Cureus
Part of SPRINGER NATURE

Open Access Review Article

Beyond Anti-aging: A Resilience-Centered Framework for Skin Longevity and the Emerging Role of Topical Adaptogens

Marianna Blyumin-Karasik [1], Jessica Colon [2]

1. Medical School, Nova Southeastern University Dr. Kiran C. Patel College of Allopathic Medicine, Davie, USA 2. Dermatology, Precision Skin and Body Institute, Fort Lauderdale, USA

Corresponding author: Jessica Colon, jc4703@mynsu.nova.edu

Review began 10/08/2026
Review ended 10/25/2026
Published 10/28/2026

© **Copyright** 2026
Blyumin-Karasik et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.118744

Abstract

Skin aging is a multifactorial process driven by intrinsic biological changes and cumulative exposure to extrinsic stressors, including ultraviolet radiation, pollution, smoking, dietary factors, sleep disruption, and psychological stress. Traditional anti-aging strategies have largely focused on correcting visible signs of damage after they occur. A skin longevity framework instead emphasizes preservation of cutaneous health, homeostasis, barrier function, repair capacity, and resilience across the lifespan. We propose that cutaneous aging should be evaluated not only by accumulated damage burden but also by recovery capacity, defined here as cutaneous resilience. This narrative review examines skin longevity through the lens of adaptation to intrinsic and extrinsic stress, building on recent efforts to formalize this concept under the term skinspan. We summarize major mechanisms of cutaneous aging, including oxidative stress, mitochondrial dysfunction, cellular senescence, inflammaging, extracellular matrix degradation, neuroendocrine dysregulation, and impaired barrier recovery. We then explore the emerging role of adaptogens, extending our prior systematic categorization of topical adaptogens in dermatology, as a heterogeneous group of bioactive compounds proposed to support homeostasis and stress adaptation through multimodal antioxidant, anti-inflammatory, barrier-supportive, neuroendocrine, and regenerative pathways. Finally, we position adaptogens within a broader longevity strategy that includes photoprotection, retinoids, senotherapeutics, and emerging biomarkers of biological skin aging. A resilience-centered model may expand dermatologic thinking from treatment of visible aging toward preservation of skin function and recovery capacity over time. Future longitudinal studies are needed to determine whether interventions that improve stress resilience can meaningfully extend skin's health span.

Categories: Dermatology
Keywords: adaptogens, exposome, inflammaging, longevity medicine, psychological stress, skin aging, skin healthspan, skin longevity, skin resilience

Introduction And Background

From anti-aging to skin longevity

The framing of dermatologic aging care has historically centered on correction, with wrinkles, pigmentation, and laxity treated once they become clinically visible. Geroscience has reoriented much of medicine away from this reactive model and toward the concept of health span, defined as the years of life spent free of significant morbidity, as distinct from lifespan, the total years lived [1]. Two recent reviews have applied this reorientation directly to skin, proposing the term skinspan to describe the period during which skin retains youthful structure and function, and using it as an organizing framework for evidence-based interventions spanning regenerative medicine, senotherapeutics, exosome-based products, and energy-based devices [2,3]. We adopt skinspan here as a useful descriptive term rather than a validated clinical endpoint, consistent with the caution both groups themselves apply.

This review takes a narrower and more conceptual approach than either prior skinspan publication. Rather than cataloging the full breadth of longevity-directed interventions, we focus on a single organizing idea: that skin longevity depends not only on the accumulation or correction of damage but also on the skin's capacity to resist, adapt to, and recover from repeated intrinsic and extrinsic insults. We refer to this capacity as cutaneous resilience. Chronological age, biological age, and visible age are related but distinct constructs, and an individual's skin may show discordance among all three depending on genetic background, cumulative exposome burden, and the efficiency of its homeostatic and repair systems [3]. A longevity-oriented dermatologist should therefore ask not only how much damage burden has accumulated but also how effectively the skin can currently recover, its recovery capacity, from ongoing stress.

Adaptogens are natural compounds, typically botanical, proposed to support the body's nonspecific resistance to stress and maintain homeostasis, and topical adaptogens are such agents applied to the skin [4]. They serve as the test case for this framework throughout the remainder of this review. We have previously undertaken a systematic categorization of topical adaptogens in dermatology, establishing

criteria for what qualifies an agent as an adaptogen in a cutaneous context and cataloging the existing preclinical and clinical evidence base [4]. This review extends that prior work by situating topical adaptogens within the skin longevity and resilience framework specifically. It asks whether their proposed mechanism, nonspecific support of homeostasis under stress, makes them a biologically plausible tool for extending skin health span while explicitly identifying where mechanistic plausibility currently outpaces demonstrated clinical benefit.

Review

Literature search strategy

A targeted narrative literature search was conducted in PubMed/MEDLINE and Google Scholar, with the final search conducted on October 4, 2026. No publication date restriction was applied, and only English-language publications were included. Search terms combined skin aging, skin longevity, skinspan, cutaneous resilience, adaptogens, psychological stress, cellular senescence, senotherapeutics, and regenerative dermatology with the name of each individual adaptogen. Priority was given to randomized controlled trials and other human studies, and preclinical studies were included only where human evidence was absent and are identified as such. Reference lists of relevant reviews were screened. No formal risk-of-bias tool was applied; study design, sample size, comparator, and duration were considered when interpreting the strength of the findings. This is a narrative rather than a systematic review, so the search was targeted rather than exhaustive.

The biology of intrinsic skin aging

Intrinsic skin aging reflects genetically programmed and chronologically driven changes that occur independently of environmental exposure. Epidermal turnover slows, the dermal-epidermal junction flattens, and keratinocyte and fibroblast function decline, reducing the skin's capacity for repair and its structural integrity [5]. Fibroblasts show reduced proliferative capacity and altered collagen and elastin synthesis, while matrix metalloproteinase activity increasingly outpaces matrix production, producing net extracellular matrix degradation over time [6].

Cellular senescence is a central hallmark of this internal process. Senescent keratinocytes, fibroblasts, and melanocytes accumulate with age and secrete factors that constitute the senescence-associated secretory phenotype, a mixture of proinflammatory cytokines, chemokines, and matrix-degrading enzymes that propagates senescence to neighboring cells and drives chronic low-grade inflammation [7,8]. Senescent melanocytes have been shown to transmit paracrine telomere dysfunction to neighboring fibroblasts and keratinocytes, positioning fibroblasts as amplifiers rather than merely targets of the aging cascade [6]. Because senescent cells resist apoptosis and continue to influence surrounding tissue, their accumulation is increasingly viewed as a druggable target, giving rise to senotherapeutic strategies [9].

Mitochondrial dysfunction and oxidative stress compound these changes. Reduced mitochondrial efficiency increases reactive oxygen species production, which in turn damages DNA, lipids, and proteins, further impairing keratinocyte and fibroblast function and accelerating the senescence cascade [10]. Hormonal and neuroendocrine shifts, including declining estrogen in women, alter collagen density, barrier lipid composition, and wound-healing capacity, adding a systemic layer to what is often described purely as a local, cutaneous process [11]. Taken together, these intrinsic mechanisms establish a baseline vulnerability against which extrinsic stressors act, and they define the biological substrate that a resilience-centered model must ultimately target. Table *1* summarizes these intrinsic stressors, together with the extrinsic stressors, alongside their associated aging pathways and measurable consequences. More comprehensive molecular and cellular manifestations of skin aging have been organized into seven hallmarks across three functional categories, two of which each comprise two related processes [12]. Primary hallmarks represent the underlying causes of damage: genomic instability together with telomere attrition, and epigenetic alterations together with loss of proteostasis. Antagonistic hallmarks represent the skin's own damage responses: deregulated nutrient sensing, mitochondrial dysfunction, and cellular senescence. Integrative hallmarks represent the resulting phenotype: stem cell exhaustion and altered intercellular communication.

