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

Samar Thiab1*, Nizam M. Mhaidat2, May Abu Taha1, Sarah Thiab1, Somaya Koraysh3, Reem Abutayeh1, Iman Basheti1
1Faculty of Pharmacy, Applied Science Private University, College of Pharmacy, Qatar University, Amman, Jordan.
2Director of Jordan Food and Drug Administration, Jordan University of Science and Technology, Ar-Ramtha, Jordan.
3Qatar University, Doha, Qatar.

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ABSTRACT
Cosmetics are marketed and used worldwide for various purposes. Several natural products are used for the development of cosmetic preparations. This paper systematically reviews randomized controlled trials (RCTs) investigating plant extracts, herbal preparations, and isolated plant-derived compounds used particularly for skin and hair care. Two independent electronic searches were conducted through PubMed and EMBASE to identify eligible RCTs. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was followed. Data extraction was performed independently by four authors based on standardized extraction forms. The risk of bias was assessed using the Cochrane Collaboration’s tool for assessing the risk of bias in randomized trials. Sixty-three RCTs were identified; 53 were using natural products for skin care and 10 for hair care. The results were summarized in tables including the population, type of intervention, comparisons with placebo or other natural products, outcomes reported, follow-up period (P: Patient; Population; I: Intervention; C: Comparison (or Control); O: Outcome; T: Time), and country in which the study was conducted. Ten plants were identified to be present in different locations in Jordan by referring to the Royal Botanic Gardens’ publication, titled “The Plants of Jordan: An Annotated Checklist.” Some plants were found to have promising findings requiring further investigations in bigger RCTs with robust design and adequate reporting.

INTRODUCTION
In the highly visual consumer culture, the appearance of body shape and beauty is gaining more attention from people as it has become an important factor in the individual’s sense of identity. The human body is the most visible expression of a person’s self (Domzal and Kernan, 1993; Shilling, 2017), and as a result, people have a high desire to be physically attractive (Kim and Seock, 2009). One way to do that is by using cosmetic products.

Cosmetics are globally used to enhance the appearance or body odor (Ashawat et al., 2009; Shivanand et al., 2010). Cosmetic products are developed in various dosage forms using natural and synthetic ingredients (Ashawat et al., 2009). The use of plants and herbs in cosmetics has gained more popularity in recent years (Ashawat et al., 2009; Gediya et al., 2011; Shivanand et al., 2010). The number of products containing natural ingredients is increasing (Antignac et al., 2011). These products are commonly used with the misconception that they are always more effective and safer than completely synthetic products (Antignac et al., 2011; Ashawat et al., 2009).

Several plants and herbs have the potential for the development of cosmetic preparations due to their chemical composition containing compounds like vitamins, minerals, flavonoids, tannins, and amino acids, which have the potential to influence the human body (Fonseca-Santos et al., 2015; Yoo et al., 2018).

The use of plants and herbs to enhance beauty is well known in the Middle East since around 3000 BC where it was commonly used by ancient Egyptians and Babylonians in Iraq (Sawicka and Noaema, 2015). In the Middle Eastern region, particularly in Jordan, a wide range of plants with medicinal activity are available (Aburjai et al., 2007; Afifi and Abu-Irmaileh, 2007).
The use of natural ingredients in cosmetics is gaining more popularity, not only for their health benefits but also due to the higher demand by consumers for ecologically friendly products (Laroche et al., 2001; Ribeiro et al., 2015).

This study systematically reviewed randomized controlled trials (RCTs) investigating plant extracts, herbal preparations, and isolated plant-derived compounds used for cosmetic purposes focusing on skin and hair care. In addition, it provides a list of the plants/herbs available in Jordan that have been studied in the literature for cosmetic purposes by referring to the Royal Botanic Gardens publication titled “The Plants of Jordan: An Annotated Checklist” (Taifour et al., 2017).

MATERIALS AND METHODS

This systematic review (SR) was based on a registered (PROSPERO CRD42020198926) protocol and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009).

Data sources and searches

RCTs reporting cosmetic clinical outcomes in adults (≥18 years old) in the English language were included. Exclusion criteria included studies involving trials with interventions requiring medical attention and postprocedural treatment, not listing a clear description of botanical/phytochemical intervention.

Eligible trials were identified by electronic searches in PubMed and EMBASE from the beginning of time on the database until 26/7/2020. A combination of the following medical subject heading (MeSH terms) and free-text terms was used: phytotherapy, herbal medicine, plant extract, volatile oil, cosmetics, and skin care.

Study selection

Two authors independently reviewed the trial inclusion and exclusion criteria. Excluded trials were listed with the reason for exclusion (Supplementary Material). Disagreements were resolved by consulting a third researcher and achieving consensus.

Data extraction and quality assessment

Data extraction was performed independently by four authors based on standardized extraction forms. Each article was independently extracted by two authors. Disagreements were resolved through discussions and the corresponding authors were contacted if any of the pieces of required information were not described in the published manuscripts.

The risk of bias was assessed by separate domains: randomization, allocation concealment, selective reporting, blinding of participants and authors, attrition, and other biases using the Cochrane Collaboration’s tool for assessing the risk of bias in randomized trials (Higgins et al., 2011). The results of these domains were graded as a “low,” “high,” or “unclear” risk of bias.

RESULTS

Skin care

The initial search yielded 1,987 abstracts. Removal of duplicates and applying the exclusion criteria identified 63 studies, 53 of which employed natural products for skin care and 10 for hair care. The process of selecting the studies included in this literature review was based on the inclusion and exclusion criteria as illustrated in Figure 1.

The 63 included studies are summarized in Tables 1 and 2 to demonstrate plants, herbs, or isolated compounds tested in the selected RCTs for skin care and hair care, respectively.

The main skin conditions addressed in selected RCTs were acne, hyperpigmentation, wrinkles, hirsutism, inflammation, stretch marks, and scars as well as testing plants and herbs for their moisturizing and skin protection properties. For hair care, the main hair issues addressed in the RCTs were hair thinning and dandruff.

The highest number of RCTs concerning selected skin conditions tested natural products for their skin protection properties (n = 12) and was published between 1997 and 2018. The investigated plants/products included Polypodium leucotomos (Gonzalez et al., 1997), Camellia sinensis (Camouse et al., 2009), Hibiscus abelmoschus (Rival et al., 2009), Calendula officinalis (Akhtar et al., 2011), Avena sativa (Michelle, 2016), Ribes nigrum (Ray et al., 2016), phenolic veratic acid (Lee et al., 2016), and Cucumis melo (Egoumenides et al., 2018), as a single ingredient within the formulation. Four other RCTs investigated the combination of extracts, including soy and jasmine (Bazin et al., 2010), dead sea water and Himalayan extracts (Wineman et al., 2012), Olea europaea and Helianthus annuus (Danby et al., 2013), and Portulaca oleracea and Prunsepia utilis (Wang et al., 2018).

The second highest number of selected RCTs addressed antiaging effects (n = 10) and was published between 2000 and 2020. The plants/herbs investigated included Centella asiatica (Gonzalez et al., 1997), date palm kernel (Bauza et al., 2002), Sanguisorba officinalis (Kim et al., 2008), Platycarya strobihaceoa (Kim et al., 2010), Oryza sativa (Kanalavatatanakul et al., 2016), Geranium thunbergii (Yoshida et al., 2019), Psoralea corylifolia (Goldberg et al., 2019), and Zanthoxylum bungeanum (Zeng et al., 2019) and two used a combination of extracts including Glycyrrhiza glabra, Angelica gigas, Prunus persica, Ophiopogon japonicus, Paeonia suffruticosa, Atractylodes japonica, Poria cocos, Rehmannia chinensis, Cimicifuga simplex, Asparagus cochinchinensis, Scutellaria baicalensis, Astragalus membranaceus, Carthamus tinctorius (Roh et al., 2019), and Coptis teeta with Trichosanthes rosthornii (Im et al., 2020).

