel openers (minoxidil), tretinoin, anti-androgens [spironolactone and finasteride, and corticosteroids **[17, 18]**. Injections of corticosteroids have been proven to be beneficial in treating localized alopecia areata in a number of investigations. In one trial, triamcinolone acetonide injections were administered, and 71 percent of patients saw hair regrowth **[19]**. These substances do have certain restrictions, though. Their efficiency and safety are in doubt, and it takes a while for them to take effect. Due to this, there is now more interest in adopting herbal and plant-based remedies to reduce hair loss. The topical application of herbal preparations provides a number of benefits, including more compliance, less adverse effects, a wider spectrum of activity,

and lower cost and greater accessibility **[20]**. Experts are always looking for new traditional medicines and their active components that can offer a feasible alternative to the currently used synthetic medication for treating hair loss. Pre-clinical and clinical research have examined the effectiveness of certain plants, their active components, and formulations incorporating various plants in encouraging hair growth. Many traditional herbs were used in treatment of baldness but there is no study carried out to prove its efficacy.

There are different herbs, which are used for treating baldness, are discussed below in detail with their basic mechanism of action, clinical studies, and observations.

Garlic and Onion

Traditional therapies for spot baldness have included the topical use of garlic **[21]**. The major substance in a garlic clove is alliin, a derivative of an amino acid that contains sulfur and has no odor. An enzyme transforms it by chopping, grinding, or crushing it into allicin [a yellow fluid], which is thought to be the source of the medicinal effects **[22]**. Sadly, less research have been conducted to far on the effectiveness of garlic in treating androgenic alopecia, and as a result, it is still unclear how garlic stimulates the growth of hair **[23]**. Garlic's regulatory effect on the immunity may have an impact because androgenic alopecia is immunological-dependent **[24]**. A steroid called betamethasone valerate was applied to the hair twice everyday along with a 5 percent odorless garlic gel in a randomized clinical trial. The control group received a gel without any garlic but with the same corticosteroid. The treatment regimen lasted for three months, and the gel was kept on the scalp for one hour to work. At the conclusion of the experiment, there were considerably more hairs in the test group than in the representative group. So, this research offered evidence that topical gel therapy, which offers long-lasting therapeutic advantages, may be successful. Also, patients appeared to like it **[21]**. Onion was also taken into consideration for topical usage because it shares many chemical properties with garlic and belongs to a similar genus **[25]**. In a comparative investigation, patients with patch baldness were treated topically with raw onion juice. Juice was not used in the representative group; instead, faucet water was used. Over a two-month period, patients received treatment twice daily. After two weeks of onion juice treatment, hair regrowth was already evident, and the test group's hair count was considerably higher than that of the representative group **[26]**.

Green Tea

The leaves of the perennial plant Camellia sinensis are used to make green tea. Although this plant is Chinese in origin, it

has ties to many other Asian nations, including Japan and the Middle East. A few catechins, such as catechin, gallocatechin, epicatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate (EGCG), are present in the tea leaf **[27]**.

In addition to their stated antioxidant qualities **[28]** and their ability to stimulate epidermal keratinocytes' normal cell development **[29]**, studies demonstrated the specific inhibition of 5α reductase **[30]**. Kwon *et al*. investigated the utilization of epigallocatechin gallate for the therapy or prevention of androgenic alopecia because of this. In this investigation, the scalps of the patients were treated with 10 percent epigallocatechin gallate in ethanol. The findings demonstrated that epigallocatechin gallate prolongs the initial stage and increases growth of hair through dermal papillae multiplication and suppression of cell death, whose protection inhibits hair loss **[31]**.

In an experimental investigation, 60 female rats with sudden baldness on the crown, neck, and posterior areas were used to investigate the impact of polyphenolic chemicals found in green tea that is not commercially accessible on rodent hair loss. 33% of the rats in the test group who drank water containing 50 percent of the catechin extract from dried green tea experienced noticeable hair regrowth. The rats in the control condition, which received faucet water, showed no signs of hair development **[32]**.