Stressor	Aging pathway	Measurable consequence	Source
Cellular senescence (keratinocytes, fibroblasts, and melanocytes)	Senescence-associated secretory phenotype release, driving chronic low-grade inflammation and propagation of senescence to neighboring cells	Accumulation of senescent cells; proinflammatory cytokine, chemokine, and matrix-degrading enzyme secretion	[7]
Senescent melanocyte paracrine signaling	Transmission of telomere dysfunction from senescent melanocytes to neighboring fibroblasts and keratinocytes	Fibroblast senescence amplification beyond the primary UV or intrinsic insult	[6]
Mitochondrial dysfunction/oxidative stress	Reduced mitochondrial efficiency increases reactive oxygen species production, damaging DNA, lipids, and proteins	Impaired keratinocyte and fibroblast function; accelerated senescence cascade	[10]
Hormonal and neuroendocrine decline (estrogen)	Altered collagen density, barrier lipid composition, and wound-healing signaling	Reduced collagen density; impaired wound-healing capacity	[11]
Extrinsic exposome (ultraviolet radiation, pollution, smoking, nutrition, and sleep)	Convergent oxidative and inflammatory pathways acting on top of intrinsic susceptibility	Photoaging; accelerated visible and structural skin damage	[13]
Chronic psychological stress	Elevated cortisol and epinephrine downregulate FGF7 and periostin expression and reduce collagen types I and III and HSP47 expression	Increased DNA damage; elevated transepidermal water loss	[14]
Chronic psychological stress (recovery-specific)	Downregulated neocollagenesis after a defined cutaneous insult	Impaired wound-healing capacity distinct from baseline skin quality	[15]

TABLE 1: Major intrinsic and extrinsic stressors, associated aging pathways, and measurable clinical or molecular consequences.

Extrinsic aging and the skin exposome

The skin exposome describes the totality of external and internal nongenetic factors that act on the skin across the lifespan and interaction with intrinsic susceptibility through epigenetic modifications. Ultraviolet radiation remains the dominant extrinsic driver of visible photoaging, but the exposome concept explicitly widens the lens to include air pollution, tobacco smoke, nutrition, physical activity, sleep disruption, and psychological stress, all of which converge on overlapping oxidative and inflammatory pathways [13].

Psychological stress has received increasing attention as a distinct and modifiable exposome factor. The adverse effects of chronic psychological stress on skin health, appearance, and aging arise in part from the bidirectional skin-stress cycle and its neuro-immuno-endocrine-cutaneous signaling pathways [16]. Chronic moderate psychological stress has been shown, in an exploratory clinical and cellular study, to significantly affect skin homeostasis, with elevated cortisol and epinephrine downregulating fibroblast growth factor 7 and periostin gene expression, increasing DNA damage, and reducing collagen types I and III and HSP47 expression, alongside a measurable increase in transepidermal water loss [14]. Survey data collected from young women, dermatologists, and psychologists in China and Japan similarly documented broad recognition of a preaging phenomenon involving self-reported signs of premature skin aging in the 20s and 30s that respondents associated with psychological stress [17]. A 2025 narrative review further detailed how the hypothalamic-pituitary-adrenal axis, neurogenic inflammation, and mast cell signaling connect chronic stress to a wide range of dermatologic manifestations, from barrier disruption to exacerbation of inflammatory dermatoses such as acne, psoriasis, and atopic dermatitis [18].

Stress also appears to blunt recovery capacity specifically, not only baseline skin quality. Psychological stress has been linked to impaired wound healing through downregulated neocollagenesis, a mechanism directly relevant to the resilience framework, since it demonstrates that stress does not simply add cumulative damage but actively degrades the skin's capacity to repair itself after a defined insult [15]. Taken together, this literature supports treating the skin exposome as a set of interacting, largely modifiable inputs rather than a fixed environmental backdrop, and it identifies psychological stress in particular as a mechanistically tractable target for adaptogen-based intervention. These extrinsic stressors and their downstream consequences are summarized in Table *1*.

Cutaneous resilience: homeostasis, adaptation, and recovery

We define cutaneous resilience as the skin's capacity to maintain or restore homeostasis following intrinsic or extrinsic stress, encompassing barrier restoration, inflammatory resolution, redox balance, and coordinated cellular repair. This framing shifts the relevant clinical question from how much cumulative damage has occurred to how efficiently the skin recovers after a given insult. Figure *1* illustrates this conceptual model, in which intrinsic aging and the extrinsic exposome converge on cumulative cellular stress, driving the decline in homeostasis and resilience that ultimately advances visible and functional skin aging. Intrinsic aging and extrinsic exposures interact through overlapping molecular, cellular, and epigenetic pathways to influence the trajectory of cutaneous aging, contributing to progressive functional decline and visible aging [19].

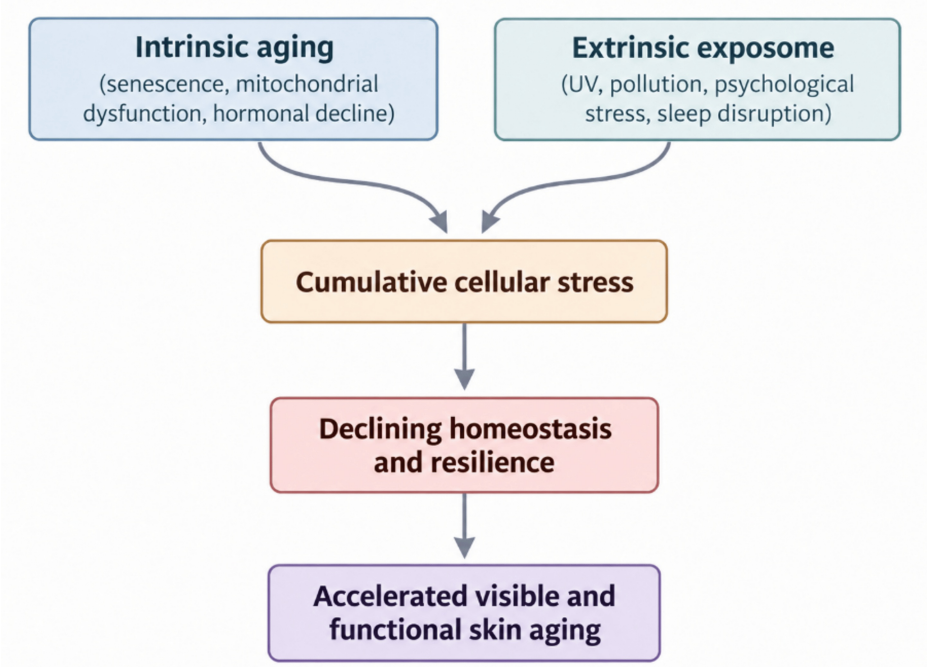


FIGURE 1: Conceptual skin resilience model.

Intrinsic aging and the extrinsic exposome converge on cumulative cellular stress, which drives declining homeostasis and resilience, producing accelerated visible and functional skin aging.

Image credit: Jessica Colon. Original, unpublished figure. This figure was prepared using generative AI (Claude Sonnet 5.5, Anthropic), based on content and instructions provided by the authors, and reviewed by the authors.

The mechanistic evidence reviewed in the "extrinsic aging and the skin exposome" section supports resilience as a measurable, stress-responsive property rather than an abstraction. The reduction in FGF7 and periostin expression under cortisol and epinephrine exposure, together with the accompanying rise in transepidermal water loss, demonstrates that acute neuroendocrine stress signaling directly impairs the molecular machinery of barrier repair [14]. Similarly, the downregulation of neocollagenesis under psychological stress shows that recovery from a defined insult, in that case a wound, is itself stress-modifiable rather than fixed [15]. An earlier industry-sponsored but frequently cited framework described this same idea as "well aging," proposing that supporting skin homeostasis under multiple simultaneous stressors, rather than targeting any single stressor in isolation, may better reflect real-world skin physiology [20].

We propose resilience as the conceptual bridge between exposome science, which characterizes the detrimental inputs acting on the skin, and longevity dermatology, which is concerned with functional outcomes over time. Under this framing, an intervention's value is judged not only by whether it reduces a single measurable stressor but by whether it preserves or restores the skin's underlying capacity to adapt and recover. This is the specific property that adaptogens, as a therapeutic category defined by nonspecific stress resistance, are proposed to support, which motivates the remainder of this review.

Adaptogens: biological rationale for skin longevity

The term adaptogen originated in Soviet pharmacology and was formalized by Panossian and colleagues to describe agents that increase an organism's nonspecific resistance to stress without disturbing normal physiological function, historically applied to systemic use in stress- and aging-related diseases [21]. This definition carries two requirements that are essential to preserve when the concept is extended topically:

that an adaptogen supports homeostasis broadly rather than correcting a single pathway, and that it does so without inducing a stress or harmful response of its own.

