International Journal of Pharmacognosy and Pharmaceutical Research 2024; 6(2): 109-116

International Journal of Pharmacognosy and Pharmaceutical Research

ISSN Print: 2664-7168
ISSN Online: 2664-7176
Impact Factor: RJIF 8
IJPPR 2024; 6(2): 109-116
www.pharmacognosyjournals.com
Received: 30-09-2024
Accepted: 06-10-2024

Pankaj Maskare
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Shrutika Patil
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Prerana Shinde
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Ameya Joshi
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Harshada Potale
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Corresponding Author:
Pankaj Maskare
Lokmanya Tilak Institute of Pharmacy, Kharghar, Navi Mumbai, Maharashtra, India

Botanical booster: Effective plant molecules for enhancing hair growth

Pankaj Maskare, Shrutika Patil, Prerana Shinde, Ameya Joshi and Harshada Potale

DOI: https://doi.org/10.33545/26647168.2024.v6.i2b.85

Abstract
Plant-derived molecules have emerged as promising agents for promoting healthy hair growth due to their natural bioactive properties and minimal side effects. They have the potential to encourage hair growth through various mechanisms, such as improving nutrient supply and blood flow to the scalp and stimulating hair follicles. Epigallocatechin-3-Gallate, Quercitrin, Sinapic acid, β-Sitosterol, Caffeine, and Ginsenosides are few key molecules known for their potential to improve hair growth and quality.
With an increasing number of individuals seeking natural hair care options, plant-based ingredients are playing a crucial role in the development of products that support healthy hair growth.
This review covers current research and provides a comprehensive overview of how botanical boosters can be used to develop natural hair care products that promote healthy hair growth. As studies on these active molecules progress, they are expected to play a crucial role in the development of future revolutionary hair care products.

Keywords: Plant-derived molecules, Hair growth, Botanical boosters, Bioactive compounds, Natural hair care.

Introduction

Hairs help in the physical defence, insulation, sebum distribution, sensory perception, and other functions of the skin. It has a significant influence on social relationships, beauty, quality of life, and self-esteem in human civilization [1]. The two primary cell types that make up the hair follicle (HF), often known as a "mini-organ" and a distinguishing feature of mammalian skin, are epithelial cells and dermal papilla cells (DPCs) [2]. Whereas the epithelial cells come from the surface epithelium, the DPCs come from the mesenchyme. Throughout adulthood, the HF cycles constantly, replicating the growth of an embryo as its constituent parts regenerate with every hair cycle [3]. Hair follicle (HF) development occurs in three stages: induction, organogenesis, and cytodifferentiation. The hair growth cycle has four phases: anagen (growth), catagen (regression), telogen (resting), and exogen (shedding). Hair grows actively during anagen, lasting two to six years, with blood nourishing the follicles. In catagen, lasting one to two weeks, the follicle collapses, cutting off its blood supply. Telogen is a five- to six-week resting phase with detached papillary cells, while exogen involves hair shedding, which can occur during anagen or telogen. [4]. The hair follicles of mammalian skin go through repeated cycles of intricacy and regeneration throughout the perinatal period [5].

Scarring alopecia, non-scarring alopecia, and structural hair diseases are the three categories of hair loss [7]. Scarring alopecia results in irreversible hair follicle loss, while non-scarring alopecia leads to temporary hair follicle suppression that can be treated for hair regrowth. Structural hair diseases arise from fragile hair shafts. Examples of non-scarring alopecia include androgenetic alopecia and trichotillomania, which cause focal, dispersed, and patterned hair loss [8]. Hair loss was treated with a variety of medications and methods. The first medication for treating hair loss that the FDA approved was minoxidil [9][10]. Sulfotransferase, which is found on the scalp, transforms minoxidil into minoxidil sulphate, which inhibits hair loss and encourages the growth of hair follicular cells [9]. Topical minoxidil side effects include hypertrichosis, irritating and allergic contact dermatitis, and sporadic skin rashes.

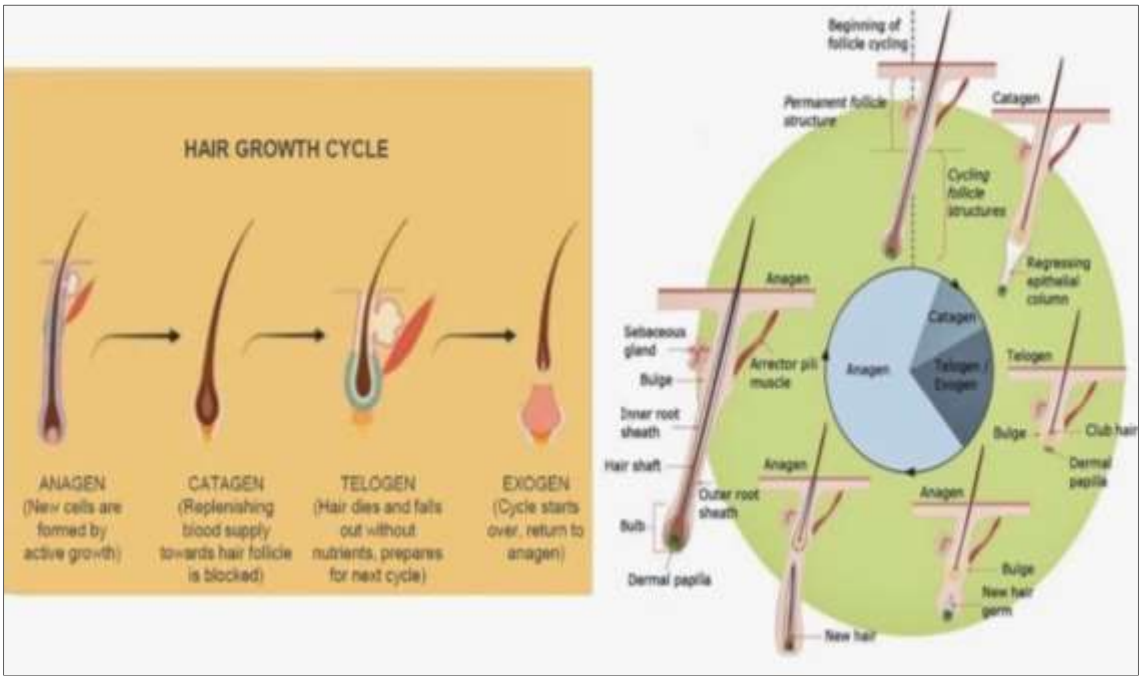

Fig 1: Stages of hair growth cycle [6]

