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ORIGINAL RESEARCH

Clinical Efficacy of a Flavo-Proxylane Topical Regimen Pre- and Post-ultrasound Procedure for Subjects Undergoing Glucagon-Like Peptide 1 (GLP-1) Receptor Agonist Therapy

Amir Moradi · Jihee H. Kim · Jemin M. Kim · Hina N. Choudhary · Patricia M. Brieva

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ABSTRACT

***Introduction*:** Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are widely used for weight management and type 2 diabetes, but reports of reduced skin laxity and volume have raised aesthetic concerns. This study evaluates the first integrated skincare protocol designed for GLP-1 RA users.

***Methods*:** This 12-week, double-blind, randomized, split-face/split-neck study included 25 GLP-1 RA users (mean age 53.36 years) with mild-to-moderate skin aging, including male and female participants with Fitzpatrick skin types II to VI. All participants applied a topical regimen featuring Proxylane and wild fruit flavonoids (Flavo-Proxylane) to one side of the face/neck and a placebo to the other. After 4 weeks of topical monotherapy, participants received a single focused ultrasound treatment, followed by an additional 8 weeks of topical therapy. Outcomes included blinded image evaluation, 13 clinical grading parameters (via modified Griffiths scale), Global Aesthetic Improvement Scale scores, tolerability, and patient-reported satisfaction.

***Results*:** All participants completed the study and lost an average of 3.7 lb. After 4 weeks of Flavo-Proxylane monotherapy, significant improvements were observed for facial skin laxity (−16%; $P<0.001$) and marionette lines (−5%; $P<0.05$), while no significant changes were observed with placebo. By week 12, the combined regimen achieved amplified improvements versus baseline, week 4, and placebo (all $P<0.001$), with total reductions of 44% in skin laxity and 34% in marionette lines. Significant improvements were observed across all 13 clinical parameters. Overall improvement rating favored Flavo-Proxylane, with 94% reporting moderate-to-significant improvement versus 30% for placebo. Flavo-Proxylane treatment was well tolerated, with 84% reporting improved skin appearance and only three mild, self-resolving adverse events.

Prior Presentation: Portions of this study were presented in preliminary form at the 2025 European Academy of Dermatology and Venereology Congress, held in Paris, September 17–20. The data presented were incomplete and prior to comprehensive quantitative analysis, and have not been previously published.

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A. Moradi
Moradi MD, Vista, CA, USA

J. H. Kim · J. M. Kim
Department of Dermatology, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, South Korea

H. N. Choudhary · P. M. Brieva (✉)
SkinCeuticals, New York, NY, USA
e-mail: patricia.brieva@loreal.com

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Conclusion: This study demonstrates that an integrated regimen with Flavo-Proxylane products and ultrasound may improve aesthetic outcomes in a diverse range of participants undergoing GLP-1 RA treatment.

Keywords: Integrated skincare; Diabetes mellitus; Aesthetic dermatology; Glucagon-like peptide 1 receptor agonist; Ultrasound; Semaglutide; Tirzepatide; Skin laxity

Key Points

Why carry out this study?

Based on associated reports of reduced skin laxity and volume, the widespread use of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) for weight management and type 2 diabetes has led to an emerging unmet aesthetic need.

This study aimed to investigate whether a targeted integrated skincare protocol combining a topical skincare regimen with Proxylane and wild fruit flavonoids (Flavo-Proxylane) plus a single ultrasound procedure could effectively mitigate adverse dermatologic changes in GLP-1 RA users. On the basis of the mechanistic properties of Flavo-Proxylane ingredients and prior research demonstrating favorable outcomes alone or integrated with ultrasound procedures, the authors hypothesized that this regimen could effectively mitigate deleterious dermatologic outcomes in the context of GLP-1 RA use.

What was learned from this study?

The Flavo-Proxylane regimen was associated with significant improvements in facial skin laxity and marionette lines over 12 weeks compared to baseline and placebo. More study participants (64%) experienced moderate-to-significant overall aesthetic improvement with Flavo-Proxylane treatment compared to placebo. Both Flavo-Proxylane and placebo treatments were well tolerated and associated with substantial improvements in clinical grading parameters, with no significant between-group differences.

This research suggests that a targeted Flavo-Proxylane regimen is well tolerated when integrated with a single ultrasound procedure and may offer synergistic effects to help mitigate deleterious dermatologic outcomes among GLP-1 RA users.

Further longitudinal research is needed to understand the complete synergistic potential and the modulatory potential of any patient-level factors that may influence the efficacy of a Flavo-Proxylane regimen combined with ultrasound treatment among GLP-1 RA users.

INTRODUCTION

Glucagon-like peptide 1 (GLP-1) is a naturally occurring incretin hormone with important physiologic implications on metabolism, glycemic response (via insulin and glucagon), appetite, gastric emptying, and body weight [1]. As part of these effects, endogenous GLP-1 inhibits advanced glycation, apoptosis induced by advanced glycation end-products (AGEs), and the production of reactive oxygen species (ROS) [2, 3]. Both AGEs and ROS have demonstrated deleterious effects on skin health, including premature skin aging, loss of elasticity, and collagen breakdown [4, 5].

GLP-1 receptor agonists (GLP-1 RAs) are a class of pharmaceutical agents being used increasingly globally in the context of type 2 diabetes mellitus (T2D) and/or obesity to activate GLP-1 receptors, thus simulating physiologic responses exhibited in the context of high endogenous GLP-1 [6]. Although GLP-1 RAs were originally approved solely for the treatment of T2D, some variations have since been approved for weight loss in individuals with overweight and obesity [7]. The added clinical utility and on-label use of GLP-1 RAs have elicited a substantial increase in usage. For example, one retrospective cohort study noted a nearly 4000% increase in the number of Ozempic (semaglutide) users from 2019 to 2022, as well as monthly growth rates of up to 119.2% among various GLP-1 RA brands [8].

