SalSphere® Hair Stimulator (SS HS)

A targeted delivery technology of natural hair stimulation

SalSphere® Hair Stimulator is a sub-micron sphere technology that addresses the need for balding men and women. This unique technology enhances the delivery and effectiveness of natural, functional, active ingredients.

The sub-micron spheres have a solid core and a semi-liquid shell (Fig 1). The core contains 6 different functional, active ingredients known to stimulate hair growth.

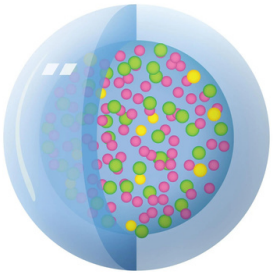

Figure 1: The sub-micron structure of SalSphere® Hair Stimulator.

SalSphere® is an advanced approach to formulating topical applications for stimulating hair growth. These submicron spheres have a core made of natural materials like lipids and waxes. These tiny particles can deliver functional, active ingredients more effectively to the hair follicles (Fig 5).

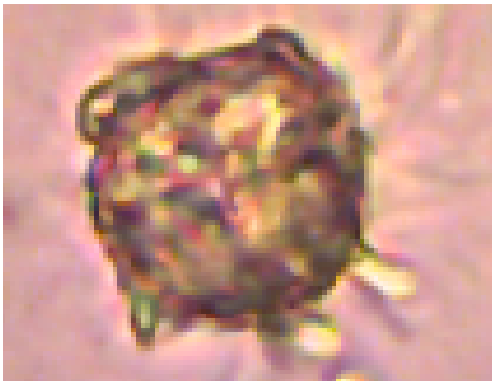

Figure 2: SalSphere® Hair Stimulator, microscopy image at 400x magnification.

SalSphere encapsulation technology provides multiple benefits:

1. Lipid-Based Encapsulation: Using lipid-based materials allows for enhanced compatibility with the skin and efficient delivery of active ingredients.

2. Targeted delivery to hair follicles: Submicron-sized spheres ranging from tens to hundreds of micrometers facilitates deeper penetration into the hair follicles.

3. Stability and Protection: The encapsulation process provides stability and protection to the active ingredients from environmental factors, such as air, light, and temperature.

Figure 3: SalSphere® Hair Stimulator technology for hair thinking and loss.

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Unique&Easy Micro-Encapsulation Solutions

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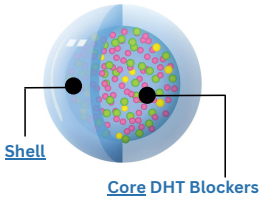

Technical Data

Key INCI of SalSphere® Hair Stimulator

Caffeine, Azelaic Acid, Serenoa Serrulata Fruit Extract [Saw Palmetto], Zinc Sulfate, Scutellaria Baicalensis Root Extract [Baicalin], Biotin, Butyrospermum Parkii (Shea) Butter

Other INCI of SalSphere® Hair Stimulator

Aqua, Arginine, Calcium Gluconate, Cetearyl Alcohol, Cetearyl Glucoside, Gluconolactone, Glycerin, Glyceryl Monostearate, Glyceryl Stearate, Glycine Soja (Soybean) Germ Extract, Hydroxypropyl Guar, Lactic Acid, Pentylene Glycol*, Phenethyl Alcohol*, Polyglyceryl-2-Stearate, Propanediol, Sodium Benzoate, Squalane, Stearyl Alcohol, Triticum Vulgare (Wheat) Germ Extract

*= Preservative Component

Table 2: Specification of SalSphere® Hair Stimulator.