Dermatology has increasingly borrowed this framework to describe a heterogeneous set of botanical and bioactive compounds applied topically, a trend documented in a 2023 bibliometric analysis of the adaptogen literature in dermatology, which mapped the pharmacophylogeny and proposed mechanisms of agents including *Centella asiatica*, curcumin, and rhodiolosides [22]. We have previously undertaken a systematic review and categorized topical agents as skin adaptogens in a dermatologic context, proposing a classification system for organizing the existing evidence base by mechanism and evidence quality [4]. The present review builds forward from that categorization rather than reproducing it, using it as the taxonomic foundation for the evidence synthesis.

Mechanistically, proposed pathways relevant to skin longevity include direct antioxidant defense, support of barrier lipid synthesis, attenuation of hypothalamic-pituitary-adrenal axis output at the level of the skin, and mitochondrial support [4]. Additional downstream pathways, including modulation of nuclear factor kappa B and Janus kinase and signal transducer and activator of transcription signaling to reduce inflammation and preservation of extracellular matrix integrity through effects on transforming growth factor beta and Smad signaling, have been demonstrated for individual agents such as *C. asiatica* but have not been established as uniform across the adaptogen category as a whole [23]. It is important not to treat this category as mechanistically uniform. Individual adaptogens differ substantially in their dominant pathway, their degree of human clinical validation, and their formulation challenges, and the strength of evidence for each claimed mechanism varies considerably by agent.

What does the topical adaptogen evidence actually show?

Table *2* summarizes the agents reviewed in this section, organized by proposed mechanism, level of clinical evidence, and key limitations, using the categorization system from our prior systematic review of topical adaptogens in dermatology [4].

Agent	Proposed mechanism	Level of evidence	Key limitations	Source
Centella asiatica	TGF beta and Smad-driven extracellular matrix synthesis; attenuation of NF kappa B and JAK/STAT3 signaling; reduced oxidative and glycation stress	Randomized, double-blind study (n = 60; *C. asiatica* plus *Phyllanthus emblica* emulsion versus placebo emulsion; 60 days); in vitro reduction in senescence and apoptosis markers; preprint, open label, uncontrolled (n = 20, 28 days; extracellular vesicle formulation)	Controlled trial tested a two-extract combination, so the *Centella* effect is not isolated; formulation and concentration vary across studies; short duration; extracellular vesicle study not yet peer-reviewed	[23-26]
Ashwagandha (*Withania somnifera*)	Proposed modulation of cortisol signaling, not measured in the randomized trial; suppression of CCN1-associated inflammatory pathways in fibroblasts (in vitro)	Randomized, double-blind study (n = 56; 8% lotion versus placebo lotion; 60 days): improved TEWL, hydration, and elasticity by day 60; no open label, uncontrolled (n = 31; no comparator; 28 days): hydration +49.0%, elasticity +27.2%, wrinkle number decreased by 25.9-33.3%	TEWL measured at baseline and day 60 with no barrier challenge, so recovery was not tested; second study open label and uncontrolled; different formulations (8% lotion versus 1% cream)	[27,28]
Curcumin	Nrf2-mediated antioxidant enzyme induction; NF kappa B inhibition; matrix metalloproteinase regulation; modulation of autophagy and apoptosis in UV-stressed keratinocytes	Strong preclinical and mechanistic evidence; limited dermatologic clinical trial data	Systemic bioavailability limitations motivate topical delivery; sparse longevity-relevant clinical trials	[29]
Aloe vera	Anti-inflammatory activity via reduction of UV-induced erythema; barrier and inflammatory support independent of corticosteroid pathways; Nrf2/ARE antioxidant activation, mitochondrial function	Randomized, double-blind, placebo-controlled trial (n = 40); significantly reduced UV erythema at 48 hours; randomized trial (n = 80); comparator (0.1% triamcinolone acetonide; 8 weeks) in plaque psoriasis: greater PASI reduction with *A. vera* (P = 0.0237), with similar DLQI improvement (P = 0.5497); in vitro and mouse studies showing reduced ROS, restored collagen, suppressed MMP-	Neither clinical trial designed around longevity outcomes; distinct from periprocedural evidence below; mechanistic studies are preclinical	[30-33]

	preservation, and senescence marker suppression	1, and reduced senescence markers.	(cell and mouse models)	
Ganoderma lucidum	Broad cosmeceutical and pharmacological activity described mechanistically; Nrf2-linked antioxidant gene upregulation and p16/SA-beta-gal senescence suppression in vitro	Extensive preclinical and mechanistic literature; in vitro senescence model (etoposide-induced) showing senolytic-like effect; no dedicated dermatologic clinical trials identified	Evidence gap between mechanistic plausibility and clinical validation; one of two tested extracts showed unfavorable IL-8 and MMP-1 upregulation	[34,35]
Cordyceps militaris	Reactive oxygen species scavenging; protection against apoptosis and senescence in fibroblasts	In vitro study (human dermal fibroblasts); reduced apoptosis and SA-beta-gal-positive cells under H_2O_2 stress	Preclinical only; *C. militaris*, not the more commonly cited *C. sinensis*; species distinction often blurred in secondary sources	[36]
Rhodiola and astragalus	Mechanistic plausibility extrapolated largely from systemic pharmacology; Nrf2/Keap1 antioxidant activation (*Rhodiola*) and mitochondrial membrane potential/ATP preservation (astragalus) shown in vitro	No dedicated topical trial of *Rhodiola* or of isolated *Astragalus* identified; one randomized, double-blind, placebo-controlled trial of a topical *Astragalus* and *Centella* saponin cream (25 per group; versus placebo cream; 4 weeks); in vitro UV-stressed fibroblast (*Rhodiola*) and keratinocyte (astragalus) studies show reduced ROS, increased collagen, and preserved mitochondrial function	The only clinical study used a combination so it does not establish independent *Astragalus* efficacy or a longevity benefit; *Rhodiola* evidence is preclinical only; clear gap for future dermatologic study.	[22,37-39]
Multi-adaptogen serum formulations	Combination botanical adaptogens targeting overall skin quality rather than a single pathway	Multicenter, open label, uncontrolled (n = 53; no comparator; 12 weeks) [40]; multicenter, open-label, uncontrolled 16-week study of an enhanced serum with 13 adaptogens in women aged 46 years and older [41]	No control group, multi-ingredient formulation complicates attribution of effect to any single adaptogen	[40,41]
Multi-adaptogen serum formulations	Combination botanical adaptogens applied post-laser to support barrier recovery and healing	Case series (n = 8); no laser only or standard aftercare comparator; improved photodamage scores, patient-reported hydration and radiance gains, and no adverse reactions	Small sample; no comparator, so added benefit beyond the procedure cannot be determined; two laser platforms (alexandrite or picosecond)	[42]

TABLE 2: Representative topical adaptogens, proposed mechanisms, level of evidence, and key limitations.

The categorization system is based on our prior systematic review [4].

Centella asiatica

C. asiatica, or gotu kola, has the most developed mechanistic and delivery-system literature among topical adaptogens. Its principal triterpenoid saponins, asiaticoside and madecassoside, and their aglycones, asiatic acid and madecassic acid, act on transforming growth factor beta- and Smad-driven extracellular matrix synthesis, attenuate nuclear factor kappa B and Janus kinase and signal transducer and activator of transcription 3 signaling, and reduce oxidative and glycation stress [23]. Human clinical data include a double-blind, placebo-controlled randomized trial of an emulsion combining 3% *C. asiatica* extract with 3% *Phyllanthus emblica* extract in 60 women aged 40 to 60, applied twice daily for 60 days, which reported improvements in skin hydration, elasticity, and wrinkle parameters, with no erythema or edema observed [26]. Because the active was a two-extract combination, this trial does not isolate the effect of *C. asiatica*. A separate 2024 review focused specifically on wound-healing applications, summarizing evidence that *Centella*-derived compounds enhance collagen synthesis, modulate inflammation, and accelerate healing across diabetic ulcers and burns when delivered through hydrogel, nanostructured, or microneedle systems [43]. In vitro work has extended this mechanistic picture directly to the senescence pathways central to this review, with *C. asiatica* extract significantly reducing hydrogen peroxide-induced cell death, reactive oxygen species generation, senescence markers, and apoptosis in cultured human keratinocytes [24]. A 28-day open-label facial study of a *C. asiatica* extracellular vesicle-based formulation in 20 adults reported improvements in hydration, elasticity, wrinkles, redness, and pore appearance. However, this work is

currently available only as a preprint and has not yet undergone peer review; this limitation should temper the weight given to it relative to the peer-reviewed trials above [25].

