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# A REVIEW ON ANTI-HAIR FALL

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## ABSTRACT

Hair loss may not be recognized as a life-threatening disorder. However, it has a great harm on a person's self-respect, mental health, and entirety quality of life. Androgenic alopecia (AGA) is the most common type of hair loss, which affects a great number of both men and women. Alopecia can be treated with various hair loss strategies, including hair transplant, cosmetics and medication. Medical treatment shows the outstanding ability in improving hair growth. Plenty of drugs prevent alopecia by inhibiting the secretion of male hormone. But these medicines exhibit some undesirable side effects. Since hair loss requires a long-term treatment,and minimizing adverse side effects is extremely urgent in drug development. Accordingly, new agents are obtained from natural products with less adverse effects. This review generalizes and analyzes the recent progress of medicinal plants for the treatment of hair loss, suggested mechanisms and outlines a number of trials taken or underway to optimize the treatment.

## INTRODUCTION

Humans are usually born with approximately 5 million follicles, and no new follicles are thought to be added after birth. The hair follicle cycle, which begins in utero, is composed of three stages: anagen, telogen, and catagen. Anagen phase is the longest, lasting an average of 3 yr and ranging from 1 to 6 yr depending on body location. It is also the most prevalent phase, with 90%–95% of all hairs existing in anagen phase at any one point in time. Anagen represents the growth period, comprising extensive mitotic activity, such that longer anagen phase means longer hair (e.g., scalp as opposed to eyebrows, eyelashes, or pubic hair). The hair then involutes during catagen phase through apoptosis of the follicular keratinocytes, leaving a club hair. Telogen is the resting period with inactivity of the organ, persisting 2 to 3 months on the

scalp or longer elsewhere. The club hair is shed and a new anagen hair grows in its place to resume the cycle.[1]

The hair follicle is a true paradigm of mesenchymal-epithelial interaction. From early morphogenesis to a fully formed organ, the hair follicle life-cycle is controlled by a dialog between mesenchymal and epithelial compartments.[2]

As the hair follicle develops, blood vessels originating from the deep dermal vascular plexus surround it. These vessels nourish the hair follicle and support nutrient delivery, waste elimination, and growth. Loss of blood supply to the hair follicles is associated with some forms of hair loss. Additionally, anagen hair follicles have demonstrated angiogenic properties. While the relationship has not been well defined, the blood supply is an essential component of successful hair follicle growth, maturation, and maintenance. The lymphatic vasculature within the dermis supplies the hair follicles as well and participates in the skin immune response.[3]

People commonly inquire about vitamin and mineral supplementation and diet as a means to prevent or manage dermatological diseases and, in particular, hair loss. Answering these queries is frequently challenging, given the enormous and conflicting body of evidence that exists on this subject. The latest findings promote new evidence-based recommendations for the prevention and treatment of atopic dermatitis, psoriasis, acne, and skin cancer and have highlighted the requirement for ongoing research studies.[4]

**Review literature**

**Nouryam M., et al 2014.** Androgenetic alopecia is the diseases of the hair fall in men. evaluated the anti-hair loss activity of the *Adiantum capillus-veneris* Linn in the testosterone-induced alopecia albino mice. Animal divided in five groups each group have Six mice. group 1(control group) received the Testosterone solution, group 2 (standard group) received the Testosterone + Finasteride solution (2%), group 3 received the Testosterone + vehicle, group 4 (test group) received Testosterone + *A. capillus-veneris* solution (1%) and group 5 received intact control (without testosterone). Testosterone (1.0 mg) administrated by subcutaneous in all groups. *A. capillus-veneris* are the test solution., which are administered to the skin of the mice in individual groups. follicle density (number of follicles/mm) and anagen/telogen are the parameter, which are used for the evaluated of hair growth by visual observation and histological study of several skin sections. *A. capillus-veneris* are given best result (less hair

loss) and compared with control group (only treated with testosterone) after 21 days. the follicular density checked in treated group (1.92 ± 0.47), compared with control group (1.05 ±0.21) and standard group (2.05 ± 0.49). Moreover, Anagen/telogen ratio was significantly concerned by test group (0.92 ± 0.06) compared with control group (0.23 ± 0.03) and standard group (1.12 ± 0.06). *A. capillus-veneris* was give the good result compared with testosterone-induced alopecia group, according to visual observation and quantitative data (follicular density and anagen/telogen ratio).[5]