Specification	Characteristic
Appearance	Opaque Cream
Color (Visual)	White to off-white
Odor	Characteristic
pH (Neat)	4.0-6.0

Figure 4: A Raw material SalSphere® Hair Stimulator 8428-38. B: Diluted version as a spray

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Targeted Deliver, Follicular Delivery

Follicular delivery refers to the targeted delivery of active ingredients directly to the hair follicles, where hair growth occurs (Fig 5). This approach enhances the effectiveness of hair growth treatments by ensuring that the active compounds reach the specific site of action in optimal concentrations. Follicular delivery is particularly advantageous for treating conditions like androgenic alopecia (pattern hair loss) and other forms of hair thinning.

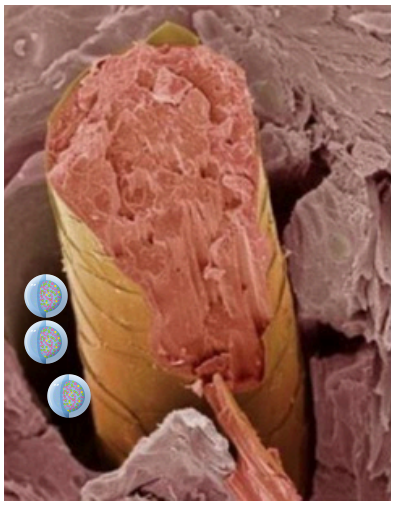

Figure 5: Illustration of follicular delivery of SalSphere® Hair Stimulator into the hair follicles.

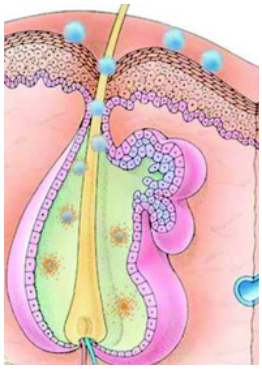

Figure 6: The diameter of the hair follicular orifice is estimated to be at 30-50µm.

SalSphere® delivery system, with a diameter of 0.8µm, can facilitate targeted delivery.

Benefits of Follicular Delivery

1. Increased Efficacy:
   - **Direct Action:** Delivering active ingredients directly to the hair follicles ensures that the compounds reach the exact location where they are needed to stimulate hair growth. This targeted approach maximizes the effectiveness of the treatment.
   - **Higher Concentrations:** Follicular delivery allows for higher concentrations of active ingredients in the follicles than traditional topical applications, leading to more potent effects on hair growth.
2. Reduced Side Effects:
   - **Localized Treatment:** Since the active ingredients are concentrated in the hair follicles and not absorbed systemically, there is a lower risk of side effects that might occur with (oral) systemic treatments.
   - **Lower Doses Required:** Targeted delivery means that lower doses of active ingredients can be used, reducing the potential for adverse reactions while still achieving effective results.
3. Improved Penetration:
   - **Overcoming the Skin Barrier:** The skin, particularly the scalp, can be a barrier to absorbing active ingredients. Follicular delivery systems, such as SalSphere® Hair Stimulator, help overcome this barrier, ensuring that the active compounds penetrate deeply enough to reach the hair follicles.
4. Sustained Release of Active Ingredients:
   - **Prolonged Action:** The SalSphere® Hair Stimulator follicular delivery system is designed to slowly release active ingredients. This sustained release ensures that the hair follicles are continuously exposed to the compounds, which can lead to better results in promoting hair growth.
5. Versatility in Treatment Options:
   - **Multiple Actives:** The SalSphere® Hair Stimulator system delivers many active ingredients. This versatility allows for the development of customized treatments tailored to individual needs.
   - **Combination Therapies:** SalSphere® Hair Stimulator delivery can also facilitate the combination of multiple active ingredients in a single formulation, allowing for synergistic effects that enhance overall hair growth outcomes.

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Functional Active Ingredeints

1. Caffeine: Stimulates hair follicles and promotes hair growth. It can extend the anagen (growth) phase of the hair cycle and inhibit the hair loss effects of dihydrotestosterone (DHT, Fig 7).

2. Azelaic Acid: Exhibits anti-inflammatory and antimicrobial properties, which may help reduce inflammation and combat scalp conditions that could contribute to hair thinning.

