Improving Body Skin Quality: Evidence-Based Development of Topical Treatment and Survey of Current Options

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ABSTRACT

The growing interest in improving the quality of body (as distinct from facial) skin may be in part attributable to the expanding use of noninvasive body contouring procedures. In this review, we describe a new framework characterizing the factors that define skin quality (including visual, textural, and biomechanical attributes) that provides a foundation for improved assessment of skin quality and its response to treatment. We then highlight critical biological pathways responsible for body skin restoration and maintenance that have been identified during the development of restorative topical products. Each of these pathways, including extracellular matrix support, suppression of lipogenesis, and enhancement of cellular/macromolecular recycling and clearance, lymphatic drainage, and lipolysis, is a potential target of 1 or more bioactive substances. A survey of available topical products marketed for skin quality improvement suggests that none target more than 2 of these pathways (including extracellular matrix support, lipolysis, and autophagy, a component of cellular recycling), leaving abundant opportunity for development of new topical formulations that target all or most of the critical pathways. Such formulations may provide improved outcomes when used as standalone products for general skin quality improvement and rejuvenation, in addition to their potential for post-procedure use, and also for pre-procedure skin conditioning.

J Drugs Dermatol. 2022;21(6):653-658. doi:10.36849/JDD.6811

INTRODUCTION

Skin is at once the largest and the most visible organ of the human body, and it can also provide an all-too-accurate reflection of internal health. Changes in skin quality attributes, such as those associated with aging, systemic disease, or injury, can substantially degrade self-image, self-esteem, and overall quality of life.[1] It is therefore unsurprising that a seemingly limitless selection of commercially available products hold out the promise of skin quality improvement and/or restoration.

Interest in the improvement of body skin (as distinct from facial skin) quality is increasing, driven in part by the growing use of noninvasive body contouring (NIBC) procedures, which employ thermal, electromagnetic, or ultrasonic energy to induce apoptosis of subcutaneous adipocytes, and consequent recontouring of subcutaneous fat deposits. NIBC procedures, because they reduce the volume of fat deposits, often lead to skin laxity, and may also affect other skin properties. Interest in NIBC procedures has increased greatly in recent years as patient outcomes have been optimized and recovery time reduced.[2]

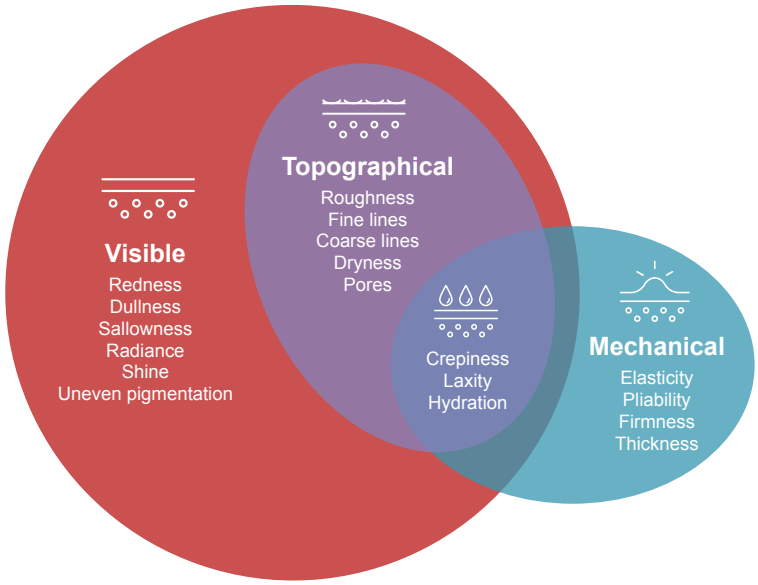
In this narrative review, we present approaches to the restoration or improvement of body skin quality. We first describe a multidimensional characterization of the elements that define high-quality skin with respect to visual, tactile, and biomechanical properties. We then explore the key physiological and signaling pathways critical to restoring or improving skin quality, as well as the potential to modulate those pathways; and finally, we review published clinical studies of topical products for skin quality improvement.