Influence of GLP-1 RAs in Dermatology

Despite the growing usage, the magnitude and rapidness of GLP-1 RA-related weight loss have shown significant implications for skin changes and facial aesthetics. Notably, aesthetic changes characterized by a loss of skin laxity and facial volume have contributed to unfavorable connotations, namely *Ozempic face* or *semaglutide face* [9–11]. Such changes are believed to result from alterations to collagen synthesis and volume, as well as potential effects on elastin (e.g., via AGEs or gene expression) [12]. GLP-1 RAs have also been linked to reports of increased wrinkles, sunken eyes, facial hollowing, and other facial alterations [9–11]. Less commonly, GLP-1 RAs have also been associated with dermatologic conditions such as allodynia, panniculitis, bullous pemphigoid, erythematosus, and hypersensitivity reactions [13–16]. To date, the overall influence of these drugs on skin health remains understudied.

Given the widespread effects of endogenous GLP-1 on metabolism and weight, its implications on skin health via inhibition of AGEs and ROS, and the anticipated alterations to facial aesthetics associated with pharmacologic GLP-1 RA use, adjunctive cosmetic treatment may be necessary to mitigate any underlying risk of adverse dermatologic effects.

Existing Evidence for Managing Skin Changes Among GLP-1 RA Users

As a result of reported concerns of facial alterations associated with GLP-1 RAs, numerous procedures have been considered to mitigate the negative dermatologic implications, specifically those related to reduced skin laxity and volume. Such procedures have included dermal fillers, neuromodulator injections, energy-based devices (e.g., lasers, radiofrequency microneedling, ultrasound), and non-energy-based procedures (e.g., physical microneedling, facial peels) [11, 17]. However, dermatologic procedures have been relatively understudied among individuals using GLP-1 RAs and have known or suspected implications depending on the type of procedure and degree of associated skin damage.

Early evidence suggests GLP-1 RAs may delay wound healing, which could have implications for invasive procedures [18]. Moreover, late facial edema has been observed with dermal fillers in those using GLP-1 RAs, although injectable fillers have otherwise shown potential to mitigate deleterious skin effects related to GLP-1 RA use [19, 20]. As a result of the lack of clinical data and the established implications of rapid weight loss observed with GLP-1 RAs, particularly near the time of drug initiation, some experts caution the use of dermatologic procedures within the first 6 months of GLP-1 RA use [17]. However, one small ($N=7$) split-face randomized placebo-controlled trial demonstrated that a targeted cosmetic regimen could improve all 13 domains (e.g., elasticity, volume, wrinkles) within the Global Ranking Scale as well as patient-reported outcomes for skin firmness and hydration [21]. As such, limited evidence supports the potential utility of non-invasive dermatologic procedures and targeted cosmetic regimens to mitigate adverse dermatologic effects of GLP-1 RAs, particularly given the lack of larger, inclusive studies.

Rationale for an Integrated Approach

Numerous procedures can improve skin laxity, sagging, and volume. A panel of dermatologists recently suggested that procedures such as injectables (e.g., neuromodulators, dermal fillers, skin boosters), energy-based devices (e.g., lasers, ultrasound), and non-energy procedures (e.g., microneedling, chemical peels) may be appropriate in the context of rapid weight loss from pharmaceuticals such as GLP-1 RAs [17]. However, given the potential influence of GLP-1 RAs on wound healing, procedures with moderate (e.g., 1927-nm non-ablative lasers, fractional ablative lasers) to severe (e.g., erbium-doped yttrium aluminum garnet lasers, fractional CO_2 lasers) skin barrier disruption may have prolonged recovery and downtime [22].

Ultrasound modalities are well-established non-invasive procedures for skin tightening and lifting in various skin types, with generally comparable utility between high-intensity focused ultrasound, microfocused ultrasound

(MFUS) with or without visualization, and newer synchronous parallel-beam technologies [23]. Ultrasound procedures generally target the mid-dermis, at depths as low as 1.5 mm, without causing significant damage to the epidermis [23–26]. Data consistently support the use of ultrasound procedures to induce collagen remodeling, tighten skin, and reduce facial skin laxity, consequently reducing facial wrinkles and improving global facial aesthetics [23–26].

In addition to procedural interventions, many topical cosmeceuticals have been shown to improve facial skin laxity, premature skin aging, and other deleterious skin effects caused by AGEs, which may be more prominent among individuals with T2D and/or obesity. For example, numerous Proxylane (or similar C-xyloside)-based formulations have been associated with improvements in skin elasticity, hydration, firmness, and wrinkles [27–30]. Mechanistically, Proxylane functions as a precursor that stimulates the synthesis of glycosaminoglycans, which bolsters the extracellular matrix by promoting the expression of type I and III collagen and essential barrier proteins (e.g., filaggrin and loricrin), thereby enhancing dermal density and epidermal differentiation to improve skin firmness and hydration [30]. Among people with T2D, a formulation with Proxylane and blueberry extract demonstrated improvements in facial skin volume, fine lines, firmness, radiance, skin tone, smoothness, creping, and overall appearance through 12 weeks [31]. Topical wild fruit flavonoids, such as those derived from blueberry, provide a synergistic effect by neutralizing ROS through suppression of oxidative stress mediators such as 4-hydroxynonenal and heme oxygenase-1, preventing AGE formation by mitigating pro-inflammatory signaling that drives glycation, and inhibiting matrix metalloproteinase expression to prevent the enzymatic degradation of collagen and protect the structural integrity of the dermal–epidermal junction [32].

When combined with MFUS in a randomized controlled trial, a formulation with 30% Proxylane solution (10.5% active) and 4% blueberry extract demonstrated significant improvements versus control in global facial aesthetics, skin elasticity, and fine lines, alongside greater patient satisfaction [33]. Despite these demonstrated benefits, no prior research has evaluated the effectiveness of a comparable topical skincare regimen, with or without ultrasound, in the context of rapid weight loss, particularly among individuals undergoing GLP-1 RA therapy. Based on previous outcomes, the current study hypothesized that a skincare regimen with Proxylane and wild fruit flavonoids (Flavo-Proxylane) could augment pre- and post-ultrasound efficacy in people actively using GLP-1 RAs, regardless of skin phototype.

Study Purpose

This study aimed to investigate the first integrated skincare protocol targeting facial aesthetic changes possibly impacted by GLP-1 RAs. Although limited data support the use of noninvasive dermatologic procedures or cosmeceutical interventions to mitigate reductions in skin laxity and volume, no studies have systematically analyzed the combined use of such interventions specifically in the context of GLP-1 RA use. Moreover, this study was designed to characterize early clinical outcomes associated with an integrated skincare approach using a randomized controlled design in this population.