Nine studies published between 2012 and 2020 tested natural products for the treatment of hyperpigmentation. These studies investigated the constituents of Silybum marianum (Altaei, 2012), Sophora flavescens (Shin et al., 2013), Polypodium leucotomos (White et al., 2013), Rumex occidentalis (Mendoza et al., 2014), Serratula quinquefolia (Morag et al., 2015), P. cocos Wolf (Lee and Cha, 2018), Vitis vinifera (Tsuchiya et al., 2020), and O. europaea (de Toledo Bagatin et al., 2020); one study used a combination of China camellia, Sanchi, P. utilis, and P. oleracea (Zhang et al., 2019).

Next were RCTs investigating natural products, examining their ability to reduce body hair growth (n = 5); these studies were published between 2003 and 2019 and included Foeniculum vulgare (Javidnia et al., 2003), Stryphnodendron...
adstringens (Vicente et al., 2009), Medicago sativa (Aali et al., 2016), and Curcuma aeruginosa (Srivilai et al., 2017, 2018).

Studies concerning the moisturizing properties of natural products (n = 4) were published between 2016 and 2019 and included *Rhododendron ferrugineum* (Filipovic et al., 2016), *C. asiatica* (Milani and Sparavigna, 2017), Scaphium scaphigerum (Kanlayavattanakul et al., 2017), and *Curcuma longa* (Asada et al., 2019).

The RCTs investigating natural products for their anti-inflammatory properties (n = 3) were published between 2014 and 2019, investigating the constituents *Prunus yedoensis* (Zhang et al., 2014) and *Glycyrrhiza inflata* (Boonchai et al., 2018) as a single ingredient preparation within the formulation; one related RCT investigated a combination of extracts of *Gentiana lutea*, *G. glabra*, and *Salix daphnoides* (Seiwerth et al., 2019).

The RCTs investigating natural products for acne treatment (n = 2) were published between 2011 and 2018 and explored combinations of extracts; the first group of studies explored retinol, rose, and hexamidine diisethionate (Lee et al., 2011), while the second group explored coco-glucoside, *Simmondsia chinensis*, *G. lutea*, *Mentha arvensis*, *Humulus lupulus*, *Leptospermum scoparium*, *S. daphnoides*, *H. annuus*, pectin, and xanthan gum (Weber et al., 2019).

Two studies, published between 2008 and 2016, tested natural products for foot care. In the former, they used a combination of mango butter and olein fraction fortified with vitamin E (Mandawgade and Patravale, 2008), whereas in the latter study, *Ziziphus mauritiana* (Akhtar et al., 2016) was used.

Rosacea was investigated in one study published in 2015 and used a cream containing medical-grade kanuka honey (Braithwaite et al., 2015). Stretch marks and scars reduction were investigated in two separate studies published in 2014 and 2010, using *O. europaea* (Soltanipour et al., 2014) and *Allium cepa* (Hosnuter et al., 2007), respectively.

Finally, three studies published in 2015, 2018, and 2019 tested plants for multiple effects; the first study investigated *Tamarindus indica* for its antisebum and antihyperpigmentation properties (Muhammad et al., 2015); the second tested *Prunus serrulata* for its moisturizing, antihyperpigmentation, antiaging, and overall improvement of skin condition and elasticity.
Table 1. Summary of RCTs conducted between 1997 and 2020 of plants, herbs, or isolated compounds used for skin care.

| 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 | Part used | Dosage form                                                                 |
|--------------------|------------|-------------------------------------|-------------------------------------------|--------------------------------------|-------------------------------------------------------------------------------------|------------------|----------|--------------------------------|-----------|--------------------------------------------------------------------------------|
| Gonzalez et al.,   | Spain      | 18–46-year-old males and females untreated or treated with oral psoralens (21) | Topical or oral *P. leucotomos* (oral dose = 1,080 mg) | Un-treated control                   | 1. Immediate pigment darkening (IPD): ultraviolet (UV) dose significantly increased (p < 0.01)   | 1. IPD           | 3 days   | *P. eucotornos*                  | –         | Capsules containing 120 mg *P. eucotornos* or lotion containing 10, 25, and 50% *P. eucotornos* extract (v/v) |
| 1997               |            |                                     |                                            |                                      | 2. Minimal erythema dose (MED): UV dose significantly increased (p < 0.01)              | 2. MED           |          |                                |           |                                                                                |
|                    |            |                                     |                                            |                                      | 3. Minimal melanogenic dose (MMD): no significant difference                          | 3. MMD           |          |                                |           |                                                                                |
|                    |            |                                     |                                            |                                      | 4. Minimal phototoxic dose (MPD): UV dose significantly increased (p < 0.01)            | 4. MPD           |          |                                |           |                                                                                |
|                    |            |                                     |                                            |                                      | 5. Langerhans cells examination of psoralen-sensitized volunteers                    | 5. Langerhans cells examination of psoralen-sensitized volunteers |          |                                |           |                                                                                |
|                    |            |                                     |                                            |                                      |                                                                                     |                  |          |                                |           |                                                                                |
| Camouse et al.,    | USA        | 19–58-year-old males and females (90) | Topical green tea or topical white tea applied minute prior to solar-simulated UV radiation irradiation, as well as immediately after it | Placebo                             | Contact hypersensitivity (CHS): no significant effect (p > 0.05)                       | CHS evaluated by the total millimetre increase in skin fold thickness | 2 days   | *C. sinensis*                    | –         |                                                                                |
| 2009               |            |                                     |                                            |                                      |                                                                                     |                  |          |                                |           |                                                                                |
| Rival et al.,      | France     | Group A: 40–50-year-old females (20) | Group A: topical product containing 3% *H. abelmoschus* | Placebo                             | 1. Skin elasticity: improved for both groups and both products                        | 1. Skin elasticity measured on the cheek using a ballistometer | 6 weeks   | *H. abelmoschus*                 | Seed      |                                                                                |
| 2009               |            | Group B: 50–60-year-old females (40) | Group B: topical product containing 3% *H. abelmoschus* and topical product containing 3% vitamin C |                                      | 2. Skin firmness, texture, and density: improved for both groups and both products Fringe projection: significantly reduced compared to the placebo in group B for both products (p < 0.05) | 2. A visual and tactile evaluation of skin firmness, texture, and density performed by an expert clinician |          |                                |           |                                                                                |
| Bazin et al.,      | Germany    | 45–65-year-old Caucasian females (24) | Emulsion containing soy and jasmine applied twice daily | Placebo                             | Global signals detected in the dermis significantly higher (p < 0.05)                 | Multilayers acquisitions using a multiphoton tomograph with subcellular resolution | 12 weeks  | –                                | –         | Emulsion                                                                     |
| 2010               |            |                                     |                                            |                                      |                                                                                     |                  |          |                                |           |                                                                                |
| Akhtar et al.,     | Pakistan   | 24–35-year-old healthy males and females (21) | W/O emulsions containing 3% *C. officinalis* | Placebo                             | Hydration and firmness of skin were significantly improved (p < 0.05)                | Mechanical parameters of the skin using noninvasive suction skin elasticity meter Cutometer 580 MPA | 8 weeks   | *C. officinalis*                 | –         | Cream                                                                         |
| 2011               |            |                                     |                                            |                                      |                                                                                     |                  |          |                                |           |                                                                                |