3. Saw Palmetto: Blocks the enzyme 5-alpha-reductase, which converts testosterone into DHT.

4. Zinc Sulfate: Supports the synthesis of keratin and prevents hair loss associated with zinc deficiency.

5. Chinese Herbal Medicine (Baicalin, Scutellaria baicalensis, Chinese skullcap): Inhibits DHT

6. Biotin: Balances skin microbiome, improves hydration and fortifies scalp defense

The enzyme 5-alpha-reductase plays a critical role in converting testosterone into dihydrotestosterone (DHT). DHT is a more potent androgen than testosterone, meaning it binds more strongly to androgen receptors, exerting stronger biological effects, such as shrinking hair follicles and shortening the anagen phase.

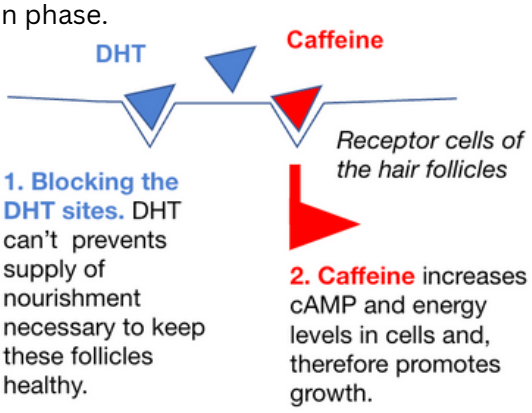

Figure 7: Caffeine potentially promotes hair growth, particularly by inhibiting the effects of dihydrotestosterone (DHT).

On their own, these active ingredients are not very effective and cannot offer targeted, sustained delivery

Figure 8: Clinical study shows the effect on of the technology on hair growth. Clinical data is available at the substaination references.

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Formulation challange

Free caffeine has a stringy, fibrous appearance, while the encapsulated caffeine in SalSphere® Hair Stimulator is finer and more uniform (Figures 9, 10).

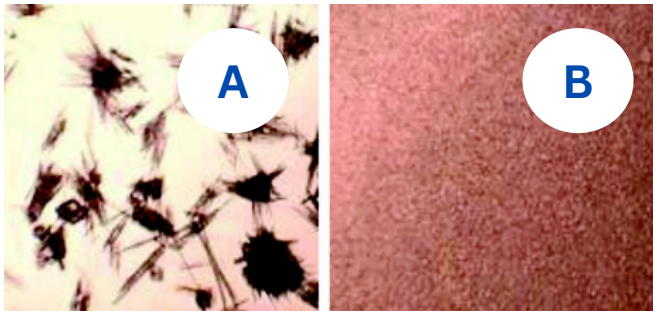

Figure 9: Microscopic images of 5% free caffeine in water (A) and 5% from SalSphere® Hair Stimulator (B). Images were taken at 100x magnification.

The crystal fibers (**Figure 9, A**) show that at 5% free, caffeine is insoluble in water. However, the SalSphere® Hair Stimulator encapsulates the caffeine (**Figure 9, B**) and is suspendable in water at 5% loading.

References

1. 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.

2. Trauer S. Permeation of topically applied caffeine through human skin - a comparison of in-vivo and in-vitro data. British Journal of Clinical Pharmacology. 2009 Aug; 68 (2): 181.

Encapsulation as a solution

Encapsulation of Caffeine at high concentration is essential to provide stability (no crystallization) and for targeted delivery

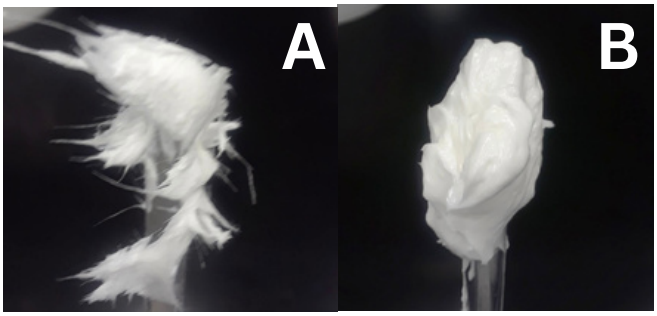

Figure 10: Cream with Free Caffeine (A) and SalSphere® Hair Stimulator (B)

(A) 5% free Caffeine crystallizes because of the solubility limitation.

