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Review Article

Snails and Skin: A Systematic Review on the Effects of Snail-based Products on Skin Health

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Relevance

The incorporation of snail-based products into skin care has increased in popularity.

Objective

The purpose of this systematic review is to gather data on the clinical use and effectiveness of secretions from *Cryptomphalus aspersa* (SCA) and snail egg extracts (IFC-CAF) in skin rejuvenation and repair.

Methods

A literature search was conducted on PubMed, Cochrane, and EMBASE databases. There was a total of 10 studies included in the review.

Results

The effects of SCA and ICF-CAF on human subjects demonstrated an improvement in signs of skin aging, increased skin hydration, decreased transepidermal water loss (TEWL), antimicrobial activity, and improved healing after radiation therapy and fractional laser treatment.

Conclusion

The popular use of snail-derived ingredients in cosmeceuticals to improve skin appearance is reinforced by the demonstration of several clinical trials on humans that have indicated significant improvement in several skin parameters. A greater understanding of the effects of topical application of snail-based products on a large sample size may further increase its utility in both medical and cosmetic purposes.

INTRODUCTION

The use of natural products in skin care has shown promising results on improving skin health.[1] Recently, increased efforts have been placed on investigating the effects of snail-derived products in skin rejuvenation. The use of snail secretions in medicine can be traced back to ancient Greece, where snail secretions were used to reduce inflammation and signs of aging.[2]

From wrinkles to burns to wounds, snail mucus possesses many qualities that allow it to act as a natural remedy.[1,3] The composition of the mucus consists of a complex matrix with a high content of allantoin and glycolic acid.[4] Allantoin has been shown to increase cell growth, stimulate regeneration of tissues, and rebuild granulation tissue.[4] The high glycolic acid content in snail secretions also shows promising effects for skin appearance. Glycolic acid is a type of alpha hydroxy acid (AHA) that acts as an exfoliant to remove dead skin cells and effectively reverses sign of aging and photodamage.[5] Thus the healing and regenerative properties of both allantoin and glycolic acid shed light on the potential dermatological uses of snail secretions. Furthermore, *in vitro* studies found that the secretions from *Cryptomphalus aspersa* (SCA), commonly known as the “brown garden snail,” contained antioxidant superoxide dismutase and glutathione S-transferase activities in addition to antimicrobial peptides.[3,6] SCA is also rich in glycosaminoglycans, which draw water into the skin and maintain skin hydration. By retaining moisture, the skin can maintain elasticity and firmness.[7]

SKIN REGENERATION

As the regenerative properties of skin decrease with age, greater research has been dedicated to investigating potential products that can minimize cutaneous aging. SCA has been shown to possess promising regenerative properties. When the skin endures external injury, keratinocytes proliferate and lead to new cell-cell adhesions. E-cadherin complexes with β-catenin to maintain integrity of epithelial cell-cell contact.[8] Further, cell migration and prolifer-

ation is established through signal transduction via phosphorylation of the Tyrosine kinase focal adhesion kinase (FAK).[8] An *in vitro* study in human keratinocyte cell lines (HaCaT) and human dermal fibroblasts (HDF) found that SCA promotes cell proliferation, migration, survival and phosphorylation of FAK, and nuclear localization of β-catenin.[8] In addition, treatment with SCA was found to increase the expression of different cell adhesion proteins in both human keratinocytes and fibroblasts.[3,8] Impaired wound healing and regeneration can be attributed to increased metalloproteinase (MMP) expression.[3] An *in vitro* study using dermal fibroblasts treated with different concentrations of SCA found that SCA significantly inhibited both MMP-1 and MMP2 expression, highlighting the regenerative properties of SCA.[3] A product derived from the eggs of *C. aspersa*, IFC-CAF, also showed the ability to induce differentiation and migration of HaCaT and HDF by promoting the production of extracellular components such as fibronectin and adhesion proteins.[9]