METHODS

This study used a 12-week double-blind, randomized, controlled, split-face and split-neck design, pairing a topical cosmeceutical skincare regimen with a single ultrasound treatment to evaluate changes to facial aesthetics with ongoing GLP-1 RA use. Participants included a total of 25 male and female participants who were actively using GLP-1 RAs, mainly for weight loss or weight management. Of all 25 participants, only one had T2D. Subjects were randomized using a split-face and split-neck design, with each subject applying the treatment regimen to one side of the face and neck, and a placebo regimen to the opposite side. Prior to participation, all subjects provided written informed consent. The study protocol, informed consent, and all patient-facing materials were approved

by the Sterling Institutional Review Board (Protocol Number SKIN2024-02, September 24, 2025). This study was performed in accordance with the Declaration of Helsinki of 1964 and all updated versions.

All study participants followed a skincare regimen applied twice daily for 4 weeks prior to the ultrasound procedure (baseline to week 4) and continued the regimen for an additional 8 weeks following the procedure (week 4 to week 12). The topical formulation was only applied once on the day of the ultrasound procedure (week 4). The Flavo-Proxylane treatment regimen included a serum (A.G.E. Interrupter Ultra Serum, SkinCeuticals) with 30% Proxylane solution (10.5% active) and 4.6% wild fruit flavonoids, alongside a complementary cream (A.G.E. Interrupter Advanced, SkinCeuticals) with 18% Proxylane concentrate (12.5% active) and 4.25% wild fruit flavonoids. Instead of the Flavo-Proxylane products, the placebo regimen included a basic serum and moisturizer, with glycerin as the sole active ingredient. All study subjects were advised to use a provided cleanser (Gentle Cleanser, SkinCeuticals) and SkinCeuticals SPF50 sunscreen.

This study used a Sofwave™ device to deliver a focused low-divergence, high-frequency ultrasound beam to the mid-dermal layer of the skin at a depth of 1.5 mm. At week 4, a single treatment was performed on the areas from cheek to neck, with energy levels ranging from 3.4 to 4.4 J, adjusted according to patient tolerability. Each pulse lasted 5.0 s, followed by a 1-s post-cooling interval between pulses.

The evaluated outcomes included clinical grading, tolerability, 2D photography, and self-assessment questionnaires. For clinical grading, 13 parameters were evaluated using a modified Griffiths 10-point scale. Tolerability was assessed using a 4-point scale based on signs and symptoms of objective or subjective irritation. Clinical grading and tolerability were assessed at baseline, week 4 (pre-ultrasound), week 5 (1 week post-ultrasound), week 8 (4 weeks post-ultrasound), and week 12 (8 weeks post-ultrasound). A five-point Global Aesthetic Improvement Scale (GAIS) was used to evaluate overall improvement at weeks 8 and 12, completed separately by both the subject and the investigator. Participants completed self-assessment and satisfaction questionnaires for additional data. The treatment area was visually assessed via 2D standardized digital photographs (Vectra M3, Canfield Scientific, Inc.). Imaging was performed at multiple angles. Two blinded dermatologists independently graded 2D images for marionette lines and skin laxity using a 5-point scale, and overall improvement of skin laxity and contour using a 4-point scale. Detailed grading scales are outlined in the Supplementary Material.

All data entry and preliminary data processing were conducted using Microsoft Excel. Final data reporting and manuscript preparation were performed using LaTeX. For objective tolerability and clinical assessment data, p values were computed using the Wilcoxon signed-rank test, incorporating Pratt's adjustment to account for tied ranks. Questionnaire responses and GAIS scores were summarized as percentage distributions for each response category. Subjective tolerability ratings and Canfield image-derived metrics were reported as mean values per data point to reflect central tendencies. Statistical evaluation of the independent photo review was conducted using repeated measures analysis of variance to compare temporal changes between the two treatment groups. Figures were generated using GraphPad Prism.

RESULTS

Overall, 25 male and female participants aged 36 to 68 years (mean 53.36) with mild-to-moderate signs of skin aging on the face and neck completed the study. Baseline weight ranged from 131 to 258.2 lb (mean 167.8). Duration of GLP-1 RA use prior to study initiation ranged from less than 1 month to up to 3 years. Additional demographic characteristics are outlined in Table 1. On average, participants lost 3.7 lb over the 12-week study period, with two subjects losing over 20 lb. Overall, weight loss appeared to follow an inverse duration–response trend with GLP-1 RA use, with greater reductions observed with shorter treatment durations (≤ 6 months) compared to longer durations (≥ 2 years), despite notable intergroup variability (Fig. 1).

Pre-procedure

At week 4 pre-ultrasound, the Flavo-Proxylane regimen decreased facial skin laxity by 16%, achieving statistical significance compared to baseline ($P<0.001$) and placebo (–1%; $P<0.05$), as observed by two blinded dermatologists. Similarly, marionette lines were significantly reduced compared to baseline (–5%; $P<0.05$).

No significant improvements were observed from baseline to week 4 with placebo treatment. Compared to baseline, significant improvements were observed across eight clinical grading parameters with the Flavo-Proxylane treatment (Fig. 2).

Although no significant differences were observed between treatments at week 4, the Flavo-Proxylane treatment demonstrated a trend toward superior performance versus placebo across five clinical grading parameters, including the overall appearance of skin condition. Additionally, the Flavo-Proxylane regimen was associated with a significantly greater frequency of mild-to-moderate overall improvement at week 4, demonstrating such improvements in 58% of participants versus 28% with the placebo treatment (Fig. 3).

Post-procedure

The ultrasound procedure was administered at week 4, after all pre-procedure analyses were performed. At week 12, the Flavo-Proxylane regimen was associated with a 44% decrease in facial skin laxity, demonstrating statistical significance compared to baseline ($P<0.001$), week 4 (–16%; $P<0.001$), and placebo (–24%; $P<0.001$). Marionette lines were also significantly reduced compared to baseline (–34%; $P<0.001$), week 4 (–5%; $P<0.001$), and placebo (–15%; $P<0.05$). Changes to skin laxity and marionette lines are demonstrated in Fig. 4.

