Ingredients of trichological shampoos with alleged beneficial effects on hair – what is really known about their efficacy? A scoping review of an area with more unknowns than knowns – Supplementary material

Table S1. An overview of clinical trials on the efficacy of the substances of interest to the present article tested individually in topical preparations against hair loss.

Name of substances	Study design	Preparation and application	Comparator preparation and application	Inclusion criteria	Number of patients, gender	Duration of treatment	Duration of follow-up	Outcome measures	Main reported outcomes	Authors' conclusion in the article	Reviewers' summary	Remarks/ Factors influencing level of evidence	Evidence level (GRADE)	Ref.
Adenosine	Prospective-randomized study	I: group II- 55 P used 1 cc of a lotion with 0,75% **adenosine**, applied twice a day- (leave on).	C: group I- 55 P used 1 cc of a lotion with 5% MNX, twice a day	M with AGA, Norwood-Hamilton stage II-V	110 M, aged under 18	6 mo	6 mo	Macro-photography and counting all visible terminal hairs at a 1-cm2	After 3 months of treatment, relative recovery was achieved in 2.4% and 1.9% of P in group 1 and group 2 (p=0.17). During 6 months, the relative recovery rate did not change either within or between the groups (p=0.99) and after 6 months none of the P achieved complete recovery. P satisfaction rate was significantly higher in group 2 (p=0.003).	"Adenosine has no statistically superiority to MNX in the treatment of AGA according to recovery rates. However, the P were significantly more satisfied with adenosine because of faster prevention of hair loss and appearance of the newly grown hairs."	Treatment with 0.75% adenosine solution gave similar results to treatment with 5% MNX, which is a promising alternative for people who experience side effects associated with the use of MNX.	No placebo group, and method of measuring effects that is not very reliable.	Low	[1]
Adenosine	Prospective-randomized study	I: 0,75% **adenosine** lotion (leave on).	C: lotion without adenosine	M with AGA	38 volunteers with AGA	6 mo	6 mo	Fototrichogram	Hair density in the adenosine group was significantly higher than in the placebo group (P = 0.0494)	"The change in thick hair proportion (classified as hair ≥60 lm in diameter) was significantly different between the two groups (P < 0.0001). The proportion of thick hair in the adenosine group was significantly higher than in the placebo group at 6 months".	After treatment of adenosine, a significant increase in hair was observed.	Study not blinded on investigators' side.	Low	[2]

Adenosine	Double-blind, randomized ,placebo-controlled trial	I: 3 ml 0,75% lotion with **adenosine** applied twice a day- (leave on).	C: 3 ml lotion without adenosine (placebo) twice a day	F with FPHL over stage 1.5	30 F, aged 22-53 years	12 mo	12 mo	Fototrichogram, Dermatologist assessments, IA and PA.	85% P in the adenosine-treated group were assessed as "improvement" or "slight improvement" while only 36% P in the placebo-treatment were assessed similarly at month 12.	"The adenosine group was significantly greater than the placebo group regarding: the change in appearance of hair at month 12, the change in hair growth at month 6; and prevention of hair loss at months 6 and 12"	Adenosine improved hair loss in Japanese women by stimulating hair growth and by thickening hair shafts.	----------	Moderate	[3]
Adenosine	Double-blind, randomized study	I: 3 ml 0,75% **adenosine** lotion, applied twice a day- (leave on).	C: 3 ml 0,1 niacinamide lotion as placebo, twice a day	M with AGA, Ogata II-IV stage	102 M, aged 30-50	6 mo	6 mo	Digital microscope, global photographs, PA	Improvements in the thick hair ratio (classified as at least 60 μm in diameter and 80 μm in diameter, P = 0.0331 and P = 0.0268, respectively) were significantly augmented for the adenosine-treated group vs. the niacinamide-treated group. Efficacy in hair density No significant differences in hair density were observed between or within the two groups (P = 0.1831, P = 0.0975, and P = 0.5539, respectively)	"Subjects classified in the 'very clear improvement', 'clear improvement' and 'fairly clear improvement' groups represented 80% of the adenosine-treated participants vs. only 32% of the niacinamide-treated participants".	The improvement in hair thickness index was significantly increased in the adenosine-treated group compared with the niacinamide-treated group.	----------	Moderate	[4]
Caffeine	Multicenter, prospective, randomized , active-controlled, open-label, noninferiority study	I: 2 ml of a 0.2% caffeine-solution applied on the scalp twice a day- (leave-on).	C: 1 ml of 5% minoxidil solution applied on the scalp twice a day (leave-on	M with AGA, Hamilton-Norwood stage III–V, ≥20% telogen hairs on trichogram	210 M recruited, aged 18-55, 82 P compl. the I arm, 79 P compl. the C arm	6 mo	6 mo	IA: anagen rate on trichogramand changes in anagen rate	Mean impr. in anagen rate I: 10.59%; C: 11.68% (difference: 1.09%, ns).	"A caffeine-based topical liquid should be considered as not inferior to minoxidil 5% solution in men with androgenetic alopecia."	Effects of 0,2% caffeine comparable to s 5% minoxidil	Lack of placebo group	Moderate	[5]