(B) At 5% Caffeine concentration, SalSphere® Caffeine has a smooth appearance with no crystals.

Encapsulating caffeine benefits both the formulator and the consumer.

The formulator can use a higher percentage of caffeine in their final formulations.

The consumer can benefit from the added available caffeine.

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Applications

Table 3: Conditioner with SalSphere® Hair Stimulator

PHASE	INCI	Wt %
A1	Aqua	80.75
A2	Glycerin	5
A3	Polyquaternium-37	0.15
B1	Cetearyl Alcohol	3
B2	Glyceryl Stearate	1
B3	Stearamidopropyl Dimethylamine Lactate	2.5
B4	Butyrospermum Parkii (Shea) Butter	0.7
C1	**SalSphere® Hair Stimulator**	**5**
C2	Phenoxyethanol, Ethylhexylglyceri	0.9
C3	Fragrance	1
	Total	**100**

Table 4: Scalp Serum with SalSphere® Hair Stimulator

PHASE	INCI	Wt %
A1	Aqua	85.35
A2	Glycerin	3.25
A3	1,3 Propandiol	4.5
A4	Xanthan Gum	1
B1	**SalSphere® Hair Stimulator**	**5**
B2	Phenoxyethanol (and) Ethylhexylglycerin	0.9
	Total	**100**

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Claim Substantiation

Claims	Substantiation
Caffeine serves as a potent, non-pharmaceutical treatment for androgenetic alopecia (AGA)	Literature: - Dhurat, R., Chitallia, J., May, T. W., Jayaraaman, A. M., Madhukara, J., Anandan, S., … Klenk, A. (2017). An Open-Label Randomized Multicenter Study Assessing the Noninferiority of a Caffeine-Based Topical Liquid 0.2% versus Minoxidil 5% Solution in Male Androgenetic Alopecia. Skin Pharmacology and Physiology, 30(6), 298–305. doi:10.1159/000481141 "In recent years, caffeine has demonstrated potential as a treatment for AGA. Due to being a phosphodiesterase inhibitor, caffeine increases cyclic adenosine monophosphate levels in cells and consequently promotes cell proliferation through stimulating cell metabolism – a mechanism that may counteract testosterone/dihydrotestosterone-induced miniaturization of the hair follicle. In a male skin organ culture model, caffeine reversed the inhibiting effect of testosterone on keratinocyte proliferation. In an in vitro study, testosterone-induced hair follicle growth suppression was reversed with addition of caffeine at concentrations of 0.001 and 0.005%; moreover, caffeine alone led to significant stimulation of hair follicle growth. In another in vitro study of male and female hair follicles, caffeine was found to enhance hair shaft elongation, prolong anagen duration and stimulate hair matrix keratinocyte proliferation. In addition, hair follicles from females appeared to be more sensitive to caffeine than hair follicles from males, and caffeine counteracted testosterone-induced transforming growth factor-β2 expression, a major antagonistic hair growth regulatory factor, in male hair follicles. Caffeine also resulted in increased expression of insulin-like growth factor-1, a promoter of hair growth, in both male and female hair follicles."
