A systematic review of randomized controlled trials assessing phytochemicals and natural ingredients for skin and hair care

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Table 2: Summary of randomized controlled trials (RCTs) conducted between 1998 and 2018 of plants, herbs, or isolated compounds used for hair care.

Hair care (*n* = 10)										
Author, year	**Country**	**Population (n)**	**Intervention (dose/method of application)**	**Comparison(s)**	**Outcome(s), p value**	**Method of testing**	**Duration**	**Scientific name of plant used**	**Parts used**	**Dosage form**
Baldness										
Hay IC et al., 1998	Aberdeen, Scotland	Alopecia areata patients (86)	Massaging aromatherapy oils into scalp for at least 2 mins, then wrapping warm towel around head every night	Placebo of carrier oil without essential oils	1. Equal distribution of patients by 4-point scale 2. Statistically significant improvement ($p<0.05$) in photographic assessment in the intervention group 3. Measurement of traced alopecia areas was reduced significantly ($p=0.05$) in the intervention group	1. Four-point severity scale to ensure equal baseline characteristics in both groups 2. Photographic assessment by 2 independent dermatologists (primary outcome) 3. Calculated area of alopecia (secondary outcome)	7 months	*Thyme vulgaris, Lavandula agustifolia, Rosmarius officinalis, Cedrus atlantica* (in jojoba and grapeseed carrier)	-	Aromatherapy oils
Kamimura A et al., 2000	Japan	30–57-year-old healthy males (29) with male pattern baldness	1%(w/w) procyanidin B-2 tonic preparation Directions for use: For 6 months, 1.8 ml of the test agent was applied to the subjects' affected area of	Placebo	1. Change in hair density: the increase in hair density in the procynadin B-2 group after 6 months was statistically significant compared to placebo ($p<0.005$) 2. Terminal hair formation: the increase in the number of terminal hairs in the procynadin B-	1. Determination of change in hair density from a predetermined site photographed by a camera fitted with macrolens 2. Determination of terminal hair formation was measured using a micrograph-equipped microscope at a	26 weeks	*Malus pumila* Miller var. domestica Schneider	Fruit juice	Tonic

			the head twice a day, resulting in a daily dose of 30 mg of procyanidin B-2. No use of other hair care products except shampoos and rinses were permitted during the clinical trial.		2 group after 6 months was statistically significant compared to placebo ($p<0.02$)	magnification of x 300				
Sasmaz S et al., 2005	Turkey	Subjects with patchy alopecia areata (31)	20% azelaic acid Direction for use: applied twice daily on the affected area for 12 weeks	0.5% anthralin (dithranol) Direction of use: applied in sparing applications for a short contact time (15 minutes) for 2 weeks and then, if tolerated, to be continued for 10 weeks with 30 minutes contact time	1. At week 20 the RGS was 1.27 ± 0.9 in the azelaic acid group versus 1.37 ± 0.8 in the anthralin group ($p>0.05$). A complete response was observed in (8 of 15) 53.3% of cases in the azelaic acid group compared with (9 of 16) 56.2% in the anthralin group ($p>0.05$) 2. No serious adverse events were observed in either group	1. Terminal hair regrowth score (RGS) with a scale ranging from 0 (inadequate response) to 2 (complete response) at week 20	12 weeks then 8 weeks of follow-up without cream use	-	-	Cream
Choi JS et al., 2015	Korea	28–68-year-old males and females suffering from alopecia areatea (50)	0.5 % Rice bran supercritical CO_2 extract (RB-SCE) tonic product Directions for	Placebo	1. Phototrichography: hair density did not differ significantly in 8 weeks (active vs placebo group) but significantly increased after 16 weeks in the active group ($p<0.034$) in	1. Phototrichography (hair density, hair count, and diameter by Folliscope) 2. Expert Panel Assessment of Global Photograph	16 weeks	*Oryza sativa* L. var. japonica	Supercritical CO_2 extract	Tonic product

