


ORIGINAL CONTRIBUTION

Comparison of topical antiaging creams in the management of lateral canthal lines

Julia M. Carroll BSC, MD, FRCPC^{1,2,3} | Sam Hanna MD, FAAD, DABD^{4,5} |
Lyn C. Guenther MD, FRCPC, FAAD⁶ | Nathalie Boucher PhD⁷ 

¹Compass Dermatology, Toronto, ON, Canada

²Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

³Dermatology, The Medcan Clinic, Toronto, ON, Canada

⁴Dermatology on Bloor, Toronto, ON, Canada

⁵Toronto Dermatology Society, Toronto, ON, Canada

⁶Dermatology, Western University, London, ON, Canada

⁷Devonian Health Group, Montmagny, QC, Canada

Correspondence

Nathalie Boucher, Devonian Health Group, Montmagny, QC, Canada.
Email: nboucher@groupe-devonian.com

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Abstract

Objective: This study compared an antiaging treatment with two currently marketed cosmetic antiaging products for the treatment of lateral canthal lines ("crow's feet").

Methods: Healthy female volunteers (72) aged of 54.6 years (mean) having fine-to-moderate wrinkles in the lateral canthal areas were randomized to one of three treatments applied daily over 28 days: Group A (Purgenesis™ Day Cream, Purgenesis™ Eye Cream, and Purgenesis™ Night Cream); Group B (Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream); or Group C (La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream). The effects on anti-wrinkle properties and for sensory attributes and general performance were evaluated on Days 1, 7, and 28.

Results: Skin hydration improved significantly at all time points in Groups A and B, and at Day 28 in Group C. Group A patients experienced significant improvements in measured skin elasticity parameters at Day 28; extensibility and maximum amplitude were significantly better at Day 28 in Groups B and C. Benefits were also seen in profilometric parameters with statistical significance only in Group A. Volunteer tolerance was good with all three treatments, although moderate and high levels of adverse events were numerically higher in Group B than in Groups A or C, and levels of slight discomfort were significantly more prevalent in Group B.

Conclusion: The Purgenesis™ antiaging treatment significantly improved skin hydration, elasticity, and profilometry parameters during a 28-day study. This therapy was found to be well tolerated and effective in countering the cutaneous signs of aging.

KEYWORDS

antiaging treatment, anti-wrinkle effects, botanic extract, cutaneous elasticity, skin hydration

1 | INTRODUCTION

Aging of the skin involves a complex mixture of multiple biological processes that varies from one person to another based on exogenous and endogenous factors.¹⁻⁴ Krutmann et al identified the following as the key environmental factors: sun radiation (ultraviolet [UV], visible light, and infrared radiation); air pollution; tobacco

smoking; poor nutrition; stress; lack of sleep; and exposure to high temperatures.⁵ Additional research highlighted the important roles of hormonal and neuroendocrine signals.⁶

Wrinkles are among the earliest and most prevalent signs of aging. They are also a principal contributor to perceived age, particularly in the face.⁷ Wrinkles can be either dynamic (ie, appearing during muscle contraction) or static (ie, present at all times and more pronounced

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with muscle activity). As the skin ages, the layers atrophy and become thinner, and elasticity is lost. Dynamic wrinkles are formed through the permanent hypercontractions that occur as compensation for age-related atrophy.⁸ A correlation was also found between repetitive facial movements and both dynamic and static facial wrinkles.⁹

Amid the high demand among consumers for safe and effective antiaging therapies, a host of strategies are currently available. Mild-to-moderate surface wrinkles and other signs of aging can be treated with topical agents, while deeper wrinkles may be managed with onabotulinumtoxinA injections and/or dermal fillers.

The primary objective of this study was to compare the efficacy of a new antiaging treatment (Purgenesis™) for which the principal ingredient is R-Spinasome®, a thylakoid extract, to two marketed antiaging cosmetic products (Prevage® and La Mer®). Secondary objectives included evaluation of consumer acceptance and tolerance of these products in normal use.

2 | MATERIALS AND METHODS

This single-centre, single-blind, parallel-design clinical study enrolled 72 healthy female volunteers aged 35–72 years (mean age 54.6 years) with fine-to-moderate wrinkles in the lateral canthal areas (“crow's feet”). Assessments were conducted over 28 days (Table 1).

Based on Material Safety Data Sheets and toxicology information available from ingredient suppliers, the sponsor provided Certificates of Innocuity for each test product, confirming their suitability for use and conformity with Canadian regulations. The study received ethics approval. Each volunteer was informed verbally and in writing of the nature of the test and of the potential risks involved. All volunteers provided informed consent to participate in the study, including consent to be photographed.

2.1 | Inclusion and exclusion criteria

Inclusion criteria for volunteers included females in good health aged 35 years or older with normal-to-dry skin on the face, fine-to-moderate¹⁰ lines, and wrinkles in the lateral canthal areas, consistent usage of a method of contraception (eg, contraceptive pill, condoms, spermicidal creams, intrauterine device, abstinence), who were regular daily users of facial care products (to ensure they were sufficiently disciplined to follow

a daily facial care routine, agreed to use only the test products in their daily facial routine, with the exception of their regular cleansing and makeup products. Patients were aware of the need for compliance with regular follow-up evaluations and tests in accordance with the established study protocol and signed informed consent forms with full knowledge of the details of the study and associated risks prior to study participation.

Exclusion criteria included previous usage of either of the comparator antiaging product lines, a history of skin irritation or allergies to the type of products to be tested (eg, antiaging products, eye serum, hydrating creams), a history of general allergies to certain food (including spinach), chemical products, glues, latex (rubber gloves) or jewelry, a history of severe acne, eczema, psoriasis, or significant skin anomalies on the areas to be tested, presence of a serious illness or health problem (eg, asthma, diabetes, cancer, immune deficiency, removed organ), use of prescription or over-the-counter medication at a frequency of ≥ 3 doses per week that could affect skin characteristics (eg, antibiotics, steroids, antihistamines, anti-inflammatories), within 7 days of study initiation, history or current significant skin pigmentation, regular use of tanning salons, or expectation of sun exposure during the study, history or current abuse of alcohol, drugs, or tobacco, and pregnancy, lactation, or plan to become pregnant during the study.