Skin aging can be attributed to both chronological and environmental factors, leading to wrinkles, changes in skin texture, reduced structural integrity and slowed wound healing.[3] Histologically, aging skin can show reduced collagen density and epidermal thinning.[10] There is an additional reduced expression of genes involved in the formation of the extracellular matrix.[10] In addition to their regenerative properties, IFC-CAF and SCA have also been shown to prevent cutaneous aging.[9] An *in vitro* study of keratinocytes and dermal fibroblasts treated with IFC-CAF found a decreased expression of aging-related markers b-GaI, p53, and p16INK in senescent dermal fibroblasts. IFC-CAF also enhanced the production of ECM fibronectin and collagen I, which prevents cutaneous aging.[9] UV radiation may induce premature aging via inducing formation of reactive oxygen species and activation of MMPs.[7] After UVB irradiation, IFC-CAF was able to improve cell survival in HaCaT cells.[9] In addition, SCA increased cell survival after irradiation with UVA light.[3] Another study using mouse models found that oral snail mucin improved UVB-induced moisture loss, decreased wrinkle formation, and improved UVB-induced elasticity.[11]

ANTIMICROBIAL ACTIVITY

Researchers observed antimicrobial peptides in the mucus of *Achatina fulica* and *C. aspersa* depicting antibacterial effects against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. This further justifies the addition of snail secretion into over-the-counter cosmeceuticals.[6]

Taken together, the demonstrated skin regenerative properties of mollusks have garnered increased interest in cosmeceutical use of snail-derived products for the treatment of skin aging. For instance, SCA and ICF-CAF have been manufactured into a commercially available topical product under the trade name Endocare (Tensage; Biopelle, Inc, Ferndale, MI, manufactured by Industrial Farmaceutica Cantabria, SA), which is marketed for its skin rejuvenation effects.[12]

The purpose of this review is to investigate the clinical efficacy of snail-derived products on skin health. This review explores the protective effects on skin of snail secretions and egg extracts in human trials.

METHODS

A PubMed, Embase, and Cochrane search for articles with the following keywords was performed: (Snail mucin OR Snail secretion OR Snail secretions OR Snail mucus OR *Cryptomphalus aspersa* OR *Achatina fulica*) AND (Skin OR Dermatolog* OR Cutaneous). Results were filtered to include clinical trials with human subjects. Sixty-three PubMed, 68 Embase, and 12 Cochrane articles resulted. Fifty-four articles were excluded due to repeats and 75 articles were removed based on title and/or abstract screening. Articles were excluded if they were written in a non-English language, conducted *in vitro* or on animal models, or if they were a review. Fifteen full texts were reviewed by three reviewers. One additional report was included via handsearching. Articles were included if they discussed the application of snail-based products in human trials. In total, 10 clinical studies were included in the review, one of which was detailed in a conference abstract.

RESULTS AND DISCUSSION

A PRISMA flow diagram outlining the screening process is provided in Figure 1.

SKIN REGENERATION AND REJUVENATION

The growth factor-like activity of SCA and ICF-CAF has been demonstrated in 7 clinical trials including 287 total patients, with results showing improvement in skin integrity and regeneration in aged skin.

The effects of SCA on photoaging were assessed in 2009 in an uncontrolled, open-label trial consisting of 15 women with clear signs of photoaging.[7] The subjects were instructed to apply an SCA 8% emulsion in the morning and a SCA 40% liquid formulation at night daily for 3 months. The Glogau scale was used to assess the severity of photodamage. The authors observed a significant reduction of photoaging signs following 3 months of SCA topical application compared to baseline. In addition, the percentage of participants with fine wrinkles and deep wrinkles decreased significantly compared to baseline. The sallowness of the skin was reduced, and the skin's dryness and roughness were improved at day 30 and day 90. A 40% reduction of irregular pigmentation was observed at day 90. Histopathological analysis revealed significant improvement in the architecture of the dermis and epidermis at day 90 with a significant increase in the number of blood vessels and a significant increase in the mean epidermal proliferation index. Profilometry at day 90 showed a statistically significant improvement in wrinkle depth and cutaneous microroughness. The tolerance of SCA treatment ranged from good to very good. Only one adverse effect was reported, unrelated to the treatment with SCA. The results suggest that clinical use of topical SCA can reduce features of photoaging, such as skin roughness and wrinkle depth, while im-