Ashwagandha

Ashwagandha, or *Withania somnifera*, is among the topical adaptogens with randomized clinical data in photoaged skin. Its proposed mechanism, modulation of cortisol signaling, was not tested in the randomized trial discussed here, which measured cosmetic and biophysical outcomes without cortisol or other stress biomarkers [27]. A randomized, double-blind, placebo-controlled trial of an 8% standardized ashwagandha lotion in 56 adults with photoaged facial skin reported significantly greater improvement than placebo across a composite physician assessment score, along with reductions in transepidermal water loss and improvements in hydration and elasticity by day 60 [27]. This trial measured barrier-related outcomes, including transepidermal water loss at baseline and day 60, alongside cosmetic outcomes, but it applied no defined barrier challenge and did not track recovery over time, so it does not test recovery capacity itself. It is nonetheless a useful starting point for the resilience-oriented endpoints discussed in the section on measuring skin longevity. A second, more recent study combined in vitro and clinical work specifically in sensitive, visibly aging skin, showing that a topical 1% ashwagandha root extract cream suppressed hydrogen peroxide-induced upregulation of CCN1 and associated proinflammatory cytokines in cultured fibroblasts, while a 28-day open-label trial in 31 women reported increases in stratum corneum hydration of 49.0% and elasticity of 27.2%, a 32.4% improvement in a facial firmness parameter, and wrinkle number reductions of 25.9-33.3% across facial regions, with no adverse events [28]. Together, these two studies provide preliminary human evidence for ashwagandha, one from a randomized, placebo-controlled trial and one from an open-label, uncontrolled study, and the mechanistic work in the second centers on CCN1-associated pathways in fibroblasts rather than cortisol signaling [28].

Curcumin

Curcumin, the principal polyphenol in turmeric, has strong preclinical support for antiphotoaging activity, acting through Nrf2-mediated antioxidant enzyme induction, inhibition of nuclear factor kappa B signaling, regulation of matrix metalloproteinase activity, and modulation of autophagy and apoptosis in ultraviolet-stressed keratinocytes [29]. Topical, rather than oral, delivery circumvents curcumin's well-documented systemic bioavailability limitations, and earlier mechanistic work specifically addressed its anti-inflammatory and antiapoptotic activity in photodamaged skin, burns, and surgical scars [44]. Clinical trial data in a longevity-relevant skin context remain comparatively sparse relative to the depth of the mechanistic literature.

Aloe vera

Topical *A. vera* has the longest history of dermatologic use among the agents reviewed here and has accumulated supporting evidence for general anti-inflammatory and barrier-related skin benefits. Mechanistic work at the molecular and cellular level provides more direct support for *A. vera* as a resilience-supporting agent specifically. Aloe-derived exosome-like nanoparticles suppressed Keap1 and promoted nuclear translocation of phosphorylated Nrf2 in ultraviolet-stressed dermal fibroblasts and keratinocytes and in a photoaged mouse model, upregulating the downstream antioxidant genes HO-1 and NQO1, reducing mitochondrial reactive oxygen species and malondialdehyde, restoring collagen and suppressing matrix metalloproteinase 1, and reducing senescence markers including senescence associated beta galactosidase, p53, p21, and senescence-associated secretory phenotype cytokines [32]. A separate study in ultraviolet B-irradiated human dermal fibroblasts found that a fermented *A. barbadensis* leaf skin extract restored mitochondrial reductase and succinate dehydrogenase activity, reduced intracellular reactive oxygen species, and increased collagen production while decreasing matrix metalloproteinase 1 secretion, outperforming an unfermented extract at comparable concentrations [33]. Both studies are preclinical and were conducted in cultured cells and in mice rather than humans, but they demonstrate that *A. vera* engages the same antioxidant, mitochondrial, and senescence pathways proposed as the mechanistic basis for topical adaptogens generally.

Multi-adaptogen Formulations and Other Agents

A multicenter, open-label, uncontrolled study of a serum comprising multiple plant-based adaptogens, involving 53 participants over 12 weeks, provides one of the few examples of a combination formulation tested clinically rather than a single isolated compound, and it is directly relevant because most commercial topical adaptogen products are multi-ingredient formulations rather than single-agent extracts [40]. Because it had no control group, it cannot separate the effect of the serum from vehicle effects or natural variation, and it is weaker evidence than the randomized trials above. A later 16-week, open-label, uncontrolled multicenter study of an enhanced serum containing 13 plant-based adaptogens in women aged 46 years and older shares this design limitation [41]. A case series of eight patients who applied a different multi-adaptogen moisturizing serum after alexandrite or picosecond laser treatments, with no laser-only or standard aftercare comparator, reported improved photodamage scores, patient-reported gains in hydration and radiance, and no adverse reactions [42]. These are preliminary observations of tolerability and cosmetic

improvement after combined treatment, and any added effect of the serum on healing remains a hypothesis for controlled evaluation. Topical *A. vera* has also been evaluated specifically in this periprocedural context, with a randomized, split-face trial in patients recovering from fractional 1,550 nm erbium-doped fiber laser resurfacing finding significantly better clinical erythema scores at days 3 and 7 and lower transepidermal water loss at days 7 and 14 compared with placebo, although no significant between-group differences emerged for erythema index, melanin index, or skin capacitance [45].

Medicinal mushrooms, including *Ganoderma lucidum*, have an extensive cosmeceutical and pharmacological literature base, but the available comprehensive reviews remain largely mechanistic and preclinical rather than grounded in dermatologic clinical trials [34]. Cell-level evidence specifically addressing senescence has since emerged from a study in which a *G. lucidum* extract applied to an etoposide-induced senescence model in human dermal fibroblasts. The extract upregulated the antioxidant genes HO-1, gamma-glutamylcysteine synthetase, and NQO1, thereby suppressing p16 expression and reducing senescence-associated beta-galactosidase-positive cells in a concentration-dependent, senolytic-like manner [35]. However, one of the two commercial extracts tested in that study showed an unfavorable increase in interleukin 8 and matrix metalloproteinase 1, underscoring that preparation-specific variability remains a real limitation even at the mechanistic level [35]. A related fungal adaptogen, *Cordyceps militaris*, distinct from the *C. sinensis* more commonly referenced in the dermatologic adaptogen literature, protected hydrogen peroxide-stressed human dermal fibroblasts from apoptosis and reduced senescence-associated beta-galactosidase-positive cells through reactive oxygen species scavenging, suggesting that this mechanistic class of evidence may extend across related Cordyceps species even though species-level distinctions are often blurred in secondary sources [36].

Rhodiola and astragalus are frequently discussed within the dermatologic adaptogen literature on mechanistic grounds, largely through extrapolation from their systemic pharmacology. We identified no dedicated topical clinical trial of *Rhodiola* and none of isolated *Astragalus*. One randomized, double-blind, placebo-controlled trial did test a topical cream combining *Astragalus membranaceus* and *C. asiatica* saponins, with 25 participants per group over four weeks [39]. It does not establish the independent efficacy of *Astragalus* or any longevity benefit, but it is relevant human evidence for an *Astragalus*-containing topical formulation. Cell-level mechanistic evidence has nonetheless accumulated for both. A *Lactobacillus plantarum*-fermented *Rhodiola rosea* extract activated the Nrf2 and Keap1 pathway in ultraviolet A-irradiated human dermal fibroblasts, raising catalase, glutathione peroxidase, HO-1, NQO1, and gamma-glutamylcysteine synthetase activity. This reduced reactive oxygen species, increased type I and III collagen and elastin, and downregulated matrix metalloproteinases 1 and 3 [37]. A purified *A. membranaceus* polysaccharide protected ultraviolet A-irradiated HaCaT keratinocytes by reducing reactive oxygen species, restoring mitochondrial membrane potential and adenosine triphosphate levels, and preserving the activity of mitochondrial complexes I and II [38]. These mechanistic findings strengthen the biological plausibility of *Rhodiola* and astragalus as resilience-supporting adaptogens, though clinical evidence for isolated agents remains absent, and clinical evidence for *Astragalus* is limited to a combination formulation.