(Continued)
| 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 | Part used | Dosage form |
|-------------|---------|----------------|------------------------------------------|---------------|---------------------|------------------|----------|-------------------------------|-----------|------------|
| Wineman et al., 2012 | Israel | ≥45-year-old females (20) | A cream containing complex of Dead Sea water and three Himalayan (Tibetan goji berries, moss lichen, and Himalayan raspberry) extracts applied once daily | Untreated control | Antiwrinkles effect: wrinkles depth significantly reduced (p < 0.05) | Antiwrinkles effect: the depth of one single wrinkle in the eye examined before and after application by PRIMOS optical 3D measuring device | Antiwrinkles effect: 4 weeks | Skin hydration: electrical capacitance (EC) measured using capacitance meter (Corneometer CM 825) | Skin hydration: 12 hours | Tibetan goji berries | Cream |
| Danby et al., 2013 | UK | Cohort 1: males and females with an average age of 46 ± 5.7 years with previous atopic dermatitis (AD), no symptoms for 6 months (7) Cohort 2: males and females with an average age of 46 ± 5.7 years with/without previous AD, no symptoms for 6 months (12) | Cohort 1: Six drops of olive oil applied to the forearm twice daily Cohort 2: six drops of olive oil or sunflower oil applied to the forearm twice daily | Untreated control | Cohort 1: 1. Transepidermal water loss (TEWL): significantly increased with tape stripping (p < 0.001) 2. Cohesiveness of stratum corneum (SC): significantly decreased in volunteers with a history of AD (p < 0.05) 3. SC hydration: no significant effect (p > 0.05) 4. Erythema: higher | Cohort 1: 1. Skin-surface pH measured using pH meter (PH905) 2. SC hydration measured using Corneometer (CM825) | Cohort 1: 1.5 weeks | O. europaea | H. annus: fruit | Oil |
| Ilnytska et al., 2016 | USA | 18–65-year-old healthy females with bilateral moderate to severe dry skin on their lower legs (50) | Colloidal lotion containing oatmeal extract applied twice daily | Untreated control | 1. Dry skin: significantly improved (p < 0.05) 2. Skin barrier integrity and hydration: significantly improved (p < 0.05) | 1. Dry skin: visual evaluation and using Dermalab 2. Skin barrier integrity and hydration assessed by TEWL measurements and using Skicon 200 EX | 5 weeks | A. sativa | – | Lotion |
| Ray et al., 2016 | UK | 40–68-year-old males (32) | Low-concentration or high concentration blackcurrant juice drink | Placebo | No significant difference (p > 0.05) | 1. Phototesting using a calibrated irradiation monochromator 2. MED | 6 weeks | – | – | Juice |
| Lee et al., 2016 | South Korea | Females with an average age of 47.7 ± 4.8 years (20) | 0.5% phenolic veratric acid cream | Placebo | 1. Visual evaluation: showed improvement 2. Photometric evaluation: significantly improved (p < 0.01) 3. Self-assessment: positive feedback | 1. Visual evaluation 2. Photometric evaluation using Skin-Visiometer SV 600 3. Self-assessment | 12-weeks | – | – | Cream |
| 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 | Part used | Dosage form |
|-------------|---------|----------------|------------------------------------------|---------------|-------------------|-----------------|----------|--------------------------------|------------|------------|
| Wang et al., 2018 | France | Females with an average age of 37.1 ± 10.6 years with dry and sensitive skin (20) | A cream containing Yunnan *P. oleracea* extract, *P. utilis* oil, beta-glucan, and sodium hyaluronate extracted from mushroom applied to 1 side of the face twice daily | A control cream containing *C. tinctorius* extract and oil | 1. Visual evaluation: a significant improvement 2. Self-assessment questionnaire: test cream was significantly favoured (p < 0.05) of dryness, erythema, and roughness was observed compared to baseline (p < 0.05). For skin desquamation, no significant difference was observed 3. Hydration index: significantly increased (p < 0.05) 4. Skin texture parameter: roughness significantly declined, and smoothness significantly increased (p < 0.05) 5. Skin barrier function (TEWL), sebum recovery (lipid index), wettability, color, and stinging test: no significant effect (p > 0.05) | Visual evaluation including dryness, roughness, desquamation, and erythema 2. Self-assessment questionnaire 3. TEWL assessment using Vapometer 4. Skin hydration assessment using Corneometer CM825 5. Lipid index assessment using Sebumeter SM 815 6. Skin texture assessment using Visioscan VC98 7. Skin-surface wettability 8. Skin color using Minolta 400 Chroma Meter 9. Skin sensitivity using a stinging test with 10% lactic acid | 4 weeks | *P. oleracea* – *P. utilis* | Cream |
| Egoumenides et al., 2018 | France | 19–50-year-old healthy Caucasian (93) | 1. A melon concentrate capsule containing 20 mg superoxide dismutase 2. Cream containing 12 U superoxide dismutase per cm² of skin | Placebo | MED: significantly higher for both cream and capsule (p < 0.05) | MED using ORIEL solar simulator as a source of radiation | 4 weeks | *C. melo* L. | Skin and seeds | 1. Hard capsule 2. Cream |
| Anti-aging | Martelli et al., 2000 | Italy | 20–25-year-old healthy female (20) | A cream containing boswellic acids, silybin, and *C. asiatica* extracts | Placebo | 1. Skin hydration: no significant difference 2. Biomechanical properties: significantly increased (p < 0.02) No adverse effects were reported | 1. Skin hydration measured by EC by Corneometer 2. Biomechanical properties (extensibility and firmness) of the skin measured using suction device (Dermaflex) | 4 weeks | *C. asiatica* | Cream |
| Bauza et al., 2002 | France | 46–58-year-old females (10) | Cream with 5% date palm kernel extract on the eye area twice daily | Placebo | 1. Skin microrelief evaluation: total surface of wrinkles was significantly reduced (p < 0.05) 2. Clinical evaluation: 60% of participants showed improvement 3. Questionnaire: 50% of participants reported improvement | 1. Skin microrelief evaluation: silicon replica analysis using a software 2. Clinical evaluation under a magnifying glass 3. Questionnaire | 5 weeks | – | Kernel |