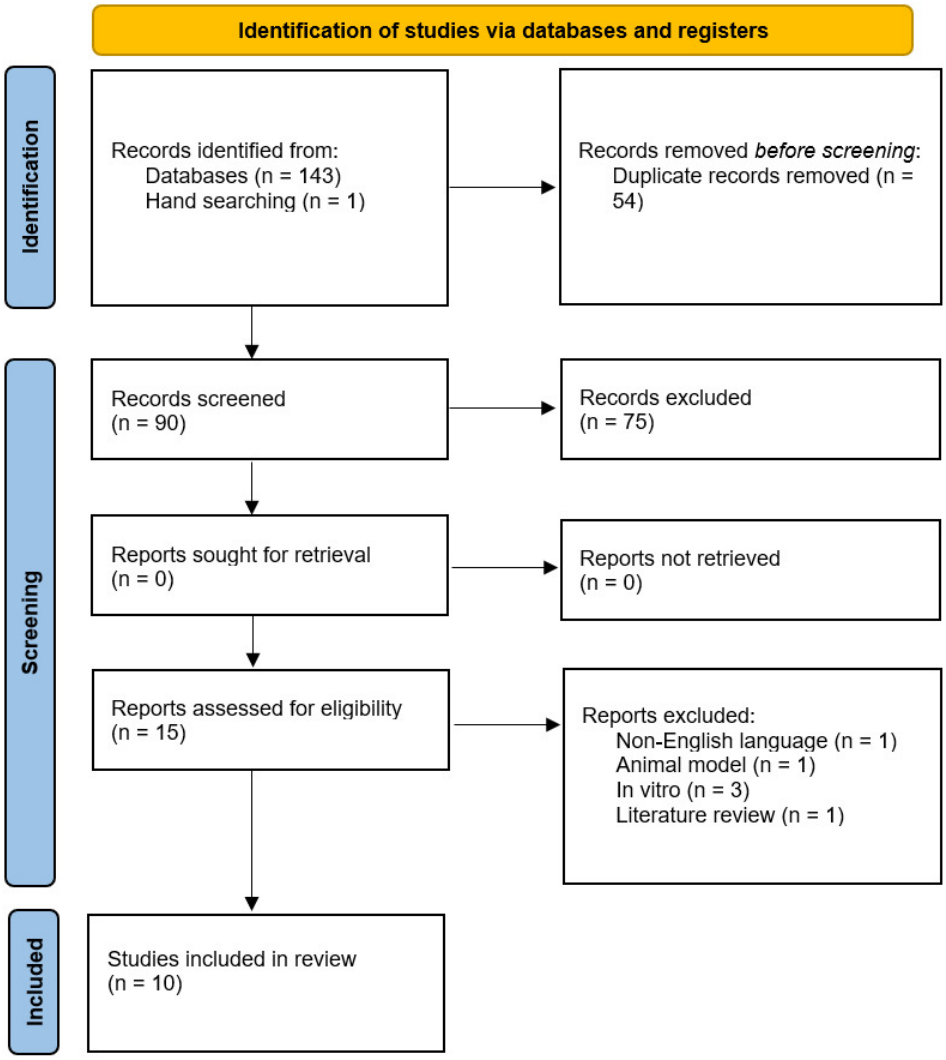

Figure 1. PRISMA Flow Diagram

proving skin sallowness and wrinkle appearance. Such effects can be attributed to antioxidant properties, inhibition of MMP expression, and promotion of extracellular matrix proteins characteristic of SCA.[3,8] However, the lack of a control group presents as a limitation in drawing clear conclusions on the efficacy of SCA in reducing photoaging.

A 2013 double-blind split-face trial assessed the efficacy of topical application of SCA in improving facial wrinkles in 25 subjects with moderate to severe facial photodamage.[13] Subjects were treated with an emulsion of 8% SCA and liquid serum of 40% SCA on one side of the face and placebo on the contralateral side for 12 weeks. Silicone skin impressions and patient and physician assessments were used to evaluate the wrinkle improvement after 12 weeks of treatments. Periocular wrinkles on the active ingredient side displayed a significant improvement after 12 weeks compared to the placebo treatment on the contralateral side. The Glogau scale indicated no change in overall photodamage severity between the two sides. Patients noted a significant improvement in fine lines on the SCA-treated side after 8-weeks. These results held constant 2 weeks after discontinuing the product, which shows the potential lasting effects of SCA on improving signs of skin aging.