**Patel S. et al., 2015** This study was designed to investigate the potential *Phyllanthus niruri* (*P. niruri)* extracts in promotion of hair growth. Here, we studied the hair growth promoting activity of petroleum ether extract of *P. niruri* following its topical administration. Alopecia was induced in albino rats by subcutaneous administration of testosterone for 21 days. Evaluation of hair loss inhibition was done by concurrent administration of extract and monitoring parameters like follicular density, anagen/telogen (A/T) ratio and histological observation of animal skin sections. Finasteride solution was applied topically as standard. *In vitro* experiments were also performed to study the effect of extract on the activity of 5α-reductase enzyme**.** Groups treated with petroleum ether extract of plant showed hair re-growth as reflected by follicular density, A/T ratio and skin sections. Histopathology and morphologic observations of hair re-growth at shaved sites showed active follicular proliferation. *In vitro* experiments results showed inhibitory activity of petroleum ether extract on type-2 5α-reductase enzyme and an increase in the amount of testosterone with increasing concentrations. It could be concluded that petroleum ether extracts of *P. niruri* might be useful in the treatment of testosterone-induced alopecia in the experimental animal by inhibiting 5α-reductase enzyme.[6]

**JI Young Oh et al., 2014** Peppermint (*Mentha piperita*) is a plant native to Europe and has been widely used as a carminative and gastric stimulant worldwide. This plant also has been used in cosmetic formulations as a fragrance component and skin conditioning agent. This study investigated the effect of peppermint oil on hair growth in C57BL/6 mice. The animals were randomized into 4 groups based on different topical applications: saline (SA), jojoba oil (JO), 3% minoxidil (MXD), and 3% peppermint oil (PEO). The hair growth effects of the 4-week topical applications were evaluated in terms of hair growth, histological analysis, enzymatic activity of alkaline phosphatase (ALP), and gene expression of insulin-like growth factor-1 (IGF-1), known bio-markers for the enhanced hair growth. Of the 4 experimental

groups, PEO group showed the most prominent hair growth effects; a significant increase in dermal thickness, follicle number, and follicle depth. ALP activity and IGF-1 expression also significantly increased in PEO group. Body weight gain and food efficiency were not significantly different between groups. These results suggest that PEO induces a rapid anagen stage and could be used for a practical agent for hair growth without change of body weight gain and food efficiency.[7]

**Begum S. et al., 2014.** *Eclipta alba* (L.) Hassk, *Asiasarum sieboldii* (Miq.) F. Maek (*Asiasari radix*), and *Panax ginseng* C. A. Mey (red ginseng) are traditionally acclaimed for therapeutic properties of various human ailments. Synergistic effect of each standardized plant extract was investigated for hair growth potential on nude mice, as these mutant mice genetically lack hair due to abnormal keratinization. Dried plant samples were ground and extracted by methanol. Topical application was performed on the back of nude mice daily up to completion of two hair growth generations. The hair density and length of *Eclipta alba* treated mice were increased significantly ($P > 0.001$) than control mice. Hair growth area was also distinctly visible in *Eclipta alba* treated mice. On the other hand, *Asiasari radix* and *Panax ginseng* treated mice developing hair loss were recognized from the abortive boundaries of hair coverage. Histomorphometric observation of nude mice skin samples revealed an increase in number of hair follicles (HFs). The presence of follicular keratinocytes was confirmed by BrdU labeling, S-phase cells in HFs. Therefore, *Eclipta alba* extract and/or phytochemicals strongly displayed incomparability of hair growth promotion activity than others. Thus, the standardized *Eclipta alba* extract can be used as an effective, alternative, and complementary treatment against hair loss.[8]

**Rambwawasvika H. et al., 2019.** Phytochemicals from *Dicerocaryum senecioides* were studied for hair rejuvenation activity using BalB/c mice. Solvent extractions and thin layer chromatography (TLC) were used to extract and isolate the phytochemicals respectively. Phytochemicals were identified by spraying with target-specific revealing reagents. *In vivo* hair growth stimulating activity for each extract was tested on denuded dorsal skin of 5-week old BalB/c mice against the controls and the standard drug minoxidil. The parameters used to evaluate hair growth were hair growth completion time, hair length, hair weight, hair follicle length, and relative hair follicle area. The identified phytochemicals from the active ethanol extract were steroidal glycosides, triterpenoid glycosides, and flavonoid glycosides. Flavonoid glycosides treatment had the uppermost hair rejuvenation capacity as measured by the shortest

hair growth completion time (19 days) versus control (29 days) and longest hair length (11.04 mm and 11.86 mm for male and female mice respectively while the control group had 5.15 mm for male mice and 5.33 mm for female mice). Hair growth stimulation by flavonoid glycosides was also dependent on dose concentration. It can be concluded from this study that flavonoid glycosides extracted from the leaves of *Dicerocaryum senecioides* have remarkable hair rejuvenation capacity in BalB/c mice. The present results provides insights on the use of *Dicerocaryum senecioides* for hair rejuvenation in traditional practices and on the potential of the plant as a source of novel compounds that can be used as hair growth promoters.[9]