2.2 | Protocol and randomization

All volunteers were instructed to arrive at the initial visit (Day 0) ≥ 2 hours after completing their regular face-washing routine and without makeup or skin treatment on their faces. Those who satisfied the inclusion and exclusion criteria were randomized to a homogeneously labeled container containing day cream, night cream, and eye product corresponding to one (1) of the three (3) test treatments:

- Group A: Purgenesis™ Eye Cream, Purgenesis™ Day Cream, and Purgenesis™ Night Cream (Devonian Health Group).
- Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream (Elizabeth Arden Canada).
- Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream (La Mer Canada).

Volunteers who entered into the study also received a follow-up sheet to be completed after every treatment application and a self-evaluation questionnaire to be completed after the 28-day course of treatment.

TABLE 1 Study schedule

Description	Day 0	Day 1	Day 7	Day 28
Completion of the medical history questionnaire and selection according to inclusion and exclusion criteria	X			
Measurement of hydration and skin elasticity (Corneometer® and Cutometer®)	X	X	X	X
Skin imprints (silicone replicates of the eye contour zones)	X	X	X	X
Digital photography (Visia-CR Imaging System)	X	X	X	X
Verification of product use according to weight of sample containers	X	X	X	X
Return completed follow-up form (log of daily application)		X	X	X
Return completed self-evaluation questionnaire				X

The volunteers were instructed to apply the products each morning, after having washed their face and hands with their regular cleansing products. The eye cream/lotion/balm was the first product to be used, to be applied to the eye contours, including the lateral canthal areas. After the eye cream/lotion/balm was absorbed into the skin, the volunteers were to cover their entire face with the day cream, avoiding the eye contour area. Every evening, the volunteers were to cover their entire face with the night cream, avoiding the eye contour area. The volunteers were not permitted to change the brand of their regular facial cleanser or makeup products during the week prior to the commencement of the study and during the study.

Before the volunteers applied their first treatment on Day 0, 12 digital photographs of the face (full front, right and left profiles, in four imaging modes: standard, cross-polarized, ultraviolet, and parallel-polarized) were taken using the Visia-CR Imaging System (Canfield Scientific Inc). After 15 minutes of stabilization in a controlled environment room (temperature $22 \pm 3^\circ\text{C}$, relative humidity $30 \pm 5\%$), skin elasticity, hydration, and profilometry were measured. These measurements were repeated at visits on Days 1, 7, and 28 (Table 1).

Volunteers were instructed to provide completed daily logs on Days 1, 7, and 28. They were also required to return the containers with the unused portion of the test products. The unused portion of the sample containers and daily logs (use diaries) was intended for verification of the volunteers' adherence to the protocol. Additionally, the volunteers had to return their completed self-evaluation questionnaires at their final follow-up evaluation on Day 28. In addition to the observations made and recorded by the contract research organization ("CRO")—Evalulab (Montreal, Canada)—the volunteers were encouraged to observe and report any immediate or delayed reactions, such as redness, irritation, itching, and/or other sensations on the application sites.

2.3 | Test methods

2.3.1 | Skin hydration

Skin hydration was measured with a Corneometer[®] CM820 (Courage & Khazaka, Germany) equipped with a 49-mm probe. The probe was gently pressed against the skin in the eye contour area (pressure of 3.56 N), and the capacitance was recorded. Triplicate measurements were taken from 6 different sites on the face (forehead, temples, chin, under-eye areas, and cheeks) of each volunteer.

2.3.2 | Cutaneous elasticity

Cutaneous elasticity was measured with a Cutometer[®] SEM 575 (Courage and Khazaka, Germany). The instrument was equipped with a probe (aperture 2 mm in diameter) that induces a controlled suction (vacuum of 400 mbar) on the skin with 4 1-second repetitions, followed by a rest period of 1 second in a reproducible manner. Two measurements were taken from the middle of each cheek.

2.3.3 | Profilometry (anti-wrinkle effect)

Imprints (negatives of the skin surface) of the eye contour zones were obtained by applying silicone polymer onto the lateral canthal areas,

with the volunteer in an upright sitting position. The polymer used for this study was silicone dental impression material (Silflo[®]; Flexico Developments Ltd., Potters Bar, England). Imprints of the lateral canthal lines were analyzed by a computerized digital image processing system coupled to Quantirides[®] software (designed by Monaderm, Monaco) to obtain the skin topography. This standard technique is based on measuring the shadows cast when an incident light is inclined at an angle of 35° on the replica. Analyzed parameters included the total area of wrinkled skin, the number and the mean depth of the depressions due to the cutaneous relief, and the depth of deep and medium wrinkles. The wrinkles were differentiated by classes of depth (Class 1 for 0–55 μm , fine; Class 2: 55–110 μm , moderate; and Class 3: 110–800 μm , profound) before and after the treatment of a given product.

2.3.4 | Qualitative survey

One section of the self-evaluation questionnaire was designed to gauge the volunteers' perception of their treatment's cosmetic quality (sensory attributes) and overall performance after 28 days of treatment. The volunteers rated the test treatment characteristics of cosmetic quality on a 4-point scale from 0 ("Did not appreciate") to 3 ("Highly appreciated"). To assess the perception of the efficacy of the treatments after 28 days of application, the volunteers were to complete questions related to the reduction of wrinkles, skin softness, firmness, hydration, smoothness, evenness of complexion, healthier looking complexion, and skin color. The responses for each criterion, expressed as "A lot," "Moderately," and "Slightly," were combined.

They were also encouraged to enter personal comments at the end of the questionnaire.

2.3.5 | Treatment acceptance

Treatment acceptance was defined by the overall participation of the volunteers in the study and the level of tolerance to the treatment they received. Tolerance to the treatment was evaluated based on the presence and severity of any observed reactions according to evaluator comment and volunteer self-reporting in the questionnaire.

2.4 | Statistical method

Statistical analysis was carried out on all pertinent parameters. Results obtained at visits on Days 1, 7, and 28 for each test treatment were compared to the baseline (Day 0) using Student's *t* test. Whenever appropriate, the results were expressed as mean of the measurements of all volunteers within each group. If relevant antiaging results were obtained, the selected statistical procedure was a hypothesis test—*t* test: paired 2 sample for means—to examine whether 2 means are equal or if there is a statistically significant difference between the 2 means.

3 | RESULTS

A total of 72 healthy volunteers were recruited: 42 in Group A, 15 in Group B, and 15 in Group C. All of the volunteers completed the

study without incidence. Compliance was found to be good in all volunteers, as indicated by the average daily use of the test products. The quantity required for covering the eye contour area was less than that for the facial application of the day and night creams.