In a 2020 double-blinded, randomized, placebo-controlled trial, 50 women with signs of photoaging were recruited to assess the efficacy of SCA and IFC-CAF on improving signs of skin aging.[12] Commercially available Endocare products containing SCA and IFC-CAF were used by 30 women, and the vehicle product was used by 20 women twice daily for 3 months. Both treatment regimens included ingredients with hydration and moisturization efficacy, but only the Endocare products had active snail-based ingredients. Subjects in the active treatment group demonstrated significantly greater reduction of transepidermal water loss (TEWL) compared to the vehicle group after 3 months. The active treatment group also had a significantly greater improvement in skin firmness after 1 month and 3 months compared to the placebo vehicle group. The elasticity of the skin after 3 months also significantly improved in the active-treatment group compared to the placebo vehicle group. Both the active and control groups showed significant improvement in periocular and perioral wrinkles after 3 months, but there were no significant differences between the groups. Physician assessment of skin roughness found that subjects in the active treatment group demonstrated a significantly greater improve-

Table 1. Summary of Clinical Studies Assessing Snail-Based Products on Skin

Intervention	Subjects	Placebo	Outcome	Major Results	Jadad Score	Author (Year), Study Design
Endocare Tensage Serum containing the secretions of Cryptomphalus aspersa (SCA), Transdermal, vitamins C and E, and nicotinamide, and Endocare/ Cellage/Cell ProConcentrate containing IFC-CAF(n=30)	Women aged 45 to 65 years old with Fitzpatrick Skin Phototypes II- V and signs of photoaging	Vehicle (n=20)	-Transepidermal water loss (TEWL), skin hydration -Skin firmness and elasticity via cutometry -Skin brightness -Rao-Goldman Five-Point Scale to assess periocular and perioral wrinkles -Subjective assessments by patients and physicians for wrinkles -Investigator (IGA) and Patient Global Assessments (PGA)	-Significant greater improvement in the reduction of TEWL in active treatment group compared to vehicle group at 90 days (p=0.026) -Subjects in the active treatment group had significantly greater improvement in skin firmness at day 30 (p=0.012) and day 90 (p=0.005) and in skin elasticity on day 90 (p=0.024) compared to the vehicle group -Nonsignificant increase in hydration index values at day 30 and day 90 in active treatment group - Nonsignificant reduction in Melanin index values in both active and vehicle groups on day 30 (p=0.051) -Both active and vehicle groups showed significant improvement in periocular (p=0.021) and perioral (p=0.033) wrinkles at the end of treatment without significant differences between the groups -Per investigator skin condition evaluation, subjects in active treatment group demonstrated significantly greater improvement in skin roughness at day 90 compared to vehicle group (p=0.002) -Significant improvement in the active group compared to vehicle group based on IGA and PGA after 1 month (p=0.005)	4	Lim et al. (2020), randomized controlled trial
Endocare Concentrate SCA 40% Ampoules with Vitamin C and E (n=10)	Women aged 40 to 65 years	Vehicle (self-controlled) (n=10)	-Microcolumn density -Transepidermal water loss (TEWL) -Photoaging based on Rao-Goldman scale -Investigator (IGA) and Patient Global Assessments (PGA)	-Significant average difference in the microcolumn density when comparing active vs vehicle hemiface (p=0.04) -Significant difference in reduction in TEWL and erythema detected in active-treated side (p<0.05) -Significant improvement in tightness in active-treated side vs vehicle-treated side (p<0.05) -Significantly greater average wrinkle decrease on SCA-treated side at the end of the 3rd week (p<0.05) -Improvement in Rao-Goldman scale in both hemifaces at one week without significant difference between hemiface -No significant difference in investigator and patients' subjective evaluation	5	Fernandez-Gonzalez et al. (2004), randomized controlled trial (split-face)
Eye and face anti-aging cream containing a *C. aspersa* egg extract	Men and women age	None	-Dermatologist investigator,	-At week 12, the investigator rated a 53% reduction in skin roughness (p<0.001), 26% improvement in skin brightness	N/A	Draelos et al. (2017), open-