**Hajhashemi V. et al., 2019** Pumpkin (*Cucurbita pepo* L.) seed oil mainly consists of saturated and unsaturated fatty acids. Previously, it was reported that oral administration of pumpkin seed oil (PSO) improved hair growth in male pattern alopecia. This study aimed to evaluate hair promoting activity of topical PSO in an animal model. Male Swiss mice (25-30 g) were used. Dorsal hair of mice (2 x 2.5 cm) was gently removed. Groups were treated as follows: (A) Intact control (did not receive testosterone) (B) Testosterone solution only (5% w/v); (C) Testosterone (5%) + PSO (5%); (D) Testosterone (5%) + PSO (10%) (E) Testosterone (5%) +minoxidil (2%). Application of drugs (100 µl) was done for six days a week, for 3 weeks. Observational and microscopic examinations were performed and results of different groups were compared. Topical application of testosterone significantly ($p<0.01$) prevented hair growth (compared with intact control). PSO (10%) increased hair growth score after 3 weeks and histopathological findings confirmed these results. After 3 weeks of treatment, the percentage of follicles in anagen phase was 95±4.6 and 44.4±15 for intact control and testosterone-only treated group, respectively. These percentages for PSO (10%) and minoxidil were 75±5.3 and 91.3±4.4, respectively and they could significantly ($p<0.001$) reverse the effects of testosterone. In conclusion, as topical application of PSO showed hair growth promotion, it might be regarded as a promising alternative for treatment of male pattern alopecia. Also, considering its composition, free fatty acids and minor components like phytoestrogens and vitamin E may have contributed to this effect.[10]

**BEGUM S. ET AL 2015** Chrysanthemum zawadskii var. latilobum (Asteraceae) (CZ) and Polygonum multiflorum Thunb. (Polygonaceae) (PM) have been used traditionally to treat different systemic diseases and acclaimed for various biological activities including hair growth. This study investigates the hair restoration efficacy of selected medicinal plant extracts on nude mice. Nude mice genetically predisposed to pattern balding were used in this

study. Topical methanol extracts of CZ and PM (10 mg/mouse/d) with standardized vehicle formulation, only vehicle (propylene glycol:ethanol:dimethyl sulfoxide, 67:30:3% v/v) and Minoxidil (2%) were applied daily for 40 consecutive days. In our study, the maximum hair score ($2.5 \pm 0.29$) was obtained in the CZ-treated group. Histological observation revealed a significant increase ($p < 0.001$) in the number of hair follicles (HF) in CZ-treated mice ($58.66 \pm 3.72$) and Minoxidil-treated mice ($40 \pm 2.71$). Subsequently, immunohistochemical analysis also confirmed the follicular keratinocyte proliferation by detection of BrdU-labeling, S-phase cells in Minoxidil and CZ-treated mouse follicular bulb and outer root sheaths. Our study revealed the underlying mechanism of stimulating hair growth in athymic nude mice by repair the nu/nu follicular keratin differentiation defect. Thus, the topical application of CZ may represent a novel strategy for the management and therapy of certain forms of alopecia.[11]

**Biosvert W.A. et al., 2017.** *Geranium sibiricum* L. has been used as a medicinal plant to treat diarrhea, bacterial infection, and cancer in Bulgaria, Peru, and Korea. However, its hair growth-promoting effect was not investigated so far. This study examined the effects of *Geranium sibiricum* L. extract (GSE) on hair growth, using in vitro and in vivo models. Antioxidant, proliferation and migration assay of GSE was performed with human dermal papilla cells (hDPCs). Hair-growth promoting effect was measured in animal model. Relative expression of interleukin-1, vascular endothelial growth factor, hepatocyte growth factor, and transforming growth factor beta 1 was determined by real time RT-PCR. Expression of Ki-67 and stem cell factor were analyzed by immunohistochemistry. GSE treatment proliferated and migrated human dermal papilla cells (hDPCs) more than treatment of 10 μM minoxidil. GSE significantly stimulated the expression of Ki-67 protein and the mRNA levels of hepatocyte growth factor and vascular endothelial growth factor in hDPCs. Topical application of 1,000 ppm GSE for 3 weeks promoted more significant hair growth on shaved C57BL/6 mice than did 5% minoxidil. The histological morphology of hair follicles demonstrated an active anagen phase with the induction of stem cell factor. GSE treatment significantly reduced the number of mast cells and the expression of transforming growth factor beta 1 in mouse skin tissues. These results demonstrated that GSE promotes hair growth in vitro and in vivo by regulating growth factors and the cellular response.[12]