3.1 | Treatment efficacy

3.1.1 | Perception of sensory attributes

Tables 2-4 present the average Total Appreciated ratings (combined "Appreciated" and "Highly Appreciated" scores) of the cosmetic qualities for the eye cream/lotion/balm, day creams, and night creams, respectively, from the volunteer self-assessment questionnaires. The overall levels of appreciation of the sensory attributes associated with the eye cream/lotion/balm, day creams, and night creams were very good for all treatments. Statistical analysis showed a significant difference between Group A and Group C.

3.1.2 | Perception of treatment efficacy

The results of the Qualitative survey are summarized as total percentage of positive responses in Table 5. The efficacy scores were similar for Groups A and B for most parameters, with the exception of skin firmness (88% for Group A versus 100% for Group B; Figure 1). Considerable differences were found between these 2 treatment groups and Group C, particularly for the criteria of softer skin, smoother skin, and more beautiful skin color. Student's *t* test calculated differences were found to be significant between Group A and Group C ($P < 0.05$) but not between Group B and Group C ($P < 0.1$).

3.2 | Skin hydration

Statistical analysis of the data revealed that the hydration of the skin for treatment Groups A and B was improved significantly ($P < 0.01$)

TABLE 2 Score averages for sensory attributes of the eye cream/lotion/balm after 28 days of application

Criteria	Total Appreciated ^a (%)		
	Group A	Group B	Group C
Ease of application	95	100	80
Texture	93	100	93
Absorption after application	88	93	100
Feeling after application	83	80	93
Fragrance	69	67	73
Average	86	88	88

^aTotal Appreciated scores represent the sums of "Appreciated" and "Highly Appreciated" ratings for each of the criteria. Group A: Purgensis™ Eye Cream; Group B: PreVage® Eye Lotion; and Group C: La Mer® Eye Balm. A statistically significant ($P < 0.05$) difference was identified between Groups A and C.

TABLE 3 Score averages for sensory attributes of the day creams after 28 days of application

Criteria	Total Appreciated ^a (%)		
	Group A	Group B	Group C
Texture	100	100	74
Ease of application	100	93	80
Absorption after application	96	93	86
Feeling after application	95	87	80
Fragrance	83	53	80
Average	95	85	80

^aTotal Appreciated scores represent the sums of "Appreciated" and "Highly Appreciated" ratings for each of the criteria. Group A: Purgensis™ Day Cream; Group B: PreVage® Day Cream; and Group C: Crème de La Mer®. A statistically significant ($P < 0.05$) difference was identified between Groups A and C.

at each follow-up appointment compared to Day 0 and at Day 28 for Group C (Figure 2). It is interesting to note the similar pattern between Group A and Group C, in which there was considerable improvement from Day 7 to Day 28, while also recognizing the significant difference in their improvements on Days 1 and 7.

3.3 | Elasticity

Skin elasticity was defined by the combination of the following skin parameters: Ue (ease of deformation, or immediate extensibility), Uf (maximum amplitude), Ur (tonicity), R9 (fatigability), and Ur/Ue (firmness; ie, net/pure elasticity). With the exception of the composite (Ur/Ue) measure, all of these criteria increase with age, and their reductions signify improvement in skin health.

A reduction in the Ue signifies improvement in firmness measured by skin's resistance to deformation. Volunteers in Group A

TABLE 4 Overall scores for sensory attributes of the night creams after 28 days of application

Criteria	Total Appreciated ^a (%)		
	Group A	Group B	Group C
Texture	100	100	74
Ease of application	100	100	60
Feeling after application	96	87	87
Absorption after application	93	100	86
Fragrance	81	47	73
Average	94	87	76

^aTotal Appreciated scores represent the sums of "Appreciated" and "Highly Appreciated" ratings for each of the criteria. Group A: Purgensis™ Night Cream; Group B: PreVage® Night Cream; and Group C: La Mer® Night Cream. A statistically significant ($P < 0.05$) difference was identified between Groups A and C.

TABLE 5 Overall scores for the perception of efficacy of the three antiaging treatments after 28 days of application

Criteria	"A lot" + "Moderately" (%)			"Slightly" (%)			Total ^a (%)		
	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C
Softer skin	81	93	60	19	7	20	100	100	80
Smoother skin	74	93	60	24	7	20	98	100	80
More hydrated skin	84	80	67	11	20	27	95	100	94
Healthier looking complexion	67	74	47	26	13	40	93	87	87
More even complexion	57	53	47	36	27	40	93	80	87
More beautiful skin color	66	67	40	24	20	27	90	87	67
Firmer skin	64	73	53	24	27	33	88	100	86
Reduction of wrinkles	48	27	33	36	60	60	84	87	93
Average	68	70	51	25	23	33	93	93	84

^aTotal scores represent the sums of all positive perceptions of efficacy ("A lot," "Moderately," and "Slightly") for each of the criteria. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream.

experienced a significant immediate (Day 1) improvement ($P < 0.05$), versus a significant ($P < 0.05$) reduction in extensibility observed in Group B and no change in Group C (Figure 3). Improvements were similar ($P < 0.05$) at Day 7 and were even more pronounced ($P < 0.01$) for all groups at Day 28.

As in the Ue responses, an immediate (Day 1) significant improvement ($P < 0.05$) was observed in maximum amplitude (Uf) in Group A, and slight worsening in Group B and Group C (Figure 4). Statistically significant improvements ($P < 0.05$) were identified in Group A and Group B, and all 3 groups exhibited significant improvements on Day 28 ($P < 0.01$).

No significant changes in skin fatigability were observed for any of the treatment groups at Day 1 and Day 7 (Figure 5). Decreases in skin fatigability were demonstrated at Day 28 for all three groups;

however, only the improvement seen in treatment Group A was statistically significant ($P < 0.05$).

Ur/Ue represents the net elasticity or firmness that diminishes with age and is considered to be the most important parameter of the skin's elasticity. No significant changes in firmness at Day 1 and Day 7 were observed in the tested treatment groups; however, treatment Group A demonstrated a statistically significant increase of 5% in firmness by Day 28 ($P < 0.05$; Figure 6).