Caffeine is a safe, non-pharmaceutical option for both oral and topical use	Literature: - Völker, J. M., Koch, N., Becker, M., & Klenk, A. (2020). Caffeine and Its Pharmacological Benefits in the Management of Androgenetic Alopecia: A Review. Skin Pharmacology and Physiology, 1–17. doi:10.1159/000508228 Recently, the effective delivery of caffeine as a hydrophilic model drug out of a topical applied formulation into and through hair follicles was demonstrated. Therefore, it was shown that hair follicles and their surrounding regions are a possible treatment route targeted by optimized formulations. In addition to that, the potential of caffeine-catalyzed gels for novel, biocompatible oral drug-delivery systems and biomedical devices has been investigated. In these tailorable systems, caffeine can act as a biocompatible catalyst to create a gel formulation that can be drug-loaded during manufacturing. These recent investigations strongly emphasize the positive impact the versatile and safe natural active ingredient caffeine can have on human health on a variety of levels. Taken together, there is a growing body of evidence highlighting the positive effects of caffeine in several disease settings, indicating that caffeine is a potent substance associated with multiple beneficial effects. When applied in adequate doses, the ingestion and cosmetic application of caffeine can considered to be safe."
Topical caffeine is observed to have good absorption and penetration though the hair follicle	Literature: - Dhurat, R., Chitallia, J., May, T. W., Jayaraaman, A. M., Madhukara, J., Anandan, S., … Klenk, A. (2017). An Open-Label Randomized Multicenter Study Assessing the Noninferiority of a Caffeine-Based Topical Liquid 0.2% versus Minoxidil 5% Solution in Male Androgenetic Alopecia. Skin Pharmacology and Physiology, 30(6), 298–305. doi:10.1159/000481141 "Caffeine has also been shown to penetrate the hair follicle even when applied as a shampoo formulation. In a study of 6 male volunteers, a caffeine-based shampoo resulted in penetration of caffeine into both the stratum corneum and hair follicles after 2-min application, with the highest values being found 2h after application. The potential efficacy of a caffeine-based topical formulation has been previously demonstrated in a prospective study of 40 men with AGA. In this study, daily use of the caffeine-based lotion resulted in an 8.14% reduction in hairs extracted at 2 months and a 15.33% reduction in hairs extracted at 4 months. In