Caffeine	Randomi-zed, controlled, double-blind, parallel group study	I : 7 ml of shampoo with caffeine (undiscl. conc.) applied once a day, kept on the scalp for 2 minutes-(rinse-off).	C : 7 ml of the same shampoo less caffeine, the same application protocol	M with AGA, Hamilton-Norwood stage II-IV;	66 M, aged 23-55, 33 P in I arm , 33 P in C arm	6 mo	6 mo	PA and IA quest.	Subjective intensity of hair loss decreased more in the I than C group (p=0.002). PA: "normalization of hair loss" more pronounced in the I than C group (p<0.001), "amount of hair in the basin" decreased more in the VI than C group (p<0.002), "strength and thickness of hair" impr. more in the I than PC group (p<0.001). More participants in I (84.8%) than C (36.4%) group wanted to continue the treatment (p<0.001). IA: "hair strength and thickness" impr. more in the I than C group (p<0.001), "balding" impr. more in the I than C group (p<0.001), "falling out of hair" impr. more in the I than C group (p<0.002), Investigator's overall preferrence of I (72.7%) higher than C (33.3%, p=0.003). Patient satisfaction rate with I greater than C (84.8% vs 36.4%, p<0.001)	"Our data support the beneficial effects of topical application of caffeine in AGA"	Impr. in subjective measures during the treatment significantly bigger after caffeine treatment than placebo.	No information on caffeine concentratio n, arbitrary scales for all measures, no pull test results reported, sponsored by producer of tested lotion	Low	[6]
Caffeine	Test with dermatologi cal control	I: 7 ml of a shampoo with caffeine (undiscl. conc.) was applied on hair and scalp once a day, and kept for 2 min. (rinse-off).	C:----------	M with AGA, Hamilton-Norwood stage II-IV;	30 M recruited, aged 18–55	6 mo	6 mo	Pull test, PA and IA quest.	Pull test: the mean number of pulled hair decreased from 20.07 at start down to 18,63 after 3 months (-7.5%) and 17.43 (-13.1%) after 6 months, both p<0.001) Increased "strength of hair", decreased "progression of balding", decreasing "extent of falling out hair" and decreased "intensity of hair loss" (self-assessment on an arbitrary scale, each p<0.001)	"Finally, we can say that caffeine is a promising substance for the cosmetic treatment of male AGA, and its formulation as a shampoo is effective as well as comfortable for male subjects, who prefer a shampoo to a lotion for daily use"	Significant impr. in objective and subjective measures during the treatment; not clear how much of it attributable to caffeine	Lack of placebo or comparator substance, no information on caffeine concentratio n, arbitrary scales for most measures, sponsored by producer of tested shampoo	Very low	[7]

									67% PA satisfied with the product					
Caffeine	Prospective, uncontro-lled, open-label	I: shampoo with caffeine (undiscl. conc.) was applied on hair and scalp once a day, and kept for 2 min. (rinse-off).	C:----------	F with TE, "copious" hair loss that begun in preceding 2 mo	30 F, aged 18-40	6 mo	6 mo	Pull-test , IA quest. after 3 and 6 mo of treatment.	Pull test: the mean number of pulled hair decreased from 21.2 at start down to 20.3 after 3 months (-4.2%, ns) and 19.2 (-9.4%) after 6 months (p=0.003) PA: impr. "intensity of hair loss" (p<0.001), decreased "number of hairs during daily combing" (p<0.001), impr. "strength of hair" (p<0.001), impr. "tension/dryness" (p=0.016). IA: impr. "strength of the hair" (p=0.002), decreased "extent of the out falling hairs" (p<0.001), decreased "progression of balding" (p=0.001), impr. "scaling/dandruff" (p=0.016).	"(…) the product has been shown to have a good cosmetic efficacy in the treatment of female TE."	Impr. in objective and subjective measures during the treatment; not clear how much of this was attributable to caffeine	Lack of placebo or comparator substance(TE is self-limiting in many cases), no information on caffeine concentration, arbitrary scales for most measures	Very low	[8]
Melatonin	Double-blind, pilot randomized, placebo-controlled study	I: 0,1% melatonin–alcohol solution applied once a day- (leave on).	C: placebo solution	28 F with diffuse alopecia and 12 with AGA	40 F, aged 20-70	6 mo	6 mo	Trichogram	The anagen hairs in frontal trichograms increased from 80,4% to 82,6% and the telogen hairs decreased from 18,9% to 15,9%.	"To the authors' knowledge, this pilot study is the first to show that topically applied melatonin might influence hair growth in humans in vivo. The mode of action is not known, but the effect might result from an induction of anagen phase."	After 6 months of treatment, a greater increase in anagen hair was observed in the melatonin group compared to the placebo group. Melatonin led to an increase in the number of frontal hairs in P with diffuse	----------	Modera te	[9]