Statistically significant decreases were observed across all 13 clinical grading parameters following Flavo-Proxylane treatment at week 12 compared to baseline. Eleven of the 13 outcomes reached high statistical significance ($P<0.001$). Percent changes ranged from 7.41% to 28.3%, with an average improvement of 15.7% across all parameters (Fig. 5). Despite these improvements, no significant differences were observed between treatments.

Additionally, the Flavo-Proxylane treatment was associated with a significantly greater frequency of moderate-to-significant overall improvement at week 12, demonstrating such improvements in 94% of participants versus 30% with the placebo treatment (Fig. 6).

Investigator-based GAIS (IGAIS) scores and subject-based GAIS (SGAIS) scores were comparable for the Flavo-Proxylane and placebo

Table 1 Demographic characteristics

Characteristic type	Subjects (*n*)
Gender	
Male	2
Female	23
Race/ethnicity	
White	22
Black/African American	2
Asian	1
Hispanic	4
Non-Hispanic	21
Fitzpatrick skin type	
II	14
III	6
IV	3
V	1
VI	1
GLP-1 RA used	
Semaglutide	12
Tirzepatide	13
Weight change during study	
Weight loss (> 1 lb)	17
No change (≤ 1 lb)	4
Weight gain (> 1 lb)	4

GLP-1 RA glucagon-like peptide 1 receptor agonist

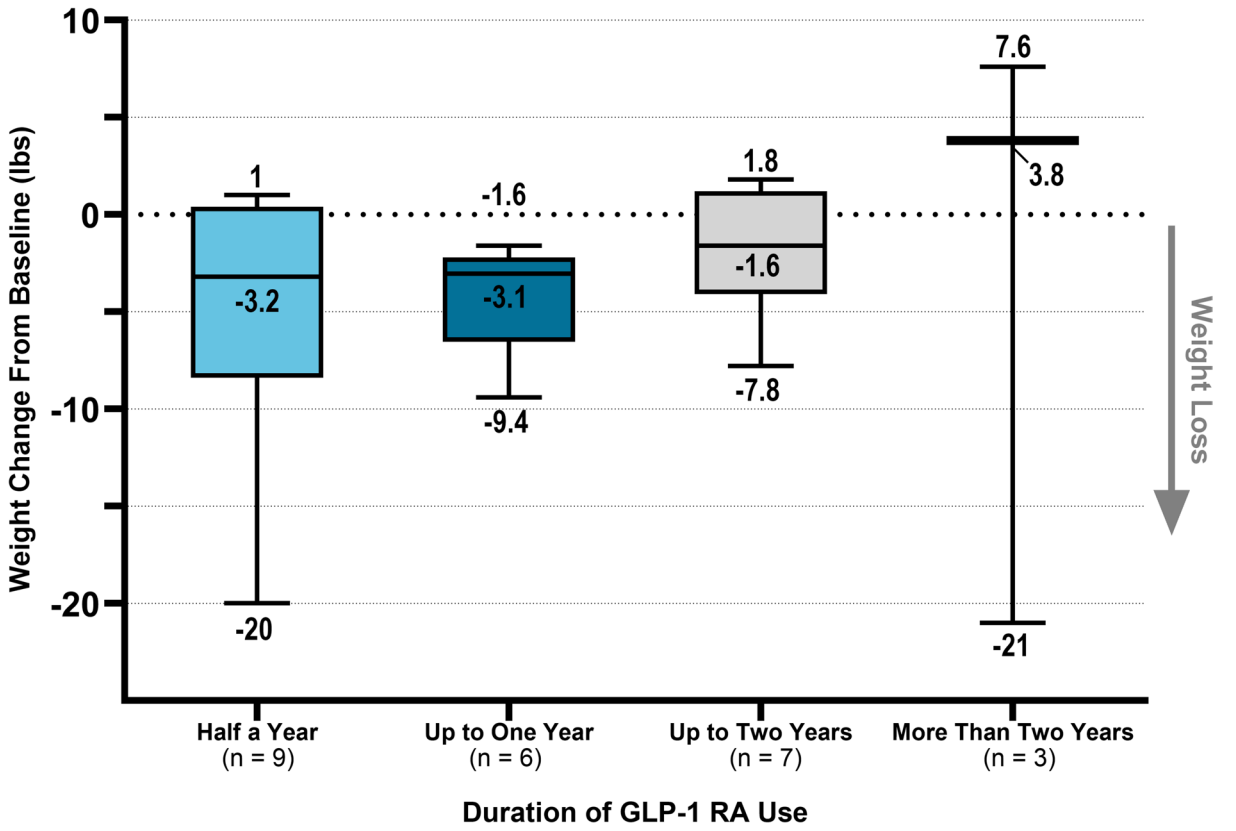

Fig. 1 Weight loss by duration of GLP-1 RA use. *Annotated data include median, minimum, and maximum values. *GLP-1 RA* glucagon-like peptide 1 receptor agonist

treatments by week 12, with 80% and 92% of participants achieving "Improved," "Much improved," or "Very much improved" scores for IGAIS and SGAIS outcomes, respectively.

Objective tolerability, based on erythema and dryness, was comparable between treatments at all timepoints. Compared to baseline, objective dryness was decreased at all timepoints and plateaued at a decrease of approximately 50% at week 8, which was sustained through week 12. A statistically significant reduction ($P<0.01$) from baseline was observed at week 5 (1 week post-procedure). Objective erythema was significantly reduced at all timepoints compared to baseline (−25.5% to −46.8%; $P<0.001$) and demonstrated a duration-dependent trend. Subjective tolerability was reduced at all timepoints for both treatments; however, the Flavo-Proxylane treatment was associated with fewer reports of dryness at weeks 5, 8, and 12.

Patient-reported survey data demonstrated high satisfaction with the Flavo-Proxylane treatment among participants for improved smoothness, hydration, protection, and overall appearance. By week 12, 84% of participants reported improved satisfaction with overall skin appearance, and 96% indicated willingness to undergo another procedure. Additionally, only 8% of subjects reported any loss of firmness throughout the 12-week study procedure. On the basis of blinded photographic assessment of 2D images by two evaluators, improvements were observed in skin laxity and marionette lines regardless of gender, skin phototype, weight change, or the GLP-1 RA used during the study (Figs. 7, 8, and 9).