Skin care (n = 53)
| 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 | Part used | Dosage form |
|-------------|---------|----------------|-----------------------------------------|--------------|------------------|------------------|---------|--------------------------------|----------|-----------|
| Kim et al., 2008 | Korea | 35–53-year-old healthy females (20) | 0.03% ziyuglycoside I cream | Placebo | 1. Visual evaluation: intervention showed a nonsignificant difference between 4 and 8 weeks, significant results were observed after 12 weeks of treatment (p < 0.05) 2. Photometric evaluation: mean depth of roughness showed a significant difference in 12 weeks (p < 0.05) | 1. Visual evaluation using photodamage score 2. Photometric evaluation using Skin-Visiometer SV 600 | 12-weeks | S. officinalis | Root | Cream |
| Kim et al., 2010 | Spain | 34-49-year-old healthy females (25) | 0.2% P. strobiacea extract | Placebo | 1. Visual evaluation: intervention showed a nonsignificant difference between 4 and 8 weeks, significant results were observed after 12 weeks of treatment (p < 0.05) 2. Photometric evaluation: average difference in roughness showed a significant difference in 12 weeks (p < 0.05) | 1. Visual evaluation 2. Photometric evaluation 3. Image analysis using Skin-Visiometer SV 600 | 12-weeks | P. strobiacea | Fruit | Cream |
| Kanlayavattanakul et al., 2016 | Thailand | 25–50-year-old healthy males and females (24) | Cream containing 0.1% or 0.2% rice panicle extract applied twice daily | Placebo | Skin hydration: significantly improved (p < 0.05) Skin lightening: significantly improved (p < 0.001) Skin firming: significantly increased (p < 0.05) Skin wrinkle: significantly reduced (p < 0.05) | Clinical evaluation using Corneometer® CM 825, Cutometer® MPA 580, Mexameter® MX 18 and Visioscan® VC 98 | 12 weeks | O. sativa cv. Indica | Rice panicle | Cream |
| Yoshida et al., 2019 | Japan | 34–56-year-old healthy females (21) | A gel containing 20 mg/ml of G. thunbergii extract | Placebo | Skin wrinkle scores: significantly reduced (p < 0.05) Skin hydration: significantly improved (p < 0.05) | 1. The antiwrinkle efficacy evaluated by visual scoring by a dermatologist, 3D skin replica images obtained from the eye corner using Silflo® and the 3D image analyzer PRIMOS system. 2. Skin elasticity measured using the Cutometer DUAL MPA 580 w | 8 weeks | G. thunbergii | Leaves | Gel |
| Roh et al., 2019 | Korea | 40–50-year-old healthy females (46) | SHYBE extract included: 0.0385% liquorice extract, 0.0765% A. gigas extract, 0.0765% peach extract, 0.0765% O. japonicus extract, 0.0765% P. suffruticosus extract, 0.0765% A. japonica | Placebo | 1. Skin hydration: significantly increased at week 4 (p < 0.05) 2. Skin elasticity: significantly increased at week 4 (p < 0.05) 3. Dermal thickness and density: significantly increased at week 4 (p < 0.05) 4. Self-assessment: no significant differences | 1. Skin hydration evaluation using Corneometer® CM 825 2. Skin elasticity evaluation using Cutometer® MPA 580 3. Dermal thickness and density evaluation Dermascan® C | 8 weeks | Licorice: G. glabra, A. gigas, Peach: P. persica, O. japonicus, P. suffruticosus, A. japonica, P. cocos, R. chinensis, G. glabra: root, A. gigas: root, P. persica: kernel, O. japonicus: root, P. suffruticosus: root, A. japonica: rhizome, P. cocos: fruit | Cream |
| Author, year       | Country | Population (n)                                      | Intervention (dose/method of application)                                                                 | Comparison(s)                                      | Outcome(s), p value                                                                 | Method of testing                                                                 | Scientific name of plant used | Part used       | Dosage form |
|-------------------|---------|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------|----------------|-------------|
| Goldberg et al., 2019 | USA     | 40–65-year-old healthy females (59)                | Night facial serum containing melatonin, bakuchiol, and ascorbyl tetraisopalmitate applied daily               | Untreated control                                 | Efficacy and tolerability study:                                                   | 1. Wrinkle roughness: significantly decreases (< 0.05)                             | P. corylifolia to obtain bakuchiol | Seeds          | Serum       |
|                    |         | Efficacy and tolerability study:                    | 2. Skin firmness: skin deformation volume and depth decreased significantly (p = 0.05)                     |                                                   | 3. Pigmentation: Significant decrease in pigmentation in comparison with baseline (< 0.05) |
|                    |         | 35–60-year-old females with bilateral visible static crow’s feet (20) | Hydration study and TEWL study:                                                                     |                                                   |                                                                                    |                                                                                   |                             |                |             |
|                    |         | Test in oily skin: 30–65-year-old healthy females (31) | 1. Sebum secretion: significantly decreased (< 0.01)                                                  |                                                   |                                                                                  |                                                                                   |                             |                |             |
|                    |         | Noncomedogenesis study: 18–55-year-old females with combination or oily facial skin with comedones (33) | Noncomedogenesis study: 1. 85% of subjects had fewer comedones after 28 days of treatment              |                                                   |                                                                                  |                                                                                   |                             |                |             |
| Zeng et al., 2019  | China   | 35–60-year-old females with bilateral visible static crow’s feet (20) | Formulation containing 2% Z. bungeanum maxim extract                                                  | Placebo                                           | 1. Skin roughness: no significant difference (> 0.05)                               | 1. Objective assessments of pictures taken using VISIA®. Crow’s feet were measured | Zanthoxylum bungeanum maxim | Fruit          |             |
| 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 | Part used | Dosage form |
|-------------|---------|------------------|------------------------------------------|---------------|----------------------|------------------|----------|-------------------------------|-----------|-------------|
| Thiab et al. | | 53 | | | | | | | |
| Im et al., 2020 | Korea | 40–59-year-old Soyang- (SY-) type females (21) | Cream including 0.3% $C. teeta$ and $T. rosthornii$ extract applied to the area around the eyes twice daily | Placebo | 1. Visual assessment of skin wrinkles: skin damage was significantly restored ($p < 0.05$) 2. Evaluation of skin wrinkle parameters using replica images: significantly decreased ($p < 0.05$) 3. Questionnaire evaluation by participants: no significant difference ($p > 0.05$) 4. Skin safety evaluation: no adverse dermatological events were observed | 1. Visual assessment of skin wrinkles under specific lighting conditions 2. Evaluation of skin wrinkle parameters using replica images analyzed using Visioline VL650 3. Questionnaire evaluation by participants 4. Skin safety evaluation performed by assessing skin irritation through an interview and by medical examination | 12 weeks | $C. teeta$ | $T. rosthornii$ | rhizome | seed | |
| Altaei, 2012 | Iraq | 28–55-year-old males and females with melasma (96) | A cream containing 0.1% or 0.2% silymarin applied twice daily | No treatment and Placebo | 1. Skin pigment evaluation melasma area and severity index (MA5I): significantly improved ($p < 0.05$) 2. Physician global assessment (PGA): significantly improved ($p < 0.05$) 3. Assessment of overall treatment: significantly satisfied ($p < 0.05$) | 1. Skin pigment evaluation by MASI 2. PGA 3. Assessment of overall treatment using a scale from 0 to 10 | 4 weeks | $S. marianum$ | – | Cream |
| 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 | Part used | Dosage form |
|----------------------|-----------|----------------|-------------------------------------------|---------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------|-----------------------------|-----------|-------------|
| Shin et al., 2013    | Korea     | 21–53-year-old participants (25) | Lotion with 0.05% *S. flavescens* extract applied twice daily | Placebo       | Significantly whitening by device and visual assessment (*p* < 0.05)                  | 1. Visual assessment by dermatologists 2. Whitening effects measured using a chromameter CR-400 | 8 weeks  | *S. flavescens* root        | Lotion    |             |
| White et al., 2013   | USA       | Hispanic females with moderate-to-severe facial melasma (40) | Oral *P. leucotomos* extract three times daily | Placebo       | 1. MASI: No significant difference (*p* = 0.14) 2. Assessment of melasma-related quality of life (MelasQOL): No significant difference (*p* = 0.62) | 1. MASI 2. Assessment of MelasQOL                                                  | 12 weeks | *P. leucotomos*             | –         | –           |
| Mendoza et al., 2014 | Philippines | 18–60-year-old males and females with epidermal and mixed melasma (45) | 3% *R. occidentalis* cream applied twice daily | Placebo       | 1. MASI: Significantly improved compared with baseline (*p* < 0.05) 2. Skin pigmentation and Mexameter MX18 readings: significantly improved compared with baseline (*p* < 0.05) | 1. MASI 2. Skin pigmentation: using Mexameter MX18                                   | 8 weeks  | *R. occidentalis*           | Cream     |             |
| Morag et al., 2015   | Poland    | 26–55-year-old females with melasma and lentigo solaris (102) | A cream with the aqueous extract from leaf of five-leaf serrata containing 2.51% of arbutin applied twice daily | Placebo       | Average level of melanin: significantly improved for patients with melasma (*p* < 0.05) | 1. Skin discoloration and measuring the average level of melanin: video dermatoscope DermoGenius (LINOS) and a probe Mexameter MX18 2. Dermatoscopic examination: probe Mexameter MX18 | 8 weeks  | *S. quinquefolia* leaves     | Cream with aqueous extract |             |
| Lee and Cha, 2018    | Korea     | 20–30-year-old females (40) | A cream with 2% (wt %) *P. cocos* Wolf extracts applied once daily in the morning | Placebo       | Skin brightness increased significantly (*p* < 0.05)                                  | Visual evaluation 2. Skin tone improvement measured using a Spectrophotometer CR 2060D | 4 weeks  | *P. cocos* Wolf             | Cream     |             |
| Zhang et al., 2019   | China     | 25–50-year-old males and females with melasma (90) | A cream containing herbal mixture [C. camellia (1%), *Sanchi* (0.5%), *P. utilis* oil (0.5%), and *P. oleracea* (1%)] | Arbutin cream and placebo | 1. MASI score: significantly improved after 12 weeks (*p* < 0.05) 2. Melanin index (MI): significantly decreased after 12 weeks (*p* < 0.05) 3. Erythema index (EI): significantly decreased after 12 weeks (*p* < 0.05) 4. The density of inflammatory cells: significantly decreased after 12 weeks (*p* < 0.05) 5. The subjective satisfaction scores: “very satisfied” increased from 13.3% at week 4%–33.3% at week 12 | 1. MASI score, MI, EI, using Mexameter and photographed using VISIA 2. Assessment of density of inflammatory cells using a reflectance confocal microscopy 3. The subjective satisfaction scores: The volunteers evaluated their satisfaction with the following criteria: 0 = not satisfied, 1 = partially satisfied, 2 = satisfied, or 3 = very satisfied | 12 weeks | C. camellia, *Sanchi*, *P. utilis*, and *P. oleracea* | Cream     |             |
| 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 | Part used | Dosage form |
|-------------|---------|----------------|------------------------------------------|--------------|---------------------|------------------|----------|-------------------------------|-----------|-------------|
| Tsuchiya et al., 2020 | Japan | 30–59-years-old females (100) | 200 ml beverage containing 200 mg of red wine oligomeric procyanidins once daily | Placebo | 1. Sunspot scores: significantly reduced (p < 0.05) 2. MI value: significantly reduced (p < 0.05) 3. Water content of the SC: significantly increased (p < 0.05) 4. Skin viscoelasticity: no significant difference (p > 0.05) 5. Wrinkle depth, and visual analog scale (VAS) questionnaire: no significant difference (p > 0.05) | 1. Sunspot score diagnosed by a dermatologist 2. MI value in sunspots, and skin color using a CIE 1976 lightness 3. Water content of the SC 4. Skin viscoelasticity 5. Wrinkle depth, and VAS questionnaire | 12 weeks | V. vinifera | Fruit |
| de Toledo Bagatin et al., 2020 | Brazil | 32–49-year-old females with center-facial melasma (42) | Topical formulation containing the olive extract and oral placebo or Topical vehicle formulation and oral capsule containing the olive extract | Placebo | 1. Modified melasma area and severity index (mMASI): no significant difference (p > 0.05) 2. MI: no significant difference (p > 0.05) | 1. mMASI score (20) evaluated based on high resolution images and luminosity using VisioFace 1000D equipment 2. MI evaluated using a spectrophotometer Mexameter | 12 weeks | O. europaea | Fruit |
| Javidnia et al., 2003 | Iran | 16–53-year-old females with mild-to-moderate forms of idiopathic hirsutism localized to the face (45) | Creams containing 1% or 2% of Fennel extract applied twice daily | Placebo | Hair diameter from the facial area: significantly reduced using fennel extract (p < 0.05) | Hair diameter measurement from the facial area | 12 weeks | F. vulgare | Seeds |
| Vicente et al., 2009 | Brazil | >18-year-old females with excess terminal hair (54) | A cream containing 6.0% of S. adstringens extract | Placebo | Significant improvement (p < 0.05) | Clinical examination | 26 weeks | S. adstringens | Bark |
| Sargazi et al. 2016 | Iran | 18–24-year-old females (60) | Eucerin as a basal cream mixed with 1%, 2%, and 5% of alfalfa extract applied twice daily | Placebo | Hair growth length and hair diameters; significantly reduced (p < 0.05) | Hair growth length and hair diameters measured using a caliper with 0.02-micrometer sensitivity | 12 weeks | M. sativa L. | Leaves |
| Srivilai et al., 2017 | Thailand | 18–23-year-old females (60) | A lotion containing 1 or 5% w/w essential oil of C. aeruginosa | Placebo | 1. Safety pretesting (hydration, irritation, etc.): There was very little erythema and no edema 2. Hair growth: significantly diminished (p < 0.05) 3. Hair density: insignificant effect (p > 0.05) | 1. TEWL assessment using a Tewameter®TM300 2. Skin hydration assessment using a Corneometer®CM825 | 12 weeks | C. aeruginosa | Rhizomes |
### Skin care ($n = 53$)