											alopecia but no such effect was achieved in P with AGA.			
Placental protein, Hydrolyzed placental protein	Double-blind, randomized controlled trial	I: Cow placenta hair tonic lotion – a commercial product (undisclosed composition and conc.), 1 ml, applied twice a day on the frontal scalp (leave-on)	C: 2% MNX solution. The same mode of application.	F with AGA, Sinclair stage 2– 5	90 F recruited, aged ≥ 18 years; 43 compl. the I arm (mean age 44), 31 compl. the C arm (mean age 41)	6 mo	6 mo	Trichoscopy, IA of photographs of the vertex scalp	Improvement in AI in both I and C groups, difference between groups ns	"Cow placenta hair tonic lotion can be as effective as minoxidil 2% in women with AGA because 67.5% of individuals treated with cow placenta showed increased hair growth at the end of the sixth month of treatment."	Effect of a cow placenta hair tonic lotion in female AGA similar to 2% MNX.	No information on the full composition and conc. in the commercial placenta product. .	Moderate	[10]
Placental protein, Hydrolyzed placental protein	.Prospective , site-to-site controlled study	I: : An in-house prepared serum with porcine placenta extract (PPE), rubbed twice a day on a shaved area (leave-on).	C: untreated shaved patch in the same P? (description imprecise)	Healthy humans	12 volunteers P, aged 25–40	1 mo	1 mo	Hair length	Re-growth of shaved hair significantly faster in treated areas (mean +23.65%, $p<0.05$ after 2 wk and +55.73%, $p<0.05$ after 1 mo) as compared to untreated areas.	"The serum-containing PPE was able to stimulate hair growth."	The tested PPE serum significantly accelerated growth of shaved hair in healthy people	Imprecise description of the human trial part, undisclosed conc. of placenta, small sample size, hair shaving not be an adequate model for effluvium or alopecia	Low	[11]

Abrreviations: AGA – androgenic alopecia; TE – telogen effluvim; FPHL- female pattern hair loss; compl. – completed; conc. - concentration; F – female(s); I – intervention (verum, test treatment); incr. – increase(d); decr. – decrease(d); C – comparator (placebo, sham treatment); P – participant(s); M – male(s); PA – participant's assessment; IA – investigator's assessment; quest. – questionnaire; ns – non significant; nass – no assessment of statistical significance reported; mo – month(s); w- week(s); d- day(s); MNX- minoxidil; nd- no data.

The publications shown in shaded fields were already used as source of data and discussed in detail in the following articles:

- Szendzielorz, E.; Spiewak, R. Placental Extracts, Proteins, and Hydrolyzed Proteins as Active Ingredients in Cosmetic Preparations for Hair Loss: A Systematic Review of Available Clinical Evidence. Appl. Sci. **2024**, 14, 10301. https://doi.org/10.3390/app142210301
- Szendzielorz, E.; Spiewak,R. Caffeine as an Active Molecule in Cosmetic Products for Hair Loss: Its Mechanisms of Action in the Context of Hair Physiology and Pathology. Molecules **2025**, 30, 167. https://doi.org/10.3390/molecules30010167
- Szendzielorz, E.; Spiewak, R.. Caffeine as an active ingredient in cosmetic preparations against hair loss: A systematic review of available clinical evidence. Healthcare. **2025**, 13, 395. https://doi.org/10.3390/healthcare13040395

- Szendzielorz, E.; Spiewak, R. Adenosine as an Active Ingredient in Topical Preparations Against Hair Loss: A Systematic Review and Meta-Analysis of Published Clinical Trials. Biomolecules **2025**, 15, 1093, doi:https://doi.org/10.3390/biom15081093

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1. Faghihi, G.; Iraji, F.; Rajaee Harandi, M.; Nilforoushzadeh, M.A.; Askari, G. Comparison of the efficacy of topical minoxidil 5% and adenosine 0.75% solutions on male androgenetic alopecia and measuring patient satisfaction rate. *Acta Dermatovenerol. Croat.* **2013**, *21*, 155-159.
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7. Bussoletti, C; Mastropietro, F.; Tolaini, M.V; Celleno, L. Use of a Caffeine Shampoo for the Treatment of Male Androgenetic Alopecia. J. Appl. Cosmetol. 2010, 28, 153-162.
8. Sisto, T.; Bussoletti, C.; Celleno, L. Role of a Caffeine Shampoo in Cosmetic Management of Telogen Effluvium. *J. Appl. Cosmetol*. **2013**, 31, 139-145.
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Table S2. An overview of clinical trials on the efficacy of the substances of interest to the present paper tested in complex topical preparations against hair loss.

Name of substances	Study design	Preparation and application	Comparator preparation and application	Inclusion criteria	Number of patients, gender	Duration of treatment	Duration of follow-up	Outcome measures	Main reported outcomes	Authors' conclusion in the article	Reviewers' summary	Remarks/ Factors influencing level of evidence	Evidence level (GRADE)	Ref.
Achillea millefolium extract, Urtica dioica root extract and 4 other "active" ingredients	Placebo-controlled, single-blind, clinical-instrumental study	I: Group A: 30 subjects that used 5ml herbal (active) shampoo with Urtica urens leaf extract, **Urtica dioica root extract**, Matricaria chamomilla flower extract, **Achillea millefolium** aerial part extract, Ceratonia siliqua fruit extract, Equisetum arvense leaf extract)- (rinse off). Group B: 30 subjects that used 3ml herbal (active) solution with the same active ingredients as shampoo-(rinse-off). Group C: 30 subjects that used 5 ml herbal (active) 3ml shampoo (rinse off) and herbal (active) solution. (leave on)	C: Group D: 30 subjects that used 5 ml placebo shampoo and 3 ml placebo solution without herbal solution.	M and F with AGA , Hamilton-Norwood stage II-III or TE	60 M and 60 F, aged 20-55, 54 P with AGA, 66 P with TE	6 mo	6 mo	Pull test for each month, phototrichogram , dermatological evaluation, PA	Pull test: Group C had the best clinical outcomes and Group D had the worst. Phototrichogram: no increase in group D during the study, the number of total hairs in groups A, B and C increased significantly in month 4 and 6 month. SE: Group C also has the best clinical outcomes and Group D the worst.	" The results obtained in this study show that the tested products have a eutrophic effect on the scalp hair due to the antiandrogenic, anti-inflammatory, antioxidant, angiogenic and hair stimulating properties of the mixture used. These properties together help prevent "hair loss" and reduce hair loss."	The best clinical outcomes had group C, and the worst group D (placebo).	More than one active ingredient makes it impossible to assess the effectiveness of Achillea millefolium.	Moderate	[1]
Adenosine, Caffeine	Randomized, controlled, single-blind study	I: Shampoo with 0.4% **caffeine** and 0.2% **adenosine**. 10 g of product applied three times a week (rinse-off)	C: Same shampoo without caffeine and adenosine. Same mode of application.	Healthy F and M with self-perceived "thinning hair", Ludwig grade I-1, I-2 or I-3 (F), Norwood Type 2, 2A,	84 P aged 20-60 , 77 P compl. the study	3 mo	3 mo	Hair density photographs, dermoscopic hair analysis system, hair loss count at combing, hair diameter micrometry, satisfaction	Mean hair density in I group incr. from 118.25 to 130.03 hairs/cm² (up 9.96%, $p<0.001$), "no significant changes" in C group (data not shown). Mean hair loss at combing decr. in I group from 27.19 to 17.53 (down 35.5%, $p<0.001$), and in C	"The shampoo containing 0.4% caffeine and 0.2% adenosine exhibited efficacy in regard to reducing hair loss and for hair density enhancement	Increased hair density and reduced hair loss after shampoo with caffeine and adenosine. No such effect after sham shampoo.	Not clear how much of the effect is attributable to adenosine. Study not blinded on investigator's side.	Low	[2]