	40 - 70 years of Fitzpatrick skin types I - IV with moderate to severe facial aging		subject, and elasticity assessments	(p<0.001), and 12% reduction in skin dyspigmentation (p=0.033) -Significant increase in skin elasticity at week 8 of 11% with a continuing elasticity increase at week 12 of 39% (p<0.001)		label, uncontrolled
Serum containing snail secretion filtrate (40%), *C. officinalis* (4%), and *G. glaba* root extract (0.3%) (n=33)	Men and women with a mean age of 29 years old	Vehicle (n=33)	-Percentage change of acne count at week 12 from baseline -Investigator Global Evaluation Acne (IGEA) -Transepidermal water loss (TEWL) -Participant satisfaction using a visual analog scale	-After 12 weeks of using the active serum product, the percentage change in total acne was reduced by 9.09%. In the placebo group, the percentage change in total acne increased by 3.92% after 12 weeks. There was no statistically significant difference in the percentage change of total acne between two groups (p=0.15) -The percentage change in inflammatory acne in the active serum group decreased by 31.40% by the end of the study. In the placebo group, the percentage change in inflammatory acne showed an upward trend and increased by 2.48% compared to baseline. The active treatment group experienced a significantly higher percentage reduction of inflammatory acne compared with the placebo. -The percentage change in non-inflammatory acne slightly increased in both groups and there was no difference between the active serum and placebo product -Both groups showed a reduction in TEWL and erythema index. -Average satisfaction score of participants in the treatment group was greater than the placebo group, but not significantly different (p=0.64)	5	Puaratanaarunkon et al. (2022), randomized controlled trial
1) Lipid-free serum containing *Cryptomphalus aspersa* secretion (SCA), low molecular weight (LMW) hyaluronic acid (HA), epidermal peptides, coffee oil, olive oil- for normal-oily skin (n=34) 2) Oil in water cream containing SCA, ectoine, LMW HA, epidermal peptides, coffee oil, olive oil- for normal-dry skin (n=37) 3) Oil in water cream containing SCA, ectoine, LMW HA, epidermal peptides, coffee oil, olive oil- for periocular	Women 40-65 years old with facial aging	None	-Skin hydration via corneometry -Elasticity and firmness via cutometry -Epidermal and dermal elements via reflectance confocal microscopy (RCM) -Coloration via	-All treatment groups depicted significant improvement in hydration, softness, firmness, wrinkles, elasticity, expression lines, nasolabial grooves, and fine lines at 45 and 90 days (p<0.05) -Both non-periocular groups depicted significant increase in epidermal thickness at 90 days (p=0.004) -Periocular group depicted significant increase in skin luminosity at 90 days (p<0.05)	N/A	Addor et al. (2019); open-label, uncontrolled

and eyelid skin (n=36)			colorimetry for periorbital group -Clinical and subjective evaluation			
Emulsion (with 8% SCA) and liquid serum (with 40% SCA) on one side of the face and placebo on the contralateral side for 12 weeks	Patients with moderate to severe facial photodamage	Vehicle on contralateral side (self-controlled)	-Silicone skin impressions of periocular rhytides -Patient and physician assessments	-Periocular rhytides on the active ingredient side showed significant improvement after 12 weeks (P=.03) and improved texture to a greater degree than placebo at 8 and 12 weeks, as well as 2 weeks after discontinuing the product (14 weeks) -Nonsignificant change in photodamage severity measured by the Glogau scale -Significant improvement reported by patients of fine lines on the SCA-treated side after 8 week-s ($p<0.05$)	4	Fabi et al. (2013); randomized controlled trial (split-face)
Two sessions with fractional nonablative laser were performed, and the cosmetic treatments (SCA 40% on one hemiface and vehicle on the other) were applied immediately after laser session and daily during the study (28 days) (n=20)	Patients with moderate aging	Vehicle on contralateral side (self-controlled)	Tewameter, Cutometer, Visioscan, VisioFace, Photography, dermoscopy, and clinical evaluation	-A significant decrease in the density of microcolumns (25%, 71%, 32%, and 61% less density, respectively, at T3 ($p=0.008$), T7 ($p=0.002$), T22 ($p<0.001$), and T24 ($p<0.001$)) was observed on the side treated with SCA compared to the vehicle-treated side -Cutaneous elasticity, area of wrinkles, and hydration on the SCA-treated side showed a significant improvement compared to the vehicle-treated side. Both the researcher and patients observed a significant improvement on the side treated with SCA compared to the vehicle-treated side -Significantly fewer side effects (erythema, burning, and dryness) were also detected	4	Truchuelo et al. (2020); randomized controlled trial (split-face)
SCA cream RadiocareTM for application to the treatment field 1-2 times a day after each RT session (n=17)	Head & Neck and Breast cancer patients; 12 Females and 5 Males; Median Age 55 years	None	Signs of Radiodermatitis were measured qualitatively with RTOG clinical scoring	-SCA cream delayed the onset of grade 2 dermatitis (Usual onset: 25 to 30 days was delayed by 5 days)	N/A	Balaji Subramanian et al. (2018); open-label, uncontrolled, case series
SCA 8% emulsion and SCA 40% liquid formulation for 3 months (n=15)	Women aged 35 to 65 years with Fitzpatrick skin types II and III with facial	None	-Presence of fine lines and wrinkles, rhytides, sallowness, pigmentation -Photodamage	-Significant reduction of photoaging signs after treatment with SCA at day 90 compared with participants at the beginning of the study ($p<0.0001$) -Significant decrease in the presence of fine wrinkles and deep wrinkles ($p<0..05$) -Significant reduction in skin's sallowness at day 30 ($p<0.02$) and day 90 ($p<0.008$)	N/A	Tribó-Boixareu M.J et al. (2009); open-label, uncontrolled