Periprocedural support represents an underexplored but clinically relevant application for topical adaptogens, given that laser resurfacing and other energy-based procedures transiently compromise the same barrier and inflammatory resolution pathways that adaptogens are proposed to support. The post-laser adaptogenic serum observations described above are compatible with tolerability and cosmetic improvement after combined treatment, but they cannot show that adjunctive topical adaptogen use enhances healing or aesthetic outcomes beyond what the procedure alone provides, which remains a hypothesis requiring larger, controlled investigation [42].

Across the agents discussed above, *A. vera*, *C. asiatica*, *G. lucidum*, *C. militaris*, *R. rosea*, and *Astragalus*, cell-level mechanistic evidence converges on a shared set of resilience pathways, Nrf2/ARE-mediated antioxidant defense, preservation of mitochondrial function, and suppression of senescence markers, rather than each agent acting through an unrelated or idiosyncratic mechanism. This convergence is consistent with the adaptogen concept, nonspecific support of homeostasis under stress, and suggests that these pathways represent a reasonable shared target for future topical development. Whether these convergent molecular mechanisms translate into meaningful clinical outcomes compared with single-ingredient formulations, and whether the concentrations used in commercial products achieve the effects demonstrated in vitro and in animal models, remain unanswered questions and represent clear directions for future targeted research.

Evaluating the Evidence as a Whole

Across the agents, the available human evidence is characterized by small sample sizes, heterogeneous outcome measures, short study durations (typically 60 days or fewer), and a near-total absence of longitudinal aging outcomes extending beyond a single treatment cycle. Formulation, concentration, and botanical standardization vary considerably between studies, complicating direct comparisons even for the two best-studied agents, *C. asiatica* and ashwagandha. Improvement in a specific skin parameter, such as transepidermal water loss or elasticity, over 60 days does not, on its own, demonstrate an effect on skin longevity as defined in this review, because this requires evidence of sustained or improved resilience over a meaningfully longer time horizon. Given the current state of the evidence, adaptogens should therefore be

characterized as mechanistically plausible and supported only for defined short-term outcomes in the cases of ashwagandha (a single randomized trial) and *C. asiatica* (a randomized trial of a two-extract combination), while remaining investigational with respect to the longevity claims this review is organized around.

One area of needed contribution identified by this evidence gap is dedicated periprocedural support. In a preliminary, conference-level analysis presented as a poster at the Science of Skin Summit and not yet peer reviewed, we searched the periprocedural literature for 29 previously identified topical adaptogens and found periprocedural evidence for 18 of 29 agents (62%) across 15 qualifying studies, with *C. asiatica*, *A. vera*, *Olea europaea*, and resveratrol showing the most independent support (Poster: Blyumin-Karasik M and Colon J. Topical Adaptogens in Periprocedural Skincare. Science of Skin Summit; 2026). Given its unpublished and conference-level status, this analysis is presented here only as a preliminary signal pointing toward periprocedural application as an underdeveloped subcategory of the topical adaptogen evidence base, not as a component of the formal evidence synthesis in Table 2.

Adaptogens within a broader skinspan strategy

Adaptogens should be positioned as one component within a multimodal longevity strategy rather than as a replacement for established interventions. Photoprotection remains foundational and among the best-supported strategies for limiting cumulative extrinsic damage and preserving the intrinsic aging trajectory. Retinoids continue to represent the most extensively validated topical class for stimulating collagen synthesis and normalizing keratinocyte differentiation, and any resilience-centered framework should explicitly situate adaptogens alongside, not above, this existing standard of care [46]. Figure 2 depicts this layered strategy, organized around three complementary categories: protection, adaptation and regulation, and repair and regeneration, that converge on cutaneous resilience as the central connecting node.

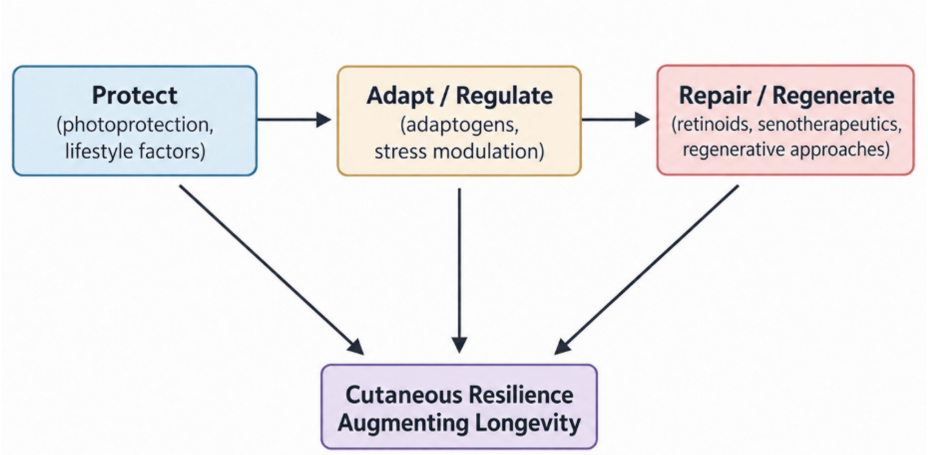


FIGURE 2: Skin longevity model.

Protect, adapt and regulate, and repair and regenerate, with cutaneous resilience positioned as the central connecting node.

Image credit: Jessica Colon. Original, unpublished figure. This figure was prepared using generative AI (Claude Sonnet 5.5, Anthropic), based on content and instructions provided by the authors, and reviewed by the authors.

The intersection of skin longevity strategies and regenerative cutaneous therapeutics may provide a framework for optimizing skinspan, defined as the period during which the skin sustains its highest functional and aesthetic performance through preservation of health, resilience, structural integrity, and regenerative capacity (Figure 3).

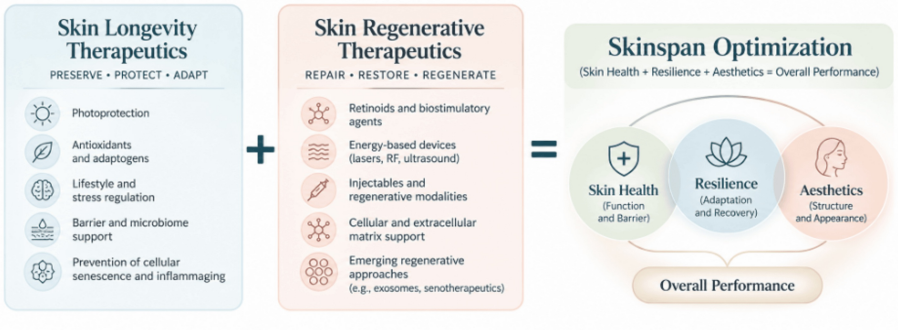


FIGURE 3: Skinspan optimization.

Skin longevity therapeutics (preserve, protect, and adapt) and skin regenerative therapeutics (repair, restore, and regenerate) jointly support skin health, resilience, and aesthetics as components of overall skinspan performance.

Image credit: Marianna Blyumin-Karasik. Original, unpublished figure. This figure was prepared using generative AI (ChatGPT image generation, OpenAI), based on content and instructions provided by the authors, and reviewed and edited by the authors.

Senotherapeutic approaches represent a mechanistically distinct but complementary strategy, targeting senescent cell burden directly rather than supporting broad stress adaptation. In laboratory models, a topically applied senotherapeutic peptide reduced senescence markers in cultured fibroblasts and human skin equivalents and lowered the estimated DNA methylation age of ex vivo skin from a 79-year-old donor on a skin-specific epigenetic clock [47]. In the ex vivo skin experiments, it also performed better than topical retinol on several skin health markers [47]. These are laboratory endpoints in ex vivo skin, not a clinical comparison, and they do not show that the peptide produces better clinical rejuvenation than retinol, which is why head-to-head clinical comparison remains necessary. Energy-based devices are increasingly discussed within this same senotherapeutic framework. A comprehensive 2024 review screening 329 articles and synthesizing 92 covering two decades of laser skin resurfacing found that fractional, ablative, non-ablative, hybrid fractional, and picosecond laser platforms each stimulate collagen remodeling through distinct microthermal or photomechanical mechanisms [48]. The review also found that repeated treatment sessions cumulatively improve collagen density and elasticity over time rather than producing only a single transient effect. Photodynamic therapy fits this same category through a distinct mechanism, with multiomics work demonstrating that it can reduce senescence markers in photoaged skin through a mitohormetic pathway, suggesting that procedural and topical longevity strategies may converge on overlapping molecular endpoints even when their delivery methods differ substantially [49].