				3 or 3A (M), age >18 years.				scores on PA (quest.)	group from 24.97 to 19.94 (down 20.1%, ns)	after 3 months compared to the baseline."		Single center study .		
Adenosine, Biotin and 5 other „active" ingredients	Open-Label Prospective Clinical Study	I: lotion with oleanolic acid, apigenin, biotinyl tripeptide-1, 2-4diamino pyrimidine-3-oxide, **adenosine**, Ginkgo biloba, and **biotin** applied once a day before bed - (leave on).	----------	M and F with AGA and TE	56 M and F, 24 P with TE and 32 with AGA, aged 25-50	6 mo	6 mo	Fototrichogram, PA quest.	In P with AGA plus TE was a statistically significant increase ($p<0.05$) in the number of anagen hairs and the total number of hairs after 90 and 180 days of treatment.	"When extrapolated from the test area to the whole scalp area (taken to be 500 cm2) this increase represented 5598.2 more hairs per patient at the end of the study."	In the self-assessment questionnaire, the product was rated highly in terms of both effectiveness and cosmetic value - 79%-86%. P were satisfied with the results and would recommend the product regardless of price.	No placebo, and method of measuring effects that is not very reliable, more than one active ingredient makes it impossible to assess the effectiveness of adenosine.	Very low	[3]
Adenosine, Panthenol and other 1 „active" ingredient	In vivo, ex vivo, and Randomized study in vitro	I: 1 ml adenosine complex (0.75% adenosine, 1% panthenol, and 2% niacinamide, APN), applied once a day (leave on)	C: 1 ml 5% MNX solution, once a day	M and F with AGA	46 volunteers with AGA, 27 M and 19 F	4 mo	4 mo	Fototrichogram	Hair density significantly increased in the MNX (from 168.1 to 176.5 number/cm2) and APN (from 168.1 to 176.5 number/cm2) groups	"Adenosine showed anti-androgenic activity in vitro and ex vivo in the elongated anagen stages."	The adenosine complex enhanced scalp health and was more susceptible to hair thickness growth via anti-androgenic activity.	More than one active ingredient makes it impossible to assess the effectiveness of adenosine.	Low	[4]
Arginine, Piroctone olamine and 3 other „active" ingredients	Open-label, observational, international real-life study	I: AC 5- product with 2,4-diamino-pyrimidine-N-oxyde (DPNO), **arginine**, 6-O glucose linoleate (SP94), **piroctone olamine,** and Vichy mineralizing water (VMW) as active ingredients applied once a day- (leave on).	----------	M and F with mild AGA, Hamilton-Norwood stage II-IV for F and Ludwig scale 0-1 for F	527 P, F= 59,9%, the mean age was 33.6±8.7 years	3mo	3 mo	PA	Hair loss was reduced in 89.0% of subjects; it was slightly higher in W (92.5%) than in M (83.8%). P satisfaction on a scale from 0 (not satisfied at all) to 10 (completely satisfied) was 7.9±1.7. Tolerance was rated good to very good by 98.6% of all P.	"Alopecia was progressive in 70.7% (251/355) of subjects more in men (83.3%, 115/138) than in women (62.7%, 136/217). Subjects applied AC5 for 82.9 ± 17.5 days; 94.8% (398/420) applied AC5 once daily while 5.2%	AC5 met the P expectations in 89.0%, more W (91%) than M (85,9%). AC5 improves hair loss and hair quality in subjects with mild AGA with an excellent tolerability, a pleasant texture, and a	No placebo group, more than one active ingredient makes it impossible to assess the effectiveness of arginine.	Very low	[5]