In addition to cardiovascular side effects such as ischemic heart disease, pericardial effusion, and pulmonary hypertension, oral minoxidil may result in fluid and sodium retention [11]. To treat male androgenetic alopecia, finasteride, and dutasteride, which are inhibitors of 5α-reductase enzyme, which transforms testosterone into dihydrotestosterone (DHT) [12]. Finasteride selectively inhibits the type II 5α-reductase enzyme, whereas dutasteride inhibits both types I and II isoenzymes [13]. However, finasteride has been associated with sexual dysfunction, including erectile dysfunction, ejaculation and libido disorders [14]. While many medications promote hair growth and prevent loss, natural plant-derived molecules provide a more appealing alternative for those preferring topical or non-chemical treatments. Complementary and alternative medicine is increasingly popular for hair loss, and natural products can act as supportive agents in a multimodal treatment approach. [15]. Many plant-based molecules including Epigallocatechin gallate (EGCG), Caffeine, Capsaicin, Ginsenosides, Procyanidin B-2, Quercitrin, Azadirachtin, Curcumin, β-Sitosterol etc. were reported to have hair growth-stimulating properties.

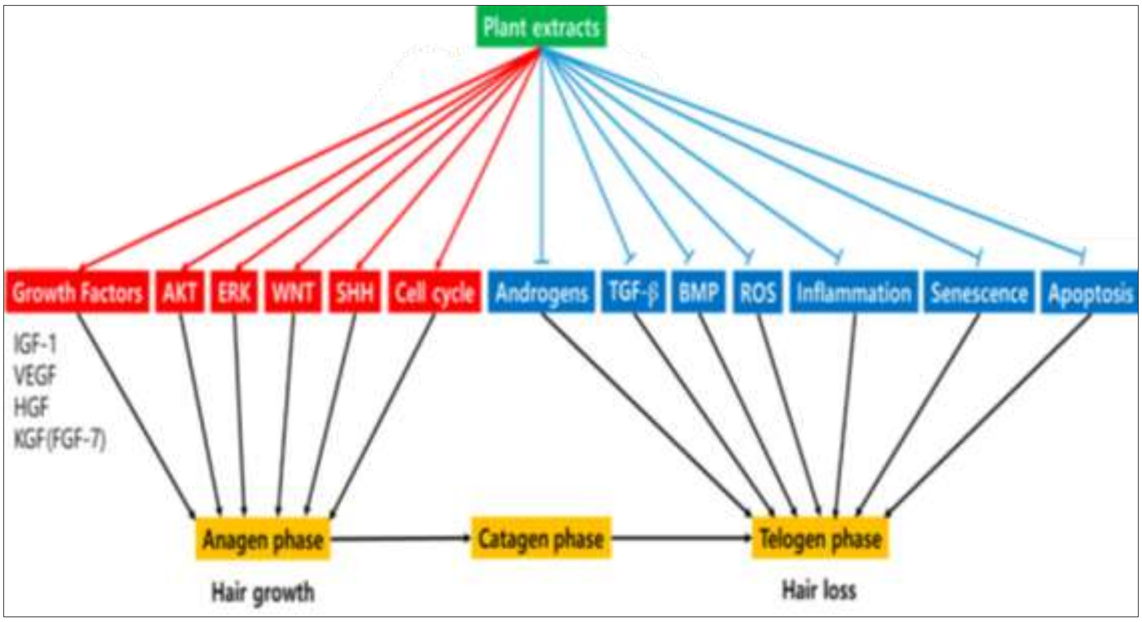

Fig 2: Sharp red arrows indicate upregulation, stimulation, or promotion, and blunted blue arrows indicate downregulation, inhibition, or suppression by plant molecules [16]

Common mechanism for hair growth

- **Insulin-like growth factor-1 (IGF-1):** Dermal papillae produce IGF-1, which regulates cellular proliferation and migration during hair follicle formation. IGF-1 stimulates hair root cells, accelerates anagen growth, and delays the catagen and telogen phases of the hair development cycle [17, 18].
- **Vascular endothelial growth factor (VEGF):** Growth factors like VEGF promote angiogenesis and vasculogenesis, which in turn increases the width of the

hair follicle's base and promotes hair growth by enabling the delivery of nutrients to the hair follicle [19][20]. It has been shown that human alopecia follicles had a considerable drop in VEGF expression when compared to normal follicles [21].