**Dehdari S. et al., 2018.** *Adiantum capillus-veneris* Linn (Maidenhair fern) is an herb belonging to the family Pteridaceae. It is named as "*Pare-siavashan*" in medical and pharmaceutical

textbooks of Iranian Traditional Medicine. The fronds of Maidenhair fern were mainly administrated by ancient physicians as single medicine or in combination with other plants in multi-herbal formulations for curing different diseases. Because of different chemical compositions, the herb fronds were also assessed for its numerous pharmacological effects. Therefore, the current study was done to review the traditional usage and modern pharmacological and toxicological effects of Maidenhair fern. Scientific databases and publications including Web of Science, PubMed, Scopus, Science direct, Cochrane Library, SID (for Persian papers) and medical and pharmaceutical textbooks of traditional medicine as well were searched for "*Adiantum capillus-veneris*", "*Maidenhair fern*" and "*Pare-siavashan*" without limitation up to 2016. Maidenhair fern exhibited to possess anti-diabetic, anticonvulsant, analgesic, hypocholesterolemic, goitrogenic, anti-thyroidal, antibacterial, antifungal, wound healing, antiobesity, anti hair loss, anti-asthmatic, anti-inflammatory, antidiarrheal and antispasmodic, antioxidant as well as diuretic, anti-urolithiatic and detoxifying effects in modern medicine. Ancient physicians declared some of the confirmed pharmacological effects. Maidenhair fern frond can be a good candidate for clinical purpose. Therefore, future researches on the other mentioned effects in traditional medicine are recommended.[13]

**Shatalebi M.A. et al., 2016.** Hair growth as a key consumer objective has important role in the hair care products researches. This study was aimed to investigate the effect of a hair wax containing propolis, a resinous mixture produced by honeybees in *Eruca sativa* seed oil base on hair growth. The hair wax was designed and formulated compared with marketed brand hair wax and evaluated for pharmaceutical parameters including pH, homogeneity, consistency, spread ability, *in vitro* drug release, and stability. After selection of the best formulation containing 10% ethanolic extract of propolis and 10% *E. sativa* seed oil, the hair growth potential was evaluated by application of 1 g hair wax daily on 4 $cm^2$ area of dorsal side of Wistar rats and compared with controls and standard medication (1 ml of 2% minoxidil). After 30 days treatment, the length and weight of hairs and percentage of hair follicles in different phases of growth in skin biopsies were assessed. The selected hair wax formulation was stable and easy to wash. The formulation significantly increased hair length on $10^{th}$, $20^{th}$, and $30^{th}$ day compared control group (5.8 ± 0.3 vs. 2.6 ± 0.4, 11.4 ± 0.6 vs. 5.8 ± 0.4, and 17.5 ± 0.5 vs. 12.7 ± 0.4 mm, respectively) and also the weight of newly grown hairs on $30^{th}$ day (0.056 ± 0.006 vs. 0.043 ± 0.005). It improved hair follicles percentages in anagen phase without any sensitivity reaction. The results of this study suggest that the formulated hair wax containing

of propolis and *E. sativa* seed oil could have significant effect on promoting hair growth.[14]

**Majeed M. et al., 2020.** Hair fall is a widespread problem among all genders, ages, and ethnicity with both physical and psychological effects.

This clinical study was designed to evaluate the efficacy and safety of a hair serum formulation containing amla extract, freeze-dried coconut water, and the micronutrient selenium along with sandalwood odorant and peanut shell extract in healthy male and female volunteers with hair fall. A total of 42 subjects were enrolled and completed the study and they used the test product daily for 90 days. TrichoScan® was used to evaluate the efficacy of the test product for improving hair growth rate, hair density, anagen hair, telogen hair, and the density of vellus and terminal hair. Hair thinning and hair fall reduction were compared to its basline by both dermatologists and subject self-assessment questionnaires. After 90 days of test product application, there was a significant improvement in hair growth rate (<0.0001), hair density (<0.0001), vellus hair density (<0.0001), and terminal hair density (<0.0001) in comparison to baseline. There was a significant reduction in hair fall with bulb (<0.0001) and without bulb (<0.0001), and hair thinning (<0.0001) compared to the baseline measurement. Adverse events were not recorded during the study. No skin intolerance was reported during the study, and the test product was considered dermatologically safe to use.[15]

**Dinh QQ. et al., 2007**. Fewer than 45% of women go through life with a full head of hair. Female pattern hair loss is the commonest cause of hair loss in women and prevalence increases with advancing age. Affected women may experience psychological distress and impaired social functioning. In most cases the diagnosis can be made clinically and the condition treated medically. While many women using oral antiandrogens and topical minoxidil will regrow some hair, early diagnosis and initiation of treatment is desirable as these treatments are more effective at arresting progression of hair loss than stimulating regrowth. Adjunctive nonpharmacological treatment modalities such as counseling, cosmetic camouflage and hair transplantation are important measures for some patients. The histology of female pattern hair loss is identical to that of male androgenetic alopecia. While the clinical pattern of the hair loss differs between men, the response to oral antiandrogens suggests that female pattern hair loss is an androgen dependant condition, at least in the majority of cases. Female pattern hair loss is a chronic progressive condition. All treatments need to be continued to maintain the effect. An initial therapeutic response often takes 12 or even 24 months. Given this delay, monitoring for treatment effect through clinical photography or standardized clinical severity scales is

helpful.[16]