			use: treat the scalp with 4 mL of solution once or twice a day at approximately 12-h intervals (total daily dose of 8 mL)		males only 2. Hair diameter: in the active group, hair diameter was significantly increased from week 8 to week 16 ($p<0.05$) compared to the placebo group in both males and females 3. Expert panel assessment of Global Photographs: at 16 weeks, the experts observed improved hair growth in the RB-SCE group compared to placebo ($p<0.05$) in males. However, outcome was insignificant at 16 weeks in the females group 4. Patient satisfaction questionnaire: the overall satisfaction of the RB-SCE group was significantly higher than that of the placebo group at 16 weeks ($p=0.005$) 3. Skin Tolerance and Safety Evaluation: in all 43 subjects, no adverse reactions (i.e. itching, prickling, burning, stinging, stiffness, tightness, burning of the eyes, weeping, erythema, edema, scaling, papule, or any other RB-SCE-related	3. The patient questionnaire assessment 4. Skin tolerance and safety evaluations by clinical observation				

					reactions) were noted					
Pekmezci E et al., 2018	Turkey	20–55-year-old adult suffering from telogen effluvium or androgenic alopecia (120)	Group A: herbal shampoo, Group B: herbal solution, Group C: herbal shampoo + placebo solution, Group D: placebo shampoo + placebo solution Directions for use: Shampoo: Every other day, three times a week, apply 5 ml on wet hair, wait for 3 to 4 minutes after foaming, and then rinse well. Solution: Every day in the morning and in the evening, apply 3 ml on dry hair and massage all over the scalp. Let it stand for at least 4 to 6 hours.	Placebo	1. Pull test: statistical analyses revealed significant improvement in all groups for all months compared to baseline. It is noted that group C (active shampoo + solution) had the best clinical outcomes ($p< 0.000001$) 2. Phototricogram: compared to baseline, the number of total hairs in groups A, B, and C (active groups) increased significantly in the 4th and 6th months. The decrease in telogen hairs and increase in anagen hairs were also significant in groups A, B, and C ($p<0.001$). The (%) changes in telogen and anagen hairs in group D were not significant ($p>0.05$) 3. Dermatological evaluation: results not reported 4. Self-assessment score: all questions showed statistically significant	1. Pull test 2. Phototricogram 3. Dermatological evaluation 4. Self-assessment score	26 weeks	*Matricaria chamomilla, Achillea millefolium, Ceratonia siliqua, Equisetum arvense, Urtica urens,* and *Urtica dioica.*	*Matricaria chamomilla:* Flower extract *Achillea millefolium:* Aerial part extract *Ceratonia siliqua :* Fruit extract *Equisetum arvense:* Leaf extract *Urtica urens:* Leaf extract *Urtica dioica:* Root extract	Shampoo or/and solution

					results based on the difference from placebo (group D) Group C had the best clinical outcomes ($p< 0.000001$) The products were well tolerated, and no side effects were recorded					
FAAD, G A M et al., 2018	US, New York	21–65-year-old healthy women with Fitzpatrick skin types I to IV and self-perceived thinning hair (40)	Oral nutraceutical supplement. Direction for use: 4 capsules daily with a meal or immediately after a meal at the same time each day	Placebo	1. Significant increase in the number of terminals, vellus, and total hair counts ($p<0.005$) in the intervention group compared to placebo 2. Significant and progressive improvement in IGHA and quality scales in the active group compared to placebo ($p<0.05$). no significant changes in terminal hair diameter 3. SAQ: there was a significant improvement in hair breakage and anxiety levels in the active group compared to the placebo group ($p<0.05$). Number of subjects who rate themselves as "improved" in the active group compared to placebo group was significantly higher changes in terminal hair diameter and	1. Determination of increase in terminal, vellus, and total hair counts using phototrichograms 2. Assessment of hair growth and quality, changes in terminal hair diameter, and bundle measurements using the blinded Investigator Global Hair Assessments (IGHA) 3. Responses in the subject self-assessment questionnaire SAQ, Ease of use, and QoL 4. Safety: changes in physical exam and potential adverse events (AEs)	6 months	Standardized extracts of *Ashwagandha*, curcumin, *Saw palmitto*, tocotrienol-rich tocotrienol/tocopherol complex, piperine, and capsaicin, hydrolyzed marine collagen, hyaluronic acid, and organic kelp	-	Capsules