Throughout the study period, the ultrasound procedure and both the Flavo-Proxylane and placebo regimens were well tolerated, with only three study-related adverse events, none

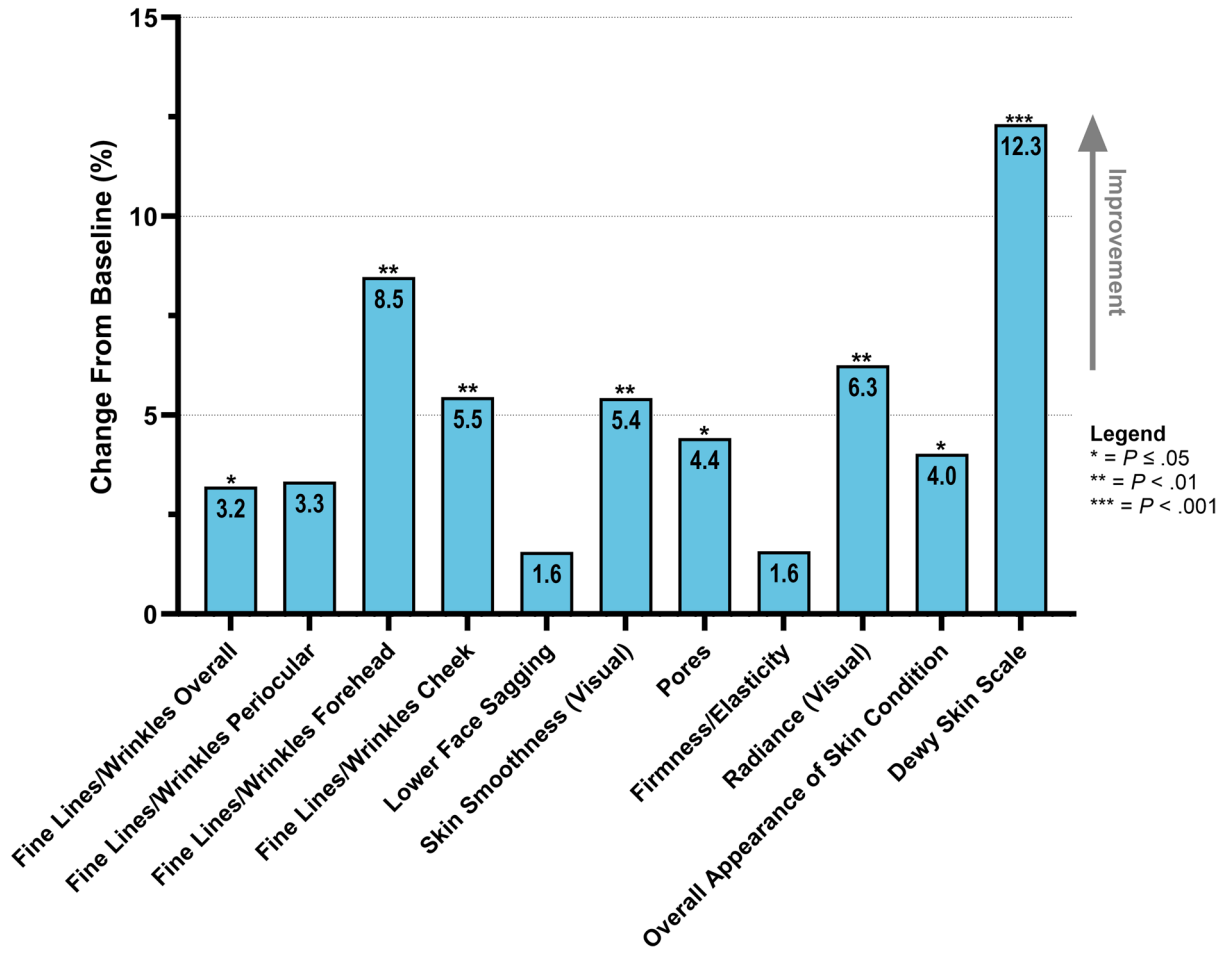

Fig. 2 Clinical grading outcomes with Flavo-Proxylane treatment before ultrasound

of which required medical intervention or discontinuation. All three study-related adverse events were attributed to transient acne that resolved without intervention.

DISCUSSION

This study demonstrated that the combination of a targeted Flavo-Proxylane cosmeceutical regimen and ultrasound could safely mitigate deleterious skin changes, including reductions in skin laxity and volume, among GLP-1 RA users. Moreover, this integrated skincare approach demonstrated improvements in various dermatologic outcomes through 12 weeks in the context of GLP-1 RA use, exemplifying the synergistic potential of a comprehensive integrated skincare regimen in this population.

The early improvements observed by week 4, prior to ultrasound administration, suggest that the topical Flavo-Proxylane regimen alone may offer measurable benefits in reducing facial skin laxity and marionette lines. Notably, these effects were not observed with the placebo treatment prior to the ultrasound procedure, reinforcing the independent value of the Flavo-Proxylane regimen. This was further supported by overall improvement ratings at week 4, in which the Flavo-Proxylane regimen was associated with