**Miao Y. et al., 2013**. Ginger (*Zingiber officinale*) has been traditionally used to check hair loss and stimulate hair growth in East Asia. Several companies produce shampoo containing an extract of ginger claimed to have anti-hair loss and hair growth promotion properties. However, there is no scientific evidence to back up these claims. This study was undertaken to measure 6-gingerol, the main active component of ginger, on hair shaft elongation *in vitro* and hair growth *in vivo*, and to investigate its effect on human dermal papilla cells (DPCs) *in vivo* and *in vitro*. 6-Gingerol suppressed hair growth in hair follicles in culture and the proliferation of cultured DPCs. The growth inhibition of DPCs by 6-gingerol *in vitro* may reflect a decrease in the Bcl-2/Bax ratio. Similar results were obtained *in vivo*. The results of this study showed that 6-gingerol does not have the ability to promote hair growth, on the contrary, can suppress human hair growth via its inhibitory and pro-apoptotic effects on DPCs *in vitro*, and can cause prolongation of telogen phase *in vivo*. Thus, 6-gingerol rather than being a hair growth stimulating drug, it is a potential hair growth suppressive drug; i.e. for hair removal.[17]

**Anjum F. et al., 2013**. *Cuscuta reflexa* (*C. reflexa*) is a parasitic climber of medicinal importance. The present study was aimed to evaluate the nutraceutical potential of *C. reflexa* stems collected from different hosts and to evaluate the role of the herbal formulation in dandruff, hair fall control as well as hair growth promoter.

Hair formulations of *C. reflexa* collected from different host plants were prepared in the form of herbal oils (10% w/v). *C. reflexa* stems were extracted using mustard oil as base oil by using direct boiling technique. Prepared oil was studied as hair tonic. The experimental protocols used were anti-dandruff hair growth activity, as well as hair fall reduction. Herbal hair oils versus mustard oil were evaluated by applying oils on human volunteers with hair fall and dandruff problem whereas promotion of hair growth activity was conducted on rats. The formulated oils were also characterised for proximate analysis, physiochemical composition, as well as antimicrobial activity.

The test oils of *C. reflexa* collected from *Azadiracta indica* and *Zizyphus jujuba* were effective in the promotion of hair growth, dandruff control, as well as reduction in hair fall activity.[18]

**Glynis A. et al., 2012**. To assess the ability of an oral supplement to increase hair growth in women with thinning hair. Healthy women aged 21 to 75 years with Fitzpatrick I to IV photo

skin types with self-perceived thinning hair. Subjects were randomized to treatment with the study medication (N=10) or placebo (N=5) twice daily for 180 days. A 4cm$^2$ area of scalp was selected for hair counts performed after 90±7 and 180±7 days of treatment. The primary efficacy measure was the change in terminal and vellus hairs in each target area. The secondary measure was changes in a self-assessment questionnaire. The mean (SD) number of terminal vellus hairs among placebo-treated subjects at baseline was 256.0 (24.1), remaining at 245.0 (22.4) and 242.2 (26.9) after 90 and 180 days, respectively. The mean baseline number of terminal hairs in control-treated subjects was 271.0 (24.2) increasing to 571 (65.7) and 609.6 (66.6) after 90 and 180 days, respectively (for each, $p<0.001$ vs. placebo). The mean number of vellus hairs among placebo-and control-treated subjects did not significantly change. Significantly more control-treated subjects perceived improvements in overall hair volume, scalp coverage, and thickness of hair body after 90 days. Additional improvement after 180 days included hair shine, skin moisture retention, and skin smoothness. No adverse events were reported.[19]

**Beoy LA. et al., 2010**. Studies have shown an association between oxidative stress and alopecia. Patients with alopecia generally exhibit lower levels of antioxidants in their scalp area as well as a higher lipid peroxidation index. Tocotrienols belong to the vitamin E family and are known to be potent antioxidants. Hence, a study was conducted to investigate the effect of tocotrienol supplementation on hair growth in volunteers suffering from hair loss. Twenty one volunteers were randomly assigned to orally receive 100 mg of mixed tocotrienols daily while 17 volunteers were assigned to receive placebo capsule orally. The volunteers were monitored for the number of hairs in a pre-determined scalp area as well as the weight of 20 strands of 1 cm length hair clippings at 0 (before supplementation), 4 and 8 months. The number of hairs of the volunteers in the tocotrienol supplementation group increased significantly as compared to the placebo group, with the former recording a 34.5% increase at the end of the 8-month supplementation as compared to a 0.1% decrease for the latter. Nevertheless, the cumulative weight of 20 strands of hair clippings did not differ much from the baseline for both supplementation groups at the end of the study period. In conclusion, this trial demonstrated that supplementation with tocotrienol capsules increases hair number in volunteers suffering from hair loss as compared to the placebo group. This observed effect was most likely to be due to the antioxidant activity of tocotrienols that helped to reduce lipid peroxidation and oxidative stress in the scalp, which are reported to be associated with alopecia.[20]