	photoaging		severity score using the Glogau scale -Roughness and wrinkle depth using profilometry	-Significant improvement on day 90 of hydration assessed by the researcher ($p<0.003$) -Significant decrease in dryness and cutaneous roughness at day 30 ($p<0.01$) and at day 90 ($p<0.008$) -Significant decrease in irregular pigmentation ($p<0.01$) -Significant increase in the number of mean blood vessels ($p<0.075$)		
2%, 5%, and 10% snail cream (*C. aspersa*) (n=20)	Women age 20 – 65 years	None (self-controlled)	-TEWL and corneometry	-Significant decrease in TEWL in snail cream 5% and snail cream 10% after 24 hr application ($p=0.047$ and $p=0.016$, respectively) -Significant increase in skin hydration measured by corneometry 24 hours after application of the 3 formulations (2%, 5%, 10%) ($p=0.0026$, $p=0.050$, $p=0.017$, respectively)	N/A	Laneri et al. (2019); open-label, self-controlled

ment compared to subjects in the placebo vehicle group after 3 months. Investigator and patient global assessments reported a significantly greater improvement in the active treatment group compared to the vehicle group after 1 month and after 3 months. Patients in the active treatment group reported significantly less stinging, burning, and erythema, suggesting the overall tolerability was equal or better in the active group than in the vehicle group. These results suggest that the synergistic activity of SCA and IFC-CAF in Endocare products can significantly improve TEWL, skin roughness, and elasticity in aging skin compared to vehicle controls.

Similarly, a 2017 study assessing the effect of mollusk egg extract on facial skin appearance in 40 subjects was conducted. The subjects applied Tensage® Stem Cell Eye Cream and Tensage® Stem Cell Cream as a facial moisturizer twice daily for 12 weeks. Both products contained ICF-CAF as an active ingredient. After 12 weeks of using the products, there was a significant reduction in global facial wrinkling. Investigator assessment demonstrated a 26% reduction in skin roughness and improvement in skin brightness. Elastomer measurements revealed a significant increase in skin elasticity over the 12-week period. While the results of the study are consistent with other studies showing that ICF-CAF can promote improvements in skin aging parameters, the absence of a control group is a significant limitation in this study.