Pumpkin

The Cucurbitaceae plant family includes the pumpkin. Several of its cultivars' fruits and seeds are frequently eaten as food. Pumpkin seed oil is a normal byproduct and is a good source of fatty acids, beta-carotene, lutein, γ and β-tocopherols, squalene, and phytostanols **[33]**. There have been some published reports on the effectiveness of pumpkin oil in the cure for symptomatic benign prostatic hypertrophy **[34]**. As demonstrated in rats, phytostanols that block 5α reductase and have androgenic antagonist effect are likely responsible for their activity. Although numerous studies in animals suggest that 5α reductase may be inhibited, the precise mechanism is still unknown **[34-36]**.

The first randomized, double-blind controlled trial assessing the safety and efficacy of pumpkin oil in male individuals who have mild to moderate forms of spot baldness was published in 2014. For 24 weeks, the representative group was provided with a dietary supplement containing 400 mg of pumpkin oil, whereas the control group received a placebo. Four outcomes the evaluation of standardized analytical pictures, patient self-examination grades, hair density, and hair counts were used to gauge changes. In comparison to the placebo-treated men, the experimental

group's mean hair count increased by 40 percent while theirs increased by 10percent. The research demonstrated that the pumpkin oil had a favorable constructive effect on hair growth, perhaps by blocking 5α-reductase. To confirm the effect mechanism of pumpkin oil, the amount of dihydrotestosterone has not been examined. Men with frontal hairline baldness were included in the trial, however the effects of the oil's action on these individuals were not reported **[37]**.

Pink and Blue Ginger

Instead of ginger, curcuma aeruginosa is a plant native to South Asia **[38]** and India and is closely related to turmeric. Its pink corolla portion and blueish tubers give it the nickname "pink and blue ginger." Traditional uses of C. aeruginosa rhizome in Eastern medicine include treating fungus infections and dysmenorrhea **[38, 39]**. It has been demonstrated in in vitro tests that *C. aeruginosa* rhizomes' 5% hexane extract suppresses testosterone's conversion to DHT more effectively than other Zingiberaceae plants **[40]**. Androgenic alopecia is reversed by its sesquiterpenes, which block the formation of DHT and the steroid 5α-reductase **[41]**.

1,8-Cyneol, Curcumenone, Curcumenol, Iso-Curcumenol, Camphor, and other active substances are present in this plant's essential oil **[42]**. Its primary sesquiterpenoid component functions as an anti-inflammatory with germacrone activity **[43]** as well as an anti-androgenic both in vitro and in vivo **[44]**. Contrary to its ability to encourage anagen on male scalps, *Curcuma aeruginosa* has been demonstrated to prevent female underarm hair growth **[41, 45]**. The effectiveness and safety of 5 percent *Curcuma aeruginosa* hexane extract vs 5 percent minoxidil solution and a combination of *Curcuma aeruginosa* extract in a minoxidil mixture were compared in a comprehensive, randomized, double-blind, placebo-controlled research. For six months, preparations were administered twice daily. The study found that *Curcuma aeruginosa* extract, especially when paired with minoxidil, encouraged hair growth and reduced hair loss. The latter supported the idea that combining these two drugs, each of which has a distinct mechanism of action, can enhance their therapeutic efficacy. All forms of baldness can be treated with minoxidil, which directly stimulates hair growth, but androgenic alopecia is the only condition that can be treated with 5α-reductase inhibitors, such as a *Curcuma aeruginosa* extract **[40]**. Minoxidil penetrates the skin more deeply when combined with *Curcuma aeruginosa* extract/essential oil, making it a more potent topical therapy for androgenic alopecia **[45]**.

Ginseng

In the family Araliaceae, the genus Panax includes 11 species of slow-growing annual