- **Fibroblast growth factor (FGF):** The growth of human hair follicles, as well as epidermal differentiation and proliferation, depend on the FGF family. The receptors for basic FGF (bFGF or FGF-2) and acidic FGF (aFGF or FGF-1) and FGF-5 have all been found inside or close to hair follicles [22][23].
- **Wnt (Wingless-Related Integration Site)/β-catenin pathways:** The Wnt/β-catenin pathways are crucial for the induction of anagen in hair growth. Hair follicle formation and growth depend on β-catenin, the transducer of Wnt signalling.[24] When Wnts bind to Frizzled receptors and lipoprotein receptor-related protein, GSK-3β activity is inhibited, leading to increased levels of free β-catenin [25]. β-catenin, activated by Wnt signaling, promotes target gene expression with T-cell factor/lymphoid enhancer factor-1 (TCF/LEF-1). Glycogen synthase kinase-3 beta (GSK-3β) controls its degradation, limiting hair follicle progenitor cell proliferation and initiating the catagen phase [26].
- **5α-reductase activity and dihydrotestosterone (DHT):** Dihydrotestosterone (DHT), a strong androgen that can cause hair follicle miniaturization and accelerated hair loss in people prone to androgenetic alopecia, is produced when testosterone is converted by 5-alpha reductase. By binding to receptors in hair follicles, DHT reduces hair density and shortens the growth phase [27].
- **Transforming growth factor beta (TGF-β):** Androgen-stimulating TGF-β1 induces the catagen phase, reducing hair growth. DHT increases TGF-β2 production in dermal papilla cells (DPC), triggering apoptosis in epithelial cells and shortening the hair cycle. TGF-β antagonists can extend hair follicles by preventing catagen-like changes. Some herbs, including *Eclipta alba*, have been shown to inhibit TGF-β1, significantly reducing its expression during the early anagen and anagen-catagen transition [28].

Bioactive molecules promoting hair growth activity
Epigallocatechin-3-Gallate
Source
With almost 50% of the total polyphenol content in green tea, epigallocatechin-3-gallate (EGCG) is the most prevalent polyphenol. It is also found in nuts, cocoa products and various fruits like apples, pears, peaches etc.

MOA
Epigallocatechin-3-Gallate a significant bioactive component of green tea, has anti-inflammatory and anti-oxidant properties. It helps in Hair follicle formation and growth, as well as the change from anagen to telogen, depend on the sonic hedgehog (Shh) and protein kinase B (AKT) signalling pathways. Hair growth can be enhanced and hair follicle cell proliferation can be encouraged by activating the Shh or AKT signals [29]. The catechins, (-) epicatechin-3-gallate and (-) epigallocatechin-3-gallate found in tea, also have an effect on Type I 5-alpha-reductase activity, which is what converts testosterone to DHT [30].

Formula: $C_{22}H_{18}O_{11}$

IUPAC Name
[(2R, 3R)-5, 7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-3,4-dihydro-2H-chromen-3-yl] 3,4,5-trihydroxybenzoate

Extraction
Epigallocatechin gallate (EGCG) is extracted from *Camellia sinensis* using subcritical water extraction, where green tea leaves are heated with water at 120°C for about 6 minutes, using a solvent-to-sample ratio of 1:40 g/mL for efficient extraction. [31].

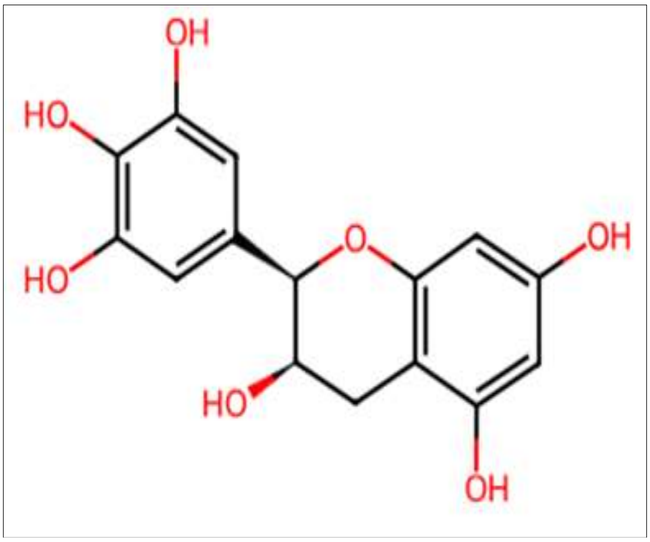

Fig 3: Structure of EGCG

Caffeine
Sources: Caffeine is a purine alkaloid, derived from several sources including coffee beans, tea leaves, cocoa, and kola nuts.

MOA
The major cause of androgenic alopecia is 5-reductase an enzyme, which changes testosterone into the more potent dihydrotestosterone (DHT) [32]. Coffee causes the 5-reductase enzyme to become less active, allowing the hair to go through a new growth phase [33]. Caffeine activates protein kinase A, reduces leukotriene formation, and decreases micro-inflammation, which enhances cellular proliferation by stabilizing cAMP levels. Its antioxidant properties also promote hair growth and maintain a healthy scalp by neutralizing harmful radicals [34].

Formula: $C_8H_{10}N_4O_2$

IUPAC Name: 1,3,7-trimethyl purine-2,6-dione

Extraction
Caffeine is extracted from tea and coffee using solid-liquid extraction with sodium carbonate, followed by vacuum filtration. The filtrate undergoes liquid-liquid extraction with dichloromethane, acetone, or ethanol. Finally, the organic layer is evaporated to compare caffeine yields, while also examining the effect of using sodium hydroxide as the base [35].

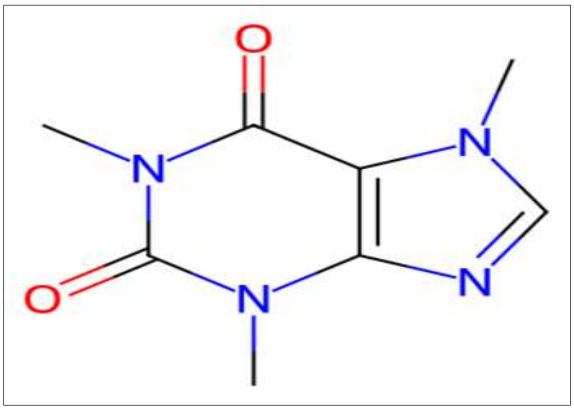

Fig 4: Structure of Caffeine

Quercitrin

Sources: This bioactive molecule can be found in Apples, berries, Brassica vegetables, capers, grapes, onions, shallots, tea and tomatoes. Quercetin is also present in therapeutic botanicals, including *Ginkgo biloba*, *Hypericum perforatum*, *Rosa damascene* and *Sambucus canadensis*.