3.4 | Profilometry

The profilometry measurements of the wrinkles evaluated the total number, surface area, total length, and mean length of the wrinkles

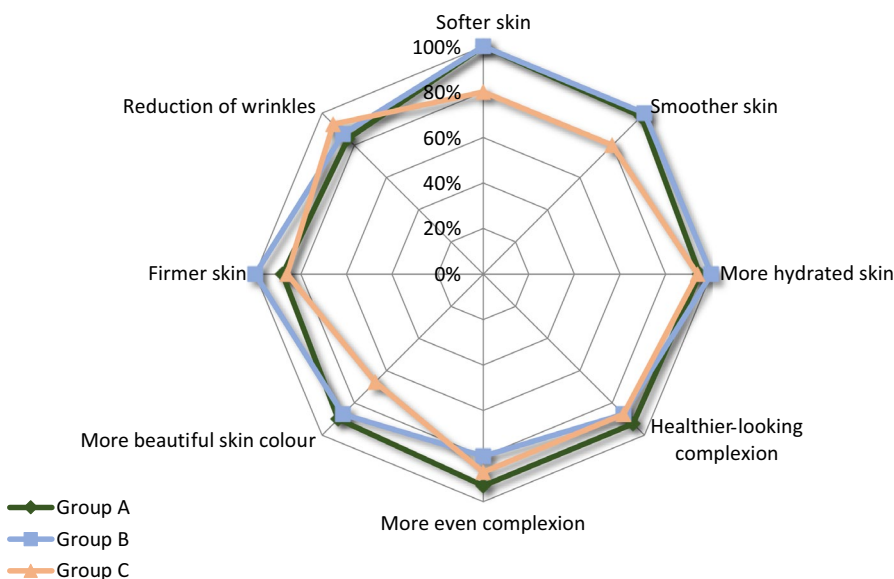


FIGURE 1 Overall scores for the perception of efficacy of the tested antiaging treatments after 28 days of application as expressed by the total positive answers. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream

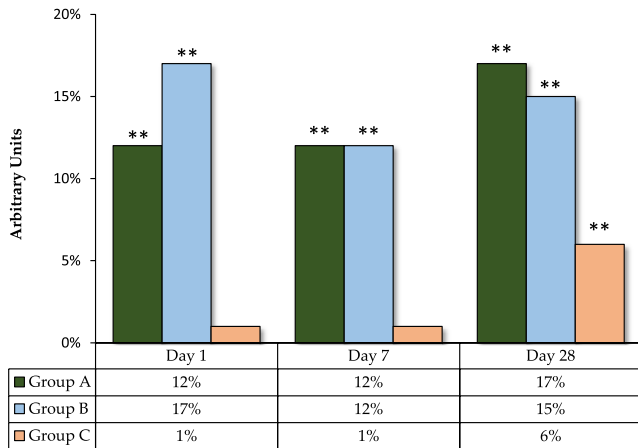


FIGURE 2 Improvement of the hydration of the skin in percentage at Days 1, 7, and 28 compared to Day 0. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. ***P* < 0.01

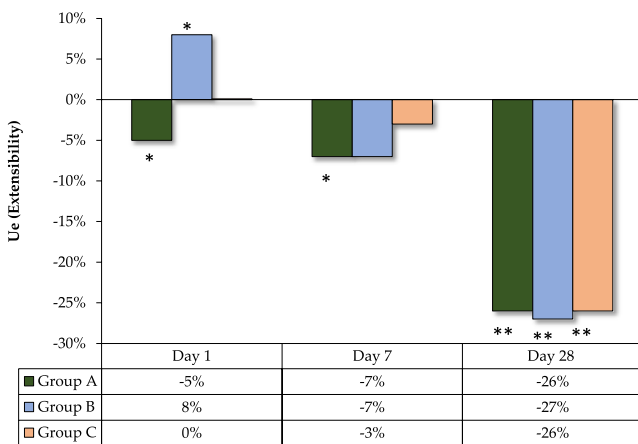


FIGURE 3 Evolution of the Ue (extensibility) at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. **P* < 0.05; ***P* < 0.01

as percentages of evolution compared to Day 0 before the initiation of the study (Figures 7-10). Group A experienced significant improvement (*P* < 0.01) in the total number of wrinkles on Day 1 but not at subsequent evaluations (Figure 7). Improvements with Group B and Group C did not achieve statistical significance at any time point. Significant benefits with respect to the area of wrinkles (*P* < 0.01 on Days 1 and 28; Figure 8), total wrinkle length (*P* < 0.01 on Days 1 and 28; Figure 9), and mean wrinkle length (*P* < 0.05 on Days 1 and 7; *P* < 0.01 on Day 28; Figure 10) were also seen in Group A alone.

Figures 11-13 illustrate the improvements in the number of wrinkles with respect to their classification based on depth—Class 1 (0-55 μm,

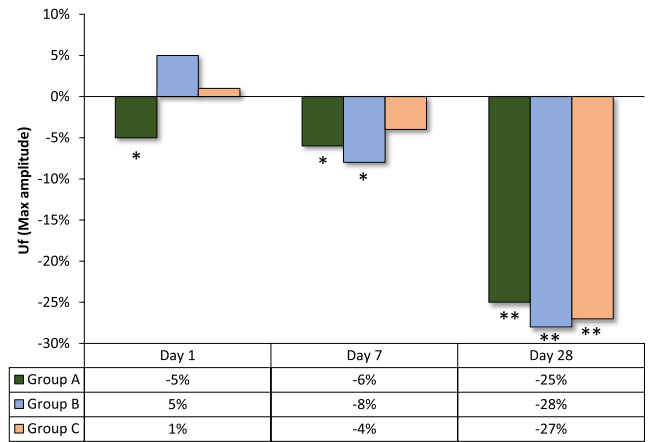


FIGURE 4 Evolution of Uf (maximum amplitude) at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. **P* < 0.05; ***P* < 0.01

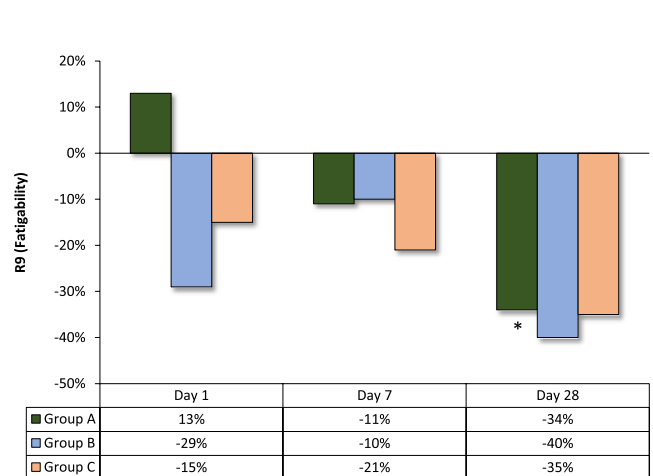


FIGURE 5 Evolution of R9 (fatigability) at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. **P* < 0.05

fine), Class 2 (55-110 μm, moderate), and Class 3 (110-800 μm, profound)—before and after treatment. Group B and Group C were numerically superior to Group A in the reduction of Class 1 wrinkles; however, no change from Day 0 achieved statistical significance for any treatment group. Patients in Group A experienced significant reductions in Class 2 (Day 1; *P* < 0.01) and Class 3 (Day 28; *P* < 0.05) wrinkles, with no statistically significant changes observed in either Group B or Group C.