with fleshy roots that contain ginsenosides. They typically flourish in eastern Asia's colder regions, particularly in northern China, Korea, and eastern Siberia, as well as in Russia. Ginseng is grown for its therapeutic properties and utilized in herbal medicine to boost the immune system and increase strength, energy, and endurance **[46]**. The red and white ginseng roots are the two varieties mentioned in Japanese pharmacopoeia. The method by which different roots are processed varies. Red ginseng is thought to have a higher level of physiological activity than white ginseng because it has more active components **[47, 48]**. Ginseng has long been used in Korea to promote healthy hair growth and stop hair loss. According to several studies, red ginseng root can effectively treat androgenic baldness **[49]**. In 2012, Oh *et al*. attempted to determine red ginseng's in vivo effectiveness as a remedy of spot baldness. Two groups of 50 individual with spot baldness were created. The first group got red ginseng extract orally along with corticosteroid intralesional injections. Just injections of corticosteroids were used to treat the second group. Scalp photos and phototrichograms were taken at the start of the treatment and 12 weeks later. Following 12 weeks, the ginseng group's hair thickness and density greatly improved, demonstrating the herb's efficiency **[50]**. The following step was to research the hair growth-increasing pathways of red ginseng extract and its ginsenosides because ginseng has been demonstrated to enhance hair growth in numerous studies. The in vivo hair growth-promoting function was tested in mice, and their impacts on patient - derived dermal papilla cells were assessed. Red ginseng extract and its ginsenosides were found to promote the growth of cutaneous papilla cells, activate the extracellular signal-regulated kinase (ERK) pathway and the AKT signaling pathway in these cells, and block dihydrotestosterone-stimulated androgen receptor expression **[51]**.

Red clover

An animal feed crop from the Fabaceae family is red clover. In traditional medicine, it is used to treat chronic skin conditions like psoriasis or dermatitis as well as stomach irritation, depression, fungal infections, cough, and other respiratory tract problems. Dried flowers preparations, particularly alcohol-water liquid concentrates with therapeutically active ingredients including isoflavonoids (estrogenic compounds), cyanogenic glycosides, cumarin derivatives, and essential oils with fragrant alcohols, are utilized for medical purposes **[52]**. Several polyphenols, including Biohanin A, phytoestrogen polyphenol, and others, have been demonstrated to obstruct 5α-reductase activity in vitro **[30]**. According to some sources, inhibition is more effective than epigallocatechin gallate found in green tea

[33]. Moreover, studies have shown that biohanin A suppressed the enzyme reductase's type I and type II isoforms more potently than epigallocatechin gallate did in intact cells **[53]**. Although the scalp contains both isomeric forms, Reductase type II is the one that causes male baldness **[54]**. Red clover extract and acetyltetrapeptide 3 were examined in clinical research for their ability to stop hair loss **[53]**.

It was measured in vivo hair growth using the TrichoScan technique, a system that integrates epiluminescence microscopy and digital image analysis. For four months, the experimental group massaged red clover extract and peptide lotion into their scalps, while the representative group utilized an inactive product. The scalp hair density and number of hairs increased after treatment with red clover and acetyltetrapeptide 3 extract. The proportion of follicles in the anagen to telogen phases increased while the density of telogen hairs dropped. The ratio may be able to stimulate hair growth if there is a considerable rise **[53]**. For the treatment of alopecia, this combination contains all the advantageous properties of biohanin A and acetyltetrapeptide 3.

Essential oils

Thyme, lavender, rosemary, and Atlas cedar essential oils have all been utilized for treating baldness for more than a century. A randomized, double-blind trial was conducted in 1998 to show that using these four essential oils is an efficient and secure method for treating spot baldness. Over seven months, patients applied the blend of oils into their scalps for two minutes each night. To improve the absorption, they covered their scalps and hair with a warm cloth. Due to the extent of the study and the exclusion of patients with more severe types of baldness, the control group in the study that used merely a combination of jojoba oil and grape seed oil was shown to be substantially less effective than the essential oil treatment group **[55]**. In 2003, research was conducted on the usage of local essential oil application combined with low-intensity electromagnetic pulses for the treatment of androgenic baldness. This 6-month, double-blind, randomized trial was conducted. Both men and women's responses to the medicine in terms of increased hair growth, baldness, hair condition, and overall tolerance were examined. Pimenta racemosa, Myrtus communis, Cedrus atlantica, Laurus nobilis, Pogostemon cablin, Rosmarinus officinalis, Salvia officinalis, Salvia sclarea, Thymus satureioides, and Cananga odorata were among the plants whose essential oils were incorporated into the lotion used by the test group **[56]**. In studies, the use of electromagnetic radiations for the therapy of androgenic alopecia was found to be successful **[57, 58]**.

In combination to these essential oils, this activation of microcirculation improved the follicular cells' nutritional status **[59]**. There were no negative outcomes from the procedure itself. In comparison to the control group, the experimental group had an average of more hairs, 83% of patients had less hair loss, and 53% of patients had an increase in hair growth of more than 20% **[56]**.