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	Review. Skin Pharmacology and Physiology, 1–17. doi:10.1159/000508228 "The results of these studies show that transdermal and follicular penetration occur simultaneously. Caffeine penetrates preferentially via the follicular route, providing immediate caffeine availability, while the slower transdermal penetration can provide a caffeine reservoir. Further penetration studies with a similar experimental setup, including the topical application of a caffeine solution (25 mg/mL, leave-on) on the chest area of 6 healthy male Caucasian volunteers, demonstrated that the follicular route contributes significantly to the absorption of caffeine through the skin."
Topical caffeine is effective in treating AGA and telogen effluvium in both men and women	Literature: - Völker, J. M., Koch, N., Becker, M., & Klenk, A. (2020). Caffeine and Its Pharmacological Benefits in the Management of Androgenetic Alopecia: A Review. Skin Pharmacology and Physiology, 1–17. doi:10.1159/000508228 "A caffeine-containing shampoo (10 mg/mL caffeine) was assessed in females with telogen effluvium (n = 30) using the hair pull test to evaluate hair loss as well as investigator and subject questionnaires to evaluate the quality of life. After 6 months of daily application on the scalp with 2 min contact time, a decrease in hair loss was noted in more than half of the participants. In addition, a good cosmetic efficacy was reported including an improvement in the strength of the hair ($p < 0.001$), a decrease in the extent of hairs falling out ($p < 0.001$), and a decrease in the progression of the balding ($p = 0.100$) assessed by the investigator's questionnaire. In females with AGA, a randomized double-blind parallel trial (n = 140) compared the efficacy of a caffeine-containing shampoo to a control shampoo without caffeine." "A randomized, controlled, double-blind, parallel group study of a caffeine-containing shampoo was conducted in males with AGA (n = 66). The contentment was significantly higher for the caffeine-containing shampoo compared to a caffeine free control ($p < 0.001$). Further parameters assessed by the subjects themselves as well as from the investigators were also improved significant differences in favor of the caffeine-containing shampoo were observed for the reduction in the intensity of hair loss ($p = 0.002$), the decrease in/normalization of the hair loss ($p < 0.001$), the decrease in the number of hairs in the basin ($p = 0.002$), and the improvement of hair strength and thickness ($p < 0.001$)."
Recent studies have shown that caffeine is considered a noninferior treatment for AGA compared to topical minoxidil	Literature: - Völker, J. M., Koch, N., Becker, M., & Klenk, A. (2020). Caffeine and Its Pharmacological Benefits in the Management of Androgenetic Alopecia: A Review. Skin Pharmacology and Physiology, 1–17. doi:10.1159/000508228 "More recently, results of a randomized, open-label, multicenter noninferiority study in males with AGA (n = 210) were published, reporting on the effects of a caffeine-containing lotion (2 mg/mL) compared to a drug-based approach (50 mg/mL minoxidil solution). Minoxidil is one of only 2 drugs in use worldwide for the treatment of hair loss, the other being finasteride. However, topical minoxidil solution has been associated with adverse effects, including contact dermatitis and hypertrichosis. On the other hand, caffeine is the most studied natural ingredient with the potential to be a topical multibenefit solution to hair loss and is not known to show any undesired effects in vivo." "Additionally, two further studies have been conducted with topically applied caffeine in combination with conventional hair loss treatments. Within a randomized, double-blind, controlled clinical trial, the topical solution consisting of 25 mg/mL caffeine with 25 mg/mL minoxidil was more effective for male and female patients suffering from AGA than the 25 mg/mL minoxidil alone in terms of patients' satisfaction (58.33% in combined treatment vs. 41.37% in minoxidil alone control group) after 150 days of treatment. Another combined treatment with 10 mg/mL caffeine, 50 mg/mL minoxidil, and 15 mg/ mL azelaic acid on male AGA