Regenerative dermatology represents a further category directed specifically at skin longevity rather than borrowed from systemic geroscience. A 2026 systematic review of 21 studies on exosome-based skin therapies reported improvements in elasticity ranging from 7% to 104%, reductions in wrinkle depth ranging from 9.6% to 16%, and increases in hydration ranging from 5.6-21% [50]. The proposed mechanisms include suppression of matrix metalloproteinases, enhanced fibroblast collagen synthesis, and reduced oxidative stress, although the review also noted a lack of standardized isolation protocols and predominantly small, short-duration trials. Platelet-rich plasma has a longer clinical track record for facial rejuvenation. A 2025 meta-analysis of nine randomized controlled trials involving 358 participants found significantly higher patient satisfaction with platelet-rich plasma than with the control across pooled outcomes, alongside a comparable safety profile [51]. However, the authors again flagged small sample sizes and heterogeneous protocols across the included trials. Both exosome-based and platelet-rich plasma approaches target the same fibroblast and extracellular matrix pathways, but through direct biologic delivery rather than pharmacologic stress modulation, and both share the adaptogen literature's central limitation: evidence concentrated in short-term cosmetic endpoints rather than longitudinal resilience or health span outcomes.

Topical peptides deserve a separate mention given their commercial prominence alongside exosomes and stem cell-derived products, though the comparative evidence here argues for caution. A 2026 systematic review and meta-analysis of 19 randomized controlled trials involving 1,341 participants included 17 oral peptide trials and only two topical peptide trials, with substantial heterogeneity, and the authors noted that the imbalance constrains definitive conclusions about the two routes [52]. The available evidence for peptides is therefore predominantly derived from oral formulations, and evidence for topical peptides remains limited. Differences between these groups of studies do not establish that oral administration is intrinsically more effective than topical administration. This is a useful methodological caution for the present review, since a category widely marketed for topical use may have most of its supporting evidence from a different route of administration, a distinction that should be verified rather than assumed for any

topical longevity active, adaptogens included.

The skin microbiome has also emerged as a resilience-relevant target in its own right. A comprehensive review of the interaction between skin microbiota and barrier function in aging skin describes age-related dysbiosis, marked by reduced Cutibacterium and diminished overall diversity, as a direct contributor to barrier dysfunction and inflammaging [53]. Commensal organisms such as Staphylococcus epidermidis and Cutibacterium acnes support resilience through pathogen antagonism, regulatory T-cell induction, ceramide production, and maintenance of the skin's acidic pH [53]. This microbiome-directed evidence base reinforces the resilience framework from a different angle than adaptogens, targeting the skin's external microbial ecosystem rather than internal cellular stress signaling, and the two approaches may ultimately prove complementary rather than competing.

Healthy lifestyle factors, including nutrition, sleep, physical activity, and smoking avoidance, remain foundational and are directly relevant to the skin exposome, particularly given the demonstrated links between psychological stress, sleep disruption, and impaired barrier recovery. A resilience-centered longevity strategy is therefore best understood as layered: photoprotection and lifestyle factors reducing the rate of new insult, retinoids and senotherapeutics addressing accumulated damage and senescent cell burden directly, and adaptogens supporting the skin's underlying stress adaptation and recovery capacity across all of these exposures simultaneously. Table *3* summarizes these established and emerging interventions, spanning photoprotection, retinoids, senotherapeutics, energy-based devices, regenerative approaches, topical peptides, microbiome support, topical adaptogens, and a holistic healthy-lifestyle foundation within this multimodal framework.

Intervention category	Representative approach	Evidence summary	Source
Photoprotection	Sunscreen and UV avoidance	Best-supported strategy for limiting cumulative extrinsic damage; foundational to intrinsic aging trajectory	[13]
Retinoids	Topical retinoid therapy	Most extensively validated topical class for stimulating collagen synthesis and normalizing keratinocyte differentiation	[46]
Senotherapeutics (topical peptide)	Topically applied senotherapeutic peptide	Reduced senescence markers in cultured cells and skin equivalents and lowered estimated DNA methylation age in ex vivo skin; performed better than retinol on several laboratory markers in ex vivo skin; no clinical data	[47]
Energy-based devices	Fractional, ablative, non-ablative, hybrid fractional, and picosecond laser platforms	Review of 92 studies; cumulative improvement in collagen density and elasticity with repeated treatment sessions	[48]
Photodynamic therapy	PDT applied to photoaged skin	Multiomics evidence of reduced senescence markers through a mitohormetic pathway	[49]
Regenerative dermatology (exosomes)	Exosome-based topical and injectable therapies	Systematic review of 21 studies; elasticity improved 7-104%, wrinkle depth reduced 9.6-16%; lack of standardized isolation protocols	[50]
Regenerative dermatology (platelet-rich plasma)	Platelet-rich plasma for facial rejuvenation	Meta-analysis of 9 randomized controlled trials (n = 358); higher patient satisfaction than the control, with comparable safety	[51]
Topical peptides	Topical peptide formulations for wrinkles, hydration, and brightness	Meta-analysis of 19 randomized controlled trials (17 oral and 2 topical), with substantial heterogeneity; evidence is predominantly from oral formulations, and evidence for topical peptides remains limited	[52]
Skin microbiome support	Maintenance of commensal diversity (*Staphylococcus epidermidis* and *Cutibacterium acnes*)	Reduced *Cutibacterium* abundance and diversity linked to barrier dysfunction and inflammaging; commensals support resilience through pathogen antagonism and ceramide production	[53]
Topical adaptogens	*Centella asiatica,* ashwagandha, curcumin, and multi-agent formulations	Mechanistically plausible stress adaptation support; strongest short-term clinical evidence for *Centella asiatica* and ashwagandha	[4,23-28,39-42]
Holistic lifestyle modification	Nutrition, sleep, physical activity, and smoking avoidance	Foundational exposome-level support; directly relevant given demonstrated links between stress, sleep and impaired barrier recovery	[13]

TABLE 3: Established and emerging interventions within a multimodal skinspan (longevity and regeneration) framework.

Measuring skin longevity: the need for better endpoints

Wrinkle counts and photographic aging scales remain the dominant outcome measures in cosmetic dermatology, but they capture cumulative visible damage rather than resilience or recovery capacity, and they are poorly suited to testing the central claims of a longevity-oriented framework. Functional biophysical measures offer a more direct window into the mechanisms discussed throughout this review: transepidermal water loss and corneometry as indices of barrier function, and as indices of recovery when measured after a standardized barrier challenge; elasticity and recovery time after a controlled mechanical or ultraviolet challenge; and pigmentation and erythema as inflammatory or vascular readouts [54].

Molecular and epigenetic measures are advancing rapidly and offer a route to biological, rather than purely visible, age assessment. Second-generation, skin-specific epigenetic clocks built from DNA methylation profiles have been developed and validated against wrinkle grade and visual age progression, moving beyond chronological age prediction toward phenotype-specific biological aging assessment [55]. Noninvasive whole-genome skin methylome profiling and newer epigenetic age predictors extend this approach toward clinical accessibility [56], and broader geroscience frameworks for validating biomarkers of aging provide a template that skin-specific research has not yet fully adopted [57].

A rigorous evaluation of adaptogens, or any other longevity-directed topical strategy, within this framework will require moving beyond the 60-day cosmetic outcome studies toward designs that pair functional recovery measures, such as time to barrier normalization after a standardized challenge, with molecular or epigenetic readouts collected over months rather than weeks. Until such endpoints are standardized and validated specifically for skin, claims of extending skin longevity, as distinct from improving a discrete skin parameter, should be made cautiously.

Future directions

Longitudinal human studies that directly evaluate resilience and recovery, rather than static improvement in a single skin parameter, represent the most pressing need identified by this review. A practical near-term design would pair a standardized barrier or wound challenge with repeated functional and molecular measurements over an extended treatment period, allowing recovery kinetics, not just endpoint values, to be compared between adaptogen-treated and control skin. Periprocedural applications in particular warrant dedicated, larger, and controlled trials, given that the current evidence for adjunctive topical adaptogen use after laser resurfacing is limited to small case series and a single randomized trial of *A. vera*.

Standardization of adaptogen definitions, extraction methods, and dosing remains a prerequisite for meaningful cross-study comparison, particularly given the botanical variability documented across *C. asiatica* and curcumin formulations. Combining clinical, biophysical, and molecular endpoints within individual studies, rather than relying on cosmetic assessment alone, would allow direct testing of whether resilience gains at the molecular level correspond to measurable functional or visible benefit.