As noted in Figure 14, the digital photographs are additional support of visual evidence of product efficacy.

3.5 | Tolerance

No adverse events or serious adverse events were observed during the study. As part of the questionnaire, the volunteers were asked to judge treatments tolerance by selecting "None," "Slight," "Moderate," or "High" for each of the intolerance criteria. The list of the intolerance criteria and the responses were expressed as the

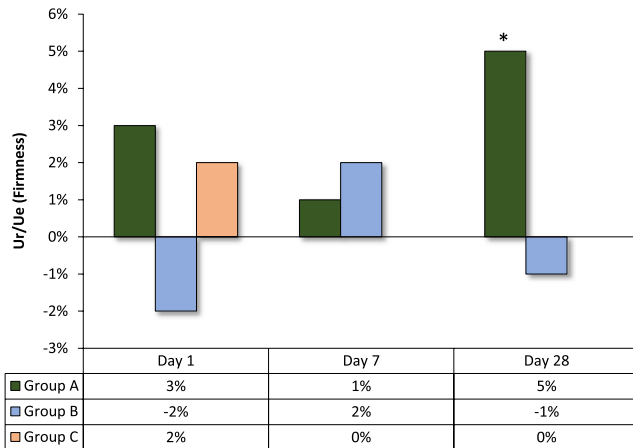


FIGURE 6 Evolution of Ur/Ue (firmness) at Day 1, Day 7, and Day 28 compared to Day 0. Group A: PurgenesiTM Eye Cream, PurgenesiTM Day Cream, and PurgenesiTM Night Cream; Group B: Prevage[®] Eye Lotion, Prevage[®] Day Cream, and Prevage[®] Night Cream; and Group C: La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream. * $P < 0.05$

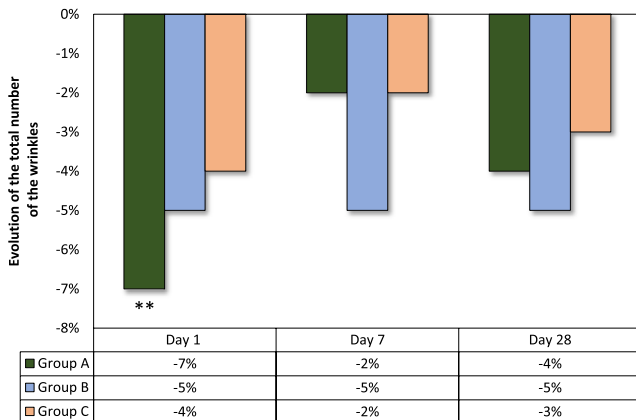


FIGURE 7 Evolution of the total number of the wrinkles at Day 1, Day 7, and Day 28 compared to Day 0. Group A: PurgenesiTM Eye Cream, PurgenesiTM Day Cream, and PurgenesiTM Night Cream; Group B: Prevage[®] Eye Lotion, Prevage[®] Day Cream, and Prevage[®] Night Cream; and Group C: La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream. ** $P < 0.01$

percentage of volunteers responding in each category after 28 days of treatment (Table 6).

Despite some numerical differences observed between the groups, all treatments were well tolerated by the majority of the

participants. Reports of moderate and high levels of redness, itching, tightness, burning sensation, stinging, eye watering, and appearance of acne lesions (pimples) were numerically higher in Group B. Group

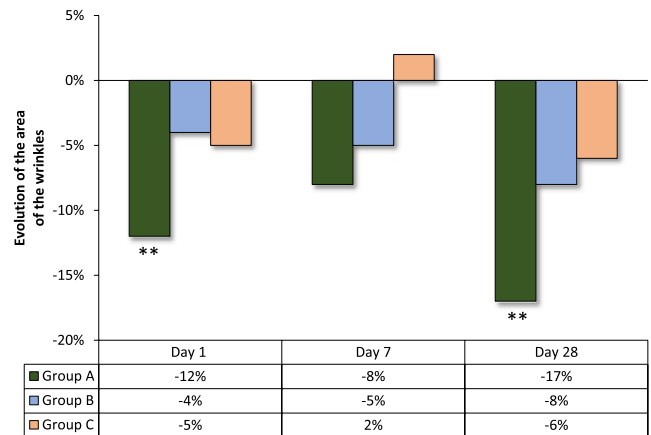


FIGURE 8 Evolution of the area of the wrinkles at Day 1, Day 7, and Day 28 compared to Day 0. Group A: PurgenesiTM Eye Cream, PurgenesiTM Day Cream, and PurgenesiTM Night Cream; Group B: Prevage[®] Eye Lotion, Prevage[®] Day Cream, and Prevage[®] Night Cream; and Group C: La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream. ** $P < 0.01$

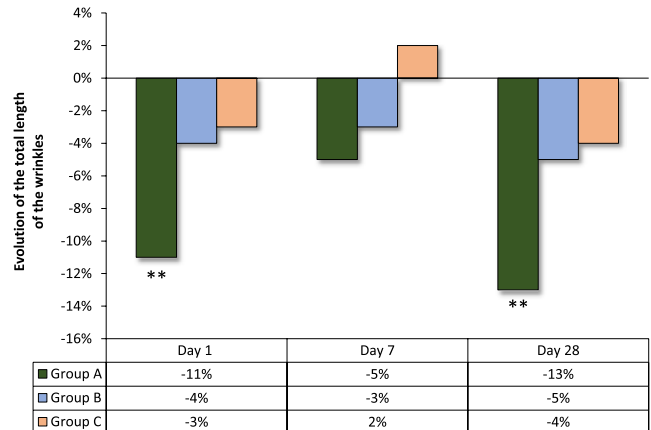


FIGURE 9 Evolution of the total length of the wrinkles at Day 1, Day 7, and Day 28 compared to Day 0. Group A: PurgenesiTM Eye Cream, PurgenesiTM Day Cream, and PurgenesiTM Night Cream; Group B: Prevage[®] Eye Lotion, Prevage[®] Day Cream, and Prevage[®] Night Cream; and Group C: La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream. ** $P < 0.01$

A and Group C had no moderate and severe intolerance criteria with the exception of stinging (2%) in Group A.