A member of the Lamiaceae family, rosemary [Rosmarinus officinalis] is an evergreen bush. As was already mentioned, rosemary essential oil is frequently considered as a potential treatment for androgenic alopecia **[55, 56]**. The advantages of this remedial herb include improving microcapillary circulation. It is used in traditional medicine to treat gastrointestinal issues, flatulence, stomach ache, cramps, to improve blood flow to the female reproductive organs, and to promote hair development **[60]**. Essential oil makes up 1.5–2.5% of the medication. The primary components of the essential oil are camphene, camphor, cineol, and borneol. The curative efficiency of rosemary oil against 2% minoxidil in treating androgenic alopecia during a 6-month period. A randomized comparison research was conducted. At the beginning, three months later, and six months later, the medication's effectiveness was evaluated. The evaluation of baldness involved microphotography. No differences in the average amount of hairs were seen in either group after 3 months of therapy. The hair count increased in both groups after 6 months of therapy. Itching of the scalp was noticed as an adverse consequence of the therapy, and it was a little adverse in the minoxidil group. Therapies with rosemary oil and minoxidil had no effect on dandruff reduction, hair dryness or greasiness **[61]**.

Procyanidins

A class of polyphenols known as procyanidins has a wide range of pharmacological actions. They have been demonstrated in vitro to have antioxidant, antiviral, antifungal, and anti-allergic properties in addition to their ability to scavenge free radicals. Procyanidins are also employed as pharmacologically active compounds in pharmaceuticals to preserve blood vessels and as skin protectants for aesthetic reasons **[62-64]**. Moreover, their potential to stimulate hair growth has been suggested **[65]**. Procyanidins are thought to induce the catagen phase and inhibit the function of the negative hair growth regulator (TGF-β) **[66, 67]**. Other aggravating variables for hair growth include lipid peroxidation and inflammation, with research showing a connection between the two and male pattern baldness. Patients' follicular biopsies revealed an increased infiltration of lymphocytes **[68, 69]**. Procyanidins can help

stop this from happening. Procyanidin B-2 is one of the procyanidin oligosaccharides that can be isolated from barley, grape seeds, and apples. Highly pure apple procyanidin B-2's effects on the scalp and hair were studied **[70]**. Men who applied 1% (w/w) procyanidin B-2 topically for six months saw outcomes that were comparable to those of finasteride and minoxidil in the therapy of androgenic alopecia. Itching and inflammation were noted as adverse effects, as well as an elevation in the proportion of the anagen to the telogen phase, stimulates growth, and density. Its strong effects on hair epithelial cells, which may be aided by its antioxidant properties, may be the main mechanism of action.

CONCLUSION

The two most typical types of baldness are spot baldness and androgenic baldness **[15, 16]**. The majority of hair loss conditions cannot be fixed, however baldness can be reduced or stopped. The perfect nutrition **[71]** and hair maintenance regimen greatly aid in this process. It has been established that a change in hair growth cannot be anticipated to occur overnight **[2]** due to the cycle of hair development itself. Future research should find out how long it takes to mend the follicles and stop the hair loss process, or the length of the therapy period. It is well known that, for some synthetic medicines, baldness might return after a certain amount of time in a more severe form. A growing number of people are interested in plant-based remedies that can either stop hair loss or encourage it. Patients are more receptive to medication, there are fewer serious adverse reactions, the expenditure on therapy is lower, and due to the diversity of plant extracts, plant preparations frequently have more than only one physiological action to treat hair loss **[20]**. Nonetheless, plant-based medicines are a valuable addition to traditional therapy and, for some patient populations, a potential alternative to therapy involving synthetic chemicals.

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Conflict of interest

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Authors' contributions

CT, SP and SP have first drafted the manuscript. DT helps in writing and editing the manuscript. CT contributed in final drafting and editing of manuscript and gave final approval for the submission of manuscript.

Ethics of Human and Animal Experimentation

Not Applicable.

Abbreviation

AKT: Ak strain transforming

DHT: Dihydrotestosterone

EGCG: Epigallocatechin gallate

ERK: Extracellular signal-regulated kinase

TGF-β: Transforming growth factor-β

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