					bundle measurements ($p<0.05$) Ease of use: 84.6% of the active subjects found it easy to add capsules to their daily routine, 88.5% of patients preferred oral capsules instead of topical application, and 73.1% would recommend the treatment to their friends 4. No treatment-related AEs were reported during the study					
Antidandruff										
Satchell AC et al., 2002	Australia	14 and older male and female patients suffering from mild-moderate dandruff (126)	5% tea tree oil shampoo Directions for use: Patients were asked to wash their hair daily, leaving the shampoo in for 3 minutes before rinsing, and were free to use a conditioner	Placebo	Tea tree oil shampoo showed significance improvement in terms of: 1. whole scalp lesion score ($p<0.001$) 2. total area of involvement score ($p<0.001$) 3. total severity score ($p<0.001$) 4. the itchiness and greasiness components of the patients' self-assessment compared to placebo ($p<0.05$)	1. Whole scalp lesion score 2. Area of involvement 3. Severity score 4. Subjective assessment of scaliness, itchiness, and greasiness using linear analog scale	4 weeks	*Melaleuca alternifolia*	Leaves extract (oil)	Shampoo
Herrera-Arellano et al., 2004	Mexico	15–45-year-old participants with pityriasis capitis who are affiliated with Mexican institute of	*S. chrysotrichun* extract (12.5%) mixed with neuter shampoo Direction for use: apply directly on	Ketoconazole (2%) mixed with neuter shampoo	1. Clinical effectiveness was similar between both groups at the end of the follow-up period (92.16% vs 86.54%; $p=0.35$) 2. Percentage of mycological effectiveness	1. Clinical effectiveness (signs and symptoms that were detected at basal condition) 2. Mycological effectiveness (direct examination and	4 weeks	*Solanum chrysotrichum*	Leaves	Shampoo

		social security (103)	damp scalp, rub until obtaining abundant lather, letting the shampoo act for 5 minutes, then rinse with clean water. to be repeated every third day for 4 weeks		was higher in ketoconazol group after two weeks of treatment ($p<0.05$), but the effect was reduced at the end of the treatment period, resulting in no statistical significance between both groups ($p>0.23$) 3. Both treatments were satisfactorily tolerated (tolerability percentage was 100% in both groups) 4. Rates of therapeutic effectiveness was similar between both groups at 2 and 4 weeks of treatment ($p>0.14$) 5. Given all of the above, therapeutic success was identical in both groups	culture) 3. Tolerability (local and systemic side effects) 4. Therapeutic success (by meeting all of the above)				
Salmanpoor R et al., 2013	Iran	14–17-year-old males and females with dandruff (203)	Group A: Liquorice 7% shampoo Direction for use: wash their hair twice weekly with the given shampoo (after discontinuing other topical products two weeks prior and during the study)	Group B: Selenium-sulfide 1% shampoo Group C: Placebo shampoo	1. The three shampoos significantly decreased DSS with the best result for selenium-sulfide 1% ($p<0.05$). 2. None of the shampoos significantly decreased scalp inflammation ($p>0.05$) 3. Pruritis decreased more in the selenium-sulfide 1% group (60%) compared to liquorice 7% group (37.5), but both treatments significantly reduced pruritis compared	)	4 weeks	*Glycyrrhiza glabra*	-	Shampoo

					to placebo 4. Around 33.8% of subjects who used liquorice reported less hair loss compared to selenium-sulfide (18.2%) and placebo (16.7%) 5. Liquorice shampoo caused the most eye irritation compared to selenium-sulfide and placebo ($p<0.05$) 6. There was no significant decrease in Pityrosporum ovale in all three groups ($p>0.05$)					
Chaijan MR et al., 2018	Iran	18–60-year-old males and females with dandruff (90)	1. *Myrtus communis* and vinegar solution 2. placebo shampoo 3. daily shampoo Directions for use: The patients were instructed to use the solution and shampoo once every 3-4 days. They used them 3 times before the second visit and 5 times between their 2nd and 3rd visits.	1. Ketoconazole 2% shampoo 2. Placebo shampoo 3. Daily shampoo	All dandruff indices improved from the baseline in both treatment arms by the end of the follow-up period ($p<0.001$) No significant difference was observed between treatment arms' efficacy, satisfaction rate, and side effects ($p>0.05$)	1. Dandruff Indices: a. Itching b. Excoriation pruritis grading (EPG) c. Adherent Scalp Flaking Score (ASFS) d. Redness of scalp skin e. Grading of scalp skin involvement 2. The patients' satisfaction and acceptance were evaluated using a visual analog scale (VAS)	1 Month	*Myrtus communis* L.	Leaves	Solution

			Also, they were asked to massage the antidandruff solutions on the scalp 3-5 minutes before going for a shower and then to wash their hair with the antidandruff shampoo. In addition, they were instructed to allow the shampoo foam to stay on their scalp for 5 minutes and after that to rinse it							