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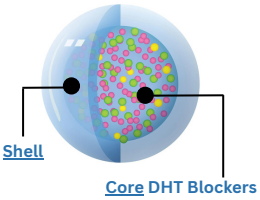
Claim Substantiation

	patients showed a higher efficacy for hair regrowth and against hair shedding, evaluated via wash test (hair shedding) as well as patient and dermatologist assessment (hair regrowth), in comparison to minoxidil alone or the placebo after 32 weeks. Both studies emphasize that the combined solutions with caffeine were more effective on male patients with AGA compared to the corresponding control group, further illustrating the efficacy of caffeine on AGA management."
Azelaic acid up-regulates cellular factors associated with inducing hair growth	Literature: - Amirfakhryan E, Davarnia B, Jeddi F, Najafzadeh N. Azelaic acid stimulates catalase activation and promotes hair growth through upregulation of Gli1 and Gli2 mRNA and Shh protein. Avicenna J Phytomed. 2020 Sep-Oct;10(5):460-471. PMID: 32995324; PMCID: PMC7508322. "In our results, the effectiveness of azelaic acid alone in inducing hair growth, was shown with respect to up-regulation of *Gli1* and *Gli2* genes and an increase in catalase activity in the bulge cells. Indeed, its combination with minoxidil also elevated Shh protein expression in the hair follicles and combination therapy had a higher effect over minoxidil alone in terms of increased Shh expression level. Similar to our results, previous studies showed that Shh/Gli1/Gli2 activation may directly promote telogen to anagen transition in the hair follicle and azelaic acid may exert various PPARγ independent effects in the hair follicle."
Azelaic acid reduces inflammatory factors associated with hair loss	Literature: - Amirfakhryan E, Davarnia B, Jeddi F, Najafzadeh N. Azelaic acid stimulates catalase activation and promotes hair growth through upregulation of Gli1 and Gli2 mRNA and Shh protein. Avicenna J Phytomed. 2020 Sep-Oct;10(5):460-471. PMID: 32995324; PMCID: PMC7508322. "Furthermore, we showed that exposure of azelaic acid to bulge cells protected them from UVB damage and caused a significant increase in the catalase activity in the bulge area. Hair loss, like acne, is strongly linked to inflammatory factors and DHT. In scarring alopecia, hair follicle stem cells (bulge cells) degenerate resulting in permanent hair loss. Some PPARγ ligands such as azelaic acid, have anti-inflammatory activity for the treatment of cicatricial (scarring) alopecia. It inhibits neutrophil mediated reactive oxygen species (ROS) production."
Topical saw palmetto has demonstrated clinical evidence to regrow hair as a non-pharmaceutical alternative therapy	Literature: - Hosking, A.-M., Juhasz, M., & Atanaskova Mesinkovska, N. (2018). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review. Skin Appendage Disorders, 1–18. doi:10.1159/000492035 "Saw palmetto (SP, *Serona repens*) is an extract from the berries of the saw palmetto palm tree (American dwarf tree) containing phytosterols (β-sitosterol), fatty acids, β-carotene, and polysaccharides. SP is a competitive, nonselective inhibitor of both forms of 5α-reductase. SP blocks nuclear uptake of DHT in target cells and decreases DHT binding to androgen receptors by approximately 50%. Additionally, the extract increases 3α-hydroxysteroid-dehydrogenase activity, increasing the conversion of DHT to its weaker metabolite, androstanediol. As a result, the pharmacodynamic profile of SP differs from finasteride due to multiple sites of action… SP has also been studied as a topical agent. A study evaluating the hair growth effect of 3.3 mL topical SP serum applied for 4 weeks and 2 mL lotion for 24 weeks, in 50 men with AGA, demonstrated increased average and terminal hair counts at 12 and 24 weeks. Although systemic SP has not demonstrated superiority to conventional systemic therapies, it does have clinical benefits and is an attractive alternative treatment for male AGA patients who are not interested in oral finasteride."
Low zinc is characteristic of hair loss disorders (alopecia areata, androgenetic alopecia, telogen effluvium), and therapies to restore zinc levels is shown to reverse	Literature: - Hosking, A.-M., Juhasz, M., & Atanaskova Mesinkovska, N. (2018). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review. Skin Appendage Disorders, 1–18. doi:10.1159/000492035 "Low zinc levels have been identified in patients with AA, AGA, and TE]. Proposed mechanisms for zinc-associated hair regrowth include antimicrobial,