| 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 | Part used | Dosage form |
|--------------|---------|----------------|------------------------------------------|---------------|----------------------|------------------|----------|------------------------------|-----------|-------------|
| Srivilai et al., 2018 | Thailand | 20–52-year-old females (30) | A lotion containing 5% sesquiterpene-Enriched Extract of *C. aeruginosa* applied twice daily | Placebo | 1. Hair growth: delayed response, retarded hair growth was observed after week 7 2. Participant questionnaire: overall satisfaction ($p < 0.05$) | 3. Hair growth and hair density: images recorded by a video imager, hair lengths, and numbers were measured using a computer software 4. Melanin measurement using a Mexameter® MX18 5. Skin irritation and skin flaking, or scaling assessed by a practicing dermatologist 6. Participant questionnaire | 13 weeks | *C. aeruginosa* | Rhizomes | – |
| Filpovic et al., 2016 | Serbia | Healthy females (76) 1. Phase I: average age = $21.15 \pm 2.05$ (52) 2. Phase II: on sodium lauryl sulfate- (SLS-) irritated skin, average age = $29.9 \pm 8.9$ (24) | Alpine Rose stem cells (ARSC), olive oil squalene, and a natural alkyl polyglucoside cream: Formula 1: 0.4% of ARSC Formula 2: 1% of squalene Formula 3: Commercially available with 0.4% of ARSC Formula 4: 1% of squalene + 0.4% of ARSC Formula 5: 6% of squalene + 0.4% of ARSC Formula 6: Placebo | Untreated control on the forearm | Phase I: 1. EC: significant change with formula 2 and 3 ($p < 0.05$) 2. TEWL: significantly decreased with formula 2 ($p < 0.05$) Phase II: 1. EC: significantly increased with formula 1, 2, and 5 ($p < 0.05$) 2. TEWL: significantly decreased with all tested creams ($p < 0.05$) 3. EI: significantly increased with formula 1, 4, and 5 ($p < 0.05$) | 1. EC using Corneometer® CMI25 2. TEWL using Tewameter® TM210 3. EI using Mexameter® MX18 4. Skin elasticity using Cutometer® MPA580 | Phase I: 21 days Phase II: 6 days | *R. ferrugineum* | Stem cells | Cream |
| Milani and Sparavigna, 2017 | Italy | Healthy females with an average age of 40 years (20) | A fluid containing *C. asiatica* meristem cell culture | Untreated control | 1. Skin hydration: significantly increased ($p < 0.05$) 2. TEWL assessed: significantly decreased ($p < 0.05$) | 1. Skin hydration evaluated using a Corneometer 2. TEWL evaluated using a Vapometer device | 1 day | *C. asiatica* | Leaves | Fluid |
| 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 | Part used | Dosage form |
|----------------------|-------------|----------------|------------------------------------------------------------------------------------------------------------|---------------|----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|--------------|-------------------------------|------------|-------------|
| Kanlayavattanakul et al, 2017 | Thailand    | 23–39-year-old healthy males and females (24) | A gel containing 0.5% Malva nut polysaccharide (0.5%) or a formulation containing 0.2% polysaccharides, tamarind, and algae | Placebo       | 1. Safety assessment: no irritation observed  
2. Skin hydration: Malva nut gel was shown to hydrate the skin more effectively than tamarind and base gel (p < 0.05) | 1. Safety assessment by a single application closed patch test  
2. Skin hydration monitored by using Corneometer® CM825 | 75–180 minutes | S. scaphigerum | Seeds | Gel |
| Asada et al., 2019 | Japan       | 21–54-year-old males and females (47) | A hot water extract of C. longa taken daily or a hot water extract + curcumin | Placebo tablets containing safflower color and kaoliang color to match the color of the other tablets | 1. Water content of the skin surface: significantly increased (p > 0.05)  
2. TEWL: no significant difference (p > 0.05)  
3. MED: no significant difference (p > 0.05) | 1. Water content of the skin surface measured with a Skicon-200EX  
2. TEWL measured using a VapoScan ASVT100RS  
3. MED performed using a solar simulator 601-300 2.5 UV Multiport | 8-weeks | C. longa | Rhizomes | Tablets |
| Zhang et al, 2014 | China       | 18–65-year-old males and females (40) | A cream containing 3% cherry blossom extract applied twice daily to forearm with induced irritation using occlusive application of 3% SLS for 24 hours | Placebo       | 1. Visual erythema scores: significantly decreased from the third day (p < 0.05)  
2. Erythema value: significantly decreased from the fifth day (p < 0.05) | 1. Visual erythema scores were evaluated by dermatologist  
2. Erythema value measurement using Mexameter MX18 | 9 days | P. yedoensis | Flowers | Cream |
| Boonchai et al., 2018 | Thailand    | 15–72-year-old males and females with mild-to-moderate facial dermatitis (80) | A cream containing 4-t-butylcyclohexanol and licochalcone applied twice daily | 0.02% triamcinolone | 1. Physician's assessment: significantly improved (p < 0.05)  
2. Skin hydration: significantly increased (p < 0.05)  
3. Patients evaluation of sensory symptoms: significantly decreased (p < 0.05) | 1. Physician's assessment and redness score using a Eucerin redness rating card  
2. Skin hydration and TEWL measured using a Corneometer CM825 and a Tewameter TM300  
3. Patients evaluation of sensory symptoms for itching, pain, burning sensation, tingling, and redness using 10 cm VAS | 4 weeks | G. inflate | – | Cream |
| Seiwther et al., 2019 | Germany     | Healthy males and females (42) | Cream with gentian, liquorice, and willow extract | 1% hydrocortisone acetate | UV-erythema test: significantly reduced compared with vehicle only (p < 0.05) | UV-erythema test using a Mexameter | 48 hours | Gentian: G. lutea  
Liquorice: G. glabra  
Willow: S. daphnoides | – | Cream |
| Lee et al., 2011    | South Korea | 15–41-year-old males and females with mild-to-moderate | APDDR-0901 (0.03% retinol, 0.7% rose extract, and 0.05% hexamidine) | 0.1% adapalene gel | 1. Median percent change in lesion count: significantly improved from baseline (p < 0.05) | 1. Median percent change in lesion count  
2. Acne grade | 12 weeks | – | – | – |
### Skin care ($n = 53$)