In 2019, an open-label study was conducted to analyze the effect of topical application of SCA on improvement of signs of skin aging.[14] 120 women with facial aging complaints were randomized to three treatment groups, based on their skin type. Subjects with normal-oily skin received a lipid-free serum containing SCA (group 1). Subjects with normal-dry skin received an oil in water cream containing SCA (group 2). Group 3 subjects received the oil in water cream, specifically for periocular and eyelid skin. Topicals were applied twice daily for 90 days. All treatment groups showed significant improvement in hydration, softness, firmness, wrinkles, elasticity, expression lines, nasolabial grooves, and fine lines at 45 and 90 days. Significant improvement in hydration was observed 2 hours following application in all treatment groups, with further improvement at day 45 and 90. Groups 1 and 2 demonstrated a significant increase in epidermal thickness at day 90 and an increase in dermal reticular collagen fibers and parallelism pattern. Group 3 was not evaluated for epidermal and dermal compositional changes due to periocular application yet depicted a significant increase in skin luminosity at day 90. The SCA-based formulations significantly improved a variety of cutaneous aging parameters, likely mediated by epidermal and dermal compositional changes. No adverse reaction related to the treatment protocol was observed. The results depict the clinical efficacy of the SCA-based formulation on a variety of cutaneous aging parameters, likely mediated by epidermal and dermal compositional changes. However, the inclusion of other regenerative and antioxidant ingredients hinders our ability to conclude the clinical efficacy of *C. aspera* secretions in isolation. Furthermore, the omission of a control group and the small number of subjects in each treatment group limits the robustness of results. Nevertheless, this study highlights the potential utility of SCA-based formulations for the improvement of cutaneous aging.

A 2019 self-controlled study analyzed the moisturizing effect of SCA on 20 female participants. Subjects applied SCA cosmetic cream of varying concentrations (2%, 5%, 10%) on their forearms. TEWL values significantly decreased after 24 hours in the snail cream 5% and snail cream 10% formulations. Skin hydration significantly improved in the snail cream 2%, 5%, and 10% formulations after 24 hours of application. These results were attributed to the high allantoin content of snail mucus. No adverse events were observed in the participants.

Lastly, a 2018 study investigated the prophylactic effect of an SCA topical cream on radiodermatitis treatment in 17 head and neck and breast cancer patients undergoing radiation therapy.[15] Patients received SCA cream Radiocare™ for application on the treatment site 1 - 2 times a day after each radiation therapy session. SCA cream delayed the onset of grade 2 dermatitis by 5 days. However, the small sample size and the lack of a control group are limitations of this study.

Seven clinical studies have demonstrated the efficacy and safety of SCA and ICF-CAF in skin regeneration. As a topical treatment, SCA and ICF-CAF can reverse the signs of aging and photodamage through the improvement of skin texture and reduction of periocular and perioral wrinkles compared to placebo. The hydrating effects on skin after application of creams containing snail-based ingredients were demonstrated in two clinical studies that showed a significant reduction in TEWL. However, the effects of SCA on photodamage differed between studies, which can be attributed to the use of the Glogau scale, a subjective visual scale of photodamage severity. While one study concluded no change in Glogau scale rating in the placebo and SCA-treated side, another study noted a significant reduction in photoaging on the Glogau scale after treatment with SCA for 3 months. The latter study, however, lacked a control group. Other limitations in the studies include the lack of large sample sizes needed to support the benefits of snail-derived ingredients in regular long-term use.

SCA APPLICATION AFTER FRACTIONAL LASER THERAPY

Ablative and nonablative fractional laser skin treatment utilize lasers to penetrate the skin surface, creating microcolumns that reduce signs of aging and improve skin texture.[16] Nonablative fractional lasers can also increase penetration of topical application of cosmetics and drugs after laser treatment.[16] In a 2020 randomized, double-blind trial, 20 patients with moderate aging were recruited to analyze the efficacy of treatment with SCA 40% on skin aging after the use of nonablative fractional laser.[16] The patients applied SCA 40% to one hemiface and a vehicle to the other immediately after a fractional nonablative laser treatment and daily for 28 days. The product was applied every 12 hours for the first 7 days and then every 24 hours until the next laser session. After the second laser session, the product was applied every 12 hours for the remaining 7 days.