add biotin substantiation



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hair loss	anti-inflammatory, antioxidant, and anti-5α-reductase activity. Zinc has been studied as both a topical and oral supplement. Zinc chelates with pyrithione to create a coordination complex that acts as an antifungal for treatment of seborrheic dermatitis. Comparing the efficacy of 1% pyrithione zinc shampoo used daily, 5% topical MXD solution used twice daily, or a combination of both, for 9 weeks in 200 AGA patients resulted in increased hair counts in all groups compared to placebo...Topical and oral zinc supplementation may prove to be an efficacious adjuvant for both AGA and AA treatment in patient populations that would like [complementary and alternative methods] modalities."
Supplementation of biotin is an effective therapy for hair loss secondary to biotin deficiency	Literature: - Hosking, A.-M., Juhasz, M., & Atanaskova Mesinkovska, N. (2018). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review. Skin Appendage Disorders, 1–18. doi:10.1159/000492035 "A recent review identified 11 cases of hair loss secondary to biotin deficiency, from either an inherited enzyme deficiency or medication, where biotin was an effective supplementation for hair regrowth. Current clinical evidence supports biotin supplementation as an effective CAM for hair loss only in cases secondary to biotin deficiency; however, apart from medications, this is rare in developed countries due to well-balanced dietary intake."
Baicalin (found in Traditional Chinese Herbal Medicine) is a safe and effective non-pharmaceutical alternative clinically shown to prevent and reverse hair loss	Literature: - Kim, A.-R., Kim, S.-N., Jung, I.-K., Kim, H.-H., Park, Y.-H., & Park, W.-S. (2014). The Inhibitory Effect of Scutellaria baicalensis Extract and Its Active Compound, Baicalin, on the Translocation of the Androgen Receptor with Implications for Preventing Androgenetic Alopecia. Planta Medica, 80(02/03), 153–158. doi:10.1055/s-0033-1360300 "These results are consistent with an inhibitory effect on the DHT and AR binding process…this moderate effect could be safe and could gradually prevent AGA. The SB-Ext and baicalin showed a proliferative effect on hDPC, which means that these materials contribute to increasing the total hair follicle DP size and induce hair growth by extending the anagen phase, which is shortened in patients with AGA. In conclusion, our results indicate that the SB-Ext and baicalin inhibited the androgen effect on target cells by antagonizing the AR and suppressing the DHT-dependent activation cascade of the AR. Our results suggest a preventive effect on androgen-associated diseases such as AGA" - Xing, F., Yi, W., Miao, F., Su, M., & Lei, T. (2018). Baicalin increases hair follicle development by increasing canonical Wnt/β-catenin signaling and activating dermal papillar cells in mice. International Journal of Molecular Medicine. doi:10.3892/ijmm.2018.3391 "The results of the present study demonstrate that baicalin promotes the growth of hair follicles likely via activation of Wnt/β-catenin signaling and increasing the ALP activity of DPCs in mice. Furthermore, baicalin was not able to overcome the Wnt/β-catenin signaling antagonism or ameliorate the inhibition of hair follicle growth caused by IWR-1 in mice. This supports the hypothesis that baicalin promotes hair follicle development by activating the Wnt pathway. Wnt pathway activity is essential for hair follicle development and the hair cycle."

Additional references

Dhurat, R., Chitallia, J., May, T. W., Jayaraaman, A. M., Madhukara, J., Anandan, S., … Klenk, A. (2017). An Open-Label Randomized Multicenter Study Assessing the Noninferiority of a Caffeine-Based Topical Liquid 0.2% versus Minoxidil 5% Solution in Male Androgenetic Alopecia. Skin Pharmacology and Physiology, 30(6), 298–305. doi:10.1159/000481141 Völker, J. M., Koch, N., Becker, M., & Klenk, A. (2020). Caffeine and Its Pharmacological Benefits in the Management of Androgenetic Alopecia: A Review. Skin Pharmacology and Physiology, 1–17. doi:10.1159/000508228 Amirfakhryan E, Davarnia B, Jeddi F, Najafzadeh N. Azelaic acid stimulates catalase activation and promotes hair growth through upregulation of Gli1 and Gli2 mRNA and Shh protein. Avicenna J Phytomed. 2020 Sep-Oct;10(5):460-471. PMID: 32995324; PMCID: PMC7508322. Hosking, A.-M., Juhasz, M., & Atanaskova Mesinkovska, N. (2018). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review. Skin Appendage Disorders, 1–18. doi:10.1159/000492035 Kim, A.-R., Kim, S.-N., Jung, I.-K., Kim, H.-H., Park, Y.-H., & Park, W.-S. (2014). The Inhibitory Effect of Scutellaria baicalensis Extract and Its Active Compound, Baicalin, on the Translocation of the Androgen Receptor with Implications for Preventing Androgenetic Alopecia. Planta Medica, 80(02/03), 153–158. doi:10.1055/s-0033-1360300 Xing, F., Yi, W., Miao, F., Su, M., & Lei, T. (2018). Baicalin increases hair follicle development by increasing canonical Wnt/β-catenin signaling and activating dermal papillar cells in mice. International Journal of Molecular Medicine. doi:10.3892/ijmm.2018.3391