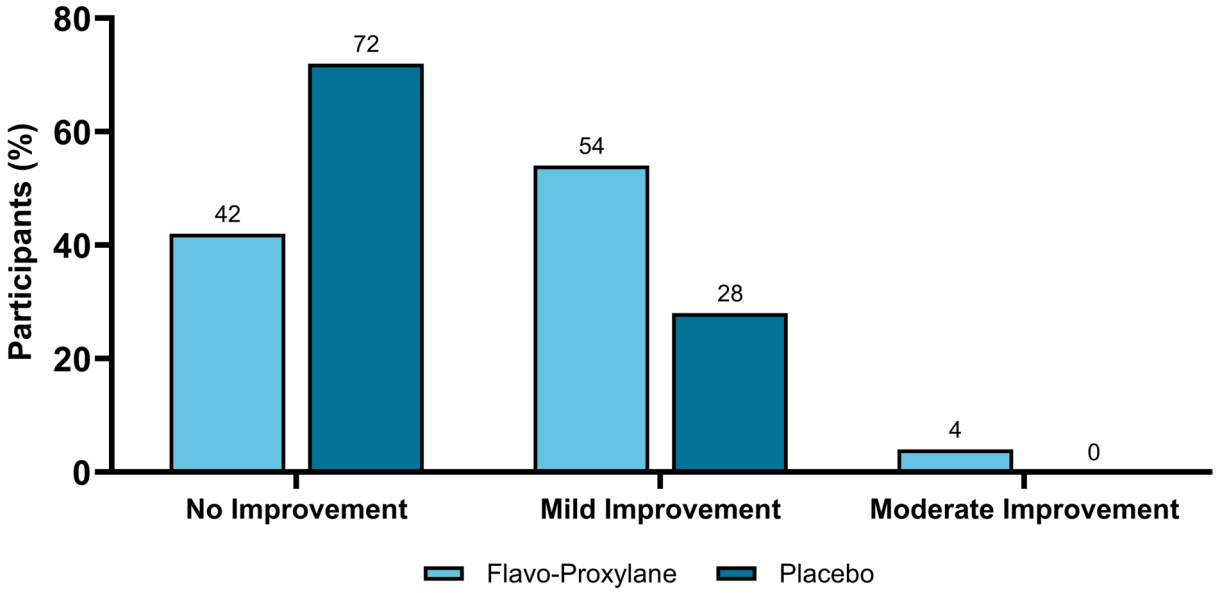

Fig. 3 Overall improvement rating between Flavo-Proxylane and placebo at week 4

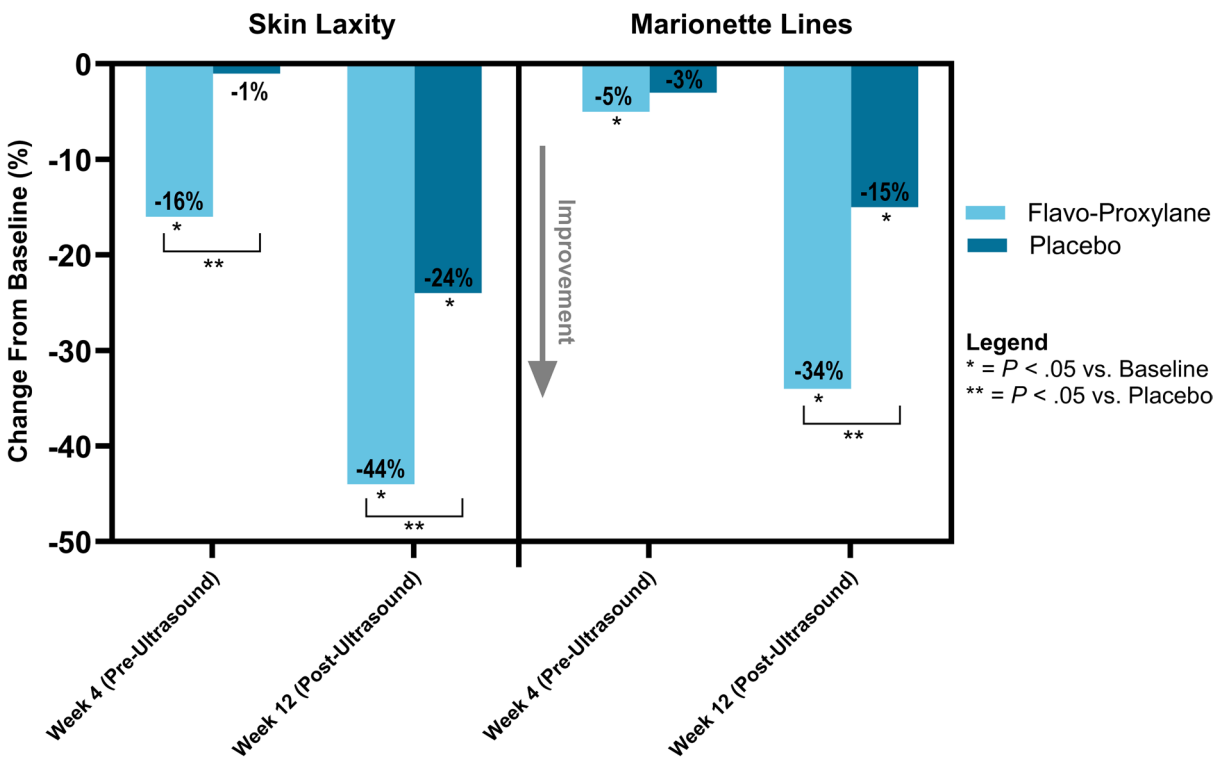

Fig. 4 Blinded clinical grading scores for skin laxity and marionette lines before and after ultrasound