Outcome measures included microcolumn density, TEWL, skin elasticity and firmness, erythema, and subjective evaluation of photoaging improvement perceived by the investigator and subjects. The results of the study found that microcolumn density induced by the laser decreased significantly faster on the active treated side compared to the vehicle-treated side. Furthermore, a significantly greater reduction in TEWL was measured on the SCA-treated hemiface 24 hours after the first laser session. The SCA-treated hemiface showed a significant improvement in elasticity after 28 days, and no significant changes were detected on the vehicle-treated hemiface. There was a significantly greater decrease in wrinkles on the SCA-treated hemiface. Investigator and patient global assessments both indicated a significant improvement on the SCA-treated hemiface after one week. A significantly greater decrease in erythema was also observed in the active hemiface on day 24 compared to the vehicle-treated hemiface. These results confirm the GF-like properties of SCA and suggest that SCA can improve skin barrier regeneration after nonablative fractional laser treatment, while also minimizing the adverse effects and enhancing the effectiveness of laser treatment in improvement of elasticity and wrinkle reduction.[3,16]

Another randomized, double-blind, vehicle-controlled study conducted in 2020 investigated whether SCA 40% could accelerate the postablative fractional CO2 laser skin recovery.[17] 10 volunteer women aged 40 - 65 years with signs of wrinkles were randomly assigned to apply SCA 40% or vehicle on their right or left hemiface. Each participant received laser treatment, and immediately after the treatment, the SCA 40% product or vehicle was applied to the right or left hemiface according to randomization. Afterwards, the product or vehicle was applied every 12 hours for the first week and then once daily for 2 more weeks. After 1 week of application of SCA, there was a statistically significant decrease in microcolumn density following fractional CO2 laser treatment. TEWL was measured before and after laser treatment, and there was a significant difference in reduction in TEWL, favoring the active-treated side. Quantitative determination of wrinkle depth was recorded immediately after laser treatment and at the end of the 3rd week, and showed a significantly greater average wrinkle decrease on the active-treated side compared to the vehicle-treated side. Additionally, side effects such as erythema and burning sensation were significantly reduced on the SCA-treated side. The reduction in microcolumn density showed that topical application of SCA 40% can accelerate the healing of microcolumns caused by fractionated ablative laser, attributed to the potential of SCA to induce fibroblast and keratinocytes migration and stimulate wound healing and matrix-remodeling.[3]

These two randomized controlled trials analyzed the effects of SCA application after nonablative and ablative fractional laser treatment. Compared to placebo, SCA application reduced adverse effects of laser treatment. SCA treatment induced faster healing of the microcolumns after both treatments and reduced side effects of erythema appearance. A significant improvement on the SCA-treated side was also observed after laser treatment in both studies, thus implying greater procedure tolerability by patients and enhanced effectiveness of the laser. However, both studies included a small sample size.

ANTIMICROBIAL ACTIVITY

A 2022 double-blind, placebo-controlled trial assessed the efficacy of snail secretion filtrate, *Calendula officinalis* and *Glycyrrhiza glaba* root extract combination serum (SCGS) in treating acne caused by prolonged face mask use in 66 subjects.[18] Subjects were randomly assigned to use SCGS (n=33) or placebo (n=33) twice daily for 12 weeks, and acne lesion count, acne severity, and TEWL were measured in the mask-covered area. The treatment group experienced a significantly greater percent reduction in inflammatory acne lesions compared to the placebo group. Both groups showed a reduction in TEWL with no significant difference between groups at all time points. These results suggest that SGCS is effective in decreasing inflammatory lesions caused by face masks. However, a limitation of this study is the inclusion of other active ingredients in addition to snail mucin, which may have potentially skewed the results. Since the treatment product was formulated with multiple natural ingredients, it is difficult to attribute the efficacy of anti-microbial activity and reduction in inflammatory acne lesions solely to the snail filtrate ingredient. Although previous in vitro studies demonstrated that snail mucin from *C. aspersa* and *A. fulica* possess antimicrobial activity against *P. aeruginosa* and *S. aureus*, other ingredients in the SCGS treatment such as *Calendula officinalis* has also shown anti-microbial activity in vitro.[6,19]

CONCLUSION

Interest in natural substances that can stimulate skin regeneration and also exhibit anti-aging protective potential has tremendously increased. The popular use of snail-derived ingredients in cosmeceuticals to improve skin appearance is reinforced by the demonstration of several clinical trials on humans that have indicated significant improvement in several skin parameters such as TEWL, skin roughness, elasticity, and wrinkle presence. Since many of the studies were limited by small sample sizes and a lack of long-term follow up to assess lasting effects of snail-derived products, future research will be instrumental in further demonstrating the efficacy of topical application of active snail ingredients in anti-microbial activity and improving signs of skin aging.

CONFLICTS OF INTEREST

None

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None

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