| 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 | Part used | Dosage form |
|--------------|---------|------------------|-------------------------------------------|---------------|-----------------------|------------------|----------|-------------------------------|-----------|-------------|
| Thiab et al., 2021 | | | acne (97) | disethionate), daily in the evening | 2. Acne grade: significantly improved from baseline ($p < 0.05$) | 3. Physician-assessed global improvement | 4. Patient self-assessment | 8 weeks | S. chinensis | seed |
| Weber et al., 2019 | Germany | 21–49-year-old males and females with oily skin (21) | A cleanser containing coco-Glucoside, S. chinensis oil, G. lutea extract, M. arvensis oil, H. lupulus extract, L. scoparium oil, S. daphnoides extract, H. annuus oil, Pectin, Xanthan gum | Face cleanser with sodium laureth sulfate | 1. Skin sebum: significantly reduced only on day 17 after the application | 2. Skin erythema measurement using a Mexameter | 3. Self-assessment: participants reported pleasant skin sensation | 8 weeks | S. chinensis: seed | G. lutea: roots |
| | | | | | | | | | M. arvensis: branch/leaf | L. scoparium: bark | S. daphnoides: seed |
| | | | | | | | | | H. annuus: bark |
| | | | | | | | | | H. annuus: seed |
| Mardawgade and Patravale, 2008 | India | Healthy males and females suffering from different foot ailments (6) | A cream containing mango butter and olein fraction, fortified with vitamin E acetate (1%w/w) | Untreated control | 1. Assessment of functional attributes: complete repair of cracked skin in all the volunteers. Antiseptic, healing, soothing, and cooling actions were predominant in most of the clinical subjects | 2. Assessment of esthetic attributes: Excellent emolliency, rebuilt protective skin barrier and replenished moisture, and improve smoothness. Had good appearance, spreadability, skin feel, smoothness, and absorption ($p < 0.05$) | 8 weeks | – | Fruit kernels | Cream |
| Akhtar et al., 2016 | Pakistan | 25–35-year-old healthy males (13) | An emulsion containing 4% Z. mauritiana extract | Placebo | Erythema: significantly decreased in both groups ($p < 0.05$) Melanin content: significantly decreased ($p < 0.05$) Skin moisture: significantly increased ($p > 0.05$) Skin elasticity: significantly increased ($p < 0.05$) Sebum content: significantly increased ($p < 0.05$) | Melanin content, skin erythema, skin elasticity, sebum content, and skin moisture were evaluated using Mexameter, Corneometer, Visioscan, and Sebumeter MPA 5 | 8 weeks | Z. mauritiana | Leaves | Emulsion |
| Rosacea | Braithwaite et al., 2015 | New Zealand | Males and females aged 16 or over with a | Cream containing medical-grade Kanuka honey with 10% | 1. Baseline assessments (the IGA-RSS): significantly improved ($p < 0.05$) | 1. Baseline assessments (the IGA-RSS) | 8 weeks | – | – | Cream |
| 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 | Part used | Dosage form |
|--------------|---------|----------------|------------------------------------------|---------------|---------------------|------------------|----------|-----------------------------|-----------|-------------|
| Soltanipour, 2014 | Iran | 20–30-year-old nulliparous females with gestational age of 18–20 weeks (150) | 1 cm³ of olive oil applied twice daily on the skin of abdomen gently without massage | Saj cream (a commercial product containing lanolin, stearin, triethanolamine, almond oil, and beizox glycerin amidine) Control (no intervention) | Striae severity: no significant effects on development and severity of striae gravidarum ($p=0.43$) | Striae severity assessed using the Davey method | The subjects were followed until gestational week of 38–40 | O. europaea | Fruit | Oil |
| Hosmuter et al., 2007 | Turkey | Males and females with hypertrophic and keloid scars and an average age of 40.3 ± 9.6 (72) | Group 1: topical onion extract only Group 2: silicone gel sheet only Group 3 ($n=20$): combined onion extract and silicone gel sheet | Groups compared with each other | 1. Clinical evaluation: (A) A significant difference in the color parameter between groups 1 and 2 and in the height parameter between the groups 1 and 3 ($p < 0.01$ and $p < 0.05$ respectively) (B) A significant reduction in scar erythema in group 1 compared with group 2 ($p < 0.05$) (C) A significant reduction in scar height in group 3 compared with group 1 ($p < 0.05$) 2. Patient assessment: (A) No significant difference in hardness, itching, and pain between all groups ($p > 0.05$) (B) A significant improvement in scar color, hardness, and pain in group 1, and a significant improvement in scar color, hardness, height, and itching groups 2 and 3 3. Evaluation of the therapeutic index (TI): The total TI of group 3 was better than the others | 1. Clinical evaluation by one plastic surgeon 2. Patients’ assessment of scar color, scar height, scar hardness, itching, and pain 3. A global assessment of the clinical course of scar development evaluated using a TI | A. cepa | – | Gel |
| Muhammad et al., 2015 | Pakistan | 25–35-year-old males (11) | W/O emulsion containing 4% w/w tamarind extract | Placebo | 1. Skin sebum contents: significantly decreased with respect to time ($p \leq 0.05$) | 1. Skin sebum contents using a Sebumeter MPA5 | 12 weeks | Tamarindus indica | Seeds | Emulsion |
# Skin care (n = 53)

| 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 | Part used | Dosage form |
|---------------------|-------------|---------------------------------|--------------------------------------------|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|----------|-------------------------------|-----------|--------------|
| Matsuyama et al., 2018 | Japan       | 35–59-year-old females with mild skin problems (20) | A capsule containing 150 mg Sakura Extract-P (cherry blossom) taken once daily | Placebo                                                                                           | 1. Advanced glycation end products (AGEs) and skin parameters: significantly decreased  
2. Skin moisture: significantly decreased in both groups (p < 0.01)  
3. TEWL: significantly increased  
4. VISHA and skin replica parameters: the number of facial spots and reddish areas decreased significantly. Skin texture and the number of pores did not change significantly. UV-reactive spots increased significantly. The other parameters showed no changes.  
5. Questionnaire results: no significant differences | 1. AGEs measured using an AGE reader  
2. Skin moisture measured using a Corneometer  
3. TEWL measured using a Tewameter  
4. Skin elasticity measured using a Cutometer  
5. Skin replica analyzed using a reflective 3-dimensional replica analysis system  
6. Facial condition assessed by a face image analyzer (VISIA Evolution)  
7. Evaluation of spots, wrinkles, texture, pores, UV reactive spots, brown spots, reddish areas, and porphyrin using an image captured with a VISHA Evolution  
8. Questionnaires regarding skin condition | 8 weeks   | *P. serrulata*                   | Flowers                                      | Capsule                                            | 12 weeks | *S. indicus*                  | Flowers                                      | Emulsion           |
## Table 2. Summary of RCTs conducted between 1998 and 2018 of plants, herbs, or isolated compounds used for hair care.