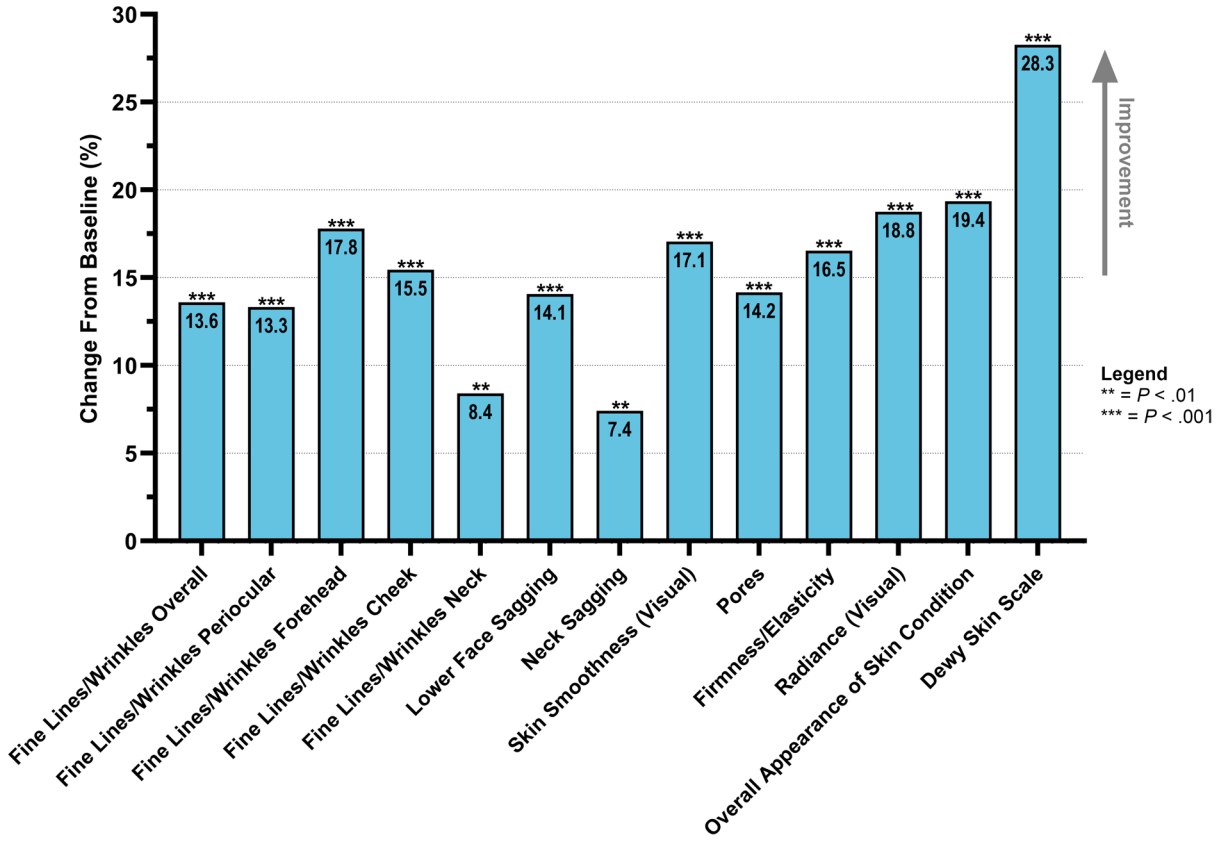

Fig. 5 Clinical grading outcomes with Flavo-Proxylane treatment after ultrasound

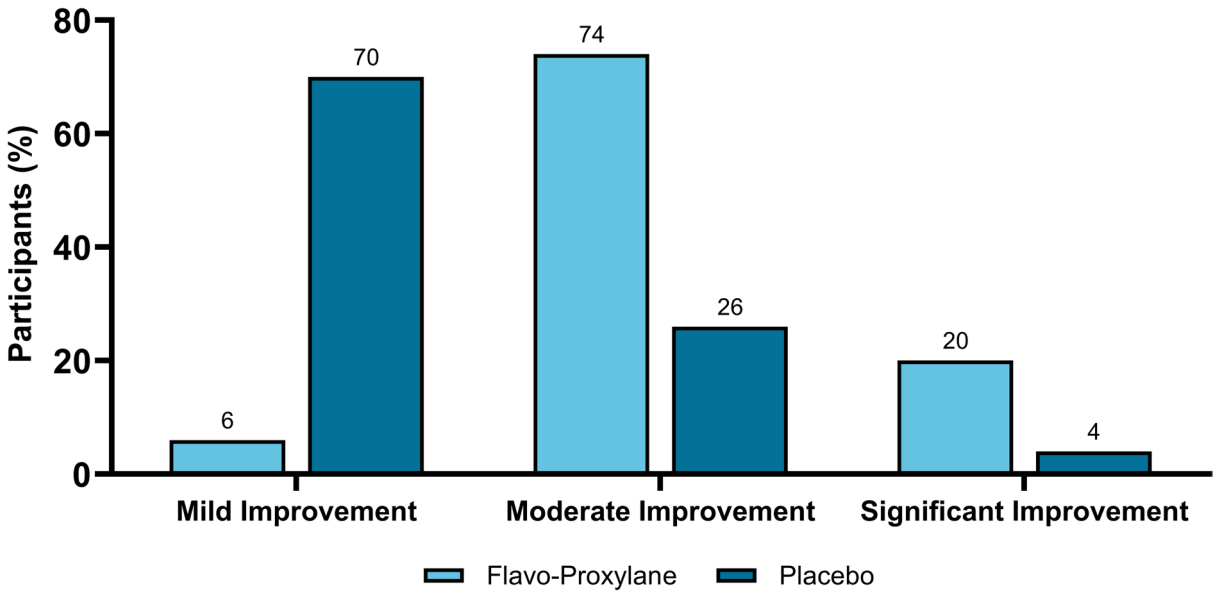

Fig. 6 Overall improvement rating between Flavo-Proxylane and placebo at week 12

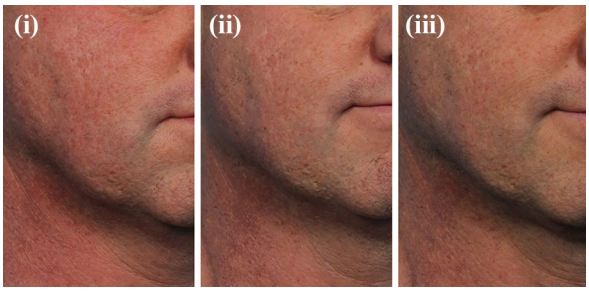

Fig. 7 Participant imaging (**i**, **ii**, **iii**). Male participant (50) with Fitzpatrick skin type III who lost 20 lb during the study while using semaglutide; Flavo-Proxylane regimen applied to the right side of the face (pictured)

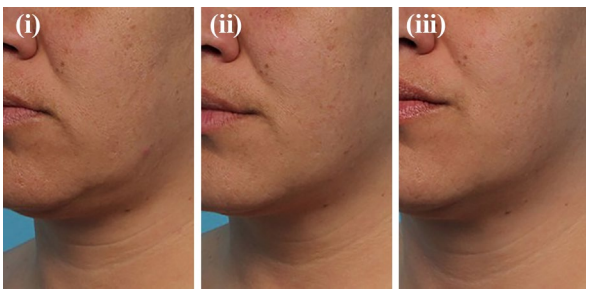

Fig. 8 Participant imaging (**i**, **ii**, **iii**). Female participant (39) with Fitzpatrick skin type III who lost 3.7 lb during the study while using tirzepatide. Flavo-Proxylane regimen applied to the left side of the face (pictured)

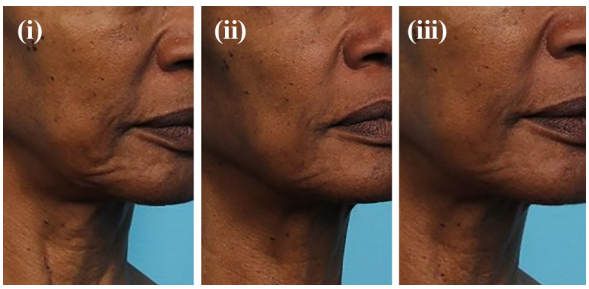

Fig. 9 Participant imaging (**i**, **ii**, **iii**). Female participant (68) with Fitzpatrick skin type VI who gained 1 lb during the study while using semaglutide. Flavo-Proxylane regimen applied to the right side of the face (pictured)

significantly greater improvements in skin laxity and contour over the placebo treatment.