MOA: Quercitrin activates the MAPK/CREB signaling pathway to enhance hair growth by increasing growth factors like basic fibroblast growth factor (bFGF), keratinocyte growth factor (KGF), platelet-derived growth factor AA (PDGF-AA), and vascular endothelial growth factor (VEGF) in human dermal papilla cells (hDPCs). It boosts cellular energy, mitochondrial membrane potential, and Bcl2 expression, while extending the anagen phase. Quercitrin also promotes phosphorylation of Akt, extracellular signal-regulated kinase (Erk), and CREB, with its effects blocked by MAPK inhibitors. [36].

Formula: $C_{15}H_{10}O_7$

IUPAC Name: 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyloxan-2-yl] oxychromen-4-one

Extraction: Supercritical fluid extraction (SFE) achieves higher extraction yields of flavonoids, particularly quercetin. Techniques include producing submicron quercetin particles with different encapsulation efficiencies and modified SFE using ethanol for quercetin extraction from *Rosa damascena* (Damask rose). Optimal conditions for this method resulted in a 32.0% extraction of quercetin at 46.3 °C, 25.5 MPa, and a 2-hour extraction time. [37].

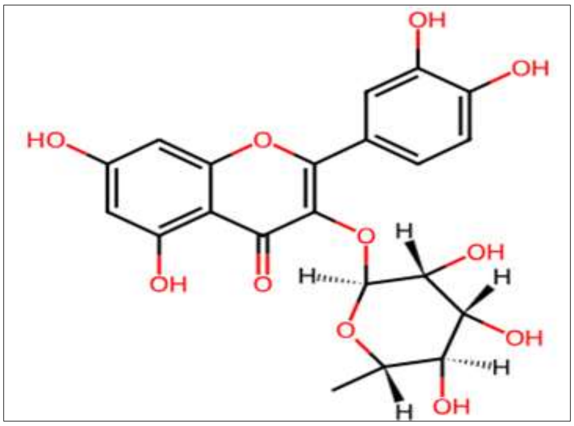

Fig 5: Structure of Quercitrin

Sinapic acid

Source: It is found in various Brassica vegetables like broccoli, and cabbage also found in seed pulses and fruits like cranberries and blackberries.

MOA: Sinapic acid (SA) promotes hair growth in human hair follicle dermal papilla cells (hHFDPC) by inducing cell proliferation and activating Akt signaling. Treatment with SA increases levels of growth factors like insulin-like growth factor 1 and vascular endothelial growth factor. It also elevates phospho-GSK-3β and β-catenin accumulation, facilitating cell cycle progression and enhancing hHFDPC growth [38][39].

Formula: $C_{11}H_{12}O_5$

IUPAC Name: (*E*)-3-(4-hydroxy-3,5-dimethoxy phenyl) prop-2-enoic acid

Extraction: The extraction of sinapic acid from mustard seed meal is pH-dependent: sinapine is more prevalent at acidic pH, while sinapic acid dominates at basic pH. Ethanol enhances the extraction, particularly at pH 12, producing ethyl sinapate and sinapic acid. Optimizing pH is crucial for maximizing antioxidant activity while considering environmental and economic impacts. [40].

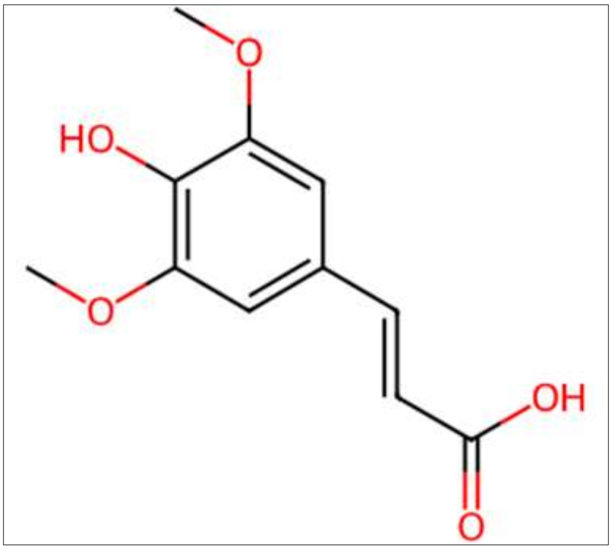

Fig 6: Structure of Sinipic acid

α-Linolenic acid

Source: Rich sources of α-Linolenic acid include flaxseeds and flaxseed oil, which contain the highest concentration of this fatty acid. Other notable sources are Chia seeds, Walnuts, Hemp seeds and Canola oil.

MOA

It acts by reducing inflammation and inhibiting 5-alpha reductase (thereby lowering dihydrotestosterone levels), and improving blood circulation to hair follicles. They enhance cell membrane integrity, promote cell regeneration, and improve hair resilience while offering antioxidant protection against oxidative stress [41].

Formula: $C_{18}H_{30}O_2$

IUPAC Name: (9*Z*,12*Z*,15*Z*)-octadeca-9,12,15-trienoic acid

Extraction: α-Linolenic acid and other oils can be extracted from plant materials using Supercritical Fluid Extraction (SFE), which utilizes supercritical carbon dioxide (CO_2). In this process, CO_2 is forced through the plant matrix at high temperatures and pressures to dissolve the oil constituents. After extraction, the oil is collected, and the CO_2 is depressurized to return to gas. This method is ideal for sensitive compounds like ALA as it preserves oil purity, avoids hazardous solvents, and operates at low temperatures. [42].