										(22/413) used it twice a day. Overall compliance was 95.9 ± 6.6%, with no notable difference between W and M."	high satisfaction rate.			
Arginine, Caffeine, Hydrolyzed Wheat Protein, Hydrolyzed Soy Protein, Prunus amygdalus dulcis, Rosmarinus officianalis and 19 other "active" ingredients	Open-label, single-center, prospective, single-arm, non-comparative study	I: 0,5 ml serum with Aqua, Hamamelis Virginiana Water, PEG/PPG-17/6 Copolymer, Propanediol, Pentavitin, Niacinamide, Pseudozyma Epicola, **Prunus Amygdalus Dulcis** Oil, Camellia Japonica seed Oil, Argania Spinosa Kernal Oil, Helianthus Annuus Seed Oil, Camellia Sinensis Seed Oil, Hydrolyzed Corn Protein, **Hydrolyzed Wheat Protein, Hydrolyzed Soy Protein, Caffeine, Arginine, Rosmarinus officianalis Lead oil,** Polysorbate 20, Acrylates/C10-30, Alkyl Acrylate Crosspolymer, Phenoxyethanol, and Ethylhexylglycerin .applied on the scalp once a day- (leave on).	C:----------	F and M with hair loss (alopecia),	32 P enrolled, 29 P compl.: 15 F and 14 M aged 18-45 years	60 d	60 d	Pull test, phototrichogram , PA and IA (quest.)	Hair growth rate incr. by 32% (p<0.01) Hair thickness incr. by 34% (p<0.01) Hair density incr. by 40% (p<0.01) Anagen hair incr. from 57% to 80% (nass) Telogen hair decr. from 43% to 20% (nass) "Up to 42% reduction in hair fall" (nass) Decr. in scalp itchiness (p<0.01), redness (p<0.01), roughness (p<0.01), scaliness (p<0.01), and dryness (p=0.02).	"(…) after 60 days of use, the hair serum demonstrated effectiveness and good tolerance in improving hair growth, thickness, and strength while reducing hair loss"	Impr. of hair condition and growth after treatment with a complex product including Prunus Amygdalus Dulcis.	Lack of randomization and control, no information on conc. of caffeine and other "active" ingredients in the products. Not clear how much of this is attributable to caffeine. Single center study. Research funded by producer of the commercial product tested.	Very low	[6]

Biotin, Panthenol and 3 other „active" ingredients	.Randomized, controlled study	I: lotion with Acetyl tetrapeptite-2, **Biotin** (vitamin B8), Creatine, Panthenol (provitamin B5), Pyridoxine HCL (vitamin B6) three times per week to a dry scalp - (leave on).	C: mild shampoo	F with Fitzpatrick skin phototypes I–IV and TE confirmed by a positive pull test	100 F, aged 19-50	16 w	16 w	Phototrichogram, pull test, global photographs	Telogen hair reduction was greater in the intervention group than in the control group at week 8 (31.8% vs. 13.5%, P = 0.0392) and week 16 (43.6% vs. 33.1%, P = 0.0584)	"The lotion reduced hair shedding earlier and led to a faster reduction in telogen hair density compared to the use of a neutral shampoo alone."	The level of P satisfaction was high with 49 P/50 P (98%) reporting improvement after 16 weeks of using the lotion.	More than one active ingredient makes it impossible to assess the effectiveness of biotin	Low	[7]
Biotin and 4 other „active" ingredients	no data	I: topical preparation with **biotin,** Thioglycoran, HUCP, Thurfyl nicotinate and Sodium pantothenate applied once a day- (leave on).	----------	Group A1- 4 healthy P, group A2- 5 P with hair loss, group B1- 4 P with AGA Hamilton stage II-IV, group B2- 5 with thinning hair and marked defluvium, but lower than the previously mentioned degrees.	18 P, aged 23-32	60 d	60 d	The morphometric computerized analysis applied to photographic images	Total mean lengths pre/post-treatment t = 3.5131 P<0.01 t, active phase growth elements pre/post-treatment t = 4.89 P <0.001 t , lengths of only active growth phase elements pre/post-treatment t =3.1552 P<0.01 t and Growth with respect to base value pre/post-treatment t = 5.7718 P<O.OOl t for coupled data.	"The pre-treatment differences, between the groups under examination and particularly between subjects with and without hair pathology, were statistically confirmed by the different percentage of elements in active growth phase as well as by the measurement of mean lengths".	The difference between the group of alopecia P and the group of apparently healthy P was remarkable.	No placebo group, the application time was to short, more than one active ingredient makes it impossible to assess the effectiveness of biotin.	Very low	[8]
Biotin and 5 other „active" ingredients	Prospective study	I: 2 ml topical formulation with minoxidil 10%, finasteride 0.1%, **biotin 0.2%,** and caffeine citrate 0.05% hydroalcoholic solution, applied twice a day- (leave on).	----------	M with AGA	5 M with AGA, aged 41-71	6 mo	6 mo	Photographs with a Nikon D-70 digital camera, PA quest.,	80% of patients stated that the appearance of their hair was "significantly improved" and 60% of patients only "agreed" that their baldness was decreasing. When asked about the effectiveness of the treatment, 60% of patients classified it as "very effective" while 40% of patients classified it as "somewhat effective".	"Clinical improvement was moderate but noticeable, as most patients had thicker, more abundant hair; scalp coverage improved; and overall hair appearance improved."	Patients demonstrated improvement in hair loss as evidenced by expert clinical evaluation, photographic evaluation, and patient satisfaction.	No placebo group, small group of P, more than one active ingredient makes it impossible to assess the effectiveness of biotin	Very low	[9]