Following ultrasound, data generally demonstrated amplified improvements in marionette lines and skin laxity, showing a cumulative and sustained effect through 12 weeks. Although the placebo treatment also showed improvements by week 12, the magnitude and frequency of response were consistently and statistically greater with the Flavo-Proxylane treatment. These findings were supported by overall improvement ratings, which revealed statistically significant between-group differences favoring Flavo-Proxylane at week 12. These data indicate that the procedural intervention was highly effective independently; however, the Flavo-Proxylane treatment further enhanced outcomes, suggesting its protective and restorative potential against adverse dermatologic changes in the context of rapid weight loss.

In addition to skin laxity and marionette lines, broader dermatologic benefits were observed. For example, significant improvements observed across 13 clinical grading parameters by week 12 indicate that the integrated skincare regimen enhances global skin aesthetics, exceeding the desired improvements in skin laxity and volume despite substantial weight loss among numerous participants. GAIS scores and patient survey data further supported these clinical outcomes, with 80% of participants rated as "Improved" or better by investigators, and 92% self-reporting similar levels of improvement in the Flavo-Proxylane group. These high satisfaction rates were echoed in patient-reported outcomes, with the majority of participants reporting improvements in overall skin appearance and a willingness to repeat the procedure. Collectively, these data suggest that the combined Flavo-Proxylane and ultrasound regimen was both efficacious and well tolerated. Tolerability remained favorable across a myriad of objective and subjective measures. For example, significant reductions in erythema and dryness were observed consistently throughout the study compared to baseline, and the Flavo-Proxylane treatment was associated with fewer subjective symptoms, such as burning, stinging, and itching, suggesting enhanced comfort and usability compared to placebo.

Overall, these findings reinforce previous research supporting the use of a targeted topical cosmetic product to improve signs of skin laxity and volume in GLP-1 RA users [21]. Moreover, this study also reinforced the synergistic potential of a Flavo-Proxylane cosmetic when

combined with ultrasound treatment to improve skin laxity [33], despite minor differences in the precise ultrasound modality between studies. Although this study supported synergy between treatments, the procedure clearly yielded standalone benefits towards skin volume and laxity, further reinforcing previous research for this relatively new technology [24–26]. The outcomes of this study suggest that GLP-1 RA use does not significantly mitigate the potential benefits of this integrated skincare regimen, regardless of the duration of GLP-1 RA use or the type of GLP-1 RA used (i.e., semaglutide, tirzepatide). As such, this integrated skincare regimen appears to be a safe and effective option to counteract the anticipated deleterious dermatologic effects of GLP-1 RA use.

Despite the notable outcomes observed in this study, several limitations are worth noting. For instance, the relatively small sample size ($N = 25$) may limit the generalizability of these findings. Similarly, despite the inclusion of both male and female participants, the small sample of male participants ($n = 2$) limits the context of gender-specific outcomes. Additionally, the single procedure and relatively short 8-week post-procedure follow-up may have limited the potential to observe complete or longer-term effects (e.g., due to sustained structural or compositional skin changes). Research suggests sustained and/or compounded improvements in some endpoints with a combined Flavo-Proxylane and ultrasound treatment through 180 days [33]. Additionally, because the ultrasound procedure was applied to both sides of the face, attribution of post-procedure outcomes to treatment alone is limited; however, this limitation was anticipated and addressed through the randomized, controlled, split-face study design, enabling relative comparisons between treatment and placebo under identical procedural conditions. Given the absence of clinical data on integrated skincare among this population, the present study was intentionally designed as foundational research to characterize early clinical and cosmetic outcomes while minimizing additional confounders (e.g., seasonal environmental exposure) and informing subsequent research. In alignment with recent expert consensus, the present study addresses an unmet need for foundational, controlled clinical data to inform aesthetic management in patients receiving medical weight-loss pharmacotherapy, including GLP-1 RAs [17]. Future studies should analyze the effects of such interventions with a larger sample and over a longer follow-up duration while controlling for potential confounders such as GLP-1 RA type, duration of therapy, and magnitude of weight change.

CONCLUSION

This study represents the first clinical investigation of an integrated skincare regimen aimed at mitigating potential deleterious dermatologic effects among GLP-1 RA users. Overall, this study found that the combination of a targeted Flavo-Proxylane cosmeceutical and ultrasound is well tolerated and may improve dermatologic outcomes in GLP-1 RA users. The cosmeceutical and procedure independently and collectively yielded statistically significant improvements across multiple clinical outcomes, including skin laxity, fine lines, and overall aesthetic improvement. However, further research is needed to better understand the complete potential of this regimen, particularly while controlling patient-level factors. Importantly, the observed outcomes suggest that this integrated approach can not only prevent deleterious skin outcomes but potentially improve such aesthetic concerns among GLP-1 RA users. These findings support the use of ultrasound-based integrated skincare strategies to proactively manage facial aesthetics in populations undergoing GLP-1 RA treatment.

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Data Availability. Raw data were generated at Moradi MD. Derived data supporting the findings of this study are available from the corresponding author [Patricia M Brieva] on request.

Declarations

Conflict of Interest. Drs. Patricia M Brieva and Hina N Choudhary are employees of SkinCeuticals. Drs. Amir Moradi, Jihee H Kim, and Jemin M Kim declare no competing interests.

Ethical Approval. Prior to participation, all subjects provided written informed consent. The study protocol, informed consent, and all patient-facing materials were approved by the Sterling Institutional Review Board (Protocol Number SKIN2024-02, September 24, 2025). This study was performed in accordance with the Declaration of Helsinki of 1964 and all updated versions.

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