**Yu JY, Gupta B. et al., 2017**. The proprietary DA-5512 formulation comprises six herbal extracts from traditional oriental plants historically associated with therapeutic and other applications related to hair. Here, we investigated the effects of DA-5512 on the proliferation of human dermal papilla cells (hDPCs) in vitro and on hair growth in C57BL/6 mice and conducted a clinical study to evaluate the efficacy and safety of DA-5512. DA-5512 significantly enhanced the viability of hDPCs in a dose-dependent manner ($p < 0.05$), and 100 ppm of DA-5512 and 1 $\mu$M minoxidil (MXD) significantly increased the number of Ki-67-positive cells, compared with the control group ($p < 0.05$). MXD (3%) and DA-5512 (1%, 5%) significantly stimulated hair growth and increased the number and length of hair follicles (HFs) versus the controls (each $p < 0.05$). The groups treated with DA-5512 exhibited hair growth comparable to that induced by MXD. In clinical study, we detected a statistically significant increase in the efficacy of DA-5512 after 16 weeks compared with the groups treated with placebo or 3% MXD ($p < 0.05$). In conclusion, DA-5512 might promote hair growth and enhance hair health and can therefore be considered an effective option for treating hair loss.[21]

**KD. et al., 2009.** The investigated the efficacy of methanol extract of Eclipta alba as hair growth promoter. Pigmented C57/BL6 mice, preselected for their telogen phase of hair growth were used. In these species, the truncal epidermis lacks melanin-producing melanocytes and melanin production is strictly coupled to anagen phase of hair growth. The extract was applied topically to assess telogen to anagen transition. Immunohistochemical investigation was performed to analyze antigen specificity. Animals in anagen phase of hair growth were positive for FGF-7 and Shh and negative for BMP4, whereas the animals in telogen phase were positive only for BMP4 antigen. The methanol extract of whole plant when tested for hair growth promoting potential, exhibited dose dependent activity in C57BL6 mice. The activity was assessed by studying the melanogenesis in resected skin, follicle count in the subcutis, skin thickness and surrogate markers in vehicle control and extract treated animals. These findings suggest that methanol extract of Eclipta alba may have potential as a hair growth promoter.[22]

**Cho YH. et al., 2014.** Pumpkin seed oil (PSO) has been shown to block the action of 5-alpha reductase and to have antiandrogenic effects on rats. This randomized, placebo-controlled, double-blind study was designed to investigate the efficacy and tolerability of PSO for treatment of hair growth in male patients with mild to moderate androgenetic alopecia (AGA). 76 male patients with AGA received 400 mg of PSO per day or a placebo for 24 weeks. Change

over time in scalp hair growth was evaluated by four outcomes: assessment of standardized clinical photographs by a blinded investigator; patient self-assessment scores; scalp hair thickness; and scalp hair counts. Reports of adverse events were collected throughout the study. After 24 weeks of treatment, self-rated improvement score and self-rated satisfaction scores in the PSO-treated group were higher than in the placebo group ($P$ = 0.013, 0.003). The PSO-treated group had more hair after treatment than at baseline, compared to the placebo group ($P < 0.001$). Mean hair count increases of 40% were observed in PSO-treated men at 24 weeks, whereas increases of 10% were observed in placebo-treated men ($P < 0.001$). Adverse effects were not different in the two groups.[23]

**Panahi Y. et al., 2015.** Rosmarinus officinalis L. is a medicinal plant with diverse activities including enhancement microcapillary perfusion. The present study aimed to investigate the clinical efficacy of rosemary oil in the treatment of androgenetic alopecia (AGA) and compare its effects with minoxidil 2%. Patients with AGA were randomly assigned to rosemary oil (n = 50) or minoxidil 2% (n = 50) for a period of 6 months. After a baseline visit, patients returned to the clinic for efficacy and safety evaluations every 3 months. A standardized professional microphotographic assessment of each volunteer was taken at the initial interview and after 3 and 6 months of the trial. No significant change was observed in the mean hair count at the 3-month endpoint, neither in the rosemary nor in the minoxidil group (P > .05). In contrast, both groups experienced a significant increase in hair count at the 6-month endpoint compared with the baseline and 3-month endpoint (P < .05). No significant difference was found between the study groups regarding hair count either at month 3 or month 6 (> .05). The frequencies of dry hair, greasy hair, and dandruff were not found to be significantly different from baseline at either month 3 or month 6 trial in the groups (P > .05). The frequency of scalp itching at the 3- and 6-month trial points was significantly higher compared with baseline in both groups (P <.05). Scalp itching, however, was more frequent in the minoxidil group at both assessed endpoints (P < .05). The findings of the present trial provided evidence with respect to the efficacy of rosemary oil in the treatment of AGA.[24]