Melatonin, Biotin and 1 other „active" ingredients	(Study 2; MEL-COS-AS01) Open-label observational study	I. lotion (leave-on) with *melatonin* 0.0033%, Ginkgo biloba, biotin	C: ----------	M with AGA, Hamilton-Norwood stage I-II, F with AGA, Ludwig stage I-II	30 M and F with AGA, aged 18-40	3 mo	3 mo	IA, PA quest.	Significant reduction in the severity of alopecia was found after just 30 days, which was again significantly increased after 90 days ($p < 0.001$)	"Satisfaction with the product was rated at 1.80 out of 2 points, and intolerance was rated at 0.54 after 30 days and 0.52 out of a maximum of 3 points after 90 days."	After 30 days, there is a significant reduction in the severity of symptoms, and after 90 days, hair loss has significantly decreased.	No placebo group and method of measuring effects that is not very reliable.	Very low	[10]
	(Study 3; MEL-COS-AS03) Open-label observational study	I: the same	C: ----------	M with AGA, Hamilton-Norwood stage I-II, W with AGA	35 M with AGA, aged 18-41	6 mo	6 mo	TrichoScan	Hair density increased by 29.1% and 40.9% at 3 and 6 months. Hair density values also differed significantly ($p < 0.001$). Improvement in hair loss was observed in 26.6% (day 30), 48.2% (day 90) and 32.1% (day 180)	"After a treatment period of 30, 90 and 180 days, according to the subjective questionnaires, 30%, 34.5% and 29% of the subjects were satisfied with the treatment and 70%, 58.6% and 58.0% were largely satisfied, whereas the proportion of subjects who were not satisfied with the treatment during the course of the study was relatively low at 0% (30 days), 6.8% (90 days) and 12.9% (180 days).	Melatonin hair solution was rated by 93.5% of respondents as good (80.6%) or very good (12.9%).	No placebo group and method of measuring effects that is not very reliable.	Very low	
	(Study 4; MEL-COS-AS04) Open observational study	I: the same	C: ----------	40 M and 20 F with early stages of hair loss or thinning hair.	60 P, average age 41 years	90 d	90 d	IA	Improvement in hair texture, which reached statistical significance in both the female and male groups ($p = 0.002$ and $p = 8 \times 10–5$, respectively). Reduction in hair loss,	"Regarding satisfaction with the treatment, a trend towards improvement was observed in the entire group, with satisfaction	Hair loss decreased significantly in the female group within the first 40 days and significantly	No placebo group and method of measuring effects that is not very reliable.	Very low	

								which was also statistically significant in both the female and male groups (p = 4 × 10–6 and p = 3 × 10–5, respectively).	increasing significantly in the female group (p = 0.002) and remaining almost unchanged in the male group."	again in the second 40 days, while remaining almost constant in the male group throughout the study.			
	(Study 5; MEL-COS-AS05) Open multicenter study	I: the same	C:----------	910 M with AGA in Hamilton stage I-II and 990 F with AGA in Ludwig stage I-II	1800 P	90 d	90 d	Pull test and semi-quantitative test to examine hair loss activity	The treatment led to significant improvement in hair loss in 59.4% and 66.4% of subjects at day 30 and 90 (p < 0.001), while 4.5% and 22.5% of subjects also showed hair growth (p < 0.001).	"The majority of 74.4% of the subjects were satisfied with the cosmetic effects after a 90-day treatment period, 23.3% were moderately satisfied, and a small percentage of 2.3% were not satisfied with the result."	According to the doctors and the subjects, the melatonin solution was more effective in improving hair loss than other previously used products.	No placebo group	Very low	
Caffeine with 9 other "active" ingredients	Prospective, singe center, randomized, double-blind, vehicle-controlled study	I: foam with a composition of 10 "active" ingredients including caffeine (undiscl. conc.). 1 g of product applied twice a day- (leave-on).	C: foam vehicle not containing the composition of 10 "active" ingredients. Same mode of application.	M with AGA, Hamilton-Norwood stage II-VII	62 M recruited, aged 19-67, 29 P compl. the I arm, 30 P compl. the C arm	6 mo	6 mo	Phototricho-gram. IA (quest.) and PA (quest.)	Reduction of telogen rate in the I group greater than in C group (p = 0.02). No significant differences between I and C groups on IA and PA.	"The study demonstrated a reduction of the telogen rate by a cosmetic foam in men affected by AGA"	The test foam (complex of 10 ingredients including caffeine) significantly reduced telogen rate in men with AGA compared to the vehicle foam after 6 months.	No information on conc. of caffeine and other "active" ingredients. Not clear how much of this effect is attributable to caffeine. Single center study.	Modera te	[11]