Skin Quality: In Search of an Elusive Goal

The improvement of "skin quality" is the objective of a wide range of aesthetic procedures, and an even wider selection of topical products, aimed both at correcting extant problems (eg, those associated with aging) and at recovery following injury or cosmetic procedures.[3-8] An initial challenge was to implement a conceptual framework that properly captures the parameters that help define skin quality.

Numerous terms (many poorly defined at best) are employed to describe components of skin quality: tone, radiance, elasticity, oiliness, uniformity, pigmentation, wrinkling, crepiness, erythema, roughness, and many others.[9] Many negative terms are applied to age-related changes arising from intrinsic or extrinsic factors; for these terms, the *absence* of the attribute in question (eg, wrinkles, hyperpigmentation, roughness) denotes skin of higher quality. Importantly, few of these terms have been

FIGURE 1. Proposed framework for defining skin quality. Three dimensions of skin attributes (visible, topographical, and mechanical) have been proposed to provide an organizational framework for the numerous descriptors of skin quality currently in use.[9]



defined operationally in ways that permit objective assessment, making clinical evaluations of effects on skin quality dependent on subjective patient- or physician-reported outcomes.

Humphrey and colleagues recently proposed a conceptual framework for skin quality that, while still in need of refinement, provides a useful foundation for clinical assessments and for developing more precise definitions of the components of skin quality. The framework postulates 3 fundamental dimensions that define skin quality: visual, topographical, and mechanical (Figure 1).[9] Some primary skin attributes involve more than 1 dimension: radiance/reflectivity and oiliness/dryness involve both visual and topographical sensations, and dryness/hydration involves all 3 categories.[9] Scars also possess elements of all 3 categories; however, as secondary skin lesions rather than basic attributes of body skin, they were excluded from the proposed framework.

Purely visual aspects of skin quality (ie, those observable via illumination of, and light reflection from, the skin with no consideration of topographic or textural variations) include overall pigmentation (ie, melanin content), hyper- and hypopigmentation, erythema, and dullness/sallowness.[9-18] Purely topographical aspects of skin quality include texture (smoothness/roughness), coarse and fine lines (wrinkles), crepiness, laxity/looseness, and pore size.[9,13,16,19] Skin mechanical attributes arise primarily from the intradermal scaffold of dermal elastic fibers; the most readily observable is elasticity, which is often measured as recoilability.[9,18] Other prominent mechanical attributes include skin firmness, which impacts elasticity, and skin thickness, which varies naturally across anatomic sites and may be affected by genetic factors, aging, and lifestyle choices, including exercise and sun exposure.[9,10,14,18-20]

A similar approach to the components of skin quality has recently been published, based on the findings of a consensus panel of dermatologists and aesthetic physicians.[4] The framework proposed by the consensus panel is broadly similar to that described above, with 4 emergent perceptual categories (skin firmness, skin surface evenness, skin tone evenness, skin glow), analogous to the 3 dimensions proposed by Humphrey et al. The descriptors for individual skin attributes are nearly identical between the 2 frameworks, with some minor terminology and grouping differences.[4,9]

Because they help define the key attributes contributing to our perception of skin quality, and are potentially applicable to all anatomic sites, these proposed frameworks are important contributions. Moreover, by also providing available objective methods for assessing these attributes (a topic beyond this article's scope), the authors have laid the groundwork for better clinical evaluations of products used for skin quality improvement.[4,9]

Body Skin Quality: Special Considerations

Skin quality is a key component affecting perception of facial attractiveness, which, in turn, influences perceptions of health and vitality, personality, age, and emotional and psychological well-being.[9,21-26] Aesthetic medicine, including treatments aimed at repair/restoration of skin quality, has been focused primarily on the face and attributes of facial skin. However, a growing desire to address cosmetic issues below the face has led both clinicians and researchers to consider the special characteristics of body skin.[27,28] Key characteristics of body skin compared with

TABLE 1.