4 | DISCUSSION

Oxidative stress (intra- and extracellular) secondary to UV exposure is among the most common factors associated with premature signs

of skin aging. Both UVA and UVB initiate the generation of reactive oxygen species (ROS) in the skin.¹¹ These ROS are central to the activation of several skin-damaging processes, including inflammation,¹² erythema,^{13,14} skin-surface oxidation,¹⁵ stimulation of sebaceous gland function,¹⁶ melanogenesis,^{17,18} and alteration of the dermal matrix.¹⁹⁻²¹ Antioxidant-containing products have been shown to protect the skin from these harmful effects.²²

Antioxidants come in many forms, including vitamins A (retinol), B3 (niacinamide), C, and E, botanicals such as resveratrol, polyphenols, and flavonoids, and the body's own coenzymeQ10. More than 8,000 polyphenol compounds have been identified.²³ The main classes are flavonoids, phenolic acids, stilbenes, and lignans.²⁴ Polyphenols are associated with a host of health benefits, including reduction in the risk of cardiovascular disease, cancer, diabetes, infections, and asthma.²³ Several studies

have also demonstrated the safety and effectiveness of topical application of polyphenols for the preservation of human skin cell longevity.²⁵⁻²⁹

The current study employed several objective and self-reported measures to compare the experimental Purgenesis™ topical antiaging product line in development, including eye, day, and night creams, with two marketed product lines: Prevage® and La Mer®. The principal ingredient of Purgenesis™ is the patented R-Spinasome®, a thylakoid extract with demonstrated antioxidant properties.^{36,37} Thylakoids play a key role in the safe processing and dissipation of harmful energy generated by the interaction of antioxidant complex-containing photosynthetic cell extracts with ROS.^{30,31} Spinach is also a rich source of phenolic compounds.^{32,33} Prevage products are made with idebenone, a synthetic analogue of ubiquinone and a stable form

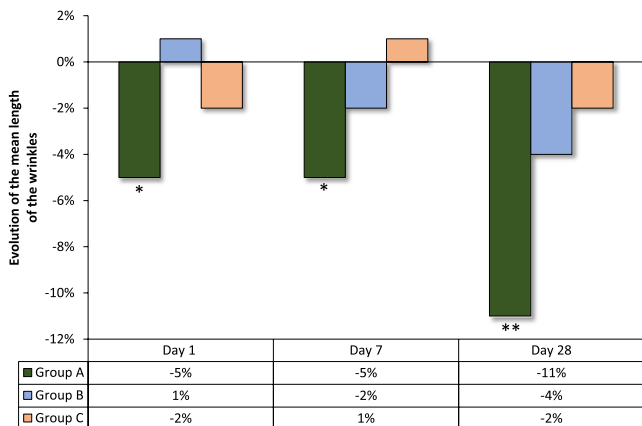


FIGURE 10 Evolution of the mean length of the wrinkles at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgenesis™ Eye Cream, Purgenesis™ Day Cream, and Purgenesis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. **P* < 0.05; ***P* < 0.01

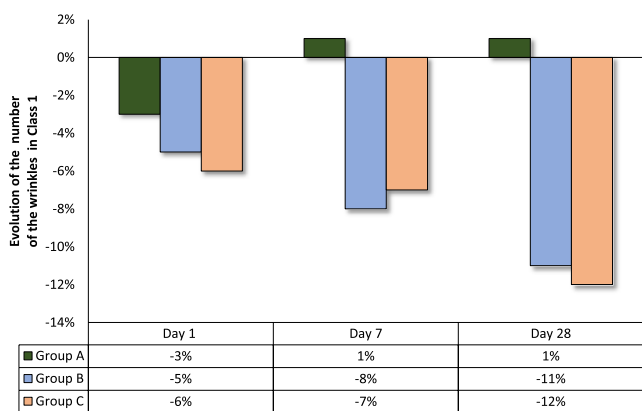


FIGURE 11 Evolution of the number of the wrinkles in Class 1 at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgenesis™ Eye Cream, Purgenesis™ Day Cream, and Purgenesis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream

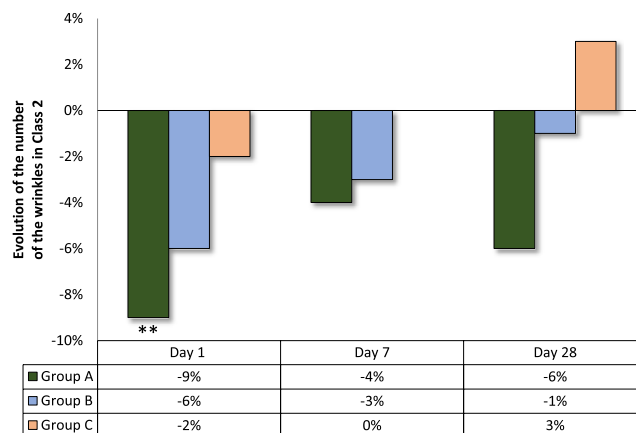


FIGURE 12 Evolution of the number of the wrinkles in Class 2 at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgenesis™ Eye Cream, Purgenesis™ Day Cream, and Purgenesis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. ***P* < 0.01

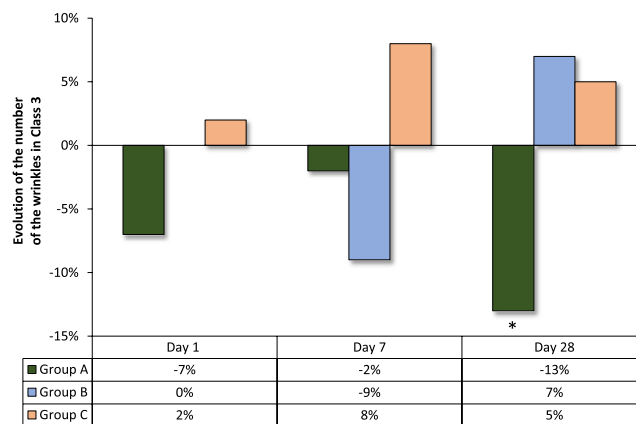


FIGURE 13 Evolution of the number of the wrinkles in Class 3 at Day 1, Day 7, and Day 28 compared to Day 0. Group A: Purgenesis™ Eye Cream, Purgenesis™ Day Cream, and Purgenesis™ Night Cream; Group B: Prevage® Eye Lotion, Prevage® Day Cream, and Prevage® Night Cream; and Group C: La Mer® Eye Balm, Crème de La Mer®, and La Mer® Night Cream. **P* < 0.05

of the naturally occurring antioxidant coenzyme Q10.³⁴ La Mer's products contain a mixture of sea kelp, vitamins, and minerals.³⁵

Skin hydration was measured with a Corneometer[®]. Epidermal moisture of the stratum corneum can be assessed by noninvasive *in vivo* instrumentation methods based on the electric capacitance of the skin.³⁶ The stratum corneum is a dielectric corpus, and all changes in its hydration status are reflected by changes in the electric capacitance, expressed in arbitrary units by Corneometer[®].