| 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 | Part used | Dosage form |
|--------------|---------|----------------|-------------------------------------------|---------------|---------------------|------------------|----------|--------------------------------|-----------|------------|
| Hay, 1998    | Aberdeen, Scotland | Alopecia areata patients (86) | Massaging aromatherapy oils into scalp for at least 2 minutes, 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 in hair density 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 | T. vulgaris, Lavandula angustifolia, Rosmarinus officinalis, C. atlantica (in jojoba and grapeseed carrier) | – | Aromatherapy oils |
| Kamimura et al., 2000 | Japan | 30–57-year-old healthy males (29) with male pattern baldness | 1% (w/w) procyanidin B-2 tonic preparation | Placebo | 1. Change in hair density: the increase in hair density in the procyanidin 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 procyanidin B-2 group after 6 months was statistically significant compared to placebo (p < 0.02) | 1. Determination of change in hair density from a predetermined site photographed by a camera fitted with macros and a microscope at a magnification of × 300 | 26 weeks | M. pumila Miller var. domestica Schneider | Fruit juice | Tonic |
| Sasmaz and Arican, 2005 | Turkey | Subjects with patchy alopecia areata (31) | 20% azelaic acid (dithranol) | 0.5% anthralin | 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 AEs 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 | – | – | Cream |
| Choi et al., 2015 | Korea | 28–68-year-old males and females suffering from alopecia areata (50) | 0.5 % Rice bran supercritical CO₂ extract (RB-SCE) tonic product | 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 males only 2. Hair diameter: in the active group, hair diameter was significantly increased | 1. Phototrichography (hair density, haircount, and diameter by Folliscope) 2. Expert Panel Assessment of Global Photograph | 16 weeks | O. sativa L. var. japonica | Supercritical CO₂ extract | Tonic product |

(Continued)
| 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 | Part used | Dosage form |
|-------------|---------|----------------|-------------------------------------------|---------------|---------------------|------------------|----------|-----------------------------|-----------|-----------|
| Pekmezci 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 | 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 < 0.00001) | Phototrichogram | 26 weeks | M. chamomilla, A. millefolium, C. siliqua, E. arvense, U. arens, and U. dioica | Shampoo or/and solution | Root extract |
| FAAD, 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. | 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 investigator global hair assessments (IGHA) and quality scales in the active group compared to placebo (p < 0.05) no significant changes in terminal hair diameter | 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 | 6 months | Standardized extracts of Ashwagandha, curcumin, Saw palmitto, tocotrienol-rich tocopherol complex, piperine, and capsacin, hydrolyzed marine | Capsules | |
| **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** | **Part used** | **Dosage form** |
|-----------------|-------------|--------------------|---------------------------------------------|-------------------|------------------------|----------------------|--------------|---------------------------------|--------------|----------------|
| Thiab et al., 2021 |             |                    |                                             |                   |                        |                      |              |                                 |              |                |
| Satchell et al., 2002 | Australia  | 14 and older male and female patients suffering from mild-moderate dandruff (126) | 5% tea tree oil shampoo | Placebo | 3. self-assessment questionnaire (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 bundle measurements ($p < 0.05$) | 3. Responses in the subject self-assessment questionnaire SAQ. Ease of use, and QoL 4. Safety: changes in physical exam and potential AEs | 4 weeks | *M. 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 Social Security (103) | *S. chrysotrichum* extract (12.5%) mixed with neuter shampoo | 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 was higher in ketoconazole group after 2 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 | 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 | *S. chrysotrichum* | Leaves | Shampoo |
| 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 | Part used | Dosage form |
|----------------------|---------|----------------|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------|----------|--------------------------------|-----------|-------------|
| Salmanpoor et al., 2012 | 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 2 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 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) | – | 4 weeks | G. glabra | – | Shampoo |
| Chaijan et al., 2018  | Iran    | 18–60-year-old males and females with dandruff (90) | 1. *M. 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. Also, they were asked to massage the antifungal solutions on the scalp 3–5 minutes before going for a shower and then to wash their hair with the antifungal 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 | 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  
c. adherent scalp flaking score  
d. Redness of scalp skin  
e. Grading of scalp skin involvement  
2. The patients’ satisfaction and acceptance were evaluated using a VAS | 1 month | *M. communis* L. | Leaves | Solution |
Table 3. Risk of bias assessment of the RCTs included in this SR.

| Random sequence generation | Allocation concealment | Selective reporting | Other sources of bias | Blinding (participants and personnel) | Blinding (outcome assessment) | Attrition bias | Incomplete outcome data |
|----------------------------|------------------------|---------------------|----------------------|---------------------------------------|-------------------------------|----------------|------------------------|
| X                          | X                      | L                   | H                    | X                                     | X                             | L              | Gonzalez et al., 1997 |
| X                          | X                      | L                   | L                    | L                                     | L                             | X              | Martelli et al., 2000 |
| L                          | X                      | L                   | L                    | L                                     | L                             | L              | Bauza et al., 2002    |
| L                          | X                      | L                   | L                    | L                                     | L                             | L              | Javidnia et al., 2003 |
| L                          | X                      | L                   | L                    | L                                     | L                             | L              | Javidnia et al., 2003 |
| H                          | X                      | L                   | L                    | X                                     | H                             | L              | Hosnabett et al., 2007 |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Camouse et al., 2009  |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Kim et al., 2008      |
| L                          | X                      | X                   | X                    | X                                     | X                             | X              | Mandawgode and Patravale, 2008 |
| L                          | X                      | L                   | L                    | L                                     | L                             | X              | Rival et al., 2009    |
| X                          | L                      | L                   | L                    | L                                     | L                             | H              | Vicente et al., 2009  |
| L                          | X                      | L                   | L                    | L                                     | L                             | L              | Bazin et al., 2010    |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Kim et al., 2010      |
| X                          | X                      | L                   | L                    | L                                     | L                             | H              | Akhter et al., 2011   |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Lee et al., 2011      |
| L                          | X                      | L                   | L                    | L                                     | H                             | L              | Altaci, 2012          |
| H                          | H                      | L                   | L                    | H                                     | H                             | L              | Wineman et al., 2012  |
| X                          | X                      | L                   | L                    | H                                     | L                             | L              | Danby et al., 2013    |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Shin et al., 2013     |
| L                          | X                      | L                   | L                    | L                                     | L                             | L              | White et al., 2013    |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Mendoza et al., 2014  |
| L                          | X                      | L                   | L                    | L                                     | L                             | H              | Soltanipoura et al., 2014 |
| X                          | X                      | L                   | L                    | H                                     | L                             | L              | Zhang et al., 2014    |
| L                          | L                      | L                   | H                    | H                                     | L                             | L              | Braithwaite et al., 2015 |
| H                          | X                      | L                   | L                    | L                                     | L                             | L              | Morag et al., 2015    |
| X                          | X                      | L                   | L                    | H                                     | L                             | L              | Muhammad et al., 2015 |
| X                          | X                      | L                   | X                    | X                                     | X                             | X              | Akhter et al., 2016   |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Filipovic et al., 2016 |
| X                          | X                      | L                   | L                    | H                                     | L                             | L              | Ilynska et al., 2016  |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Kanlayavattanakul et al., 2016 |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Lee et al., 2016      |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Ray et al., 2016      |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Srivilai et al., 2017 |
| L                          | X                      | L                   | H                    | L                                     | L                             | L              | Boonchai et al., 2018 |
| X                          | X                      | L                   | H                    | L                                     | X                             | L              | Kanlayavattanakul et al., 2017 |
| X                          | X                      | L                   | H                    | L                                     | L                             | L              | Milani and Sparavigna, 2017 |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Srivilai et al., 2017 |
| X                          | X                      | L                   | L                    | L                                     | L                             | L              | Wang et al., 2018     |
| X                          | X                      | L                   | H                    | L                                     | L                             | L              | Egoumenides et al., 2018 |
| X                          | X                      | L                   | L                    | H                                     | L                             | L              | Goldberg et al., 2019 |
| X                          | X                      | L                   | L                    | L                                     | L                             | X              | Lee and Cha, 2018     |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Matsuyama et al., 2018 |
| L                          | X                      | L                   | L                    | X                                     | L                             | X              | Weber et al., 2019    |
| X                          | L                      | L                   | H                    | L                                     | L                             | L              | Yoshida et al., 2019  |
| X                          | L                      | L                   | H                    | L                                     | L                             | L              | Asada et al., 2019    |
| L                          | L                      | L                   | L                    | L                                     | L                             | L              | Roh et al., 2019      |

(Continued)
(Hay, 1998); and the third study tested *Sphaeranthus indicus* for its moisturizing, antihyperpigmentation, antisebum, elasticity properties, and overall improvement of the skin condition (Ahmad et al., 2020).