Characteristics of Body Skin in Comparison With Facial Skin[27,28]		
Skin Attribute	**Body Skin Characteristics (vs Facial Skin)**	**Implications**
Thickness	Thicker stratum corneum, with more corneocyte layers Thickness may contribute to slower/uneven differentiation rate	Rougher, uneven surface microrelief Reduced permeability to topical agents
Sebaceous glands	Substantially fewer and smaller glands, especially on extremities Reduced sebum deposition in some areas	Drier skin
Subcutaneous fat	Variable over body; less deposition on hands and chest	Affects appearance of plumpness/smoothness
Sun exposure	Mostly less than for facial skin, except in certain areas (forearms, décolletage)	Uneven skin tone in exposed areas
Sensitivity to external stimuli	Reduced in proportion to increased thickness	Reduced sensation in areas with thicker skin

TABLE 2.

Age-Related Changes and Processes in Body Skin[28]	
Dermal Layer	**Key Changes**
Epidermis	Decreased stratum corneum thickness (especially neck, chest, back of hands) Increased corneocyte size (secondary to reduced epidermal differentiation)
Dermis	Changes in epidermal-dermal junction Loss of extracellular matrix proteins (especially elastin, collagen) Reduced levels of hyaluronic acid, glycosaminoglycans
Subcutaneous fat	Overall reduction in thickness and volume Redistribution to various sites, with increased thickness in some areas and reduced thickness in others

facial skin, as well as age-related changes in body skin, are described in Tables 1 and 2.

Pathways to Improving Body Skin Quality

In considering the key goals for a topically administered product designed to improve the quality of body skin, we concluded that the most desirable goals from the patient viewpoint were to improve skin health and quality generally across multiple parameters, improve the appearance/reduce the extent of cellulite, and complement in-office body-contouring procedures and facilitate rapid recovery and improvement in skin quality.

Based on our collective experiences and knowledge of dermal anatomy and physiology, as well as the extant literature, we translated these broad goals into modulation of critical biological target areas and pathways (Figure 2)[29]:

Support for and remodeling of the extracellular matrix (ECM): Promoting expression of ECM protein elements (chiefly collagens, fibronectin, and elastic fiber proteins) to improve the skin's biomechanical properties (firmness, elasticity) and facilitate skin tightening via ECM reconstruction/recovery.[30-33]

Support cellular clearance and recycling: This involves support for autophagy and promotion of proteasome activity. Autophagy leads to the clearance of damaged and worn-out cellular components and organelles via lysosomes. Proteasomes are largely responsible for clearance/removal of damaged/misfolded proteins.[34]

Improve lymphatic drainage: This facilitates the removal of released fatty acids and cellular/macromolecular debris and promotes the discharge of excess tissue fluids to reduce edema.[35,36]

Promote lipolysis: Induction of and increasing the rate of lipolysis to release free fatty acids (FFAs) and glycerol into the circulation to regulate lipid accumulation, adipocyte volume, and fat mass.[37,38]

Inhibit lipogenesis: Suppressing lipogenesis (ie, lipid synthesis and storage in adipocytes) maintains healthy cell activity and prevents adipocyte volume increase; this also involves inhibiting adipocyte reuptake of FFA and other lipid components.[37,38]

Topical Products for Body Skin Quality Improvement

We review here published clinical evaluations of 3 body skin treatments promoted for skin restoration and skin quality improvement (Table 3) in which skin quality parameters were evaluated.

Published Clinical Results

In a case series, 5 female subjects (age range, 23–69 years) applied Body Tightening Concentrate (BTC; SkinCeuticals, Garland, TX) twice daily for 18 weeks, following laser lipolysis using the SculpSure system (Cynosure, Westford, MA) for

FIGURE 2. Potential biological target pathways and mechanisms for improving skin health and quality. The use of topical products to modulate these pathways may lead to improvements in skin quality both as standalone treatments as well as to facilitate recovery from NIBC.[29-38]

reduction of abdominal or posterior flank adiposity. Subjects could opt for a second laser treatment at the same or different site at a 6-week follow-up.[7] Based on photographic evidence from follow-up visits, all 5 blinded investigators correctly assigned the photos to their proper sequence based on overall treatment results over time and concurred with improved skin quality and reduced laxity. No adverse events were reported.[7] Limitations of this study included lack of objective outcome measures and the small number of subjects; moreover, there was no historical or concurrent control group, making it impossible to discern whether the observed effects simply reflected normal recovery following SculpSure treatment.