Caffeine and 24 other "active" ingredients	.Single center, open-label, prospective, observational, real-world study	I: serum in a roller with a complex mixture of 24 (M) or 27 (F) ingredients, including caffeine at position 6 (undiscl. conc.). Roller applied twice a day (leave-on).	C:----------	M and F with mild to severe AGA	150 P enrolled (90 F, 60 M), all compl. the study, aged 18-75	8 w	8 w	Photography, P-filled quest. Phototrichogram in 7 P.	Hair thickness incr. in crown (17%, p<0.05), vertex (15%, p<0.05) and frontal (10%, ns) areas. Hair density incr. in crown (24%, p<0.05), vertex (12%, p<0.05) and frontal (2%, ns). PA: Decr. in hair shedding declared by 100% P, incr. frequency of new hair (90%), incr. in hair growth, hair volume, scalp coverage and amount of hair regrowth (each 80%).	"we show that twice-daily use of the novel topical serum (...) led to meaningful improvements in hair growth with high patient satisfaction and no side effects."	Significant impr. in hair parameters in crown and vertex, but not frontal area. High satisfaction rates.	Lack of randomization, no comparator, short follow-up, small group on trichogram (7 P). No information on conc. of caffeine and other "active" ingredients in the products. Not clear how much of this is attributable to caffeine. Single center study. Research funded by producer of the commercial product tested.	Very low	[12]
Caffeine and 2 other "active" ingredients	Single center, open-label, prospective study	I: liquid with a complex mixture of Procapil™ 3%*, caffeine (undiscl. conc.), and zinc PCA (undiscl. conc.). Undiscl. amount of product was applied on the scalp once a day-(leave-on).	C: ----------	M with AGA, Hamilton-Norwood stage II–IV	20 P enrolled (all M), aged 18-57	12 w	12 w	Photography, combing test, trichoscopic assessment, P satisfaction	IA: "impr. hair growth" by 68.5% and 68.4% after 6 and 12 w. Decr. in hair loss by 26.9% in combing test after 12 w (p=0.026). Terminal/vellus hair ratio incr. by 53% after 12 w (p=0.028). Incr. in the anagen/telogen ratio by 12.8% after 12 w (ns). No change in total hair count and density after 6 and 12 w (ns). PA: "impr. hair" reported by 12.8% after 6 and 84.2% after 12 w.	"this study found a 12-week treatment course with a topical formulation containing caffeine and Procapil 3% a beneficial and promising treatment for AGA"	Improvement in hair growth, decrease in hair loss, incr. terminal hair. High satisfaction rates.	Lack of randomization and control, no information on conc. of caffeine and other "active" ingredients in the products. Not clear how much of this is attributable to caffeine. Single center study.	Very low	[13]

											Research funded by producer of the commercial product tested.			
Panax ginseng and 3 other „active" ingredients	Prospective, Randomized, Triple-blind, Controlled Trial	I: 1 ml herbal extract with acetyl tetrapeptide-3, biochanin A (red clover extracts), **Panax Ginseng extract**, and Salvia officinalis oil. twice a day- (leave on).	C: 1 ml 3% MNX, twice a day	16 M with AGA Hamilton-Norwood stage III- IV and 16 F with FPHL Ludwig stage I-II	32 M and F, aged 18-55	24 w	24 w	Global photographs, dermoscopic photographs, Hair Mass Index (HMI) using cross-section trichometry, P quest.	12.5% and 21% of the herbal extract combination and 3% minoxidil groups showed excellent improvement. The response in the frontal region was lower than in the vertex region in both the herbal extract combination (87.5%) and 3% minoxidil (85%) groups. At week 24, significant clinical improvement was observed, with an increase in terminal hair count of 8.3% (P=0.009) and 8.68% (P=0.002) with the herbal extract combination	"Expert panel photographic evaluation of the top of the head at week 24 revealed a 100% response in both the herbal extract combination and 3% minoxidil treatment groups."	The lack of difference in clinical efficacy and safety between herbal extract and 3% minoxidil solution suggests that a combination of herbal extracts may be an alternative treatment for AGA	More than one active ingredient makes it impossible to assess the effectiveness of Panax ginseng	moderate	[14]
Panthenol, Placental protein, Hydrolyzed placental protein and other 2 "active" ingredients	Prospective study without a control group	I: shampoo and the hair tonic with equine **placental growth factor** (PIGF), pumpkin extract, **panthenol**, and niacinamide applied 2-3 times a day- (rinse off).	C:----------	F with postpartum hair loss	25 F, aged 27-40	3 mo	3 mo	Photographs with a Folliscope P quest.	Both hair thickness and density improved. Hair thickness at the vertex improved from 0.089 μm at baseline to 0.094 μm at 3 months (P= 0.028), and hair density at the occiput increased significantly from 75.24/cm2 at baseline to 81.33/cm2 at 3 months (P<0.001). Hair density at the vertex improved from 79.28/cm2 at baseline to 87.56/cm2 at 3 months (P= 0.866), and hair thickness at the occiput increased from 0.085 μm at	"After 3 months, some participants complained of pain and "discomfort, such as itching and slippery, respectively. When participants rated their satisfaction with the shampoo and toner on a scale of 1 to 5 points, fragrance received 3.22 points, refreshing feeling received 3.87 points, hair shine	A significant number of participants subjectively felt that their hair loss worsened after childbirth, although a trend towards overall satisfaction was observed.	No placebo group. More than one active ingredient makes it impossible to assess the effectiveness of panthenol and the effectiveness of the preparations was mainly attributed to horse	Very low	[15]