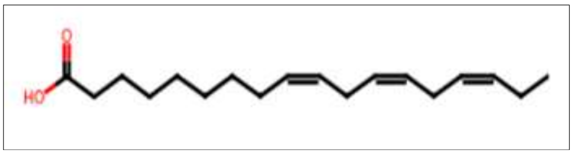

Fig 7: Structure of α-Linolenic Acid

β-Sitosterol:

Source: Saw Palmetto (*Serenoa repens*) and Pygeum (*Prunus africanum*) are well-known natural sources of β-Sitosterol, a plant sterol that has gained recognition for its health benefits, particularly for prostate health and cholesterol management.

MOA: β-Sitosterol exhibits effect by inhibiting the enzyme 5α-reductase, thus preventing the conversion of testosterone into dihydrotestosterone (DHT), a key factor in the development of androgenic alopecia [43].

Formula: $C_{29}H_{50}O$

IUPAC Name

(3*S*, 8*S*, 9*S*, 10*R*, 13*R*, 14*S*, 17*R*)-17-[(2*R*, 5*R*)-5-ethyl-6-methylheptan-2-yl]-10, 13-dimethyl-2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3-ol

Extraction: The dried roots of *Hemidesmus indicus* were powdered and extracted with 70% methanol by continuous stirring. The filtrate was vacuum-evaporated to dryness. β-sitosterol was isolated from the root extract using column chromatography with a mobile phase of chloroform, ethyl acetate, and methanol by gradient elution. The isolated β-sitosterol was further characterized using HPTLC and TLC [44].

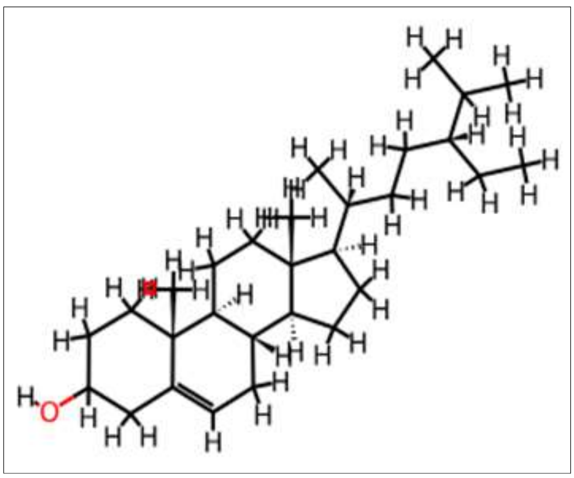

Fig 8: Structure of β-Sitosterol

Procyanidin B-2

Sources: Procyanidin B-2 is a type of proanthocyanidin commonly found in various plant sources. Notable sources include apples, particularly in the skin, as well as grapes, especially in the seeds and skins. Other fruits such as cranberries, blueberries, and blackberries are also rich in procyanidin B-2.

MOA: Procyanidin B-2 method of action is based on its strong growth-promoting effect on hair epithelial cells. Furthermore, its anti-oxidative properties may add to its effects. It reduces inflammation, which is commonly related with male pattern baldness. This suppression helps restore scalp health, perhaps resulting in hair growth [45].

Formula: $C_{30}H_{26}O_{12}$

IUPAC Name: (2*R*, 3*R*)-2-(3, 4-dihydroxyphenyl)-8-[(2*R*, 3*R*, 4*R*)-2-(3, 4-dihydroxyphenyl)-3, 5, 7-trihydroxy-3,4-dihydro-2*H*-chromen-4-yl]-3, 4-dihydro-2*H*-chromene-3, 5, 7-triol

Extraction: The extraction of procyanidin B-2 from grape seeds uses infrared-assisted extraction (IRAE). The ideal parameters for this method are a 50% methanol solution as the extraction solvent, a solid-to-liquid ratio of 1:150 g/mL, and a 30-minute illumination time under a 275 W infrared light. The extracted solution is examined using high-performance liquid chromatography (HPLC) [46].

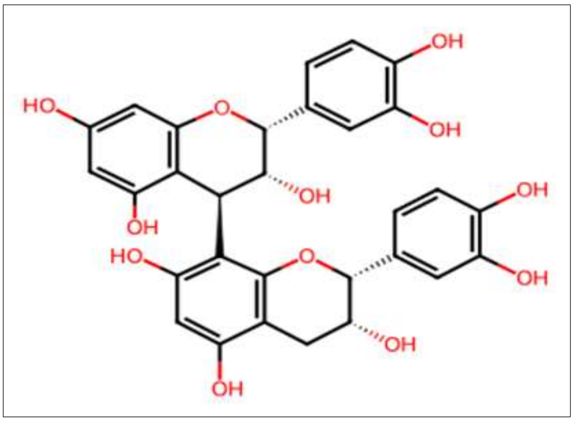

Fig 9: Structure of Procynadine B-2

Ginsenosides

Sources: Ginsenosides is a bioactive molecule primarily found in ginseng, particularly the roots of *Panax ginseng* (Asian ginseng) and *Panax quinquefolius* (American ginseng)

MOA: Ginsenosides from *Panax ginseng* exhibit several mechanisms that promote hair growth. They inhibit the 5α-reductase enzyme, reducing the conversion of testosterone to dihydrotestosterone (DHT) [47], which is linked to androgenic alopecia. Ginsenoside enhances hair growth by modulating Wnt/Dickkopf Homologue 1 (DKK1) signaling, promoting the expression of β-catenin to initiate the anagen phase of hair follicles [48]. Additionally, ginsenosides activate Sonic Hedgehog (Shh) signaling pathways, facilitating the transition from the resting to the growth phase of hair follicles [49]. They also have anti-apoptotic effects, enhancing dermal papilla cell proliferation via ERK and AKT/PKB signaling pathways [50].