An earlier study evaluating skin quality improvements using the same formulation following bipolar radiofrequency (RF) treatment for posterior buttock/thigh adiposity showed consistent results.[3] In an 8-week, split-body study, 20 female subjects received RF treatment (Accent XL; Alma Lasers Inc., Buffalo Grove, IL) plus BTC on one buttock/thigh, while the other buttock/thigh received RF treatment only. At week 8, the buttock/thigh receiving the RF treatment plus BTC experienced significant improvements in skin tone, radiance, texture, firmness/tightness, and overall appearance compared with RF treatment alone. Although thigh circumference was significantly reduced from baseline on both sides at 8 weeks, the reduction was consistent on each side (≈1%).[3]

In a randomized, split-body study, Kavali and colleagues evaluated BodiFirm (Revision Skincare, Irving, TX) for skin quality improvement in female patients (N=40; mean age,

TABLE 3.

Evidence Base for Selected Topical Body Skin Treatments		
Topical Product	**Key Ingredients**	**Target Pathways**
Body Tightening Concentrate[3,7]	Tripeptide, yeast extract, hydrolyzed rice protein	Support dermal ECM
BodiFirm[39]	Peptides (tripeptides, tetrapeptide, and hexapeptide), *Bambusa vulgaris* (bamboo) stem/leaf extract, *Manihot esculenta* (cassava) tuber extract; methylsilanol carboxymethyl theophylline alginate	Support dermal ECM Lipolysis
TransFORM Body Treatment with TriHex Technology[8,40]	Tripeptide-1 and hexapeptide-12 Hexapeptide-11 Acetyl tetrapeptide-2	Support dermal ECM Autophagy

ECM, extracellular matrix

52 years; range, 40–60 years) with mild to moderate signs of aging (laxity, crepiness, overall photodamage); subjects were randomized as to arm treatment (one with BodiFirm, the other with placebo).[39] At 8 and 12 weeks, the proportion of patients with specific improvements impacting skin quality, as judged by a blinded clinical grader, was significantly greater for BodiFirm than for placebo ($P \leq 0.05$). At 12 weeks, BodiFirm treatment was associated with improvements in skin crepiness in 97% of subjects, underarm laxity in 83% of subjects, and photodamage in 83% of subjects; and BodiFirm also demonstrated significantly greater response rates versus baseline for skin roughness, firmness (visual), skin tone evenness (lack of red areas), and hyperpigmentation. However, only the percentage of responders (not the degree of improvement) was directly compared between treatments.[39]

In a randomized, double-blind, split-body pilot study, TransFORM Body Treatment with TriHex Technology (TBT; Alastin Skincare, Inc., Carlsbad, CA) was compared with a bland moisturizer in women (N=11; age range, 25–65 years) following cryolipolysis (CoolSculpting System; Allergan Aesthetics, an AbbVie Company, Irvine, CA) for bilateral reduction of upper arm adiposity.[8] Subjects applied each treatment to opposing arms (treatment assignment was randomized) twice daily for 24 weeks post-procedure. TBT demonstrated a nonsignificant trend toward greater improvements versus the comparator in mean investigator-assessed skin laxity score (graded on a 5-point scale [0=none, 4=extreme]). The strength of the finding is constrained by the lack of statistical analysis for the investigator ratings.