Cutaneous elasticity, another key parameter, is measured with a Cutometer[®]. Cutometric measurement was demonstrated to be an objective, precise, and noninvasive technique to measure a patient's skin's viscoelastic properties.³⁷ The skin's appearance is related to and highly affected by its elastic properties. The elasticity of the skin is subject to change with the use of cosmetic products. Changes in the mechanic and viscoelastic properties of the skin reflect the elasticity of the skin. Profilometry evaluated the total area of wrinkled skin, the number and mean depth of wrinkles, and change from baseline in the number of fine (Class 1), moderate (Class 2), and profound (Class 3) wrinkles.

Patients receiving the Purgensis™ product line (Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group A) experienced more statistically significant improvements in objective measures than those in Group B (Prevage[®] Eye Lotion,

Prevage[®] Day Cream, and Prevage[®] Night Cream) or Group C (La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream). The Prevage[®] products were particularly beneficial in profilometric analyses; no parameters measured by profilometry in the other treatment groups achieved statistical significance.

Subjective feedback from volunteer questionnaires on the sensory attributes was highly positive for all three treatments. Total appreciation rates were generally higher for the Purgensis™ treatments (86% for eye cream, 95% for day cream, and 94% for night cream) than for the Prevage[®] (88%, 85%, and 87%, respectively) and La Mer[®] (88%, 80%, and 76%, respectively) products.

All treatments were well tolerated by the majority of the participants. Recipients of Purgensis™ and La Mer[®] products generally experienced less intolerance adverse effects than those using Prevage[®] products. The Prevage[®] group had numerically higher rates of moderate-high intolerance and significantly higher rates of slight discomfort than the Purgensis™ and La Mer[®] groups.

5 | CONCLUSIONS

Benefits were observed with all three antiaging treatments tested in this study according to subjective and objective parameters.

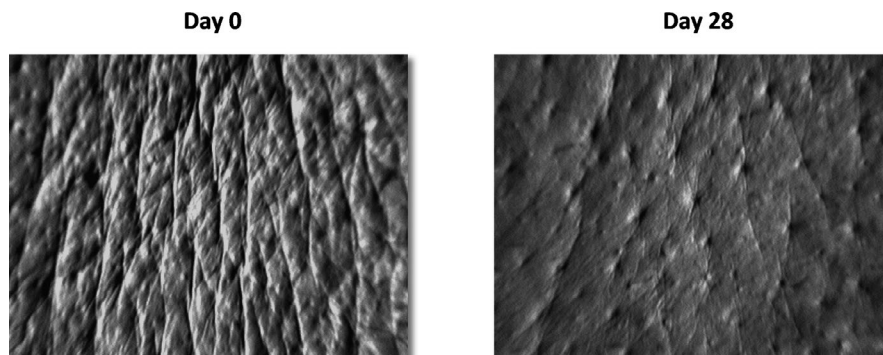


FIGURE 14 Improvement experienced by subject VOLA009VWPP using Purgensis™ antiaging skincare after 28 days of use. Digital photography (Visia-CR Imaging System) Day 28 compared to Day 0

TABLE 6 Overall scores for skin tolerance to each treatment after 28 days of application

Intolerance Criteria	"None" (%)			"Slight" (%)			"Moderate" & "High" (%)		
	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C
Residue left by the products on the skin (eg, pills, balls)	98	100	93	2	0	7	0	0	0
Redness	98	80	87	2	13	13	0	7	0
Itching	98	73	100	2	20	0	0	7	0
Skin flaking	95	93	100	5	7	0	0	0	0
Tightness	95	93	87	5	0	13	0	7	0
Burning sensation	95	67	93	5	26	7	0	7	0
Stinging	93	73	93	5	20	7	2	7	0
Pimples	90	80	93	10	7	7	0	13	0
Eye watering	88	73	93	12	20	7	0	7	0

Note: Group A: Purgensis™ Eye Cream, Purgensis™ Day Cream, and Purgensis™ Night Cream; Group B: Prevage[®] Eye Lotion, Prevage[®] Day Cream, and Prevage[®] Night Cream; and Group C: La Mer[®] Eye Balm, Crème de La Mer[®], and La Mer[®] Night Cream.

Specifically, the three treatments were shown to be effective in hydrating the skin. Only the treatment used by Group A (Purgenesis™ antiaging treatment) significantly improved elasticity and profilometry parameters during a study period of 28 days. The combined effect of improved parameters may be considered as an antiaging effect, and the Purgenesis™ treatment may be considered an effective treatment to counter the cutaneous signs and symptoms of aging. A longer-term study is recommended to further elucidate the maximal effects on elasticity and profilometric parameters.

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AUTHOR CONTRIBUTIONS

The authors reviewed the results and the related report in the preparation of this paper.