									baseline to 0.093 µm at 3 months (P= 0.068).	received 2.78 points, hair elasticity received 3.13 points, and residual odor received 3.00 points."		placenta, which is the main constituent of PIGF.			
Piroctone olamine and 2 other „active" ingredients	Pilot study	I: 5,5 ml lotion with antimicrobials**, 0,25 % piroctone olamine** and 0,3 % triclosan one a day and nonmedicated mild shampoo- (leave on).	C: ----------	M with AGA, Hamilton-Norwood and Olsen stage I-IV	20 M with AGA, aged 26-48	18 mo	18 mo	Trichogram, clinical photographs and biopsy	"Long-term use of the lotion resulted in a gradual decrease in the severity of AGA, as assessed by both clinical photographs and the HCD index. A negative logarithmic correlation (r = -0.64, Pc0.01) was found between the HCD index and the treatment time. Compared to the initial HCD index (48.6 f 15.6), significant (Pc 0.05) improvement was achieved at month 6 (37.8 f 13.3) and was maintained thereafter. Self-assessments of hair loss by the subjects followed a similar negative logarithmic (t = -0.56, Pc 0.01) trend of improvement"	"The mean size of the sebaceous glands and the mean diameter of the hair shaft remained unchanged during the study."	Clinical photographs and a trichogram showed that long-term use of the lotion led to a significant reduction in some immunoinflammatory aspects and, consequently, changes in the hair cycle.	No placebo group	Very low	[16]
Rosmarinum officinalis, Serenoa serrulata and other 2 „active" ingredients	Randomized, double-blind controlled trial	I: 5% minoxidil in the morning and the topical herbal solution with **Rosmarinus officinalis** Linn., Olea europaea L., and lipidosterolic extract of **Serenoa serrulata** in the evening- (leave on).	C: 5% MNX applied twice a day	M with AGA, Hamilton-Norwood stage III-V	24 M with AGA, aged 18-50	36 w	36 w	Hair diameter was recorded by a digital micrometer, global photographic and PA quest.	The mean hair density in Group C was 94.67 hairs/cm2, which increased slightly from the mean hair density at baseline of 94.08 hairs/cm2 (P = 0/171). In contrast, the mean hair density in Group C was 96.92 hairs/cm2, which increased from the mean hair density at baseline of 93.83 hairs/cm2 (P = 0.003). After completing the questionnaire, there were statistically significant differences between the two groups in terms of increased hair growth, decreased hair loss, and	"During the 36-week treatment period, the mean hair diameter decreased in group C and increased in group I in both treatment groups, mean hair density increased at week 36 of treatment."	The most important observation of this study was that the topical herbal solution as a part of combined therapy can enhance the efficacy of single-agent preparations.	More than one active ingredient makes it impossible to assess the effectiveness of Rosmarinum officinalis.	Moderate	[17]

									improved hair appearance ($P < 0.05$).					
Serenoa serrulata, Piroctone olamine and other 3 "active" ingredients	pilot, prospective, open, within-subject	I: 3,3 ml serum for the first 4 weeks with **Saw palmetto (serenoa serrulata)** Green tea extract Peony root extract **Piroctone-olamine** Oligopeptides- (leave on), and 2 ml lotion until the end of study shampoo with the same ingredients as serum but not as Concentrated and shampoo with Oligopeptides Multivitamins- (rinse off).	C:----------	M volunteers with AGA, Norwood–Hamilton stage III, IIIv, IV and V	50 M with AGA, aged 20-50	24 w	24 w	Macrophotographic technique using the Canfield photography system, global photographic, IA and P quest.	"The number of terminal hairs increased at both weeks 12 and 24, with week 24 being better than week 12. There was also a significant decrease in the number of vellus hairs (statistically significant between weeks 0 and 24 and weeks 12 and 24). For the photographic assessments, the investigators reported a slight increase in hair on the anterior and vertex scalp, statistically significant at time points 0 to 12, 12 to 24, and 0 to 24 weeks."	"On the hair growth satisfaction scale, median scores were significantly higher by two to three points out of seven in all categories at weeks 12 and 24, compared to baseline."	The best results were achieved in the first 12 weeks, after which the effects decreased, suggesting that the use of a more concentrated serum is a more effective method than the use of a lotion.	No placebo group. More than one active ingredient makes it impossible to assess the effectiveness of Serenoa serrulate.	Very low	[18]

Abrreviations: AGA – androgenic alopecia; TE – telogen effluvim; FPHL- female pattern hair loss; compl. – completed; conc. - concentration; F – female(s); I – intervention (verum, test treatment); incr. – increase(d); decr. – decrease(d); C – comparator (placebo, sham treatment); P – participant(s); M – male(s); PA – participant's assessment; IA – investigator's assessment; quest. – questionnaire; ns – non significant; nass – no assessment of statistical significance reported; mo – month(s); w- week(s); d- day(s); MNX- minoxidil; nd- no data.

The publications shown in shaded fields were already used as source of data and discussed in detail in the following articles:

- Szendzielorz, E.; Spiewak, R. Placental Extracts, Proteins, and Hydrolyzed Proteins as Active Ingredients in Cosmetic Preparations for Hair Loss: A Systematic Review of Available Clinical Evidence. Appl. Sci. **2024**, 14, 10301. https://doi.org/10.3390/app142210301
- Szendzielorz, E.; Spiewak,R. Caffeine as an Active Molecule in Cosmetic Products for Hair Loss: Its Mechanisms of Action in the Context of Hair Physiology and Pathology. Molecules **2025**, 30, 167. https://doi.org/10.3390/molecules30010167
- Szendzielorz, E.; Spiewak, R.. Caffeine as an active ingredient in cosmetic preparations against hair loss: A systematic review of available clinical evidence. Healthcare. **2025**, 13, 395. https://doi.org/10.3390/healthcare13040395
- Szendzielorz, E.; Spiewak, R. Adenosine as an Active Ingredient in Topical Preparations Against Hair Loss: A Systematic Review and Meta-Analysis of Published Clinical Trials. Biomolecules **2025**, 15, 1093, doi:https://doi.org/10.3390/biom15081093

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