Psychological stress and sleep, as modifiable contributors to impaired skin recovery, warrant more direct inclusion as both study variables and intervention targets in future adaptogen research, given that the proposed mechanism of adaptogens, nonspecific stress adaptation, is most directly testable in a population with demonstrable stress exposure rather than in a general cosmetic population. Finally, as exposome burden and epigenetic aging signatures become more accessible, personalized approaches that match specific interventions to an individual's dominant stress exposures and resilience deficits, rather than a uniform anti-aging regimen, represent a plausible long-term direction for longevity-oriented dermatology.

Conclusions

Reframing skin aging as reflecting not only accumulated damage burden but also a progressive loss of adaptive and recovery capacity offers a complementary lens to existing longevity and regenerative frameworks such as skinspan. Skin longevity, under this framing, may be supported both by strategies that reduce new injury, photoprotection foremost among them, and by strategies that preserve the underlying resilience of the cutaneous tissue itself.

Topical adaptogens are biologically plausible candidates for this resilience-supporting role, extending the taxonomy and evidence base established in our prior systematic review of topical adaptogens in dermatology. Current evidence is strongest for individual mechanistic and short-term clinical effects, particularly for ashwagandha and for a *C. asiatica*-containing combination, and considerably weaker for any claim of extending skin longevity specifically. A rigorous framework for longevity-oriented dermatology will require validated resilience-focused biomarkers, functional recovery endpoints, and longitudinal clinical studies before adaptogens, or any other single intervention category, can be positioned as more than a promising and mechanistically coherent piece of a much larger multimodal skinspan strategy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Jessica Colon, Marianna Blyumin-Karasik

Acquisition, analysis, or interpretation of data: Jessica Colon, Marianna Blyumin-Karasik

Drafting of the manuscript: Jessica Colon, Marianna Blyumin-Karasik

Critical review of the manuscript for important intellectual content: Jessica Colon, Marianna Blyumin-Karasik

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have

no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

Generative AI tools were used to prepare the figures in this manuscript. Figures 1 and 2 were created using Claude Sonnet 5.5 (Anthropic), and Figure 3 was created using ChatGPT image generation (OpenAI). In each case, the authors provided the content and the instructions for how each figure should look, and the authors reviewed and edited the resulting images. Generative AI was also used to help with reference formatting, and Grammarly was used to help review grammar, spelling, and style. The authors take full responsibility for the content and accuracy of the figures and the manuscript.

References

1. Kennedy BK, Berger SL, Brunet A, et al.: Geroscience: linking aging to chronic disease . Cell. 2014, 159:709-13. 10.1016/j.cell.2014.10.039
2. Kream E, Fabi SG, Boen M: Skinspan: a holistic roadmap for extending skin longevity with evidence based interventions. J Cosmet Dermatol. 2025, 24:e70432. 10.1111/jocd.70432
3. Wyles SP, Maredia HS, Ansaf RB, et al.: Skinspan(TM): a healthy longevity framework for skin aging . Mayo Clin Proc. 2025, 100:1976-91. 10.1016/j.mayocp.2025.07.027
4. Blyumin-Karasik M, Colon J, Karasik D, Nguyen S, Woolery-Lloyd H, Lain E: What are topical adaptogens? A systematic review and proposed system to identify and categorize skin adaptogens in dermatology. J Clin Aesthet Dermatol. 2025, 18:28-35.
5. Chin T, Lee XE, Ng PY, Lee Y, Dreesen O: The role of cellular senescence in skin aging and age-related skin pathologies. Front Physiol. 2023, 14:1297637. 10.3389/fphys.2023.1297637
6. Zhang J, Yu H, Man MQ, Hu L: Aging in the dermis: fibroblast senescence and its significance . Aging Cell. 2024, 23:e14054. 10.1111/acel.14054
7. Bulbiankova D, Díaz-Puertas R, Álvarez-Martínez FJ, Herranz-López M, Barrajón-Catalán E, Micol V: Hallmarks and biomarkers of skin senescence: an updated review of skin senotherapeutics . Antioxidants (Basel). 2023, 12:444. 10.3390/antiox12020444
8. Dańczak-Pazdrowska A, Gornowicz-Porowska J, Polańska A, et al.: Cellular senescence in skin-related research: targeted signaling pathways and naturally occurring therapeutic agents. Aging Cell. 2023, 22:e13845. 10.1111/acel.13845
9. Wyles SP, Carruthers JD, Dashti P, et al.: Cellular senescence in human skin aging: leveraging senotherapeutics. Gerontology. 2024, 70:7-14. 10.1159/000534756
10. de Afonso Bonotto NC, Musachio E, Felin GD, Felin GD, Schwanke CH, da Cruz IB, Barbisan F: Skin aging and mitochondrial dysfunction: structural changes, mechanistic insights, and therapeutic perspectives. Oxid Med Cell Longev. 2026, 2026:e5140711. 10.1155/omcl/5140711
11. Zomer HD, Cooke PS: Targeting estrogen signaling and biosynthesis for aged skin repair . Front Physiol. 2023, 14:1281071. 10.3389/fphys.2023.1281071
12. Jin S, Li K, Zong X, Eun S, Morimoto N, Guo S: Hallmarks of skin aging: update . Aging Dis. 2023, 14:2167-76. 10.14336/AD.2023.0321
13. Krutmann J, Bouloc A, Sore G, Bernard BA, Passeron T: The skin aging exposome. J Dermatol Sci. 2017, 85:152-61. 10.1016/j.jdermsci.2016.09.015
14. Pujos M, Chamayou-Robert C, Parat M, Bonnet M, Couret S, Robiolo A, Doucet O: Impact of chronic moderate psychological stress on skin aging: exploratory clinical study and cellular functioning. J Cosmet Dermatol. 2025, 24:e16634. 10.1111/jocd.16634
15. Mochel K, Bronte J, Kasaba M, Vempati A, Tam C, Hazany S: The impact of psychological stress on wound healing: implications for neocollagenesis and scar treatment efficacy. Clin Cosmet Investig Dermatol. 2025, 18:1625-37. 10.2147/CCID.S528730
16. Zhang H, Wang M, Zhao X, Wang Y, Chen X, Su J: Role of stress in skin diseases: a neuroendocrine-immune interaction view. Brain Behav Immun. 2024, 116:286-302. 10.1016/j.bbi.2023.12.005
17. Anwar SS, Apolinar MA, Ma L: Perception, understanding, and association between psychological stress and skin aging: quantitative surveys of Asian women aged 18-34 years, dermatologists, and psychologists in China and Japan. J Cosmet Dermatol. 2023, 22:2297-307. 10.1111/jocd.15732
18. Bobok N, Taskesen T: Stress-induced changes of the skin: a narrative review . Cureus. 2025, 17:e96285. 10.7759/cureus.96285
19. Haykal D, Flament F, Mora P, Balooch G, Cartier H: Unlocking longevity in aesthetic dermatology: epigenetics, aging, and personalized care. Int J Dermatol. 2025, 64:2204-14. 10.1111/ijd.17725
20. De Tollenaere M, Meunier M, Scandolera A, et al.: Well-aging: a new strategy for skin homeostasis under multi-stressed conditions. J Cosmet Dermatol. 2020, 19:444-55. 10.1111/jocd.13047
21. Panossian AG, Efferth T, Shikov AN, et al.: Evolution of the adaptogenic concept from traditional use to medical systems: pharmacology of stress- and aging-related diseases. Med Res Rev. 2021, 41:630-703. 10.1002/med.21743
22. Liu XX, Chen CY, Li L, et al.: Bibliometric study of adaptogens in dermatology: pharmacophylogeny, phytochemistry, and pharmacological mechanisms. Drug Des Devel Ther. 2023, 17:341-61. 10.2147/DDDT.S395256
23. Handayani R, Febriyanti RM, Muhaimin M, Chearunisaa AY: Centella asiatica (L.) Urb. in skin health and cosmeceuticals: mechanisms, clinical evidence, and advanced delivery systems. Pharmacia. 2025, 72:1-3. 10.3897/pharmacia.72.e167217
24. Tan Y, Hu A, Lu J, et al.: Protective effects of Centella asiatica against senescence and apoptosis in epidermal cells. Biology (Basel). 2025, 14:202. 10.3390/biology14020202