Formula: $C_{30}H_{52}O_2$

IUPAC Name: (3*S*,5*R*,8*R*,9*R*,10*R*,14*R*,17*S*)-17-(2-hydroxy-6-methylhept-5-en-2-yl)-4,4,8,10,14-pentamethyl-2,3,5,6,7,9,11,12,13,15,16,17-dodecahydro-1*H*-cyclopenta[a]phenanthren-3-ol

Extraction: Ultrasound-assisted extraction (UAE) efficiently extracts ginsenosides from *Panax ginseng* and *Panax quinquefolius* by using ultrasonic vibrations to break plant cell walls. This low-temperature method prevents compound degradation, yielding higher amounts in less time than traditional processes. [51].

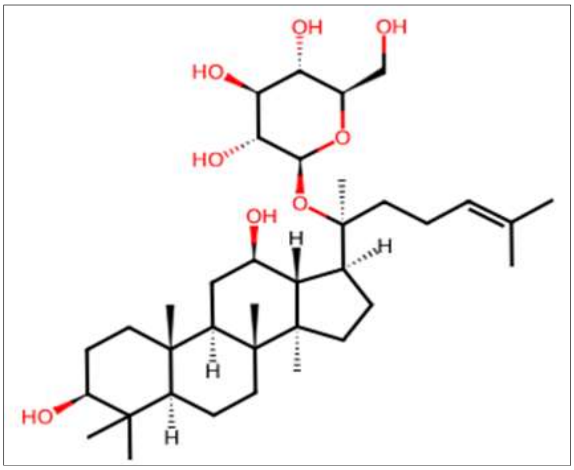

Fig 10: Structure of Ginsenoside

Rosmarinic acid
Sources: Rosmarinic acid is found in *Rosmarinus officinalis* (rosemary), *Ocimum basilicum* (basil), *Mentha* spp. (mint), and *Thymus vulgaris* (thyme). Other notable sources are *Salvia* spp. (sage) and *Melissa officinalis* (lemon balm).

MOA: Rosmarinic acid when injected into dermal papilla cells, inhibits the enzyme 5α-reductase. This enzyme converts testosterone into dihydrotestosterone (DHT), a stronger androgen that plays a crucial role in diseases like androgenic alopecia (hair loss). Rosmarinic acid inhibits this conversion, reducing DHT binding to androgen receptors and avoiding hair follicle shrinking while increasing hair growth [52].

Formula: $C_{18}H_{16}O_8$

IUPAC Name: (2*R*)-3-(3,4-dihydroxyphenyl)-2-[(*E*)-3-(3,4-dihydroxyphenyl) prop-2-enoyl] oxypropanoic acid

Extraction: Rosmarinic acid is extracted from *Rosmarinus officinalis* using ultrasound-assisted extraction. The plant is soaked in 1.0 M Br for two hours, then subjected to ultrasound at 250 W for 30 minutes, enhancing the extraction by breaking down plant cells [53].

Capsaicin
Source: Capsaicin is predominantly found in the fruits of the *Capsicum* genus, particularly in chili peppers. Notable sources include *Capsicum annuum* (bell peppers and red chili peppers), *Capsicum chinese* (habanero peppers), and *Capsicum frutescens* (bird's eye chili).

MOA
Capsaicin activates vanilloid receptor-1, increasing calcitonin gene-related peptide (CGRP) release, which boosts insulin-like growth factor-I (IGF-I) production essential for hair growth. Combining capsaicin with isoflavone may enhance IGF-I levels in hair follicles, promoting hair growth. [17].

Formula: $C_{18}H_{27}NO_3$

IUPAC Name: (*E*)-*N*-[(4-hydroxy-3-methoxyphenyl) methyl]-8-methylnon-6-enamide

Extraction
The capsaicinoids were extracted using pressurized liquid extraction (PLE). The sample, combined with sea sand, was put in a stainless-steel cell containing a cellulose filter. The chamber was filled with solvent (Methanol, ethanol, or water), pressured at 100 atm, and heated to between 50-200^o C. The extracts were then examined using HPLC with fluorescence detection and mass spectrometry [54].

Table 1: Molecule overview: Formulation types and additional uses

Molecule name	Formulation Type	Other uses
Epigallocatechin-3-Gallate	Hair serums, topical treatments	Antitumor, antiviral, antifibrosis, antiobesity
Caffeine	Scalp shampoos, topical solutions	Increased metabolism, improved physical performance, diuretic effect, enhanced cognitive function
Quercitrin	Hair growth lotions, serums	Anti-inflammatory, antimicrobial, anti-cancer
Sinapic acid	Scalp serums, topical treatments	Anti-inflammatory, antimicrobial properties, cognitive benefits
α-Linolenic acid	Hair oils, conditioning treatments	Supports cognitive function, improves skin hydration, precursor to other fatty acids
β-Sitosterol	Scalp treatments, creams	Anti-inflammatory, support wound healing
Procyanidin B-2	Hair restoration serums	Antioxidant, blood sugar regulation, neuroprotective effects, weight management.
Ginsenosides	Anti-hair loss serums	Regulation of blood sugar levels, neuroprotective effects, stress reduction and adaptogenic Effects
Rosmarinic acid	Scalp lotions, topical treatments	Weight management, gastroprotective effects, anticancer and neuroprotective effects
Capsaicin	Hair growth creams, topical applications	Pain Relief, pest repellent, anti-inflammatory effect

Conclusion

Bioactive compounds from plants, such as epigallocatechin gallate, caffeine, and curcumin, are gaining recognition for their potential to promote hair growth and overall wellness. These natural agents stimulate hair follicles, enhance blood flow to the scalp, regulate growth factors, and inhibit harmful enzymes like 5-alpha reductase, linked to hair thinning. Their organic nature offers significant advantages over synthetic treatments like finasteride and minoxidil, often associated with side effects. As consumer interest in holistic solutions grows, these compounds are poised to transform the hair care market, providing safer and more effective alternatives for addressing hair loss and improving hair quality.