ORCID

Nathalie Boucher  <https://orcid.org/0000-0002-7925-215X>

REFERENCES

- Landau M. Exogenous factors in skin aging. *Curr Probl Dermatol*. 2007;35:1-13.
- Naylor EC, Watson RE, Sherratt MJ. Molecular aspects of skin ageing. *Maturitas*. 2011;69(3):249-256.
- Cevenini E, Invidia L, Lescai F, et al. Human models of aging and longevity. *Expert Opin Biol Ther*. 2008;8(9):1393-1405.
- Steveton K. Types of skin aging. *Cosmetics & Toiletries*. 2013;128(5):298-299.
- Krutmann J, Bouloc A, Sore G, Bernard BA, Passeron T. The skin aging exposome. *J Dermatol Sci*. 2017;85(3):152-161.
- Quatresooz P, Piérard-Franchimont C, Kharfi M, et al. Skin in maturity: the endocrine and neuroendocrine pathways. *Int J Cosmet Sci*. 2007;29(1):1-6.
- Gunn DA, Rexbye H, Griffiths CE, et al. Why some women look young for their age. *PLoS ONE*. 2009;4(12):e8021.
- Beylot C. Skin ageing-General features of facial ageing and therapeutic choices [Article in French]. *Ann Dermatol Venereol*. 2019;146(1):41-74. <https://doi.org/10.1016/j.annder.2018.10.015>.
- Fujimura T, Hotta M. The preliminary study of the relationship between facial movements and wrinkle formation. *Skin Res Technol*. 2012;18(2):219-224.
- Lemperle G, Holmes RE, Cohen SR, Lemperle SM. A classification of facial wrinkles. *Plast Reconstr Surg*. 2001;108(6):1735-1750.
- Masaki H. Role of antioxidants in the skin: anti-aging effects. *J Dermatol Sci*. 2010;58(2):85-90.
- Rhodes LE, Gledhill K, Masoodi M, et al. The sunburn response in human skin is characterized by sequential eicosanoid profiles that may mediate its early and late phases. *FASEB J*. 2009;23(11):3947-3956.
- Warren JB. Nitric oxide and human skin blood flow responses to acetylcholine and ultraviolet light. *FASEB J*. 1994;8(2):247-251.
- Ahn SM, Yoon HY, Lee BG, et al. Fructose-1,6-diphosphate attenuates prostaglandin E2 production and cyclo-oxygenase-2 expression in UVB-irradiated HaCaT keratinocytes. *Br J Pharmacol*. 2002;137(4):497-503.
- Chiba K, Kawakami K, Sone T, Onoue M. Characteristics of skin wrinkling and dermal changes induced by repeated application of squalene monohydroperoxide to hairless mouse skin. *Skin Pharmacol Appl Skin Physiol*. 2003;16(4):242-251.
- Akitomo Y, Akamatsu H, Okano Y, Masaki H, Horio T. Effects of UV irradiation on the sebaceous gland and sebum secretion in hamsters. *J Dermatol Sci*. 2003;31(2):151-159.
- Schallreuter KU, Moore J, Wood JM, et al. In vivo and in vitro evidence for hydrogen peroxide (H2O2) accumulation in the epidermis of patients with vitiligo and its successful removal by a UVB-activated pseudocatalase. *J Invest Dermatol Symp Proc*. 1999;4(1):91-96.
- Sasaki M, Horikoshi T, Uchiwa H, Miyachi Y. Up-regulation of tyrosinase gene by nitric oxide in human melanocytes. *Pigment Cell Res*. 2000;13(4):248-252.
- Scharffetter-Kochanek K, Wlaschek M, Briviba K, Sies H. Singlet oxygen induces collagenase expression in human skin fibroblasts. *FEBS Lett*. 1993;331(3):304-306.
- Ohuchida M, Sasaguri Y, Morimatsu M, Nagase H, Yagi K. Effect of linoleic acid hydroperoxide on production of matrix metalloproteinases by human skin fibroblasts. *Biochem Int*. 1991;25(3):447-452.
- Chung K-Y, Agarwal A, Uitto J, Mauviel A. An AP-1 binding sequence is essential for regulation of the human $\alpha 2(I)$ collagen (COL1A2) promoter activity by transforming growth factor- β . *J Biol Chem*. 1996;271(6):3272-3278.
- Dunaway S, Odin R, Zhou L, Ji L, Zhang Y, Kadarko AL. Natural antioxidants: multiple mechanisms to protect skin from solar radiation. *Front Pharmacol*. 2018;9:392.
- Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. *Oxid Med Cell Longev*. 2009;2(5):270-278.
- Spencer J, Abd El Mohsen MM, Minihaane A-M, Mathers JC. Biomarkers of the intake of dietary polyphenols: strengths, limitations and application in nutrition research. *Br J Nutr*. 2008;99(1):12-22.
- Zillich OV, Schweiggert-Weisz U, Eisner P, Kerscher M. Polyphenols as active ingredients for cosmetic products. *Int J Cosmet Sci*. 2015;37(5):455-464.
- Martorana M, Arcoraci T, Rizza L, et al. In vitro antioxidant and in vivo photoprotective effect of pistachio (*Pistacia vera* L., variety Bronte) seed and skin extracts. *Fitoterapia*. 2013;85:41-48.
- Ruszová E, Cheel J, Pávek S, et al. Epilobium angustifolium extract demonstrates multiple effects on dermal fibroblasts in vitro and skin photo-protection in vivo. *Gen Physiol Biophys*. 2013;32(3):347-359.
- Li YH, Wu Y, Wei HC, et al. Protective effects of green tea extracts on photoaging and photoimmunosuppression. *Skin Res Technol*. 2009;15(3):338-345.
- Chuarienthong P, Lourith N, Leelapornpisid P. Clinical efficacy comparison of anti-wrinkle cosmetics containing herbal flavonoids. *Int J Cosmet Sci*. 2010;32(2):99-106.
- Bissonnette EY, Proulx LI, Turmel V, Drouin R, Purcell M. PCT-233, a novel modulator of pro- and anti-inflammatory cytokine production. *Clin Exp Immunol*. 2004;135(3):440-447.
- Cruz JA, Avenson TJ, Kanazawa A, Takizawa K, Edwards GE, Kramer DM. Plasticity in light reactions of photosynthesis for energy production and photoprotection. *J Exp Bot*. 2005;56(411):395-406.
- Chu YF, Sun J, Wu X, Liu RH. Antioxidant and antiproliferative activities of common vegetables. *J Agric Food Chem*. 2002;50(23):6910-6916.
- Issa AY, Volate SR, Wargovich MJ. The role of phytochemicals in inhibition of cancer and inflammation: new directions and perspectives. *J Food Compos Anal*. 2006;19(5):405-419.

34. Constantin M-M, Poenaru E, PoenRU C, et al. Skin hydration assessment through modern non-invasive bioengineering technologies. *Maedica - J Clin Med*. 2014;9(1):33-38.
35. Sin P, Stupka I, Brychta P. Evaluation and comparison of composite and split-thickness skin grafts using cutometer MPA 580. *Ann Burns Fire Disasters*. 2010;23(4):208-213.
36. Boulet A, Maes P. The use of a photosynthetic cell extract comprising functional thylakoids in cosmetic compositions. 2011. (WO2011127559) Patents No: EUR 11768299.7/JPS5952261/CAN 2699676/ US13261472.
37. St-Pierre A., Blondeau D., Boivin M., Beaupré V., Boucher N., Desgagné-Penix I.. Study of antioxidant properties of thylakoids

and application in UV protection and repair of UV-induced damage. *J Cosmet Dermatol*. 2019;1-12. <https://doi.org/10.1111/jocd.12936>. [Epub ahead of print]

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