25. Chang TM, Wu CC, Huang HC, et al.: Evaluation of effects on skin quality of a Centella asiatica extracellular vesicle-based skin care formulation: a 28-day facial skin quality study. medRxiv. 2025, 10.1101/2025.03.04.25323195
26. Poomanee W, Yaowiwat N, Pattarachaidaecharuch T, Leelapornpisid P: Optimized multiherbal combination and in vivo anti-skin aging potential: a randomized double blind placebo controlled study. Sci Rep. 2023, 13:5633. 10.1038/s41598-023-32738-7
27. Narra K, Naik SK, Ghatge AS: A study of efficacy and safety of ashwagandha (Withania somnifera) lotion on facial skin in photoaged healthy adults. Cureus. 2023, 15:e36168. 10.7759/cureus.36168
28. Kang L, Liu Y, Xin Y, et al.: Ashwagandha root extract and its potential modulation of CCN1-associated pathways in sensitive-skin aging. J Cosmet Dermatol. 2026, 25:e71010. 10.1111/jocd.71010
29. Nie Y, Li Y: Curcumin: a potential anti-photoaging agent . Front Pharmacol. 2025, 16:1559032. 10.3389/fphar.2025.1559032
30. Reuter J, Jocher A, Stump J, Grossjohann B, Franke G, Schempp CM: Investigation of the anti-inflammatory potential of Aloe vera gel (97.5%) in the ultraviolet erythema test. Skin Pharmacol Physiol. 2008, 21:106-10. 10.1159/000114871
31. Choonhakarn C, Busaracome P, Sripanidkulchai B, Sarakarn P: A prospective, randomized clinical trial comparing topical aloe vera with 0.1% triamcinolone acetonide in mild to moderate plaque psoriasis. J Eur Acad Dermatol Venereol. 2010, 24:168-72. 10.1111/j.1468-3083.2009.03377.x
32. Sun Z, Zheng Y, Wang T, et al.: Aloe vera gel and rind-derived nanoparticles mitigate skin photoaging via activation of Nrf2/ARE pathway. Int J Nanomedicine. 2025, 20:4051-67. 10.2147/IJN.S510352
33. Lee H, Choi W, Ro H, Kim G, Lee H: Skin antiaging effects of the fermented outer layers of leaf skin of Aloe barbadensis miller associated with the enhancement of mitochondrial activities of UVB-irradiated human skin fibroblasts. Appl Sci. 2021, 11:5660. 10.3390/app11125660
34. Ahmad R, Riaz M, Khan A, Aljamea A, Algheryafi M, Sewaket D, Alqathama A: Ganoderma lucidum (Reishi) an edible mushroom; a comprehensive and critical review of its nutritional, cosmeceutical, mycochemical, pharmacological, clinical, and toxicological properties. Phytother Res. 2021, 35:6030-62. 10.1002/ptr.7215
35. Kühnel H, Seiler M, Feldhofer B, Ebrahimian A, Maurer M: Ganoderma lucidum extract modulates gene expression profiles associated with antioxidant defense, cytoprotection, and senescence in human dermal fibroblasts: investigation of quantitative gene expression by qPCR. Curr Issues Mol Biol. 2025, 47:130. 10.3390/cimb47020130
36. Park JM, Lee JS, Lee KR, Ha SJ, Hong EK: Cordyceps militaris extract protects human dermal fibroblasts against oxidative stress-induced apoptosis and premature senescence. Nutrients. 2014, 6:3711-26. 10.3390/nu6093711
37. Fu H, Zhang Y, An Q, et al.: Anti-photoaging effect of Rhodiola rosea fermented by Lactobacillus plantarum on UVA-damaged fibroblasts. Nutrients. 2022, 14:2324. 10.3390/nu14112324
38. Li Q, Wang D, Bai D, et al.: Photoprotective effect of Astragalus membranaceus polysaccharide on UVA-induced damage in HaCaT cells. PLoS One. 2020, 15:e0235515. 10.1371/journal.pone.0235515
39. Chan L-P, Liang C-H: Natural plant-based rejuvenating compositions: human study on Astragalus membranaceus and Centella asiatica saponins for skin health. Cosmetics. 2025, 12:131. 10.3390/cosmetics12040131
40. Draelos ZD, Grimes PE, Watchmaker J, Nelson DB: A multi-center trial evaluating a serum comprised of plant-based adaptogens targeting skin quality. J Clin Aesthet Dermatol. 2024, 17:15-9.
41. Draelos ZD, Moradi A, Smathers A: A multicenter trial of an enhanced serum comprised of 13 plant-based adaptogens targeting skin quality in females impacted by hormonal decline. J Cosmet Dermatol. 2026, 25:e70802. 10.1111/jocd.70802
42. Blyumin-Karasik M, Colon J, Nguyen S, Rosen J: Laser and skin-care synergy: a post-laser application of novel adaptogenic moisturizing serum for improving healing and cosmesis on the face. J Cosmet Dermatol. 2025, 24:e16668. 10.1111/jocd.16668
43. Witkowska K, Paczkowska-Walendowska M, Garbiec E, Cielecka-Piontek J: Topical application of Centella asiatica in wound healing: recent insights into mechanisms and clinical efficacy. Pharmaceutics. 2024, 16:1252. 10.3390/pharmaceutics16101252
44. Heng MCY: Topical curcumin: a review of mechanisms and uses in dermatology . Int J Dermatol Clin Res. 2017, 3:010-7. 10.17352/2455-8605.000020
45. Udompataikul M, Chalermchai T, Boonnarisarangkoon U: The efficacy of aloe vera gel in postprocedural wound care after fractional 1,550 nm erbium-doped fiber laser. J Med Assoc Thai . 2017, 100:1303-8.
46. Mukherjee S, Date A, Patravale V, Korting HC, Roeder A, Weindl G: Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. Clin Interv Aging. 2006, 1:327-48. 10.2147/ciia.2006.1.4.327
47. Zonari A, Brace LE, Al-Katib K, et al.: Senotherapeutic peptide treatment reduces biological age and senescence burden in human skin models. NPJ Aging. 2023, 9:10. 10.1038/s41514-023-00109-1
48. Haykal D, Cartier H, Goldberg D, Gold M: Advancements in laser technologies for skin rejuvenation: a comprehensive review of efficacy and safety. J Cosmet Dermatol. 2024, 23:3078-89. 10.1111/jocd.16514
49. Yan Y, Chang Q, Wu Y, et al.: Multi-omics analysis reveals photodynamic therapy ameliorating skin photoaging by improving cellular senescence through mitohormesis-mediated reduction of citrate content. Aging Cell. 2026, 25:e70328. 10.1111/acel.70328
50. Alzahrani A, Alghamdi S, Alahmadi M, et al.: Exosomes in skin rejuvenation: systematic review of anti-aging effects and clinical applications. Dermatol Pract Concept. 2026, 16:6462. 10.5826/dpc.1601a6462
51. Chen H Sr, Zhou X: Meta-analysis of the efficacy of platelet-rich plasma in treating skin aging . Aesthet Surg J Open Forum. 2026, 8:ojaf150. 10.1093/asjof/ojaf150
52. Nukaly HY, Halawani IR, Irtaza HM, et al.: Oral and topical peptides for skin aging: systematic review and meta-analysis of randomized controlled trials. Front Med (Lausanne). 2026, 13:1618306. 10.3389/fmed.2026.1618306
53. Woo YR, Kim HS: Interaction between the microbiota and the skin barrier in aging skin: a comprehensive review. Front Physiol. 2024, 15:1322205. 10.3389/fphys.2024.1322205

54. Cohen S, Thor D: From skin aging biomarkers to precision esthetic longevity: a translational diagnostic framework. Front Med (Lausanne). 2026, 13:1902741. 10.3389/fmed.2026.1902741
55. Bienkowska A, Raddatz G, Söhle J, et al.: Development of an epigenetic clock to predict visual age progression of human skin. Front Aging. 2023, 4:1258183. 10.3389/fragi.2023.1258183
56. Menendez Vazquez A, Katsanos D, Vasile M, et al.: Epigenetic age predictors for non-invasive assessment of human skin. NPJ Aging. 2025, 12:11. 10.1038/s41514-025-00314-0
57. Moqri M, Herzog C, Poganik JR, et al.: Biomarkers of aging for the identification and evaluation of longevity interventions. Cell. 2023, 186:3758-75. 10.1016/j.cell.2023.08.003