**Lee H. et al., 2016.** *Rumex japonicus* Houtt. is traditionally used as a medicinal plant to treat patients suffering from skin disease in Korea. However, the beneficial effect of *Rumex japonicus* Houtt. on hair growth has not been thoroughly examined. Therefore, the present study aims to investigate the hair growth-promoting effect of *Rumex japonicus* (RJ) Houtt. root extract using human dermal papilla cells (DPCs), HaCaT cells, and C57BL/6 mice model. RJ

induced antiapoptotic and proliferative effects on DPCs and HaCaT cells by increasing Bcl-2/Bax ratio and activating cellular proliferation-related proteins, ERK and Akt. RJ also increased *β*-catenin via the inhibition of GSK-3*β*. In C57BL/6 mice model, RJ promoted the anagen induction and maintained its period. Immunohistochemistry analysis demonstrated that RJ upregulated Ki-67 and *β*-catenin expressions, suggesting that the hair growth effect of RJ may be mediated through the reinforcement of hair cell proliferation. These results provided important insights for the possible mechanism of action of RJ and its potential as therapeutic agent to promote hair growth.[25]

**Hughes K. et al., 2020.** Hair loss is becoming increasingly prevalent as dietary and living habits change. The search for natural products to limit hair loss has led to tapping into traditional cosmetic knowledge. We studied three plants of the Polynesian cosmetopoeia, *Bidens pilosa*, *Calophyllum inophyllum* and *Fagraea berteroana*, to determine their ability to promote hair growth. Their chemical content was characterized by liquid chromatography coupled to mass spectrometry (LC-MS). Their proliferative activity on dermal papilla cells (DPCs) was assessed via MTT assay and molecular targets were evaluated by RT-qPCR analysis of seven factors involved in the modulation of the hair cycle, *CCND1*, *LEF1*, *DKK1*, *WNT5A PPARD*, *TGFB1*, *PPARD* and *RSPO2*. Our results show that our extracts significantly increased proliferation of dermal papilla cells. Furthermore, LC-MS/MS analysis revealed a diversity of molecules, flavonoids, iridoids and organic acids, some known for hair-inducing properties. Finally, specific extracts and fractions of all three plants either upregulated *CCND1*, *LEF1* and *PPARD* involved in stimulating hair follicle proliferation and/or lowered the gene expression levels of hair growth inhibiting factors, *DKK1* and *TGFB1*. Our findings suggest that extracts from *B. pilosa*, *C. inophyllum* and *F. berteroana* are interesting candidates to stimulate hair growth.[26]

**Choi S.H. et al., 2015.** BP201, porcine lung tissue-derived phospholipids, consists of phosphatidylcholine as a major phospholipid species. BP201 promoted hair growth after application onto the shaved backs of BALB/c and C3H mice. Its effect was enhanced when applied together with minoxidil (MNX) in C3H mice. When the tissue specimens prepared from the shaved skins of BP201-treated and control mice were microscopically examined, the total numbers of hair follicles in both anagen and telogen phases of BP201-treated mice were significantly higher than those of control mice. The numbers of hair follicles in the anagen phase of BP201-treated mice were also higher than those of control mice. In combination with

MNX, BP201 further increased the total number of hair follicles, but did not alter the percentage of hair follicles in the anagenic phase. BP201 also increased the proliferation of human hair follicle dermal papilla cells. Collectively, BP201 possesses hair growth promoting potential, which would suggest its use singly or in combination for hair growth products.[27]

**Li Y. and Han M. et al., 2015.** *Polygonum multiflorum* Radix (PMR) has long history in hair growth promotion and hair coloring in clinical applications. However, several crucial problems in its clinic usage and mechanisms are still unsolved or lack scientific evidences. In this research, C57BL/6J mice were used to investigate hair growth promotion activity and possible mechanism of PMR and *Polygonum multiflorum* Radix Preparata (PMRP). Hair growth promotion activities were investigated by hair length, hair covered skin ratio, the number of follicles, and hair color. Regulation effects of several cytokines involved in the hair growth procedure were tested, such as fibroblast growth factor (FGF-7), Sonic Hedgehog (SHH), *β*-catenin, insulin-like growth factor-1 (IGF-1), and hepatocyte growth factor (HGF). Oral PMR groups had higher hair covered skin ratio (100 ± 0.00%) than oral PMRP groups (48%~88%). However, topical usage of PMRP had about 90% hair covered skin ratio. Both oral administration of PMR and topically given PMRP showed hair growth promotion activities. PMR was considered to be more suitable for oral administration, while PMRP showed greater effects in external use. The hair growth promotion effect of oral PMR was most probably mediated by the expression of FGF-7, while topical PMRP promoted hair growth by the stimulation of SHH expression.[28]