References

1. Ji S, Zhu Z, Sun X, Fu X. Functional hair follicle regeneration: an updated review. Signal Transduction and Targeted Therapy. 2021;6:66.
2. Alzoabi NM, Alsharif HM Sr, Alawami AM, Habarah HH, Alhawaj HA, *et al*. Assessing the impact of alopecia on quality of life, depression, and self-esteem in Saudi Arabia. Cureus. 2023;15:12.
3. Houschyar KS, Borrelli MR, Tapking C, Popp D, Puladi B, Ooms M, *et al*. Molecular mechanisms of hair growth and regeneration: Current understanding and novel paradigms. Dermatology. 2020;236:271–280.
4. Schmidt-Ullrich R, Paus R. Molecular principles of hair follicle induction and morphogenesis. Bioessays. 2005;27:247–261.
5. Oh JW, Kloepper J, Langan EA, Kim Y, Yeo J, Kim MJ, *et al*. A guide to studying human hair follicle cycling *in vivo*. Journal of Investigative Dermatology. 2016;136:34–44.
6. Sharma A, Mohapatra H, Arora K, Babbar R, *et al*. Bioactive compound-loaded nanocarriers for hair growth promotion: current status and future perspectives. Plants. 2023;12:37-39.
7. Mulinari-Brenner F, Bergfeld WF. Hair loss: diagnosis and management. Cleveland Clinic Journal of Medicine. 2003;70:705–712.
8. Gupta M, Mysore V. Classifications of patterned hair loss: A review. Journal of Cutaneous and Aesthetic Surgery. 2016;9:3–12.
9. Messenger AG, Rundegren J. Minoxidil: Mechanisms of action on hair growth. British Journal of Dermatology. 2004;150:186–194.
10. Rogers NE, Avram MR. Medical treatments for male and female pattern hair loss. Journal of American Academy of Dermatology. 2008;59:547–566.
11. Suchonwanit P, Thammarucha S, Leerunyakul K. Minoxidil and its use in hair disorders: A review. Drug Design, Development and Therapy. 2019;13:2777–2786.
12. Zhongbao Z, Shiqiang S, Zhenli G, Jitao W, *et al*. The efficacy and safety of dutasteride compared with finasteride in treating men with androgenetic alopecia: A systematic review and meta-analysis. Clinical Interventions in Aging. 2019;14:399–406.
13. Escamilla-Cruz M, Magaña M, Escandón-Perez S, Bello-Chavolla OY. Use of 5-Alpha reductase inhibitors in dermatology: A narrative review. Dermatology and Therapy. 2023;13:1721-1731.
14. Kiguradze T, Temps WH, Yarnold PR, Cashy J, *et al*. Persistent erectile dysfunction in men exposed to the 5α-reductase inhibitors, finasteride, or dutasteride. PeerJ. 2017;5:20-30.
15. Hosking AM, Juhasz M, Atanaskova MN. Complementary and alternative treatments for alopecia: a comprehensive review. Skin Appendage Disorders. 2019;5:72-89.
16. Choi JY, Boo MY, Boo YC. Can plant extracts help prevent hair loss or promote hair growth? A review comparing their therapeutic efficacies, phytochemical components, and modulatory targets. Molecules. 2024;29:2287-2289.
17. Harada N, Okajima K, Arai M, Kurihara H, Nakagata N. Administration of capsaicin and isoflavone promotes hair growth by increasing insulin-like growth factor-I production in mice and in humans with alopecia. Growth Hormone & IGF Research. 2007;17:408-415.
18. Su HY, Hickford JG, Palmer BR, Bickerstaffe R. Insulin-like growth factor 1 and hair growth. Dermatology Online Journal. 1999, 5.
19. Yano K, Brown LF, Detmar M. Control of hair growth and follicle size by VEGF-mediated angiogenesis. Journal of Clinical Investigation. 2001;107:409-417.
20. Gnann LA, Castro RF, Azzalis LA, Feder D, Perazzo FF, *et al*. Hematological and hepatic effects of vascular epidermal growth factor (VEGF) used to stimulate hair growth in an animal model. BMC Dermatology. 2013;13:1-5.
21. Goldman CK, Tsai H, Chang J, *et al*. Loss of vascular endothelial growth factor in human alopecia hair follicles. Journal of Investigative Dermatology. 1995;104:18-20.
22. Du Cros DL. Fibroblast growth factor and epidermal growth factor in hair development. Journal of Investigative Dermatology. 1993;101:106-113.
23. Cros DD, Isaacs K, Moore GP. Distribution of acidic and basic fibroblast growth factors in ovine skin during follicle morphogenesis. Journal of Cell Science. 1993;105:667-674.
24. Huelsken J, Vogel R, Erdmann B, Cotsarelis G, Birchmeier W. β-Catenin controls hair follicle morphogenesis and stem cell differentiation in the skin. Cell. 2001;105:533-545.
25. Van Mater D, Kolligs FT, Dlugosz AA, Fearon ER. Transient activation of β-catenin signaling in cutaneous keratinocytes is sufficient to trigger the active growth phase of the hair cycle in mice. Genes & Development. 2003;17:1219-1224.
26. Aoki M, Hecht A, Kruse U, Kemler R, Vogt PK. Nuclear endpoint of Wnt signaling: neoplastic transformation induced by transactivating lymphoid-enhancing factor 1. Proceedings of the National Academy of Sciences. 1999;96:139-144.
27. Azzouni F, Godoy A, Li Y, Mohler J. The 5 alpha-reductase isozyme family: a review of basic biology and their role in human diseases. Advances in Urology. 2012;(1):17-19.
28. Herman A, Herman AP. Mechanism of action of herbs and their active constituents used in hair loss treatment. Fitoterapia. 2016;114:18-25.
29. Zhang H, Nan W, Wang S, Song X, *et al*. Epigallocatechin-3-gallate promotes the growth of mink hair follicles through sonic hedgehog and protein kinase