### Skin care

Ten RCTs concerned with hair care were identified for reducing hair loss and baldness, six of which were published between 1998 and 2018. The studies used *O. sativa* (Choi et al., 2015), *Malus pumila* (Kamimura et al., 2000), and anthralin (Sasmaz and Arican, 2005), and three used a combination of natural products. Of those combinations, one study used *Melaleuca alternifolia* (Satchell et al., 2002), *Solanum chrysotrichum* (Herrera-Arellano et al., 2004), *G. glabra* (Salmanspoor et al., 2012), and *Myrtus communis* (Chaijan et al., 2018).

### Risk of Bias of the Included Studies

The risk of bias of the included studies in this review was conducted by the researchers, with the bias assessment for all the studies included in detail in Table 3.

### Skin care

Eighteen studies were at low risk of randomization bias, as they were randomized using either sequence generation or block randomization. On the other hand, 3 studies were at a high risk due to inadequate randomization. The rest did not provide sufficient information regarding the randomization method; thus, the risk was considered unclear (*n* = 32). Most studies (*n* = 42) did not describe the allocation concealment process, so the risk of bias was noted as unclear, whereas 10 studies were considered of low risk as proper concealment techniques were described. Only one study was considered high risk regarding the allocation concealment, as the participants were unblinded. Fifty-two other studies were considered of low risk as proper concealment techniques were described. The participants were not blinded in 9 studies, so these were considered at a high risk of performance bias. Additionally, the assessors were not blinded in 6 studies, so these were at a high risk of detection bias. If it was unclear whether...
the participants and/or assessors were blinded, the studies were considered to be at an unclear risk of performance/detection bias. For the attrition bias, attrition rates above 20% were considered of high risk; 2 studies were found to have high dropout rates and were at a high risk of attrition bias, 43 were stated as low risk, and 8 were of unclear risk because it was unclear whether the data of all participants were considered or if any failed to complete the study. Many studies (n = 43) were stated as low risk in the domain of other biases, six were stated as high risk as the researchers were funded from the same companies providing the test products, and eight were considered unclear because the conflict of interest was not declared in these studies.

Hair care

Four studies were at low risk of randomization bias, while six were considered of unclear risk, because the randomization methods were not mentioned. One study was considered at low risk of allocation bias, and nine were considered of unclear risk. In the reporting bias domain, nine were considered low risk and one was of unclear risk. Some studies (n = 7) were double-blinded, so they were at low risk of both performance and detection biases, while the remaining three studies followed an open-label strategy and thus were at a high risk for both performance and detection biases. In the attrition bias domain, seven studies were at low risk, two were at an unclear risk, and one was stated high risk. Regarding other biases, five studies were considered low risk, and the other five were stated as unclear risk.

Outcomes

Skin care

Thirty-six RCTs compared natural product(s) or derived compound(s) with a placebo; 29 preparations were found effective. Nine RCTs compared natural product(s) or derived compound(s) with another treatment; eight preparations were found effective. Eight RCTs compared natural product(s) or derived compound(s) with untreated controls, all of which yielded statistically significant results. One RCT compared silymarin cream with untreated control and placebo was found effective in both cases. The results of the remaining studies were statistically insignificant.

Hair care

Six RCTs compared natural product(s) or derived compound(s) to placebo, and all were found to have statistically significant outcomes. Four RCTs compared natural product(s) or derived compound(s) with active treatments, and the efficacy outcomes were found to be statistically insignificant.

The tested natural product(s) or derived compound(s) showed good tolerability in most studies, but adverse events (AEs) including dryness, scaling, erythema, edema, itching, and pricking were reported with a formulation containing retinol and rose extract (Lee et al., 2011).

Plants present in Jordan

From the above discussed studies, ten plants were identified to be present in different locations in Jordan, as illustrated in Table 4. The plants that are found in Jordan and can be used for skin and hair care were as follows: A. sativa, which was investigated in a study conducted in the United States of America (USA), was found effective in improving skin barrier integrity and increasing its hydration (Garay, 2016). Portulaca oleracea was reported to be useful in the treatment of melasma in China (Zhang et al., 2019). In addition, it was found to improve skin health and reduce sensitization when used in combination with other plants (Wang et al., 2018). Silybum marianum was also reported to be useful for melasma as was found in an Iraqi study (Altai, 2012). Foeniculum vulgare and M. sativa were effective in reducing facial hair in two studies, both conducted in Iran (Javidnia et al., 2003; Sargazi et al., 2016). Glycerrihiza glabra was used in combination with other plants to improve the overall skin condition (Roh et al., 2019; Seiwerth et al., 2019) and in a hair shampoo as an antiandrogen agent (Salmanpoor et al., 2012). Myrtus communis was also found useful for the treatment of dandruff when mixed with vinegar in a study conducted in Iran (Chaijan et al., 2018). Ceratonia siliqua and U. vrens were used in a combination used to improve hair growth and strength with other plants in a study conducted in Turkey (Pekmezci et al., 2018).

DISCUSSION

The worldwide growth of the cosmetic sector is partially driven by the input of natural products (Cervellon and Carey, 2011). The global market value for natural cosmetics is expecting a positive increase with the upcoming years (Shahbandeh, 2020). This SR is unique as it explored plant extracts, herbal preparations, and isolated plant-derived compounds used for cosmetic purposes, particularly for skin and hair care. Fifty-three RCTs exploring natural products used for skin care were identified. Most of the RCTs were published between the years 2013 and 2019 (n = 34). Thirty-seven RCTs used natural products as a single ingredient (around 70% of the RCTs), while 16 RCTs used them in combinations (around 30% of the RCTs). Creams were the most frequently used dosage form (49% of the topical preparations). Other tested dosage forms were lotions, serums, gels, emulsions, beverages, oils, tablets, and capsules. Ten RCTs were designed to test natural products for hair care, seven of which used natural products as a single ingredient (70% of the RCTs), while the other three used them in combinations (30% of the RCTs). Shampoos were the most common form used (40%); aromatic oils, creams, solutions, capsules, and hair tonics were also used. The population included in this review added up to 3,439 subjects, and about 50% of the studies included females exclusively. The smallest number of participants was 3 and the highest was 203. The most common duration of the RCTs was 12 weeks (around 27% of the RCTs). The shortest duration was 75 minutes (0.0074 weeks), and the longest duration was 7 months (30.42 weeks). Around 87.3% of the reviewed RCTs found the tested natural products to have statistically significant efficacy outcomes. In addition, several treatment preparations were described, highlighting the diverse possibilities for incorporating botanicals into cosmetics. However, these reported outcomes should be interpreted cautiously for several reasons. Firstly, the majority of RCTs did not include power calculations indicating whether the number of participants is representative of the population or not. Secondly, participants were usually from a certain background, and thus the findings might not be applicable to all people of diverse ethnicities, lacking external generalizability.
Thirdly, statistical significance may not necessarily indicate clinical significance, as the outcomes of interest are sometimes surrogate markers. It is important to explore local plants for their cosmetic potential, which may add to the diversity of the local market. In our case, plants that are present in Jordan are of particular interest, as these can be used in developing cosmetics locally and can be marketed internationally to help the country’s economy flourish (Workman, 2020). This discussion sheds light on each of these plants to provide needed information for policy makers and investors in the country.

CONCLUSION

Cosmetics are marketed and used worldwide for various purposes, which makes them a subject for academic and market research (Infante et al., 2016). This SR provided a summary of the plants/herbs in the literature which were clinically tested in RCTs from 1997 until 2020 for their cosmetic purposes, particularly skin and hair care. Such information can be helpful for policy makers and investors to make informed decisions regarding the production of cosmetics that can be of benefit locally and internationally. Additionally, this SR provided a list of plants/herbs found in Jordan which evidently showed cosmetic potential. In order to provide clear and comparative results, plants with promising findings are worth further investigations in robust RCTs.

AUTHORS’ CONTRIBUTION

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

ETHICAL APPROVAL

Not applicable.

CONFLICT OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

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