**Zhang N. et al., 2013.** *Thuja orientalis* has been traditionally used to treat patients who suffer from baldness and hair loss in East Asia. The present study sought to investigate the hair growth-promoting activity of *T. orientalis* hot water extract and the underlying mechanism of action. After *T. orientalis* extract was topically applied to the shaved dorsal skin of telogenic C57BL/6 N mice, the histomorphometric analysis was employed to study induction of the hair follicle cycle. To determine the effect of *T. orientalis* extract on the telogen to anagen transition, the protein expression levels of β-catenin and Sonic hedgehog (Shh) in hair follicles were determined by immunohistochemistry. We observed that *T. orientalis* extract promoted hair growth by inducing the anagen phase in telogenic C57BL/6 N mice. Specifically, the histomorphometric analysis data indicates that topical application of *T. orientalis* extract induced an earlier anagen phase and prolonged the mature anagen phase, in contrast to either the control or 1% minoxidil-treated group. We also

observed increases in both the number and size of hair follicles of the *T. orientalis* extract-treated group. Moreover, the immunohistochemical analysis reveals earlier induction of β-catenin and Shh proteins in hair follicles of the *T. orientalis* extract-treated group, compared to the control or 1% minoxidil- treated group. These results suggest that *T. orientalis* extract promotes hair growth by inducing the anagen phase in resting hair follicles and might therefore be a potential hair growth- promoting agent.[29]

**Boisvert WA. et al., 2017.** *Geranium sibiricum* L. has been used as a medicinal plant to treat diarrhea, bacterial infection, and cancer in Bulgaria, Peru, and Korea. However, its hair growth-promoting effect was not investigated so far. This study examined the effects of *Geranium sibiricum* L. extract (GSE) on hair growth, using in vitro and in vivo models. Antioxidant, proliferation and migration assay of GSE was performed with human dermal papilla cells (hDPCs). Hair-growth promoting effect was measured in animal model. Relative expression of interleukin-1, vascular endothelial growth factor, hepatocyte growth factor, and transforming growth factor beta 1 was determined by real time RT-PCR. Expression of Ki-67 and stem cell factor were analyzed by immunohistochemistry. GSE treatment proliferated and migrated human dermal papilla cells (hDPCs) more than treatment of 10 μM minoxidil. GSE significantly stimulated the expression of Ki-67 protein and the mRNA levels of hepatocyte growth factor and vascular endothelial growth factor in hDPCs. Topical application of 1,000 ppm GSE for 3 weeks promoted more significant hair growth on shaved C57BL/6 mice than did 5% minoxidil. The histological morphology of hair follicles demonstrated an active anagen phase with the induction of stem cell factor. GSE treatment significantly reduced the number of mast cells and the expression of transforming growth factor beta 1 in mouse skin tissues. These results demonstrated that GSE promotes hair growth in vitro and in vivo by regulating growth factors and the cellular response.[30]

**Akanda MR. et al., 2017.** Keratin biomaterial has been used in regenerative medicine owing to its in-vivo and in-vitro biocompatibility. The present study was aimed to investigate the hair growth promoting activity of keratin extract and its mechanism of action. Keratin extract was topically applied on the synchronized depilated dorsal skin of telogenic C57BL/6 mice and promoted hair growth by inducing the anagen phase. The histomorphometric observation indicated significantly increases the number, shaft of hair follicles and deep subcutis area in the keratin extract treated group in contrast to the control group, which was considered an indication of anagen phase induction. Subsequently, the quantitative real-time polymerase

chain reaction analysis revealed that fibroblast growth factor-10, vascular endothelial growth factor, insulin-like growth factor-1, β-catenin, and Shh were expressed earlier in the keratin extract-treated group than in the control group. Besides, keratin extract has been observed to be biocompatible when analyzed with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and 4',6-diamidino-2-phenylindole staining using immortalized human keratinocyte cells, showing more than 90% cell viability. Our study demonstrated that keratin extract stimulating hair follicle growth by inducing the growth phase; anagen in telogenic C57BL/6 mice and thus the topical application of keratin extract may represent a promising biomaterial for the management and applications of hair follicle disorder.[31]

## CONCLUSION

After the study many reviews article and research paper we found that there are many plants and synthetic Anti-hair fall drugs. Which have a medicinal value in the anti-hair fall activity in their different pharmaceutical preparation.

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