B signaling pathways. Frontiers in Pharmacology. 2018;9:673-674.
30. Jain PK, Das DE, Das C. Prospect of herbs as hair growth potential. Innovare Journal of Medical Sciences. 2017;5:25-33.
31. Hiep NT, Duong HT, Anh DT, Hoai Nguyen N, *et al*. Subcritical water extraction of epigallocatechin gallate from Camellia sinensis and optimization study using response surface methodology. Processes. 2020;8:1027-1029.
32. Fischer TW, Herczeg-Lisztes E, Funk W, Zillikens D, *et al*. Differential effects of caffeine on hair shaft elongation, matrix and outer root sheath keratinocyte proliferation, and transforming growth factor-β2/insulin-like growth factor-1-mediated regulation of the hair cycle in male and female human hair follicles *in vitro*. British Journal of Dermatology. 2014;171:1031-43.
33. Herman A, Herman AP. Caffeine's mechanisms of action and its cosmetic use. Skin Pharmacology and Physiology. 2012;26:8-14.
34. Fischer TW, Hipler UC, Elsner P. Effect of caffeine and testosterone on the proliferation of human hair follicles *in vitro*. International Journal of Dermatology. 2007;46:27-35.
35. Chaugule A, Patil H, Pagariya S, Ingle P. Extraction of caffeine. International Journal of Advanced Research in Chemical Science. 2019;6:11-9.
36. Kim J, Kim SR, Choi YH, Shin JY, *et al*. Quercitrin stimulates hair growth with enhanced expression of growth factors via activation of MAPK/CREB signaling pathway. Molecules. 2020;25:4004-5.
37. Manzoor MF, Hussain A, Sameen A, Sahar A, Khan S, Siddique R, *et al*. Novel extraction, rapid assessment and bioavailability improvement of quercetin: A review. Ultrasonics Sonochemistry. 2021;78:105686-7.
38. Woo H, Lee S, Kim S, Park D, Jung E. Effect of sinapic acid on hair growth promoting in human hair follicle dermal papilla cells via Akt activation. Archives of Dermatological Research. 2017;309:381-8.
39. Nićiforović N, Abramovic H. Sinapic acid and its derivatives: natural sources and bioactivity. Comprehensive Reviews in Food Science and Food Safety. 2014;13:34-51.
40. Chadni M, Flourat AL, Reungoat V, Mouterde LMM, *et al*. Selective extraction of sinapic acid derivatives from mustard seed meal by acting on pH: Toward a high antioxidant activity rich extract. Molecules. 2021;26:212-3.
41. Kesika P, Sivamaruthi BS, Thangaleela S, Bharathi M, Chaiyasut C. Role and mechanisms of phytochemicals in hair growth and health. Pharmaceuticals. 2023;16:206-5.
42. Afzal MF, Khalid W, Armghan Khalid M, Zubair M, *et al*. Recent industrials extraction of plants seeds oil used in the development of functional food products: A Review. International Journal of Food Properties. 2022;25:2530-50.
43. Patil S, Tilak P, Surve M, Bichave A, Deshmukh M. Fruit derived beta sitosterol: A natural gift for baldness. International Journal of Creative Research Thoughts. 2024;12:556-81.
44. Salunkhe PS, Patil SD, Dhande SR. Anti-thrombotic activity of isolated β-sitosterol from roots of Hemidesmus indicus Linn in rat model. Journal of Pharmacognosy Phytochemistry. 2018;7:10-4.
45. Kamimura A, Takahashi T, Watanabe Y. Investigation of topical application of procyanidin B-2 from apple to identify its potential use as a hair growing agent. Phytomedicine. 2000;7:529-36.
46. Cai Y, Yu Y, Duan G, Li Y. Study on infrared-assisted extraction coupled with high performance liquid chromatography (HPLC) for determination of catechin, epicatechin, and procyanidin B2 in grape seeds. Food Chemistry. 2011;127:1872-7.
47. Lee Y, Kim SN, Hong YD, Park BC, *et al*. Panax ginseng extract antagonizes the effect of DKK 1-induced catagen-like changes of hair follicles. International Journal of Molecular Medicine. 2017;40:1194-200.
48. Truong VL, Bak MJ, Lee C, Jun M, *et al*. Hair regenerative mechanisms of red ginseng oil and its major components in the testosterone-induced delay of anagen entry in C57BL/6 mice. Molecules. 2017;22:1505-6.
49. Qian YU, Ke-Wu ZE, Xiao-Li MA, Jiang Y, *et al*. Ginsenoside Rk1 suppresses pro-inflammatory responses in lipopolysaccharide-stimulated RAW264.7 cells by inhibiting the Jak2/Stat3 pathway. Chinese Journal of Natural Medicines. 2017;15:751-7.
50. Park GH, Park KY, Cho HI, Lee SM, *et al*. Red ginseng extract promotes the hair growth in cultured human hair follicles. Journal of Medicinal Food. 2015;18:354-62.
51. Jegal J, Jeong EJ, Yang MH. A review of the different methods applied in Ginsenoside extraction from Panax ginseng and *Panax quinquefolius* roots. Natural Product Communication. 2019;14:1934578-839.
52. Murata K, Noguchi K, Kondo M, Onishi M, *et al*. Promotion of hair growth by Rosmarinus officinalis leaf extract. Phytotherapy Research. 2013;27:212-7.
53. Zu G, Zhang R, Yang L, Ma C, *et al*. Ultrasound-assisted extraction of carnosic acid and rosmarinic acid using ionic liquid solution from Rosmarinus officinalis. International Journal of Molecular Science. 2012;13:11027-43.
54. Barbero GF, Palma M, Barroso CG. Pressurized liquid extraction of capsaicinoids from peppers. Journal of Agricultural and Food Chemistry. 2006;54:3231-6.