Carruthers and colleagues also evaluated TBT as a standalone treatment for forearm skin quality improvement in a randomized split-body study (N=13 [4 men and 9 women]; mean age, 57 years; range, 38–74 years). Subjects applied TBT or bland moisturizer to the extensor and volar surfaces of opposing forearms (arm assignment was randomized) twice daily.[40] After 3 months of treatment, TBT, compared with bland moisturizer, was associated with significant improvement in photographically assessed volar skin roughness (P=0.004) and a trend toward improvement in extensor skin roughness (P=0.174). There were no significant between-treatment differences observed with respect to skin elasticity or skin thickness, or in a patient-reported assessment of wrinkle severity; however, numerical trends generally favored TBT.[40]

DISCUSSION

Skin quality substantially impacts quality of life, self-esteem, and psychological health, as well as interpersonal interactions.[41] In this narrative review, we have described our efforts to characterize not only the important elements of skin quality but also the key biological pathways that are crucial to restoring or repairing those elements when they are lost or compromised by aging or other causes.

The critical pathways for skin quality improvement and/or restoration spotlighted here should be considered appropriate targets for intervention via topical agents. These targeted pathways have demonstrated their central role in skin quality maintenance and restoration, and patterns of gene expression underlying these pathways have been shown to be responsive to bioactive botanical preparations.[29]

Clinical studies of available topical agents marketed for skin quality improvement and/or restoration have suggested their efficacy with respect to certain skin quality attributes. Based on our review of their components, the pathways targeted by the agents evaluated thus far include ECM support and restoration and lipolysis, along with autophagy, one aspect of cellular clearance and recycling. The limited target range of currently available topical agents leaves ample opportunity for development of products targeting additional pathways, potentially further improving outcomes.

The rapid growth of aesthetic procedures, including NIBC, shows no sign of abating, as outcomes improve and downtime is reduced. At the same time, "body contouring" has begun to tilt toward "body idealization," encompassing not only NIBC and fat reduction but also desirable skin and body outcomes. Because of their potential to address multiple skin quality issues, topical products are destined to play a crucial role in achieving these outcomes, not only in the post-procedural arena but potentially as standalone products.

As the use of NIBC procedures and the range of available topical agents for skin quality improvement continue to expand, the reviewed studies have also highlighted the need to implement objective evaluations of the various skin parameters potentially affected by treatment agents, in order to supplant the current range of patient- and physician-rated evaluations as current status and outcome measures in clinical trials and clinical practice. This will involve establishing benchmarks/ranges for each assessment to define appropriate ranges for the defined parameter (ie, minimal, moderate, or severe), as well as the minimal meaningful change defining improvement/deterioration.

One area deserving of future study is the use of topical products for skin quality improvement as adjunctive *pretreatments* to improve the results of NIBC procedures. This approach could conceivably reduce the incidence of undesirable post-NIBC effects (eg, bruising/ecchymosis, redness, sensitivity) and also reduce the need for post-procedure treatment.

DISCLOSURES

Kuniko Kadoya and Tsing Cheng are employees of AbbVie and may own stock in the company. Janet Allenby has served on advisory boards or received honoraria from AbbVie/Allergan,

Alastin Skin Care, and Endo Laboratories; is associated with the equipment program from Soliton; is owner of and is salaried by Allenby Cosmetic Dermatology; is owner of Body Squad LLC; and is a stockholder in Endo Laboratories. Sabrina G. Fabi is a consultant, investigator, and stockholder for Allergan Aesthetics, an AbbVie Company. David McDaniel has received grant/investigator funding from AbbVie/Allergan, Cynosure, Dermforce, Pharma Cosmetix, RegenX Science, and Anne Arundel Dermatology; has received equipment loan from Canfield Scientific and Cynosure; has received consulting fees from AbbVie/Allergan, Dermaforce, and Cynosure; has received salary from Anne Arundel Dermatology; holds ownership in McDaniel Institute of Aging Research LLC and Senescence LLC; has served on advisory boards for AbbVie/Allergan and Cynosure; and is a stockholder in Anne Arundel Dermatology, Northcell Pharmaceuticals, and RegenX Science.

Funding Disclosures:

This study was sponsored by Allergan Aesthetics, an AbbVie Company. Writing and editorial assistance was provided to the authors by Stephen Collins, PhD of Peloton Advantage, an OPEN Health company, and was funded by Allergan Aesthetics, an AbbVie Company, Irvine, CA. All authors meet the ICMJE authorship criteria. Neither honoraria nor other form of payment was made for authorship.

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